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A TEXTBOOK OF
ORGANIC CHEMISTRY

The English Translation
from the German of
A. BERNTHSEN. Ph.D.

EDITED AND REVISED TO DATE BY
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BLACKIE AND SON LIMITED
50 OLD BAILEY, LONDON
GLASGOW AND BOMBAY
1912

Companion Volume

PRACTICAL ORGANIC CHEMISTRY

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Nature: "Altogether the book is probably the most complete among those of home manufacture on the subject that has yet appeared"

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PREFACE

The present edition is on much the same lines as the former, but contains the following new chapters:—XLVIII. Fermentation and Enzyme Action, XLIX. Catalytic Action of Finely-divided Metals and Metallic Oxides; L. Unsaturation; LI. Aliphatic Diazo- and Triazo-compounds.

The Chapters on Alkaloids, Terpenes and Camphors, and Proteins have been rewritten.

The earlier Chapters give an outline of General Systematic Organic Chemistry, and the later ones deal in somewhat more detail with some of the problems which have attracted a considerable amount of attention within recent years.

Numerous references to original papers are given in the text, and the following works are recommended for special study:—

Meyer and Jacobson. *Handbuch der organischen Chemie.*

Lassar-Cohn. *Arbeitsmethoden.*

Th. Weyl. *Die Methoden der organischen Chemie.*

Werner. *Lehrbuch der Stereochemie.*

Landolt. *Das optische Drehungsvermogen.*

O. Aschan. *Chemie der alicyclischen Verbindungen.*

E. Fischer. *Aminosauren und Polypeptide*, 1906.

Do. *Purin Gruppe*, 1907.

Do. *Kohlenhydrate und Fermente*, 1909.

Cain. *The Diazo-compounds.*

Smiles. *Relations between Chemical Constitution and Physical Properties.*

Stewart. *Stereo-chemistry.*
Do. *Recent Advances in Organic Chemistry.*
Sidgwick. *Organic Chemistry of Nitrogen.*
Harden. *Alcoholic Fermentation.*
E. F. Armstrong. *Simple Carbohydrates and Glucosides.*
Bayliss. *Enzyme Action.*
Schryver. *Proteins.*

Valuable Summaries of certain fields of Organic Work, such as Combustion, Diazo-compounds, Grignard's Reagents, Camphor, Tautomerism, Stereo-chemistry of Nitrogen, &c., will be found in the Reports of the British Association since 1900, and also in Ahren's *Sammlung chemischer und chem.-technischer Vortrage* from 1897 onwards.

J. J. SUDBOROUGH.

BANGALORE, *March, 1912.*

ABBREVIATIONS

A. = Liebig's *Annalen der Chemie.*
Abs = *Journal of the Chemical Society.* Abstracts.
Am. = *American Chemical Journal.*
Annales = *Annales de Chemie et de Physique.*
Arch. f. Phys. = *Archiv fur Physiologie.*
B. = *Berichte der deutschen Chemischen Gesellschaft.*
B A. Rep. = *British Association Report.*
Bull. Soc. Chim. = *Bulletin de la Société Chimique à Paris.*
C. C. = *Chemisches Central-blatt.*
C. R. = *Comptes rendus de l'Académie des Sciences.*
J A C. S. = *Journal of the American Chemical Society.*
J. C. S. = *Journal of the Chemical Society.* Transactions.
J. Ind. = *Journal of the Society of Chemical Industry.*
J. pr. = *Journal fur praktische Chemie.*
M. = *Monatshefte fur Chemie* (Wien).
P. = *Proceedings of the Chemical Society.*
Phil. Mag. = *Philosophical Magazine.*
Rec. = *Recueil des Travaux Chimiques des Pays Bas.*
S. J. = Sudborough and James's *Practical Organic Chemistry.*
Walker, Phys. Chem. = James Walker's *Introduction to Physical Chemistry.*
Zeit. phys. = *Zeitschrift fur physikalische Chemie.*

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n = normal.
O-ether = Oxygen ether.
N-ether = Nitrogen ether.
B.-pt. = Boiling-point.
M.-pt. = Melting-point.
d = dextro.
l = lævo.
r = racemic.
s = symmetrical.
i = inactive.
R = alkyl radical.
Me = Methyl, CH_3.
Et = Ethyl, C_2H_5.
Ph = Phenyl, C_6H_5.
o = ortho.
m = meta.
p = para.

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ORGANIC CHEMISTRY

INTRODUCTION

Organic Chemistry is the Chemistry of the Carbon Compounds Formerly those compounds which occur in the animal and vegetable worlds were classed under Organic, and those which occur in the mineral world under Inorganic Chemistry, the first to adopt this arrangement having been *Lémery* in his Cours de Chimie (1675). After the recognition of the fact that all organic substances contain carbon, it was thought that the difference between organic and inorganic compounds could be explained by saying that the latter were capable of preparation in the laboratory, but the former only in the organism, under the influence of a particular force, the life force—vis vitalis—(*Berzelius*). But this assumption was rendered untenable when *Wohler* in 1828 synthetically prepared urea, CON_2H_4, a typical secretion of the animal organism, from cyanic acid and ammonia, two compounds which were at that time held to be inorganic; and when, shortly afterwards, the synthesis of acetic acid, by the use of carbon, sulphur, chlorine, water, and zinc, was effected.

Since then so many syntheses of this kind have been achieved as to prove beyond doubt that the same chemical forces act both in the organic and inorganic worlds.

The separation of the two branches, Organic and Inorganic Chemistry, from each other is, however, still retained for convenience sake, although the original reasons for this separation, which at the time was more or less a matter of necessity, have since been found to be erroneous. In consequence of the great capacity of combining with one another which carbon atoms possess, the number of organic compounds is extraordinarily large, and in order to be in a position to study them, it is necessary to have a knowledge of the other elements, including

the metals. The carbon compounds, many of the most important of which contain only carbon and hydrogen, or carbon, hydrogen, and oxygen, also stand in a closer relationship to each other than do the compounds of the other elements. Partly upon grounds of convenience, carbon itself and some of its principal compounds, such as carbonic acid, which is so widely distributed in the mineral kingdom, are treated of under Inorganic Chemistry.

The expressions "organic" and "organized" substances should not be confused; organized substances, *e.g.* leaves, nerves and muscles, and also the life-processes which go on in the interior of the organism, are treated of under Physiology and Physiological Chemistry.

Constituents of the Carbon Compounds

Many organic substances are composed of carbon and hydrogen only, and are then termed hydrocarbons, for instance, ethylene, benzene, petroleum, naphthalene, and oil of turpentine; a vast number consist of carbon, hydrogen, and oxygen, for instance, wood spirit, alcohol, glycerine, aldehyde, oil of bitter almonds, formic acid, acetic acid, stearic acid, tartaric acid, benzoic acid, carbolic acid, tannic acid, and alizarin; many compounds contain carbon, hydrogen, and nitrogen, for instance, prussic acid, aniline, and coniine; as examples of compounds containing carbon, hydrogen, nitrogen, and oxygen, may be taken urea, uric acid, indigo, morphine, and quinine. In addition to these, sulphur, chlorine, bromine, iodine, phosphorus, and, generally speaking, the larger number of the more important elements, are also frequent constituents of the carbon compounds.

Qualitative Analysis of Organic Compounds

The presence of **Carbon** in a compound is often proved by the "carbonization" of the latter, *e.g.* starch, sugar, &c., when heated in a glass tube, or when warmed with concentrated sulphuric acid. Carbon compounds which readily volatilize, *e.g.* alcohol, chloroform, acetic acid, do not give these tests; but many of them deposit carbon when their vapours are led through a red-hot tube. The best proof of the presence of carbon is obtained by completely oxidizing the organic compound by either heating it with copper oxide (see below), or

by leading its vapour over the glowing oxide. The carbon present is thus converted into carbon dioxide, and the **Hydrogen** into water.

Nitrogen in organic compounds is recognized—

(*a*) Frequently by a smell resembling that of burnt hair, upon heating;

(*b*) Frequently by the presence of red fumes, or by explosion, upon heating (nitro- and diazo-compounds);

(*c*) In many cases by the liberation of ammonia upon heating with soda-lime (*Wohler*);

(*d*) In all cases by heating with potassium (and in most cases with sodium), and testing the metallic cyanide formed —(see Cyanogen Compounds)—by dissolving the fused mass in water, adding a few drops of ferrous sulphate solution, boiling, and acidifying with hydrochloric acid (formation of Prussian Blue); or by converting the cyanide into thiocyanate, and proving the presence of the latter by means of the blood-red coloration with ferric chloride. [See tests for hydrocyanic acid (*Lassaigne*).] If sulphur be likewise present, iron filings must be added.

Testing for the **Halogens.** Direct precipitation by nitrate of silver is usually not practicable; thus, no chlorine can be detected in chloroform even upon boiling it with $AgNO_3$. The halogens are therefore tested for:

(*a*) By heating the substance on a platinum wire with cupric oxide in the *Bunsen* flame, or by causing the vapour of the compound to pass over glowing copper gauze; in this way chlorine gives first a blue and then a green flame coloration, and iodine a green (*Beilstein*);

(*b*) By heating the substance strongly with pure lime, and testing the solution of the haloid calcium salt produced with silver nitrate;

(*c*) By heating in a sealed tube with fuming nitric acid and nitrate of silver, when the haloid silver salt is produced (*Carius*).

Testing for **Sulphur:**

(*a*) In many cases, upon boiling with an alkaline solution of lead oxide, brown sulphide of lead is formed (*e.g.* white of egg);

(*b*) By heating with sodium, and testing the resulting sodium sulphide with water upon a silver coin (black stain); or by means of sodium nitroprusside solution (purple-violet coloration) (*Schönn*);

(*c*) By complete oxidation in the dry way, by fusing with potassium carbonate and nitre, or by heating with mercuric oxide and sodium carbonate; or in the wet way, by fuming nitric acid (*Carius*), and testing the sulphuric acid produced, by barium chloride solution.

In like manner **Phosphorus** is converted by complete oxidation into phosphoric acid; or, upon heating with powdered magnesia, and moistening the resulting mass with water, the presence of phosphuretted hydrogen can be recognized (*Schonn*).

All the **other Elements** are tested for, after complete oxidation of the compound (preferably by *Carius'* method), in the usual way.

Another method (B. 1904, **37**, 2155) is to heat a small amount of the substance with sodium peroxide and twenty-five times its weight of naphthalene or cinnamic acid in an iron tube, and then test for haloids, sulphates, phosphates, &c.

Quantitative Organic or Elementary Analysis

Estimation of Carbon and Hydrogen (Combustion). The substance is oxidized by heating it to redness with cupric oxide (*Liebig*), or with other substances which readily give up oxygen, such as lead chromate, platinum and oxygen (*Dennstedt*),* &c., in a tube of difficultly fusible glass, which is open either at one or at both ends.

The carbon dioxide, thus produced by the oxidation of the carbon, is absorbed by a concentrated solution of caustic potash contained in specially shaped bulbs,* and the water, produced by the oxidation of the hydrogen; in a U-shaped calcic chloride tube, both tubes being weighed before and after the combustion. If the substance—(0·2 to 0·3 grm.)—is solid, it is either mixed with fine, dry copper oxide (*Liebig*, *Bunsen*), or placed in a porcelain or platinum boat and burnt in a stream of air or oxygen (open tube). Liquids are weighed out in small tubes or thin sealed glass bulbs. When nitrogen is present, a coil of tightly-rolled copper-wire gauze is placed in the front part of the combustion tube and heated to redness, in order to reduce any oxides of nitrogen which may be formed in the subsequent combustion. In the presence of sulphur or of the halogens, lead chromate, which has been

* For details see Sudborough and James' *Practical Organic Chemistry*, Chap. V, B.

fused and then powdered, is used instead of copper oxide, so as to convert any Cl, SO_2, &c., into $PbCl_2$, $PbSO_4$, &c., and thus prevent them from passing into the potash solution. When only halogens, without sulphur, are present, the combustion is carried out with copper oxide, a copper, or still better a silver spiral, which is kept cool, being placed in the fore-part of the tube to retain the halogens.

In the presence of alkalis or alkaline earths (which would retain carbon dioxide), lead chromate mixed with $\frac{1}{10}$ of its weight of potassic bichromate is used; the chromic acid then expels all the carbonic acid.

Explosive compounds must be burnt in a vacuum. From the weights of carbon dioxide and water found, the percentages of C and H are readily calculated:

$$C = \tfrac{3}{11} CO_2; \quad H = \tfrac{1}{9} H_2O.$$

Estimation of Nitrogen. This estimation is either relative or absolute. In the former case the proportion between the nitrogen and the carbon dioxide evolved is determined (*Liebig, Bunsen*); in the latter the nitrogen is either estimated as such volumetrically, or as ammonia.

The conversion into **Ammonia** is effected by heating the substance strongly with soda-lime (*Will, Varrentrapp*), or by treating it with strong sulphuric acid and permanganate of potash (*Kjeldahl*; Z. Anal. Ch. **22**, 366; also B. **19**, Ref. 852; **24**, 3241; **27**, 1633). The ammonia is then either titrated directly by absorption in standard acid, or transformed into ammonium platinichloride, $(NH_4)_2PtCl_6$, which is weighed, or else ignited, and the weight of the residual metallic platinum noted.

In the **Gasometric Estimation of Nitrogen** the substance is mixed with copper oxide, a copper spiral being also used in the front part of the tube, and the combustion is carried out in the usual way, but in a stream of carbon dioxide; the CO_2 is either generated from magnesite in the tube itself, or led through it. The nitrogen is collected over mercury and aqueous caustic potash (*Dumas*), or directly over potash (*Zulkowsky, Schwarz, Schiff*, &c.), in some special form of nitrometer.

Its percentage is obtained by reducing the volume to the volume at normal temperature and pressure, determining the weight of this volume of nitrogen from the fact that 1 c.c. of

dry nitrogen at 0° and 760 mm. weighs 1·2489 mg., and expressing the result in percentage.

The Gasometric method may be used for all classes of nitrogen compounds, but the Soda-lime method cannot be used for nitro compounds, certain bases, and various other groups of compounds, as the nitrogen of these is not completely transformed into ammonia upon heating with soda-lime.

For the simultaneous determination of carbon, hydrogen, and nitrogen the combustion must be carried on in a stream of pure oxygen, the mixture of gases escaping from the potash bulbs being collected over a solution of chromous chloride, which absorbs the oxygen, but not the nitrogen (A. 1886, **233**, 375).

Estimation of Sulphur and Phosphorus. The **Sulphur** is estimated as sulphuric acid, being converted into this—

(*a*) In the wet way, by heating the substance with fuming nitric acid at 150°–300° in a sealed tube (*Carius*), or in a combustion-tube in a mixed stream of nitric oxide and oxygen (*Claesson*), or nitric acid vapour (*Klason*).

(*b*) In the dry way—(and this method is only available in the case of the less volatile compounds)—by fusing the substance with potassic hydroxide and nitre, or with soda and chlorate or chromate of potash, also by heating with soda and mercuric oxide, or with lime in a stream of oxygen.

Phosphorus is estimated by analogous methods.

Estimation of the Halogens. Here also the organic substance is completely decomposed—

(*a*) After *Carius*, as above, in a sealed tube, with fuming nitric acid and solid silver nitrate, by which means the halogen is converted into its silver salt;

(*b*) By heating the compound strongly with pure lime in a hard glass tube, or in two crucibles, one of which is inverted in the other, or with sodic carbonate and nitre in a tube. The chloride formed is precipitated with silver nitrate in the usual way;

(*c*) By the action of nascent hydrogen (sodium and alcohol), the halogen in the organic substance can frequently be converted into its hydrogen compound (*Stepanow*).

Dennstedt, B. 1897, **30**, 1590, 2861, has described methods for estimating C, H, Cl, and S in one operation.

Metallic and acidic radicals, contained in organic salts, can often be estimated directly by the usual methods.

Oxygen is almost invariably determined by difference; direct

methods of estimation have been proposed by *Baumhauer*, *Ladenburg*, *Stromeyer*, and others.

The carbon estimation is usually too low (0·05 — 0·1), owing to leakage and incomplete absorption, that of hydrogen too high (0·1 — 0·2), owing to the difficulty of completely drying the cupric oxide. Nitrogen estimations are also usually too high, owing to the difficulty of completely freeing the carbon dioxide from air.

The Calculation of the Empirical Formula

The same principle applies here as in the case of inorganic compounds, *i.e.* the percentage numbers found are divided by the atomic weights of the respective elements, the relative proportions of the quotients obtained being expressed in whole numbers. For instance, acetic acid being found to contain 40·11 p.c. carbon, 6·80 p.c. hydrogen, and, consequently, 53 09 p.c. oxygen, the quotients are to each other as 3·34 : 6·80 · 3·32 = 1 : 2 : 1. The simplest analysis-formula of acetic acid would therefore be CH_2O. Sometimes figures are obtained which correspond with equal nearness to different formulæ, between which it is therefore impossible, without further data, to choose.

For instance, a sample of naphthalene yields on analysis 93·70 p.c. carbon and 6·30 p.c. hydrogen; the quotient proportion here is 7·81 to 6·30 = 1 239 : 1, which corresponds equally well with the numbers 5 : 4 or 11 : 9. The formula C_5H_4 requires 93·75 p.c. carbon and 6·25 p.c. hydrogen, and the formula $C_{11}H_9$, 93 62 p.c. carbon and 6 38 p.c. hydrogen, the deviations from the actual numbers found being in both cases within the limits of experimental error. Therefore other considerations must be taken into account here, in order to decide between the two formulæ.

The formula derived from the results of analyses is termed the **Empirical Formula**, and expresses the simplest numerical relationship between the atoms of the elements present. The actual molecular formula may be a multiple of this, and has to be determined according to special principles.

Determination of Molecular Weight

1. By Chemical Methods.

Our chemical formulæ (*e.g.* CH_2O) express not merely a

percentage relation, but at the same time the smallest quantity of the compound which is capable of existing as such, *i.e.* a molecule of it. This molecule is ideally no longer divisible by mechanical means, but only by chemical, and then into its constituent atoms. If the formula CH_2O were the correct one for acetic acid, then the amount of oxygen (or carbon) contained in a molecule would be indivisible, and that of hydrogen divisible only by 2. Since, however, it has been observed that one-fourth of the total hydrogen in acetic acid is replaceable, *e.g.* by a metal, with the formation of a salt, it is obvious that the quantity of hydrogen in the molecule must be divisible by 4, and so the formula must contain at least 4 atoms of hydrogen, and must therefore be $C_2H_4O_2$, or some multiple of it. This is, in fact, the case. Acetate of silver contains 64·67 p.c. silver, and therefore 35·33 p.c. of the acetate radical; or, to 1 atom of silver = 108 parts by weight, there are 59 parts by weight of the acid radical. This 59, together with 1 atom of hydrogen = 1, makes the molecular weight of acetic acid 60, = 2×30, = $2 \times CH_2O$, = $C_2H_4O_2$.

This is a determination of molecular weight by **chemical means** Such determinations are carried out in the case of acids generally by means of their silver salts; these are usually normal salts, are easy to purify, are almost always free from water of crystallization, and are readily analysed. It is, however, *absolutely necessary* to know whether the acid is mono- or polybasic In the case of a di-, tri-, &c., basic acid, the above calculation must be made with reference to 2, 3, &c., atoms of silver, whereas acetic acid— being monobasic— contains only one replaceable atom of hydrogen, which is therefore exchanged for one atom of silver. Consequently, its formula cannot be a multiple of $C_2H_4O_2$.

In the determination of the molecular weights of **Bases**, their platinichlorides are similarly made use of, these being almost always constituted on the type of ammonium platinichloride: $(NH_3)_2H_2PtCl_6$: *i.e.* they contain two molecules of a monoacid base such as ammonia combined with one atom of platinum.

To determine the molecular weights of **Neutral Compounds**, derivatives must be prepared and examined for the proportion of the total hydrogen which is replaceable, *e.g.*, by chlorine. For example, by the action of chlorine upon naphthalene, there is first formed the substance monochloronaphthalene, which contains 73·8 per cent C, 4·3 per cent H, and 21·9 per

cent Cl, these numbers giving the formula $C_{10}H_7Cl$. In the same way benzene yields the compound C_6H_5Cl. In both these cases the halogen acts by replacing hydrogen, and at least one atom of the latter in the molecule must be replaced, since fractions of an atom are necessarily out of the question If, then, the compound obtained has the formula $C_{10}H_7Cl$, it follows that $\frac{1}{8}$th of the H present has been replaced by Cl, and there must consequently be 8, 8 × 2, or 8 × 3, &c., atoms of hydrogen in the compound, and likewise 10 atoms, or some multiple of 10, of carbon. But a multiple of 8 or 10 may be rejected, since no compounds have been observed which would indicate the replacement of $\frac{1}{8}$th of the total hydrogen. This leads to the formula $C_{10}H_8$ for naphthalene, the other possible formula got by analysis viz $C_{11}H_9$ (see p. 7), being now untenable In a similar way the formula of benzene is found to be C_6H_6.

2. By Physical Methods.

(*a*) *By Estimating the Vapour Density.*

According to the law of *Avogadro* (1811) and *Ampère* (1814), all gases under similar conditions, *i.e.* in the perfectly gaseous state and under the same temperature and pressure, contain in equal volumes equal numbers of molecules. It follows from this that the weights of equal volumes of different gases are proportional to the weights of equal numbers of their constituent molecules, in other words, the molecular weight is proportional to the specific gravity of the gas. Thus, if M_x be the molecular weight of any given substance required, M_o that of oxygen, S the vapour density or specific gravity of the former as compared with oxygen taken as 16*,

$$M_x : M_o = S : 16.$$

And since $M_o = 32$, $M_x = S \times 2$. To determine, therefore, the molecular weight of a gas or vapour, one has only to find its density, and to multiply this by 2.

To take an example, the specific gravity of acetic acid vapour being found to be 30, then M = 60, and the molecular formula is $C_2H_4O_2 = 60$.

* Oxygen is taken as standard (O = 16) for vapour density, since it is now customary to take it as standard in atomic-weight determinations. For all practical purposes, one may take the density compared with hydrogen as unity.

It is essential to the application of this method that the temperature of the vapour shall be so high above the boiling-point of the substance that the latter is in the perfectly gaseous state, remaining at the same time undecomposed.

The only common method employed in the chemical laboratory for vapour-density determinations is that due to Victor and Carl Meyer. In this process the small tube containing the substance is dropped into a vertical glass tube, the lower and wider part of which is cylindrically shaped and sealed. This is kept warm at a constant temperature, being surrounded by a long glass mantle in which a suitable liquid boils, the upper part of the mantle itself serving for the condensation of the vapour. The displaced air alone escapes, and is collected over water and measured. No determination, therefore, of the temperature of the vapour of the substance in question is required. Only about 0·1 grm. substance is required. In all cases the vapour density is the weight of the vapour, divided by the weight of an equal volume of hydrogen (see note, p. 9), which can readily be calculated in the usual manner.

If, instead of having the apparatus filled with air, hydrogen is employed, the greater molecular velocity of the latter allows of the conversion of substances into vapour at 30°–40° below their ordinary boiling temperatures (*V. Meyer* and *Demuth*, B. 1890, **23**, 311).

Until a few years ago, the determination of molecular weights by physical means was restricted to the different modifications of the method which has just been described, and consequently it could only be carried out with substances which were either already gaseous, or which could be rendered so without decomposition.

The recent important researches of *van't Hoff*, *Raoult*, *Arrhenius*, *Ostwald*, and others, upon the nature of solution—in particular, the proof that the laws of *Boyle*, *Gay-Lussac*, and *Avogadro* are applicable to solutions as well as to gases—now permit, however, of the ready determination of the molecular weights of substances in solution, and therefore of *compounds which could not be volatilized without decomposition*. This is accomplished as follows:—

(*b*) *By Measuring the Depression of the Freezing Temperature of Solutions, or Cryoscopic Method.*

This method is based upon the following data:—Each solvent has a perfectly definite freezing-point (*e.g.* water 0°, benzene,

5·0°, and glacial acetic acid, 16·75°), but the introduction of a solute into such a solvent lowers the freezing-point, and within certain limits the lowering is directly proportional to the concentration of the solute. Raoult has shown that gram molecules of different substances dissolved in equal weights of the same solvent lower the freezing-point of the solvent to the same extent, or "equimolecular solutions have the same freezing-point". The molecular lowering of the freezing-point is the lowering which would be produced when the gram molecule (M) of the substance was dissolved in 100 grams of solvent, and is usually denoted by C. This varies for different solvents, and may be determined experimentally by using substances of known molecular weight, *e.g.*, p grams of a substance of molecular weight M dissolved in 100 grams of solvent caused a depression of $\Delta°$ in the freezing-point of the solvent.

Δ = depression for p grams in 100 grams of solvent

$M\frac{\Delta}{p}$ = " M " 100 "

$$\therefore C = M\frac{\Delta}{p}.$$

The value C may also be calculated theoretically from van't Hoff's equation $C = \frac{2T^2}{100L}$, where T = absolute freezing-point of the solvent, and L is the latent heat of fusion of the solvent.

Having determined the value C (for water C = 18·5, for glacial acetic acid 39, and for benzene 50), we may use the same equation

$$C = M\frac{\Delta}{p} \quad \text{or} \quad M = \frac{Cp}{\Delta}$$

for calculating M when Δ = lowering of the freezing-point produced by dissolving p grams of a substance of unknown molecular weight M in 100 grams of solvent.

It is obvious that this method cannot be employed with satisfactory results for determining the molecular weights of electrolytes in ionizing media. It has also been found that certain hydroxylic substances give abnormal values in benzene solution, owing to the fact that benzene tends to cause the association of molecules of such compounds.

Ebulliscopic Method. Molecular weights may also be determined by the raising of the boiling-point of a suitable

solvent produced by the introduction of known weights of the substance into a given weight (or volume) of the solvent. The principles involved are exactly the same as those discussed above in the cryoscopic method, but the forms of apparatus are different. (J. C. S. 1898, **73**, 502.)

Descriptions of apparatus employed in these physical methods are given in Sudborough and James' *Practical Organic Chemistry*, Chap. VIII.

(*c*) *By Measurement of the Osmotic Pressure.*

According to *van't Hoff* (Z. phys. Chem. I. 481), equimolecular solutions exert the same osmotic pressure, or are isotonic, equality of temperature being assumed. From this it follows, by reasoning analogous to that in section (*b*), that the molecular weight of a compound can be ascertained by measuring the osmotic pressure of its solution. The method is rarely used in chemical laboratories (*Ladenburg*, B. 1889, **22**, 1225; *M. Planck*, Z. phys. Chem., 1890, 6, 187.)

(*d*) *By Measurement of the Lowering of the Vapour Pressure.*

According to *Raoult*, the same generalizations hold for the lowering of the vapour pressure of a solvent by the introduction of a solute, as for the lowering of the freezing-points or the raising of the boiling-point. Three methods of applying the principle for the determination of molecular weights have been described. This law can be deduced theoretically from the preceding one (*c*), and it also stands in theoretical continuity with that of (*b*). (See *Wall & Biedig*, B. 1889, **22**, 1084; *Barger*, J. C. S. 1904, **85**, 206, *Perman*, *ibid.* 1905, **87**, 194; *Blackman*, *ibid.* 1474.)

(*e*) *By Measuring the Decrease in Solubility.*

(*Nernst*, B. **23**, Ref. 619. See also *Ostwald-Luther.*)

Polymerism and Isomerism

The determination of molecular weight is of the first importance, because different substances very frequently have the same percentage composition and therefore the same empirical formula, and yet are totally distinct from one another. This difference is often due to differences in the complexities of the molecules. Thus formic aldehyde, CH_2O; acetic acid, $C_2H_4O_2$; lactic acid, $C_3H_6O_3$; and grape-sugar, $C_6H_{12}O_6$, have all the same percentage composition; as have also ethylene, C_2H_4;

propylene, C_3H_6; and butylene, C_4H_8. Compounds standing in such relation to each other are termed **polymers**. Very frequently, however, substances which are totally distinct from each other possess both the same percentage composition and the same molecular weight; that is to say, these compounds are made up not only of the same elements, but also of an equal number of atoms of these elements; such substances are termed **isomers** or **metamers**. (See Ethers.) Thus, for instance, common alcohol and methyl ether, the latter of which is obtained by heating methyl alcohol with sulphuric acid, have one and the same molecular formula, C_2H_6O.

The striking phenomenon of isomerism is most readily explicable on the assumption that for the molecule of each compound there is a definite arrangement of the atoms, and that this arrangement or grouping is different in the molecules of the two isomerides. This difference in grouping may be considered as being due to a difference in the linking powers of the atoms, as is indicated by the dissimilar chemical behaviour of isomers, and explained by the theory of valency.

Chemical Theories; the Theory of Valency

After the fall of the Electro-Chemical theory, unitary formulæ—in contradistinction to the earlier dualistic formulæ—were much used; thus alcohol had the formula $C_4H_6O_2$ (using the old equivalent weights). The necessity for comparing substances of complicated composition with simpler ones, taken as "Types", had already repeatedly led to the propounding of new theories for representing the constitution of organic compounds, *e.g.* the older Type theory (*Dumas*), and the Nucleus theory (*Laurent*).

These obtained a firmer basis through *Gerhardt's* **Theory of Types**, which received support more especially from the discovery of ethylamine and other ammonia bases (*Wurtz*, 1849, and *Hofmann*, 1849, 1850), the proper interpretation of the formulæ of the ethers (*Williamson*, 1850), and the discovery of the acid anhydrides (*Gerhardt*, 1851). All compounds, inorganic as well as organic, were in this way compared with simpler inorganic substances taken as "**Types**", of which *Gerhardt* named four, viz.—

$$\left.\begin{matrix}H\\H\end{matrix}\right\rangle \qquad \left.\begin{matrix}H\\Cl\end{matrix}\right\rangle \qquad \left.\begin{matrix}H\\H\end{matrix}\right\rangle O \qquad , \qquad \left.\begin{matrix}H\\H\\H\end{matrix}\right\rangle N.$$

The first two of these really belong to the same type. Thus the following formulæ were arrived at:—

$\left.\begin{matrix}H\\Cl\end{matrix}\right\}$ $\left.\begin{matrix}K\\Cl\end{matrix}\right\}$ $\left.\begin{matrix}C_2H_5\\Cl\end{matrix}\right\}$ $\left.\begin{matrix}C_2H_3O\\Cl\end{matrix}\right\}$

Potassium chloride Ethyl chloride Acetyl chloride

$\left.\begin{matrix}H\\H\end{matrix}\right\}O$ $\left.\begin{matrix}K\\H\end{matrix}\right\}O$ $\left.\begin{matrix}NO_2\\H\end{matrix}\right\}O$ $\left.\begin{matrix}C_2H_5\\H\end{matrix}\right\}O$ $\left.\begin{matrix}C_2H_3O\\H\end{matrix}\right\}O$

Potassium hydroxide Nitric acid Alcohol Acetic acid

$\left.\begin{matrix}K\\K\end{matrix}\right\}O$ $\left.\begin{matrix}NO_2\\NO_2\end{matrix}\right\}O$ $\left.\begin{matrix}C_2H_5\\C_2H_5\end{matrix}\right\}O$ $\left.\begin{matrix}C_2H_3O\\C_2H_3O\end{matrix}\right\}O$

Potassium oxide Nitric anhydride Ether Acetic anhydride

$\left.\begin{matrix}H\\H\\H\end{matrix}\right\}N$ $\left.\begin{matrix}C_2H_5\\H\\H\end{matrix}\right\}N$ $\left.\begin{matrix}C_2H_3O\\H\\H\end{matrix}\right\}N$

Ethylamine Acetamide

&c. &c. Organic compounds could thus, like inorganic, be referred to inorganic types by assuming in them the presence of Radicals (*e.g.* ethyl, C_2H_5; acetyl, C_2H_3O, &c.), *i.e.* of groups of atoms which play a part analogous to that of an atom of an element, and which can be transferred by double decomposition from one compound to another. Thus ethyl chloride, C_2H_5Cl; alcohol, C_2H_6O; ethylamine, C_2H_7N; ether, $C_4H_{10}O$; &c., were represented as containing the same radical C_2H_5, ethyl, and the close relationship existing between these compounds now found expression in the type formulæ.

Sulphuric acid, H_2SO_4, was derived from the double water type, thus—

$$\left.\begin{matrix}H_2\\H_2\end{matrix}\right\}O_2 \qquad \left.\begin{matrix}(SO_2)''\\H_2\end{matrix}\right\}O_2;$$

and chloroform, $CHCl_3$, and glycerin, $C_3H_8O_3$, from the triple hydrochloric acid and water types—

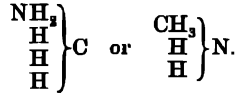
$$\left.\begin{matrix}H_3\\Cl_3\end{matrix}\right\} \quad \left.\begin{matrix}(CH)'''\\Cl_3\end{matrix}\right\}; \qquad \left.\begin{matrix}H_3\\H_3\end{matrix}\right\}O_3 \quad \left.\begin{matrix}(C_3H_5)'''\\H_3\end{matrix}\right\}O_3;$$

the assumption being made that the radicals $(C_2H_5)'$, $(SO_2)''$, $(CH)'''$, and $(C_3H_5)'''$ could replace a number of hydrogen atoms corresponding with the number of accents (') marked upon them, i.e. that they were monatomic, diatomic, &c. To the above

three types *Kekulé* afterwards added a fourth, of especial importance as regards the carbon compounds, viz.—



It was then found that many compounds could be referred equally well to one or another of these types, methylamine, for instance, either to CH_4 or to NH_3, thus—



The assumption, already mentioned, of the atomic groups (radicals) which in these types replaced hydrogen, led further to more exact investigations of the chemical value, *i.e.* the replaceable value, of those groups as compared with that of hydrogen. In this way chemists learnt to distinguish between mono-, di-, tri-, &c., valent groups, and, generally speaking, to pay more attention to equivalent proportions

As the outcome of his researches upon organo-metallic compounds, *Frankland* formulated in 1852 (A. **85**, 368) the law that the elements nitrogen, phosphorus, arsenic, and antimony tend to form compounds which contain three or five equivalents of other elements.

Kekulé then, in 1857–58 (A. **104**, 129; **106**, 129), proceeded to show that a more profound idea (the "Type idea") lay at the root of the types themselves, viz., that there are mono-, di-, tri-, and tetravalent, &c., elements, which possess a corresponding replacing or combining value as regards hydrogen; and that hydrogen is therefore monovalent, oxygen divalent, nitrogen trivalent, carbon tetravalent, and so on.

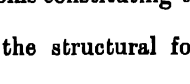
With the introduction of the CH_4 type by *Kekulé*, and the establishment of the tetravalent nature of the carbon atom accompanying this, were connected the endeavours of *Kolbe* to derive the constitution of organic compounds from carbonic acid (according to *Kolbe* C_2O_4, C = 6, O = 8), by the exchange of oxygen for organic radicals (A. **113**, 293); see also, for further details, *Kopp's* "Entwickelung der Chemie in der neueren Zeit" (Oldenbourg, Munich, 1873), and *E. V. Meyer's*

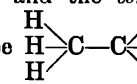
"History of Chemistry" (Macmillan, 1891), *Schorlemmer's* "Rise and Development of Organic Chemistry" (Macmillan).

The question of the valency of elements, a point which it is often difficult to decide in inorganic chemistry, is infinitely easier of determination in the case of the carbon compounds, because the carbon atom is **tetravalent** towards hydrogen as well as towards chlorine and oxygen. Since the atom of hydrogen, as the unit of valency, is monovalent, and, further, since the divalence of the oxygen atom cannot reasonably be doubted, the valency of the three "organic" elements hydrogen, oxygen, and carbon may be considered as resting upon a sure basis, as may also the conclusions drawn therefrom, and this all the more since the most important carbon compounds are made up of those three elements.

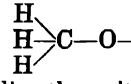
Within the past few years the divalency of the oxygen atom in many organic compounds has been brought into question. The readiness with which many oxy-derivatives form definite compounds with mineral acids and with metallic salts would appear to indicate that in many cases the oxygen atom can even be tetravalent (see Oxonium Salts). In certain compounds it has also been suggested that the carbon atom may be trivalent (see Triphenylmethyl).

Explanation of Isomerism; Determination of the Constitution of Organic Compounds

The phenomenon known as isomerism is elucidated to a great extent by the theory of valency. If two substances have the same molecular formula, *i.e.* both contain the same elements and the same number of atoms of the respective elements in their molecules, then the obvious conclusion to be drawn is that in the two molecules the atoms are differently arranged. The methods adopted in determining the manner in which the atoms are linked together, or, as it is called, the determination of the chemical constitution of the compound, is usually based on the following points:—(*a*) The respective valencies of the atoms constituting the molecule. A compound C_2H_6 must have the structural formula  , or, as it is often more shortly written, $CH_3 \cdot CH_3$, if each atom of carbon is to be represented as tetravalent, and each hydrogen atom as monovalent. Similarly the compound CH_4O must be

represented as  , or $CH_3 \cdot OH$ if the carbon atom is tetravalent, the oxygen atom divalent, and the hydrogen atoms monovalent. (*b*) A study of the more important methods of formation and of the chemical reactions in which the compound in question can take part. To select as an example ethyl alcohol, C_2H_6O. We can start from ethane, $CH_3 \cdot CH_3$, and by the action of chlorine replace one of the hydrogen atoms by a chlorine atom, and thus obtain the compound $CH_3 \cdot CH_2Cl$. When this is boiled with dilute alkalis (KOH), it gives potassic chloride and ethyl alcohol, $C_2H_5Cl + KOH = C_2H_6O + KCl$ From this it is obvious that the monovalent chlorine atom becomes replaced by an atom of oxygen and an atom of hydrogen. This can be readily understood if we assume that these two atoms enter in the form of the monovalent hydroxyl group, —O—H, and the *constitutional formula* for ethyl alcohol would then be  or $CH_3 \cdot CH_2 \cdot OH$. This formula is further supported by a study of most of the chemical reactions in which ethyl alcohol can take part. It can react with metallic sodium, yielding a compound, sodic ethoxide, C_2H_5NaO; however much sodium is employed, only one of the six hydrogen atoms present in the alcohol molecule can be replaced by sodium, and this atom is presumably the one differently situated from the remaining five, namely, the one attached to oxygen. The presence of the hydroxyl, —O—H, group is further confirmed by the action of hydric chloride or of phosphorus trichloride on the alcohol, when an atom of chlorine takes the place of the $\cdot OH$ group.

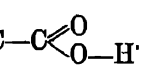
$$CH_3 \cdot CH_2 \cdot OH + HCl = CH_3 \cdot CH_2Cl + H \cdot OH$$
$$\text{and } 3\,CH_3 \cdot CH_2 \cdot OH + PCl_3 = 3\,CH_3 \cdot CH_2Cl + P(OH)_3.$$

Isomeric with ethyl alcohol is the substance known as dimethyl ether. Although it has the same molecular formula, it differs altogether from ethyl alcohol in its chemical and physical properties. The only other possible method of linking up the atoms 2 C, 6 H, and O, is  , in which the two carbon atoms are not directly united to one another, and in which the six hydrogen atoms are all similarly

situated. The chemical reactions of dimethyl ether are in perfect harmony with this constitutional formula. It does not react with metallic sodium, and hence presumably does not contain an ·OH group. When acted upon by hydriodic acid, under suitable conditions, the molecule is ruptured, as represented by the following equation:—

$$CH_3 \cdot O \cdot CH_3 + HI = CH_3I + CH_3 \cdot OH.$$

Similarly, whenever the oxygen atom is removed a rupture of the molecule occurs, and the two carbon atoms in the molecule become separated.

The constitutional formula for acetic acid is written  . This formula corresponds perfectly with the chemical behaviour of acetic acid and explains the following facts:—(*a*) that one of the hydrogen atoms of the acid possesses properties different from those of the three others, the first-named being easily replaceable by metallic radicals; (*b*) that the two oxygen atoms behave differently, not being equally readily exchangeable for other radicals; (*c*) that different functions appertain to the two carbon atoms, so that one of them—being already joined to two atoms of oxygen—easily gives rise to carbonic acid, while the other—connected as it is with three atoms of hydrogen—readily passes into methane or methyl compounds.

On account of the innumerable cases of isomerism which have been observed, simple molecular formulæ alone are in most cases insufficient for the discrimination of organic compounds; it generally requires the constitutional formulæ to give a clear idea of their behaviour and of their relations to other substances. Careful study has made it possible within the last few decades to find out the mode in which the atoms are combined in the molecules of most organic compounds, and from this to deduce new methods for their preparation. The constitutional formulæ thus arrived at are sometimes very simple, sometimes, however, very complicated, as, for instance, in the cases of citric acid and grape-sugar (which see).

Rational Formulæ

Great latitude is permissible as regards the mode of writing constitutional formulæ, according to the particular points which it is desired to emphasize. A formula on paper is not as a rule intended to represent the symmetrical or spatial arrangement of the atoms in a compound.

A shortened constitutional formula, which indicates more chemical relations than an empirical one does, is called a *rational* formula; *e.g.* C_2H_5OH, alcohol; $(CH_3)_2O$, methyl ether.

For acetic acid, instead of the constitutional formula already given on page 18, the following rational formulæ may be used:—

$CH_3—C\begin{matrix}O\\ \diagdown OH\end{matrix}$, $CH_3—CO\cdot OH$, $CH_3—CO_2H$, $CH_3\cdot CO_2H$, $(CH_3\cdot CO)OH$, $C_2H_3O\cdot OH$, $H(C_2H_3O_2)$; and so on.

The Nature of the Carbon Atom

The theoretical views and the knowledge thereby gained of the nature of the carbon atom may be expressed somewhat as follows:—

1. The carbon atom is tetravalent.

2. Its four valencies are all equal; a mono-substituted derivative of methane exists in only one form, that is, isomerism is not met with.

3. The atoms or atomic groups which are held bound by these four valencies cannot readily exchange places with each other (the *Le Bel–van't Hoff* law, 1874). Proof: there are in nearly every case two physically different tetra-substitution products, C, a, b, c, d of methane (see Stereochemistry).

4. Several carbon atoms can be connected together by either one, two, or three valencies (see p. 23): C·C, C:C, C⋮C.

5. Similarly, three or more carbon atoms may be united, forming in this way the so-called "carbon chains" (see p. 32), thus—

$C\cdot C\cdot C\cdot C$; $C\cdot C\cdot C:C\cdot C\cdot C$; $C⋮C\begin{matrix}\diagup\\ C\\ \diagdown\end{matrix}C\cdot C$.

The number of the atoms so linked together may be very large, in some cases probably several hundreds.

6. These carbon atoms form either open or ring shaped closed chains.

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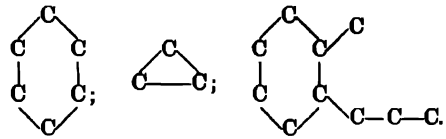
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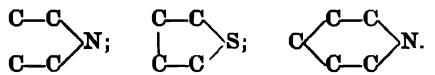
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Open chains are those which have separate constituent atoms at either end, as in (5). In *closed chains* or *rings*, on the contrary, the first and last constituent atoms are linked together (although there may at the same time be subsidiary branches from them), thus—



7. The atoms of other elements, with the exception, of course, of monovalent ones, may likewise take part in the formation of such chains, both open and closed, for example:



The above figures (the hexagon, &c.), which are made use of to represent such chains or rings, are merely meant to be pictorial (*schematisch*) and not geometrical; the question of the spatial arrangement of atoms in compounds will be dealt with later.

Homology

In the study of carbon compounds it is customary to group together all the compounds with similar chemical structure and similar chemical properties, and to arrange the members of such a group, or *homologous series* as it is termed, according to the order of their molecular complexity, *i.e.* according to the number of carbon atoms contained in the molecule.

For example:—

Paraffins.		Fatty acids
CH_4 methane	.....	CH_2O_2 formic
C_2H_6 ethane	.....	$C_2H_4O_2$ acetic
C_3H_8 propane	.....	$C_3H_6O_2$ propionic
C_4H_{10} butane	.....	$C_4H_8O_2$ butyric
&c.		

It is found that in any such *homologous series* a number of generalizations can be drawn. Some of the more important of these are:—

1. For each homologous series we can write a *general for-*

mula which will represent the composition of all the members of the series; for example, the general formula for the paraffins is C_nH_{2n+2}, and for the saturated fatty acids $C_nH_{2n}O_2$.

2. If any particular member in a series is selected, it is found to differ in composition from the member immediately preceding, and also from the one immediately succeeding, it by a definite amount, namely, CH_2. Or, expressed in other words, any member of the series may be regarded as derived from the member immediately preceding it by the introduction of a methyl group, $\cdot CH_3$, for an atom of hydrogen It follows, therefore, that all the members of the paraffin series may be regarded as derived from CH_4 by the addition of a given number of CH_2 groups, and the general formula is for this series $CH_4 + xCH_2$, or more simply C_nH_{2n+2}.

3. The chemical properties of the different members of the series vary but slightly, so that a description of the chemical properties of any one member may be taken, as a rule, to apply to the other members.

4. In studying the physical properties, well-marked gradations are observed as the number of carbon atoms increases. In the case of liquids, the boiling-point is found to rise as the complexity of the molecule increases. In certain series, *e.g.* the paraffins, the first few members are gases, then follow liquids with gradually increasing boiling-points, and ultimately solids with extremely high boiling-points. Other physical data, such as melting-point, specific gravity, solubility, &c., are affected in very much the same manner.

In the paraffin series the grouping together of the carbon atoms must be conditioned by themselves, since hydrogen, as a monovalent element, cannot be the cause of it. In all the higher hydrocarbons the carbon atoms are therefore combined together in the form of a chain, as shown in the following graphical representations:—

C,	C,	C·C·C·C, or C·C; and so on.
C	C	C
in C_2H_6	in C_3H_8	in C_4H_{10}

Various cases can occur in the mode of combination of the carbon atoms (Isomers). (See Hydrocarbons of the Methane Series.)

Law of Even Numbers of Atoms.—The number of hydrogen

atoms in the above hydrocarbons is always divisible by two. Should they therefore be partially replaced by other elements, the sum of these latter, if their valencies are expressed by odd numbers, *e.g.* Cl, N, and P, and of the remaining hydrogen atoms taken together must, as a necessary consequence of the law of equivalent proportions, remain an even number.

Radicals

According to *Liebig*, radicals were groups of atoms capable of a separate existence, which played the parts of elements, and, like these latter, could combine among themselves and be exchanged from one compound to another.

Later on, the postulate that such radicals must also be capable of existing in the free state was allowed to lapse, and they were frequently defined shortly as "the residues left unattacked by certain decompositions".

Now, however, it is usual to designate as radicals only those atomic groups which are found repeating themselves in a comparatively large number of compounds derived from one another, and which play in these compounds the part of a simple element, *e.g.* CH_3, methyl; C_2H_3O, acetyl; by this definition the question of their existence or non-existence in the free state does not arise. The radical methyl, for example, is not known in the free state, since, when its formation might be expected, ethane (dimethyl), $CH_3—CH_3$, is obtained instead (see p. 37). Such radicals may be mono-, di-, or trivalent, &c., according to the number of monovalent atoms which they are capable either of replacing or of combining with, so as to form a saturated compound; for instance, $(C_2H_4)''$, ethylene, is divalent; $(C_3H_5)'''$, glyceryl, trivalent; $(CH)'''$, methine or methenyl, likewise trivalent, &c. The monovalent residues, C_nH_{2n+1} (methyl, ethyl, &c.), which form the radicals of the monovalent alcohols, $C_nH_{2n+1}OH$, are frequently termed *alkyls*, or *alphyls*, while the divalent residues, C_nH_{2n}, are known as *alkylenes*.

At the present time it is also customary to speak of single atoms as radicals; *e.g.* we have the chloride or iodide radical, and further, the hydric radical which is characteristic of acids.

Classification of the Hydrocarbons, &c.

The hydrocarbons which have already been described are termed "saturated" compounds, since they cannot take up more hydrogen. But besides these there are hydrocarbons, &c., poorer in hydrogen, or "unsaturated", such as C_2H_4, ethylene, and C_2H_2, acetylene, corresponding with which there are numerous homologous series.

The constitution of these is explained, as will be seen later, by the assumption of a double or triple bond between neighbouring carbon atoms, for instance—

C_2H_4 is written $CH_2:CH_2$,
C_2H_2 is written $CH:CH$.

From these different hydrocarbons, as starting-points, the most various substitution products, such as alcohols, aldehydes, ketones, acids, amines, &c., are derived by exchange of the hydrogen for halogen, oxygen, nitrogen, &c.

To another class of hydrocarbons belongs that most important compound benzene, C_6H_6, which contains eight atoms of hydrogen less than hexane, C_6H_{14}. With regard to its constitution, the theory of the existence of a closed chain of six carbon atoms has been advanced. (See Benzene Derivatives.) From benzene are derived an immense number of the most different homologous and analogous hydrocarbons and substitution products, alcohols, aldehydes, acids, and so on. Thus benzene, like methane, is the mother substance of numerous organic compounds.

What has just been said with regard to benzene also holds good for various other compounds, which are characterized from a chemical point of view by containing a closed (ring) chain. These are:—

(*a*) Trimethylene, C_3H_6; Tetramethylene, C_4H_8; and Pentamethylene, C_5H_{10}.

(*b*) Pyridine, C_5H_5N, a strongly basic nitrogenous compound, but one which at the same time resembles benzene closely in many respects.

(*c*) Furane, C_4H_4O; Pyrrol, C_4H_5N; Thiophene, C_4H_4S; Pyrazole, $C_3H_4N_2$; Thiazole, C_3H_3NS; &c.

Some of these latter compounds are extremely like benzene, others like pyridine; several of them are as yet only known in the form of derivatives. Like benzene, they are all mother-substances of—in many cases—long series of compounds.

Organic chemistry is therefore divided into the following sections:—

1. **Chemistry of the Methane Derivatives or Fatty Compounds, or Aliphatic Compounds** (from ἀλοιφή, fat), so called because the fats and many of their derivatives belong to this group. This section comprises all carbon compounds with open chains. A few compounds, which are really closed-chain or ring compounds, will be mentioned in this section on account of their close relationship to certain open-chain compounds; as an example, we may take succinic anhydride $\begin{matrix}CH_2\cdot CO\\ CH_2\cdot CO\end{matrix}\!\!>\!O$, which is formed by the elimination of water from succinic acid, $OH\cdot CO\cdot CH_2\cdot CH_2\cdot CO\cdot OH$.

2. **Cyclic or closed-chain compounds.** This section is usually divided into two sub-sections.

(*a*) Chemistry of the *carbocyclic compounds*, which comprises the study of all compounds built up of a ring of carbon atoms. As examples we have $\begin{matrix}CH_2\\ CH_2\end{matrix}\!\!>\!CH_2$, Trimethylene; $CH_2\!<\!\begin{matrix}CH_2\\ CH_2\end{matrix}\!>\!CH\cdot CO_2H$, Tetramethylene carboxylic acid, $CH\!<\!\begin{matrix}CH:CH\\ CH\cdot CH\end{matrix}\!>\!CH$, Benzene; &c.

(*b*) Chemistry of the *heterocyclic compounds*, comprising the study of all ring compounds which contain other atoms, in addition to carbon atoms, as part of the ring, *e.g.*

$\begin{matrix}CH\cdot CH\\ CH\cdot CH\end{matrix}\!\!>\!O$ Furane, $\begin{matrix}CH\cdot CH\\ CH\cdot CH\end{matrix}\!\!>\!S$ Thiophene, $CH\!<\!\begin{matrix}CH:CH\\ CH\cdot CH\end{matrix}\!>\!N$ Pyridine, &c.

Physical Properties of Organic Compounds

The physical properties of organic compounds are often of the greatest importance for their characterization, and physical data are frequently made use of in determining the purity of a chemical compound.

Solubility. — The carbon compounds vary enormously as regards their solubility in various solvents. As a rule, a given solvent dissolves those substances which are chemically closely allied to it. As example of this, we have the fact that water tends to dissolve hydroxylic compounds, especially if

there are several hydroxy groups in the molecule, *e.g.* mannitol, glucose, and pyrogallol.

Benzene tends to dissolve most hydrocarbons, and ether dissolves the majority of simple organic compounds, with the exception of salts of acids.

The usual method of determining the solubility of the given substance is to prepare a saturated solution of the substance at the temperature required. This is accomplished by one of two methods:—(*a*) Shaking the finely-divided solute for some time in contact with the solvent at the given temperature, care being taken that there is always some undissolved solute left over. (*b*) If the solute is more soluble in hot than in the cold solvent, a concentrated hot solution is prepared, and is then allowed to cool down to the temperature required, care being taken to stir the solution so that the excess of solute crystallizes out and a supersaturated solution is not obtained. A known weight or volume of the clear saturated solution is taken, and the solvent removed by evaporation, and the residual solute weighed. The result is usually expressed in the form 100 grams of solvent dissolve x grams of solute at $t°$.

Specific Gravity and Specific Volume.—The specific gravity of a liquid is an important criterion for the purity of the substance. This is usually determined in a specific-gravity bottle, Sprengel tube, or Pyknometer. The pyknometer is filled with pure water at a given temperature (usually 4° or 15°) and carefully weighed. It is then dried, filled with the liquid at a fixed temperature, and again weighed. The ratio $\frac{\text{wt. of liquid}}{\text{wt. of water}}$ is the specific gravity. It is usual in giving the specific gravity to denote the temperature at which the determination was made, as this varies with the temperature, and also the temperature of the water, *e.g.* $d_{4°}^{20°}$ denotes the specific gravity of the liquid at 20° compared with that of water at 4°. The reciprocal of the specific gravity is known as the *specific volume*, and the product of this and the molecular weight as the *molecular volume*.

Melting-Point.—Each fusible compound has a fixed definite melting-point, and this constant is often made use of in determining the purity of a solid, as the introduction of even small amounts of impurities lowers the melting-point considerably. When appreciable amounts of impurities are present, the

melting-point is not sharp, but ranges over a number of degrees. The melting-point is best defined as the temperature at which the liquid and solid phases of the compound are in equilibrium. The most direct and most accurate method of determining the melting-point is to place a thermometer in the molten substance and allow it to partially solidify, and note the temperature at which the mercury remains constant when the mixed solid and liquid is stirred by the thermometer. As this method involves the use of a relatively large amount of the substance, the determination is usually made by introducing a very small amount of the finely-divided substance into a narrow capillary tube closed at one end. This tube is then attached to a thermometer, the substance being at the same level as the middle of the bulb of the thermometer, and the two are carefully heated in a bath of sulphuric acid. Just before the melting-point is reached the flame is removed occasionally, so that the temperature rises very slowly, and the melting-point can be read accurately to within ·5 or ·25 of a degree. As a rule, a short thermometer is used, so that the whole thread of mercury is in the bath, otherwise a correction has to be made for the length of the mercury thread which is not immersed in the hot bath.

Boiling-Point.—The purity of a volatile substance can usually be determined by means of the boiling-point, *i.e.* the temperature at which the vapour pressure of the substance is equal to the atmospheric pressure. It is usually determined by placing the bulb of the thermometer in the vapour, and if a short thermometer is employed, and the whole of the mercury thread is surrounded by the vapour, no correction is required. In each case the barometric pressure should be stated, and also whether the thread of mercury was completely immersed in the vapour.

Many substances which decompose when heated under atmospheric pressure, may be distilled without undergoing decomposition under reduced pressure. This is accomplished by attaching the flask, condenser, and receiver to a mercury or water pump and exhausting. When the pressure is sufficiently reduced the substance is distilled, care being taken that the pressure under which the distillation occurs is measured by means of a manometer. As a rule, considerable difficulty in avoiding bumping is encountered in distillations under diminished pressure; this is most readily got over by placing a piece of porous material (unglazed pot) in the liquid,

or by slowly aspirating bubbles of air through the boiling liquid. (Compare *Auschutz* and *Reilter*, Brochure. Bonn, 1895).

Fractional Distillation.—Two miscible liquids with widely differing boiling-points, *e.g.* alcohol, 78°, and aniline, 185°, can be separated by the process of fractional distillation, as the lower boiling liquid distils over first. In all cases an intermediate fraction consisting of a mixture of the substances is obtained, but, as a rule, the greater the difference between the boiling-points of the two substances the smaller is this fraction. In many cases where the boiling-points are not very far removed, *e.g.* benzene, 80°, and toluene, 111°, the two compounds cannot be separated by a single fractionation; it is thus customary to collect fractions every 5° and to subject each of these fractions to further distillation, using the same flask for distillation, and again collecting every 5°. It is then found that there is a large fraction boiling at 80–85° and consisting of nearly pure benzene, and a large fraction, 110–111°, consisting of pure toluene, and a number of small fractions boiling at 85–90°, 90–95°, &c., and consisting of mixtures of benzene and toluene. The process is often quickened by using some form of fractionating column. This consists of a long tube with bulbs blown on, and serves to lengthen the neck of the flask. The Linneman tube contains small wire-gauze cups in the constricted parts, and in these drops of the higher boiling liquid collect, and thus all the vapour has to pass through or be washed by these drops. The same purpose is served in the Glynsky tube by placing a glass ball in each constriction. (See *S. Young*, "Fractional Distillation". London, 1903.)

It is not always possible to separate liquids by fractional distillation, for example, when the boiling-points are very close, or when the two substances form a mixture of definite boiling-point. When dilute nitric acid is distilled, water first passes over, and then a mixture of water and nitric acid, until the residue in the flask is 68 per cent nitric acid, and then it boils constantly at 126°, since the vapour and the liquid in the flask have the same composition.

Mixtures of constant boiling-point are always characterized by the fact that they have a vapour pressure either higher or lower than that of either of the constituents, or than that of any other mixture of the same compounds.

Steam Distillation.—This is the process frequently resorted to in the separation of a compound readily volatile in steam

from other substances, *e.g.* tars or inorganic salts, which are not volatile. It consists in blowing steam through the mixture, and condensing the steam and volatile compound by means of a Liebig condenser. Very often the volatile compound is practically insoluble in water, and separates as an oil or solid in the distillate. The rapidity with which a given substance distils with steam depends on the vapour pressure of the substance at the given temperature, and also on its molecular weight or vapour density compared with that of water. Thus a mixture of nitro-benzene and water, which may be regarded as non-miscible liquids, boils at 99°; *i.e.* the vapour pressure of the mixture at 99° is 760 mm. The vapour pressure of water at 99° is 733 mm., and therefore the partial pressure of the nitro-benzene is 27 mm. In a given volume of the mixed vapours $\frac{733}{760}$ will consist of steam and $\frac{27}{760}$ of nitro-benzene, and the relative weights of these volumes will be the volumes × relative densities, *i.e.* $\frac{9 \times 733}{760} : \frac{61 \times 27}{760}$ *i.e.* 4 : 1; or, in other words, $\frac{1}{5}$th by weight of the total distillate will consist of nitro-benzene.

Other methods very frequently used in the purification of solid compounds are crystallization and fractional crystallization. The method employed is essentially the same as that made use of in purifying inorganic compounds, except that organic solvents, *e.g.* alcohol, chloroform, benzene, carbon disulphide, and low-boiling petroleums, are largely used. Often a mixture of two solvents is more serviceable than a single one, *e.g.* substances are often crystallized by solution in warm alcohol and addition of water, or solution in benzene and addition of petroleum, until a slight turbidity ensues. The fact that a substance crystallizes from a given solvent in well-defined crystals does not necessarily indicate that the substance is a single chemical individual, as numerous examples of mixed crystals with definite melting-points are known, and these are not resolved when repeatedly crystallized from the same solvent.

Extraction with Ether, Benzene, &c.—Partition Coefficient.—An organic compound can often be separated from other substances, especially inorganic salts, by shaking out with ether, separating the ethereal layer by means of a separating funnel, drying the solution with granular calcium chloride or some other suitable drying agent, and removing the ether by

distillation. The method gives very good results when the compound to be extracted is much more soluble in ether than in water, and when the substances from which it is to be separated are insoluble in ether. When there is no marked difference in the solubilities of the given compound in ether and in water, the extraction must be repeated a number of times, in some cases even twenty, since for each compound the ratio $\frac{\text{conc. of ethereal solution}}{\text{conc. of aqueous solution}}$ is a constant, and is usually termed the *partition coefficient* or *coefficient of distribution* of the particular substance between the two solvents. In extractions with ether it must be borne in mind that ether dissolves to an appreciable extent in water, and also water in ether. Other liquids, such as benzene, carbon-disulphide, chloroform, &c., may be used in place of ether.

When the amount of solvent to be used is limited, it is more economical to extract two or three times with small amounts of solvent rather than only once with the whole amount. As an illustration. 11 grams of a substance and 1 litre each of the non-miscible liquids, water and benzene. The solubility of the substance in benzene is ten times its solubility in water, and it has the same molecular weight in both solvents.

Case I.—Extracting at once with the litre of benzene, $\frac{\text{conc. of benzene solution}}{\text{conc. of water solution}} = \frac{10}{1}$, *i.e.* $\frac{1}{11}$th of the whole, or 1 gram, remains in the water.

Case II.—Extract twice with 500 c.c. of benzene. After first extraction, suppose x grams passes into the benzene, then conc. of aqueous solution is $11 - x$, and of the benzene $2x$, $\therefore \frac{2x}{11 - x} = \frac{10}{1}$, or $x = 9$ (approx.), and 2 grams are left in the water.

After extraction with second quantity of benzene, y grams go into the benzene. Then $\frac{2y}{2 - y} = \frac{10}{1}$, or $y = 1{\cdot}7$ (approx.), and only 0·3 gram remains in the aqueous solution. Whereas, after the single extraction with a litre of benzene 1 gram was left.

For applications of this method in determining the relative strengths of acids and amines, compare *Farmer* and *Warth* (J. C. S. 1904, 1713).

Class I.—ALIPHATIC OR OPEN-CHAIN COMPOUNDS

I. HYDROCARBONS

A. Saturated Hydrocarbons, C_nH_{2n+2}

This constitutes the simplest homologous series of carbon compounds, and all the saturated open-chain compounds may be regarded as derived from these.

The following list includes the more important *normal* hydrocarbons:—

Formula.	Name.	Melting-point.	Boiling-point.	Specific gravity.
CH_4	Methane	−186°	−164°	0·415 at b.-p.
C_2H_6	Ethane	−172°	−84°	0·446 at 0°
C_3H_8	Propane		−37°	0·536 at 0°
C_4H_{10}	Butane		+1°	0·600 at 0°
C_5H_{12}	Pentane		37°	0·627 at 14°
C_6H_{14}	Hexane		69°	0·658 at 20°
C_7H_{16}	Heptane		98°	0·683 at 20°
C_8H_{18}	Octane		125°	0·702 at 20°
C_9H_{20}	Nonane	−51°	150°	0·718 at 20°
$C_{10}H_{22}$	Decane	−31°	173°	0·730 at 20°
$C_{11}H_{24}$	Undecane	−26°	195°	0·774 at m.-p.
$C_{12}H_{26}$	Dodecane	−12°	214°	0·773 at m.-p.
$C_{14}H_{30}$	Tetradecane	+4°	252°	0·775 at m.-p.
$C_{16}H_{34}$	Hexadecane	18°	287°	0·775 at m.-p.
$C_{20}H_{42}$	Eicosane	37°	205°*	0·778 at m.-p.
$C_{21}H_{44}$	Heneicosane	40°	215°*	0·778 at m.-p.
$C_{23}H_{48}$	Tricosane	48°	234°*	0·779 at m.-p.
$C_{31}H_{64}$	Hentriacontane	68°	302°*	0·781 at m.-p.
$C_{35}H_{72}$	Pentatriacontane	75°	331°*	0·782 at m.-p.
$C_{60}H_{122}$	Hexacontane	101°		

* Under 15 mm. pressure.

The first members of the series, including those with about four atoms of carbon, are gases, which gradually become more easily condensable as the number of carbon atoms in the molecule increases. The members which follow are liquid at the

ordinary temperature, their boiling-point rising with increasing number of carbon atoms. An increase of CH_2 in the molecular formula does not necessarily denote a definite increase in the boiling-point. The difference in boiling-point between hexane and heptane is 29°, and between undecane and dodecane only 19°; thus with compounds of high molecular weight an increase of CH_2 does not produce so marked an effect on the boiling-point as with simpler compounds. The higher homologues, from about $C_{16}H_{34}$ (melting-point 18°) on, are solid at the ordinary temperature, and their melting-point gradually rises up to about 100°. The highest members can be distilled under diminished pressure only. The methane homologues are almost or quite insoluble in water; alcohol dissolves the gaseous members to a slight extent, the liquid members easily, and the solid with gradually increasing difficulty. Their specific gravities at the melting-point increase with increasing number of carbon atoms from 0·4 up to 0·78, which is the maximum limit. This value is already almost reached by the hydrocarbon $C_{11}H_{24}$, so that for the higher members of the series the following law holds good: "the molecular volumes are proportional to the molecular weights" (*Krafft*).

They are incapable of combining further with hydrogen or halogens (see p. 23), and absorb neither bromine nor sulphuric acid. They are therefore termed the Saturated Hydrocarbons. Even fuming nitric acid has little or no action upon the lower members of the series; thus, methane is not attacked by a mixture of fuming nitric and sulphuric acids, even at 150°. They are also very indifferent towards chromic acid and permanganate of potash in the cold,* when oxidation does take place, they are mostly converted directly into carbonic acid. The name of "The Paraffins" (from *parum affinis*), which was originally applied only to the solid hydrocarbons from lignite, has therefore been extended to the whole homologous series.

By the action of the halogens (Cl, Br), **substitution** takes place, the substituted hydrogen combining with an amount of halogen equal to that which has entered the hydrocarbon (see Substitution products of the Hydrocarbons):

$$CH_3H + ClCl = CH_3Cl + HCl.$$

As the number of carbon atoms increases, the percentage composition of these hydrocarbons approaches a definite limit,

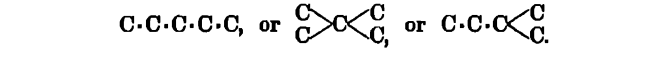
* With the exception of compounds containing the grouping R'R''R'''CH

viz. that of the hydrocarbons, C_nH_{2n}, or CH_2, as is shown by the following table:—

Per cent.	CH_4	C_2H_6	C_3H_8	C_6H_{14}	$C_{18}H_{34}$	$C_{22}H_{46}$	$C_{24}H_{50}$	$C_{35}H_{72}$	Limit Value, C_nH_{2n}
C	75·00	80·00	81·82	83·72	84·60	85·16	85·21	85·36	85 71
H	25 00	20·00	18·18	16·28	15·40	14·84	14·79	14·64	14·29

It is therefore impossible to distinguish by elementary analysis between two of the neighbouring higher homologues, *e.g.* C_{22} and C_{24}, C_{24} and C_{30}; the only reliable data here are the methods of formation from compounds in which the number of carbon atoms in the molecule is already known, and the melting-points.

Isomers.—Only one representative each of the formulæ CH_4, C_2H_6, and C_3H_8 is known, but of C_4H_{10} there are two, of C_5H_{12} three, and of C_6H_{14} already five isomers, and most of the higher hydrocarbons are known in various isomeric forms. From this the conclusion is drawn that in these different isomers the carbon atoms are differently combined, in the one case in a straight line without branching, like the links of a chain; in the other, with the formation of a branching chain. (This is of course not to be taken as meaning that they are grouped together in space in straight lines.) Thus:—



The first of these hydrocarbons, with a non-branching chain, are termed the normal hydrocarbons; the last, the iso-hydrocarbons.

The principles by which such constitutional formulæ are arrived at will be explained under Butane and Pentane.

Only those homologues are comparable whose constitutions are similar, as in the case of the normal hydrocarbons.

Occurrence.—The hydrocarbons of the paraffin series occur naturally in great variety. Thus, methane is exhaled from the earth's crust, as "fire-damp" and as marsh-gas. The next higher homologues are found dissolved in petroleum, which also contains the higher hydrocarbons in large amount. Solid hydrocarbons occur as ozokerite or earth-wax. By the fractional distillation of petroleum a large number of these com-

pounds have been isolated. Heptane and hexadecane are also found in the vegetable kingdom.

Modes of formation.—A. Various members of this series are obtained by the distillation of lignite (Boghead, Cannel coal), wood, bituminous shale, and, in very much smaller quantity, from pit coal. Paraffins are also obtained by dissolving carbide of iron in acids, and by heating wood, lignite, and coal, but not graphite, with hydriodic acid.

B. From substances containing an equal number of carbon atoms in the molecule.

1. From the halogen alkyls,* $C_nH_{2n+1}X$, and, generally speaking, from the substitution products of the hydrocarbons by exchange of the halogen for hydrogen (**inverse substitution**). This is effected by the action of reducing agents, that is, agents which give rise to nascent hydrogen. Some of the commoner reducing agents employed for such purposes are sodium amalgam and water, zinc and a dilute acid, zinc and water at 160°, the copper-zinc couple in presence of water and alcohol (*Gladstone-Tribe*), aluminium- or magnesium-amalgam and alcohol, and one of the most vigorous reducing agents, concentrated hydriodic acid at high temperatures, especially in contact with red phosphorus, which serves to continually renew the hydrogen iodide. (See chapter on Reduction.)

2. From monohydric alcohols, $C_nH_{2n+1}\cdot OH$, polyhydric alcohols, $C_nH_{2n}(OH)_2$, $C_nH_{2n-1}(OH)_3$, &c., also from aldehydes, $C_nH_{2n+1}\cdot CHO$, ketones, $C_nH_{2n+1}\cdot CO\cdot C_nH_{2n+1}$, and other compounds containing oxygen, by heating with hydriodic acid and red phosphorus at relatively high temperatures. In all these reactions the oxygen is ultimately removed as water.

3. From hydrocarbons poorer in hydrogen, *i.e.* unsaturated hydrocarbons (see these), by the addition of hydrogen; *e.g.* ethane from ethylene or acetylene and hydrogen, either in presence of platinum black or finely-divided nickel or by heating the mixture of gases to 400°–500°. Also by heating with hydriodic acid (*Krafft*), or by addition of halogen or halogen hydride, and exchange of the halogen for hydrogen, according to 1. Thus:—

$$C_2H_4 + H_2 = C_2H_6, \qquad \begin{cases} C_2H_4 + HBr = C_2H_5Br, \\ C_2H_5Br + 2H = C_2H_6 + HBr. \end{cases}$$
$$C_5H_{10} + 2HI = C_5H_{12} + I_2;$$

* The monovalent residues, C_nH_{2n+1}, methyl, ethyl, &c., which are at the same time the radicals of the monohydric alcohols, $C_nH_{2n+1}OH$, are frequently termed alkyl groups.

4. By decomposing the organo-zinc compounds (zinc-alkyls) with water (*Frankland*)—

$$Zn(C_2H_5)_2 + 2\,H_2O = Zn(OH)_2 + 2\,C_2H_6.$$

Or more readily by decomposing Grignard's organo-magnesium compounds with water. Thus ethyl iodide and magnesium, in presence of dry ether, yield ethyl magnesium iodide, $C_2H_5 \cdot Mg \cdot I$, and this with water evolves ethane:

$$C_2H_5 \cdot Mg \cdot I + H \cdot OH = C_2H_6 + OH \cdot Mg \cdot I.$$

C. From acids containing more carbon, with separation of carbon dioxide. Thus, by heating acetate of calcium with soda-lime, methane and carbonic acid are formed.

$$(CH_3COO)_2Ca + Ca(OH)_2 = 2\,CH_4 + 2\,CaCO_3.$$

In the case of the acids of higher molecular weight, this separation of carbonic acid is conveniently effected by heating with sodic ethoxide.

D. By the combination of two radicals containing a smaller number of carbon atoms.

1. By the action of sodium upon the alkyl iodides in ethereal solution (*Wurtz*); or by heating with zinc in a sealed tube (*Frankland*):

$$2\,CH_3I + 2\,Na = C_2H_6 + 2\,NaI.$$

By this method also two different radicals can be combined, *e.g.* $C_2H_5I + C_4H_9I$ give $C_2H_5 + C_4H_9 = C_6H_{14}$, ethyl-butyl (*Wurtz's* "Mixed Radicals").

2. By the electrolysis of solutions of the potassic salts of fatty acids (*Kolbe*, 1848). The anions, for example, $CH_3 \cdot COO$, when discharged at the anode, break up into CH_3 and CO_2, and two of the CH_3 groups immediately combine to form a molecule, $CH_3 \cdot CH_3$, viz. ethane. The hydrogen is here evolved at the cathode, and the hydrocarbon at the anode; the carbon dioxide is to a large extent retained in the solution.

Methane, CH_4 (*Volta*, 1778). *Occurrence.*—As an exhalation from the earth's crust, more especially at Baku in the neighbourhood of the Caspian Sea (the "Holy Fire" of Baku); from the large gas wells at Pittsburg, in North America, and in numerous other places; in the exhalations from mud volcanoes, for instance at Bulganak in the Crimea, where the gas is almost pure methane (*Bunsen*); and as pit gas or "fire-damp" in mines, where, wher mixed with air, it is apt to cause explosions.

As marsh-gas, together with carbon dioxide and nitrogen,

by the decomposition of organic substances under water; further, by the fermentation of cellulose, *e.g.* by river mud, by means of Schizomycetes (fission-fungi).

It is also found in rock-salt (the Knistersalz of Wieliczka), and in the human intestinal gases (up to 57 per cent CH_4 after eating pulse).

The illuminating gas obtained by the destructive distillation of coal contains about 40 per cent methane.

Modes of preparation.—1. Methane is formed synthetically by the direct union of carbon and hydrogen. Pure sugar carbon freed from all traces of hydrogen by treatment with chlorine is heated in a current of dry hydrogen in a porcelain tube, and the issuing gas is found to contain one per cent of methane (*Bone* and *Jordan*, J C S, 1897, 41; 1901, 1042, *Pring*, 1910, 489; *Pring* and *Fanlie*, 1911, 1796, 1912, 91); and is also formed by the decomposition of ethane, ethylene, and acetylene at moderate temperatures (*Bone* and *Coward*, 1908, 1197).

2. When carbon monoxide and hydrogen are passed over reduced nickel at 200°–250°. The nickel acts as a catalytic agent, and apparently undergoes no change. Carbon dioxide may be substituted for the monoxide. (*Sabatier* and *Senderens.*) The reactions are:—

$$CO + 3H_2 = CH_4 + H_2O \quad \text{and} \quad CO_2 + 4H_2 = CH_4 + 2H_2O$$

3. By leading sulphuretted hydrogen and carbon bisulphide vapour over red-hot copper (*Berthelot*); $CS_2 + 2H_2S + 8Cu = CH_4 + 4Cu_2S$. Steam may be substituted for the sulphuretted hydrogen.

4. It is usually prepared by heating anhydrous sodic acetate with baryta, or, less advantageously, with soda-lime (cf. p. 34), ethylene, C_2H_4, and hydrogen (up to 8 per cent) being formed at the same time.

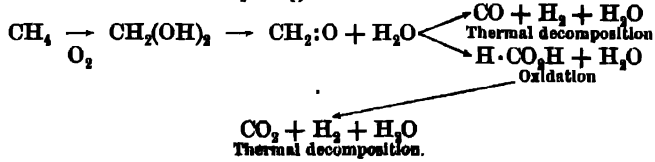
5. Pure methane is obtained from magnesium methyl iodide and water, $CH_3 \cdot Mg \cdot I + H \cdot OH = CH_4 + OH \cdot Mg \cdot I$; also (see B, 1) by the reduction of methyl iodide, CH_3I, *e.g.* in alcoholic solution by means of zinc in the presence of precipitated copper (the *Gladstone-Tribe* "Copper-zinc Couple");* also by the inverse substitution of chloroform, $CHCl_3$, or carbon tetrachloride, CCl_4.

Properties.—It is a gas with a density = 8 (H = 1), and is condensed under a pressure of 140 atmospheres at 0°. It boils at −164°, and solidifies at −186°. Absorption coefficient in cold water about 0·05, in cold alcohol 0·5. It burns with a

pale and only faintly luminous flame, yielding carbon dioxide and water, and when mixed with air or oxygen in certain proportions forms an explosive mixture. It is decomposed by the electric spark into its elements, and a similar decomposition occurs when the gas is led through a red-hot tube; but there are formed at the same time C_2H_6, C_2H_4, C_2H_2, and, in smaller quantity, C_6H_6, benzene, $C_{10}H_8$, naphthalene, and other products. The first three hydrocarbons just mentioned, ethane, &c., behave similarly.

Combustion of Hydrocarbons.—When methane and hydrocarbons generally are burnt or exploded with excess of air or oxygen, the final products are carbon dioxide and water vapour, and the reaction is generally represented, *e.g.*, by the equation $CH_4 + 2O_2 = CO_2 + 2H_2O$. This undoubtedly represents the final products which are formed, and also their relative amounts, but does not give an idea of the mechanism of combustion. Numerous investigators have conducted experiments on combustion, especially on combustion in the presence of limited amounts of oxygen. The conclusion was first drawn that with a defective supply of oxygen the hydrogen is oxidized in preference to the carbon. Somewhat later, *Kersten* (1861) suggested the preferential burning of the carbon, since when ethylene is exploded with its own volume of oxygen, carbon monoxide and hydrogen are the chief products. (Cf. *Smithells*, J. C. S. 1892, **61**, 220.)

The recent work of *Bone* and others on the slow combustion of methane, ethane, ethylene, and acetylene (J. C. S. 1902, 535; 1903, 1074; 1904, 693, 1637; Proc. 1905, 220; B. A. Report, 1910, 469), shows that by passing a mixture of methane and oxygen in a continuous stream through a tube filled with porous material (pot or magnesia), at a fixed temperature between 350° and 500°, appreciable amounts of formaldehyde are obtained. Gaseous products are also obtained, but these are probably due to secondary reactions, *e.g.* either the further oxidation of the aldehyde to carbon monoxide, carbon dioxide, and steam, or the thermal decomposition of the aldehyde into carbon monoxide and hydrogen. Thus:—



By the expression thermal decomposition is meant that at the temperature mentioned the aldehyde is unstable, and immediately decomposes into the simpler products, CO and H_2.

Ethane behaves similarly, and the reactions can be represented by the following scheme:—

$$CH_3{\cdot}CH_3 \xrightarrow[O_2]{} CH_3{\cdot}CH(OH)_2 \longrightarrow CH_3{\cdot}CH{:}O + H_2O \xrightarrow[O_2]{} OH{\cdot}CH_2{\cdot}CO_2H \downarrow CH_2{:}O + CO + H_2O.$$

Secondary reactions are the thermal decompositions of the formaldehyde into CO and H_2, and of the acetaldehyde into CH_4 and CO. In reality some 80 per cent of the ethane can be collected as formaldehyde. With ethylene the reactions are probably—

$$CH_2{:}CH_2 \xrightarrow[O_2]{} OH{\cdot}CH{:}CH{\cdot}OH \longrightarrow 2\,CH_2{:}O \xrightarrow[O]{} H{\cdot}CO_2H \xrightarrow[O]{} OH{\cdot}CO{\cdot}OH,$$

and the thermal decomposition products of the formaldehyde, formic acid, and carbonic acid, viz. H_2, CO, CO_2, H_2O.

It is thus obvious that at the temperatures mentioned (350–500°) combustion consists primarily in the addition of oxygen and the production of hydroxylic compounds, which then yield aldehydes. It is highly probable that reactions of a similar nature occur during explosive combination and detonation at high temperatures (B. A. Report, 1910, 492).

Ethane, C_2H_6, occurs in crude petroleum and constitutes the gas of the Delamater gas well in Pittsburg, and is there utilized for technical purposes.

Preparation.—By the electrolysis of acetic acid (*Kolbe*, 1848), and therefore formerly called "methyl" since it was supposed to be CH_3; subsequent molecular-weight determinations proved it to have the double formula C_2H_6. It is also obtained from ethyl iodide, alcohol, and zinc dust, or from zinc ethyl (*Frankland*), hence the name "ethyl hydride". "Ethyl hydride" and "methyl", which were formerly supposed by *Frankland* and *Kolbe* to be different substances, were proved to be identical by *Schorlemmer* in 1863 by their conversion into C_2H_5Cl, which may be prepared from both in exactly the same way.

It is a gas which can be condensed under a pressure of 46 atmospheres at 4°, and is somewhat more soluble than

methane in water and alcohol. It burns with a faintly-luminous flame.

Propane, C_3H_8, and the two butanes, C_4H_{10}, are also gaseous at the ordinary temperature, and are present to a certain extent in crude petroleum.

Theoretically propane can exist in only one form, represented by the constitutional formula $CH_3 \cdot CH_2 \cdot CH_3$, as this is the only manner in which three carbon and eight hydrogen atoms can be grouped up if we assume that the carbon atoms are tetravalent and the hydrogen atoms monovalent.

ISOMERISM, NOMENCLATURE, CONSTITUTION

To determine whether the next homologue, C_4H_{10}, can theoretically exist in more than one modification, we can start with propane, $\overset{\alpha}{C}H_3 \cdot \overset{\beta}{C}H_2 \cdot \overset{\alpha}{C}H_3$, and replace one of the eight hydrogen atoms by a methyl group. It is obvious that we can obtain two distinct compounds according to whether we replace one of the six terminal hydrogens (α) or one of the central hydrogens (β). The two compounds would have the respective formulæ

$$CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_3 \text{ and } \begin{matrix} CH_3 \\ CH_3 \end{matrix} \!\!> CH \cdot CH_3,$$

and are known as normal butane and iso-butane (or trimethyl methane).

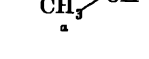
Two compounds having the formula C_4H_{10} are actually known, and their constitutional formulæ derived from their methods of formation agree with the two formulæ $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_3$ and $(CH_3)_2 : CH \cdot CH_3$, as the *n*-compound may be obtained by the action of zinc on ethyl iodide, $CH_3 \cdot CH_2I$, and the *iso*-compound by the reduction of tertiary butyl iodide, $(CH_3)_2 : CI \cdot CH_3$.

All the succeeding hydrocarbons can, according to theory, exist in various isomeric modifications. The number of modifications possible can be derived in exactly the same manner as already described for the butanes.

As an example, take the hydrocarbons C_5H_{12}, the pentanes. Starting with *n*-butane, $\overset{\alpha}{C}H_3 \cdot \overset{\beta}{C}H_2 \cdot \overset{\beta}{C}H_2 \cdot \overset{\alpha}{C}H_3$, and replacing one H atom by a CH_3 group, we can get either

(1) $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_3$ or (2) $CH_3 \cdot CH_2 \cdot CH \!\!< \begin{matrix} CH_3 \\ CH_3 \end{matrix}$

according as we replace an H atom in the α or β position. Starting from iso-butane,



we can similarly get

(3) $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!CH\cdot CH_2\cdot CH_3$ or (4) $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C\!<\!\begin{matrix}CH_3\\CH_3\end{matrix}$;

but formulæ (2) and (3) are identical, and the three isomerides possible are therefore $CH_3\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_3$, $(CH_3)_2{:}CH\cdot CH_2\cdot CH_3$ and $(CH_3)_2{:}C{:}(CH_3)_2$. Of hydrocarbons with six carbon atoms, five isomers are possible, and they are all known. Of the nine possible heptanes, C_7H_{16}, the existence of five has already been proved.

The number of theoretically possible isomers increases very rapidly with the number of carbon atoms, so that, according to *Cayley*, 802 isomeric hydrocarbons of the formula $C_{13}H_{28}$ are possible.

Of these isomers only one can be **normal**, *i.e.* can have a single chain of carbon atoms, in which each of the two terminal carbon atoms is combined with three atoms of hydrogen, and all the middle ones with two, according to the formula, $CH_3\cdot(CH_2)_n\cdot CH_3$.

A convenient *Nomenclature* for the more complicated paraffins is arrived at by making methane the starting-point for all of them, that carbon atom from which the branching chain emanates being considered as originally belonging to CH_4, in which the hydrogen atoms are supposed to be wholly or partially replaced by hydrocarbon radicals, thus:—

$CH_3\cdot CH_2\cdot CH\!<\!\begin{matrix}CH_3\\CH_3\end{matrix}$ = dimethyl-ethyl-methane.

The names of the well-known lower hydrocarbon radicals (alkyls) are also frequently used as a basis; for instance, the group $(CH_3)_2CH$ is termed isopropyl (see Isopropyl Alcohol), hence the compounds:

$\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!CH\cdot CH_2\cdot CH_3$: ethyl-isopropyl.

$\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!CH\cdot CH\!<\!\begin{matrix}CH_3\\CH_3\end{matrix}$: di-isopropyl.

The boiling-points of the normal hydrocarbons are always

higher than those of the isomers; indeed the boiling-point becomes lowered continuously the more the carbon atom chain is branched, *i.e.* the more methyl groups are gathered together in the molecule.

The *Constitution* of the higher paraffins can in most cases only be arrived at with certainty from their synthetical formation (*e.g.* normal butane and hexane), or from their chemical relation to oxygenated derivatives whose constitution is already known, especially to the ketones and acids. (See Ketones.)

If, for instance, by the action of PCl_5 upon acetone, for which the constitution $CH_3 \cdot CO \cdot CH_3$ is proved, the substance $CH_3 \cdot CCl_2 \cdot CH_3$ (acetone chloride) be formed, and this be then treated with zinc methyl, the resulting hydrocarbon, a pentane, will have the constitution $(CH_3)_4C$.

$$(CH_3)_2{:}CCl_2 + Zn(CH_3)_2 = ZnCl_2 + (CH_3)_2{:}C{:}(CH_3)_2.$$

As a second example, we have *n*-hexane, which can be obtained by the action of metals upon *n*-propyl iodide, as represented by the equation:

$$2\,CH_3 \cdot CH_2 \cdot CH_2I + Zn = ZnI_2 + CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_3.$$

The system of nomenclature suggested by the International Congress at Geneva is as follows:—The normal paraffins retain their present names. Thus hexane means the compound $CH_3 \cdot (CH_2)_4 \cdot CH_3$. In the case of those with branching chains the longest normal chain gives the name, the branches being regarded as substituents, and the position of substitution being indicated by the successive numbering of the atoms of the carbon chain (the carbon atom which is nearest to the point of ramification is numbered 1; should there be more than one branching—say, a longer and a shorter—then No. 1 begins with the end carbon atom which stands nearest to the shorter branching). Trimethyl-methane is therefore called 2-methyl-propane; dimethyl-ethyl-methane, 2-methyl-butane; and tetramethyl-methane, 2:2-dimethyl-propane.

The following paraffins have been obtained from crude petroleum: *n*- and *iso*-pentane, *n*-hexane and an isomer, and *n*-heptane, all these being present in the so-called "gasoline", which is obtained by the distillation of petroleum, and is used for carburetting coal-gas; further, normal Heptane, *n*-Octane, *n*-Nonane, and *n*-Decane, besides an isomer of each, and ir

* The petroleum ether and ligroin of commerce consist principally of the hydrocarbons C_5H_{12}, C_7H_{16}, and C_9H_{20}.

addition to these (as also from the distillation of cannel and Boghead coal), a large number of the higher hydrocarbons. In all probability these products are not chemical individuals, but mixtures of homologues and isomers standing very near to each other, as is shown by a comparison with the artificially-prepared normal hydrocarbons.

F. Krafft has prepared those normal hydrocarbons from $C_{11}H_{24}$ to $C_{35}H_{72}$ which are mentioned in the table on p. 30, from the acids C_{12}, C_{14}, C_{16}, and C_{18} of the acetic acid series (see these), for which the normal constitution, *i.e.* non-branching carbon chain, has been demonstrated; and also from the ketones, $C_nH_{2n}O$, which are obtained by subjecting the barium salts of these acids to dry distillation, either alone or together with acetate or heptoate of calcium, and which, as a consequence of their mode of formation, yield normal hydrocarbons. (See Ketones.) *Krafft* has further isolated the normal hydrocarbons $C_{17}H_{36}$ to $C_{23}H_{48}$, also $C_{24}H_{50}$, $C_{26}H_{54}$, and $C_{28}H_{58}$, by subjecting the paraffin obtained from lignite to fractional distillation *in vacuo*.

These are, from about $C_{16}H_{34}$ (m.-pt. 18°) on, solid at the ordinary temperature. When distilled under atmospheric pressure, or heated with $AlBr_3 + HI$, the higher hydrocarbons partially decompose into lower ones of the formulæ C_nH_{2n+2} and C_nH_{2n}; this process is known as "cracking". But they may be distilled in a vacuum, whereby their boiling-points are reduced by 100° or more. (See table.)

Petroleum, *Mineral Oils*.—These are probably produced by the decomposition of animal or vegetable organisms* (*Engler*, C. C. 1906, II, 1017), and are found between Pittsburg and Lake Erie in America; between Lake Erie and Lake Huron in Canada; in Hanover, Holstein, and Elsass in Germany; in Boryslaw in Galicia; in the Crimea; in the Caucasus; in Borneo, &c. The American oil consists mainly of paraffin hydrocarbons, whereas the Russian oil contains large quantities of hydrocarbons of the general formula C_nH_{2n}. These latter have been shown to be closed-chain compounds, they are known as *naphthenes*, and are isomeric with the olefines.

The American and Russian oils are worked up on a large scale for the preparation of commercial products. The crude petroleum is a thick, oily liquid of dark colour and sp. gr. 0·3 to 0·92. It is usually washed with alkalis and sulphuric acid,

* This view is supported by the fact that many paraffin oils have a slight optical activity.

and then subjected to fractional distillation. The fraction 50–60° is termed petroleum ether or petrol, the fraction 70–90° is termed benzoline or benzine, ligroin is the fraction 90–120°. Burning oil is the fraction 150–300°, and from the higher fractions are obtained lubricating oils, vaseline, and paraffin-wax.

Paraffin-Wax, obtained by *Reichenbach* in 1830 from wood tar, is got by the distillation of lignite or peat. It also is a mixture of many hydrocarbons, about 40 per cent of it consisting of the compounds $C_{22}H_{46}$, $C_{24}H_{50}$, $C_{26}H_{54}$, and $C_{28}H_{58}$.

Liquid Paraffin (*Reichenbach's* "Eupion") and the butter-like **Vaseline** are high-boiling distillation products of lignite or petroleum, and the same applies to many lubricating oils.

Ozokerite, green, brown, and red, and of the consistency of wax, melting-point 60°–80°, is a natural paraffin found at Boryslaw in Galicia, at Tscheleken near Baku (also called Neftgil), on the Caspian Sea, and forms the ceresine of commerce when bleached.

Asphalt, or **Earth Pitch**, found in India, Trinidad, Java, and Cuba, is a transformation product of the higher-boiling mineral-oils, produced by the action of the oxygen of the air just as paraffin absorbs oxygen and becomes brown upon prolonged heating in the air. It is used for cements and salves, and in asphalting, photo-lithography, &c.

B. Olefines or Hydrocarbons of the Ethylene Series (Alkylenes): C_nH_{2n}

There are two series of hydrocarbons of the general formula C_nH_{2n}, the members of which differ from the corresponding paraffins by containing two atoms of hydrogen less in the molecule. The one series is that of the **Olefines**, of which ethylene, C_2H_4, is the first member; the other is that which contains **Trimethylene, Tetramethylene, Hexamethylene**, &c. (Cf. Polymethylenes.)

The properties exhibited by these two series are so different that different constitutions must be accorded to them. The olefines form additive compounds with exceptional facility, being thus converted into the paraffins or their derivatives; from this the conclusion is drawn that, like the latter, they contain an open carbon chain.

The names given to the hydrocarbons are similar to those for the paraffins, *except* that the termination *ane* is replaced by *ene*, or often by *ylene*.

SUMMARY

		Melting-point	Boiling-point.
Ethylene	C_2H_4	−169°	−103°
Propylene	C_3H_6		−48
Butylene (3)	C_4H_8 α		−5°
	C_4H_8 β		+1°
	C_4H_8 γ		−6°
Amylene (5)	C_5H_{10}*		+39°
Hexylene	C_6H_{12}		68°
Heptylene	C_7H_{14}		95°
Octylene	C_8H_{16}		124°
Nonylene	C_9H_{18}		153°
Decylene	$C_{10}H_{20}$		172°
Undecylene	$C_{11}H_{22}$		195°
Dodecylene	$C_{12}H_{24}$	−31°	{96°†
Tridecylene	$C_{13}H_{26}$		233°
Tetradecylene	$C_{14}H_{28}$	−12°	{127°
Pentadecylene	$C_{15}H_{30}$		247°
Hexadecylene (Cetene)	$C_{16}H_{32}$	+4°	274° / {155°
Octadecylene	$C_{18}H_{36}$	18°	{179°
Eicosylene	$C_{20}H_{40}$		
Cerotene	$C_{27}H_{54}$	58°	
Melene	$C_{30}H_{60}$	62°	

The general formula C_nH_{2n} for this series indicates that each member differs from the corresponding member of the paraffins by two hydrogen atoms.

In their physical properties they resemble the methane homologues very closely. C_2H_4, C_3H_6, and C_4H_8 are gases, C_5H_{10} a volatile liquid, the higher members liquids with rising boiling-point and diminishing mobility, while the highest are solid and similar to paraffins. The boiling-points of members of both series containing the same number of carbon atoms, and whose constitutions are comparable, lie very close together, but the melting-points of the olefines are somewhat the lower of the two; *e.g.* $C_{16}H_{34}$, m.-pt. 21°, b.-pt. {157°, and $C_{16}H_{32}$, m.-pt. 4°, b.-pt. {155°.

* The melting- and boiling-points given from C_5H_{10} on, are those of the normal hydrocarbons.

† { signifies boiling-point under 15 mm. pressure.

Most of the olefines are readily soluble in alcohol and ether but insoluble in water, only the lower members dissolving slightly in the latter. The specific gravities of the normal olefines, determined at the melting-points, rise from about 0·63 upwards, and approach with increasing carbon to a definite limit, viz. about 0·79.

In their chemical relations, the olefines differ materially from the paraffins. Most of their special chemical characteristics are undoubtedly due to the presence of a double or olefine bond in the molecule, *e.g.* ethylene, $CH_2{:}CH_2$. (Cf. Constitution of Olefines.)

(*a*) They combine readily with nascent hydrogen, with chlorine, bromine, iodine, and their hydracids, fuming sulphuric acid, hypochlorous acid, nitrous acid, and, generally speaking, with two monad atoms or monovalent groups, whereby members of the methane series or their derivatives ensue; hence their name of "Unsaturated Hydrocarbons".

$$\begin{aligned} C_2H_4 + H_2 &= C_2H_6. \\ C_2H_4 + Cl_2 &= C_2H_4Cl_2. \\ C_2H_4 + HI &= C_2H_5I. \\ C_2H_4 + H_2SO_4 &= C_2H_5(SO_4H). \end{aligned}$$

In the formation of these additive compounds the double bond present in the molecule becomes converted into a single bond, and the two monovalent groups (*e.g.* Br, H, OH, &c.) add themselves on to the two carbon atoms between which the double bond previously functionated, *e.g.* $CH_2{:}CH_2 + Br_2$ gives $CH_2Br{\cdot}CH_2Br$. Thus by the addition of bromine to an olefine the two bromine atoms must always be attached to two adjacent carbon atoms. (Cf. Polymethylene Hydrocarbons.)

Combination with hydrogen is sometimes effected, *e.g.* in the case of ethylene, by the aid of platinum black at the ordinary temperature, by means of finely-divided nickel at a higher temperature, or by heating the olefines or their dichlor-, &c., additive products with fuming hydriodic acid and phosphorus. (Cf. Modes of Formation of the Saturated Hydrocarbons.)

Ethylene chloride, $C_2H_4Cl_2$, obtained by the combination of ethylene with chlorine, was formerly called the oil of the Dutch chemists, hence the name of "Olefines" for the whole class of hydrocarbons C_nH_{2n} (*Guthrie*).

Chlorine adds itself on more easily than iodine, but hydrochloric acid less readily than hydriodic, bromine and hydro-

bromic acid standing midway. When a halogen hydride is used, the halogen attaches itself to that carbon atom to which the smaller number of hydrogen atoms are already united,* *e.g.*

$$CH_3 \cdot CH : CH_2 + HI = CH_3 \cdot CHI \cdot CH_3.$$

Particular olefines, *e.g.* isobutylene, also combine slowly with water to alcohols under the influence of dilute acids.

Ethylene combines with fuming sulphuric acid at the ordinary temperature, and with the concentrated acid at 160°–170°.

Amylene forms with nitrogen tetroxide, N_2O_4, amylene nitrosate (A. **248**, 161); nitrogen trioxide and nitrosyl chloride also unite directly with the olefines.

(*b*) They readily polymerize, especially in presence of sulphuric acid or zinc chloride. Thus amylene, C_5H_{10}, in presence of sulphuric acid yields the polymers $C_{10}H_{20}$, $C_{15}H_{30}$, and $C_{20}H_{40}$; and tertiary butyl alcohol, warmed with acid of a definite strength, di-isobutylene.

(*c*) Unlike the paraffins, they are readily oxidized by $KMnO_4$ or CrO_3, but not by cold HNO_3.

In this reaction, two hydroxyl groups are added to the molecule of the olefine if a dilute (1 per cent) solution of permanganate is used, and a dihydric alcohol (a glycol) is formed.

$$CH_2 : CH_2 \longrightarrow OH \cdot CH_2 \cdot CH_2 \cdot OH.$$

But if stronger solutions are used, or if chromic anhydride is employed, the molecule of the olefine is ruptured at the point where the double bond exists and a mixture of simpler acids or ketones is obtained. The readiness with which unsaturated compounds discharge the colour of acidified permanganate is frequently made use of as a qualitative test for such compounds.

The "official name" (p. 40) of the olefines is formed by replacing the last syllable "ane" of the paraffins by "ene". The position of the double bond is denoted by the number of the carbon atom from which it proceeds. In a branching chain the numbering is the same as in the case of the corresponding saturated hydrocarbons; in a normal chain it begins at the end carbon atom which is nearest to the double bond.

Example: $\overset{1}{CH_3} \cdot \overset{2}{CH} : \overset{3}{CH} \cdot \overset{4}{CH} \langle \begin{matrix} \overset{5}{CH_3} \\ CH_3 \end{matrix}$ is 4-methyl-2-pentene.

Modes of formation.—(*a*) Together with paraffins by the destructive distillation of many substances, such as wood,

* Cf. *Michael*, J. pr. 1888, [ii] 37, 524; 1903, 68, 487; B. 1906, 39, 2138.

lignite, and coal, and also by the distillation of the higher paraffins (process of "cracking", p. 41); illuminating gas consequently contains the olefines C_2H_4, C_3H_6, C_4H_8, &c.

(*b*) By abstraction of water from the alcohols, $C_nH_{2n+1}OH$, by heating them with sulphuric acid, phosphorus pentoxide, zinc chloride, anhydrous formic acid, syrupy phosphoric acid, &c. When sulphuric acid is used, an alkyl-sulphuric acid, *e.g.* ethyl hydrogen sulphate, $C_2H_5O \cdot SO_2 \cdot OH$, is first formed, and this decomposes upon further warming into alkylene and sulphuric acid. This method is especially applicable in the case of the lower homologues. Many alcohols yield olefines when heated alone, or with finely divided solids (Chap. XLIX).

The palmitic esters of the higher alcohols, when distilled under somewhat diminished pressure, yield palmitic acid and an olefine.

(*c*) By heating the halogen compounds $C_nH_{2n+1}X$ with alcoholic potash, or by passing their vapour over red-hot lime or hot oxide of lead, &c.; sometimes by simple distillation:

$$C_5H_{11}I + KOH = C_5H_{10} + KI + H_2O.$$

The iodine and bromine compounds are particularly suited for this. The reaction may be regarded as the elimination of a molecule of halogen hydracid from the molecule of the compound, the halogen coming from the one carbon atom and the hydrogen from an adjacent. (Cf. also *Nef*, A. 1901, **318**, 3.)

(*d*) Sometimes from the haloid compounds $C_nH_{2n}X_2$ by abstraction of the halogen,* *e.g.* ethylene from ethylene bromide by treatment with zinc, magnesium, or zinc dust and alcohol:

$$C_2H_4Br_2 + Zn = C_2H_4 + ZnBr_2.$$

(*e*) By the electrolysis of potassic salts of dibasic acids of the succinic acid series; thus succinic acid itself yields ethylene:

$$C_2H_4(COOH)_2 = C_2H_4 + 2\,CO_2 + H_2.$$

The complex anion $O \cdot CO \cdot \overline{CH_2} \cdot \overline{CH_2} \cdot CO \cdot O$, when discharged decomposes into ethylene and carbon dioxide.

Constitution of the Olefines.—For ethylene the following formulæ may be given:—

(I) $\begin{matrix} CH_3 \\ | \\ CH= \end{matrix}$ (II) $\begin{matrix} CH_2- \\ | \\ CH_2- \end{matrix}$ (III) $\begin{matrix} CH_2 \\ \| \\ CH_2 \end{matrix}$

* Only when the halogen atoms are attached to adjacent carbon atoms.

In the formulæ I and II, two free carbon bonds or valencies are assumed in the ethylene molecule. Formula III follows from the assumption that the bonds which are not used up in attaching the hydrogen atoms to carbon are used in uniting the carbon atoms themselves.

Now the ethylene bromide which is formed by the addition of bromine to ethylene has, for reasons which will be given under that compound, the constitution $CH_2Br \cdot CH_2Br$, and likewise the compound obtained by the addition of ClOH (*i.e.* Cl and OH), viz. glycol chlorhydrin, the constitution $CH_2Cl \cdot CH_2OH$; consequently formula I, according to which these substances would have the constitutions $CH_3 \cdot CHBr_2$ and $CH_3 \cdot CHCl(OH)$, is excluded.

Formula III is more probable than formula II:—

(*a*) Since methylene, CH_2:, appears to be incapable of existence; all attempts to isolate it have yielded ethylene, C_2H_4 (see below), so that free valencies attached to the carbon atom probably cannot exist.

(*b*) Because the free affinities to be assumed according to II are never found singly (which should in that case be possible), but invariably in pairs only, and indeed only on neighbouring carbon atoms This is proved from the constitution of the compounds obtained by the addition, for instance, of Br_2. Unsaturated compounds containing only one carbon atom, and unsaturated hydrocarbons containing an *odd* number of hydrogen atoms, are unknown.

It is therefore to be concluded that in ethylene and its homologues a double carbon bond, corresponding with formula III, exists.

By this term "double bond" is not, however, to be understood a closer or more intimate combination. The olefines, on the contrary, are more readily oxidized than the paraffins, being thereby attacked at the point of the double bond. Other properties, especially physical ones, also give indications that a double bond between two carbon atoms is looser, and therefore more easily broken, than a single one. (Cf. *Bruhl*, A. **211**, 162.)

1. **Methylene** (*Methene*), CH_2, does not exist. Numerous attempts to prepare it, *e.g.* by the withdrawal of hydrogen and chlorine from methyl chloride, or of iodine from methylene iodide, have invariably yielded ethylene, thus:—

$$2\,CH_3Cl - 2\,HCl = C_2H_4.$$

Here the two resulting CH_2-residues have united together, in the same way as the two methyl-groups coalesced to ethane (p. 34).

2. **Ethylene** (*Ethene*), olefiant gas, $CH_2:CH_2$.

This compound was discovered in 1795 by four Dutch chemists. Its formula was established by *Dalton*.

Illuminating gas generally contains 4 to 5 per cent of ethylene. For formation from elements see *Pring* and *Fairlie*, J. C. S. 1911, **99**, 1806. It is usually prepared by heating alcohol with excess of concentrated sulphuric acid, with addition of sand, a mixture of equal portions of the two liquids being subsequently dropped into the evolution flask; sulphur dioxide, &c., are produced at the same time by secondary reactions. A better method is to heat alcohol with syrupy phosphoric acid at 200° (*Newth*). Small quantities can be conveniently prepared from ethylene bromide and zinc or magnesium. It is further formed by heating ethylidene chloride, $CH_3 \cdot CHCl_2$, with sodium.

It may be liquefied at 0° under a pressure of 44 atmos., is very slightly soluble in water and alcohol; burns with a luminous flame, and forms an explosive mixture with oxygen. When rapidly mixed with two volumes of chlorine and set fire to, it burns with a dark-red flame, with formation of hydrochloric acid and deposition of much soot. It is converted at a red heat into methane, CH_4, ethane, C_2H_6, acetylene, C_2H_2, &c., with separation of carbon. (See p. 36.) It combines with hydrogen in presence of spongy platinum to ethane, C_2H_6.

3. **Propylene** (*Propene*), C_3H_6, $CH_2:CH \cdot CH_3$. Only one olefine, C_3H_6, is theoretically possible and only one is known, viz. methylethylene. It can be prepared from isopropyl iodide and caustic potash, or by heating glycerol with zinc dust. It is isomeric with trimethylene (see Polymethylenes).

4. **Butylene**, C_4H_8. Three butylenes are possible according to theory, and three are known. All of them are gaseous, their boiling-points lying between $-6°$ and $+3°$. Butylene and pseudo-butylene are derived from normal butane, and isobutylene from isobutane, since they severally combine with H_2 to form these hydrocarbons. The first, α-butylene, is prepared from normal; the second, β-butylene, from secondary; and the third, γ-butylene, from tertiary butyl iodide, by the action of caustic potash upon these; the last can also be obtained from isobutyl alcohol and sulphuric acid. The isomerism of the two

butylenes derived from normal butane is explained by the assumption of a double bond at different points, thus:—

$CH_2:CH\cdot CH_2\cdot CH_3$ (α-butylene (1-*butene*)) $CH_3\cdot CH:CH\cdot CH_3$ (β-butylene (2-*butene*))

Isobutylene has the formula $(CH_3)_2C:CH_2$ (*methylpropene*). The behaviour of these isomers upon oxidation is in accordance with the above formulæ, the oxidation always taking place at the point of the double bond.

The butylenes are isomeric with tetra-methylene (*cyclobutane*, see Polymethylenes).

5. **Amylene**, C_5H_{10}. A large number of isomeric amylenes are known, among them being **Amylene** (b.-pt. 35°), which is obtained, together with an isomer, Iso-amylene, by heating ordinary amyl alcohol with chloride of zinc. For it the constitutional formula $(CH_3)_2C:CH\cdot CH_3$ (=trimethylethylene) is assumed. This is known in the pure form under the name of "pental".

The higher Olefines of normal constitution, with 12, 14, 16, and 18 atoms of carbon, have been prepared by *Krafft* according to method *b*.

Cerotene and **Melene** (m.-pt. 62°) are obtained by the distillation of Chinese wax and bees'-wax respectively. They are like paraffin in appearance, and are only sparingly soluble in alcohol.

C. Hydrocarbons, C_nH_{2n-2}: Acetylene Series

The hydrocarbons of this series again differ from those of the preceding by containing two atoms of hydrogen less. In physical properties they closely resemble both the latter and those of the methane series; thus the lowest members up to C_4H_6 are gaseous, the middle ones liquid, and the highest solid, and in their melting- and boiling-points they do not differ to any extent from those of the other series with an equal number of carbon atoms. The specific gravities of the normal hydrocarbons C_{12}, C_{14}, C_{16}, and C_{18}, at the melting-point, gradually approach with increasing carbon to a definite limit (0·80), and are somewhat higher than those of the corresponding members of the ethylene series throughout.

Constitution.—Upon grounds similar to those which have already been explained under ethylene, the constitutional formula for acetylene, C_2H_2, is assumed to be $CH:CH$, according to which the carbon atoms are joined together by a triple bond.

For a compound C_3H_4, the two following constitutional formulæ are possible:—

$$CH{:}C\cdot CH_3 \text{ (allylene)} \quad \text{and} \quad CH_2{:}C{:}CH_2 \text{ (allene).}$$

As a matter of fact, two hydrocarbons C_3H_4 do exist, only one of which, allylene, yields metallic compounds. It is therefore to be considered the true homologue of acetylene, containing a triple bond, according to the first of the two above formulæ, while to allene the second formula, with the two double bonds, is to be ascribed. The constitution of the tetrabromopropanes, which are formed from these by the addition of bromine, agrees with this conception.

In their chemical relations the acetylenes stand nearer to the olefines than to the paraffins, in so far that they are unsaturated and therefore capable of forming additive products.

1. A molecule of an acetylene can combine either (*a*) with two atoms of hydrogen or halogen, or with one molecule of halogen hydride, to olefines or their substitution products, thus:—

$$\begin{aligned} CH{:}CH + 2\,H &= CH_2{:}CH_2 \\ CH{:}CH + HBr &= CH_2{:}CHBr \text{ (vinyl bromide)} \\ CH{:}CH + Br_2 &= CHBr{:}CHBr, \end{aligned}$$

or (*b*) with four atoms of hydrogen or halogen, or two molecules of halogen hydride, to paraffins or paraffin substitution products, thus.—

$$\begin{aligned} CH_3\cdot C{:}CH + 4\,H &= CH_3\cdot CH_2\cdot CH_3 \\ &\quad \text{(in presence of platinum black)} \\ CH{:}CH + 2\,Br_2 &= CHBr_2\cdot CHBr_2 \\ CH_3\cdot C{:}CH + 2\,HI &= CH_3\cdot CI_2\cdot CH_3. \end{aligned}$$

Like many of the olefines, various members of this series combine with water under the influence of dilute acids, thus allylene, C_3H_4, gives acetone, C_3H_6O; and acetylene, C_2H_2, gives crotonic aldehyde, with intermediate formation of acetic aldehyde. The combination with water may be accomplished (*a*) by the action of sulphuric acid when, as in the case of the olefines, alkyl hydrogen sulphates are formed as intermediate products; (*b*) by means of mercuric chloride solution; or (*c*) by directly heating the hydrocarbon with water at 300° in sealed tubes. $HgCl_2$ and other mercury salts also induce such hydration:

$$\begin{aligned} CH{:}CH + H_2O &= CH_3\cdot CHO \\ CH_3\cdot C{:}CH + OH_2 &= CH_3\cdot CO\cdot CH_3. \end{aligned}$$

2. Many of the acetylene hydrocarbons are readily polymerized; thus, acetylene is transformed into benzene when led through a red-hot glass tube. This is an important synthesis of benzene:

$$3\,C_2H_2 = C_6H_6.$$

At the same time the compounds C_8H_8, $C_{10}H_8$, &c., are formed. Similarly allylene, C_3H_4, gives mesitylene, C_9H_{12}, in contact with sulphuric acid and a little water. (See Benzene Derivatives.)

3. Acetylene and some of its homologues react even at the ordinary temperature, in a manner which is peculiar to them, with an ammoniacal solution of cuprous or argentic oxide, to form reddish-brown or yellow-white precipitates, *e g.* CCu:CCu; CAg:CAg; $CH_3 \cdot C{:}CAg$, &c, which are explosive, and which are decomposed by acids, such as HCl, with regeneration of the hydrocarbon.

The hydrogen of acetylene can be replaced by potassium or sodium; thus, when the hydrocarbon is heated with sodium, the compounds C_2HNa and C_2Na_2 are obtained. These are decomposed by water or acids with evolution of acetylene.

All the hydrocarbons C_nH_{2n-2} do not, however, give such metallic compounds, but only the true homologues of acetylene containing the grouping $\cdot C{:}CH$.

Hydrocarbons such as allene, $CH_2{:}C{:}CH_2$, which do not contain a triple bond, and even acetylene compounds such as $CH_3 \cdot C{:}C \cdot CH_3$, where no hydrogen atoms are attached to the C atoms between which the triple bond is supposed to exist, do not yield these metallic derivatives.

In the case of the higher homologues, isomerism may be due either to the difference in position of the triple carbon bond in the molecule, or to the presence and different positions of the two double bonds. The constitution of a compound is fixed by the formation or otherwise of metallic derivatives, and by its behaviour upon oxidation. (See Oxidation of the Butylenes, p. 49.)

The official name of the acetylene homologues proper, with a triple carbon-linking, ends in "ine"; that of the isomeric hydrocarbons, with two double bonds, in "diene".

Formation.—1. They are obtained, together with the hydrocarbons already described, by the distillation of wood, lignite, coal, &c.; thus illuminating gas contains acetylene, allylene, and crotonylene.

2. By treating the haloid, preferably the bromine, compounds $C_nH_{2n}X_2$ and $C_nH_{2n-1}X$ with alcoholic potash or sodium ethoxide (C_2H_5ONa):



$$\mathrm{H{-}C{\cdot}C{-}H - 2\,HBr = H{\cdot}C{\equiv}C{\cdot}H.}$$

With alcoholic potash, even when excess is used, the reaction tends to stop at the first stage, and a brominated olefine is formed, *e.g.* vinyl bromide (p. 65) from ethylene dibromide; with sodic ethoxide, the elimination of hydric bromide proceeds more readily.

Further, from the unsaturated alcohols, $C_nH_{2n-1}\cdot OH$, by the separation of the elements of water from them.

3. By the electrolysis of potassium salts of the acids of the fumaric acid series (*Kekulé*).

4. Certain acetylene hydrocarbons, $R\cdot C{\equiv}C\cdot CH_3$, when heated with sodium, pass into the sodium compounds of their isomers, $R\cdot CH_2\cdot C{\equiv}CH$; on the other hand, when the latter are warmed with alcoholic potash, the opposite reaction takes place (*Faworsky*, B. **20**, Ref. 781; **25**, Ref. 81; **25**, 2244).

Acetylene (*Ethine*), C_2H_2, was first obtained impure by *E. Davy* from calcium carbide in 1839, and pure by *Berthelot* in 1849. Illuminating gas contains 0·06 per cent. It is synthesised from its elements, when an electric arc is caused to pass between two carbon poles in an atmosphere of hydrogen (*Berthelot*), but other hydrocarbons are formed at the same time (*Bone* and *Jerdan*, J. C. S. 1901, 1042; cf. also *Hutton* and *Pring*, 1906, 1591). It may be obtained from ethylene bromide and sodium ethoxide solution; also by the incomplete combustion of many carbon compounds, for instance, when the gas in a *Bunsen* lamp burns at the base; and from ethane, ethylene, and methane at a red heat, or by the action of the induction spark. (See pp. 36 and 48.) The simplest method of preparation is by the action of water on calcium carbide, the water being allowed to drop gradually on to the carbide:

$$CaC_2 + H_2O = CaO + C_2H_2.$$

It becomes liquid at 1° under a pressure of 48 atmospheres, burns with a luminous and very sooty flame, and has a peculiar disagreeable smell. Its flame has a high illuminating power when burnt in specially-constructed burners, and is now largely made use of as an illuminating agent. It dissolves in its own

volume of water, and in six times its volume of alcohol; is poisonous, combining with the hæmoglobin of the blood. It is decomposed into its elements with detonation by explosive fulminate of silver, and also by the electric spark. It combines with hydrogen to ethane, when heated with the latter in presence of platinum black, or to ethylene, upon treating its copper compound with zinc and ammonia. A mixture of acetylene and oxygen explodes violently when a light is applied to it. Chromic acid oxidizes acetylene to acetic acid, and permanganate of potash to oxalic acid. It combines with nitrogen under the influence of the induction spark to hydrocyanic acid (see this), and detonates upon being mixed with chlorine, but additive products, *e.g.* $C_2H_2Cl_2$, can, however, be prepared. As little as $\frac{1}{200}$ milligramme of it can be detected by the formation of the dark-red copper compound C_2Cu_2. This latter explodes when struck, or when heated to a little over 100°.

Allylene (*Propine*), C_3H_4, or $CH_3 \cdot C{:}CH$, can be prepared from propylene bromide, $CH_3 \cdot CHBr \cdot CH_2Br$. It resembles acetylene.

Allene (*Propadiene*), C_3H_4, or $CH_2{:}C{:}CH_2$, is obtained by the electrolysis of itaconic acid. It is gaseous, and does not yield metallic compounds.

Diallyl (*Hexa-1:5-diene*), $CH_2{:}CH \cdot CH_2 \cdot CH_2 \cdot CH{:}CH_2$, is obtained from allyl iodide, $CH_2{:}CH \cdot CH_2I$, and sodium.

Isomeric with these hydrocarbons are certain hydro-derivatives of aromatic hydrocarbons, *e.g.* tetrahydrobenzene, C_8H_{14}; decahydronaphthalene, $C_{10}H_{18}$. (See Aromatic Compounds.)

D. Hydrocarbons C_nH_{2n-6}

Di-acetylene (*Butadiine*), C_4H_2, or $CH{:}C \cdot C{:}CH$. This is prepared by heating the ammonic salt of diacetylene-dicarboxylic acid (see this) with ammoniacal copper solution, whereby it is transformed into the cuprous compound of diacetylene, and then warming this with potassium cyanide. It is a gas of a peculiar odour, which yields a violet-red copper compound and a yellow silver one, the latter exploding upon being rubbed, even when moist. (*Baeyer*, B. **18**, 2269.)

Di-propargyl (1:5-*Hexadiine*), C_6H_6, or $CH{:}C \cdot CH_2 \cdot CH_2 \cdot C{:}CH$, is obtained by the conversion of diallyl into its tetra-bromide, and the subsequent elimination of four molecules of hydric bromide from each molecule of the tetra-bromide; b. pt.

85°. It gives copper and silver compounds, and takes up eight atoms of bromine, &c. It possesses an especial interest, as it is isomeric with benzene. Another isomeride is 2:4-*Hexadiine*, $CH_3 \cdot C \vdots C \cdot C \vdots C \cdot CH_3$. (B. **20**, R. 564.)

II. HALOID SUBSTITUTION PRODUCTS OF THE HYDROCARBONS

A. Halogen Derivatives of the Paraffins

These are to be regarded as paraffin hydrocarbons in which one or more hydrogen atoms have become replaced by one or more halogen atoms.

General Properties.—Only a few of these compounds, *e.g.* CH_3Cl, C_2H_5Cl, and CH_3Br, are gaseous at the ordinary temperature, most of them being liquid, and those with a very large number of carbon atoms in the molecule solid, *e.g.* cetyl iodide, $C_{16}H_{33}I$. The introduction of a halogen atom in any hydrocarbon in place of an atom of hydrogen always tends to raise the boiling-point; the introduction of iodine has the most marked effect, and chlorine the least (cf. Table, p. 56). Such, also, as contain a large number of halogen atoms, *e.g.* CI_4, C_2Cl_6, are solid. Under comparable conditions, the boiling-points of the iodides lie, for each atom of halogen, about 50° (40°–60°), and those of the bromides about 22° (20°–24°), above those of the chlorides.

The lowest members of the series have, in the liquid form, at first a higher specific gravity than water, *e.g.* CH_3I, sp. gr. 2·2, C_2H_5Br, sp. gr. 1·47. With an increasing number of carbon atoms, however, they become more like the paraffins, the influence of the halogen diminishes, and they are lighter than water.

The halogen substitution products of the hydrocarbons are very sparingly soluble in water, but readily in, and therefore miscible to any extent with, alcohol or ether; they also dissolve in glacial acetic acid. They often possess a sweet ethereal odour, but this becomes less marked with diminishing volatility. Most of them are combustible; thus methyl and ethyl chloride burn with a green-bordered flame, while ethyl iodide and chloroform can only be set fire to with difficulty. Many

members of the series containing one or two atoms of carbon produce insensibility and unconsciousness when inhaled, *e.g.* $CHCl_3$, $C_2H_3Cl_3$, C_2H_5Br, and C_2HCl_5. The liquid iodine derivatives are readily decomposed, and on exposure to light turn deep-brown in colour, owing to the liberation of free iodine, *e.g.* ethyl iodide liberates iodine and gives C_4H_{10}.

In all these compounds the halogen is more firmly bound than in inorganic salts, so that, for instance, when silver nitrate is added to an aqueous solution of a chlorine compound, *e.g.* chloroform, it causes no precipitation of AgCl. Nevertheless, the halogen is in most cases readily exchangeable for other elements or groups, a circumstance of the utmost importance for many organic reactions. This is especially true for the iodine and bromine compounds, which react more readily than the chlorides, and, on account of their lesser volatility, are easier to work with; thus C_2H_5Br reacts with $AgNO_3$ at the boiling temperature, and C_2H_5I in the cold even.

In all these halogen compounds the halogen can be again replaced by hydrogen by inverse substitution, *e.g.* by sodium amalgam, by zinc dust and hydrochloric or acetic acid, or by heating with hydriodic acid. (See p. 33.)

Of fluorine compounds, only a few are known as yet; CH_3F and C_2H_5F are gases.

Nomenclature.—The best system of nomenclature is to regard them as derived from the corresponding hydrocarbons, *e.g.* $CHCl_3$ trichloro-methane, CH_3I mono-iodo-methane, and if necessary to indicate the carbon atoms to which the halogen radicals are attached, *e.g.* $CH_2Cl \cdot CH_2Cl$ 1:2-dichloro-ethane, $CH_3 \cdot CHBr_2$ 1:1-dibromo-ethane, $CH_2Br \cdot CH_2 \cdot CH_2Br$ 1:3-dibromo-propane, $CH_3 \cdot CH(CH_3) \cdot CHBr \cdot CH_2 \cdot CH_2Br$ 2-methyl-3:5-dibromo-pentane.

The following are some of the most important methods employed for the preparation of these halogen derivatives:—

1. By **Substitution.**—*Chlorination and Bromination.* Chlorine and bromine act for the most part as direct substituents (see p. 31). With the gaseous hydrocarbons their action even in the cold is an extremely energetic one (*e.g.* chlorine mixed with methane easily causes an explosion, so that dilution with CO_2 is necessary); the higher members require to be heated.

HALOGEN SUBSTITUTION PRODUCTS

Saturated Compounds

(*a*) *Mono-substituted Derivatives.*

	Chloride		Bromide.		Iodide	
	B.-p	Sp gr	B.-p	Sp gr	B.-p	Sp. gr.
Methyl.....	−23·7°	0·952	+4·5°	1·732	+45°	2·293
Ethyl.....	+12·2°	0 918	38·4°	1·468	72·3°	1·944
n-Propyl.. ...	46 5°	0·912	71°	1·383	102 5°	1·786
iso-Propyl....	36 5°	0·882	60°	1·340	89°	1·744
Prim. *n*-Butyl	78°	0·907	101°	1·305	130°	1 643

(*b*) *Di-substituted Derivatives.*

	Chloride		Bromide.		Iodide	
	B.-p	Sp gr.	B.-p	Sp gr.	B.-p.	Sp. gr
Methylene ...	42°	1·337	97°	2·498	180°	3·292
Ethylene.....	84°	1·260	131°	2 189	solid; m.-p. 81–8	
Ethylidene...	58°	1·189	110°	2·080	178°	2·84

(*c*) *Tri-substituted Derivatives.*

	Chloroform	Bromoform	Iodoform.
CHX_3.....	b.-p. 61°	b.-p. 151°	melts at 11 sublimes

(*d*) *Tetra-substituted Derivative.*

	Chloride	Bromide
CX_4... ..... . Carbon tetra-	76°	solid; m.-p 92°; b.-p. 189°

Unsaturated Compounds

	Chloride.	Bromide	Iodide.
Vinyl, $CH_2{:}CHX$	−18°	+23°	56°
Allyl, $CH_2{:}CH\cdot CH_2X$.....	46°	70°	101°

Trichlorethylene boils at 88°, tetrachlorethylene at 121 Monochlor- and monobrom-acetylene are gaseous.

Compounds of the type CCl_3Br, CCl_2Br_2, CCl_2I_2, &c., a also known.

The first halogen atom enters most easily into the cor pound, the substitution becoming more difficult as the numb of those atoms present increases. In the case of the high hydrocarbons there usually result two isomeric mono-subst tution products. The action of the halogens is further facil tated by sunlight, and by the presence of iodine, this latt acting as a carrier of chlorine by the alternate formation ICl_3 and ICl, thus: $ICl_3 = ICl + 2\,Cl$. Antimony pent

chloride and ferric chloride act in the same way (and also for brominating and iodating,—B. **18**, 2017; A. **231**, 195); iron wire is especially useful in brominating (B. **24**, 4249). When complete chlorination is required, the substance in question is repeatedly saturated with chlorine in presence of iodine, and heated in a tube to a high temperature.

From methane are formed the whole series of substitution products up to CCl_4.

Ethane first yields ethyl chloride, C_2H_5Cl, then ethylidene chloride, $C_2H_4Cl_2$, and so on up to C_2Cl_6.

From propane is first produced normal propyl chloride, C_3H_7Cl, and finally C_3Cl_8. The latter decomposes, upon vigorous chlorination, first into C_2Cl_6 and CCl_4, and the perchloro-ethane subsequently into two molecules CCl_4. On chlorinating butane and the higher hydrocarbons strongly, an analogous splitting up of the molecule is effected. Strong chlorination or bromination readily gives rise at the same time to hexachloro- or hexabromo-benzene.

Iodine seldom acts as a direct substituent, since by this reaction hydrogen iodide would be formed, which would then reduce the iodine compound back to the hydrocarbon. (See p. 33.) To induce the action, therefore, the HI formed must be removed by HIO_3 or HgO. The iodine substitution products of the hydrocarbons are usually prepared indirectly (according to 2 or 3).

2. From **Unsaturated Hydrocarbons**. These combine readily with halogen or halogen hydride. (See p. 44.)

Ethylene gives with hydrochloric, hydrobromic, and hydriodic acids, ethyl chloride, &c., *i.e.* mono-substitution products of ethane; with chlorine, &c., it gives di-substitution products.

The compound $C_2H_4Cl_2$, obtained by the action of chlorine, is called ethylene chloride, has the constitutional formula $CH_2Cl \cdot CH_2Cl$, and is isomeric with the ethylidene chloride $CH_3 \cdot CHCl_2$, obtained by the chlorination of C_2H_5Cl. (For an explanation of this isomerism, see p. 62.)

Propylene combines with hydriodic acid to isopropyl iodide, C_3H_7I, which is reconverted into propylene by elimination of HI. But the same propylene results from a compound isomeric with isopropyl iodide, viz. normal propyl iodide (and also, of course, from the above-mentioned normal propyl chloride), by the elimination of hydrogen iodide (or chloride), so that by this reaction normal propyl iodide can be transformed into isopropyl iodide. (See p. 60.) From the three butylenes there

are formed two butyl iodides, viz. secondary and tertiary, which, as well as the two other existing butyl iodides, yield these butylenes again with alcoholic potash; in this way the two last-mentioned butyl iodides are convertible into their isomers, the two first (see p. 61).

A study of the constitution of the compounds formed, shows that in these additive reactions the *halogen invariably attaches itself to that carbon atom with which are combined the least number of hydrogen atoms*, e.g.

$$CH_3 \cdot CH : CH_2 + HI = CH_3 \cdot CHI \cdot CH_3 \text{ (\textit{not } } CH_3 \cdot CH_2 \cdot CH_2I);$$

from C_3H_7X onwards, therefore, we obtain only "secondary" and "tertiary"* compounds.

3. From **Compounds containing oxygen.**

(*a*) From the alcohols $C_nH_{2n+1}OH$. In these the OH is readily exchangeable for chlorine, bromine, or iodine by the action of halogen hydride, thus:—

$$C_2H_5OH + HBr \rightleftarrows C_2H_5Br + H_2O.$$

In such exchange the halogen takes the place of the hydroxyl, so that the constitution of the haloid product corresponds with that of the alcohol used.

These reactions are reversible or balanced, and a state of equilibrium is reached; according to the law of mass action, it is therefore necessary either to use a large excess of halogen hydride (*e.g.* to saturate with the gas or to heat in a sealed tube), or to remove the water formed, by sulphuric acid, zinc chloride, &c.

Methyl and ethyl chlorides are easily prepared by distilling the corresponding alcohol with common salt and sulphuric acid, or by leading hydrochloric-acid gas into the warmed alcohol containing half its weight of zinc chloride in solution (*Groves*).

The chlorides of phosphorus are also applicable for the substitution of OH by Cl, since they react in the same way with alcohols as with water, thus:

$$PCl_3 + 3\,HOH = P(OH)_3 + 3\,HCl$$
$$PCl_3 + 3\,C_2H_5OH = P(OH)_3 + 3\,C_2H_5Cl.$$

* The names "primary", "secondary", and "tertiary" compounds are founded upon those of the alcohols—primary, secondary, and tertiary—in question, from which they can be prepared according to method 8, *a*.

Phosphorus pentachloride is most frequently used for this purpose,

$$PCl_5 + C_2H_5OH = C_2H_5Cl + HCl + POCl_3.$$

Phosphorus oxychloride itself is also sometimes employed. Of especial importance here is the application of the halogen compounds of phosphorus in the production of bromine and iodine compounds. The former need not be prepared beforehand, the end being achieved by gradually bringing phosphorus and iodine or bromine together in presence of the alcohol:

$$3\,CH_3OH + P + 3\,I = 3\,CH_3I + H_3PO_3.$$

This is the method usually employed for the preparation of methyl and ethyl iodides.

(*b*) The halogen derivatives may also be prepared from polyhydric alcohols, *e.g.* trichlorhydrin, $C_3H_5Cl_3$, from glycerol, $C_3H_5(OH)_3$, and PCl_5; isopropyl iodide, C_3H_7I, or allyl iodide, C_3H_5I, from glycerol and PI_3 according to the conditions of the experiment (see p. 60); hexyl iodide, $C_6H_{13}I$, from mannitol, $C_6H_8(OH)_6$ and HI, the latter acting here as a reducing agent also.

(*c*) From aldehydes and ketones (see these), dichloro-substitution products are formed by the action of PCl_5, *e.g.* ethylidene chloride, $CH_3 \cdot CHCl_2$, from aldehyde, $CH_3 \cdot CH{:}O$; acetone chloride, $CH_3 \cdot CCl_2 \cdot CH_3$, from acetone $CH_3 \cdot CO \cdot CH_3$.

4. Chlorine and bromine compounds are frequently formed from the corresponding iodine or bromine ones by direct exchange, *e.g.* isopropyl bromide from the iodide, or methylene bromide from methylene iodide; (also by treatment with mercuric chloride, stannic chloride, or fuming hydrochloric acid). Conversely the chlorides and bromides may be transformed into the iodides by heating with sodium iodide in alcoholic or acetone solution (B. **18**, 519), dry calcium iodide (B. **16**, 392), or with fuming hydriodic acid.

MONO-SUBSTITUTION PRODUCTS

The **methyl** and **ethyl** compounds are usually obtained from the corresponding alcohols by one or other of the following methods:—(*a*) Grove's method (p. 58); (*b*) action of concentrated sulphuric acid and sodium halide; (*c*) phosphorus and halogen.

Methyl chloride is often obtained by heating trimethylamine hydrochloride at 360°. (For physical properties, see

Table.) Methyl chloride is used for the production of artificial cold, for extracting perfumes from flowers, and for methylating dyes in the colour industry. It burns with a green-bordered flame.

Ethyl Fluoride, C_2H_5F. A gas of ethereal odour, which liquefies at $-48°$; it burns with a blue flame, and does not attack glass.

Each **Propyl halide**, C_3H_7X, exists in two isomeric forms, the normal propyl and the isopropyl compounds, the former boiling at a somewhat higher temperature than the latter. To the normal compounds the constitutional formula $CH_3 \cdot CH_2 \cdot CH_2X$ is ascribed, and to the iso-compounds the formula $CH_3 \cdot CHX \cdot CH_3$, since they are derivable respectively from normal propyl alcohol and from isopropyl alcohol or acetone, the constitutions of which can readily be determined.

According to theory only these two cases are possible, since propane, $CH_3 \cdot CH_2 \cdot CH_3$, contains but two types of hydrogen atoms, viz.: (1) six combined with the end carbon atoms, and (2) two combined with the middle ones. For the transformation of the normal into the iso-compounds, see p. 57.

Isopropyl iodide, 2-iodopropane, is prepared from glycerol, phosphorus, iodine, and water (see p. 59); allyl iodide (p. 65) is formed as intermediate product, and at the same time some propylene (p. 48):

$$C_3H_5(OH)_3 + 3\,HI - 3\,H_2O = C_3H_6I_2 = C_3H_5I + I_2.$$
$$C_3H_5I + HI = C_3H_6 + I_2. \qquad C_3H_6I + 2\,HI = C_3H_7I + I_2.$$

Each **Butyl-haloid compound**, C_4H_9X, is known in four isomeric forms, which differ from one another in boiling-point (up to 30°).

Four isomers are theoretically possible; thus from normal butane, $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_3$, are derived:

(*a*) $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2I$ — Normal butyl iodide (1-*iodobutane*)

and

(*b*) $CH_3 \cdot CH_2 \cdot CHI \cdot CH_3$ — Secondary butyl iodide (2-*iodobutane*)

according to whether a "terminal" or "central" hydrogen atom is replaced; similarly from trimethylmethane, $CH(CH_3)_3$, are derived:

(*c*) $\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!CH \cdot CH_2I$ — Isobutyl iodide (2-*methyl*-3-*iodopropane*)

and

(*d*) $\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!CI \cdot CH_3$ — Tertiary butyl iodide (2-*methyl*-2-*iodopropane*)

The constitutions of these four compounds follow from

those of the four corresponding butyl alcohols (p. 67), from which they can be prepared by the action of halogen hydride.

For transformations, see p. 58. Isobutyl bromide changes into the tertiary compound when heated at 230°–240°, probably owing to the intermediate formation of butylene.

The **Isobutyl compounds** are the easiest to prepare (from isobutyl alcohol). The **Tertiary** readily react with H_2O to form the alcohol and halogen hydride, this taking place even in the cold in the case of the iodide.

These mono-halogen derivatives are one of the most important groups of reagents employed by the organic chemist, on account of the readiness with which the halogen atoms may be replaced by other radicals.

Some of the more characteristic reactions are:—

1. Replacement of halogen by hydrogen. Inverse substitution (see p. 33).

2. Replacement of halogen by OH (hydroxyl) (p. 71),

$$C_2H_5I + H_2O = C_2H_5OH + HI,$$

generally by the aid of aqueous alkali, moist silver oxide, or lead oxide and water.

3. Alkalis in alcoholic solution, or alcoholic solutions of sodium methoxide ($CH_3 \cdot ONa$) or sodium ethoxide ($C_2H_5 \cdot ONa$), as a rule, eliminate halogen hydracids, and yield olefines, $CH_2I \cdot CH_3 - HI = CH_2{:}CH_2$. For the reaction it is necessary that the halogen derivative contain at least two carbon atoms, and that a hydrogen atom should be attached to a carbon atom adjacent to the one to which the halogen is united.

4. The halogen may be replaced by the **amino** group $\cdot NH_2$ by the aid of ammonia under pressure, by the **nitro** group $\cdot N\leqslant^{O}_{O}$ or **nitrite** radical $\cdot O \cdot N{:}O$ (p. 94), and by the **nitrile** radical $\cdot C{:}N$ (p. 100).

For their use as synthetical reagents, see pp. 121, 228, 237.

DI-SUBSTITUTION PRODUCTS

Methylene chloride, CH_2Cl_2, **Methylene bromide**, CH_2Br_2, and **Methylene iodide**, CH_2I_2, are colourless liquids which are obtained either from the tri-haloid substitution products by inverse substitution or from the mono-substitution products by the introduction of more halogen. (See table, p. 56.)

The compounds $C_2H_4X_2$ are known in two isomeric forms, to which are assigned the constitutional formulæ:

$CH_2X \cdot CH_2X$ (ethylene) and $CH_3 \cdot CHX_2$ (ethylidene).

The former result from the addition of halogen to ethylene, or from the action of halogen hydride or phosphorus haloids upon glycol, $C_2H_4(OH)_2$ (see this), *e.g.* ethylene bromide, by passing ethylene into bromine and water at the ordinary temperature.

The ethylene compounds yield acetylene with alcoholic potash, or better, alcoholic solution of sodium ethoxide, and are transformed into glycol by exchanging their halogen atoms for hydroxyl under the influence of potassium carbonate solution. Glycol, $CH_2(OH) \cdot CH_2 \cdot OH$, with hydrochloric acid yields glycol mono-chlorhydrin, $CH_2Cl \cdot CH_2 \cdot OH$, and this on oxidation yields mono-chloracetic acid, $CH_2Cl \cdot CO \cdot OH$. In this acid it can be shown that the chlorine and hydroxyl radicals are attached to distinct carbon atoms, hence in glycol the two hydroxyl groups, and in ethylene dibromide the two bromine atoms, are almost certainly united to distinct and not to the same carbon atoms.

The **Ethylidene compounds** are obtained from aldehyde (para-aldehyde) by exchange of the oxygen for halogen by means of phosphorus chloride, &c

Ethylidene chloride, also called ethidene chloride, or 1:1-dichloroethane, is, however, most conveniently prepared with phosgene, $COCl_2$, thus:—

$$CH_3 \cdot C\lessgtr^{H}_{O} + COCl_2 = CH_3 \cdot CHCl_2 + CO_2.$$

It is also formed by the further chlorination of C_2H_5Cl, and is a by-product in the manufacture of chloral. Its boiling-point (57°) is lower than that of ethylene chloride (84°). It is an anæsthetic.

Propylene chlorides, $C_3H_6Cl_2$, bromides and iodides, are likewise known. One group is formed by the addition of halogen to propylene, and thus has an unsymmetrical constitution, *e.g.* propylene chloride, 1 : 2 - dichloropropane, $CH_3 \cdot CHCl \cdot CH_2Cl$. Isomeric with this group are the symmetrically-constituted **Trimethylene derivatives**, of which trimethylene-bromide, 1:3-dibromo-propane, $CH_2Br \cdot CH_2 \cdot CH_2Br$, results from the addition of hydrobromic acid to allyl bromide:

$$CH_2:CH \cdot CH_2Br + HBr = CH_2Br \cdot CH_2 \cdot CH_2Br.$$

TRI-SUBSTITUTION PRODUCTS

Chloroform, $CHCl_3$ (*Liebig* and *Soubeiran*, 1831; formula established by *Dumas*, 1835).

Formation.—1. From methane and methyl chloride (see p. 57). 2. By heating alcohol, or even better, acetone, with bleaching-powder and water. When alcohol is used, the bleaching-powder probably first oxidizes it to aldehyde, then chlorinates to chloral, and ultimately hydrolyses (see below) to chloroform. 3. Together with alkali formate by warming chloral or chloral hydrate with aqueous alkali:

$$CCl_3 \cdot CHO + NaOH = CHCl_3 + HCO_2Na.$$

This last method of formation is the best for the preparation of pure chloroform.

It is a colourless liquid of a peculiar ethereal odour and sweetish taste, is sparingly soluble in water, and solidifies below −70°. B.-pt 61·2°. Sp gr. 1·527. It dissolves fats, resins, caoutchouc, iodine, &c, and is also a most valuable anæsthetic (*Simpson*, Edinburgh, 1848).

The carbylamine reaction (see Iso-nitriles) furnishes a delicate test for the presence of chloroform

Bromoform, $CHBr_3$, is sometimes present in commercial bromine

Iodoform, CHI_3 (*Serullas*, 1822; formula established by *Dumas*), is prepared by warming alcohol with iodine and alkali or alkaline carbonate:

$$C_2H_5OH + 4I_2 + 6KOH = CHI_3 + HCO_2K + 5KI + 5H_2O.$$

It can also be prepared in the same way from acetone, aldehyde, lactic acid, and, generally, from compounds which contain the group $CH_3 \cdot CH(OH) \cdot C$, or $CH_3 \cdot CO \cdot C$ (*Lieben*).

An electrolytic method consists in passing an electric current through a solution containing potassium iodide, sodium carbonate, and alcohol, the temperature being kept at 65°. Some 85 per cent of the potassium iodide is thus converted into iodoform.

It crystallizes in yellow hexagonal plates, melts at 119°, has a peculiar odour, is volatile with steam, and is an important antiseptic. It contains only 0·25 per cent H, which at first caused the presence of the latter to be overlooked.

Methyl chloroform, $CH_3 \cdot CCl_3$. This compound, the trichloride of acetic acid, also acts as an anæsthetic.

Glyceryl chloride, *Trichlorhydrin*, 1:2:3-trichloropropane, $CH_2Cl \cdot CHCl \cdot CH_2Cl$, is obtained from glycerol and PCl_5 (p. 59). B.-pt. 158°. The corresponding bromine compound is also known, but not the iodine one, $C_3H_5I_3$, which decomposes in the nascent state (*i.e.* when glycerine, phosphorus, and iodine react together) into allyl iodide, C_3H_5I, and I_2.

HIGHER SUBSTITUTION PRODUCTS

Carbon tetrachloride, CCl_4. Can be prepared from chloroform or carbon disulphide and chlorine. It is a colourless liquid, boils at 77°, and is used as a solvent for fats, &c.

Perchloro-ethane, C_2Cl_6. Rhombic plates of camphor-like odour. Melts and sublimes at 185°.

The chemical properties of these polyhalogen derivatives are somewhat similar to those of the monohalogen derivatives. They may be reduced, transformed into the corresponding alcohols, or the halogen atoms replaced by NH_2 radicals, &c. The action of alkalis on the polyhalogen derivatives, in which the halogen atoms are attached to the same carbon atom, is interesting, *e.g.* CH_2Cl_2 gives not $CH_2{<}^{OH}_{OH}$, but $CH_2{:}O$ formaldehyde and H_2O; $CHCl_3$ gives not $CH(OH)_3$, but this compound $-$water, viz. $O{:}CH \cdot OH$, formic acid. Similarly, CCl_4 gives not $C(OH)_4$, but $CO_2 + 2H_2O$, and $CH_3 \cdot CHBr_2$ gives $CH_3 \cdot CH(OH)_2 - H_2O$, *i.e.* $CH_3 \cdot CHO$.

Many of these reactions require high temperatures; the substances must be heated with the alkali in sealed tubes under pressure. It is characteristic of carbon derivatives that **compounds which contain two or more hydroxyl radicals attached to the same carbon atom are unstable**, and, as a rule, immediately eliminate water yielding an aldehyde, acid, &c. Ammonia and chloroform at a red heat yield HCN and HCl.

B. Haloid Derivatives of the Unsaturated Hydrocarbons

These compounds are obtained either by partially withdrawing halogen or halogen hydride from the halogen derivatives of the saturated hydrocarbons, or by incompletely saturating the hydrocarbons poorer in hydrogen with halogen or halogen hydride, *e.g.*:

$$C_2H_4Br_2 - HBr = C_2H_3Br. \quad C_2H_2 + HBr = C_2H_3Br.$$

The allyl compounds, C_3H_5X, are obtained from allyl alcohol and halogen hydride or phosphorus haloids.

These unsaturated products are very similar to the corresponding saturated ones, but they are, of course, capable of combining further with halogen or halogen hydride, and they exist in stereo-isomeric modifications. (See Fumaric Acid.)

In the unsaturated compounds the halogen atoms are, as a rule, not so readily replaced by other radicals, *e.g.* OH, NH_2, as in the saturated halogen derivatives.

The following may be mentioned:—

Vinyl bromide, *bromo-ethylene*, $CH_2:CHBr$; is usually prepared from ethylene di-bromide and alkali.

Allyl-chloride, -bromide, and **-iodide**, 3-*iodo*-1-*propene*, $CH_2:CH\cdot CH_2X$.

These are of importance on account of their relation to the allyl compounds found in nature, *e.g.* oil of mustard and oil of garlic. The iodide is prepared from glycerol, phosphorus, and iodine, and from it, by means of $HgCl_2$, the chloride.

Isomeric with these are the **propylene compounds**, *e.g.* **α-chloro-propylene** (1-*chloro*-1-*propene*), $CHCl:CH\cdot CH_3$.

III. MONOHYDRIC ALCOHOLS, OR ALKYL HYDROXIDES

Alcohols may be regarded as paraffins in the molecules of which one or more hydrogen atoms have been replaced by one or more monovalent *hydroxyl* groups, $\cdot O\cdot H$. The $\cdot O\cdot H$ group is thus characteristic of alcohols. For the proof of the presence of the OH group, see p 17. They are usually divided into groups, according to the number of such radicals contained in the molecule: *dihydric*, e.g. $C_2H_4(OH)_2$; *trihydric*, e.g. $C_3H_5(OH)_3$; *hexahydric*, e.g $C_6H_8(OH)_6$, &c.

The monohydric alcohols are either saturated or unsaturated, according to the hydrocarbons from which they are derived. The unsaturated closely resemble the saturated, except that they are capable of forming additive compounds.

A. Monohydric Saturated Alcohols, $C_nH_{2n+1}OH$

(See Table, p. 67.)

The lowest members of this series are colourless mobile liquids, the middle ones are more oily, and the highest—from dodecyl alcohol, $C_{12}H_{25}OH$, onwards—are solid at the ordinary temperature, and like paraffin in appearance. Gaseous alcohols are unknown; and it is thus obvious that the introduction of OH for H raises the boiling-point of a substance. Compare—

	B.-p.		B.-p.
CH_4	−164°	CH_3OH	66°
C_3H_8	−93°	C_2H_5OH	78°
$C_2H_5(OH)$	78°	$C_2H_4(OH)_2$	197°

With compounds of analogous constitution the boiling-point rises with tolerable regularity; in the case of the lower members by about 19°, and higher up in the series by a smaller number.

The lowest members are miscible with water, but this solubility rapidly diminishes as the molecular weight increases; thus butyl alcohol requires 12 parts, and amyl alcohol 40 parts of water for solution, while the higher members are no longer soluble in water. The former can be separated or "salted out" from their aqueous solution by the addition of salts, *e.g.* K_2CO_3 and $CaCl_2$.

The specific gravity is always < 1. The highest members (over C_{16}) can be distilled undecomposed only in a vacuum; at the ordinary pressure they break up into olefine and water. The lowest members possess a spirituous odour, those with more than five C atoms an odour of fusel, and both have a burning taste, while the highest members are like paraffin in appearance and without either taste or smell.

CONSTITUTION AND ISOMERS; CLASSIFICATION OF THE ALCOHOLS

Propyl alcohol, $C_3H_7 \cdot OH$, and the higher members exist in different isomeric modifications; thus there are two propyl, four butyl, and eight amyl alcohols, &c.

The number of isomeric forms theoretically possible can be determined by taking the formulæ for the corresponding saturated hydrocarbons, and seeing in how many different positions

NORMAL MONOHYDRIC SATURATED ALCOHOLS

Name.	Syst Name	Const Formula	Melting-pt.	Boiling-pt.	Sp. gr. at 0°.
Methyl alcohol	Methan-1-ol	$CH_3 \cdot OH$		66°	0·812
Ethyl alcohol	Ethan-1-ol	$CH_3 \cdot CH_2 \cdot OH$	− 130°	78°	0·806
n-Propyl alcohol	Propan-1-ol	$CH_3 \cdot [CH_2]_2 OH$	...	97°	0·817
n-Butyl alcohol	Butan-1-ol	$CH_3 [CH_2]_3 OH$	...	117°	0·823
n-Amyl alcohol	Pentan-1-ol	$CH_3 [CH_2]_4 OH$	...	138°	0 829
n-Hexyl alcohol	Hexan-1-ol	$CH_3 [CH_2]_5 OH$	...	157°	0·833
n-Heptyl alcohol	Heptan-1-ol	$CH_3 [CH_2]_6 OH$	...	176°	0·836
n-Octyl alcohol	Octan-1-ol	$CH_3 [CH_2]_7 OH$	...	195°	0 839
n-Nonyl alcohol	Nonan-1-ol	$CH_3 [CH_2]_8 OH$	− 5°	213°	0·842
n-Decyl alcohol	Decan-1-ol	$CH_3 [CH_2]_9 OH$	+ 7°	231°	0·839
n-Dodecyl alcohol	Dodecan-1-ol	$CH_3 [CH_2]_{11} OH$	24°	...	0·831 at 24°

ISOMERIC PROPYL, BUTYL, AND AMYL ALCOHOLS

Name.	Syst Name.	Const Formula.	B.-pt.	Sp gr at 20°.
Propyl alcohols—$C_3H_7 \cdot OH$.				
Normal	Propan-1-ol	$CH_3 \cdot CH_2 \cdot CH_2 \cdot OH$	97°	0 804
Iso or secondary	Propan-2-ol	$CH_3 \cdot CH(OH) \cdot CH_3$	81°	0 789
Butyl alcohols—$C_4H_9 \cdot OH$.				
Norm. primary	Butan-1-ol	$CH_3 \cdot [CH_2]_3 \cdot OH$	117°	0·810
Norm. secondary	Butan-2-ol	$CH_3 \cdot CH_2 \cdot CH(OH) \cdot CH_3$	110°	
Prim. isobutyl	2-Methyl-propan-1-ol	$(CH_3)_2 \cdot CH \cdot CH_2 \cdot OH$	107°	0·806
Tertiary	2-Methyl-propan-2-ol	$(CH_3)_3C \cdot OH$	83°	0 786
Amyl alcohols—$C_5H_{11} \cdot OH$.				
Norm. primary	Pentan-1-ol	$CH_3 [CH_2]_4 \cdot OH$	138°	...
Isobutyl carbinol	2-Methyl-butan-4-ol	$(CH_3)_2 \cdot CH \cdot CH_2 \cdot CH_2 \cdot OH$	131°	...
Secondary butyl carbinol	2-Methyl-butan-1-ol	$CH_3 \cdot CH_2 \cdot CH(CH_3) \cdot CH_2 \cdot OH$	128°	...
Methyl-propyl carbinol	Pentan-2-ol	$CH_3 \cdot CH_2 \cdot CH_2 \cdot CH(OH) \cdot CH_3$	119°	...
Methyl-isopropyl carbinol	2-Methyl-butan-3-ol	$(CH_3)_2 \cdot CH \cdot CH(OH) \cdot CH_3$	112·5°	...
Diethyl carbinol	Pentan-3-ol	$CH_3 \cdot CH_2 \cdot CH(OH) \cdot CH_2 \cdot CH_3$	117°	...
Dimethyl-ethyl carbinol	2-Methyl-butan-2-ol	$(CH_3)_2 \cdot C(OH) \cdot CH_2 \cdot CH_3$	102°	...

the OH group can be introduced, *e.g.* $CH_3 \cdot CH_2 \cdot CH_3$, propane, can obviously give—

$$CH_3 \cdot CH_2 \cdot CH_2 \cdot OH \quad \text{and} \quad CH_3 \cdot CH(OH) \cdot CH_3$$

two distinct propyl alcohols.

Butane exists in two forms:

$$CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_3 \text{ or } \textit{normal} \quad \text{and} \quad (CH_3)_3CH \text{ or } \textit{iso}$$

From the *n* we can get—

$$CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot OH \quad \text{and} \quad CH_3 \cdot CH_2 \cdot CH(OH) \cdot CH_3;$$

from the *iso*—

$$(CH_3)_2CH \cdot CH_2 \cdot OH \quad \text{and} \quad (CH_3)_3C \cdot OH;$$

but no more.

Of these isomerides, some only are oxidizable to acids, $C_nH_{2n}O_2$, containing an equal number of carbon atoms, an aldehyde, $C_nH_{2n}O$, being formed as intermediate product. Such alcohols are termed **primary** alcohols (primary propyl, butyl, and isobutyl alcohols, &c.).

Another class of alcohols is not oxidizable to acids with an equal number of atoms of carbon, but to ketones, $C_nH_{2n}O$, by the removal of 2 atoms of hydrogen, *e.g.* isopropyl alcohol yields acetone, C_3H_6O. These are termed **secondary** (secondary butyl alcohol). Upon further oxidation the ketones do indeed yield acids, which, however, contain not an equal but always a smaller number of carbon atoms, the carbon chain having thus been broken up.

Lastly, the third class of alcohols, the **tertiary**, yield upon oxidation neither aldehydes, ketones, nor acids with an *equal* number of carbon atoms, but only ketones or acids containing fewer atoms of carbon.

Constitution of the Alcohols.—In the molecule of a monohydric alcohol one of the hydrogen atoms plays a part different from that of the others; thus it is replaceable by metals (K and Na), and by acid radicals, and, together with the oxygen atom, combines with the hydrogen of a halogen hydride to form water, while the other hydrogen atoms of the alcohol remain unchanged. This hydrogen atom, which has already been formulated under the Theory of Types apart from the others, is called the "typical" or "extra-radical" hydrogen atom. It is not joined directly to the carbon atom, but through the oxygen one, a conclusion which is confirmed by

the formation of alcohols by the action of alkalis (KOH) on monohalogen derivatives of the paraffins. (See p. 71.) This point has been previously discussed (p. 17) for ethyl alcohol.

The alcohols therefore contain a hydroxyl group, OH, and their general constitutional formula is $(C_nH_{2n+1})\cdot OH$.

According to theory, this hydroxyl can either replace an atom of hydrogen in a methyl group, in which case an alcohol containing the group $\cdot CH_2OH$ (one carbon atom being joined to the other by a single bond) results, *e.g.* $CH_3\cdot CH_2\cdot OH$. Or it can replace the hydrogen of a CH_2: group in a hydrocarbon, so that the resulting compound contains the group $:CH\cdot OH$, the carbon being here joined to two other carbon atoms. Or, lastly, it is possible that in a hydrocarbon with a branching carbon chain, the hydrogen of a methine group CH: may be replaced by hydroxyl, when the resulting alcohol would contain the group $:C\cdot OH$, in which one carbon atom is joined to three others.

Now, it is easy to see that the group $\cdot C\lessdot^{H_2}_{O\cdot H}$ can, by further oxidation, be transformed into $\cdot C\lessdot^{O}_{O\cdot H}$. The latter, which is termed carboxyl, is contained in the acids $C_nH_{2n}O_2$, or $C_{n-1}H_{2n-1}COOH$, which are formed by the oxidation of the primary alcohols. Consequently it is the **primary** alcohols which contain the group $\cdot CH_2\cdot OH$.

The group $:CH\cdot OH$ can likewise be changed into $:C:O$ $\left(i.e.\ C\lessdot^{OH}_{OH} - H_2O\right)$, which is the characteristic group of the ketones, by oxidation. A further introduction of O or OH, whereby acids containing the group $\cdot CO\cdot OH$ would ensue, is not possible in this case without a rupture of the carbon chain, since the carbon atom is tetravalent. Since then it is the **secondary** alcohols which upon oxidation yield ketones, and not acids with an equal number of carbon atoms, the group $:CH\cdot OH$ is characteristic of these.

Finally, the group $:C\cdot OH$ already contains the maximum of oxygen which can be combined with a carbon atom already linked to 3 other atoms of carbon. A compound, therefore, in which this atomic group is present, cannot yield, when oxidized, an aldehyde, acid, or ketone with an equal number of carbon atoms in the molecule, but the result of such oxidation must be the breaking of the carbon chain, and the formation of acids or ketones containing a smaller number of carbon

atoms in the molecule. This being the behaviour of tertiary alcohols, the group $\vdots C \cdot OH$ is peculiar to them.

The existence of the three classes of alcohols finds in this way a thoroughly satisfactory explanation from theory.

The secondary and tertiary alcohols were predicted by *Kolbe* in 1859 from theoretical considerations (A. **113**, 301; **132**, 102).

Among the isomeric alcohols the primary possess the highest, and the tertiary the lowest boiling-points (cf. p. 67). Similar generalizations appear to hold good for other physical properties, *e.g.* specific gravity, specific refractive indices, and capillarity constants. The tertiary have the highest melting-points.

Determination of Constitution.—The determination of the constitution of any special alcohol is based largely on its method of formation and on its products of oxidation. *E.g.* Isopropyl alcohol may be obtained by the reduction of acetone $(CH_3)_2 C:O$, and must therefore have the constitutional formula $(CH_3)_2 \cdot CH \cdot OH$, and not $CH_3 \cdot CH_2 \cdot CH_2 \cdot OH$. This is confirmed by the fact that on oxidation it yields the ketone acetone, and must necessarily be a secondary alcohol with the grouping $:CH \cdot OH$.

Similarly isobutyl alcohol must be represented as $(CH_3)_2 \cdot CH \cdot CH_2 \cdot OH$, since on oxidation it yields *iso*-butyric acid, the constitution of which is known to be $(CH_3)_2 \cdot CH \cdot CO \cdot OH$.

Occurrence.—Different alcohols are found in nature combined with organic acids as esters in ethereal oils and waxes; *e.g.* methyl, ethyl, butyl, hexyl, and octyl alcohols, and also those with 16, 27, and 30 carbon atoms; ethyl alcohol also occurs in the free state.

I. General Methods of Formation.—1. By "**saponification**" or "**hydrolysis**" of their esters, *i.e.* by boiling these with alkalis or mineral acids, or by the action of superheated steam, thus:—

$$\underset{\text{Ethyl benzoate}}{C_6H_5 \cdot CO \cdot OC_2H_5} + KOH = \underset{\text{Potassium benzoate}}{C_6H_5 \cdot CO \cdot OK} + C_2H_5OH.$$

Some esters, *e.g.* ethyl hydrogen sulphate, decompose when simply warmed with water:

$$C_2H_5 \cdot \ddot{O} \cdot SO_2 \cdot OH + H \cdot OH = C_2H_5 \cdot OH + SO_2(OH)_2.$$

Most of these processes of hydrolysing require some little time, and the ester is boiled with the alkali (KOH solution) in a flask fitted with a reflux condenser.

2. From the halogen compounds $C_nH_{2n+1}X$, and therefore indirectly from the paraffins and olefines (pp. 55 and 57). In the latter case secondary or tertiary alcohols, from C_3 on, are obtained since the halogen of the haloid compounds becomes attached to that carbon atom to which the smaller number of hydrogen atoms are united.

(*a*) By warming these, especially the iodides, with excess of water to 100°; sometimes by simply allowing the mixture to stand (tertiary iodides):

$$C_2H_5I + HOH = C_2H_5{\cdot}OH + HI.$$

When but little water is used, a state of equilibrium is reached as the reaction is reversible. These halogen compounds may also be termed the esters of the halogen hydracids, so that, strictly speaking, the mode of formation 2 *a* is included in 1.

(*b*) Frequently by digesting with moist silver oxide (which acts here like the unknown hydroxide, AgOH), or by boiling with lead oxide and water:

$$C_2H_5I + Ag{\cdot}OH = C_2H_5{\cdot}OH + AgI.$$

(*c*) Upon warming with silver or potassium acetate, the acetate of the alcohol in question is formed, and this is then hydrolysed:

$$C_2H_5I + CH_3{\cdot}COOAg = CH_3{\cdot}COOC_2H_5 + AgI$$
$$CH_3{\cdot}COOC_2H_5 + HOK = C_2H_5{\cdot}OH + CH_3{\cdot}COOK.$$

3. By the fermentation of the carbohydrates (*e g.* grape-sugar), the alcohols with 2, 3, 4, 5, and, under certain conditions, even 6 atoms of carbon are produced. (Yeast fermentation.)

4. On treating the primary amines (see these) with nitrous acid:

$$\begin{matrix} C_2H_5{\cdot}NH_2 \\ HO{\cdot}N:O \end{matrix} = C_2H_5{\cdot}OH + N_2 + H_2O.$$

5. From polyhydric alcohols by replacing several of the hydroxyl groups by halogen atoms, and then reducing the halogen derivative:

$$\underset{\text{Glycerol}}{C_3H_5(OH)_3} + 2\,HCl = \underset{\text{Dichlor-hydrin}}{C_3H_5Cl_2(OH)} + 2\,H_2O.$$

$$C_3H_5(OH)Cl_2 + 4\,H = \underset{\text{Isopropyl alcohol}}{C_3H_7{\cdot}OH} + 2\,HCl.$$

Secondary alkyl iodides are often obtained by the action

of HI and P on polyhydric alcohols, and these on hydrolysis yield secondary alcohols, *e.g.*:

$$\underset{\text{Glycerol}}{C_3H_5(OH)_3} \longrightarrow \underset{\text{s-Propyl iodide}}{C_3H_7I} \longrightarrow \underset{\text{s-Propyl alcohol}}{C_3H_7\cdot OH}.$$

$$\underset{\text{Erythritol}}{C_4H_6(OH)_4} \longrightarrow \underset{\text{s-Butyl iodide}}{C_4H_9I} \longrightarrow \underset{\text{s-Butyl alcohol}}{C_4H_9\cdot OH}.$$

II. Special Methods of Formation.—1. **Primary alcohols** are obtained from aldehydes by reduction with sodium amalgam and very dilute sulphuric acid (*Wurtz*), or with acetic acid and zinc dust, when the alkyl acetates are formed:

$$CH_3\cdot CH{:}O + 2H = CH_3\cdot CH_2\cdot OH.$$

This reaction is somewhat similar to the reduction of an olefine to a paraffin. In both cases a double bond is converted into a single bond, and an atom of hydrogen is added on to each atom between which the double bond originally existed

Similarly from acid anhydrides (or esters, but not the free acids) and nascent hydrogen, or by the reduction of the acid chlorides, when an ester of the alcohol is formed by the action of the unreduced chloride on the alcohol.

2. **Secondary alcohols** are formed by the action of nascent hydrogen (sodium amalgam) on the ketones, $C_nH_{2n}O$:

$$CH_3\cdot CO\cdot CH_3 + 2H = CH_3\cdot CH(OH)\cdot CH_3.$$

Pinacones are obtained here as by-products. (See Ketones.)

3. **Secondary alcohols** are also formed by the action of aldehydes on dry ethereal solutions of magnesium alkyl halides (p. 120), and treating the product which results with water or dilute acid:

$$CH_3\cdot CH{:}O + CH_3\cdot Mg\cdot I = CH_3\cdot CH(OMgI)\cdot CH_3$$
$$CH_3\cdot CH(OMgI)\cdot CH_3 + H\cdot OH = CH_3\cdot CH(OH)\cdot CH_3 + I\cdot Mg\cdot OH.$$

4. **Tertiary alcohols** are formed by the action of (*a*) ketones, (*b*) acid chlorides, or (*c*) esters of organic acids, on magnesium alkyl haloids (*Grignard*, Ann. Chem. Phys. 1901, **24**, 433), and decomposing the products with water:

(*a*) $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C{:}O + C_2H_5\cdot Mg\cdot Br = \begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C\!<\!\begin{matrix}C_2H_5\\O\cdot MgBr\end{matrix}$

$\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C\!<\!\begin{matrix}C_2H_5\\O\cdot MgBr\end{matrix} + H\cdot OH = \begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C\!<\!\begin{matrix}C_2H_5\\OH\end{matrix} + Br\cdot Mg\cdot OH.$

(*b*) $CH_3\cdot CO\cdot Cl + 2CH_3\cdot Mg\cdot I = (CH_3)_3C\cdot O\cdot MgI + MgICl.$

(*c*) $CH_3\cdot CO\cdot OC_2H_5 + 2CH_3\cdot Mg\cdot Br = (CH_3)_3C\cdot OMgBr + Br\cdot Mg\cdot OC_2H_5.$

A somewhat similar reaction is that between acid chlorides and zinc alkyl compounds—an older and less effective method due to *Butleroff*.

5. **Secondary** or **tertiary alcohols** sometimes ensue by the direct combination of an olefine with water, *e.g.* tertiary butyl alcohol, $(CH_3)_3C \cdot OH$, from isobutylene. This often gives a simple method for converting a primary into a secondary or tertiary alcohol.

The *Nomenclature* of the alcohols, especially of the secondary and tertiary, is based upon a comparison of them with methyl alcohol, also called carbinol. They are looked upon as carbinol, $CH_3 \cdot OH$, in which the three hydrogen atoms are wholly or partially replaced by alkyl radicals, thus:—

Tertiary butyl alcohol, $(CH_3)_3C \cdot OH$ = trimethyl carbinol:
Secondary butyl alcohol, $CH_3 \cdot CH_2 \cdot CH(OH) \cdot CH_3$
= $CH(OH)(CH_3)(C_2H_5)$, = methyl-ethyl carbinol

The systematic name of the alcohols terminates in "ol" As examples:—

$CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot OH$ Butanol
$CH_3 > CH \cdot CH(CH_3) \cdot CH(OH) \cdot CH_3$ 2.3-Dimethylpentan-4-ol.
CH_3

Behaviour.—1. The typical hydrogen atom (p 68) is replaceable by metals, *e.g.* readily by K or Na, less readily by Ca, Mg, or Al, with formation of alcoholates, EtONa, $Mg(OEt)_2$, &c.

$$2C_2H_5OH + 2Na = 2C_2H_5ONa + H_2.$$

These react with water, giving rise to a state of equilibrium as represented in the equation

$$Et \cdot ONa + H \cdot OH \rightleftarrows Et \cdot OH + Na \cdot OH.$$

Brühl (B. 1904, **37**, 2066) has described a method for preparing the compound $CH_3 \cdot ONa$ free from water and alcohol.

Primary and secondary, but not tertiary, alcohols combine with baryta and lime to alcoholates at 130°. Crystalline compounds are formed with calcium chloride, so that this salt cannot be used for drying the alcohols; these compounds are decomposed by water.

2. They enter into the composition of many compounds, as "alcohol of crystallization". (See pp. 75 and 79.)

3. They react with acids both mineral and organic in some-

what the same manner as metallic hydroxides do, yielding **alkyl salts** or **esters** and water (cf. Esterification):

$$KOH + \underset{\text{Acetic acid.}}{CH_3 \cdot COOH} = CH_3 \cdot COOK + H_2O$$

$$C_2H_5OH + CH_3 \cdot COOH \rightleftarrows CH_3 \cdot COOC_2H_5 + H_2O.$$

The methyl and ethyl esters derived from certain substituted benzoic acids, *e.g.* paranitrobenzoic acid, $NO_2 \cdot C_6H_4 \cdot CO_2H$, are solids with definite melting-points, and are sometimes used in identifying small amounts of these alcohols.

4. Dehydrating agents convert them into olefines

5. With halogen hydracids or phosphorus halides, they yield monohalide derivatives of the hydrocarbons (p. 58).

6. For the behaviour of primary, secondary, and tertiary alcohols upon oxidation, see p. 68 *et seq.*

Methyl alcohol is oxidized to carbon dioxide as the primary product (formic acid) is itself readily oxidized

7. The primary, secondary, and tertiary alcohols can also be distinguished from one another by the behaviour of the nitro-compounds, which are formed by the action of silver nitrite on the iodides (cf. *Meyer* and *Jacobson*, I, p. 221).

8. Halogens do not substitute but oxidize.

9. Many alcohols when heated with excess of soda lime yield the sodium salts of the corresponding acids.

Methyl alcohol, Methanol, *Wood Spirit*, CH_3OH, was discovered in wood-tar by *Boyle* in 1661, and its difference from ordinary alcohol recognized in 1812 by *Phillips Taylor*. Its composition was established in 1834 by *Dumas* and *Péligot*. It occurs as methyl salicylate in *Gaultheria procumbens* (oil of winter green, Canada), as butyric ester in the unripe seeds of *Heracleum giganteum*, and as ester of benzoylecgonin in cocain.

Formation.—1. By chlorinating methane, CH_4, and hydrolysing the resulting methyl chloride (*Berthelot*). Methyl iodide may be hydrolysed in a similar manner.

2. By the destructive distillation of wood (beech wood) at about 350°.

By this distillation there are obtained (*a*) Gases (CH_4, C_2H_6, C_2H_4, C_2H_2, C_3H_6, C_4H_8, CO, CO_2, H_2). (*b*) An aqueous distillate of "pyroligneous acid", containing methyl alcohol (1–2 per cent), acetic acid (10 per cent), acetone (0·1–0·5 per cent), methyl acetate, allyl alcohol, &c. (*c*) Wood-tar, containing paraffins, naphtnalene, phenol, guaiacols, &c. (*d*) Wood charcoal.

3. Also by the dry distillation of vinasse.

It is prepared commercially from the crude pyroligneous acid by repeated distillation after neutralization with lime, and is purified by formation of the $CaCl_2$ compound, which is a solid, and stable at 100°; or, better, by transformation into the oxalic or benzoic ester, both of which are easy to purify and hydrolyse.

Properties.—It is a colourless liquid, boils at 66°, and has a specific gravity about 0·8. The alcohol of commerce usually contains acetone. It burns with a non-luminous flame, dissolves fats, oils, &c, and acts as an intoxicant like ethyl alcohol. It also enters into the composition of compounds as "alcohol of crystallization", *e.g.* $BaO + 2\,CH_4O$, $MgCl_2 + 6\,CH_4O$; $CaCl_2 + 4\,CH_4O$ (six-sided plates). It is readily oxidized to formic aldehyde and formic acid, being also converted into the latter when heated with soda-lime. Potassium methoxide, CH_3OK, is a white crystalline powder, and forms a definite crystalline compound $CH_3OK + CH_3OH$.

The anhydrous alcohol dissolves a small amount of dehydrated cupric sulphate to a blue-green solution. Distilled over heated zinc dust, it decomposes almost quantitatively into $CO + 2\,H_2$.

Uses.—For tar colours—(also as CH_3I and CH_3Cl); as methyl ether in the manufacture of ice, for polishes and varnishes; as *Wiggersheim's* preservative liquid; for methylating spirits of wine, &c.

Ethyl alcohol, Ethanol, *Spirits of Wine*, C_2H_5OH. Liquids containing spirits of wine have been known from very early times, and their concentration either by distillation or by dehydration with carbonate of potash is also an old art. We read of it as "alcohol" in the sixteenth century. *Lavoisier* arrived at the qualitative, and *de Saussure* in 1808 the quantitative composition of alcohol.

In the vegetable kingdom alcohol is only found occasionally, as ethyl butyrate, but in the animal kingdom it occurs in various forms, *e.g.* in diabetic urine. It is also present in small quantity in coal-tar, bone oil, wood spirit, and bread, fresh English bread containing 0·3 per cent.

Formation.—1. From C_2H_6 by conversion into C_2H_5Cl and hydrolysis of the latter according to modes of formation 1 and 2.

2. Ethylene and concentrated H_2SO_4 react at 160°, yielding ethyl hydrogen sulphate,

$$C_2H_4 + H_2SO_4 = C_2H_5HSO_4;$$

and this when boiled with water gives ethyl alcohol. (See pp. 44 and 70.) This method was discovered by *Faraday*, and corroborated in 1855 by *Berthelot*.

3. By the reduction of acetaldehyde

$$CH_3 \cdot CH{:}O + 2H = CH_3 \cdot CH_2 \cdot OH.$$

4. *Preparation by the Alcoholic Fermentation of Sugar.*—Directly from grape and fruit sugars, $C_6H_{12}O_6$, and indirectly from cane-sugar, $C_{12}H_{22}O_{11}$, after previous hydrolysis to two molecules of $C_6H_{12}O_6$; also indirectly from malt-sugar, from starch, &c.

Fermentations are peculiarly slow decomposition-processes of organic substances which are accompanied, as a rule, with liberation of gas and evolution of heat, and which are induced by micro-organisms, or by complex organic nitrogenous substances (*enzymes*) of animal or vegetable origin. The alcoholic fermentation of sugar, *i.e.* the fermentation which produces spirit, is caused by the varieties of the genus *Saccharomyces*, the *yeast ferment*, which forms small oval microscopic cells, multiplying by gemmation. As plants, these require for their sustenance inorganic salts, *e.g.* phosphates, potassium salts, and nitrogen in the form of ammonium salts, but, as non-assimilating fungi, no carbon dioxide.

In the vinous fermentation 94 to 95 per cent of the sugar breaks up into alcohol and carbon dioxide,

$$C_6H_{12}O_6 = 2C_2H_6O + 2CO_2,$$

with 2·5 to 3·6 per cent glycerol, $C_3H_5(OH)_3$, and 0·4 to 0·7 per cent succinic acid, $C_4H_6O_4$, as invariable by-products. In addition to these, most of the higher homologues of ethyl alcohol are also formed—the so-called *fusel oil*—the latter resulting largely from the presence of foreign micro-organisms.

The chief constituent of fusel oil is fermentation amyl alcohol (isobutyl carbinol), $C_5H_{11}OH$, but it has also been proved to contain the two propyl alcohols (chiefly isopropyl), normal, iso, and tertiary butyl alcohols, normal and active amyl alcohols, together with higher homologues and esters. They can be separated by means of their hydrobromic esters.

Conditions of Fermentation.—Fermentation can only go on between the limits of 3° and 35°, the most favourable temperature being between 25° and 30°. The solution must not be too concentrated, as the organism cannot live in a solution of alcohol of greater concentration than 14 per cent; the presence of air is not strictly necessary, but it has a favouring influence.

Yeast loses its activity upon the addition of any reagents which destroy the cells, also when it is thoroughly dried, when heated to 60°, when treated with alcohol, acids, and alkalis; the addition of small quantities of salicylic acid, phenol, corrosive sublimate, &c., also prevents fermentation.

For a number of years it was thought that the presence of the living yeast plant, or of some other similar organism, was essential for the production of alcoholic fermentation. The recent work of *E. Buchner* (B. 1897, **32**, 2086, 2372; 1898, **33**, 971, 2764) has shown that the fermentation is brought about by an enzyme called *Zymase*, which is contained in the cell. If the yeast cells are crushed with "Kieselguhr" (a siliceous earth) and water, so that the cell walls are broken, and the mass then filtered through a Chamberland filter under considerable pressure, an extract is obtained which, although practically free from yeast cells, can yet induce alcoholic fermentation. The zymase is relatively unstable and easily decomposed, *e.g.* when the solution is heated or even kept for some time, but it may be preserved by the addition of certain antiseptic substances, such as chloroform, thymol, &c., which readily kill the yeast plant itself. (Compare Chap. XLVIII.)

Buchner's researches indicate that fermentations induced by organized ferments are probably due to certain unorganized ferments (enzymes) contained in the cells of the organism

The following materials are used for the preparation of alcohol or of liquids containing alcohol:—

(*a*) Grape-sugar, fruit-sugar, *i.e.* grapes and other ripe fruits, for wine, &c (*b*) Cane or beet sugar and molasses for brandy. Solutions of cane-sugar are fermented by yeast, since ordinary yeast always contains small amounts of an enzyme (*invertase*), which can hydrolyse cane-sugar to glucose and fructose:

$$C_{12}H_{22}O_{11} + H_2O = C_6H_{12}O_6 + C_6H_{12}O_6$$

and these are then directly fermented by the yeast organism. (*c*) The starch of cereals for beer and corn brandy, and of potatoes for potato brandy. The starch is first converted into malt-sugar and dextrine under the influence of diastase, or into grape-sugar, by boiling with dilute acids, and these sugars are then fermented.

The transformation of starch into malt-sugar (maltose) and dextrine is a typical example of fermentation by an *enzyme*, the special enzyme in this case being *diastase*, a complex organic nitrogen derivative produced during the germination of the

barley in the process of malting. The transformation of the starch into maltose, &c., is in reality a process of hydrolysis induced by the ferment. The maltose $C_{12}H_{22}O_{11}$ in its turn is hydrolysed by a second ferment (*maltase*) to grape-sugar, $C_6H_{12}O_6$, which is then transformed into alcohol and carbon dioxide.

A wine of medium strength contains 8½ to 10 per cent alcohol, port wine 15 per cent, sherry up to 21 per cent, champagne 8 to 9 per cent, and beer an average of 2 to 6 per cent.

The different varieties of brandy or spirits obtained by "burning", *i.e.* by distilling fermented liquids, contain 30 to 40 per cent alcohol, and cognac even over 50 per cent.

Purification of alcohol. It is difficult to separate alcohol completely from water by distillation, since their boiling-points are only 22° apart from one another. Even after repeated rectification the distillates are found to contain water. The same reason applies to the difficulty of separating alcohol from its higher homologues (fusel oil). From an alcohol containing 30 per cent of water the fusel oil can be extracted by chloroform.

On the large scale this separation is excellently effected by the use of dephlegmators or fractionating columns, which are based upon the principle of partial volatilization and partial cooling of the vapours (*Adam* and *Berard*; improved by *Savalle*, *Pistorius*, *Coffey*, and others). In this way an alcohol containing 98 to 99 per cent can be obtained.

Aqueous alcohol can be deprived of the greater part of its water by the addition of strongly heated carbonate of potash or anhydrous copper sulphate, or by distillation over quicklime, and the last portions can be extracted by baryta, or by several additions of metallic calcium and repeated distillation. Alcohol containing water becomes turbid on being mixed with benzene, carbon bisulphide, or liquid paraffin oil, and it gives a white precipitate of $Ba(OH)_2$ on the addition of a solution of BaO in absolute alcohol, and is capable of restoring the blue colour to anhydrous copper sulphate. Alcohol free from water is termed *absolute* alcohol. Ordinary absolute alcohol usually contains at least 0·2 per cent of water.

Contraction takes place on mixing alcohol and water together, 53·9 volumes alcohol + 49·8 volumes water giving, not 103·7, but 100 volumes of the mixture. The percentage of alcohol in any spirit is determined either from its specific

gravity by reference to a specially-calculated table, or by areometers of particular construction, or by its vapour tension as estimated by *Geissler's* vaporimeter.

Properties.—It is a colourless mobile liquid with characteristic spirituous odour; boils at 78·3°, or at 13° under 21 mm. mercury pressure Solidifies at −112·3°, and has sp. gr. 0·79 at 15°. It burns with an almost non-luminous flame, is exceedingly hygroscopic, and miscible with water and with ether in all proportions. Forms several cryo-hydrates with water (+12 Aq., +3 Aq., +$\frac{1}{3}$ Aq.). Is an excellent solvent for many organic substances such as resins and oils, and also dissolves sulphur, phosphorus, &c., to some extent. With concentrated sulphuric acid it yields, according to the conditions, ethyl hydrogen sulphate, ether, or ethylene. It diffuses through porous membranes into a dry atmosphere more slowly than water, and coagulates albumen, being therefore used for preserving anatomical preparations.

It is very readily oxidized by the oxygen of the air, either in presence of finely-divided platinum or in dilute solutions in presence of certain ferments, first to aldehyde and then to acetic acid; thus, beer and wine become sour, but not the pure alcohol itself. $K_2Cr_2O_7$ or $MnO_2 + H_2SO_4$ oxidize it in the first instance to aldehyde; fuming nitric acid attacks it with explosive violence, yielding numerous products; but, by the action of colourless concentrated HNO_3, ethyl nitrate can be obtained under suitable conditions; in dilute solution glycollic acid is formed. Alkalis also induce a gradual oxidation in the air; thus, alcoholic potash or soda solutions quickly become brown with formation of aldehyde resin, this latter resulting from the action of the alkali upon the aldehyde first produced. Alcoholic potash therefore frequently acts as a reducing agent, *e.g.* upon aromatic nitro-compounds. (See these.) Chlorine and bromine first oxidize alcohol to aldehyde and then act as substituents. (See Chloral.) Chlorinated alcohols can therefore only be prepared indirectly (cf. Ethylene chlorhydrin). When the vapour of alcohol is led through a red-hot tube, H, CH_4, C_2H_4, C_2H_2, C_2H_6, $C_{10}H_8$, CO, C_2H_4O, $C_2H_4O_2$, &c., are formed.

Of the compounds containing alcohol of crystallization may be mentioned, $KOH + 2\,C_2H_6O$, $LiCl + 4\,C_2H_6O$, $CaCl_2 + 4\,C_2H_6O$, and $MgCl_2 + 6\,C_2H_6O$.

Sodium ethoxide, C_2H_5ONa, is of special importance among the alcoholates It is formed by the action of sodium upon

absolute alcohol. The crystals of $C_2H_5 \cdot ONa + 2\,C_2H_6O$, at first obtained, lose their alcohol of crystallization at 200° and change into a white powder of C_2H_5ONa. (See also *Bruhl.*) Sodium ethoxide is of especial value for syntheses, and can frequently be employed in alcoholic solution. This compound is sometimes termed sodium ethylate, but the better name is ethoxide, in order to indicate its close relationship to sodium hydroxide, NaOH.

When taken in small quantity alcohol acts as a stimulant, in larger quantity as an intoxicant. Absolute alcohol is poisonous, and quickly causes death when injected into the veins. The presence of considerable amounts of fusel oil has detrimental physiological effects.

Detection of Alcohol.—1. By the iodoform reaction* (see Iodoform), when 1 part in 2000 of water can be recognized.

2. By means of benzoyl chloride, C_6H_5COCl, which yields with alcohol the characteristically smelling ethyl benzoate, or of *p*-nitrobenzoyl chloride, which yields ethyl *p*-nitrobenzoate melting at 57°; the corresponding methyl ester melts at 97°.

Propyl alcohols, C_3H_7OH.

1. **Normal propyl alcohol**, 1-*Propanol*, $CH_3 \cdot CH_2 \cdot CH_2 \cdot OH$ (*Chancel*, 1853), is obtained from fusel oil by means of its hydrobromic ester (*Fittig*), or directly by fractionation. It has also been obtained from propionic aldehyde and propionic anhydride by reduction with sodium amalgam (*Rossi*). It is a liquid with a pleasant spirituous odour, and boils 19° higher than ethyl alcohol. It is miscible with water in all proportions, but may be salted out on addition of calcium chloride. Its *constitution* follows from that of propionic acid, into which it is converted on oxidation.

Of the higher alcohols, ***n*-butyl alcohol**, $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot OH$, may be obtained from the fusel oil formed when certain special species of yeast (*Saccharomyces ellipsoideus*) are used in the alcoholic fermentation.

Isobutyl carbinol, $(CH_3)_2 : CH \cdot CH_2 \cdot CH_2 \cdot OH$, is the chief constituent of the so-called "fermentation amyl alcohol" obtained by fractional distillation of fusel oil, the other constituent being secondary butyl carbinol,

$$C_2H_5 \cdot CH(CH_3) \cdot CH_2 \cdot OH.$$

This latter, on account of its action on polarized light, is

* Acetaldehyde, acetone, and isopropyl alcohol also give this reaction, but not methyl alcohol.

generally known as *active* (*i.e.* optically active) amyl alcohol. It is lævo-rotatory, *i e* rotates the plane of polarization to the left (cf. active valeric acid), and has $[\alpha]_D - 5{\cdot}9°$ at 20°.

Normal hexadecyl-alcohol, or **cetyl alcohol**, forms as palmitic ester the chief constituent of spermaceti. The cetyl alcohol of commerce contains, in addition, a homologous alcohol, $C_{18}H_{38}O$.

Ceryl alcohol, *Cerotin*, $C_{26}H_{53}OH$, forms as cerotic ester Chinese wax.

Melissic, or **miricyl alcohol**, $C_{30}H_{61}OH$ or $C_{31}H_{63}OH$, is present as palmitic ester in bees'-wax and in Carnauba wax, and is most conveniently prepared from the latter. The alcohols are obtained from all these esters (wax varieties) by hydrolysis with boiling alcoholic potash.

B. Monohydric Unsaturated Alcohols, $C_nH_{2n-1}OH$

These are very similar to the saturated alcohols both in physical properties and in general chemical behaviour, but are sharply distinguished from the latter by the formation of additive compounds with hydrogen, halogens, halogen hydracids, &c., *e.g.*:

$$CH_2{:}CH{\cdot}CH_2{\cdot}OH + Br_2 = CH_2Br{\cdot}CHBr{\cdot}CH_2{\cdot}OH.$$

They thus resemble the olefines owing to the presence of a double bond, and the products are saturated alcohols or their halide derivatives, the latter of which cannot be prepared directly by substitution of the alcohols These unsaturated alcohols are to be considered as olefines in which an atom of hydrogen is replaced by hydroxyl.

According to theory, the existence of alcohols which contain the hydroxy-methylene group, :CH(OH), linked to a carbon atom by a double bond, might be predicted. To this class belongs **vinyl alcohol** (*ethenol*), $CH{:}CH{\cdot}OH$, which occurs in commercial ether, but which has not yet been isolated (B. **22**, 2863), although derivatives of it are known. By the reactions in which one would expect it to be formed, its isomer, $CH_3{\cdot}CHO$ (acetaldehyde), is formed; in fact, the grouping $:C{:}CH{\cdot}OH$ is usually unstable, passing as it does into the more stable one, $:CH{\cdot}CH{:}O$, a transformation which is most readily explained upon the assumption that water is taken up and again split off. Similarly, instead of the group $CH_2{:}C(OH){\cdot}CH_3$, we always get $CH_3{\cdot}CO{\cdot}CH_3$.

Allyl alcohol (1-*Propene*-3-*ol*), $CH_2{:}CH{\cdot}CH_2OH$ (*Cahours* and *Hofmann*, 1856), is present to the extent of 0·1 to 0·2 per cent in wood spirit, and is formed (1) from allyl iodide; (2) by reduction of its aldehyde, acrolein (see this); (3) by heating glycerol, $C_3H_5(OH)_3$, with oxalic or formic acid and a little ammonium chloride to 220°. The reaction is somewhat similar to the production of formic acid, and in both cases the same product is first formed, viz. glyceryl monoformate—

$$\begin{array}{l} CH_2{\cdot}OH \\ CH{\cdot}OH \\ CH_2{\cdot}OH \end{array} \longrightarrow \begin{array}{l} CH_2{\cdot}OH \\ CH{\cdot}OH \\ CH_2{\cdot}O{\cdot}CO{\cdot}H \end{array} \longrightarrow \begin{array}{l} CH_2{\cdot}OH \\ CH \\ CH_2 \end{array}$$

and this when heated to the required temperature, 220°, decomposes into CO_2, H_2O, and allyl alcohol. Allyl alcohol is a mobile liquid of suffocating smell, having almost the same boiling-point (97°) as *n*-propyl alcohol; like the latter, it is miscible with water. It does not take up nascent hydrogen directly, but chlorine, bromine, cyanogen, hypochlorous acid, &c. If cautiously oxidized, it yields glycerol, but stronger oxidation converts it into its aldehyde, acrolein, and acid, acrylic acid, containing the same number of carbon atoms, and it is therefore a primary alcohol; hence the above *constitutional formula.*

C. Monohydric Unsaturated Alcohols, $C_nH_{2n-2}{\cdot}OH$

These alcohols are derivatives of acetylene and its homologues. The compounds possess:—(1) The characteristic properties of alcohols. (2) The properties of unsaturated compounds. Each molecule of such an alcohol can combine with 1 or 2 molecules of a halogen or halogen hydracid. (3) Most of them possess the further peculiarity of forming explosive compounds with ammoniacal copper and silver solutions, *e.g.* C_3H_2AgOH, the former being coloured yellow and the latter white; acids decompose these compounds into the unsaturated alcohol. Those of them which do not yield such metallic compounds contain, not a triple bond, but two double ones between the carbon atoms. The most important of these alcohols is—

Propargyl alcohol, or *propinyl alcohol* (1-*Propin*-3-*ol*),

$$C_3H_3OH, = CH{:}C{\cdot}CH_2OH,$$

a mobile liquid of agreeable odour, lighter than water, and boiling at 114°, *i.e.* somewhat higher than normal propyl alcohol.

For further examples of unsaturated alcohols, see Open-chain Terpenes (Chap. XLI, A).

IV. DERIVATIVES OF THE ALCOHOLS

These may be classed in the following divisions:—

A. Ethers of the alcohols, or alkyl oxides, *e.g.* $C_2H_5 \cdot O \cdot C_2H_5$, ethyl ether.

B. Thio-alcohols and ethers, or alkyl hydrosulphides and sulphides, *e.g.* $C_2H_5 \cdot SH$ and $(C_2H_5)_2S$.

C. Nitrogen bases of the alcohol radicals.

D. Other metalloid compounds of the alcohol radicals.

E. Metallic compounds of the alcohol radicals, or organo-metallic compounds.

A. Ethers Proper (Alkyl- or Alphyl-Oxides)

The ethers of the monohydric alcohols are compounds of neutral character derived from the alcohols by elimination of the elements of water (1 molecule water from 2 molecules alcohol). They can frequently be prepared by treating the alcohols with sulphuric acid, and are distinguished from the latter by not reacting with acids to form esters, and by being substituted and not oxidized by the halogens, &c. Only the lowest member of the series is gaseous, most of them are liquid, and the highest are solid. The more volatile ethers are characterized by a peculiar odour which is not shown by the higher members.

Constitution.—The hydrogen atoms cannot be replaced by sodium or other metallic radicals (see p. 18), and are all presumably attached to carbon.

Their structure as alkyl oxides, or anhydrides of monohydric alcohols (cf. metallic oxides), follows largely from modes of formation 2 and 3, from the non-reactive character of the hydrogen atoms, and from reactions 4 and 5, p. 85.

$$\begin{matrix} KOH \\ KOH \end{matrix} = K_2O + H_2O; \quad \begin{matrix} C_2H_5OH \\ C_2H_5OH \end{matrix} = \begin{matrix} C_2H_5 \\ C_2H_5 \end{matrix}\!\!>\!O + H_2O.$$

The alkyl groups contained in them may either be the same, as in ordinary ether and in methyl ether, $(CH_3)_2O$, in

which case they are termed "**simple ethers**"; or they may be different, as in methyl-ethyl ether, $CH_3 \cdot O \cdot C_2H_5$, when they are known as "**mixed ethers**".

Ethers derived from tertiary alcohols are not known.

Modes of Formation.—1. By heating the alcohols, $C_nH_{2n+1} \cdot OH$, with sulphuric acid. The reaction proceeds in two phases, *e.g.*:

(*a*) $C_2H_5 \cdot OH + OH \cdot SO_2 \cdot OH = OH \cdot SO_2 \cdot OC_2H_5 + H \cdot OH.$
(*b*) $OH \cdot SO_2 \cdot OC_2H_5 + C_2H_5 \cdot OH = OH \cdot SO_2 \cdot OH + C_2H_5 \cdot O \cdot C_2H_5.$

In phase *a* an alkyl hydrogen sulphate is formed, which, when further heated with alcohol, as in *b*, yields ether and regenerates sulphuric acid. The latter is therefore free to work anew, and in this way to convert a very large quantity of alcohol into ether.

This process is theoretically a continuous one, but practically it has its limits, through secondary reactions, such as the formation of SO_2, &c. A modification of the method consists in heating the alcohol with benzene-sulphonic acid $C_6H_5 \cdot SO_2 \cdot OH$ in place of sulphuric acid. No sulphur dioxide is formed, and the reaction becomes in reality continuous. The method is only suitable for primary alcohols; secondary and tertiary under similar conditions yield olefines. Hydrochloric, hydrobromic, and hydriodic, among other acids, act similarly to sulphuric acid; thus ether is obtained when alcohol is heated with dilute hydrochloric acid in a sealed tube to 180°, ethyl chloride, C_2H_5Cl, being formed as an intermediate product. When alcohol is heated with hydrochloric acid, a state of equilibrium is established between the alcohol, ether, ethyl chloride, hydrochloric acid, and water, after which the same quantity of each of these products is destroyed as is formed in unit of time.

2. By the action of alkyl halides on sodium-alkylate, or also upon alcoholic potash:

$$C_2H_5I + C_2H_5 \cdot ONa = C_2H_5 \cdot O \cdot C_2H_5 + NaI.$$

3. From alkyl halides and dry silver oxide, Ag_2O (also HgO and Na_2O):

$$2\,C_2H_5I + Ag_2O = C_2H_5 \cdot O \cdot C_2H_5 + 2\,AgI.$$

Modes of formation 1 and 2 yield mixed as well as simple ethers, *e.g.*:

$$C_2H_5 \cdot SO_4H + CH_3 \cdot OH = C_2H_5 \cdot O \cdot CH_3 + H_2SO_4.$$
$$C_6H_{11}I + CH_3 \cdot ONa = C_6H_{11} \cdot O \cdot CH_3 + NaI.$$

Properties. — 1. The ethers are very stable, *e.g.* ammonia, alkalis, dilute acids, and metallic sodium have no action upon them, nor has phosphorus pentachloride in the cold.

2. When superheated with water in presence of some acid, such as sulphuric, the ethers take up water and are retransformed into alcohols, the secondary more readily than the primary; this change also proceeds, but extremely slowly, at the ordinary temperature.

3. When warmed with concentrated sulphuric acid, alcohol and ethyl hydrogen sulphate are formed:

$$C_2H_5 \cdot O \cdot C_2H_5 + H\,HSO_4 = C_2H_5 \cdot OH + C_2H_5 \cdot HSO_4.$$

4. When saturated with hydriodic acid gas at 0°, the ethers yield alcohol and alkyl iodide:

$$C_2H_5 \cdot O \cdot C_2H_5 + HI = C_2H_5 \cdot OH + C_2H_5I.$$

When the ethers are "mixed", the iodine attaches itself to the smaller alkyl group; further interaction yields, of course, two molecules of alkyl iodide.

5. When heated with phosphorus halides the oxygen atom is replaced by two halogen atoms, and two molecules of an alkyl halide are formed.

6. Like the alcohols, the ethers are oxidized by nitric and chromic acids, but halogens substitute in them and do not oxidize; in this latter respect they resemble the hydrocarbons.

7. Many ethers form definite compounds with acids, especially complex acids like $H_4FeC_6N_6$ (B. 1901, **34**, 2688), also with bromine, with metallic salts, &c. (J. C. S. 1904, 85, 1106; Proc. 1904, 165).

Ethyl ether, Ethane-oxy-ethane, "*Ether*" $(C_2H_5)_2O$, was discovered by *Valerius Cordus* about 1544, and possibly before that time by *Raymond Lully*. It was also called "sulphuric ether", and "vitriol ether", on account of its being supposed to contain sulphur. Its composition was established by *Saussure* in 1807, and *Gay-Lussac* in 1815.

Preparation.—By the continuous process from ethyl alcohol and sulphuric acid at 140°, with gradual addition of the alcohol, according to *Boullay*. It is freed from alcohol by shaking with water, and dried by distillation over lime or calcium chloride, and finally over metallic sodium.

Theories of the Formation of Ether.—At first the action of the sulphuric acid was considered to consist in an abstraction of water. Later on, it was thought that the acid gave rise to

a contact action (*Mitscherlich, Berzelius*), but *Liebig* showed that this view was incorrect, since ethyl hydrogen sulphate is formed. *Liebig* assumed that the ethyl hydrogen sulphate decomposed, when heated, into ether and SO_3; but *Graham*, on the other hand, proved that the acid gives no ether when heated alone to 140°, but only when heated along with more alcohol.

After this, *Williamson* propounded the theory of etherification at present held, a theory based on the opinion of *Laurent* and *Gerhardt* that ether contains two ethyl radicals. Its correctness was proved by mode of formation 2, and also by the preparation of mixed ethers.

Properties.—It is a mobile liquid with powerful ethereal odour, and is very volatile, even at the ordinary temperature. It melts at −113°, boils at +34·9°, has specific gravity = 0·72 at 17·4°, and at 120° has a vapour pressure of 10 atmospheres. It produces considerable lowering of temperature when evaporated. It is easily inflammable, and therefore dangerous as a cause of fire, from the dissemination of its very heavy vapour; a mixture of it with oxygen or air is explosive. It is somewhat soluble in water (1 part in 10), and, conversely, 3 volumes of water dissolve in 100 volumes of ether; the presence of water can be detected by the milkiness which ensues upon the addition of carbon disulphide. Ether is an excellent solvent or extractive for many organic substances, and also for I_2, Br_2, CrO_3, $FeCl_3$, $AuCl_3$, $PtCl_4$, and other chlorides. It forms crystalline compounds with various substances, *e.g.* the chlorides and bromides of Sn, Al, P, Sb, and Ti, being present in them as "ether of crystallization".

When dropped upon platinum black it takes fire, and when poured into chlorine gas an explosion results, hydrochloric acid being set free. In the dark, however, and in the cold, substitution by chlorine is possible; the final product of the substitution, **perchloro-ether**, $C_4Cl_{10}O$, is solid and smells strongly like camphor.

Ether was first employed as an anæsthetic by *Simpson* in 1848, but this property had been previously observed by *Faraday*. It is further used as an extractive in the colour industry, as *Hofmann's* drops when mixed with 1 to 3 volumes of alcohol, for ice machines, and for the preparation of collodion, &c.

Methyl ether, $(CH_3)_2O$ (*Dumas, Péligot*), closely resembles common ether, is gaseous at the ordinary temperature, but

liquid under $-20°$, and is prepared on the large scale for the production of artificial cold.

Ethyl-cetyl- and **dicetyl ethers** are solid at the ordinary temperatures.

Several ethers with unsaturated alcohol radicals are also known, *e.g.* **allyl ether**, $(C_3H_5)_2O$, and **vinyl-ethyl ether**, $C_2H_3 \cdot O \cdot C_2H_5$. B.-pt. 35°·5. These can combine directly with bromine.

Isomers.—The general formula of the saturated ethers is $C_nH_{2n+2}O$. Isomeric with each ether is a saturated alcohol, thus C_2H_6O = methyl ether or ethyl alcohol, $C_4H_{10}O$ = di-ethyl ether or butyl alcohol. From $C_4H_{10}O$ on, however, several different isomeric ethers are not only possible, but are also known, *e.g.* di-ethyl ether, $(C_2H_5)_2O$, is isomeric with methyl-propyl ether, $CH_3 \cdot O \cdot C_3H_7$; similarly methyl-amyl ether, $CH_3 \cdot O \cdot C_5H_{11}$, ethyl-butyl ether, $C_2H_5 \cdot O \cdot C_4H_9$, and dipropyl-ether, $C_3H_7 \cdot O \cdot C_3H_7$, are all isomeric. Isomerism of this kind depends upon the fact that the alkyl radicals—and hydrogen—are homologous, so that if the numbers of carbon atoms are equal, so also must be the numbers of hydrogen.

Such isomerism in which the compounds belong to the same class and differ only in the nature of the alkyl group present is termed **metamerism**.

The determination of the *constitution* of the ethers is based upon (*a*) their syntheses according to modes of formation 1 or 2, and (*b*) their decomposition by HI according to Reaction 4.

Varieties of Isomerism.—The cases of isomerism which have been mentioned up to now are of three kinds. The first was the isomerism of the higher paraffins, which, since it is based upon the dissimilarity of the carbon chains, is often termed **chain-isomerism**. The isomerism between ethylene and ethyl-idene chlorides or between primary and secondary propyl alcohols depends upon the differences in position of the substituting halogen or hydroxyl in the same carbon chain, and is termed **position isomerism**. In addition to these there is the third kind, **metamerism**. Further cases will be spoken of under the Benzene derivatives.

B. Thio-alcohols and -ethers

The relationship between oxygen and sulphur, indicated by their positions in the periodic classification of the elements, is supported by a study of their carbon derivatives. We have

a group of sulphur compounds analogous to the monohydric alcohols. These are known as thio-alcohols or "thiols". Similarly a group corresponding with the ethers is known as the thio-ethers or alkyl sulphides. These are liquids of a most unpleasant and piercing odour, something like that of leeks; they are nearly insoluble in water, and the lower members are very volatile. The higher homologues are not so soluble in water, but continue to be soluble in alcohol and ether, and their smell is less strong on account of the rise in the boiling-point. They are readily inflammable.

The **thio-alcohols**, also called **mercaptans** or **alkyl hydrosulphides**, *e.g.* mercaptan, ethan-thiol, $C_2H_5 \cdot SH$, although of neutral reaction, possess the chemical characters of weak acids and are capable of forming salts, the "mercaptides", especially mercury compounds. The name "mercaptan" is derived from "corpus mercurio aptum". They are soluble in a strong solution of potash, and their boiling-points are distinctly lower than those of the corresponding alcohols. The **thio-ethers**, also termed **alkyl sulphides**, *e.g.* ethyl sulphide, $(C_2H_5)_2S$, are on the other hand neutral volatile liquids without acid character.

Both classes of compounds are derived from hydrogen sulphide by the replacement of either one or both atoms of hydrogen by alkyl groups, just as alcohol and ether are derived from water:

$$\left.\begin{matrix}H\\H\end{matrix}\right\}S. \qquad \left.\begin{matrix}C_2H_5\\H\end{matrix}\right\}S. \qquad \left.\begin{matrix}C_2H_5\\C_2H_5\end{matrix}\right\}S$$

The boiling-points are methyl mercaptan 6°, ethyl mercaptan 36°, methyl sulphide 37°, ethyl sulphide 92°.

The *constitution* of these compounds follows at once from their modes of formation.

Formation.—The mercaptans may be obtained—

1. By warming an alkyl halide or sulphate with potassium hydrosulphide in concentrated alcoholic or aqueous solution:

$$C_2H_5Br + KSH = C_2H_5 \cdot SH + KBr.$$

2. By heating alcohol with phosphorus pentasulphide, the oxygen being thus replaced by sulphur (*Kekulé*).

The thio-ethers are similarly obtained—

1. From an alkyl halide or potassium alkyl sulphate and normal potassium sulphide:

$$2C_2H_5 \cdot SO_4K + K_2S = (C_2H_5)_2S + 2K_2SO_4.$$

2. By treating ethers with phosphorus pentasulphide

"Mixed sulphides", comparable with the "mixed ethers", can also be prepared, *e.g.* methyl-ethyl sulphide, $C_2H_5 \cdot S \cdot CH_3$.

Behaviour.—A. **The Mercaptans.**

1. Sodium and potassium act upon the mercaptans to form sodium and potassium salts, white crystalline compounds, which are decomposed by water. The mercury salts are obtained by warming an alcoholic solution of mercaptan with mercuric oxide, *e g* **mercuric mercaptide**, $Hg(C_2H_5S)_2$ (white plates). With mercuric chloride sparingly soluble double compounds are formed, *e.g.* $(C_2H_5 \cdot S)Hg \cdot Cl$, a white precipitate. The lead salts are yellow-coloured, and are formed when alcoholic solutions of a mercaptan and of lead acetate are mixed

2 When oxidized with nitric acid the mercaptans are transformed into **alkyl-sulphonic acids**:

$$C_2H_5 \cdot SH + 3O = \begin{matrix} C_2H_5 \\ HO \end{matrix} \!\!>\!\! S \!\!<\!\! \begin{matrix} O \\ O \end{matrix} \text{ (ethyl-sulphonic acid).}$$

3. The mercaptans in the form of sodium salts are oxidized by iodine or by sulphuryl chloride, SO_2Cl_2 (B **18**, 3178), and also frequently in ammoniacal solution in the air to **disulphides**, *e.g* **ethyl disulphide**, $(C_2H_5)_2S_2$, thus:—

$$2\,C_2H_5S \cdot Na + I_2 = C_2H_5 \cdot S \cdot S \cdot C_2H_5 + 2\,NaI.$$

These are disagreeably-smelling liquids, which have much higher boiling-points than the mercaptans. They are reduced by nascent hydrogen, and with nitric acid yield **disulphoxides**, *e.g.* **ethyl disulphoxide**, $(C_2H_5)_2S_2O_2$.

B **The Thio-ethers.**—1. They yield additive compounds with metallic salts, *e.g.* $(C_2H_5)_2S$, $HgCl_2$, which can be crystallized from ether.

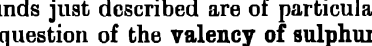
2. They are capable of combining with halogen or oxygen. Thus ethyl sulphide forms with bromine a **dibromide**, $(C_2H_5)_2S:Br_2$, crystallizing in yellow octohedra, and with dilute nitric acid, **diethyl sulphoxide**, $(C_2H_5)_2S:O$, a thick liquid soluble in water, which combines further with nitric acid to the compound, $(C_2H_5)_2SO$, HNO_3. Concentrated nitric acid or potassic permanganate oxidizes the sulphides or sulphoxides to **sulphones**, *e.g.* ethyl sulphide to **(di)-ethyl sulphone**, $(C_2H_5)_2SO_2$, and methyl-ethyl sulphide to **methyl-ethyl sulphone**, $(CH_3)(C_2H_5)SO_2$. The sulphones are solid well-characterized compounds which boil without decomposition.

The sulphoxides are reduced by nascent hydrogen to sulphides, but not the sulphones.

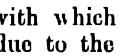
3. The behaviour of the sulphides towards the alkyl haloids is of especial interest. Thus the substances $(CH_3)_2S$ and CH_3I combine even in the cold to the white crystalline **trimethyl-sulphine iodide**, $(CH_3)_3SI$, or **trimethyl-sulphonium iodide**, as it is now generally called in order to emphasize its similarity to the ammonium salts; this is soluble in water, and when heated is resolved into its components. It behaves exactly like a salt of hydriodic acid, and yields with moist silver oxide —(but not with alkali)—an oily base, **trimethyl-sulphonium hydroxide**, $(CH_3)_3S \cdot OH$, which cannot be volatilized without decomposition. This is as strong a base as caustic potash, and resembles the latter so closely that it absorbs carbon dioxide, cauterizes the skin, drives out ammonia, and gives salts with acids even with hydrogen sulphide; these latter closely resemble the alkali sulphides, *e.g.* they dissolve Sb_2S_3 (*Oefele*, 1833; *Cahours*).

The compounds just described are of particular interest with regard to the question of the **valency of sulphur**.

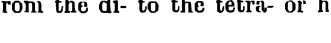
The readiness with which these sulphur compounds are oxidized, and the ease with which they yield additive compounds, is undoubtedly due to the readiness with which the S atom passes from the di- to the tetra- or hexa-valent state; for example:—



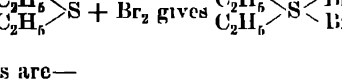
The sulphoxides are—



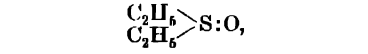
the sulphones—



the sulphonic acids—



and the sulphonium compounds—



Since in ethyl sulphide both the alkyl radicals are bound to the sulphur, this will also be the case in ethyl sulphone, otherwise the sulphones would manifestly be easily saponifiable. (See Ethyl-hydrogen sulphite.) The sulphonium hydroxides also can only be explained very insufficiently as molecular compounds, on the assumption of the divalence of sulphur. The formula $(CH_3)_2S + CH_3OH$ for trimethylsulphine hydroxide does not indicate in the least the strongly basic character of this substance, since it is not explicable why the mere addition of the neutral methyl alcohol to the equally neutral methyl sulphide should produce such an effect.

With respect to **isomers**, the same general conditions prevail in the sulphur as in the corresponding oxygen compounds.

SULPHIDES OF UNSATURATED ALCOHOL RADICALS

Allyl sulphide, $(C_3H_5)_2S$ (*Wertheim*, 1844), present in the oil of *Allium sativum*—oil of garlic,—in *Thlaspi arvense*, &c, may be prepared from allyl iodide and K_2S (*Hofmann*, *Cahours*). B.-pt. 140°.

Analogous **alkyl selenium** and **tellurium compounds** are also known. They are in part distinguished by their excessively disagreeable, nauseous, and persistent odour.

C. Esters of the Alcohols with Inorganic Acids and their Isomers

The esters or alkyl salts may be considered as derived from the acids (see p. 74) by the exchange of the replaceable hydrogen of the latter for alkyl radicals, just as metallic salts result by exchanging the hydrogen for a metallic radical:

HNO_3. KNO_3. $(C_2H_5)NO_3$.

Or they are derived from the alcohols by exchange of the hydroxyl radical for acid radicals, *e.g.* $C_2H_5 \cdot NO_3$, ethyl nitrate; $C_2H_5 \cdot SO_4H$, ethyl hydrogen sulphate; and $C_2H_5 \cdot Cl$, ethyl chloride.

Monobasic acids yield only one kind of ester, "**neutral** or **normal esters**", which are analogous to the normal metallic salts of those acids.

Dibasic acids yield two series of esters—(1) **acid esters** and (2) **neutral esters**—corresponding respectively with acid and normal salts, thus, $C_2H_5 \cdot HSO_4$ and $(C_2H_5)_2 : SO_4$ are the acid

and normal ethyl esters of sulphuric acid. Tribasic acids yield three series of esters, &c.

The composition of the esters or alkyl salts is therefore exactly analogous to that of metallic salts, so that in the definition of polybasic acids their behaviour in the formation of esters may also be included.

The normal esters are mostly liquids of neutral reaction, and often of very agreeable odour, with relatively low boiling-points, and volatilize, eventually in a vacuum, without decomposition. Most of them are very sparingly soluble in water. The acid esters, also called ester-acids, on the other hand, are of acid reaction, without smell, usually very readily soluble in water, much less stable than the neutral esters, and not volatile without decomposition. They act as acids, *i.e.* form salts and esters.

All esters are able to combine with water, and are by this means resolved again into their components, namely, alcohol and acid, *e.g.*—

$$C_2H_5NO_3 + H_2O = C_2H_5OH + HNO_3.$$

This process occurs when the ester is boiled with alkalis or acids, or when heated with steam to over 100°, *e.g.* 150°–180°, and is termed **hydrolysis**, or *saponification*, when alkalis are used (see Soaps, p. 158). The reaction is usually conducted in a flask fitted with a reflux condenser, but in a few cases the reaction takes place when the ester is mixed with water at the ordinary temperature.

General Modes of Formation.—1. The simplest method for obtaining an ester is by the action of the acid on the alcohol, water always being formed as a by-product. As the reactions are reversible,

$$C_2H_5\cdot OH + O{:}N\cdot OH \rightleftarrows C_2H_5\cdot O\cdot N{:}O + H\cdot OH,$$

it is essential that the water formed should be removed from the sphere of action by the aid of concentrated sulphuric acid, fused zinc chloride, &c., or that a large excess of acid should be employed, otherwise after a short time a state of chemical equilibrium is reached, all four compounds are present, and the direct and reverse reactions are proceeding at the same rate; even prolonged heating will then not transform any further amounts of acid and alcohol into ester.

Esters are therefore often prepared by adding an excess of

concentrated sulphuric acid to a mixture of the alcohol and sodium salt of the acid

2. The alcohol is heated with the acid chloride, thus.—

$$\begin{matrix}O\\O\end{matrix}\!\!\gg\!S\!<\!\begin{matrix}Cl\\Cl\end{matrix} + 2\,C_2H_5\cdot OH = \begin{matrix}O\\O\end{matrix}\!\!\gg\!S\!<\!\begin{matrix}OC_2H_5\\OC_2H_5\end{matrix} + 2\,HCl.$$

3. The silver salt of the acid is heated with an alkyl iodide; this is a method of very general application, although it often leads to isomers of the expected ester (see also p. 94):

$$C_2H_5\cdot I + O{:}N\cdot OAg = O{:}N\cdot OC_2H_5 + AgI.$$

Besides the true esters, there are also included in this division several other classes of acid derivatives isomeric with them, but distinguished from them by not being readily hydrolysed, *i.e.* by being more stable, *e.g.* nitro-compounds, sulphonic and phosphinic acids, &c. The hydrocyanic derivatives of the alcohols will also be described here for the sake of convenience These, also, are not hydrolysed in the normal manner into alcohol and acid, but are decomposed in quite a different manner.

ESTERS OF NITRIC ACID

Methyl nitrate, $CH_3\cdot O\cdot NO_2$, is a colourless liquid, boiling at 66°. **Ethyl nitrate**, $C_2H_5\cdot O\cdot NO_2$ (*Millon*), is a mobile liquid of agreeable odour and sweet taste, but with a bitter after-taste; it boils at 86°, and burns with a white flame. Both esters are soluble in water. The latter is prepared directly from the alcohol and acid, with the addition of urea in order to destroy any nitrous acid as fast as it is formed.

Nitric esters contain a large proportion of oxygen in a form in which it is readily given up; they therefore explode when suddenly heated. They are very readily hydrolysed to nitric acid and the alcohol when boiled with alkalis Tin and hydrochloric acid reduce them to hydroxylamine.

$$C_2H_5\cdot O\cdot N\!<\!\begin{matrix}O\\O\end{matrix} + 6\,H = C_2H_5\cdot OH + H_2N\cdot OH + H_2O.$$

These two reactions indicate that the nitrogen atom is not directly united to carbon, as it is so readily removed either as nitric acid or as hydroxylamine.

DERIVATIVES OF NITROUS ACID

The compound $C_2H_5O_2N$ exists in two isomeric forms, represented by the formulæ $C_2H_5 \cdot O \cdot N:O$ and $C_2H_5 \cdot N\leqslant^{O}_{O}$. The former is termed ethyl nitrite, as it is the true ester of nitrous acid, $H \cdot O \cdot N:O$; the isomeride is termed nitro-ethane, as it contains the nitro group $\cdot N\leqslant^{O}_{O}$ attached to carbon.

α. **Alkyl nitrites.**—These are obtained by the action of nitrous fumes (from arsenious oxide and nitric acid), or of potassium nitrite and sulphuric acid, or of copper and nitric acid upon the alcohols. They are neutral liquids of aromatic odour, with very low boiling-points, and are readily hydrolysed to the corresponding alcohol and acid. When reduced they yield the alcohol, ammonia, and water.

Methyl nitrite is a gas; **ethyl nitrite** boils at 18°, has a characteristic odour, and in the impure state, as obtained from alcohol, copper, and nitric acid, is used medicinally under the name of "sweet spirits of nitre".

Amyl nitrite, $C_5H_{11} \cdot O \cdot N:O$, is a pale-yellow liquid boiling at 96°, and is used in medicine; it produces expansion of the blood-vessels and relaxation of the contractile muscles

β. **The Nitro-derivatives** are colourless liquids of ethereal odour, practically insoluble in water, and boiling at temperatures some 100° higher than their isomers. Like the latter they distil without decomposition, and occasionally explode when quickly heated. They are fundamentally distinguished from the alkyl nitrites by not being readily hydrolysed, and by yielding amino-compounds (see these) on reduction, the nitrogen remaining attached to carbon:

$$CH_3 \cdot N\leqslant^{O}_{O} + 6\,H = CH_3 \cdot NH_2 + 2\,H_2O.$$

Nitro-methane boils at 99°–101°. **Nitro-ethane,** $C_2H_5 \cdot NO_2$ (*V. Meyer* and *Stuber*, 1872), boils at 113°–114°, burns with a bright flame, and the vapour does not explode even at a high temperature.

Formation.—1. The nitro-compounds may be obtained by treating an alkyl iodide with solid silver nitrite (*V. Meyer*). When methyl iodide is used nitro-methane alone is formed, with ethyl iodide about equal weights of nitro-ethane and ethyl nitrite, and the higher homologues in regularly decreas-

ing amounts as compared with those of their isomers, from which, however, they may be readily separated by distillation. Tertiary alkyl iodides do not yield nitro-compounds:

$$CH_3I + AgNO_2 = CH_3 \cdot NO_2 + AgI.$$

Nitromethane is most readily prepared by the action of sodium nitrite solution on sodium chloroacetate, carbon dioxide being eliminated

2. The nitro-derivatives of the lower paraffins cannot be obtained by the direct action of nitric acid on the hydrocarbons, but with some of the higher derivatives this is possible, *e.g.* heptane, octane, &c. With decane a 30-per-cent yield of a mono nitro-derivative may be obtained by means of fuming nitric acid. (*Worstall*, Am. 1898, **20**, 202; 1899, **21**, 211; *Konowaloff*, Abs. 1905, i, 764, 1907, **1**, 1.) This method is largely employed in the aromatic series (see Nitrobenzene).

The *constitution* of the nitro-compounds is based on the fact that they are not readily hydrolysed, and that the nitrogen is not removed during reduction, but remains directly bound to carbon in the resulting amines (see these). Consequently the nitrogen of the nitro-compound is directly joined to the alkyl radical *i.e.* to carbon, for instance

$$CH_3 \cdot N\langle \overset{O}{\underset{O}{|}}, \text{ or more probably } CH_3 \cdot N\langle \overset{O}{\underset{O}{\diagdown\!\!\diagup}}$$

Nitrogen which is attached directly to an alkyl radical is therefore not removed by hydrolysing agents Since the nitrogen of the isomeric alkyl nitrites, on the other hand, is easily split off from the alkyl radical either by hydrolysis or by reduction, it is manifestly not directly combined with the carbon but with the oxygen The alkyl nitrites, therefore, receive the constitutional formula $R \cdot O \cdot N:O$, where R represents the alkyl radical

From this follows for the hypothetical hydrated nitrous acid the formula $H \cdot O \cdot N:O$, and for the anhydride the formula $(NO)_2O$. The aromatic hydrocarbons, *e.g.* benzene, C_6H_6, yield with nitric acid nitro-compounds, thus:—

$$C_6H_5 \cdot H + HNO_3 = C_6H_5 \cdot NO_2 + H_2O.$$

Nitric acid, therefore, contains a nitro-group bound to hydroxyl, corresponding with the formula $H \cdot O \cdot NO_2$.

Behaviour.—1. They yield primary amines with acid reducing agents, *e.g.* iron and acetic acid, tin and hydrochloric acid,

&c., substituted hydroxylamines being formed as intermediate products (*V. Meyer*, B. 1892, **25**, 1714).

2. **Primary** ($\cdot CH_2 \cdot NO_2$) and **secondary** ($:CH \cdot NO_2$) nitro-compounds can yield metallic derivatives, and hence possess certain acidic properties. For example, nitro-methane and nitro-ethane react with alcoholic sodium hydroxide, yielding sodium compounds, $CH_2Na \cdot NO_2$ and $CH_3 \cdot CHNa \cdot NO_2$. It is almost certain that these sodium salts are not true derivatives of the nitro-compound, but are derived from an isomer, the so-called *iso-nitro*-compound $CH_2 : N \overset{O}{\underset{O \cdot H}{\swarrow}}$, and thus sodic nitro-methane has the constitutional formula $CH_2 : NO \cdot ONa$ (*Hollemann*, B. 1900, **33**, 2913). The nitro-derivatives are thus not true acids, but *pseudo acids* (*Hantzsch*, B. 1899, **32**, 577; see also Phenylnitromethane). These sodium salts are crystalline solids, and are highly explosive.

Tertiary nitro-compounds ($:C \cdot NO_2$) contain no hydrogen joined to the carbon atom which is united to the nitro-group, and they have not an acid character, the acidifying influence of the nitro-group does not, therefore, extend to those hydrogen atoms which are attached to other carbon atoms.

The hydrogen in the primary and secondary nitro-derivatives, which is attached to the same carbon atom as the NO_2 group, can also be replaced by bromine. So long as hydrogen, as well as this bromine and the nitro-group, remains joined to the carbon atom in question, the compound is of a strongly acid character; but when it also is substituted by bromine, the compound becomes neutral, *e.g.* dibromo-nitro-ethane, $CH_3 \cdot CBr_2 \cdot NO_2$, is neutral.

The reactivity of the hydrogen atoms of the $-CH_2 \cdot NO_2$ and $>CH \cdot NO_2$ groups, characteristic of primary and secondary nitro-compounds, is exemplified in the reactions of these compounds with aldehydes in the presence of sodium carbonate. A primary nitro-compound can combine with one or with two molecules of formaldehyde, yielding compounds of the types $-CH(NO_2)CH_2 \cdot OH$ and $-C(NO_2)(CH_2 \cdot OH)_2$.

3. The primary nitro-compounds yield, with concentrated hydrochloric acid at 140°, acids of the acetic series containing an equal number of carbon atoms, and hydroxylamine.

4. The reaction of the nitro-compounds with nitrous acid is very varied. The primary yield **nitrolic acids** and the

secondary **pseudo-nitrols**, while the tertiary do not react with it at all. Thus from nitro-ethane, $CH_3 \cdot C \lessdot^{H_2}_{NO_2}$, **ethyl-nitrolic acid**, $CH_3 \cdot C \lessdot^{N \cdot OH}_{NO_2}$, an acid crystallizing in light-yellow crystals and yielding intensely red alkali salts, is formed. Normal nitro-propane acts similarly. Secondary nitro-propane, $(CH_3)_2 : CH \cdot NO_2$, gives, on the contrary, **propyl-pseudo-nitrol**, $(CH_3)_2C(NO)(NO_2)$, a white crystalline, indifferent, non-acid substance, which is blue either when fused or when in solution. These reactions, which are only given with compounds of low molecular weight (in the primary up to C_8, and in the secondary up to C_5), are specially applicable for distinguishing between the primary, secondary, or tertiary nature of an alcohol (see p. 74) The nitro-hydrocarbons, which are readily prepared from the iodides, are dissolved in a solution of potash to which sodium nitrite is added, the solution acidified with sulphuric acid and again made alkaline, and then observed for the production of a red coloration (primary alcohol), a blue coloration (secondary alcohol), or no coloration (tertiary alcohol).

Chloropicrin, CCl_3NO_2, a heavy liquid of excessively suffocating smell, b.-pt 112°, is formed from many hydrocarbon compounds by the simultaneous action of nitric acid and chlorine, chloride of lime, &c. It is best obtained from picric acid and bleaching-powder.

Polynitro-derivatives are also known **Dinitromethane**, $CH_2(NO_2)_2$, an unstable yellow oil, **dinitroethane**, $CH_3 \cdot CH(NO_2)_2$, obtained from $CH_3 \cdot CHBr \cdot NO_2$ and potassium nitrite, b.-pt. 185°, **trinitromethane** or **nitroform**, $CH(NO_2)_3$, colourless crystals, m.-pt. 15°, **tetranitromethane**, $C(NO_2)_4$, colourless crystals, m.-pt. 13° and b.-pt 126°, is prepared by the action of nitric acid (D = 1·53) on acetic anhydride (*Chattaway*, J. C. S. 1910, 2100). Good yields (50 per cent) of dinitro-compounds of the type $NO_2 \cdot [CH_2]_n \cdot NO_2$ can be obtained from the corresponding di-iodo-derivatives and silver nitrite (*Von Braun* and *Sobecki*, B. 1911, **44**, 2526) provided $n > 3$. The compounds are stable and react with bromine, nitrous acid, &c., in much the same manner as mono-nitro-compounds They are accompanied by alkylene dinitrites, $O:N \cdot O[CH_2]_n \cdot O \cdot N:O$, and nitro-nitrites, $NO_2 \cdot [CH_2]_n \cdot O \cdot N:O$, from which they can be separated by fractional distillation. The dinitro-compounds can be used for the preparation of dialdehydes, since when

reduced with stannous chloride they yield dioximes, and these on hydrolysis give dialdehydes:

$$\underset{\text{1 5 Dinitro pentane}}{NO_2\cdot[CH_2]_5\cdot NO_2} \longrightarrow OH\cdot N{:}CH\cdot[CH_2]_3\cdot CH{:}N\cdot OH \longrightarrow \underset{\text{Glutaric aldehyde}}{O{:}CH\cdot[CH_2]_3\cdot CH{:}O}$$

ESTERS OF SULPHURIC ACID

As a dibasic acid sulphuric acid can give rise to both **neutral or normal esters**, *e.g.* $(C_2H_5)_2SO_4$, and **acid esters or alkyl hydrogen sulphates**, *e.g.* $C_2H_5HSO_4$

The neutral esters are formed by the three general methods: (*a*) from fuming sulphuric acid and alcohol, (*b*) from silver sulphate and alkyl iodide; (*c*) from sulphuryl chloride and alcohol:

$$SO_2Cl_2 + 2C_2H_5OH = SO_2(OC_2H_5)_2 + 2HCl$$

The acid esters of the primary alcohols are generally prepared directly from their components. Secondary and tertiary alcohols do not yield them.

Ethyl sulphate, $(C_2H_5)_2SO_4$, is a colourless oily liquid of an agreeable peppermint odour, insoluble in water, and solidifying on exposure to a low temperature. It boils at 208°, is quickly hydrolysed with boiling water, but only slowly with cold water, yielding alcohol and sulphuric acid

Methyl sulphate, $(CH_3)_2SO_4$, is a syrupy oil, b.-pt. 188°, it is extremely poisonous, does not adhere to glass, and is a common reagent used instead of methyl iodide for the formation of methyl derivatives of phenols, alcohols, and amines (cf. S. J., Exp 127)

Ethyl hydrogen sulphate, $C_2H_5O\cdot SO_2\cdot OH$ (*Dabit*, 1802), is obtained from a mixture of alcohol and sulphuric acid, but not quantitatively, on account of the state of equilibrium that ensues. It is also formed from ethylene and sulphuric acid at a somewhat higher temperature. It differs from sulphuric acid by its Ba-, Ca-, and Pb-salts being soluble, and it can therefore be easily separated from the former by means of $BaCO_3$, &c. It yields salts which crystallize beautifully, *e.g.* $KC_2H_5SO_4$, but which slowly decompose into sulphate and alcohol on boiling their concentrated aqueous solution, especially in presence of excess of alkali.

These salts are frequently used instead of ethyl iodide for the preparation of other ethyl derivatives (process of ethylation).

The free acid ester is prepared by adding the requisite amount of sulphuric acid to the barium salt. It is a colourless oily liquid which does not adhere to glass, and which slowly hydrolyses when its solution is evaporated or kept. When heated alone it is decomposed into ethylene and sulphuric acid; with alcohol it yields ethyl ether and sulphuric acid.

DERIVATIVES OF SULPHUROUS ACID

α. **Alkyl Sulphites.** — **Ethyl sulphite,** $SO_3(C_2H_5)_2$, is an ethereal liquid of peppermint odour, which can be prepared from alcohol and thionyl chloride, $SOCl_2$, and which is rapidly hydrolysed by water. It has b.-pt. 161°, and its probable constitution is $O:S(OEt)_2$.

Ethyl Hydrogen Sulphite — The very unstable potassium salt, $OEt \cdot SO_2K$, is formed by the action of dry sulphur dioxide on potassium ethoxide (*Rosenheim*, B. 1905, **38**, 1301). It is decomposed by water, yielding alcohol and potassium sulphite.

The action of sodium hydroxide on ethyl sulphite does not hydrolyse the ester to sodium ethyl sulphite, but to sodium ethyl sulphonate, $C_2H_5 \cdot SO_2 \cdot ONa$ (B. 1898, **31**, 406.)

β. **Sulphonic Acids.** — Sulphonic acids contain the monovalent group $\cdot SO_2 \cdot OH$. They are colourless oils or solids, extremely hygroscopic, readily soluble in water, and are strong monobasic acids. They are much more stable than the isomeric alkyl hydrogen sulphites, for example, they are not hydrolysed when boiled with aqueous alkalis or acids, but are decomposed when fused with potash. They are non-volatile with steam, and when strongly heated decompose.

Ethyl-sulphonic acid, $C_2H_5 \cdot SO_2 \cdot OH$ (*Lowig*, 1839; *H. Kopp*, 1840), is a strong monobasic acid, and yields crystalline salts, *e.g.* $C_2H_5 \cdot SO_3K + H_2O$ (hygroscopic), $C_2H_5 \cdot SO_3Na + H_2O$.

Methyl-sulphonic acid, $CH_3 \cdot SO_3H$, is a syrupy liquid, and was prepared by *Kolbe* in 1845 from trichloro-methyl-sulphonic chloride, $CCl_3 \cdot SO_2Cl$ (produced from CS_2, Cl, and H_2O).

Modes of Formation. — 1. From sodium or ammonium sulphite and alkyl iodide (or alkyl hydrogen sulphate).

$$C_2H_5 \cdot I + Na_2SO_3 = C_2H_5 \cdot SO_3Na + NaI.$$

Sulphonic esters are formed by the action of alkyl iodides on silver sulphite.

$$2C_2H_5I + Ag_2SO_3 = (C_2H_5)_2SO_3 + 2AgI.$$

2. By the oxidation of mercaptans by $KMnO_4$ or HNO_3:

$$C_2H_5 \cdot SH + 3O = C_2H_5 \cdot SO_3H.$$

The sulphonic acids yield chlorides with PCl_5, *e.g* ethyl-sulphonic acid gives **ethyl-sulphonic chloride**, $C_2H_5 \cdot SO_2Cl$, a liquid which boils without decomposition at 177°, fumes in the air, and is reconverted by water into ethyl-sulphonic and hydrochloric acids. Nascent hydrogen reduces it to mercaptan, and with zinc dust it yields the zinc salt of a syrupy, readily soluble acid, viz. **ethyl-sulphinic acid**, $C_2H_5 \cdot SO_2H$, which may also be reduced to mercaptan Sodium ethyl sulphinate yields ethyl sulphone when treated with ethyl bromide, C_2H_5Br. When esterified the acid forms an unstable ester, isomeric with ethyl sulphone (B **24**, 2272).

Ethyl Ethyl-sulphonate, $C_2H_5 \cdot SO_2 \cdot OC_2H_5$, is isomeric with ethyl sulphite, and, being an ester of the more stable ethyl-sulphonic acid, can only be partially hydrolysed It is prepared from silver sulphite and ethyl iodide It boils at 213°, and the sulphonic esters generally have considerably higher boiling-points than the isomeric alkyl sulphites.

Constitution.—From the formation of the sulphonic acids from mercaptans by oxidation, and the (indirect) reversibility of this reaction, it follows that the sulphur in them is directly attached to the alkyl radical, if, then, sulphur is regarded as hexavalent, ethyl-sulphonic acid has the constitution

$$C_2H_5 \cdot SO_2 \cdot OH = \begin{matrix} C_2H_5 \\ HO \end{matrix} \!\!>\!\! S \!<\!\! \begin{matrix} O \\ O. \end{matrix}$$

This constitution is in perfect harmony with the reaction of the acids with phosphorus pentachloride and also with their monobasicity. From this we might conclude, assuming that the conversion of metallic sulphites into sulphonic acid derivatives is a simple exchange of alkyl and metallic radicals, that the constitution of sodium sulphite is $Na \cdot SO_2 \cdot ONa$, of the hypothetical sulphurous acid $H \cdot SO_2 \cdot OH$, and of sulphuric acid $OH \cdot SO_2 \cdot OH$. The alkyl sulphites formed from thionyl chloride probably have the alkyl groups attached to oxygen, *e.g.* ethyl sulphite, $SO(OC_2H_5)_2$.

Esters of phosphoric acid $PO(OR)_3$, $PO(OR)_2(OH)$, and $PO(OR)(OH)_2$, (R = alkyl), exist, as do also similar compounds of phosphorous and hypophosphorous acids. The phosphinic acids, &c., are related to the two last-mentioned classes. Esters of boric and silicic acids are also known.

ALKYL DERIVATIVES OF HYDROCYANIC ACID

Hydrocyanic acid, HCN, yields two classes of derivatives by the exchange of its hydrogen atom for alkyl radicals, neither of which can be regarded as esters, in the sense that they are hydrolysed to the acid and alcohol.

α. **Alkyl Cyanides or Nitriles**, R·C⋮N.—These are either colourless liquids, which volatilize without decomposition, or solids, with an ethereal odour slightly resembling that of leeks; they are lighter than water, and are relatively stable. The lower members are miscible, with water, but the higher ones not, and they boil at about the same temperatures as the corresponding alcohols

Formation.—1. By heating an alkyl iodide with an alcoholic solution of potassium cyanide, or potassium ethyl sulphate with potassium ferrocyanide

$$CH_3I + KCN = KI + CH_3\cdot CN \text{ (methyl cyanide).}$$

2 From fatty acids, *e.g* acetic acid, $CH_3\cdot CO\cdot OH$ The ammonium salt when distilled loses water and yields the acid amide, *e.g.*.

$$CH_3\cdot CO\cdot ONH_4 = H_2O + CH_3\cdot CO\cdot NH_2 \text{ (acetamide).}$$

The amide when heated with a dehydrating agent, *e.g.* P_4O_{10}, loses a second molecule of water and yields the cyanide.

$$CH_3\cdot CO\cdot NH_2 = H_2O + CH_3\cdot C{\vdots}N.$$

As a consequence of this mode of formation these compounds are also termed **nitriles** of the monobasic acids, *e.g.* $CH_3\cdot CN$, methyl cyanide or aceto-nitrile, $C_2H_5\cdot CN$, propio-nitrile, &c

3. The higher nitriles, in which $C > 5$, are formed from the amides of acids of the acetic series containing 1 atom of carbon more in the molecule, and also from the primary amines with the same number of carbon atoms, upon treatment with bromine and caustic-soda solution (*Hofmann*). See Amides.

4. From the oximes of the aldehydes, by warming with acetic anhydride. See Aldoximes.

Reactions.—The nitriles are chemically active. Most of the reactions are of an additive nature, and are somewhat similar to those characteristic of the olefines. These reactions are in harmony with the constitutional formula usually attributed to the nitriles, *e.g.* R·C⋮N, according to which a triple bond exists between a nitrogen and a carbon atom.

1. When hydrolysed with acids or alkalis, or superheated with water, they take up water (2 mols.) and yield the ammonium salts of fatty acids (with alkalis, the alkali salt, and free ammonia). The reaction undoubtedly proceeds in two distinct stages, and an acid amide is first formed

$$\begin{aligned} CH_3\cdot C{:}N \\ +\ O{:}H_2 \end{aligned} = CH_3\cdot CO\cdot NH_2.$$

$$CH_3\cdot CO\cdot NH_2 + H_2O = CH_3\cdot CO\cdot ONH_4$$

It is generally impossible to stop the hydrolysis at the first stage in the case of aliphatic nitriles, but this is readily accomplished with aromatic cyanides This is a reaction of considerable interest, as it enables us to pass from a saturated alcohol, $C_nH_{2n+1}\cdot OH$, to the aliphatic acid, $C_nH_{2n+1}\cdot COOH$, which contains 1 atom of carbon more than the alcohol

$$CH_3\cdot OH \longrightarrow CH_3I \longrightarrow CH_3\cdot CN \longrightarrow CH_3\cdot COOH$$

2 Just as acetamide is formed by the taking up of water, so is thio-acetamide by the addition of sulphuretted hydrogen,

3. By the addition of hydrochloric acid, amido-chlorides or imido-chlorides are formed, by the addition of ammonia bases, amidines Halogens also form decomposable additive-products.

4 Primary amines are obtained by the reduction of nitriles with sodium and alcohol (p 106)·

$$CH_3\cdot C{:}N + 4H = CH_3\cdot CH_2\cdot NH_2 \text{ (ethylamine).}$$

5 Metallic potassium or sodium frequently induces polymerization, thus methyl cyanide yields in this way **cyanmethine**, a mono-acid base crystallizing in prisms

Aceto-nitrile, *Ethane-nitrile*, $CH_3\cdot CN$, b-pt 82 is present in the products of distillation from the vinasse of sugar beet and in coal-tar. **Propio-nitrile**, (*Propane-nitrile*), $C_2H_5\cdot CN$, **butyro-nitrile**, $C_3H_7\cdot CN$, and **valero-nitrile**, $C_4H_9\cdot CN$, are liquids of agreeable bitter-almond-oil odour, **palmito-nitrile**, $C_{15}H_{31}\cdot CN$, is like paraffin.

β. **Isocyanides, Isonitriles or Carbylamines** – These are colourless liquids readily soluble in alcohol and ether, but only slightly soluble in water. They have a feeble alkaline reaction, an unbearable putrid odour, and poisonous properties, and boil somewhat lower than the isomeric nitriles.

Formation. —1. By heating an alkyl iodide with silver cyanide instead of potassium cyanide (*Gautier*), a double com-

pound with silver cyanide being first formed, according to *Wade*:

$$Ag\cdot N{:}C{:} + EtI = \begin{matrix} Ag \\ Et \\ I \end{matrix}\!\!>\!N{:}C{:} = AgI + Et\cdot N{:}C{:}$$

(ethyl carbylamine)

2 In small quantity, along with the nitrile, when a potassium alkyl-sulphate is distilled with potassium cyanide.

3. By the action of chloroform and alcoholic potash upon primary amines (*Hofmann*, 1869) (see pp. 63 and 108)·

$$CH_3\cdot NH_2 + CHCl_3 + 3KOH = CH_3\cdot N{:}C + 3KCl + 3H_2O.$$

Behaviour.—1. The isonitriles differ fundamentally from the nitriles in their behaviour with water or dilute acids. When strongly heated with water, or with acids in the cold, they decompose into formic acid and a primary amine containing an atom of carbon less than themselves:

$$CH_3\cdot NC + 2H_2O = CH_3\cdot NH_2 + HCO_2H.$$

Unlike the nitriles, they are very stable towards alkalis.

2. The isonitriles are also capable of forming additive products with the halogens, HCl, H_2S, &c., compounds different from those given by the nitriles, thus, with HCl they yield crystalline salts which are rapidly decomposed by water into amine and formic acid.

3 Some of the isonitriles change into the isomeric nitriles when heated. According to *Wade* this change does not occur at all readily in the fatty series if the carbylamines are thoroughly dry. (J. C. S. 1902, **81**, 1596.)

Methyl isocyanide, $CH_3\cdot NC$, boils at 58°, and **ethyl isocyanide**, $C_2H_5\cdot NC$, at 82°.

Constitution of the Nitriles and Isonitriles.—The constitution of the nitriles follows from the readiness with which they can be hydrolysed to acids of the acetic series. In acetic acid we know that we have a methyl group directly attached to a carbon atom, *e.g.* $CH_3\cdot CO\cdot OH$, and since methyl cyanide on hydrolysis yields acetic acid, it also presumably contains the methyl group attached to carbon. The nitrogen atom, on the other hand, is eliminated, and is thus probably not directly bound to the alkyl radical Consequently aceto-nitrile has the constitution $CH_3\cdot C{:}N$.

This constitutional formula is supported by a study of the product formed on reduction, namely $CH_3\cdot CH_2\cdot NH_2$.

In the case of the isonitriles, however, it is the nitrogen which must be directly bound to the alkyl radical, as their close connection with the amine bases shows, the amines being easily prepared from and reconverted into the isonitriles. The carbon atom of the cyanogen group, on the contrary, is eliminated as formic acid on decomposition with acid, and is consequently not directly united to the alkyl radical, but only through the nitrogen. The constitutional formula of methyl isocyanide is therefore either $CH_3 \cdot N \vdots C$ or $CH_3 \cdot N : C :$, with an unsaturated carbon atom (cf. Chap. LII).

D. Amines or Nitrogen Bases of the Alkyl Radicals

By the introduction of alkyl radicals in place of hydrogen into the ammonia molecule, the important class of **ammonia bases** or **amines** is formed.

The amines containing small alkyl groups bear the closest resemblance to ammonia, and are even more strongly basic than the latter. They have an ammoniacal odour, give rise to white clouds with volatile acids, combine with hydrochloric acid, &c., to salts with evolution of heat, and yield platini- and auri-chlorides. Their aqueous solutions precipitate insoluble hydroxides from solutions of the salts of the heavy metals, and these precipitates are frequently soluble in excess.

The lowest members of this class are combustible gases readily soluble in water. The next are liquids of low boiling-point, also at first readily soluble, but the solubility in water, and also the volatility, decrease with an increase in molecular weight, until the highest members of the series, such as tricetylamine, $(C_{16}H_{33})_3N$, are at the ordinary temperature odourless solids of high boiling-point, insoluble in water but soluble in alcohol and ether, and readily combining with acids to form salts. All amines are considerably lighter than water.

The quaternary ammonium hydroxides are solid and very hygroscopic, and exceedingly like potash in properties.

Classification.—The bases are divided into **primary, secondary, tertiary,** and **quaternary bases,** according as they contain 1, 2, 3, or 4 alkyl radicals; the three first are derived from ammonia, and the last from the hypothetical ammonium hydroxide, $NH_4 \cdot OH$. Characteristic of primary amines is the *amino* group, $\cdot NH_2$, of secondary, the *imino* group, $:NH$, and of tertiary, the N radical attached to three alkyl groups.

The system of *nomenclature* is simple, as indicated by the following examples:—$CH_3 \cdot NH_2$, **methylamine**; $C_3H_7 \cdot NH_2$, **propylamine**, $(C_2H_5)_2NH$, **di-ethylamine**; $(CH_3)_3N$, **trimethylamine**, and $N(C_2H_5)_4I$, **tetraethylammonium iodide.**

The alkyl radicals may be either saturated or unsaturated.

Modes of Formation.—1. Primary amines, *e.g.* methylamine, ethylamine, are obtained by heating alkyl cyanates with potash solution (*Wurtz*, 1848), just as cyanic acid itself yields ammonia and carbon dioxide:

$$\begin{matrix} O:C:N \cdot C_2H_5 \\ O:H_2 \end{matrix} = CO_2 + NH_2 \cdot C_2H_5.$$

2 By the direct introduction of the alkyl radical into ammonia by heating a concentrated solution of the latter with methyl iodide, chloride, or nitrate, ethyl iodide, &c. In this reaction an atom of hydrogen is first exchanged for an alkyl radical, and then the base produced combines with the halogen hydride, formed at the same time, to a salt, thus:—

(I) $$NH_2H + CH_3I = NH_2 \cdot CH_3, HI.$$

From the methylamine hydriodide thus produced, free methylamine can readily be obtained by distillation with potash:

$$NH_2(CH_3), HI + KOH = NH_2(CH_3) + KI + H_2O.$$

The methylamine can now combine further with methyl iodide to hydriodide of dimethylamine.

(II) $$NH_2(CH_3) + CH_3I = NH(CH_3)_2HI,$$

which, in its turn, yields the free base with potash. This latter can again combine with methyl iodide:

(III) $$NH(CH_3)_2 + CH_3I = N(CH_3)_3HI,$$

the salt so produced yielding trimethylamine as before. Finally, the trimethylamine can once more take up methyl iodide:

(IV) $$N(CH_3)_3 + CH_3I = N(CH_3)_4I.$$

The compound obtained, tetramethylammonium iodide, is, however, no longer a salt of an amine, but of an ammonium base, and is not decomposed on distillation with potash solution. The velocities of formation of quaternary ammonium iodides from tertiary amines and alkyl iodides have been determined by *Menschutkin*. The reaction has been shown

to be a bimolecular one. The velocity varies with the alkyl iodide employed, decreasing as the alkyl group becomes more complex. The solvent employed, for example, acetone, hexane, methyl alcohol, &c., also affects the velocity of formation to an enormous extent, *e.g.* the combination of ethyl iodide and tri-ethylamine takes place some 250 times as readily in ethyl alcohol as in hexane solution.

Primary and secondary bases can also be transformed into secondary and tertiary by warming with potassium alkyl-sulphates (B. 1891, **24**, 1678).

When several alkyl iodides are used in place of methyl iodide, **mixed amines**, *i.e.* amines containing different alkyl groups in the molecule, are obtained, *e.g.* **methyl-propylamine**, $NH(CH_3)(C_3H_7)$, **methyl-ethyl-propylamine**, $N(CH_3)(C_2H_5)(C_3H_7)$.

The reactions I to IV given above do not in reality follow each other in perfect order but go on simultaneously, the bases being partly liberated from the hydriodides by the ammonia, and so being free to react with more alkyl haloid. The product obtained by distillation with potash is therefore a mixture of all the three amines and ammonia.

These cannot be separated by fractional distillation, and so their different behaviour with ethyl oxalate, $OEt \cdot CO \cdot CO \cdot OEt$, is made use of for the purpose. Methylamine reacts with this ester to form chiefly (1) **dimethyl-oxamide**, $CH_3NH \cdot CO \cdot CO \cdot NH \cdot CH_3$ (solid), and (2) some **methyl-oxamic ester**, $OEt \cdot CO \cdot CO \cdot NH \cdot CH_3$ (liquid); dimethylamine yields (3) the **ethyl ester of dimethyl-oxamic acid**, $OEt \cdot CO \cdot CO \cdot N(CH_3)_2$ (liquid), while trimethylamine does not react with the ethyl oxalate Upon warming the product of the reaction on the water-bath, the latter base distils over, and the remaining compounds can then be separated by special methods (for which see B. **3**, 776; **8**, 760), and individually decomposed by potash, (1) and (2) yielding methylamine, and (3) dimethylamine.

3. The nitro-compounds yield primary amines when treated with acid reducing agents (see p. 95), thus:—

$$CH_3 \cdot NO_2 + 6H = CH_3 \cdot NH_2 + 2H_2O.$$

4. The nitriles, including hydrocyanic acid, are capable of taking up four atoms of hydrogen (see p. 102) and forming primary amines (*Mendius*, 1862):

$$CH_3 \cdot C{:}N + 4H = CH_3 \cdot CH_2 \cdot NH_2 \text{ (ethylamine).}$$

5. Primary amines, in which $C < 6$, are prepared according to *Hofmann's* method, by the action of bromine and caustic-soda solution upon the amides of acids containing 1 carbon atom more than themselves (see Amides).

6. Primary amines likewise result from the reduction of the oximes or hydrazones (see pp. 127 and 135): for example, acetaldoxime:

$$CH_3 \cdot CH{:}N \cdot OH + 4H = CH_3 \cdot CH_2 \cdot NH_2 + H_2O.$$

7. See p. 463 for preparation of amines from phthalimide.

Isomers.—Numerous isomers exist among the amines, as the following table shows:—

	C_2H_7N	C_3H_9N.	$C_4H_{11}N$.
Isomers	$NH_2(C_2H_5)$ $NH(CH_3)_2$	$NH_2(C_3H_7)$ $NH(CH_3)(C_2H_5)$ $N(CH_3)_3$	$NH_2(C_4H_9)$ $NH(CH_3)(C_3H_7)$ and $NH(C_2H_5)_2$ $N(CH_3)_2(C_2H_5)$

This kind of isomerism is the same as that of the ethers (p. 87), *i.e.* metamerism From (C_3H_7) onwards, isomerism can also occur in the alkyl radicals. According to theory, as many amines C_n as alcohols C_{n+1} are capable of existence.

Behaviour —1. The amines combine directly with acids (organic or inorganic) to form **salts** in exactly the same way as ammonia; the quaternary ammonium bases, however, react with acids, forming salts and eliminating water like potassium or ammonium hydroxide:

$$CH_3 \cdot NH_2 + HCl = CH_3 \cdot NH_2, HCl = CH_3 \cdot NH_3Cl.$$
$$(CH_3)_4N \cdot OH + HCl = (CH_3)_4N \cdot Cl + H_2O.$$

The salts so obtained are white, crystalline compounds, readily soluble in water, and frequently hygroscopic. The chlorides form, with platinic chloride, sparingly soluble **platinichlorides** analogous to ammonium platinichloride, $(NH_4)_2PtCl_6$, *e.g.* methylamine platinichloride, $(CH_3NH_3)_2PtCl_6$.

The same applies to the **aurichlorides**, *e.g.* $C_2H_5NH_3AuCl_4$.

Strong alkalis, *e.g.* potassium hydroxide, decompose all the salts with the exception of the quaternary ammonium compounds yielding the free bases (and not ammonia).

2. Hydrolysing agents such as alkalis and acids do not affect the nitrogen bases of the alcohol radicals.

3. The different classes of amines are distinguished from

each other by the primary having 2 hydrogen atoms, the secondary 1, but the tertiary none replaceable by alkyl groups; the same applies to acid radicals (acyl groups). The ultimate products obtained from isomeric amines by the action of methyl iodide are distinguished from one another by analysis. Thus of the three isomeric amines C_3H_9N, propylamine gives with methyl iodide, $C_3H_7 \cdot N(CH_3)_3I$, propyl-trimethylammonium iodide $= C_6H_{16}NI$, methyl-ethylamine gives $C_2H_5 \cdot N(CH_3)_3I$, ethyl-trimethylammonium iodide $= C_5H_{14}NI$; and trimethylamine gives $N(CH_3)_4I$, tetramethylammonium iodide $= C_4H_{12}NI$. An iodine estimation in the final product would immediately enable us to settle the constitution of the original amine.

The primary bases further differ from the others in their behaviour with chloroform, carbon disulphide, and nitrous acid.

4. Only the primary bases react with chloroform and alcoholic potash, with formation of isonitriles (p. 103).

5. When warmed with carbon disulphide in alcoholic solution, the primary and secondary, but not the tertiary, bases react to form derivatives of thiocarbamic acids. (See Carbonic Acid Derivatives) Should the amines be primary ones, the characteristically smelling isothiocyanates are produced upon heating the thiocarbamic derivatives with a solution of $HgCl_2$ ("Senfol" reaction)

6. Nitrous acid reacts with the primary amines, forming alcohols, *e.g.*—

$$CH_3 \cdot NH_2 + H \cdot O \cdot NO = CH_3 \cdot OH + N_2 + H_2O.$$

A molecular rearrangement is occasionally met with, *e.g.* the production of isopropyl alcohol from *n*-propylamine.

Secondary bases yield with nitrous acid nitroso-compounds, *e.g.* "**dimethyl-nitrosamine**":

$$(CH_3)_2NH + NO \cdot OH = (CH_3)_2N \cdot NO + H_2O.$$

These nitrosamines are yellow-coloured volatile liquids of aromatic odour (*Geuther*). When reduced with acid-reducing agents, or when heated with alcohol and hydrochloric acid, they regenerate the secondary amines. Weak reducing agents, however, convert them into hydrazines (p. 112). The nitrosamines are frequently of great service in the purification of the secondary bases.

Nitrous acid has no action upon tertiary amines.

7. By the indirect action of nitric acid (B. **22**, Ref. 295),

nitramines result, *i.e.* amines in which an amino-hydrogen atom has been replaced by the nitro-group, *e.g.* $CH_3 \cdot NH \cdot NO_2$, **methyl-nitramine**. Similarly, by the indirect introduction of an amino-group, hydrazines are formed, *e.g* $CH_3 \cdot NH \cdot NH_2$, methyl-hydrazine.

8. While the amines are liberated from their salts by alkalis, the free bases of the quaternary ammonium salts, *e g.* tetramethylammonium iodide, cannot be prepared from these by treatment with potash, because the products are soluble and non-gaseous, and hence an equilibrium is attained. The salts behave normally in aqueous solutions, for example, the iodides yield precipitates with silver nitrate, and are good electrolytes, The corresponding hydroxides, *e g.* $N(CH_3)_4OH$, are obtained most readily by acting upon the iodides with moist silver oxide. These hydroxides are extraordinarily like caustic potash. They are colourless hygroscopic solids, readily soluble in water, and abstract carbon dioxide from the air. The solutions have strongly alkaline properties, are good electrolytes, and precipitate metallic hydroxides from solutions of their salts. When distilled they decompose, yielding the tertiary base, the tetramethyl base yielding in addition methyl alcohol, and the homologous bases olefine and water (*Braun*, A. **382**, 1):

$$N(CH_3)_4 \cdot OH = N(CH_3)_3 + CH_3 \cdot OH.$$
$$N(C_2H_5)_4 \cdot OH = N(C_2H_5)_3 + C_2H_4 + H_2O.$$

They are of importance for the study of the valency of nitrogen. Their formation and general properties are most in harmony with the assumption of a penta- or quinque-valent nitrogen atom, *e.g.* $\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!\!N\!\!<\!\!\begin{matrix} CH_3 \\ CH_3 \\ I \end{matrix}$, and not as a so-called molecular compound, $N(CH_3)_3$, CH_3I. (Cf Trimethyl-sulphonium hydroxide.) The fact that the salts $N(CH_3)_2(C_2H_5) + C_2H_5Cl$ and $N(CH_3)(C_2H_5)_2 + CH_3Cl$ are identical, is in agreement with the former assumption. (*Meyer* and *Lecco.*) Lastly, optically active isomers are met with among the quaternary ammonium salts, a point which receives its readiest explanation from the asymmetry of the molecule containing a quinquevalent nitrogen atom. (See Stereochemistry of Nitrogen Derivatives.)

9. The quaternary iodides are resolved into tertiary base and alkyl iodide when heated. They combine with 2 or 4 atoms of bromine or iodine to tri- and penta-bromides or -iodides, *e.g.* $N(CH_3)_4 \cdot I \cdot I_4$ (dark needles), and $N(C_2H_5)_4I \cdot I_4$

(azure-blue needles). Such periodides readily lose the excess of iodine, and are hence relatively unstable. Hepta- and Ennea-iodides also exist.

The following table gives the boiling-points of the various amines:—

	Primary.	Secondary	Tertiary
Methyl	— 6°	7°	3·5°
Ethyl	19°	56°	90°
n-Propyl.....	49°	98°	156°
n-Butyl.....	76°	160°	215°
n-Octyl	180°	297°	366°

Methylamine, $CH_3 \cdot NH_2$, occurs in *Mercurialis perennis* and *annua* ("mercurialin"), in the distillate from bones and wood, and in herring brine. It is produced in many decompositions of organic compounds, *e.g.* from alkaloids, as when caffeine is boiled with barium hydroxide; also by heating trimethylamine hydrochloride to 285°.

It is most readily prepared from acetamide, caustic soda, and bromine. (*B.* **18**, 2737.) It is more strongly basic and even more soluble in water than ammonia, has a powerful ammoniacal and at the same time fishlike odour, and burns with a yellowish flame. Its aqueous solution, like that of ammonia, precipitates many metallic salts, frequently redissolving the precipitated hydroxides; unlike ammonia, it does not dissolve $Ni(OH)_2$ and $Co(OH)_2$.

The **hydrochloride**, $CH_3 \cdot NH_2$, HCl, forms large glistening plates, is very hygroscopic and readily soluble in alcohol; the **platinichloride** crystallizes in golden scales, and the sulphate forms an alum.

Dimethylamine, $(CH_3)_2NH$, occurs in Peruvian guano and pyroligneous acid, and is formed by decomposing nitroso-dimethyl-aniline by caustic-soda solution.

Trimethylamine, $(CH_3)_3N$, is widely distributed in nature, being found in considerable quantity in *Chenopodium vulvaria*, also in *Arnica montana*, in the blossom of *Cratægus oxyacantha*, and of pear, and in herring brine. (*Wertheim.*)

It is a decomposition product of the betaine of beet-root, and therefore along with ammonia, dimethylamine, &c., methyl alcohol and aceto-nitrile by the distillation of

vinasse. It has an ammoniacal and pungent fishlike odour.

The tertiary amines can be oxidized by means of hydrogen peroxide to compounds of the type $(CH_3)_2N{:}O$, **trimethylamine oxide**, which are colourless crystalline bases.

Tetramethylammonium iodide, $N(CH_3)_4I$, is obtained in large quantity directly from $NH_3 + CH_3I$. It crystallizes in white needles or large prisms, and has a bitter taste

Tetramethylammonium hydroxide, $N(CH_3)_4OH$, crystallizes in hygroscopic needles, and can be obtained by the action of alcoholic potash on an alcoholic solution of its chloride; potassium chloride is precipitated, and the hydroxide remains in solution. It forms salts, *e g* a platinichloride, sulphide, polysulphide, cyanide, &c.

Ethylamine, $C_2H_5NH_2$. Crude ethyl chloride (obtained as a by-product in the manufacture of choral) is used for its preparation. It has a strongly ammoniacal smell and biting taste, mixes with water in every proportion, and burns with a yellow flame It dissolves $Al(OH)_3$, but not $Fe(OH)_3$, also $Cu(OH)_2$ with difficulty, but not $Cd(OH)_2$. With bleaching powder it yields **ethyl-dichloro-amine**, $C_2H_5{\cdot}NCl_2$, as a yellow oil of a most unpleasant piercing odour.

Tri-ethylamine, $(C_2H_5)_3N$, is an oily strongly alkaline liquid. The precipitates which it gives with solutions of metallic salts are mostly insoluble in excess of the precipitant.

HYDROXYLAMINES, HYDRAZINES

The **Alkyl-hydroxylamines**, which are derived from hydroxylamine, $NH_2{\cdot}OH$, just as the amines are from ammonia, belong to two different series, in accordance with the constitution of hydroxylamine, thus. —

$NH_2{\cdot}OCH_3$	and	$CH_3{\cdot}NH{\cdot}OH$
α-Methyl-hydroxylamine		β-Methyl hydroxylamine

The compounds of the first series, which are obtained from the oxime ethers (p 138), are—as ethereal compounds—tolerably stable, and do not reduce *Fehling's solution*. Those of the second series, which likewise result from certain oxime derivatives, but at the same time also from the reduction of the nitro-hydrocarbons (p. 96), very readily undergo change, reduce *Fehling's solution* even in the cold, and yield primary amines when further reduced (B **23**, 3597; **24**, 3528; **25**, 1714).

E. Fischer (A. **190**, 67; **199**, 281, 294) has given the name of **hydrazines** to a series of peculiar bases, mostly liquid and

closely resembling the amines, but containing two atoms of nitrogen in the molecule, and differing from the latter especially by their capability of reducing *Fehling's solution*, for the most part even in the cold, and by the ease with which they are oxidized. They are derived from "Diamide" or "Hydrazine", $NH_2 \cdot NH_2$ (*Curtius* and *Jay*, J. pr. Ch. 1889, (2), **39**, 27). They are formed by the action of nascent hydrogen on the nitrosamines (p. 108):

$$(CH_3)_2N \cdot NO + 4H = (CH_3)_2N \cdot NH_2 + H_2O.$$

Primary, secondary, tertiary, and quaternary hydrazines are known, according as 1, 2, 3, or 4 of the hydrogen atoms in $NH_2 \cdot NH_2$ are replaced by alkyl groups.

The secondary hydrazines exist in two isomeric forms, namely, $NHR \cdot NHR$ and $NH_2 \cdot NR_2$, which are known respectively as *symmetrical* and *unsymmetrical* secondary hydrazines.

Methyl-hydrazine, $CH_3 \cdot NH \cdot NH_2$ (cf. A. 1889, **253**, 5). An excessively hygroscopic liquid, which fumes in the air, and has an odour similar to that of methylamine. B.-pt. 87°.

Ethyl-hydrazine, $C_2H_5 \cdot NH \cdot NH_2$. When di-ethyl urea is treated with nitrous acid a nitroso-compound is formed, which, on reduction with zinc dust and acetic acid, yields the so-called "diethyl-semicarbazide", and this decomposes, when heated with hydrochloric acid, into carbon dioxide, ethylamine, and ethyl-hydrazine:

$CO<^{NH \cdot C_2H_5}_{NH \cdot C_2H_5}$ Di-ethyl-urea — $CO<^{NH \cdot C_2H_5}_{N(NO) \cdot C_2H_5}$ Nitroso-compound — $CO<^{NH \cdot C_2H_5}_{N(NH_2) \cdot C_2H_5}$ Diethyl semicarbazide

$$C_2H_5 \cdot NH \cdot CO \cdot N(NH_2) \cdot C_2H_5 + H \cdot O \cdot H = CO_2 + NH_2C_2H_5 + NH_2 \cdot NHC_2H_5.$$

Ethyl-hydrazine is a colourless mobile liquid of ethereal and faintly ammoniacal odour, boiling at 100°. It is very hygroscopic, forms white clouds with moist air, dissolves in water and alcohol with evolution of heat, and corrodes cork and caoutchouc.

Diethyl-hydrazine, $(C_2H_5)_2N \cdot NH_2$, is prepared from diethylamine by transforming it into diethyl-nitrosamine by the nitrous-acid reaction, and then reducing the latter. It resembles ethyl-hydrazine closely:

$$(C_2H_5)_2N \cdot NO + 4H = (C_2H_5)_2N \cdot NH_2 + H_2O.$$

Tetra-ethyl-tetrazone, $(C_2H_5)_2 : N \cdot N : N \cdot N : (C_2H_5)_2$, a

colourless, strongly basic oil, volatile with steam, is formed when diethyl-hydrazine is heated with mercuric oxide.

The *constitution* of the hydrazines follows from their modes of formation. Since in diethyl-nitrosamine, $(C_2H_5)_2N \cdot NO$, for instance, the nitroso-group NO must be attached to the nitrogen of the amine and not to the carbon, judging from the case with which it can be separated (p. 108), so the same linking of the atoms must be assumed in the hydrazines, which are formed from the nitroso-compounds by reduction, *i e* by exchange of O for 2H. The readiness with which diethyl-hydrazine is oxidized to diethylamine, *e.g.* by alkaline cupric oxide, is an agreement with such a formula. The hydrazines are relatively stable towards reducing agents.

For aliphatic Diazo and Triazo Compounds, see Chap. LI.

E Alkyl Derivatives of Phosphorus, Arsenic, &c.

1. PHOSPHORUS

Just as amines are derived from ammonia, so from phosphuretted hydrogen, PH_3, are derived **primary, secondary,** and **tertiary phosphines** by the exchange of hydrogen for alkyl radicals, and to these must likewise be added quaternary compounds, the **phosphonium bases**. The phosphines correspond closely with the amines in composition and in some of their properties, *e g* they are not saponifiable But they differ from them in the following points.—

1 Like phosphuretted hydrogen itself, the alkyl phosphines are only feebly basic; thus ethyl phosphine does not affect litmus, and its salts are decomposed by water The salts of the secondary and tertiary compounds are not decomposed, thus showing that the presence of alkyl radicals tends to strengthen the basic properties of the compound

2 Like phosphuretted hydrogen they are readily inflammable, and they are consequently rapidly oxidized in the air and readily take fire of themselves.

3. As the phosphorus atom in these compounds shows a tendency to pass from the ter- to the quinque-valent state, many of the phosphines behave as unsaturated compounds; they combine with oxygen, sulphur, halogens, &c., for example, $(CH_3)_3PO$, $(CH_3)_3PS$, $(CH_3)_3PCl_2$, and a compound $(CH_3)_3P$, CS_2, in the form of red plates. The products obtained on oxidation are characteristic, and may be regarded

as derived from phosphoric acid, $O:P(OH)_3$, by the replacement of one or more OH groups by one or more alkyl radicals:

$CH_3 \cdot PH_2$, with nitric acid, yields $CH_3 \cdot PO \cdot (OH)_2$, **methyl phosphonic acid.**

$(CH_3)_2PH$, with nitric acid, yields $(CH_3)_2 \cdot PO \cdot OH$, **dimethyl phosphinic acid.**

$(CH_3)_3P$, on oxidation in the air, yields $(CH_3)_3PO$, **trimethyl phosphine oxide.**

4. Corresponding with the disagreeable smell of phosphuretted hydrogen, they possess an excessively strong stupefying odour; thus ethyl phosphine has a perfectly overpowering smell, and excites on the tongue and deep down in the throat an intensely bitter taste.

Formation.—1. The tertiary phosphines and quaternary compounds are formed directly from phosphine and an alkyl iodide. (Cf. Amines, formation 2.)

$$PH_3 + 3C_2H_5I = P(C_2H_5)_3 + 3HI.$$

2. According to *Hofmann* (1871), primary and secondary phosphines are formed by heating phosphonium iodide and an alkyl iodide with zinc oxide, *e.g.*:

$$2C_2H_5I + 2PH_4I + ZnO = 2P(C_2H_5)H_2, HI + ZnI_2 + H_2O$$

They can be separated from one another by decomposing the salts of the primary phosphines by water, as already mentioned.

3. The tertiary phosphines are produced from calcium phosphide and an alkyl iodide, a reaction first observed by *Thenard* in 1846;

4. Also from phosphorus trichloride and zinc methyl, or magnesium alkyl iodides (*Auger* and *Billy*, C. 1904, **139**, 597).

5. The phosphonium salts are formed by the combination of tertiary phosphines with an alkyl haloid, and closely resemble the corresponding ammonium compounds.

Tri-ethyl phosphine, $P(C_2H_5)_3$, has no alkaline reaction. When concentrated it possesses a stupefying, and when dilute a pleasant hyacinth-like odour.

Tetramethyl-phosphonium hydroxide, $P(CH_3)_4OH$. Unlike the analogous ammonium hydroxide, this compound decomposes into trimethyl-phosphine oxide and methane when heated:

$$P(CH_3)_4OH = P(CH_3)_3O + CH_4.$$

2. ARSENIC

The similarity of arsenic to phosphorus and nitrogen is further exemplified by the analogous compounds which it forms with alkyl radicals. In virtue, however, of the more metallic character of arsenic, it does not show the same tendency to combine with alkyl radicals and hydrogen at the same time, but forms derivatives containing alkyl groups and electro-negative elements like chlorine or oxygen. Arsenic analogues of methylamine have been recently prepared, and are very unstable Trimethyl-arsine, analogous to trimethylamine and trimethylphosphine, is well known As **primary** and **secondary compounds** we have methyl-arsine dichloride, $CH_3 \cdot AsCl_2$, dimethyl-arsine chloride, $(CH_3)_2AsCl$, and analogous substances They are colourless liquids of stupefying odour, exerting in some cases an unbearable irritating action upon the mucous membrane. They do not possess basic properties. In addition to these there exist also quaternary compounds, **arsonium salts**, which are exactly analogous to the quaternary phosphonium salts.

The halogen of the chlorine compounds is easily replaceable by its equivalent of oxygen Thus, corresponding with the compound $R \cdot AsCl_2$ there is an oxide $R \cdot AsO$ and a sulphide $R \cdot AsS$, and with the chloride R_2AsCl an oxide $(R_2As)_2O$. These oxides, liquid or solid, are compounds of stupefying odour, and behave like basic oxides, hydrochloric acid reconverts them into the corresponding chlorides

Here, also, the tendency of arsenic to change from the tervalent to the quinquevalent state is especially marked. The above chlorides and trimethyl-arsine itself all combine with two atoms of chlorine to compounds of the type AsX_5. The above oxygen compounds of the type AsX_3 and also trimethyl-arsine are consequently oxidizable to compounds containing one O atom or two OH groups more, acids or oxides which are also formed from the chlorides of the type AsX_5 by exchange of halogen for O or OH, *e.g.* cacodyl oxide, $(Me_2As)_2O$, to cacodylic acid, $Me_2As\lessdot^{OH}_{O}$. These products are therefore completely analogous to the phosphonic and phosphinic acids and phosphine oxides already described.

The compounds $As(CH_3)_xCl_{5-x}$, of the type AsX_5, when heated, decompose into methyl chloride and compounds $As(CH_3)_{x-1}Cl_{4-x}$, of the type AsX_3, this elimination of methyl

chloride taking place the more readily the fewer methyl groups are present in the molecule; thus $As(CH_3)_3Cl_2$ breaks up when somewhat strongly heated, $As(CH_3)_2Cl_3$ at 50°, and $As(CH_3)Cl_4$ at 0°, *i.e.* the last-named is only stable when in a freezing-mixture. When, therefore, chlorine acts upon $As(CH_3)Cl_2$ at the ordinary temperature, the reaction appears to be one of direct exchange of alkyl for chlorine, thus:

$$As(CH_3)Cl_2 + Cl_2 = AsCl_3 + CH_3Cl.$$

It is interesting to note that, like free "methyl" ($CH_3\cdot$), the radical $\cdot As(CH_3)_2$ has no separate existence; cacodyl possesses the doubled formula $As_2(CH_3)_4$ ("Di-arsene-dimethyl").

The *tertiary arsines* are formed:

1. From sodium arsenide and alkyl iodide (*Cahours* and *Riche*):

$$AsNa_3 + 3C_2H_5I = As(C_2H_5)_3 + 3NaI.$$

2. From arsenious chloride and (*a*) zinc alkyl (*Hofmann*), or (*b*) magnesium alkyl haloid (*Pfeiffer*, B. 1904, **37**, 4620, *Sauvage*, C. 1904, **139**, 674).

Trimethyl-arsine, $As(CH_3)_3$, and **triethyl-arsine**, $As(C_2H_5)_3$, are liquids sparingly soluble in water. They fume in the air, and are thereby oxidized to tri-methyl- or -ethyl-arsine oxide.

The **secondary arsines** are obtained from cacodyl and cacodyl oxide, which are formed when a mixture of potassic acetate and arsenious oxide is distilled (*Cadet*, 1760).

$$O\langle^{As:O}_{As:O} + 4CH_3\cdot CO_2K = O\langle^{As(CH_3)_2}_{As(CH_3)_2} + 2CO_2 + 2CO_3K_2$$

The distillate of cacodyl and cacodyl oxide so obtained, and termed "alkarsin", fumes in the air and is spontaneously inflammable (*Cadet's* "fuming arsenical liquid"). Hydrochloric acid acts upon it to form cacodyl chloride (*Bunsen*, 1838), and caustic-potash solution gives pure **cacodyl oxide**, $As_2(CH_3)_4O$, a liquid of stupefying odour which produces nausea and unbearable irritation of the nasal mucous membrane; it boils without decomposition, and is insoluble in water and of neutral reaction. It yields salts with acids, *e.g.* **cacodyl chloride** with hydrochloric acid:

$$O(AsMe_2)_2 + 2HCl = 2AsMe_2Cl + H_2O.$$

The chloride is a liquid of even more stupefying odour and violent action than the oxide, and its vapour is spontaneously

inflammable. When heated with zinc clippings in an atmosphere of carbon dioxide, it yields the free **cacodyl**, $As_2(CH_3)_4$ (from κακώδης, "stinking"), a colourless liquid insoluble in water and boiling undecomposed at 170°, and of a horrible nauseous odour which produces vomiting. It is as readily inflammable in the air as the vapour of phosphorus, yielding the oxide when slowly brought in contact with it, and also combining directly with sulphur, chlorine, &c. Cacodyl plays, therefore, even down to the most minute particulars, the part of a simple electro-positive element, it is a true "organic element" (*Bunsen*).

Cacodylic acid, $\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!As\!-\!O\!-\!OH$ is crystalline, soluble in water, odourless, and poisonous. It forms crystallizable salts.

SUMMARY

		Compounds with Chlorine	Oxides	Acids
Primary ..	Methyl-arsine dichloride, $AsMeCl_2$ B.-p. 133°.	Methyl-arsine tetra-chloride, $AsMeCl_4$.	Methyl-arsine oxide, $AsMeO$. B.-p. 95°.	Methyl-arsonic acid, $O:AsMe(OH)_2$. Solid plates.
Secondary	Cacodyl chloride, $AsMe_2Cl$ B.-p. 100°.	Cacodyl trichloride, $AsMe_2Cl_3$.	Cacodyl oxide, $(AsMe_2)_2O$. B.-p. 150°.	Cacodylic acid, $O:AsMe_2\cdot OH$. Prisms. M.-p. 200°.
Tertiary..	Trimethyl-arsine, $AsMe_3$ B.-p. 70°.	Trimethyl-arsine dichloride, $AsMe_3Cl_2$.	Trimethyl-arsine oxide, $AsMe_3O$. Solid.	

3 ANTIMONY, BORON, AND SILICON COMPOUNDS

Antimony also forms compounds with the alkyls precisely similar to those of arsenic; primary and secondary compounds do not exist. **Trimethyl-stibine**, $Sb(CH_3)_3$ (*Landolt*), is a highly disagreeable and spontaneously inflammable liquid of onion-like smell; and **Antimony pentamethyl**, $Sb(CH_3)_5$, an oily liquid of weak odour, which can be distilled, and is not

spontaneously inflammable. **Tetramethyl-stibonium-hydroxide**, $Sb(CH_3)_4OH$, is very like caustic potash.

Bismuth yields tri-alkyl derivatives, *e.g.* $Bi(CH_3)_3$, which are relatively unstable. No bismuthonium compounds are known.

Boron tri-ethyl, $B(C_2H_5)_3$ (*Frankland*), is a spontaneously inflammable liquid which burns with a green flame with deposition of much soot; and **boron trimethyl**, $B(CH_3)_3$, an analogous gas of an unbearable stinking smell.

The silicon compounds (*Friedel* and *Crafts*), in contradistinction to the foregoing, resemble methane and the paraffins rather than the spontaneously inflammable silicon hydride, and are very stable in the air.

Tetramethyl silicane, $Si(CH_3)_4$, is a mobile liquid similar to pentane, and floats on water. **Tetraethyl silicane** or **Silicononane**, $SiEt_4$, is also known, and gives rise to numerous derivatives corresponding with those of tetraethyl methane, *e.g.* $SiC_8H_{19}Cl$, $SiC_8H_{19}\cdot O\cdot CO\cdot CH_3$, $SiC_8H_{19}\cdot OH$, **Silicononyl alcohol**, &c. Compare B. 1911, **44**, 2640.

F. Organo-Metallic Compounds

Most of the important metals form definite compounds with alkyl groups. The composition of these organo-metallic or metallo-organic compounds almost always corresponds with that of the metallic chlorides from which they are derived by the replacement of halogen by alkyl. They are colourless, mobile liquids which boil without decomposition at relatively low temperatures; they often decompose violently with water and burn explosively in the air, but in other cases they are stable, both in water and air. To the former category belong the magnesium, zinc, and aluminium alkyls, and to the latter the mercury, lead, and tin compounds. As most of the compounds are volatile, their molecular weights can be determined, and hence the valencies of the respective metals determined, as, the alkyl radicals are monovalent. Examples are: $ZnMe_2$, $CdMe_2$, $HgEt_2$, $AlMe_3$, $PbMe_4$, $SnEt_4$, &c.

Compounds are also known which contain halogen as well as alkyl radicals combined with a metal. They behave like salts. The halogen in them can be replaced by hydroxyl, whereby basic compounds result, compounds which are often much more strongly basic than the corresponding metallic hydroxides, in accordance with the electro-positive character

of the alcohol radical. Such hydroxides or oxides cannot be volatilized without decomposition. Compounds of this type, *e.g.* $CH_3 \cdot Mg \cdot I$, are very readily prepared from their components ($Mg + CH_3I$) in dry ethereal solution, and are largely made use of as synthetical reagents.

The organo-metallic compound may be prepared—

1. By treating the alkyl haloid with the metal in question. In this way zinc-, magnesium-, and mercury-alkyls are got:

$$Mg_2 + 2CH_3I = Mg(CH_3)_2 + MgI_2.$$

The mixed organo-metallic compounds (p. 121), *e.g.* $CH_3 \cdot Mg \cdot I$ or $C_2H_5 \cdot Zn \cdot I$, are probably formed as intermediate products.

2. Numerous metallic compounds have been prepared by double decomposition between zinc-alkyl and the metallic chloride, or more recently by the action of the mixed magnesium compounds on the metallic chloride. *Pfeiffer* (B. 1904, **37**, 319, 1125, 4617) has prepared numerous tin, lead, and mercury compounds by this method:

$$2Zn(C_2H_5)_2 + SnCl_4 = Sn(C_2H_5)_4 + 2ZnCl_2.$$
$$2C_2H_5 \cdot Mg \cdot I + HgCl_2 = Hg(C_2H_5)_2 + MgCl_2 + MgI_2.$$

Potassium- and **Sodium methide**, $K(CH_3)$ and $Na(CH_3)$, and **Potassium-** and **Sodium ethide**, $K(C_2H_5)$ and $Na(C_2H_5)$, are not known in the free state. When metallic sodium is added to zinc ethyl (or ethide), zinc separates out and a crystalline compound of sodium ethide and zinc ethide is formed, from which, however, the former cannot be prepared pure, since decomposition sets in upon warming. On distilling in a stream of carbon dioxide, the potassium methide combines with the latter to form potassic acetate; the ethyl compound behaves in a similar way.

Zinc methyl or **methide**, $Zn(CH_3)_2$ (*Frankland*, 1849), is prepared according to method 1:

$$(I)\ CH_3I + Zn = Zn(CH_3I);\quad (II)\ 2Zn(CH_3)I = Zn(CH_3)_2 + ZnI_2.$$

The first stage is completed upon warming, and the second upon distilling the resulting product. The zinc is conveniently used in the form of the "copper-zinc couple", and the reaction is facilitated by the addition of ethyl acetate, the reason for this not being known. Zinc methyl is a colourless, mobile, strongly refracting liquid of very piercing and repulsive smell.

B.-pt. 46°; sp. gr. 1·39. It is spontaneously combustible, and burns with a brilliant reddish-blue flame (the zinc flame), with formation of zinc oxide, but may be distilled in an atmosphere of carbon dioxide. When the supply of oxygen is limited, zinc methoxide, $Zn(OCH_3)_2$, is formed. It reacts violently with water, yielding methane and $Zn(OH)_2$, and with methyl iodide gives ethane. It is employed in the preparation of secondary and tertiary alcohols and of ketones. Iodine converts it into **zinc-methyl iodide**, $ZnCH_3I$, white plates (see above), and methyl iodide; an excess of iodine yields zinc iodide and methyl iodide.

Zinc ethyl, $Zn(C_2H_5)_2$, b.-pt. 118°, sp. gr. 1·18, closely resembles zinc methide.

The mercury compounds, $HgMe_2$ and $HgEt_2$, are produced by method of formation 1, also by method 2. They are colourless liquids of peculiar sweetish and unpleasant odour, and boil respectively at 95° and 159°. They are permanent in the air, but inflammable, and both—especially the methyl compound—are very poisonous.

Aluminium methyl, $Al(CH_3)_3$, is spontaneously inflammable and decomposes violently with water. B.-pt. 130°. For vap. dens. see B. **22**, 551.

Lead tetramethyl, $Pb(CH_3)_4$, and **ethyl**, $Pb(C_2H_5)_4$ (*Cahours*). These are formed according to method 2, curiously with separation of lead:

$$2PbCl_2 + 2Zn(CH_3)_2 = Pb(CH_3)_4 + Pb + 2ZnCl_2.$$

They are stable in the air, and are interesting from the lead in them being tetravalent. The **hydroxide**, $Pb(CH_3)_3 \cdot OH$, forms pointed prisms, smells like mustard, and is a strong alkali; thus, it saponifies fats, drives out ammonia from its salts, precipitates metallic salts, &c. The compound $Pb_2(C_2H_5)_6$ is also known.

The tin compounds are similar (*Ladenburg*, *Frankland*).

Tin tetramethyl, $Sn(CH_3)_4$, **Tin tetraethyl**, $Sn(C_2H_5)_4$, **Tin triethyl**, $Sn_2(C_2H_5)_6$, **Tin dimethyl**, $Sn_2(CH_3)_4$, &c., are of interest as indicating the tetravalence of tin.

For a number of years the zinc alkyl compounds were largely used for the synthesis of various groups of compounds, viz. hydrocarbons, tertiary alcohols, and ketones (see these). To a large extent these compounds are now replaced by *Grignard's* reagents (C. 1900, **130**, 1322; 1901, **132**, 336, 558).

Any alkyl haloid, when added to dry magnesium powder suspended in pure anhydrous ether, yields a compound of the type $CH_3 \cdot Mg \cdot I$. This reaction occurs in ethyl ether, amyl ether, and in dimethylaniline, but not readily in solvents like benzene unless ether or dimethylaniline is also present. It would appear that the ether forms a definite compound, with the magnesium alkyl compound, of the type $CH_3 \cdot Mg \cdot I$, $(C_2H_5)_2O$. Probably $\begin{matrix} C_2H_5 \\ C_2H_5 \end{matrix}\!>\!O\!<\!\begin{matrix} MgCH_3 \\ I \end{matrix}$ (*Baeyer* and *Villiger*, B. 1902, **35**, 1201). These *Grignard* compounds in ethereal solution are extremely reactive They have been largely made use of for the preparation of hydrocarbons; primary, secondary, and tertiary alcohols; aldehydes, acids, thio-acids, &c. (see these); also for the detection and estimation of hydroxyl groups (B. 1902, **35**, 3912, and *Hibbert* and *Sudborough*, J. C. S. 1901, **85**, 933) by measuring the volume of methane evolved when a given weight of the hydroxyl compound is mixed with an excess of the *Grignard* reagent dissolved in amyl ether. They may also be used for differentiating between primary, secondary, and tertiary amines (*Sudborough* and *Hibbert*, Proc. 1904, **20**, 165).

V. ALDEHYDES AND KETONES, $C_nH_{2n}O$

The aldehydes and ketones are substances which are respectively formed by the oxidation of the primary and secondary alcohols, the oxidation consisting in the elimination of two atoms of hydrogen from each molecule of alcohol.

The aldehydes are formed from the primary alcohols, and are easily converted by further oxidation into the corresponding acids containing an equal number of carbon atoms, oxygen being taken up. They possess in consequence strongly reducing properties.

The ketones result from the oxidation of the secondary alcohols, and are more difficult to oxidize further; they do not possess reducing properties. Their oxidation does not lead to acids containing an equal number of carbon atoms in the molecule, but to others containing a smaller number, the carbon chain being broken.

The lower members of both classes are neutral liquids of peculiar smell, readily soluble in water and readily volatile, only CH_2O being gaseous. As the number of carbon atom-

increases they become less soluble, and their odour becomes less marked with rise of boiling-point until the highest members are solid, odourless like paraffin, and only capable of being distilled under reduced pressure.

The aldehydes closely resemble the ketones as regards modes of formation and also in many of their properties.

Both groups of compounds contain the carbonyl :C:O group, but in the aldehydes this is always attached to a hydrogen atom, and also to an alkyl group or a second hydrogen, *e.g.* $CH_3 \cdot CO \cdot H$ and $H \cdot CO \cdot H$, whereas in a ketone it is attached to two alkyl groups, *e.g.* $C_2H_5 \cdot CO \cdot C_2H_5$.

A. Aldehydes

The homologous series of the aldehydes, $C_nH_{2n}O$, corresponds exactly with that of the acids, $C_nH_{2n}O_2$. They form a group of compounds exactly intermediate between the primary alcohols and the fatty acids. Each primary alcohol by the loss of hydrogen yields an aldehyde, and this by the addition of oxygen yields a fatty acid:

$$H \cdot CH_2 \cdot OH \xrightarrow[-2H]{} H \cdot C\lessdot^{H}_{O} \xrightarrow[+O]{} H \cdot C\lessdot^{O \cdot H}_{O}$$

$$CH_3 \cdot CH_2 \cdot OH \longrightarrow CH_3 \cdot C\lessdot^{H}_{O} \longrightarrow CH_3 \cdot C\lessdot^{O \cdot H}_{O}, \text{ \&c}$$

Their boiling-points are decidedly lower than those of the corresponding alcohols, and rise, in the normal aldehydes, at first by about 27° for each CH_2, and later on by a less amount.

Nomenclature. The name aldehyde is derived from *al*(cohol), *dehyd*(rogenatus), *i.e.* an alcohol from which hydrogen has been removed. The various aldehydes are named according to the acids to which they give rise on oxidation. For example, $H \cdot CHO$ formaldehyde, $CH_3 \cdot CHO$, acetaldehyde, &c. According to the Geneva Congress, the aldehydes receive names ending in *al*, *e.g.* ethanal for acetaldehyde.

Modes of Formation.—1. By the regulated oxidation of the primary alcohols, $C_nH_{2n+1}OH$, by potassium dichromate or manganese dioxide and dilute sulphuric acid; often slowly by atmospheric oxygen, especially in the presence of bone-black or platinum:

2. From the acids of the acetic series, by distilling a mixture of their calcium or barium salts with calcium or barium formate (*Limpricht*). The formic acid acts in this instance as a reducing agent, producing calcium carbonate, thus:—

$$CH_3\cdot COOca + HCOOca = CH_3\cdot CHO + CaCO_3 \quad (ca = \tfrac{1}{2}Ca.)$$

3. From the dihalogen substitution products of the hydrocarbons containing the group $\cdot CHX_2$, by superheating with water or by boiling with water and PbO:

$$CH_3\cdot CHCl_2 + H_2O = CH_3\cdot CHO + 2HCl.$$

4. From *Grignard* reagents (p. 120), and ethyl formate or ethyl orthoformate. Also by heating alcohols with metals or metallic oxides (Chap. XLIX).

Constitution. — In the oxidation of the primary alcohols, $R\cdot CH_2\cdot OH$, to their corresponding acids, $R\cdot CO\cdot OH$, the alkyl radical R remains unaltered. It must consequently also remain unchanged in the intermediate products of the oxidation, viz. the aldehydes, which therefore possess the constitution $R\cdot CHO$:

$CH_3\cdot CH_2\cdot OH$	$CH_3\cdot CHO$	$CH_3\cdot CO\cdot OH$
Alcohol	Aldehyde	Acetic acid.

The aldehydes thus contain the group $\cdot CHO$, either $\cdot C\cdot OH$ or $\cdot C\lessdot^{O}_{H}$. The former is not correct, since the aldehydes do not give the reactions characteristic of compounds containing hydroxyl radicals. All their properties point to the presence of the :C:O group. The characteristic grouping of all aldehydes is thus the $\cdot C\lessdot^{H}_{O}$ group. This is confirmed by the fact that an acid chloride $R\cdot C\lessdot^{O}_{Cl}$ on reduction yields a primary alcohol and undoubtedly an aldehyde as an intermediate product:

$$R\cdot C\lessdot^{O}_{Cl} \rightarrow R\cdot C\lessdot^{O}_{H} \rightarrow R\cdot C\lessdot^{OH}_{H}{}_{H}.$$

Isomers.—Isomerism in the aldehydes is caused solely by isomerism in the alkyl radicals R, which are combined with the group $\cdot CHO$, and therefore contain an atom of carbon less. Otherwise the aldehydes—from C_3H_6O on—are isomeric with the ketones, with the oxides of the olefines (*e.g.* aldehyde with

ethylene oxide, C_2H_4O), and with the alcohols of the allylic series.

Behaviour. — The aldehydes are distinguished by being exceptionally chemically active.

1. The aldehydes are very readily oxidizable, slowly even by the air alone, and quickly by chromic acid, salts of the noble metals, &c. They consequently reduce an ammoniacal solution of silver and often one of copper, this reaction is characteristic and is especially delicate in the presence of caustic-soda solution. (Formation of silver mirror.)

2. The aldehydes are easily reduced by nascent hydrogen, *e.g.* sodium amalgam and dilute acid or zinc dust and glacial acetic acid, to the primary alcohols from which they are derived by oxidation, *e.g.*:

$$CH_3 \cdot CHO + 2H = CH_3 \cdot CH_2 \cdot OH.$$

A glycol is formed as a by-product, *e.g.* butylene glycol, $C_4H_8(OH)_2$, from C_2H_4O

3. Phosphorus pentachloride and trichloride convert the aldehydes into ethylidene chloride and analogous dichloro-substitution products of the hydrocarbons:

$$CH_3 \cdot CHO \rightarrow CH_3 \cdot CHCl_2.$$

4. Additive reactions. According to *Perkin* (J. C. S 1887, 808), a solution of acetaldehyde in water contains a certain amount of the hydrate, $CH_3 \cdot CH(OH)_2$. (Cf. Chloral hydrate.) This compound is extremely unstable, and has never been isolated in a pure form. In those reactions in which it might be formed, its anhydride (acetaldehyde) is invariably produced, *e.g.* $CH_3 \cdot CHCl_2$ with alkali yields $CH_3 \cdot CH:O$ as final product, and not $CH_3 \cdot CH(OH)_2$, although this is probably formed as an intermediate substance.

Thus we conclude *that two hydroxyl groups attached to the same carbon atom cannot as a rule exist together*, but a molecule of water is eliminated, and an aldehyde or ketone is formed. In particular cases only can compounds with two such hydroxyl groups exist (see Chloral).

If, in place of water, $NaHSO_3$, NH_3, HCN, &c., be employed, direct addition to the aldehydes is readily observed, and in all these reactions it is concluded that the addition occurs at the expense of the doubly-united oxygen atom. A hydrogen atom of the substance in question attaches itself to the oxygen of the aldehyde, with formation of a hydroxyl group, while

the residual X (*e.g.* NH_2), which was originally bound to the afore-mentioned H atom, becomes united to the carbon:

$$CH_3 \cdot CH{:}O + HX = CH_3 \cdot CH\!<\!\begin{matrix}OH\\X\end{matrix}.$$

Cf. additive reactions of the olefines (p. 44).

The most important additive reactions are:—

(*a*) Combination with water, which would lead to a dihydric alcohol, does not as a rule take place, for the reasons already given. Should the alkyl radical of the aldehyde, however, contain several negative atoms, *e.g.* Cl, then the hydrates are capable of existence, for instance chloral hydrate:

$$CCl_3 \cdot CHO + H_2O = CCl_3 \cdot CH(OH)_2.$$

But even in these cases the tendency for water to separate is too great to allow of such hydrates behaving as dihydric alcohols, they react rather, for the most part, exactly like the aldehydes themselves. (Cf. Pyroracemic and Mesoxalic acids.)

(*b*) Occasionally, compounds with alcohol or acetic acid, *e.g.* $R \cdot CH(OEt)(OH)$, or $R \cdot CH(OH)(OAc)$, are met with. They are, however, extremely unstable. When the aldehyde is heated with alcohol or acetic anhydride, stable ethers or esters of the hypothetical glycols are obtained

$$CH_3 \cdot CHO + 2C_2H_5 \cdot OH = CH_3 \cdot CH(OC_2H_5)_2 + H_2O$$
$$CH_3 \cdot CHO + (C_2H_3O)_2O = CH_3 \cdot CH(OC_2H_3O_2)_2$$

The compounds obtained from alcohols, the so-called "**acetals**" (see p. 129), are also formed by the partial oxidation of primary alcohols, and are hydrolysed by sulphuric acid.

(*c*) The aldehydes combine with sodium hydrogen sulphite, $NaHSO_3$, &c., to crystalline compounds, readily soluble in water but sparingly in alcohol, *e.g.* C_2H_4O, $NaHSO_3$, $\frac{1}{2}H_2O$. These are to be regarded as sulphite derivatives of the ethylidene glycols, for instance, $CH_3 \cdot CH(OH)(\cdot O \cdot SO_2Na)$. They are almost invariably decomposed when heated with alkalis or acids and regenerate the aldehydes. They are, therefore, of great importance for the separation of aldehydes from mixtures.

(*d*) The aldehydes combine with ammonia to aldehyde-ammonias, *e.g.* **aldehyde-ammonia**, $(CH_3 \cdot CHO, NH_3)_3$. These are crystalline compounds, for the most part readily soluble in water, sparingly in alcohol, and insoluble in ether. Like the bisulphite compounds, they are advantageously used for the

purification of aldehydes, as they readily yield the aldehydes when warmed with dilute acid. (See p. 128.)

(*e*) The aldehydes combine with hydrocyanic acid to form nitriles of higher acids, thus, acetic aldehyde yields the compound $CH_3 \cdot CH<^{OH}_{CN}$, **ethylidene cyanhydrin.** This reaction is largely made use of in the preparation of certain hydroxy acids, as the cyanhydrins, when hydrolysed, yield hydroxy acids, *e.g.* $CH_3 \cdot CH<^{OH}_{COOH}$, lactic acid.

(*f*) An interesting additive reaction is that between an aldehyde and a *Grignard* compound (p. 121). Thus acetaldehyde and magnesium ethyl iodide yield $\frac{CH_3}{C_2H_5}>CH \cdot OMgI$, and this with water gives methyl-ethyl-carbinol, $\frac{CH_3}{C_2H_5}>CH \cdot OH$. (Cf. Secondary Alcohols.)

5. The aldehydes show great tendency to polymerize. (See pp. 12 and 45.) In the case of formaldehyde this polymerization occurs spontaneously at the ordinary temperature Acetaldehyde is polymerized upon the addition of small quantities of hydrochloric, sulphuric, or sulphurous acid, zinc chloride, carbonyl chloride, &c., to para-aldehyde, $C_6H_{12}O_3$, $= (C_2H_4O)_3$, at the ordinary temperature, and to meta-aldehyde, $(C_2H_4O)_3$, at 0°. Why the above-mentioned substances should induce this polymerization is not known.

Another type of polymerization is the aldol condensation (see pp. 127 and 131).

6. Towards alkalis the aldehydes behave differently. Aldehyde and several of its homologues, when heated with caustic-soda solution, are transformed into a reddish-brown resin termed **aldehyde-resin**, a product insoluble in water but soluble in alcohol, and possessing a peculiar odour. Other aldehydes are transformed by alkalis into a mixture of equivalent amounts of alcohol and acid, thus:—

$$2RCOH + H_2O = RCH_2OH + R \cdot CO_2H.$$

7. The aldehydes show a great tendency to form *condensation* products with aldehydes, ketones, acids, &c. (See Crotonic Aldehyde, Cinnamic Acid, &c.)

(*a*) $CH_3 \cdot CHO + CH_3 \cdot CHO = CH_3 \cdot CH:CH \cdot CHO + H_2O.$
(*b*) $CH_3 \cdot CO \cdot CH_3 + R \cdot CHO = CH_3 \cdot CO \cdot CH:CHR + H_2O.$
(*c*) $CH_3 \cdot CO_2H + R \cdot CHO = R \cdot CH:CH \cdot CO_2H + H_2O.$

It is probable that in all these condensations direct addition first occurs, for example, in (*a*) aldol, $CH_3 \cdot CH(OH) \cdot CH_2 \cdot CHO$, is first formed, and then by the loss of water forms croton aldehyde, $CH_3 \cdot CH:CH \cdot CHO$. (See p. 131.)

8. With hydroxylamine the aldehydes yield the so-called **Aldoximes**, water being eliminated (*V. Meyer*, B. **15**, 2778).

$$CH_3 \cdot CHO + H_2N \cdot OH = CH_3 \cdot CH:N \cdot OH + H_2O.$$

For the conditions under which oximes are formed, see B. **23**, 2769

9. The aldehydes react with hydrazines to form the so-called **Hydrazones**, water being eliminated. Phenylhydrazine is the reagent usually employed:

$$CH_3 \cdot CHO + H_2N \cdot NHC_6H_5 = \underset{\text{Aldehyde-phenyl-hydrazone.}}{CH_3 \cdot CH:N \cdot NH \cdot C_6H_5} + H_2O$$

Most of the phenylhydrazones are somewhat sparingly soluble in alcohol, crystallize very readily, and are made use of in identifying different aldehydes On reduction they yield primary amines.

$$CH_3 \cdot CH:N \cdot NH \cdot C_6H_5 + 4H = CH_3 \cdot CH_2 \cdot NH_2 + NH_2 \cdot C_6H_5.$$

10. Moist chlorine and bromine act upon the aldehydes as substituents, thus, from acetaldehyde chloral is obtained:

$$CH_3 \cdot CHO + 3Cl_2 = CCl_3 \cdot CHO + 3HCl.$$

11. Sulphuretted hydrogen converts the aldehydes into thio-aldehydes These are compounds of unpleasant aromatic odour, which show the same peculiarities of polymerization as the aldehydes (*Klinger*). (Cf. *E. Baumann*, B. **23**, 60, **24**, 1419, 3591.)

Reactions 8 and 9 may also be regarded as condensations. It is possible that in all these reactions direct addition first occurs, and that water is subsequently eliminated.

Tests for aldehydes:

(1) Behaviour with ammoniacal silver-nitrate solution (p. 124, and also B. **15**, 1629).

(2) Behaviour with alkaline bisulphites (p. 125).

(3) Behaviour with phenyl-hydrazine and hydroxylamine (see above).

(4) Aldehydes colour a solution of fuchsine which has been

decolorized by sulphurous acid (*Schiff's* reagent) an intense violet-red, some ketones and chloral, but not chloral hydrate, produce the same effect. (B. **13**, 2343; Bull. Soc. Chim. 1894, **11**, 692.)

Formaldehyde, *Methanal*, H·CH:O, may be regarded as the oxide of the divalent methylene radical, CH_2:. It is obtained dissolved in water and excess of methyl alcohol by leading the vapour of the latter, mixed with air, over a glowing platinum or copper spiral or platinum asbestos (*Hofmann*, 1869). Other oxidizing agents lead directly to formic acid.

It is a gas, condensible by cold to a clear mobile liquid, which boils at $-21°$. A solution of about 40 per cent is an article of trade, and is known as formalin. In solution it has apparently the hydrate formula, $CH_2(OH)_2$, and is used as an antiseptic and disinfectant.

Its chief polymeric forms are:

(1) **Para-formaldehyde**, probably $(CH_2O)_n$, a white mass soluble in water, (2) **trioxy-methylene**, probably $(CH_2O)_n$, a crystalline compound which passes into formaldehyde again when volatilized, (3) **formose** (which see), a mixture of several compounds of the nature of glucose. On account of this facility for undergoing polymerization, formic aldehyde in all probability plays an important part in assimilation by plants.

It does not form an additive compound with ammonia, but condenses to the complex compound $C_6H_{12}N_4$, hexamethylenetetramine.

By its combination with hydrochloric acid, **chloro-methyl alcohol** (*chloro-methanol*), $CH_2Cl(OH)$, and **hydroxy-chloro-methyl ether** (*chloromethane-oxy-methanol*), $CH_2Cl·O·CH_2OH$, are formed. Both of these are colourless liquids, which react in many respects like formic aldehyde itself.

Methylal, $CH_2(OCH_3)_2$ (see Acetals, p. 125), is frequently made use of instead of formaldehyde, for carrying out condensation reactions. It is employed in medicine as a soporific, and is also used as an extractive for certain scents. B.-pt. 42°.

Acetaldehyde, *Ethanal*, *Aldehyde*, $CH_3·CHO$, was formerly termed "acetyl hydride", $C_2H_3O·H$ (*Fourcroy* and *Vauquelin*, 1800; composition established by *Liebig* in 1835). It is prepared by passing ammonia gas into an ethereal solution of the crude aldehyde, obtained by oxidizing alcohol with $K_2Cr_2O_7 + H_2SO_4$ and drying over $CaCl_2$, washing the precipitated aldehyde-ammonia with ether, and finally distilling it with dilute sulphuric acid. It is obtained in large quantity as a by-product in the first portions of the distillate "**First Runnings**"

in the manufacture of spirit. For its production in place of vinyl alcohol, $C_2H_3 \cdot OH$, from acetylene, see pp. 50 and 81.

It is a colourless mobile liquid, boils at 21°, and has sp. gr. about 0·8. Its odour is aromatic and suffocating, and produces a kind of cramp in the chest when inhaled. It burns with a luminous flame, dissolves sulphur, phosphorus, and iodine, and is readily soluble in water, alcohol, and ether.

Para-aldehyde, $C_6H_{12}O_3$, is a liquid sparingly soluble in water. It melts at 10°, and boils at 124°, *i.e.* more than 100° above that of aldehyde, and is used as a soporific.

Meta-aldehyde, $(C_2H_4O_3)_2$, crystallizes in white prisms insoluble in water, and sublimes at a little over 100°, but is partially reconverted into aldehyde. (B. **14**, 2271. **40**, 1341.)

Meta-aldehyde is changed back again into ordinary aldehyde by prolonged heating to 115° in sealed tubes, and also, as is the case with para-aldehyde, by distillation with somewhat dilute sulphuric acid. Para-aldehyde reacts in the same way as ordinary aldehyde with PCl_5, but not with NH_3, $NaHSO_3$, $AgNO_3$, and NH_2OH. The constitution of para aldehyde may be represented as:

$$CHMe\begin{matrix} O\cdot CHMe \\ O\cdot CHMe \end{matrix}\!\!>\!O \quad (\textit{Kekulé} \text{ and } \textit{Zincke})$$

(The union of three molecules of aldehyde by means of the valencies of carbon atoms cannot be assumed, on account of the readiness with which para-aldehyde breaks up into aldehyde.)

With regard to these and other polymeric compounds, the general rule has been proved to hold that, in the case of bodies of similar constitution, the one of simpler composition is the more soluble, possesses the lower melting-point, and is the more easily vaporized

Acetal, $CH_3 \cdot CH(OC_2H_5)_2$, boils at 104°. It is usually obtained by the partial oxidation of ethyl alcohol with manganese dioxide and sulphuric acid, the acetaldehyde first formed condensing with the alcohol with the production of acetal. This, as well as methylal, is frequently used instead of aldehyde for the carrying out of condensation reactions (see p. 126).

Propylaldehyde, $C_2H_5 \cdot CHO$, is present in wood-tar. Normal **heptylic aldehyde** (*œnanthol*), $C_7H_{14}O$, is obtained by the dry distillation of castor-oil under diminished pressure, &c.

Chloral, 2-*trichloro-ethanal*, $CCl_3 \cdot CHO$, is a liquid which boils at 98°, and which—when impure—easily changes into

a solid polymeric modification, meta-chloral, but is regenerated from this upon heating. It combines readily with water to **chloral hydrate**, $CCl_3 \cdot CH(OH)_2$ (see p. 125, *a*), and with alcohol to **chloral alcoholate**, $CCl_3 \cdot CH(OH)(OC_2H_5)$, and **trichloro-acetal**, $CCl_3 \cdot CH(O \cdot C_2H_5)_2$. The end product of the action of chlorine upon alcohol consists chiefly of the last three substances. They are all colourless crystalline compounds, which are converted into chloral by distilling with sulphuric acid, and rectifying over lime.

Chloral is an oily liquid with a sharp, characteristic odour. It combines with sodium bisulphite, ammonia, hydrocyanic acid, and acetic anhydride, and reduces an ammoniacal solution of silver oxide. It is readily oxidized to trichloracetic acid, and decomposed by alkali into chloroform and an alkali formate:

$$CCl_3 \cdot CHO + HKO = CCl_3H + HCO_2K.$$

Chloral hydrate, $CCl_3 \cdot CH(OH)_2$, forms large colourless crystals readily soluble in water, melting at 57°, and boiling with dissociation at 97°. It acts as a soporific and antiseptic. Sulphuric acid converts it into chloral.

UNSATURATED ALDEHYDES

Acrolein, *Acrylic aldehyde*, *propenal*, $CH_2:CH \cdot CHO$, is produced by the oxidation of allyl alcohol, by the distillation of fats, and by heating glycerol with potassium hydrogen sulphate. It is a liquid boiling at 52°, of pungent odour (the smell of burning fat being due to it), and of violent action upon the mucous membrane of the eyes. It unites in itself the properties of an aldehyde and of an unsaturated carbon compound, and therefore combines with ammonia and with bromine; it also unites with hydrogen bromide to *bromopropyl aldehyde*, $CH_2Br \cdot CH_2 \cdot CHO$.

When distilled, acrolein-ammonia yields picoline, C_6H_7N (see Pyridine bases); and crotonic aldehyde-ammonia, by an analogous reaction, collidine, $C_8H_{11}N$.

Acrolein can combine with two atoms of bromine to acrolein dibromide (dibromopropyl aldehyde), $CH_2Br \cdot CHBr \cdot CHO$, a compound which is of importance in the synthesis of the sugars. (See Synthesis of Monoses.)

Crotonic aldehyde, $CH_3 \cdot CH:CH \cdot CHO$. When acetaldehyde is left for some time in contact with dilute hydrochloric acid or sodium hydroxide, polymerization occurs, and

a substance termed **aldol**, or α-hydroxy-butyraldehyde, is obtained, $CH_3 \cdot CH(OH) \cdot CH_2 \cdot CHO$. The constitution of aldol follows from its properties. It cannot be readily converted back into acetaldehyde, and in this respect differs from the other polymeric forms, viz. meta- and para-aldehyde. This difference is due to the fact that in the aldol condensation the union of the molecules has been brought about between carbon atoms, and hence the relative stability. Aldol when distilled or in presence of dehydrating agents yields croton-aldehyde, water being eliminated.

$$CH_3 \cdot CH(OH) \cdot CH_2 \cdot CHO = CH_3 \cdot CH{:}CH \cdot CHO + H_2O.$$

On oxidation it yields crotonic acid.

B. Ketones

The lowest member of the series, Acetone, contains three atoms of carbon. The higher members, from C_{12} on, are solid. They are all lighter than water; *e.g.* the sp. gr. of acetone is 0·81 at 0°.

Occurrence.—Acetone is present in urine, methyl-nonyl ketone in oil of rue (*Ruta graveolens*).

Modes of Formation.—1. By the oxidation of secondary alcohols; just as in the conversion of a primary alcohol to an aldehyde, this oxidation consists in the withdrawal of two hydrogen atoms from each molecule of the alcohol:

$$\underset{\text{Isopropyl alcohol}}{CH_3 \cdot CH(OH) \cdot CH_3} + O = \underset{\text{Acetone.}}{CH_3 \cdot CO \cdot CH_3} + H_2O$$

Many primary and secondary alcohols are decomposed into hydrogen and aldehyde (or ketone) when heated in contact with a catalyst (see Chap. XLIX).

2. By the dry distillation of the calcium or barium salts of fatty acids, the metallic carbonate being also formed:

$$\begin{matrix} CH_3 \cdot CO \cdot O \\ CH_3 \cdot CO \cdot O \end{matrix} \!\!> Ca = CaCO_3 + CH_3 \cdot CO \cdot CH_3.$$

Some of the ketones of high molecular weight may be obtained by heating fatty acids with phosphorus pentoxide (*Kipping*):

$$\begin{matrix} R \cdot CO \cdot O \cdot H \\ R \cdot CO \cdot O \cdot H \end{matrix} = R \cdot CO \cdot R + CO_2 + H_2O.$$

When two different acids are employed, **mixed ketones**, *i.e.* ketones containing different alkyl radicals, are formed, thus:—

$$CH_3\cdot COOca + CH_3\cdot CH_2\cdot COOca = \begin{matrix} CH_3 \\ C_2H_5 \end{matrix}\!\!>\!CO + CO_3Ca$$

Calcium acetate and propionate — Methyl-ethyl ketone

As a rule, in addition to the mixed ketone, the two simple ketones, *e.g.* $(CH_3)_2CO$ and $(C_2H_5)_2CO$, are also formed.

3. From dichlorides containing the group $C\cdot CCl_2\cdot C$:

$$(CH_3)_2CCl_2 + H_2O = (CH_3)_2CO + 2HCl$$

Acetone chloride — Acetone

It is probable that the chlorine atoms are first replaced by hydroxyls, yielding the glycol, $CMe_2(OH)_2$, which immediately eliminates H_2O, yielding the ketone, CMe_2O.

4. By the action of zinc alkyl upon an acid chloride, *e.g.* acetyl chloride, $CH_3\cdot COCl$.

An additive compound is first formed, $CH_3\cdot C\!<\!\begin{matrix} OZnCH_3 \\ CH_3 \\ Cl \end{matrix}$

which must be quickly decomposed by water, otherwise tertiary alcohols are produced.

$$CH_3\cdot C\!<\!\begin{matrix} O\,ZnCH_3\,OH \\ CH_3 \\ Cl \qquad H \end{matrix} = CH_3\cdot CO\cdot CH_3 + HCl + CH_3\cdot Zn\cdot OH.$$

This method of formation, which was devised by *Freund* in 1861, allows of the preparation of any possible ketone by using the requisite zinc alkyl and acid chloride.

At the same time it elucidates, together with method 2, the *constitution* of the ketones from the constitution of the corresponding acids. Conclusions regarding constitution based on the latter method must be accepted with a considerable amount of reserve unless supported by other arguments, since in reactions which occur at high temperatures intramolecular rearrangements can readily occur. Theoretically, therefore, ketones are compounds which contain the carbonyl group, CO, linked on both sides with an alkyl radical, $R\cdot CO\cdot R$. If the alcohol radicals are the same, "**simple**" ketones result; and if different, "**mixed**" ketones. A compound with less than 3 C atoms is thus impossible.

Ketones have been synthesised by the action of organo-magnesium compounds on nitriles or acid amides, *e.g.*:

$$R\cdot C{\equiv}N + I\cdot Mg\cdot R' = \begin{matrix} R \\ R' \end{matrix}\!\!>\!C{:}N\cdot MgI,$$

$$R\cdot CO\cdot NH_2 + 2I\cdot Mg\cdot R' = \begin{matrix} R \\ R' \end{matrix}\!\!>\!C\!<\!\begin{matrix} OMgX \\ NHMgX \end{matrix} + R'H,$$

and these with water yield R·CO·R'. (*Blaise*, C 1901, **132**, 38, **133**, 299.)

5. From the ketone acids or their esters, *e.g.* acetoacetic ester, $CH_3\cdot CO\cdot CH_2\cdot CO\cdot OC_2H_5$, by warming with moderately dilute sulphuric acid or with dilute alkalis. This important reaction will be treated of at greater length under acetoacetic ester.

6. By the addition of water to homologues of acetylene, $CH_3\cdot C{\equiv}CH + H_2O = CH_3\cdot CO\cdot CH_3$. This reaction occurs at relatively high temperatures, or may be brought about indirectly by the aid of sulphuric acid, or solutions of mercuric salts.

Isomers.—The ketones exhibit the same isomerism as the secondary alcohols. This isomerism depends on the one hand upon the isomerism within the alkyl groups, *e.g.* dipropyl ketone and di-*iso*propyl ketone, which are linked together by the CO group, and on the other by the position of the oxygen atom in the carbon chain (position isomerism); thus, $C_4H_9\cdot CO\cdot CH_3$ is isomeric with $C_3H_7\cdot CO\cdot C_2H_5$.

The aldehydes containing an equal number of carbon atoms in the molecule are always isomeric with the ketones, since both classes of compounds are formed from isomeric alcohols by the withdrawal of 2 H.

Further, acetone is isomeric with allyl alcohol. Such an isomerism of a saturated with an unsaturated compound is termed "**saturation isomerism**" (cf. p. 87).

Nomenclature.—The usual name is formed by adding the suffix ketone to the name of the alkyl groups present, *e.g.* $(C_2H_5)_2CO$, diethyl ketone; $CH_3\cdot CO\cdot C_2H_5$, methylethyl ketone, &c. The names of the simple ketones are also derived from the acids which yield them, *e.g.* "**Valerone**" $(C_4H_9)_2CO$, from valeric acid.

The systematic names of the ketones are formed by taking the name for the corresponding hydrocarbon, adding the suffix one to indicate the O replacing 2 H, and then a number to indicate the position of the O atom, *e.g.* $CH_3\cdot CO\cdot CH_2\cdot CH_3$, **butan-2-one**, &c.

Behaviour.—1. Reagents which give rise to nascent hydrogen reduce the ketones to secondary alcohols: $(CH_3)_2CO + 2H = (CH_3)_2CH \cdot OH$. Small amounts of pinacones (see these) are formed at the same time.

2. Oxidizing agents, *e.g.* $K_2Cr_2O_7$, and dilute H_2SO_4, slowly convert the ketones into acids or ketones containing a smaller number of carbon atoms in the molecule (not—as in the case of the aldehydes—into acids containing an equal number), the carbon chain being broken:

$$CH_3 \cdot CO \cdot CH_3 + 4O = CH_3 \cdot COOH + CO_2 + H_2O.$$

Since the carbon atom is tetravalent, the CO group in the ketone, being already linked to 2 alkyl radicals, can only yield the COOH group, characteristic of acids (p. 110), by the removal of one of the alkyl groups. In this process of oxidation of a mixed ketone the molecule usually becomes ruptured in such a manner that the CO group remains attached to the smaller alkyl group. Thus $CH_3 \cdot CO \cdot C_3H_7$ on oxidation yields mainly acetic $CH_3 \cdot CO_2H$ and propionic $C_2H_5 \cdot CO_2H$ acids; but at the same time a small amount is oxidized to a mixture of carbonic and butyric acids (B. **25**, R. 121).

Since the acids formed by oxidation bear no reciprocal relation to the ketone, and the oxidation process is more complicated than in the case of the aldehydes, it is easy to understand why the ketones do not possess reducing properties.

3. Phosphorus pentachloride, PCl_5, converts the ketones into the corresponding dichlorides, acetone, for instance, into acetone chloride, $(CH_3)_2CCl_2$.

4. Additive reactions. (*a*) The ketones do not as a rule combine with water and alcohol, for the reasons given under the aldehydes and at p. 132.

(*b*) With ammonia they yield complex condensation products, *e.g.* di-acetone-amine, $C_6H_{13}NO$, tri-acetone-amine, $C_9H_{17}NO$ (*Heintz*); this reaction is more complicated than that with the aldehydes, 2 or 3 molecules of acetone combining with 1 molecule of ammonia, with elimination of water.

(*c*) The ketones which contain the group $CH_3 \cdot CO \cdot$, and a few other relatively simple ketones, combine with sodium hydrogen sulphite to crystalline compounds, *e.g.* acetone to $(CH_3)_2C\langle^{OH}_{O \cdot SO_2Na}$, H_2O, which can be converted back into the ketone by distillation with sodium-carbonate solution. This

very important reaction is made use of in separating and purifying the ketones. *Stewart* has recently (J. C. S. 1905, **87**, 185) studied the comparative rates at which some of these compounds are formed.

(*d*) With hydrocyanic acid they yield hydroxy-nitriles, as in the case of the aldehydes; *e.g.* $(CH_3)_2C\langle^{OH}_{CN}$.

(*e*) Ketones readily form additive compounds with *Grignard's* reagents, and when decomposed with water these yield tertiary alcohols (see p. 72):

$$Me_2CO + MeMgI = Me_3C\cdot O\cdot MgI,$$
$$Me_3C\cdot O\cdot MgI + H\cdot OH = Me_3C\cdot OH + OH\cdot Mg\cdot I.$$

5 The ketones, unlike the aldehydes, do not possess the property of polymerizing, but they form condensation products. Just as aldehyde is converted into crotonic aldehyde, so is acetone, by the action of many reagents—*e.g.* CaO, KOH, HCl, and H_2SO_4—converted, with elimination of water, into **mesityl oxide**, $C_6H_{10}O$, **phorone**, $C_9H_{14}O$, or **mesitylene**, C_9H_{12}, according to the conditions (see these substances):

$$2C_3H_6O = C_6H_{10}O + H_2O. \qquad 3C_3H_6O = C_9H_{14}O + 2H_2O.$$
$$3C_3H_6O = C_9H_{12} + 3H_2O.$$

Analogous condensations also ensue with other ketones or aldehydes under the influence of dilute caustic soda or of sodium ethoxide (B. **20**, 655). In this way the more complicated ketones are formed (A. **218**, 121).

6. Sulphuretted hydrogen converts the ketones into thio-compounds, *e.g.* acetone into thio-acetone, $CH_3\cdot CS\cdot CH_3$ (B. **16**, 1368), or their polymers.

7. Halogens give rise to substitution products.

8. Like the aldehydes, the ketones—even C_{35}—react with hydroxylamine, yielding oximes, which are termed **Ketoximes** (*V. Meyer*, B. **15**, 1324, 2778; **16**, 823, 1784, &c.):

$$(CH_3)_2CO + H_2N\cdot OH = H_2O + (CH_3)_2C{:}N\cdot OH \text{ (acetoxime).}$$

9. They react in an analogous manner with phenyl-hydrazine, $C_6H_5\cdot NH\cdot NH_2$ (*E. Fischer*, B. **17**, 572), with the formation of **phenyl-hydrazones** (p. 127):

$$(CH_3)_2CO + H_2N\cdot NH\cdot C_6H_5 = \underset{\text{Acetone-phenyl-hydrazone.}}{(CH_3)_2C{:}N\cdot NH\cdot C_6H_5} + H_2O.$$

Phenyl-hydrazine and hydroxylamine are therefore of great value for the recognition of the aldehydic or ketonic character of a substance. Semicarbazide, $NH_2 \cdot CO \cdot NH \cdot NH_2$, reacts in an analogous manner (A. 1898, **303**, 79), and it or its hydrochloride is now largely used as a reagent for aldehydes and ketones, as the products (**semicarbazones**) crystallize well and have definite melting-points:

$$(CH_3)_2CO + NH_2 \cdot NH \cdot CO \cdot NH_2 = H_2O + (CH_3)_2C{:}N \cdot NH \cdot CO \cdot NH_2.$$

Acetaldehyde-semicarbazone melts at 162°, and **acetone-semicarbazone** at 187°.

10. Nitrous acid (ethyl nitrite and sodium ethylate) gives rise to **iso-nitroso-ketones**, *e.g.* iso nitroso-acetone, $CH_3 \cdot CO \cdot CH{:}N \cdot OH$, by replacement of H_2 by the group $:N \cdot OH$ (oximino). When hydrolysed, the $:N \cdot OH$ group is replaced by oxygen, and diketones or aldehydo-ketones are formed.

Acetone, 2-*Propanone*, $CH_3 \cdot CO \cdot CH_3$. The formula was established by *Liebig* and *Dumas* in 1832. It is present in very small quantity in normal urine, in the blood, in serum, &c., but in much larger quantity in pathological cases such as acetonuria and diabetes mellitus. It is produced, among other ways, by the distillation of sugar, gum, cellulose, &c., and is therefore present in wood spirit, also by the addition of water to allylene, C_3H_4 (p. 50). On the large scale it is prepared by the dry distillation of calcium acetate.

It is a liquid of peculiar pungent odour, boils at 56°, and has sp. gr. 0·81 at 0°. It is soluble in water, but may be salted out from its aqueous solution, and is also miscible with alcohol and ether. $KMnO_4$ does not oxidize it in the cold, but CrO_3 converts it into acetic and carbonic acids.

Metallic sodium reacts with acetone, yielding the derivative $CH_3 \cdot C(ONa){:}CH_2$.

Detection.—Acetone may be detected by the formation of indigo when its solution in sodium hydroxide is warmed with *o*-nitro-benzaldehyde.

Sulphonal, $(CH_3)_2{:}C(SO_2 \cdot C_2H_5)_2$, is formed when a mixture of acetone and mercaptan is treated with hydrochloric acid, and the **mercaptol**, $(CH_3)_2C(SC_2H_5)_2$ [a derivative of the hypothetical acetone-glycol, $(CH_3)_2C(OH)_2$], which is thus formed, is oxidized by potassium permanganate to the corresponding sulphone. It crystallizes in prisms, melts at 125°, and acts as a soporific.

Mesityl oxide, $C_6H_{10}O$, $= CH_3 \cdot CO \cdot CH{:}C(CH_3)_2$ (*Kane*, 1838; *Baeyer*), is a liquid of aromatic odour, boiling at 132°.

Phorone, $C_9H_{14}O$, $= (CH_3)_2C{:}CH \cdot CO \cdot CH{:}C(CH_3)_2$, forms readily fusible yellow crystals. Both of these compounds are obtained by saturating acetone with hydrochloric acid gas (A. **180**, 1).

Methyl ethyl ketone (2-*Butanone*), $CH_3 \cdot CO \cdot C_2H_5$, is present in crude wood spirit, and is also formed by the oxidation of secondary butyl alcohol. B.-pt. 81°.

Pinacoline (2-*Dimethyl-3-butanone*), *methyl tertiary-butyl ketone*, $CH_3 \cdot CO \cdot C(CH_3)_3$, is produced by the action of dilute sulphuric acid upon pinacone (p. 193). This involves a characteristic rearrangement known as the "pinacoline reaction". B.-pt. 106°.

A number of ketones have been obtained from the higher fatty acids. These have been converted by *Krafft* into the corresponding paraffins, by first transforming them into the chlorides, $C_nH_{2n}Cl_2$, by means of PCl_5, and then heating the latter with hydriodic acid and phosphorus.

ALDOXIMES AND KETOXIMES

The aldoximes and ketoximes are the compounds obtained by the action of hydroxylamine on the aldehydes and ketones respectively. They both contain the bivalent oximino group $:N \cdot OH$ attached to carbon, *e.g.*:

$CH_3 \cdot CH{:}N \cdot OH$ and $(CH_3)_2C{:}N \cdot OH$
Acetaldoxime Acetoxime

They are either colourless crystalline compounds or liquids, and are both basic and acidic in properties. With metallic hydroxides they yield salts of the type $CH_3 \cdot CH{:}NOK$; with mineral acids they form salts in much the same manner as ammonia does, *e.g.* $CMe_2{:}NOH, HCl$.

The oximes are fairly readily hydrolysed by dilute acids, yielding hydroxylamine and either an aldehyde or a ketone.

On reduction they all yield primary amines, $:N \cdot OH \rightarrow \cdot NH_2$.

Dehydrating agents, *e.g.* acetic anhydride or acetyl chloride, transform the aldoximes into nitriles, water being eliminated:

$$CH_3 \cdot CH{:}N \cdot OH = CH_3 \cdot C{:}N + H_2O.$$

The ketoximes with acetyl chloride undergo an interesting intramolecular rearrangement known as the *Beckmann transformation*, the final product being an acid amide or anilide. It

is probable that the hydroxyl group of the oxime changes place with one of the alkyl groups attached to the carbon atom, and this then leads to a wandering of a hydrogen atom and a shifting of the double bond:

$$\begin{matrix} R\cdot C\cdot R' & & R\cdot C\cdot OH & & R\cdot C{:}O \\ \ddot{N}\cdot OH & \longrightarrow & \ddot{N}\cdot R' & \longrightarrow & \dot{N}HR'. \end{matrix}$$

Constitution.—In the formation of the oximes the water eliminated is undoubtedly formed from the oxygen of the carbonyl group and the hydrogen atoms of the hydroxylamine, otherwise the reaction would be of the type

$$CH_3\cdot CO\cdot CH_3 + NH_2\cdot OH = CH_3\cdot CO\cdot CH_2\cdot NH_2 + H_2O,$$

and an aminoketone would result. There are two possible ways in which water can be thus eliminated, yielding a compound $CMe_2{:}N\cdot OH$ or $CMe_2\langle{}^{O}_{NH}\rangle$. That the first of these two formulæ is correct is demonstrated by the fact that when an alkyl derivative, $:C{:}N\cdot OR$ or $:C\langle{}^{O}_{N\cdot R}\rangle$, is hydrolysed with hydrochloric acid an alkyl derivative of hydroxylamine, $NH_2\cdot OR$, is obtained, and hence the alkyl group is presumably attached to oxygen in the alkylated oxime, and the oxime itself thus contains an OH group. This constitution formula is in perfect harmony with the reactions characteristic of oximes.

The oxime derived from an aldehyde or ketone often exists in isomeric forms. This is especially true of those derived from aromatic aldehydes and from mixed (unsymmetrical) ketones of the aromatic series. According to *Goldschmidt* and *V. Meyer*, these isomers are structurally identical, and are **stereo-isomeric** (*i.e.* the isomerism is due to the spatial relationship of the various atoms and radicals).

According to *Hantzsch* and *Werner*, the isomerism is readily explicable if we assume that two of the three valencies of the nitrogen atom, when N is united by a double bond to C, lie in the same plane, but that the third valency lies outside this plane. Thus

$$\begin{matrix} R\cdot C\cdot H \\ \ddot{N} \end{matrix}$$

with the oxime derived from an aldehyde, if the two valencies attaching N to C lie in a plane at right angles to the plane of the paper, then the OH radical must fall either close to the alkyl group R or to the H atom; in fact, two configurations are possible, viz.:—

$$\begin{array}{ll} R\cdot C\cdot H & R\cdot C\cdot H \\ \| & \| \\ N\cdot OH & HO\cdot N. \end{array}$$

These are known (1) as *syn*-aldoximes when the H and OH are close together, and as a rule they readily lose water, yielding nitriles, (2) as *anti*-aldoximes when the H and OH are far removed from one another. As a rule, these yield acetyl derivatives, and not nitriles, on treatment with acetyl chloride.

The oximes derived from unsymmetrical ketones also often exist in stereo-isomeric forms, which can be explained in a similar manner:

$$\begin{array}{ll} R\cdot C\cdot R' & R\cdot C\cdot R' \\ \| & \| \\ N\cdot OH & HO\cdot N. \end{array}$$

No isomerism should occur, and so far none has been met with, in the case of the oxime derived from a symmetrical ketone when R = R'. The configurations of these isomeric ketoximes are generally derived from a study of the *Beckmann* transformation.

$$\begin{array}{l} R\cdot C\cdot R' \\ \| \\ N\cdot OH \end{array} \text{ gives } R\cdot CO\cdot NHR' \text{ and } \begin{array}{l} R\cdot C\cdot R' \\ \| \\ OH\cdot N \end{array} \text{ gives } NHR\cdot CO\cdot R$$

(See also Aromatic Aldoximes and Ketoximes.)

VI. MONOBASIC FATTY ACIDS

A. Saturated Acids, $C_nH_{2n}O_2$, or $C_nH_{2n+1}\cdot CO_2H$

(See Table, p. 140.)

The monobasic fatty acids are formed by the oxidation of the saturated primary alcohols or of their corresponding aldehydes. These acids are monobasic, *i.e.* contain in the

molecule only one replaceable atom of hydrogen, since, as a rule, they give rise to only one series of salts or of esters. They are known as the **fatty acids**, because many of them are contained in fats or are formed from fats by processes of oxidation or hydrolysis. They are often spoken of as acids of the aliphatic series.

The characteristic group of the monobasic acids is the carboxylic group $\cdot C\begin{matrix}O\\ \diagdown O\cdot H\end{matrix}$, and it is the hydrogen of this group which becomes replaced in the formation of salts. The basicity of an acid, as a rule, depends on the number of such carboxylic groups present in the molecule.

NORMAL FATTY ACIDS AND THEIR PHYSICAL DATA

$C_nH_{2n+1}\cdot CO_2H$, where C_nH_{2n+1} is a **normal** alkyl group

		Melting-pt	Boiling pt.
Formic acid	CH_2O_2	8·3°	101°
Acetic acid	$C_2H_4O_2$	17°	118°
Propionic acid	$C_3H_6O_2$	— 36°	141°
Butyric acid	$C_4H_8O_2$	— 8°	162°
Valeric acid	$C_5H_{10}O_2$		186°
Caproic acid	$C_6H_{12}O_2$	+ 8°	205°
Heptoic acid	$C_7H_{14}O_2$	— 10°	224°
Caprylic acid	$C_8H_{16}O_2$	+ 16°	236°
Nonylic acid	$C_9H_{18}O_2$	12°	254°
Capric acid	$C_{10}H_{20}O_2$	31°	269°
Undecylic acid	$C_{11}H_{22}O_2$	28°	{213°
Lauric acid	$C_{12}H_{24}O_2$	43°	{226°
Tridecylic acid	$C_{13}H_{26}O_2$	40	{236°
Myristic acid	$C_{14}H_{28}O_2$	54°	{248°
Pentadecylic acid	$C_{15}H_{30}O_2$	51°	{257°
Palmitic acid	$C_{16}H_{32}O_2$	63°	{269°
Margaric acid	$C_{17}H_{34}O_2$	60°	{277°
Stearic acid	$C_{18}H_{36}O_2$	69°	{287°
Nondecylic acid	$C_{19}H_{38}O_2$	66°	{298°
Arachidic acid	$C_{20}H_{40}O_2$	75°	...
Behenic acid	$C_{22}H_{44}O_2$	83°	...
Lignoceric acid	$C_{24}H_{48}O_2$	80°	...
Cerotic acid	$C_{26}H_{52}O_2$	78°	...
Melissic acid	$C_{30}H_{60}O_2$	90°	...

The lower members of the series are liquids of pungent

odour and corrosive action, and boil without decomposition. They dissolve readily in water, and the aqueous solutions exhibit a strongly acid reaction, although most of the anhydrous acids are without action on dry litmus paper. The intermediate members have an unpleasant smell like that of rancid butter or perspiration, and are oily and but slightly soluble in water. Mobility, odour, and solubility diminish as the percentage of carbon increases. The higher members, from C_{10}, are solids, like paraffin, insoluble in water, and can only be distilled without decomposition in a vacuum. Their acid character no longer finds expression in their reaction with litmus, but in their capability of forming salts with bases. These higher acids are readily soluble in alcohol, and especially in ether.

In this series the boiling-point rises regularly for each increase in the number of C atoms in the molecule. The rise is roughly 19° for each increment of CH_2. The melting-points do not exhibit the same regularity: the melting-point of any acid containing an even number of C atoms in the molecule is higher than the melting-point of the acid with an odd number of C atoms which immediately succeeds it

Similar phenomena have been observed in other homologous series. (See section on Physical Properties and Constitution.)

The specific gravity of the liquid acids is at first > 1, and from C_3 onwards < 1, and it decreases continuously to about 0·8, the paraffin character of the hydrocarbon radical becoming preponderant.

Occurrence.—Many of the acids of this series are found in nature in the free state, but more frequently as esters, viz.:—(*a*) esters of monohydric alcohols (see wax varieties), (*b*) esters of glycerol or glycerides, in most of the vegetable and animal fats and oils. For further particulars see pp. 157 and 158.

Formation. -1. By the oxidation of the primary alcohols, $R \cdot CH_2 \cdot OH$, or their aldehydes, $R \cdot C\lesssim^{H}_{O}$, by means of $K_2Cr_2O_7$ or MnO_2 and dilute H_2SO_4, or by the oxygen of the air in presence of platinum or of nitrogenous substances, *e.g.* acetic acid from alcohol. The acids thus formed contain the same number of carbon atoms as the alcohol or aldehyde. Many complex carbon compounds, *e.g.* ketones, unsaturated compounds, &c., when oxidized yield acids containing a smaller number of carbon atoms. The higher acids of this series are converted into their lower homologues when oxidized.

2. Several acids have been prepared from the halogen compounds containing the group $\cdot CX_3$, *e.g.*:—

$$HCCl_3 + 4KOH = H \cdot CO_2K + 3KCl + 2H_2O.$$

We should expect an exchange of the three chlorine atoms for three hydroxyls, with formation of the intermediate compounds $CH(OH)_3$ or $R \cdot C(OH)_3$. Such compounds are, however, extremely unstable, and immediately eliminate water yielding the acids (cf. p. 124):

$$R \cdot C(OH)_3 = R \cdot C(=O)OH + H_2O.$$

But derivatives of these trihydric alcohols, or **ortho-acids** as they are termed, are known; for example, **ethyl ortho-formate** $HC(OC_2H_5)_3$, a neutral liquid of aromatic odour, insoluble in water, and boiling at 146°.

3. From the alkyl cyanides or nitriles, $C_nH_{2n+1}CN$. The cyanides, which are prepared by warming the alkyl iodide with cyanide of potassium, are converted into the fatty acid and ammonia by hydrolysis with potassium hydroxide solution, with dilute or concentrated hydrochloric acid, or with sulphuric acid diluted with its own volume of water.

The reaction may be regarded as the addition of two molecules of water to each molecule of nitrile:

$$CH_3 \cdot C{:}N \xrightarrow{+H_2O} CH_3 \cdot CO \cdot NH_2 \xrightarrow{+H_2O} CH_3 \cdot CO \cdot ONH_4,$$

first yielding the acid amide, and then the ammonium salt of the acid, which is decomposed by the hydrolysing agent employed. The process, in the case of aromatic nitriles, can be stopped at the point when the acid amide is formed, but in the aliphatic series this is almost impracticable. The reaction is the exact reverse of the formation of nitriles from the ammonium salts of fatty acids:

$$CH_3 \cdot CO \cdot ONH_4 \xrightarrow{-H_2O} CH_3 \cdot CO \cdot NH_2 \xrightarrow{-H_2O} CH_3 \cdot C{:}N.$$

The great importance of this reaction, by means of which we can obtain an acid C_{n+1} from an alcohol C_n, has been already indicated (p. 101). And since the acids can be converted indirectly by reduction into the corresponding alcohol

it is thus possible to build up synthetically, step by step, the alcohols richer in carbon from those poorer in carbon, a circumstance which is of especial importance in the case of the normal alcohols (*Lieben* and *Rossi*). As an example:

$$CH_3\cdot OH \xrightarrow[P \text{ and } I]{} CH_3I \xrightarrow[KCN]{} CH_3\cdot CN \xrightarrow[Hydrolysis]{} CH_3\cdot COOH \xrightarrow[With\ calcium\ formate]{} CH_3\cdot CHO \xrightarrow[Reduction]{} CH_3\cdot CH_2OH$$

4. The acids may be regarded as resulting from the paraffins, *e.g.* acetic acid from CH_4 and CO_2, and formic acid from H_2 and CO_2. The two components can be made to combine indirectly; thus, carbon dioxide and sodium methyl (p. 119) combine when heated together (*Wanklyn*):

$$CH_3Na + CO_2 = CH_3\cdot CO_2Na.$$

Formic acid is obtained in an analogous manner from hydrogen and carbon dioxide, under the influence of the silent electric discharge:

$$H_2 + CO_2 = H\cdot CO_2H;$$

or from hydrogen, potassium, and carbon dioxide, when the potassium is placed in a bell-jar filled with moist carbon dioxide (*Kolbe* and *Schmitt*, 1861): or by treating carbonate of ammonia, &c., with sodium amalgam.

5. By passing carbon monoxide over heated caustic alkali or alcoholate, thus:

$$CH_3\cdot ONa + CO = CH_3\cdot CO_2Na \text{ (at } 160^\circ).$$
$$H\cdot ONa + CO = H\cdot CO_2Na.$$

6. By the action of carbon dioxide on ethereal solutions of organo-magnesium haloids, a magnesium compound,

$$C_nH_{2n+1}\cdot Mg\cdot I + CO_2 = C_nH_{2n+1}\cdot CO\cdot OMgI,$$

is obtained, which gives the free acid on the addition of dilute sulphuric acid (C. 1904, **138**, 1048).

7. By the addition of hydrogen to unsaturated acids, *e.g.* propionic acid, $CH_3\cdot CH_2\cdot CO_2H$, from acrylic acid, $CH_2{:}CH\cdot CO_2H$. This addition of hydrogen may be effected (*a*) directly by hydriodic acid and phosphorus, sodium amalgam and water, or by the aid of hydrogen and reduced nickel at a temperature of about 100° (Ostr. 1903, **1**, 547), or hydrogen and colloidal

palladium at the ordinary temperature, Chap. XLIX; (*b*) indirectly, by addition of hydrobromic acid and inverse substitution. Unsaturated acids also yield saturated ones containing fewer carbon atoms when fused with potash, *e.g.* 1 mol. crotonic acid, $C_4H_6O_2$, yields 2 mols. acetic acid, $C_2H_4O_2$.

8. From the hydroxy acids, by reduction with hydriodic acid:

$$\underset{\text{Lactic acid}}{CH_3\cdot CH(OH)\cdot CO_2H} + 2HI = \underset{\text{Propionic acid.}}{CH_3\cdot CH_2\cdot CO_2H} + I_2 + H_2O$$

9. From many polybasic acids, by the elimination of CO_2, for example, formic from oxalic, $COOH\cdot COOH$, and acetic from malonic, $CO_2H\cdot CH_2\cdot CO_2H$.

10. *Aceto-acetic ester syntheses.*—The homologues

$$R\cdot CH_2\cdot COOH \text{ and } \begin{matrix}R\\R'\end{matrix}\!\!>\!CH\cdot COOH$$

can be prepared from acetic acid by first converting the latter into aceto-acetic ester, $CH_3\cdot CO\cdot CH_2\cdot COOC_2H_5$, introducing alkyl groups into this, and then decomposing the compound so obtained by concentrated alcoholic potash. (Cf. Aceto-acetic Ester, p. 228, and Malonic Ester, p. 238.)

Separation.—Natural fats are nearly all glycerides, *i.e.* esters derived from the trihydric alcohol, glycerol, and various fatty and other acids, so that a mixture of acids is obtained when any natural fat is hydrolysed. This mixture may be separated into its components as follows:—

(*a*) By fractional distillation in a good vacuum; (*b*) by fractional precipitation of an alcoholic solution of the acids by means of magnesium acetate, calcium chloride, &c., the acids richer in carbon being precipitated first, (*c*) by fractional solution: the dry barium salts of formic, acetic, propionic, and butyric acids are very differently soluble in alcohol, the solubility increasing rapidly with the number of carbon atoms; (*d*) by fractional neutralization, and distillation of the non-combined acid.

Behaviour.—1. *Salts.* The acids are monobasic, and thus form **normal salts**, *e.g.* $CH_3\cdot CO_2Na$. They also yield **acid salts**—the so-called **per-acid salts**—from the existence of which we might feel inclined to doubt their monobasic nature. These salts can, however, be crystallized from a strongly acid solution only; they decompose on the addition of water, and also lose their excess of acid when heated. The formation of

such acid salts is now usually regarded as being due to the tetravalency of one of the oxygen atoms, *e.g.*:

$$\begin{matrix} R\cdot CO \\ R\cdot CO\cdot O \end{matrix}\!\!>\!O\!<\!\!\begin{matrix} Na \\ H \end{matrix}.$$

All the other chemical characteristics of the acids go to prove their monobasicity, especially the non-formation of acid esters.

2. The monobasic acids give rise to different groups of derivatives in much the same manner as the monohydric alcohols. The typical hydrogen atom is replaceable by an alkyl group with formation of an **ester** or **alkyl salt**, *e.g.* $CH_3\cdot CO\cdot OC_2H_5$, ethyl acetate, or by a second acid radical with formation of an **anhydride**, the hydroxyl may further be replaced by halogen, especially chlorine, to an **acid chloride** by SH to a **thio-acid**, by NH, to an **amide**, &c. (See Acid Derivatives, p. 171.)

3. Halogens act upon the acids as substituents (see p. 167).

4. When the alkali salts are heated with soda lime, or frequently when the silver salts are heated alone, carbon dioxide is eliminated and a paraffin formed (see *e.g.* Methane). Paraffins are also formed when the alkali salts are electrolysed (see Ethane).

5. Most of the acids are relatively stable towards oxidizing agents, formic acid alone being readily oxidized to carbonic acid, and thus possessing strong reducing properties.

6. When the lime salts of the acids are heated with calcium formate they are reduced to aldehydes, and when heated for a lengthened period with hydriodic acid and phosphorus, to paraffins.

6*a*. When the lime salts are distilled alone, or are heated with phosphorus pentoxide, they are transformed into the ketones, $(C_{n-1}H_{2n-1})_2CO$.

Constitution.—It follows from their modes of formation, especially 3, 4, and 6, and also from their behaviour (see 4 above), that acetic acid and its higher homologues contain alkyl radicals. The conversion of the alcohols into acids containing 1 atom of carbon more, by means of the cyanides, is especially strong proof of this. The latter contain the alkyl radical bound to the nitrile group $\cdot C\vdots N$, and when they are hydrolysed the alkyl radical remains unchanged, and the tervalent nitrogen is replaced by O'' and $(OH)'$, both of these attaching themselves to the carbon atom of the original cyanogen, and so forming the group

$$\cdot CO_2H = \cdot C\!\!<\!\!\begin{matrix} O \\ OH \end{matrix}.$$

Consequently all the oxygen in the acid is united to a single carbon atom in the form of the group CO_2H. This group, which is termed carboxyl, is characteristic of the existence of acid properties. Further proof of the presence of the carboxyl group is based largely on the reactions of the acids. The alkyl group which they contain must be directly attached to C, as it is not removed by the action of acids or alkalis. We thus have $C_nH_{2n+1}\cdot C$. The presence of an OH group follows from the reaction of the acids with PCl_3 or PCl_5, when an atom of O and an atom of H become replaced by an atom of Cl, and they must presumably therefore be present in the form of the univalent $\cdot O\cdot H$ group. There is only 1 oxygen atom left over to account for, and this is presumably attached to the C by a double bond, and thus we have $C_nH_{2n+1}\cdot C\lessdot^{O}_{OH}$. The monobasic acids may therefore be regarded as compounds of the alkyl radicals with carboxyl, or, in other words, as derived from paraffins by the replacement of one hydrogen atom by a carboxyl group, thus:—

$$C_{n-1}H_{2n-1}\cdot CO_2H = C_nH_{2n}O_2.$$

Formic acid is, in this way, the hydrogen compound of carboxyl, $H\cdot CO_2H$.

The acids are distinguished as *primary*, *secondary*, or *tertiary*, according as the alkyl radicals which they contain are primary, &c. Thus:—

Primary	Secondary	Tertiary
$R\cdot CH_2\cdot CO_2H$	$RR'CH\cdot CO_2H$	$RR'R''C\cdot CO_2H$.

There is no room for doubt that it is the hydrogen atom of the carboxyl group, the so-called "typical" hydrogen atom, which is replaced by metals in the formation of salts, for the foregoing acids are all monobasic, and consequently the number of hydrogen atoms present in the alkyl radical is of no moment for the acid character. In the di- and polybasic acids, the presence of two or more carboxyls can usually be demonstrated.

If the composition of the primary alcohols, $R\cdot CH_2\cdot OH$, is compared with that of the corresponding acids, $R\cdot CO\cdot OH$ (R = alkyl or hydrogen), the latter are seen to be derived from the former by the exchange of two atoms of hydrogen for one atom of oxygen. The character of the original

substance is thus completely changed by the entrance of the electro-negative (acidifying) oxygen.

Nomenclature.—The names for the first five acids are special; from C_6 onwards, with a few exceptions, the names for the *normal* acids indicate the number of carbon atoms, *e.g.* hexoic, heptoic, or heptylic, &c. The systematic name (Geneva Congress) of the normal compound is obtained by adding the word acid to the name of the paraffin containing the same number of carbon atoms, *e.g.* acetic acid = ethane acid

The monovalent radicals left when OH is removed from the molecule of each acid are often spoken of as **acid** or **acyl radicals**. (Cf. Alkyl Radicals.) The commonest of these radicals are $CH_3 \cdot CO \cdot$, **acetyl**; $C_2H_5 \cdot CO \cdot$, **propionyl**; $C_3H_7 \cdot CO \cdot$, **butyryl**, &c.

The aldehydes may be looked upon as hydrogen compounds of the acyl radicals, and the ketones as compounds of the latter with alkyl radicals, thus.—

$(CH_3 \cdot CO)H$ (aldehyde) $(CH_3 \cdot CO)CH_3$ (acetone).

The constitution of aldehydes and ketones, and of compounds derived from them, is based on the constitution of the monobasic acids.

Isomers.—The acids of the acetic series show the same isomerism as the alcohols containing 1 atom of carbon less, since they are formed from these by means of the cyanides. Thus we have 1 propionic acid, 2 butyric acids corresponding with the 2 propyl alcohols, 4 valeric acids corresponding with the 4 butyl alcohols, and so on.

Formic acid (*Methane acid*), *acidum formicicum*, CH_2O_2 (*Samuel Fisher* and *John Wray*, 1670, *Marggraf*), occurs free in ants, especially *Formica rufa*, in the processionary caterpillar (*Bombyx processionea*), in the bristles of the stinging nettle, the fruit of the soap-tree (*Sapindus saponaria*), and in tamarinds and fir cones; also in small quantity in various organic liquids, in perspiration, urine, and the juice of flesh.

Formation.—From HCN, $CHCl_3$, CH_3OH, CO_2, &c. (See General Methods of Formation.) Its salts are obtained by the reducing action of sodium amalgam upon ammonium carbonate or solutions of the alkali hydrogen carbonates (*Lieben*); the free acid by the dry distillation or oxidation of many organic substances, *e.g.* starch (*Scheele*).

Preparation.—1. Sodium formate is obtained by absorbing carbon monoxide in soda lime at 210° (*Merz*).

2. When oxalic acid is heated, formic acid is obtained in small quantity together with carbon monoxide, carbon dioxide, and water, and the same effect is produced by the direct action of sunlight upon its aqueous solution containing uranic oxide:

$$C_2H_2O_4 = CO_2 + CH_2O_2.$$

This decomposition is best effected by heating crystallized oxalic acid with glycerol to 100°–110° (*Berthelot, Lorin*), the formic acid produced combining with the glycerol to an ester, **monoformin** (see Glyceryl Esters):

$$\begin{array}{l} CH_2\cdot OH \\ CH\cdot OH \\ CH_2\cdot O\,H + HO\cdot C\!\!<\!\!\begin{matrix}O\\H\end{matrix} \end{array} = \begin{array}{l} CH_2\cdot OH \\ CH\cdot OH \\ CH_2\cdot O\cdot C\!\!<\!\!\begin{matrix}O\\H\end{matrix} \end{array} + H_2O$$

This remains behind in the flask, and practically only water and carbon dioxide pass over. The monoformin is then hydrolysed either by boiling it with excess of water or by the addition of more oxalic acid, the water of crystallization of the latter acting as the hydrolysing agent. The formic acid distils over with the water, and then the anhydrous oxalic reacts again with the glycerol, yielding monoformin and carbon dioxide, the process repeating itself time after time, a very small amount of glycerol being thus sufficient to convert considerable quantities of oxalic into formic acid. (B. **15**, 928.) The anhydrous acid is obtained by decomposing the solid lead or copper salt with sulphuretted hydrogen.

Properties.—It is a colourless liquid which solidifies in the cold and fumes slightly in the air. M.-pt. +9°; b.-pt. 101°; sp. gr. 1·22. It has a pungent acid and ant-like odour, acts as a powerful corrosive, and produces sores on the soft parts of the skin. It is a much stronger acid than acetic acid, is a powerful antiseptic, and decomposes completely into carbon monoxide and water when heated with concentrated sulphuric acid: $CH_2O_2 = CO + H_2O$.

Salts.—**Potassium-**, HCO_2K, **sodium-**, HCO_2Na, and **ammonium formate**, HCO_2NH_4, form deliquescent crystals. The first two yield oxalates when strongly heated, with evolution of hydrogen (see Oxalates); the ammonium salt yields formamide and water at 180°:

$$HCO_2\cdot NH_4 = H\cdot CO\cdot NH_2 + H_2O.$$

The **lead** salt, $Pb(HCO_2)_2$, forms glistening, sparingly soluble needles, the **copper** salt, $Cu(HCO_2)_2 + 4H_2O$, large blue monoclinic crystals, and the **silver** salt colourless crystals. The last-mentioned deposits silver when warmed, consequently a solution of nitrate of silver is reduced when heated with formic acid.

A solution of the soluble **mercuric** salt, $Hg(HCO_2)_2$, evolves carbon dioxide when gently warmed, and yields free formic acid together with the sparingly soluble **mercurous** salt, $Hg_2(HCO_2)_2$, which separates in white plates, on further heating, carbon dioxide, formic acid, and metallic mercury are obtained. Similarly an aqueous solution of mercuric chloride is reduced by formic acid to the mercurous salt, Hg_2Cl_2.

Formic acid is thus a strong reducing agent, and in this respect differs from the other members of the series.

$$HCO{\cdot}OH = CO_2 + 2H.$$

It decomposes into carbonic acid and hydrogen when heated alone to 160°, or when brought into contact with finely-divided rhodium.

This power of reduction may be attributed to the aldehydic grouping contained in its constitutional formula, $H{\cdot}O{\cdot}CH{:}O$.

Acetic acid (*Ethane acid*), $CH_3{\cdot}COOH$, was known in the dilute form, as crude wine vinegar, to the ancients. *Stahl* prepared the concentrated acid about 1700. *Glauber* mentions wood vinegar (1648). Its constitution was established by *Berzelius* in 1814. Salts of acetic acid are found in various plant juices, especially those of trees, and in the perspiration, milk, muscles, and excrementa of animals. Esters of acetic acid also occur, *e.g.* triacetin in croton-oil (see p. 158, and also under Glycerol).

Formation (see p. 140 *et seq.*).—It is the final product of the oxidation of a great many compounds, and also of their treatment with alkalis.

The following synthesis is of historical interest:—Perchloroethylene, C_2Cl_4, which is prepared from CCl_4, *i.e.* from Cl and CS_2, yields with chlorine in presence of water in direct sunlight trichloracetic acid, carbon hexachloride, C_2Cl_6, being obviously formed as intermediate product (*Kolbe*, 1843):

$$CCl_3{\cdot}CCl_3 + 2H_2O = CCl_3{\cdot}CO_2H + 3HCl.$$

The latter acid is reduced to acetic by nascent hydrogen (*Melsens*).

Preparation.—1. *From alcohol.*—A dilute aqueous solution of alcohol, containing up to 15 per cent, is slowly converted into acetic acid on exposure to the oxidizing action of the air and in presence of certain low forms of plant life known as bacteria, especially *Bacterium aceti*. These organisms are contained in the air, and hence become deposited in alcoholic liquors exposed to the air, and thus produce the souring of wines, &c. For the growth of the micro-organisms it is essential that nitrogenous matter, phosphates, &c., shall be present, and hence pure alcohol mixed with water does not turn sour. In the "quick process" dilute alcoholic liquors are allowed to trickle over beechwood shavings which have been previously coated with the required bacteria (mother of vinegar), and the temperature is kept at about 35°.

Vinegar is an aqueous solution of acetic acid, usually containing only 3 to 5 per cent, but containing also small quantities of alcohol, of the higher acids, *e.g.* tartaric and succinic, the ethyl esters of the acids, albuminoid matters, &c.

2. *From wood.*—The dry distillation of wood, which is conducted in cast-iron retorts, yields: (1) gases, *e.g.* hydrogen 15 per cent, methane 11 per cent, carbon dioxide 26 per cent, carbon monoxide 41 per cent, and higher hydrocarbons 7 per cent; (2) an aqueous solution known as pyroligneous acid, which, in addition to acetic acid, contains methyl alcohol, acetone, homologues of acetic acid, and strongly smelling combustible products (empyreuma); and (3) wood-tar, which contains compounds of the nature of carbolic acid. The pyroligneous acid is worked up for acetic acid by converting it into the sodium or calcium salt, heating these—the former up to its melting-point and the latter to 200°—to get rid of empyreumatic substances, and then distilling with sulphuric acid.

Properties.—Acetic acid is a strongly acid liquid of pungent odour, which feels slippery to the touch and burns the skin, and which solidifies on a cold day to large crystalline plates melting at 17°; (glacial acetic acid). It boils at 118°, and its vapour burns with a blue flame; sp. gr. at 15°, 1·055. When mixed with water, contraction and consequent increase in density ensue, the maximum point corresponding with the hydrate $CH_3 \cdot CO_2H + H_2O$, $= CH_3 \cdot C(OH)_3$ (ortho-acetic acid), which contains 77 per cent acid and has a sp. gr. of 1·075 at 15·5°; after this, the specific gravity decreases with further addition

of water, so that a 50-per-cent acid has almost the same density as one of 100 per cent. The amount of acid present in a solution is determined either by its sp. gr., this contraction being borne in mind, or by titration with standard alkali, using phenolphthalein as indicator, or with very concentrated acid by a careful determination of its melting- (freezing-) point in the *Beckmann* apparatus. The vapour density near the boiling-point is much higher than that required by theory, but is normal above 250°. The high values are due to the association of the molecules at the lower temperatures, and in the liquid state the molecular formula is undoubtedly $(C_2H_4O_2)_x$, &c. The acid is hygroscopic, and stable towards chromic acid and cold permanganate of potash. It dissolves phosphorus, sulphur, and many organic compounds, is corrosive, and gives rise to painful wounds on tender parts of the skin

Salts.—All the normal acetates are soluble in water. The following **potassic** salts are known:—(*a*) $KC_2H_3O_2$, (*b*) $KC_2H_3O_2$, $HC_2H_3O_2$, and (*c*) $KC_2H_3O_2$, $2\,HC_2H_3O_2$.

Sodium acetate, $CH_3 \cdot COONa$, $3\,H_2O$, forms transparent readily soluble rhombic prisms. **Ammonium acetate**, $CH_3 \cdot CO \cdot ONH_4$, resembles the potassium salt. It is used in medicine as a sudorific (liquor ammonii acetici). Its solution loses ammonia on evaporation, and it yields acetamide when distilled **Ferrous acetate**, $Fe(C_2H_3O_2)_2$, is largely used in the form of "iron liquor" as a mordant in dyeing. The normal **ferric** salt, $Fe(C_2H_3O_2)_3$, which is employed for the same purpose, is obtained when a soluble ferric salt is mixed with sodium acetate. Its solution is deep red in colour, and deposits the iron as **basic salt**, $CH_3 \cdot CO \cdot OFe(OH)_2$, when heated with excess of water. It is used in medicine as "liquor ferri acetici". The analogous **aluminic acetate** is known only in solution, and finds a wide application as "red liquor" mordant in calico printing and dyeing. Its use depends upon the fact that it is readily hydrolysed by water, *e.g.* when exposed to the action of steam, and on the insolubility of the compound (lake) formed from the residual alumina and the colouring matter. It is employed in small doses as an astringent in cases of diarrhœa, &c. Lead salts. (1) **Normal lead acetate** or sugar of lead, $(CH_3 \cdot COO)_2Pb + 3\,H_2O$, is manufactured from sheet-lead and acetic acid. It forms colourless lustrous four-sided prisms, which are poisonous and of a nauseous sweet taste. It combines with lead oxide to (2) **basic salts** of alkaline reaction, termed **sub-acetates.**

The simplest basic salt has the composition $OH \cdot Pb \cdot O \cdot CO \cdot CH_3$, but there also exist others, *e.g.* $OH \cdot Pb \cdot O \cdot Pb \cdot O \cdot CO \cdot CH_3$, &c. Two molecules of acetic acid can combine with as many as 5 molecules of lead oxide. These basic acetates are used as *Goulard's* lotion, and on the large scale for the preparation of white-lead, &c

Cupric acetate, $Cu(C_2H_3O_2)_2 + 2H_2O$, dark-green crystals, also forms basic salts (verdigris). **Silver acetate**, $AgC_2H_3O_2$, forms characteristic glistening needles.

Detection of Acetic Acid.—(1) When an acetate is heated with alcohol and sulphuric acid, the pleasant-smelling ethyl acetate is formed, (2) by means of the silver salt, (3) by the odour of cacodyl produced upon heating the potassium or sodium salt with arsenious oxide. (See p. 116.)

Propionic acid, $CH_3 \cdot CH_2 \cdot CO_2H$ (*Gottlieb*, 1844), may be obtained by the reduction of acrylic or lactic acid (see pp. 143 and 144), also from lactate or malate of calcium by suitable *Schizomycetes* fermentation (*Fitz*). It is usually prepared by the hydrolysis of ethyl cyanide (propionitrile) with alkalis. (See pp. 101 and 142.)

Calcium chloride separates it from its aqueous solution in the form of an oil, whence its name πρῶτος, the first, and πῖων, fat, the first oily acid.

Butyric acids, $C_4H_8O_2$.

1. **Normal butyric acid**, *butane acid*, *ethylacetic acid*, $CH_3 \cdot CH_2 \cdot CH_2 \cdot CO_2H$, occurs free in perspiration, in the juice of flesh, in the contents of the large intestine, and in the solid excrementa; as hexyl ester in the oil of the fruit of *Heracleum giganteum*, as octyl ester in *Pastinaca sativa*, and to the extent of 2 per cent as glyceride in butter (*Chevreul*, 1822).

Formation.—(See also General Modes of Formation.) It is produced (1) by the decay of moist fibrin and of cheese (being therefore contained in Limburg cheese); (2) by a *Schizomycetes* fermentation of glycerol, and of carbohydrates (*Pelouze* and *Gélis*; *Fitz*; see below); (3) by the oxidation of albuminoids with chromic acid, of fats with nitric acid, of coniine, &c., and (4) by the dry distillation of wood.

Preparation.—In the "butyric fermentation" of sugar or starch by fission ferments (*e.g. Bacillus butylicus*), $CaCO_3$ or ZnO being added at the same time, to neutralize the acid formed.

If the fermentation is brought about by impure materia

(decaying cheese, &c.), lactic acid is first produced by other micro-organisms, this being then converted into butyric acid by the butyric bacillus.

Properties.—It is a thick liquid of unpleasant rancid odour, in presence of ammonia like that of perspiration, is miscible with water, and separates from its aqueous solution on the addition of salts. B.-pt. 163°. The calcium salt, $Ca(C_4H_7O_2)_2 + H_2O$, forms glistening plates, and is characterized by being more soluble in cold than in hot water, it therefore separates on warming the concentrated cold aqueous solution. On prolonged heating of the solution, however, it is transformed into the calcium salt of isobutyric acid.

2. **Isobutyric acid,** *2-methyl-propane acid, dimethyl-acetic acid,* $(CH_3)_2:CH\cdot CO_2H$, is present in the free state in the carob (*Redtenbacher*), in the root of *Arnica montana*, and as esters in *Pastinaca sativa* and Roman chamomile oil.

It is obtained from isopropyl cyanide (*Erlenmeyer*), by the oxidation of isobutyl alcohol, by the aceto-acetic ester synthesis (p 229), &c. It resembles *n*-butyric acid, but is more sparingly soluble in water (1 in 5), and boils 9° lower, *i.e* at 154°. Unlike the latter, however, it is easily oxidized to acetone or acetic acid, and carbonic acid. The calcium salt, $Ca(C_4H_7O_2)_2$, differs from its isomer in being more soluble in hot water than in cold. The solution is accompanied by a slight absorption of heat, whereas the solution of the salt of the *n*-acid is accompanied by a slight evolution of heat.

Valeric acid, $C_5H_{10}O_2$, exists in the four different modifications which are theoretically possible:

1. **Normal Valeric acid** (*Pentane acid*), *propyl-acetic acid*, $CH_3\cdot(CH_2)_3\cdot CO_2H$, from normal butyl cyanide (*Lieben* and *Rossi*, 1871), is best prepared from propyl-malonic acid. (See B. **21**, Ref 649; also malonic ester synthesis.) It boils at 185°, and is soluble in 27 parts of water.

2. **Isovaleric acid,** *3-methyl-butane acid, isopropyl-acetic acid,* $(CH_3)_2:CH\cdot CH_2\cdot CO_2H$, is obtained from isobutyl cyanide. It is found in the free state and in the form of esters in the animal kingdom and in many plants, especially (free) in the valerian root (*Valeriana officinalis*), and in the angelica root (*Angelica archangelica*), from which it is obtained by boiling with soda; further, in the blubber of the dolphin (*Chevreul*, 1817), in the berries of *Viburnum opulus*, in the perspiration from the foot, &c. The natural acid is usually mixed with the active valeric acid, and is therefore optically

active; the oxidation of fermentation amyl alcohol by chromic acids yields a similar mixture. When pure it is optically inactive, boils at 175°, and has an unpleasant pungent acid odour, like that of old cheese, and a corrosive action. It is used in medicine.

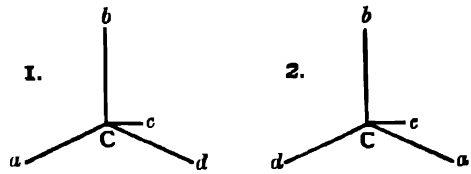
3. **Methyl-ethyl-acetic acid,** *active valeric acid, 2-methyl-butane acid,* $\begin{matrix}CH_3\\C_2H_5\end{matrix}\!\!>\!CH\cdot CO_2H$, occurs in nature, as already mentioned, and results from the oxidation of the active (−) amyl alcohol; it is in this case (+) optically active, while, if prepared synthetically, *e.g.* by the aceto-acetic ester reaction, it is optically inactive, but can be resolved by suitable methods into a + valeric acid and a − valeric acid. [For determination of optical activity, see section on Physical Properties.]

There are thus three distinct acids, one dextro-rotatory, one lævo-rotatory, and the third optically inactive, which have to be represented by the same structural formula, viz. $\begin{matrix}CH_3\\C_2H_5\end{matrix}\!\!>\!CH\cdot CO_2H$.

As regards their ordinary chemical and physical properties, the two active acids are exactly alike, and differ only in their action on polarized light. This difference is not due to the different arrangements of the molecules, as all three are liquids, and in liquids the molecules are not usually regarded as having definite arrangements. A further proof that the cause of the activity, and hence of the isomerism, is to be sought for in the molecules themselves, and not in any special arrangements of the molecules, is the fact that the optical properties of the acids in the gaseous state are similar to those in the liquid. The investigations of *Pasteur, Le Bel,* and *Van't Hoff* have shown that this kind of isomerism, which is now usually termed **stereo-isomerism,** is due to the fact that the compound contains a carbon atom to which 4 different radicals are attached; in the case of valeric acid these are, H, CH_3, C_2H_5, CO_2H. Such a carbon atom is usually termed an asymmetric carbon atom. (This expression does not mean that the carbon atom itself is asymmetric in shape, but that it is attached to four distinct radicals, and as we shall see later this produces an asymmetric molecule.)

Van't Hoff showed that if we assume that these radicals are arranged around the carbon atom, not in a single plane, but in the three dimensions of space, then every compound con

taining a single asymmetric carbon atom should exist in the modifications represented by the figures 1 and 2.

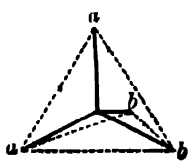


Such modifications are not identical, since they cannot be brought to superposition (this can be shown readily by the aid of models), but they are very similar; in fact, they stand in the relationship of the right to the left hand, or, in other words, in the relationship of an asymmetric object to its mirror image

The spatial relationship of the radicals is often expressed by stating that if the asymmetric carbon atom is situated as the centre of a regular tetrahedron, then the four radicals occupy the solid angles of the tetrahedron. The arguments in favour of the spatial representation of the molecules of carbon compounds are largely based on a consideration of the number of isomeric forms in which simple carbon derivatives occur. For example, no simple compound of the type C a a b b is known to exist in more than one modification. If, however, the radicals and carbon atom were arranged in a single plane, we should expect the two modifications:



but with the spatial or tetrahedral arrangement we can get but the one modification.



An examination of models* will clearly show that in whatever way we exchange the radicals *a* and *b*, we always arrive at a figure which can be superimposed on the one depicted.

Similarly with regard to compounds C a a b c, in which 2 of the 4 radicals are alike. The tetrahedral arrangement allows of one modification only, and in these cases only one is actually known. When, however, all four radicals are distinct, *e.g.* C a b c d, the spatial arrangement, as we have already seen, admits of two **configurations**, which are in the relationship of object to mirror image, and these two modifications undoubtedly represent the two optically active isomerides, in which almost every compound of the type C a b c d has been shown to exist. An examination of the models representing the two modifications shows that they are both asymmetric, *i.e.* a plane of symmetry cannot be drawn through them, and the optical activity which such compounds exhibit when in the liquid state, or in solution, is undoubtedly connected with the asymmetry of their molecules. Since the two configurations contain the same radicals and are very similar, in the one case containing the 4 radicals arranged in what we may term a positive, and in the other, in the opposite or negative direction, we should expect the molecules of the two compounds to produce rotations of the polarized ray equal in magnitude but of opposite sign. This is the case with the two optically active valeric acids: the pure dextro-acid has a rotation of + 17·85°, and the lævo-acid − 17·85°.

In addition to the two optically active modifications, a third isomeride is usually known which is optically inactive. As it can be synthesised by mixing together equal weights of the *d* and *l* compounds, it follows that such a compound is either a mixture or a definite compound of the two active isomerides, *i.e.* its optical inactivity is owing to the fact that the two components are present in equal quantities. Such isomerides are often spoken of as **racemic compounds, and are optically inactive by external compensation.** Such racemic compounds may be resolved into their optically active components by

* In using models it must be remembered that the models are not supposed to represent in the least the actual shapes of the atoms, but merely their spatial relationships. It must also be borne in mind that the atoms and radicals in the molecules are in a state of motion, and the fixed position represented in the model may be supposed to represent the mean position of the centre of gravity of any particular atom in its oscillatory motion, or the position which the centre of gravity would occupy at absolute zero.

several methods, most of which were devised by *Pasteur*. (See Racemic Acid.)

Relationship between Asymmetry of the Molecule and Optical Activity.—Since the two isomerides of the type C a b c d are optically active, it should follow that any derivative of valeric acid in which the four radicals attached to the central carbon atom are still different should be also optically active, but that a derivative in which two of the radicals become similar should become inactive. This question has been examined by *Le Bel* in the case of some forty derivatives of active amyl alcohol, $\begin{matrix}CH_3\\C_2H_5\end{matrix}\!\!>\!C\!<\!\!\begin{matrix}H\\CH_2OH\end{matrix}$. The alcohol, its chloride, amine, all its esters, its oxidation product, viz. valeric acid, and all its salts, esters, &c., are optically active, the hydrocarbon $\begin{matrix}CH_3\\C_2H_5\end{matrix}\!\!>\!C\!<\!\!\begin{matrix}H\\CH_3\end{matrix}$ obtained by reducing the chloride is, however, optically inactive, and cannot be resolved into active components.

4. **Trimethyl-acetic acid**, *pivalic acid*, $(CH_3)_3C\cdot CO_2H$, can be prepared from tertiary butyl cyanide (*Butlerow*, 1873). It melts at 35°, boils at 164°, and has an odour like that of acetic acid.

Of the **hexylic acids**, eight are theoretically possible, and of these seven are already known. The most important among them is **normal caproic acid**, $CH_3\cdot(CH_2)_4\cdot CO_2H$ (*Chevreul*, 1822), which is found in nature, *e.g.* in cocoa-nut oil, Limburg cheese, and as a glyceride in the butter made from goats' milk, and is produced in the butyric fermentation of sugar, and by the oxidation of albuminous compounds and of the higher fatty acids, &c. Like valeric acid, it has a very unpleasant and persistent odour of perspiration and rancid butter. B.-pt. 205°.

The higher acids which are found in nature are all of normal constitution, and contain for the most part an even number of carbon atoms. Goats' butter contains the acids C_8, C_8, and C_{10}, hence the names **caproic**, **caprilic**, and **capric** acids, and cocoa-nut oil—in addition to those three—the acid C_{12}. This last, **lauric acid**, is contained more especially in oil of laurels (*Laurus nobilis*); **myristic acid**, C_{14}, is present in oil of iris and nutmeg butter (from *Myristica moschata*); **arachidic acid**, C_{20}, in the oil of the earth-nut (*Arachis hypogæa*); **behenic acid**, C_{22}, in oil of ben (*Moringa oleifera*); **cerotic acid**, C_{26}, forms in the free state the chief constituent of bees'-wax, and as ceryl ester that of Chinese wax. **Palmitic acid**, $C_{16}H_{32}O_2$, and **stearic acid**, $C_{18}H_{36}O_2$ (pp. 158 and 161), are very widely distributed, being nearly always accom-

panied by a third acid poorer in hydrogen, viz. **oleic acid**, $C_{18}H_{34}O_2$ (see Unsaturated Acids).

Most animal and vegetable fats and oils, *e.g.* tallow, suet, butter, palm, olive and seal oils, consist almost entirely of a mixture of the glyceryl esters of palmitic, stearic, and oleic acids, these esters being termed, for the sake of brevity, **palmitin**, $C_3H_5(O\cdot CO\cdot C_{15}H_{31})_3$, **stearin**, $C_3H_5(O\cdot CO\cdot C_{17}H_{35})_3$, **olein**, $C_3H_5(O\cdot CO\cdot C_{17}H_{33})_3$. Palmitin and stearin being solid and olein liquid, the consistence of a fat or oil depends on the preponderance or otherwise of the solid esters. The constitution of the fats was elucidated by *Chevreul* in 1811.

Rancidity consists, in the case of many fats, of a partial saponification, whereby strongly smelling fatty acids are set free.

Most of the varieties of wax are, on the contrary, esters of monohydric alcohols; thus bees'-wax consists of the **melissic ester of palmitic acid**, $C_{30}H_{61}O\cdot CO\cdot C_{15}H_{31}$, together with free **cerotic acid**, Chinese wax (from *Croton sebiferum*, the tallow-tree) of the ester $C_{27}H_{55}O\cdot CO\cdot C_{26}H_{53}$, and spermaceti (Cetaceum, in the skull of *Physiter macrocephalus*) of the ester $C_{16}H_{33}O\cdot CO\cdot C_{15}H_{31}$.

From all these esters the acids are obtained in the form of potassium salts by saponification with alcoholic potash, thus:—

$$\underset{\text{Stearin}}{C_3H_5(O\cdot CO\cdot C_{17}H_{35})_3} + 3\,KOH = \underset{\text{Potassic stearate}}{3\,C_{17}H_{35}CO_2K} + \underset{\text{Glycerol}}{C_3H_5(OH)_3}$$

The separation of the acids is effected by fractional crystallization, fractional precipitation with magnesium acetate, or by fractional distillation either of the fats themselves or of their esters in a vacuum. Oleic acid can be separated from palmitic and stearic by taking advantage of the solubility of its lead salt in ether.

The stearine candles of commerce consist of a mixture of palmitic with excess of stearic acid, some paraffin or wax being usually added to prevent them becoming crystalline. The manufacture of candles depends upon the saponification of the solid fats, especially of beef and mutton tallow, by means of water and lime, of concentrated sulphuric acid, or of superheated steam.

Soaps consist of the alkaline salts of palmitic, stearic, and oleic acids, hard soaps containing sodic salts, chiefly of the solid acids, while soft soaps contain potassic salts, principally oleate. By the addition of common salt to a solution of a potassic soap, the latter is converted into a sodic soap, which is insoluble in

a solution of sodic chloride. This process is usually termed "*salting out*", and is analogous to the precipitation of sodic chloride by the addition of hydric chloride to its saturated solution. (Cf. *Walker*, "Phys. Chem.", p. 314.) These alkali soaps dissolve to a clear solution in a little water, but with excess of water are hydrolysed to a certain extent, yielding free alkali and free fatty acid or acid salt, analogous to potassic peracetate. The cleansing action of soap is usually attributed to the presence of the small amount of free alkali thus formed:

$$C_{17}H_{35}\cdot CO_2Na + H\cdot OH \rightleftharpoons C_{17}H_{35}\cdot CO_2H + NaOH.$$

This hydrolysis is similar to that observed in the case of inorganic salts derived from a feeble acid and a strong base, and increases with increasing dilution. The production of free alkali (or free hydroxyl ions) can be readily understood by aid of the theory of ionization. The salt $R\cdot CO_2Na$, when dissolved in water, may be assumed to be ionized to a certain extent in the normal manner, thus giving rise to cations $\overset{+}{Na}$ and anions $R\cdot\overset{-}{CO_2}$. But water itself is ionized to a slight extent to $\overset{+}{H}$ and $\overset{-}{OH}$ ions, and we should thus have $\overset{+}{H}$ and $R\cdot\overset{-}{CO_2}$ ions in the same solution; the acid from which the sodic salt is derived is a feeble acid, and hence shows little tendency to ionize, and thus the $\overset{+}{H}$ and $R\cdot\overset{-}{CO_2}$ ions will unite to form non-ionized molecules $R\cdot CO_2H$. This implies removal of hydrions from the sphere of chemical action, and a certain number of water molecules will be ionized in order to supply fresh hydrions; these will again unite with the acid ions, and the two reactions will proceed until a state of equilibrium is established. In this state of equilibrium we shall have $R\cdot\overset{-}{CO_2}$, $\overset{+}{Na}$, $\overset{+}{H}$, $\overset{-}{OH}$ ions and $R\cdot CO_2H$ and H_2O molecules; but it is obvious that the $\overset{-}{OH}$ ions will be largely in excess of the $\overset{+}{H}$ ions, since a considerable number of these latter have been used up in forming non-ionized molecules of acid. The solution, as a whole, will thus possess more or less pronounced alkaline properties. (Cf. *Walker*, "Phys. Chem", p. 290.) The calcium, barium, and magnesium salts are insoluble in water, but partly crystallizable from alcohol. The precipitates produced by the action of hard waters on soaps consist

largely of those insoluble salts. The lead salts are prepared by boiling fats with lead oxide and water, and form the so-called plaisters or lead plaisters.

The higher acids with an uneven number of carbon atoms, C_{11}, C_{13}, C_{15}, and C_{17}, are prepared synthetically from the acids containing 1 atom of carbon more, by transforming them into the ketones $C_{n-1}H_{2n-1}\cdot CO\cdot CH_3$ (p. 131), and oxidizing these, when acids $C_{n-2}H_{2n-3}\cdot COOH$ are obtained. (*Krafft*)

On these reactions a method for proving that the higher fatty acids, *e.g.* palmitic and stearic, are normal in constitution has been based. (See Caution, p. 132.)

The acid $C_{15}H_{31}\cdot CO_2H$ is converted into the ketone $C_{15}H_{31}\cdot CO\cdot CH_3$; this on oxidation yields $C_{14}H_{29}\cdot CO_2H$ and acetic acid. The conversion into ketone and subsequent oxidation is repeated, and an acid, $C_{13}H_{27}\cdot CO_2H$, obtained. The processes are repeated until an acid, $CH_3\cdot(CH_2)_7\cdot CO_2H$, *n*-nonylic acid, is obtained. This can be shown to have a normal structure by synthetical methods, and hence all the higher acids must also have a normal structure, since if the acid $C_{19}H_{37}\cdot CO_2H$ had not a normal structure, but contained a side chain, *e.g.* $C_{11}H_{23}\!>\!\!\begin{matrix}CH_3\\ \\ \end{matrix}\!\!>CH\cdot CO_2H$, on conversion into the ketone and subsequent oxidation it would not yield the acid, $C_{12}H_{25}\cdot CO_2H$, but a ketone, $CH_3\cdot CO\cdot C_{11}H_{23}$, or the oxidation products of this ketone

Dissociation constant. — One of the most characteristic physical constants of the organic acids is what is termed the dissociation or affinity constant K, which is derived from the equation $k = \frac{a^2}{v(1-a)}$, where v = volume of solution in litres containing 1 gram mol. of the acid, a is the amount ionized, and $1 - a$ the amount not ionized. This equation is based on the law of mass action. In the case of any feeble organic acid, *e.g.* acetic acid, where we have 1 gram molecule dissolved in v litres of solution, a state of equilibrium represented by the equation

$$CH_3\cdot COOH \rightleftarrows CH_3\cdot \overset{-}{C}OO + \overset{+}{H}$$

occurs. Then if k_1 and k_2 represent the velocity constants of the direct and reverse reactions, we have, according to *Guldberg* and *Waage's* law, at the stage of equilibrium:—

$$k_1 \times \frac{1-a}{v} = k_2 \times \frac{a}{v} \times \frac{a}{v}, \quad \text{or} \quad \frac{a^2}{v(1-a)} = \frac{k_1}{k_2} = k.$$

The extent of ionization in a solution containing 1 gram molecule in v litres is determined by electrical conductivity determinations. $\alpha = \frac{\mu_v}{\mu_\infty}$, *i.e.* the degree of ionization at a dilution v is the ratio of the molecular conductivity at this dilution to the molecular conductivity at infinite dilution when all the acid molecules are ionized. (Cf. *Walker*, pp. 232–235.) For a weak acid, k remains constant, and affords a convenient measure of the strength of an organic acid. As a rule, the constant is usually taken as 100 times k, or $K = 100\,k$.

Acid	Formic	Acetic	Propionic	*n*-Butyric	*iso*-Butyric
K.....	0·0214	0·00180	0·00134	0·0015	0·00144

Formic acid is obviously much the strongest of the fatty acids, but they are all comparatively weak acids compared with the strong mineral acids. Close comparison cannot be drawn between the two groups, as the equation $k = \frac{\alpha^2}{(1-\alpha)v}$ does not hold good for strong acids.

Palmitic acid (*hexadecane acid*), $CH_3\cdot(CH_2)_{14}\cdot CO_2H$, is most conveniently prepared from palm-oil, which is a mixture of palmitin and olein, also by fusing oleic acid or cetyl alcohol with potash. M.-pt. 60°.

Stearic acid, $CH_3\cdot(CH_2)_{16}\cdot CO_2H$, is formed, among other methods, by reducing oleic acid, and is also obtained from the so-called shea-butter or from mutton suet. M.-pt. 68°. "Artificial ivory" consists of gypsum which has been saturated with liquid stearic acid.

B. Unsaturated Acids, $C_nH_{2n-2}O_2$ or $C_mH_{2m-1}\cdot CO_2H$

	Melting pt	Boiling pt
Acrylic acid, $C_3H_4O_2$	7°	140°
Crotonic acids, $C_4H_6O_2$.... 1*a*	72°	182
1*b*	15°	172°
2	16°	160°
Angelic acid } $C_5H_8O_2$	45°	185°
Tiglic acid }	65°	198
Oleic acid, $C_{18}H_{34}O_2$	14°	...
Erucic acid, $C_{22}H_{42}O_2$.....	33	...

These acids are known as the acids of the oleic series. In their physical properties they closely resemble the saturated acids, apart from differences in melting-point, which are sometimes considerable. They have the chemical properties characteristic of monobasic acids; they yield salts, esters, amides, &c., in much the same manner as the saturated acids; but in addition they resemble the olefines in the readiness with which they yield additive compounds with hydrogen, halogens, or halogen hydrides, thus forming fatty acids or their substitution derivatives. Thus oleic acid, $C_{18}H_{34}O_2$, when treated with H_2 in presence of colloidal Pd, yields stearic acid, $C_{18}H_{36}O_2$, and with bromine, dibromo-stearic acid, $C_{18}H_{34}Br_2O_2$. In this way they characterize themselves as derivatives of the unsaturated hydrocarbons of the ethylene series, from which we may imagine them to be formed by the replacement of an atom of hydrogen by carboxyl. They may therefore be termed olefine-carboxylic acids.

Upon the addition of halogen hydride, the halogen does not always attach itself to that carbon atom to which the smaller number of hydrogen atoms is united.

The presence of the double bonds renders them much more sensitive to oxidizing agents than are the fatty acids. When a very dilute oxidizing agent is employed, *e.g.* 1 per cent permanganate, dihydroxy derivatives of fatty acids are obtained:

$$CH_3 \cdot CH{:}CH \cdot CO_2H + O + H_2O = CH_3 \cdot CH(OH) \cdot CH(OH) \cdot CO_2H;$$

but if stronger oxidizing agents are employed, a rupture of the molecule occurs at the position where the double bond exists, and a mixture of acids is obtained:

$$CH_3 \cdot CH{:}CH \cdot CH_2 \cdot CO_2H \longrightarrow CH_3 \cdot CO_2H \text{ and } CO_2H \cdot CH_2 \cdot CO_2H.$$

This affords an excellent method for determining the position of the double bond in the molecule of the acid. Fusion with caustic alkalis also causes a breaking up of the molecules, and the formation of a mixture of fatty acids; but this reaction is of no use for determining the position of the double bond, as treatment with alkali tends to shift the double bond, if possible, nearer to the carboxylic group. *Fittig* (B. 1891, **24**, 82, &c.) has studied the action of dilute alkalis on a number of unsaturated acids, and always observed the same effect, *e.g.* hydrosorbic acid, $CH_3 \cdot CH_2 \cdot CH{:}CH \cdot CH_2 \cdot COOH$, passes into

$CH_3 \cdot CH_2 \cdot CH_2 \cdot CH : CH \cdot COOH$ (2-*hexene*-1-*acid*). Such changes, which are termed "molecular transformations", are explained by the assumption that atoms or radicals (in this case the elements of water) are added on to the original compound, and then eliminated in a different manner, *e.g.*:

$$CH_3 \cdot CH : CH \cdot CH_2 \cdot CO_2H \longrightarrow CH_3 \cdot CH_2 \cdot CH(OH) \cdot CH_2 \cdot CO_2H \longrightarrow CH_3 \cdot CH_2 \cdot CH : CH \cdot CO_2H.$$

The presence of the double bond in the molecule has a considerable effect upon certain properties of the acid; for example, the dissociation constant and the rate of esterification by the catalytic method.

Fichter and *Pfister* have shown (Abs 1904, i. 965) that the introduction of a double bond usually increases the strength of an acid, and that the effect is most marked when the double bond is in the β-γ-position, *e.g.* butyric acid, K = 0·00154; crotonic acid, K = 0·00204; and for vinyl acetic, K = 0·00383.

Sudborough (J. C. S. 1905, 1840; 1907, 1033; 1909, 315, 975) has shown that the introduction of the double bond in the α-position greatly retards esterification. The rates for hydrocinnamic, $C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CO_2H$, and for cinnamic acid, $C_6H_5 \cdot CH : CH \cdot CO_2H$, are as 40·1.

Modes of Formation.—1. By oxidizing the corresponding alcohols or aldehydes, *e.g.* acrylic acid from allyl alcohol or acrolein.

$$CH_2 : CH \cdot CH_2 \cdot OH \longrightarrow CH_2 : CH \cdot CHO \longrightarrow CH_2 : CH \cdot CO_2H.$$

2. From the unsaturated alcohols or their iodides, by converting them into nitriles and hydrolysing these, *e.g.* crotonic acid from allyl iodide (intramolecular rearrangement, p. 164).

$$CH_2 : CH \cdot CH_2I \longrightarrow CH_3 \cdot CH : CH \cdot CN \longrightarrow CH_3 \cdot CH : CH \cdot CO_2H$$

Both these methods of formation are analogous to those of the fatty acids.

3. From the monohalogen substitution products of the saturated fatty acids, by warming with alcoholic potash, sometimes upon simply heating with water. This reaction is analogous to the formation of the olefines from alkyl haloids; it occurs in the case of those substituted acids which contain the halogen in the β-position to the carboxyl (see p. 167 *et seq.*).

4. From the halogen substitution products of the unsatu rated acids by inverse substitution:

$$CH_3 \cdot CH{:}CCl \cdot CO_2H \longrightarrow CH_3 \cdot CH{:}CH \cdot CO_2H.$$

5. By the elimination of water from hydroxy fatty acids.

$$\underset{\text{Ethylene-lactic acid}}{CH_2(OH) \cdot CH_2 \cdot COOH} = \underset{\text{Acrylic acid}}{CH_2{:}CH \cdot CO_2H} + H_2O$$

This reaction corresponds with the formation of the olefines from monohydric alcohols.

Constitution and Isomers.—The constitution of the unsaturated acids, $C_nH_{2n-2}O_2$, follows from their behaviour as monobasic acids and as unsaturated compounds, and the position of the double bond is ascertained by the process of oxidation. The number of isomeric acids, $C_mH_{2m-1} \cdot CO_2H$, is the same as the number of isomeric unsaturated alcohols, $C_mH_{2m-1} \cdot OH$

Acrylic acid, *propene acid, ethylene-carboxylic acid*, $CH_2{:}CH \cdot CO_2H$ (*Redtenbacher*), is prepared by the oxidation of acrolein by oxide of silver, or by the distillation of β-iodopropionic acid with oxide of lead. (Cf. mode of formation 3.) It is very similar to propionic acid. Mixes with water and readily polymerizes. It is reduced to propionic acid when warmed with zinc and sulphuric acid, and is decomposed when fused with alkali into acetic and formic acids.

Acids, $C_4H_6O_2$. Four isomeric acids with this formula are known. 1. Ordinary or **solid crotonic acid** (2-*Buten* 1-*acid*), $CH_3 \cdot CH : CH \cdot CO_2H$, occurs along with isocrotonic acid in crude pyroligneous acid, and is prepared from allyl iodide by means of the cyanide, which, instead of having the anticipated formula, $CH_2 : CH \cdot CH_2 \cdot CN$, has the isomeric one, $CH_3 \cdot CH{:}CH \cdot CN$; this affords another example of molecular transformation.

It is also prepared by heating malonic acid with paraldehyde and glacial acetic acid:

$$CH_3 \cdot CH{:}O + H_2C\!\!<\!\!\begin{matrix}CO_2H\\CO_2H\end{matrix} = H_2O + CO_2 + CH_3 \cdot CH{:}CH \cdot CO_2H.$$

It crystallizes in large prisms, melts at 72°, boils at 189°, has an odour like that of butyric acid, and is fairly soluble in water. On reduction it yields *n*-butyric acid, and on careful oxidation, oxalic acid, hence the constitution.

2. **Isocrotonic acid**, $CH_3 \cdot CH{:}CH \cdot CO_2H$, obtained by the

action of sodium amalgam upon chloro-isocrotonic acid, melts at 15°, boils at 172°, and changes into ordinary crotonic acid at 180°. It is present in croton-oil. For preparation of the pure acid see *Morrell* and *Bellars*, J. C. S. 1904, 345.

Isocrotonic acid was formerly regarded as $CH_2{:}CH{\cdot}CH_2{\cdot}CO_2H$, but it shows almost the same chemical behaviour as crotonic acid, *e.g.* on reduction and oxidation, or on addition of hydrogen bromide, and is now regarded as having the same structural formula as, but being stereo-isomeric with, solid crotonic acid. (Cf. Fumaric and Maleic acids.)

3. **Meth-acrylic acid**, *2-methyl-2-propene-1-acid*, $CH_2{:}C{<}^{CH_3}_{CO_2H}$ is found in small quantity in Roman chamomile oil, and may be obtained by the withdrawal of HBr from bromo-isobutyric acid:

$$CH_3{\cdot}CBr{<}^{CH_3}_{CO_2H} \rightarrow CH_2{:}C{<}^{CH_3}_{CO_2H}.$$

It smells like decaying mushrooms, and melts at 15°.

4 **Vinyl-acetic acid**, $CH_2{:}CH{\cdot}CH_2{\cdot}CO_2H$, *1 Butene-4 acid*, may be obtained synthetically.

Angelic acid, $CH_3{\cdot}CH{:}C(CH_3)CO_2H$, is present in the angelica root, and, together with its stereo-isomer, **tiglic acid**, in Roman chamomile oil. (Cf. A **250**; **259**, 24; **272**, 1, **273**, 127.) The relationship of these two acids is exactly the same as that of crotonic and isocrotonic acids.

Oleic acid, $C_{18}H_{34}O_2$ (*Chevreul*), is present as olein (glyceryl oleate) in the fatty oils especially, *e.g.* olive, almond, and train oils. It is a colourless oil, solidifies to white needles in the cold, melts at 14°, and cannot be volatilized without decomposition. It is tasteless and odourless, and has no action upon litmus, but quickly becomes yellow and acid by oxidation in the air, and also acquires a rancid odour. Its lead salt is soluble in ether, and by this means the acid may be separated from numerous other organic acids. It yields, on fusion with potash, the saturated acids, palmitic and acetic. Nitrous acid converts it into the stereo-isomeric crystalline **elaïdic acid**, melting at 45°. It contains a normal chain, since on reduction it yields stearic acid. When carefully oxidized, it yields **pelargonic acid**, $CH_3{\cdot}(CH_2)_7{\cdot}CO_2H$, and **azelaic acid**, $CO_2H{\cdot}(CH_2)_7\ CO_2H$, and hence the constitutional formula:

$$CH_3{\cdot}(CH_2)_7{\cdot}CH{:}CH{\cdot}(CH_2)_7{\cdot}CO_2H.$$

Erucic acid, $C_{22}H_{42}O_2$, occurs in rape-seed oil, melts at 33°, and on treatment with nitrous acid yields the stereo-isomeric **brassidic acid**, melting at 60°. The constitution is probably:

$$CH_3[CH_2]_7 \cdot CH{:}CH[CH_2]_{11} \cdot CO_2H.$$

For the stereo-chemistry of the unsaturated acids, see Fumaric and Maleic acids.

C. Propiolic Acid Series, $C_nH_{2n-4}O_2$

The acids of this series again contain two atoms of hydrogen less than those of the former, and are to be regarded as carboxylic acids of the acetylene hydrocarbons, *e g.* propiolic acid, $CH{:}C \cdot CO_2H$, as acetylene-carboxylic acid. They can accordingly be prepared by the addition of CO_2 to the sodium derivatives of the acetylenes (analogously to mode of formation 4 of the saturated acids, p. 143).

They closely resemble the unsaturated acids which have been already described, but differ from them by the fact that each molecule of such an acid can combine with either 2 or 4 atoms of hydrogen, chlorine, bromine, &c., and can yield explosive compounds with ammoniacal silver and copper solutions. There are, however, acids of the formula $C_nH_{2n-4}O_2$ which do not possess this last peculiarity, viz., those which are derived, not from the homologues of acetylene proper, but from their isomers, and which therefore contain two double bonds instead of a triple one. (Compare Acetylene Hydrocarbons, p. 51.)

The most important member of the series is **propiolic** or **propargylic acid**, *propine acid*, $CH{:}C \cdot CO_2H$, which corresponds with propargyl alcohol, and is prepared by warming an aqueous solution of the acid potassium salt of acetylene-dicarboxylic acid, the latter being itself obtained from dibromo-succinic acid. (See p. 241, also B. **18**, 677.) In its physical properties it resembles propionic acid, forms silky crystals below 6°, and boils at 144°. It is readily soluble in water and alcohol, and becomes brown in the air. It gives, even in dilute solution, the characteristic explosive silver precipitate.

Tetrolic acid, $CH_3 \cdot C{:}C \cdot CO_2H$, is obtained from β-chloro crotonic acid and aqueous potash, and melts at 76°.

Sorbic acid, $CH_3 \cdot CH{:}CH \cdot CH{:}CH \cdot CO_2H$, is contained in the juice of the unripe sorb apple (*Sorbus Aucuparia*), and has relatively high melting- and boiling-points.

D. Halogen Substitution Products of the Monobasic Acids

The saturated monobasic acids yield halogen substitution products, *e.g.*.

Name.	Formula	Melting-pt	Boiling-pt.	K
Acetic acid	$CH_3 \cdot CO_2H$	17°	118°	0·00180
Chlor-acetic acid	$CH_2Cl \cdot CO_2H$	62°	186°	0·155
Dichlor-acetic acid	$CHCl_2 \cdot CO_2H$	liq.	191°	5·14
Trichlor-acetic acid	$CCl_3 \cdot CO_2H$	52°	195°	121·0
Brom-acetic acid	$CH_2Br \cdot CO_2H$	50°	208°	0·138
Dibrom-acetic acid	$CHBr_2 \cdot CO_2H$	48°	232°	...
Tribrom-acetic acid	$CBr_3 \cdot CO_2H$	135°	dec.	...
Iodo-acetic acid	$CH_2I \cdot CO_2H$	82°	dec.	0 075
Cyano-acetic acid	$CN \cdot CH_2 \cdot CO_2H$	65°	dec.	0 370
Propionic acid	$CH_3 \cdot CH_2 \cdot CO_2H$	— 23°	140·7°	0 00134
α-Chloro-propionic acid	$CH_3 \cdot CHCl \cdot CO_2H$	oil	186°	...
β-Chloro-propionic acid	$CH_2Cl \cdot CH_2 \cdot CO_2H$	41·5°(?)	204°	...
α-Bromo-propionic acid	$CH_3 \cdot CHBr \cdot CO_2H$	24·5°	203·5°	...
β-Bromo-propionic acid	$CH_2Br \cdot CH_2 \cdot CO_2H$	62·5°	...	...
α-Iodo-propionic acid	$CH_3 \cdot CHI \cdot CO_2H$	oil	...	...
β-Iodo-propionic acid	$CH_2I \cdot CH_2 \cdot CO_2H$	82°	...	0·009
α:β-Dibromo-propionic acid	$CH_2Br \cdot CHBr \cdot CO_2H$	64°	...	
α:α-Dibromo-propionic acid	$CH_3 \cdot CBr_2 \cdot CO_2H$	61°	...	3 3
β:β-Dibromo-propionic acid	$CHBr_2 \cdot CH_2 \cdot CO_2H$	71°	..	. .

The acids poorer in hydrogen also yield similar substitution products, *e.g.* $CH_2:CCl\cdot CO_2H$, α-chlor-acrylic acid; $CHBr:CH\cdot CO_2H$, β-brom-acrylic acid; $CH_3\cdot CH:CCl\cdot CO_2H$, α-chlor-crotonic acid; $CI:C\cdot CO_2H$, iodo-propiolic acid, &c.

All these halogen derivatives have the properties of monobasic acids; in many respects they resemble the parent substances, but as a rule are much stronger acids. This is extremely well shown in a comparison of the dissociation constants K. (See table.)

Since their acid nature remains unaltered, they still contain the carboxyl group; the halogen has therefore replaced the hydrogen of the hydrocarbon radical. They may also be looked upon as haloid substitution products of the hydrocarbons, in which 1 atom of hydrogen is replaced by carboxyl:

CH_3Cl (chloro-methane) $CH_2Cl\cdot CO_2H$ (chlor-acetic acid).

The modes of formation and properties of these substituted acids also coincide with this view. Thus, while they show a behaviour perfectly analogous to that of the non-substituted acids, forming salts, esters, chlorides, anhydrides, and amides, their halogen atoms are as readily exchangeable for OH, CN, or SO_3H, as are those of the substitution products of the hydrocarbons. (See p. 61.)

Isomers and Constitution.—While in each case only one mono-, di-, &c., halide acetic acid exists, two isomeric monohaloid propionic acids are known. This is readily explicable from the fact that in propionic acid, $CH_3\cdot CH_2\cdot CO_2H$, the two α-hydrogen atoms are differently situated from the three β- ones, the former being attached to the carbon atom nearer to the carboxyl, and the latter to that one farther from it. According to theory, therefore, with which the observed facts agree, the following two isomers are possible:—

$CH_3\cdot CHX\cdot CO_2H$ and $CH_2X\cdot CH_2\cdot CO_2H$
α-Haloid-propionic acid β-Haloid-propionic acid

These acids yield two isomeric lactic acids by exchange of their halogen for hydroxyl, thus:—

$CH_3\cdot CH(OH)\cdot CO_2H$ and $CH_2(OH)\cdot CH_2\cdot CO_2H$
Common lactic acid Ethylene-lactic acid

The constitution of both of these lactic acids follows from their other modes of formation (see p. 207, *et seq.*). The

positions of the halogens in the α- and β- substituted propionic acids are thus also fixed.

Those substituted acids which contain the halogen attached to the α-carbon atom, *i.e.* to the same carbon atom to which the carboxyl group is united, are termed α-acids, and the others β, γ, &c., acids, the successive carbon atoms in their order from the carboxyl group being designated as α, β, γ, &c.

We thus distinguish, for instance, between α-, β-, and γ-chloro-butyric acids, αα-, αβ-, and ββ- dibromo-propionic acids, &c.

Two stereo-isomeric forms of the α- or β- mono-chloro- and -bromo-crotonic acids are known (A. **248**, 281), being derived from crotonic and isocrotonic acids respectively.

Formation.—(*a*) Of the saturated substituted acids.

1. Chlorine and bromine can substitute directly, the halogen taking up the α-position to the carboxyl.

The reaction is often carried out in sunlight and in the presence of a halogen carrier. One of the commonest methods is to transform the acid into the acid bromide by the aid of phosphorus and bromine, and then to brominate. The product obtained, *e.g.* $CH_3 \cdot CHBr \cdot COBr$, on treatment with water yields the α-bromo acid, $CH_3 \cdot CHBr \cdot CO_2H$. This is generally known as the *Hell-Volhard-Zelinsky* method. Trimethyl acetic acid, $CMe_3 \cdot CO_2H$, which contains no α-hydrogen atom, cannot be brominated in this manner (B 1890, **23**, 1594).

2. From hydroxy acids of the glycollic series by the action of PCl_5, HBr, &c., *e.g.*:

$$CH_3 \cdot CH_2 \cdot CH(OH) \cdot CO_2H \longrightarrow CH_3 \cdot CH_2 \cdot CHCl \cdot CO_2H.$$

3. By the addition of halogen or halogen hydride to the unsaturated acids.

(*b*) Of the unsaturated substituted acids. These are often prepared by the elimination of HCl, HBr, or HI from polyhalogen derivatives of the fatty acids:

$$CH_3 \cdot CHBr \cdot CHBr \cdot CO_2H \longrightarrow CH_3 \cdot CH{:}CBr \cdot CO_2H,$$

or by the addition of hydrogen halide to propiolic acids.

Behaviour.—1. For the replacement of chlorine, bromine, and iodine by hydroxyl, see p. 206. This exchange takes place with more difficulty in the α-monochloro-substituted acids than in the corresponding bromine and iodine compounds, but more easily than in the case of the alkyl chlorides, and it is effected by means of moist silver oxide,

or frequently by prolonged boiling with water alone (A. **200**, 75). In this way monochlor-acetic yields glycollic acid:

$$CH_2Cl \cdot CO_2H + H_2O = OH \cdot CH_2 \cdot CO_2H + HCl.$$

β-halogen acids, on the other hand, lose halogen hydride when boiled with water, and yield unsaturated acids, together with CO_2 and olefines $C_{n-1}H_{2n-2}$. γ-halogen acids break up under these conditions (even with cold soda solution) into HCl, &c., and a lactone, *i.e.* an anhydride of a γ-hydroxy-acid (see p. 217; cf. *Fittig*, A. **208**, 116).

2. When boiled with an alcoholic solution of potassium cyanide, cyano-fatty acids are produced:

$$CH_2Cl \cdot CO_2K + KCN = CN \cdot CH_2 \cdot CO_2K + KCl.$$

These compounds are on the one hand monobasic acids, and on the other nitriles, and they consequently yield dibasic acids when hydrolysed. In the above case malonic acid, $CO_2H \cdot CH_2 \cdot CO_2H$, is formed.

3. They form sulphonic acids with sodium sulphite, *e.g.*:

$$CH_2Cl \cdot CO_2Na + Na \cdot SO_3Na = NaSO_3 \cdot CH_2 \cdot CO_2Na + NaCl.$$

These latter are compounds which, apart from the acid character they derive from the carboxyl group, are actual sulphonic acids, like ethyl-sulphonic acid, and are thus dibasic. Their sulpho-group can, however, be replaced by OH on boiling with alkalis.

4. With $AgNO_2$, under favourable conditions, nitro-derivatives of the fatty acids are formed, and these yield amino-acids on reduction, *e.g.* $NH_2 \cdot CH_2 \cdot CO_2H$. (B. 1910, **43**, 3239.)

Chloroformic acid, $Cl \cdot CO_2H$, has so far not been prepared, although derivatives of it are known. (Cf. Chloro-carbonic acid.)

The chlorinated acetic acids are formed by the direct substitution of acetic acid, or better, of acetyl chloride, chlorinated acetyl chlorides ensuing in the latter case as intermediate products.

Monochlor-acetic acid (*Chloro-ethane acid*), $CH_2Cl \cdot CO_2H$, is prepared by chlorinating acetic acid, preferably in the presence of acetic anhydride, sulphur, or phosphorus. It forms rhombic prisms or tables and corrodes the epidermis. **Dichlor-acetic acid**, $CHCl_2 \cdot CO_2H$, is more conveniently obtained by warming chloral hydrate with potassium cyanide (B. **10**, 2120), and **trichlor-acetic acid**, $CCl_3 \cdot CO_2H$, by

oxidizing chloral hydrate with nitric acid. The former decomposes with boiling alkali to oxalic and acetic acids, and the latter to chloroform and carbon dioxide. Inverse substitution reconverts tri-, di-, and monochlor-acetic acids into acetic acid (*Melsens*, 1842).

Sulpho-acetic acid, $SO_3H \cdot CH_2 \cdot CO_2H$, forms deliquescent prisms containing $1\frac{1}{2}$ mols. H_2O of crystallization. Its salts crystallize well. **Cyano-acetic acid**, $CN \cdot CH_2 \cdot CO_2H$, is a crystalline substance melting at 65°–66° and readily soluble in water; it decomposes into aceto-nitrile, $CH_3 \cdot CN$, and CO_2 when heated, and yields malonic acid on hydrolysis.

α-Chloropropionic acid, $CH_3 \cdot CHCl \cdot CO_2H$, is obtained by the action of PCl_5 upon lactic acid, and decomposition of the lactyl chloride, $CH_3 \cdot CHCl \cdot COCl$, by water. **β-iodopropionic acid**, $CH_2I \cdot CH_2 \cdot CO_2H$, is prepared by acting upon glyceric acid, $CH_2(OH) \cdot CH(OH) \cdot CO_2H$, with iodide of phosphorus (exchange of 2 OH for 2 I and of I for H), also by acting on acrylic acid with hydriodic acid. It forms colourless six-sided tables of a peculiar odour; m.-pt. 82°. The two **cyanopropionic acids**, $C_2H_4(CN) \cdot CO_2H$, give the two succinic acids when hydrolysed.

Chloro- and **Bromo-crotonic acids**, **β-Chloro-crotonic acid** (*2-Chloro 2-Butene acid*) (m.-pt. 94°) and the stereo-isomeric **β-Isochloro-crotonic acid** (m.-pt 59·5°) are formed by the action of PCl_5 on ethyl acetoacetate, and treatment of the product with water. The β-chlor-iso-acid volatilizes with steam, but the β-chloro-acid does not.

VII. ACID DERIVATIVES

A general idea of the kind of derivatives to which acids give rise is obtained by comparing these derivatives with corresponding derivatives of the saturated monohydric alcohols, *e.g.* those of acetic acid with those derived from ethyl alcohol:

$CH_3 \cdot CH_2 \cdot OH$	Alcohol.	$CH_3 \cdot CO \cdot OH$	Acetic acid.
$CH_3 \cdot CH_2 \cdot ONa$	Sodium ethylate.	$CH_3 \cdot CO \cdot ONa$	Sodium acetate.
$CH_3 \cdot CH_2 \rangle O$ $CH_3 \cdot CH_2 \rangle$	Ethyl ether.	$CH_3 \cdot CO \rangle O$ $CH_3 \cdot CH_2 \rangle$	Ethyl acetate.
		$(CH_3 \cdot CO)_2O$	Acetic anhydride.
$CH_3 \cdot CH_2 \cdot Cl$	Ethyl chloride.	$CH_3 \cdot CO \cdot Cl$	Acetyl chloride.
$CH_3 \cdot CH_2 \cdot SH$	Mercaptan.	$CH_3 \cdot CO \cdot SH$	Thiacetic acid.
$CH_3 \cdot CH_2 \cdot NH_2$	Ethylamine.	$CH_3 \cdot CO \cdot NH_2$	Acetamide.

It is seen that as regards formulæ there is a close resemblance, the acetyl group taking the place of the ethyl group. Stated generally, the acid derivatives contain acyl radicals in place of the alkyl groups contained in the corresponding derivatives of alcohols.

These derivatives are obtained by methods many of which are perfectly analogous to the modes of formation of the corresponding alkyl derivatives, but they differ characteristically from these by being less stable towards hydrolysing agents.

A number of other derivatives, viz. amido- and imido-chlorides, thiamides, imido-thio-compounds, and amidines, are peculiar to the acids:

$CH_3 \cdot CCl_2 \cdot NHR$*	Amido-chlorides.	$CH_3 \cdot C(NH)OH$	Imino-compounds.
$CH_3 \cdot CCl{:}NR$	Imido-chlorides.	$CH_3 \cdot C(NH)SR$	Imino-thio- ,,
$CH_3 \cdot CS \cdot NH_2$	Thiamides.	$CH_3 \cdot C(NH)(NH_2)$	Amidines.

These compounds are also characterized by being readily hydrolysed.

A. Esters of the Fatty Acids

We have already seen that mineral acids readily give rise to esters by the replacement of their acidic hydrogen radicals by alkyl groups, *e.g.* $SO_2(OH)_2 \rightarrow SO_2(OEt)_2$. In exactly the same manner the typical hydrogen of the fatty acids can be replaced by alkyl groups, and we get esters derived from the fatty acids, *e.g.* ethyl acetate, $CH_3 \cdot CO_2Et$. Since these esters correspond with the metallic salts, they are sometimes termed alkyl salts. (Cf. $CH_3 \cdot CO_2K$ and $CH_3 \cdot CO_2Et$.)

Methods of Formation.—1. By direct **esterification**, *i.e.* by direct action of the acid on the alcohol·

$$CH_3 \cdot CO \cdot OH + Na \cdot OH = CH_3 \cdot CO \cdot ONa + H \cdot OH$$
$$CH_3 \cdot CO \cdot OH + C_2H_5 \cdot OH = CH_3 \cdot CO \cdot OC_2H_5 + H \cdot OH$$

Although the equation representing the reaction is analogous to that representing the neutralization of acetic acid by an alkali, the process of esterification differs from that of neutralization in two respects.

(1) The reaction proceeds but slowly; thus, in the esterification of acetic acid by ethyl alcohol the limit of the reaction at the boiling-point is not reached until after the lapse of

* R signifies an alkyl radical either alphyl or aryl.

several hours, and even then only two-thirds of the acid have been transformed into ester.

(2) The reaction is a reversible or balanced one, and hence is never complete. The water which is formed during the process of esterification tends to hydrolyse the ester back into acid and alcohol:

$$CH_3 \cdot CO \cdot OH + C_2H_5 \cdot OH \rightleftarrows CH_3 \cdot CO \cdot OC_2H_5 + H \cdot OH.$$

Thus, when equivalent quantities of acetic acid and ethyl alcohol are employed, only some 66 per cent of the acid becomes transformed into ester. It can readily be shown, by aid of *Guldberg-Waage's* law of mass action, that by employing an excess of alcohol a larger proportion of acid will be converted into ester. Thus, in the above equation, if the original concentrations of the four substances expressed in gram molecules be denoted by a, b, o and o, and the velocity constants of the direct and reverse reactions by k_1 and k_2 respectively, then after time t equilibrium will be established; and if we assume x gram molecules of acid have been esterified, then the concentrations of the four substances will be $a - x$, $b - x$, x and x. The rate of the direct reaction can be denoted by $k_1 (a - x) (b - x)$, and that of the reverse by $k_2 x^2$ (*Guldberg and Waage*). When equilibrium is established, the two reactions will proceed at the same rate, and

$$k_1 (a-x) (b-x) = k_2 x^2,$$

$$\text{or } \frac{(a-x)(b-x)}{x^2} = \text{constant for a given temperature.}$$

In the case of acetic acid and ethyl alcohol, using gram molecular proportions, *i.e.* $a = b = 1$, we find that equilibrium is established when some two-thirds of acid are esterified. Thus

$$\frac{(1-\frac{2}{3})(1-\frac{2}{3})}{(\frac{2}{3})^2} = \text{constant},$$

and the constant becomes equal to $\frac{1}{4}$.

Then, supposing we alter the proportions of acid and alcohol, using 2 gram molecules of alcohol to 1 of acid, we have—

$$\frac{(1-x)(2-x)}{x^2} = \frac{1}{4}.$$

$$x = \cdot 85 \text{ (approx.)},$$

and thus 85 per cent of the acid will have been esterified in place of the 66 per cent when only 1 gram. mol. of alcohol was used. The reversible nature of the reaction is of especial importance in the preparation of ethyl acetate, and in this case the difficulty is overcome by the addition of a moderate amount of concentrated sulphuric acid, which is ordinarily supposed to react with the water, and thus prevent its hydrolysing the ester. (Compare also *Wade*, J. C. S. 1905, 1656.)

It is worthy of note that the limit of esterification does not vary to any large extent with the temperature. Thus, in the case mentioned above, the limit at 10° is 65·2 per cent, and at 220° it is only 66·5 per cent.

With most of the higher esters, and more especially the esters in the aromatic series, the limit of esterification is much higher, as the esters are not so readily hydrolysable. In these cases, however, the rates at which the esters are formed are extremely slow, and a catalytic agent is therefore introduced. The two common catalytic agents employed are: (1) A small amount of dry hydrogen chloride. At one time it was customary to saturate the boiling alcoholic solution of the acid with hydrogen chloride, but the researches of *E. Fischer* and *Speier* (B. 1895, **28**, 3201, 3252) have shown that the addition of 3 per cent of dry hydrogen chloride to the alcoholic solution is quite sufficient. (2) A small amount of concentrated sulphuric acid, which acts in much the same manner as the hydrogen chloride. The use of these reagents is not to raise the limit of esterification, but to accelerate the production. In most cases, using the catalytic method at the boiling-point of the alcohol, the reaction is complete after three hours, and a 90–95 per cent yield of ester can be obtained by pouring into water.

A number of researches have been made as to the influence of the constitution of the acid and of the alcohol on the rate of esterification, *i.e.* the amount of ester formed in unit time. *Menschutkin*, who employed the direct esterification method without a catalytic agent, *i.e.* the so-called auto-catalytic method, found that primary acids, *i.e.* $R \cdot CH_2 \cdot CO_2H$, were esterified most quickly; secondary acids, $RR'CH \cdot CO_2H$, were intermediate; and tertiary acids, $RR'R''C \cdot CO_2H$, least readily when the same alcohol was employed. Other researches tend to show that strong acids react with alcohol more readily than feeble acids in the absence of a catalyst.

The velocity of esterification has also been determined for

a number of acids employing the catalytic method (HCl). From the equation we should expect the reaction to be a bimolecular reaction, or a reaction of the second order; by altering the conditions, namely, by taking a large excess of alcohol as compared with the acid, the concentration of the alcohol may be regarded as constant, and the reaction then becomes unimolecular (*H. Goldschmidt*) and may be studied by the aid of the equation for unimolecular reactions, $K = \frac{1}{t} \log. \frac{a}{a-x}$; where K = the velocity constant, t = time, a = concentration of the acid at the beginning of the experiment expressed in c.c. of standard alkali, and $a - x$ = concentration of the acid after the lapse of time t.

Using this method, it is found that the introduction of any substituent (CH_3, Cl, Br, I, C_6H_5, &c.) into the acetic acid molecule always lowers the velocity of esterification, the introduction of two such radicals, *e.g.* $CHBr_2 \cdot CO_2H$, lowers the constant to a still greater extent, and when all three hydrogens are replaced by substituents, *e.g.* $C(CH_3)_3 \cdot CO_2H$, the acid is esterified very slowly indeed as compared with acetic acid.

These examples afford an extremely good instance of what is now generally termed **steric retardation**, or the retardation of a chemical reaction by the spatial relationships of radicals introduced into a molecule.

The common theory of the process of esterification is that there is first direct union between a molecule of the acid and of the alcohol:

$$R \cdot C\begin{matrix}O\\OH\end{matrix} + R'OH = R \cdot C\begin{matrix}OR'\\OH\\OH,\end{matrix}$$

yielding a dihydroxylic compound, which immediately eliminates water, yielding the ester $R \cdot C\begin{matrix}OR'\\O\end{matrix}$. The introduction of radicals into the CH_3 group of the acetic acid molecule by filling up the space renders the formation of such additive compounds much more difficult, and hence the retardation of esterification (*Wegscheider*).

The influence of the hydrogen chloride is purely catalytic; it remains unchanged at the end of the reaction. Its catalysing effect is undoubtedly due to to the hydrions it generates, as strong acids (HCl, HBr) are much better catalysing agents

than weaker acids (picric acid). (Cf. *Goldschmidt*, B. 1895, **28**, 3218; *Sudborough* and others, J. C. S. 1898, 81; 1899, 467; 1904, 534; 1905, 1840.)

2. By the action of an acid chloride upon an alcohol or its sodium compound (cf. p. 179):

$$CH_3 \cdot CO \cdot Cl + C_2H_5 \cdot OH = CH_3 \cdot CO \cdot O \cdot C_2H_5 + HCl.$$

3. By the action of an alkyl haloid upon the salt of the acid:

$$C_2H_5Cl + CH_3CO \cdot ONa = CH_3 \cdot CO \cdot OC_2H_5 + NaCl$$

As a rule, an alkyl iodide and the silver salt of the acid are employed. The ester can then be separated from the solid silver iodide and distilled. Occasionally the potassium salt and methyl sulphate are used. Reactions 2 and 3 are of very general application, and are largely made use of when an ester cannot readily be obtained by the catalytic method of esterification.

Properties.—The esters are mostly neutral liquids which volatilize without decomposition; only those which contain a small number of carbon atoms in the molecule are soluble in water, *e.g.* ethyl acetate (1:14).

1. **Hydrolysis.**—They are all hydrolysed (saponified), *i.e.* resolved back into alcohol and acid, when heated, or better, superheated, with water, or when boiled with aqueous solutions of strong alkalis or mineral acids, with the simpler esters this hydrolysis is complete when the ester is allowed to remain for some time in contact with water or dilute alkali.

The hydrolysis of an ester under the influence of water or of mineral acids may be represented by the equation:

$$R \cdot CO_2R' + H \cdot OH = R \cdot CO_2H + R' \cdot OH,$$

and may be studied by the aid of the general equation for a uni-molecular reaction, $K = \frac{1}{t} \log. \frac{a}{a - x}$, since the concentration of the water, if a large excess is used, may be regarded as constant.

The action of the mineral acid is purely catalytic. The same result might ultimately be obtained by using water alone, but is considerably accelerated by using a small amount of a strong mineral acid (HCl, H_2SO_4). Weak acids also accelerate the hydrolysis of the ester, but to a less extent. It

has been found, using the same ester and equivalent quantities of different acids, that the rate of hydrolysis is directly proportional to the strength of the acid. In other words, the catalysing influence of different acids is due to the hydrions.

The hydrolysis of an ester by alkalis is represented by the equation, $R \cdot CO \cdot OR' + NaOH = R \cdot CO \cdot ONa + R' \cdot OH$, and as it is analogous to the preparation of soaps by the action of alkalis on fats (p. 158), is commonly termed Saponification. This is a bimolecular reaction, and if equivalent quantities of ester and alkali are employed in solution, can be studied by aid of the equation $K = \frac{1}{t} \cdot \frac{x}{a(a-x)}$, where t = time, a = initial concentration of alkali and of ester, $a - x$ = concentration of these after time t. The concentrations can readily be determined by direct titration with standard acid, and the number of cubic centimetres of acid introduced directly into the equation.

It has been found that when different alkalis are employed, their hydrolysing effect is proportional to their strengths, *i.e.* is due to the free hydroxyl ions. Different esters are hydrolysed at very different rates by the same alkali; the rate appears to depend on the complexity of the molecule, *i.e.* the number of substituents present, and also on the nature of these substituents, viz. whether they are of a positive or negative nature. It has been found that $CCl_3 \cdot CO_2C_2H_5$ is hydrolysed by alcoholic potash much more readily than ethyl acetate itself, owing to the negative nature of the chlorine substituents. (Compare A. **228**, 257, **232**, 103, J. C. S. 1899, 182.)

In all cases it has been found that, comparing solutions of equal strength, *e.g.* N/10, a strong alkali is a much better hydrolysing agent than a strong acid.

2. A characteristic reaction of methyl and ethyl esters is that they exchange OMe (**methoxy**) or OEt (**ethoxy**) groups for NH_2 on treatment with strong ammonia, thus yielding acid amides, *e.g.* $CH_3 \cdot CO \cdot NH_2$.

3. Phosphorus pentachloride decomposes most esters, yielding an alkyl chloride and an acyl chloride, the O of the $\cdot OEt$ group being replaced by two chlorine atoms.

4. Ethyl esters are readily transformed into methyl esters, $R \cdot CO_2Et \rightarrow R \cdot CO_2Me$, by warming with methyl alcohol and a catalyst (CH_3ONa, HCl). The reaction is reversible, and is termed **alcoholysis**.

5. Sodium methoxide combines with the esters to form un-

stable additive compounds, $R \cdot C(ONa)(OCH_3)(OR')$, which are derivatives of "ortho-acids" (See p. 142; also B. 20, 646.)

The odour and taste of many of the esters is so agreeable that they are manufactured upon a large scale, and employed as fruit essences.

Ethyl formate, $H \cdot CO \cdot OC_2H_5$, b.-pt. 55°, is employed in the manufacture of artificial rum or arrak. **Ethyl acetate**, *acetic ether*, $CH_3 \cdot CO \cdot OC_2H_5$, b.-pt. 75°, is used internally as a medicine. **Amyl acetate**, $CH_3 \cdot CO \cdot OC_5H_{11}$, b.-pt. 148°. The alcoholic solution of this forms the essence of pears. **Ethyl butyrate**, $CH_3(CH_2)_2CO \cdot OC_2H_5$, is the essence of pine-apples. **Iso-amyl iso-valerate**, $C_4H_9 \cdot CO \cdot O \cdot OC_5H_{11}$, b.-pt. 196°, finds application as apple oil or apple ether. **Cetyl palmitate**, $C_{15}H_{31} \cdot CO \cdot OC_{16}H_{33}$, **ceryl cerotate**, $C_{25}H_{51} \cdot CO \cdot OC_{26}H_{53}$, and **melissic palmitate**, $C_{15}H_{31} \cdot CO \cdot O \cdot C_{30}H_{61}$, are constituents of waxes. (See Wax Varieties, p. 158.)

When the esters of the acids of high molecular weight are distilled under the ordinary pressure and not in a vacuum, they decompose into an olefine and a fatty acid. (See p. 46.)

Isomers.—All esters containing the same number of C atoms in the molecule, and derived from the monohydric saturated alcohols and the fatty acids, are isomeric. Thus methyl butyrate is isomeric not only with ethyl propionate but also with propyl acetate and with butyl formate. Further, all esters are isomeric with the monobasic acids which contain an equal number of carbon atoms, *e.g.* the esters just mentioned are isomeric with the valeric acids. (See Metamerism, p. 87.)

Further cases of isomerism occur when the alcohol on the one hand, or the acid on the other, is unsaturated, *e g.* allyl propionate and propyl acrylate.

B. Acid Chlorides, Bromides, &c.

Acid chlorides are the compounds derived from the acids by the replacement of the hydroxyl group by chlorine:

$$R \cdot CO \cdot OH \longrightarrow R \cdot CO \cdot Cl.$$

1. They are usually prepared by the action of the chlorides of phosphorus, PCl_3 and PCl_5, upon the acids or their salts:

$$C_2H_7 \cdot CO \cdot OH + PCl_5 = C_2H_7 \cdot CO \cdot Cl + POCl_3 + HCl.$$

The acid chloride is separated from the $POCl_3$ formed at the same time by fractional distillation. In the case of acetic acid PCl_3 is conveniently used:

$$3CH_3\cdot CO\cdot OH + PCl_3 = 3CH_3\cdot CO\cdot Cl + PO_3H_3.$$

Phosphorus oxychloride, $POCl_3$, may also be allowed to act upon the alkali salts of the acids; when the latter are present in excess, acid anhydrides are produced (p. 180). Thionyl-chloride, $SOCl_2$, and the acid are frequently used, as the only other product is SO_2

2. By the action of chlorine upon the aldehydes in the absence of water: $CH_3\cdot CHO + Cl_2 = CH_3\cdot COCl + HCl$.

Properties.—The acid chlorides are suffocating liquids which fume in the air, distil without decomposition, and are reconverted by water, in many cases at the ordinary temperature, into the corresponding acids and hydrochloric acid:

$$CH_3\cdot CO\cdot Cl + H_2O = CH_3\cdot CO\cdot OH + HCl.$$

They are thus more readily decomposed than the alkyl chlorides When the chlorides are warmed with alcohols, the chlorine is replaced by alkyloxy groups, *e g.* OCH_3, OC_2H_5, and in this way esters are formed. With ammonia they yield acid amides, $R\cdot CO\cdot NH_2$. With the sodium salts of the fatty acids they yield acid anhydrides. With organo-magnesium compound they first form ketones, and then tertiary alcohols (see p. 72) With silver cyanide acyl cyanides (*e g.* $CH_3\cdot CO\cdot CN$, acetyl cyanide) are formed, and these on hydrolysis with concentrated hydrochloric acid yield ketonic acids, $CH_3\cdot CO\cdot COOH$.

Formyl chloride is not known.

Acetyl chloride (*Ethanoyl chloride*), $CH_3\cdot COCl$, is a mobile, colourless liquid of suffocating odour. Boils at 55°, has a sp. gr. 1·13 at 0°, reacts extremely vigorously with water and ammonium hydroxide, and is a reagent of exceptional importance, since it serves for the conversion of the alcohols and primary and secondary amines into their acetyl derivatives. It is thus frequently used for detecting OH, NH_2 or NH groups in organic compounds. The compound under examination is heated with acetyl chloride (or even better, acetic anhydride), and the pure product either analysed or hydrolysed, and acetic acid tested for in the products of hydrolysis (see p. 201).

The boiling-points of the acid chlorides are always considerably lower than those of the corresponding acids.

Acid bromides and iodides are known and closely resemble the chlorides. Their boiling-points are higher.

C. Acid Anhydrides

Corresponding with the monobasic fatty acids there are anhydrides, which may be regarded as derived from two molecules of the acid by the elimination of a molecule of water, *e g.*

$$\begin{matrix} CH_3\cdot CO\cdot OH \\ CH_3\cdot CO\cdot OH \end{matrix} = \begin{matrix} CH_3\cdot CO \\ CH_3\cdot CO \end{matrix}\!\!>\!O + H_2O.$$

They may also be considered as **acyl oxides**. For instance, $(CH_3\cdot CO)_2O$ = **acetyl oxide**.

Preparation.—1. They cannot as a rule be obtained by the direct withdrawal of water from the acids, but by the action of acid chlorides upon the alkali salts of the acids:

$$CH_3\cdot CO\cdot Cl + Na\,O\cdot CO\cdot CH_3 = (CH_3\cdot CO)_2O + NaCl.$$

A very convenient method for preparing them is by the action of phosphorus oxychloride on the sodium salts of the acids, care being taken that sufficient of the dry sodium salt is used to decompose the acid chloride first formed (see p. 179)

$$2CH_3\cdot CO\cdot ONa + POCl_3 = 2CH_3\cdot COCl + NaCl + NaPO_3$$

2. By the action of phosgene on the acids (B. **17**, 1286):

$$2CH_3\cdot CO\cdot OH + COCl_2 = (CH_3\cdot CO)_2O + CO_2 + 2HCl$$

3. The anhydrides of the higher acids are conveniently prepared by the action of acetic anhydride on their sodium salts.

Properties.—The majority of the acid anhydrides are liquids, but those of higher molecular weight solids, of neutral reaction, and soluble in alcohol and ether. They are non miscible with water, but are gradually hydrolysed by it to the free acids Dilute alkalis decompose them readily. When warmed with alcohols they yield esters; with ammonia, acid amides; and with hydrogen chloride, free acid and acid chloride:

$$(CH_3\cdot CO)_2O + HCl = CH_3\cdot CO\cdot Cl + CH_3\cdot CO\cdot OH.$$

The boiling-point of an acid anhydride is higher than that

of the corresponding acid, although an ether boils at a lower temperature than the corresponding alcohol, *e.g.* EtOH 78°; Et_2O 35°; AcOH 118°; Ac_2O 137°.

Acetic anhydride, $(CH_3 \cdot CO)_2O$, is a mobile liquid of suffocating odour, boiling at 137°, and having a sp. gr. of 1·073 at 20°. Like acetyl chloride it is a reagent of great importance, and is largely made use of in testing for and estimating hydroxyl groups in carbon compounds, and for converting primary and secondary amines into acetyl derivatives.

Mixed anhydrides containing two different acyl groups are also known (*Gerhardt, Williamson*), *e.g.* $\begin{matrix} C_2H_3O \\ C_5H_{11}O \end{matrix}\!\!>\!O$. When distilled they yield the two simple anhydrides.

Acyl peroxides have also been prepared. **Acetyl peroxide**, $(C_2H_3O)_2O_2$, is a thick liquid insoluble in water, which acts as a strong oxidizing agent and explodes when heated, it is prepared by the action of barium peroxide, BaO_2, upon acetic anhydride.

Numerous other **peroxides** have been prepared recently by *Baeyer* and *Villiger* (B 1901, **34**, 738) by means of hydrogen peroxide in the presence of potassium hydroxide Among the simpler of these peroxides may be mentioned **ethyl hydrogen peroxide**, $C_2H_5 \cdot O \cdot O \cdot H$, a colourless liquid, **diethyl peroxide**, $C_2H_5 \cdot O \cdot O \cdot C_2H_5$, a liquid boiling at 65 , **acetone peroxide**, $(C_3H_6O_2)_2$, boiling at 132°; and **triacetone peroxide**, $(C_3H_6O_2)_3$, melting at 97°. Many of these compounds are explosive.

D. Thio-acids and Thio-anhydrides

Just as sulphur can replace oxygen in the alcohols and ethers, giving rise to mercaptans and alkyl sulphides, so it can replace oxygen in the carboxylic acids, giving rise to (1) R·CO·SH, **thiolic acids**; (2) R·CS·OH, **thionic acids**; and (3) R·CS·SH, **thion-thiolic acids**.

Thiacetic acid (*Ethane-thiolic acid*), $CH_3 \cdot CO \cdot SH$, is a colourless liquid boiling below 100°; it smells of acetic acid and sulphuretted hydrogen, and is readily decomposed by water into these two components. It is prepared from acetic acid and phosphorus pentasulphide, P_2S_5. The other thio-compounds are likewise readily hydrolysed, yielding acetic acid and hydrogen sulphide.

E. Acid Amides and Hydrazides

Amides.—An acid amide is the compound derived from the acid by the introduction of the amido* group in place of the hydroxyl radical of the carboxylic group:

$$R{\cdot}CO{\cdot}OH \longrightarrow R{\cdot}CO{\cdot}NH_2.$$

They may also be regarded as derived from ammonia by the replacement of a hydrogen atom by an acyl group, *e.g.* $NH_2{\cdot}CO{\cdot}CH_3$. **Secondary** and **tertiary amides**, *e.g.* $NH(CO{\cdot}CH_3)_2$, and $N(CO{\cdot}CH_3)_3$, are known, but are of relatively small importance.

Modes of Formation. — 1. By the dry distillation of the ammonium salts of the fatty acids:

$$CH_3{\cdot}CO{\cdot}ONH_4 = CH_3{\cdot}CO{\cdot}NH_2 + H_2O.$$

2. By addition of water to the alkyl cyanides (nitriles).

$$CH_3{\cdot}CN + H_2O = CH_3{\cdot}CO{\cdot}NH_2.$$

This addition of water is frequently effected by dissolving the nitrile in concentrated sulphuric acid, or in acetic and concentrated sulphuric acids, or by shaking with concentrated hydrochloric acid in the cold; also, and often quantitatively, by hydrogen peroxide, H_2O_2, in alkaline solution. In some cases a further addition of water occurs, and the ammonium salt of the acid is formed.

3. By the action of acid chlorides or acid anhydrides upon aqueous ammonia or solid ammonium carbonate; if amines are employed here, in place of ammonia, **alkylated amides** are formed:

$$CH_3{\cdot}COCl + 2NH_3 = CH_3{\cdot}CONH_2 + NH_4Cl.$$

4. By heating esters with ammonia solution, sometimes even on shaking in the cold:

$$CH_3{\cdot}CO{\cdot}OC_2H_5 + NH_3 = CH_3{\cdot}CO{\cdot}NH_2 + C_2H_5OH.$$

Properties.—1. With the exception of formamide they are colourless crystalline compounds, volatile without decomposition, but with relatively high boiling-points. The following

* *The* NH_2 *group is usually termed an* **amino** *group when present in a primary amine, but an* **amido** *group when present in an acid amide.*

comparison of boiling-points is interesting, as the order is the same for most groups:—

	Acetyl chloride	Ethyl acetate.	Acetic acid	Acetic anhydride	Acetamide
Boiling-point	55°	78°	117°	137°	222°

2. The lower members are soluble in water, and although derivatives of ammonia are, unlike most amines, practically neutral, the strongly positive character of the hydrogen atoms of the ammonia being cancelled by the entrance of the negative acyl radical. Still, the primary amides are capable of forming additive compounds with some acids, *e.g.* acetamide yields the compound $(C_2H_3O\cdot NH_2)_2HCl$, "**acetamide hydrochloride**"; these are, however, unstable, and are decomposed for the most part by water alone. On the other hand, the hydrogen of the amido group can be replaced by particular metals, especially mercury (also sodium; cf. B. **23**, 3037; **28**, 2353), the amides, therefore, playing the part of weak acids in the compounds so obtained, *e.g.* **mercury acetamide**, $(CH_3\cdot CONH)_2Hg$.

3. The amides are readily hydrolysed, more especially by alkalis, to the free acid and ammonia. Alkylated amides on hydrolysis yield the acid (or sodium salt) and an amine (not ammonia). Amines are not decomposed by alkalis.

$$CH_3\cdot CO\cdot NHC_2H_5 + NaOH = CH_3\cdot CO\cdot ONa + C_2H_5NH_2.$$

Hydrolysis of Acid Amides —The velocity of hydrolysis of the amides of the common fatty acids has been determined by *Crocker* and *Lowe* (J. C. S. 1907, **91**, 593 and 952), using an electro-conductivity method. With sodium hydroxide and also hydrochloric acid, formamide is hydrolysed most readily, and valeramide least readily.

4. Nitrous acid converts the primary amides into the corresponding acids, with liberation of nitrogen:

$$CH_3\cdot CO\cdot NH_2 + NO_2H = CH_3\cdot CO\cdot OH + N_2 + H_2O.$$

This reaction is a general one, and corresponds exactly with the action of nitrous acid upon the primary amines (p 108).

5. Nitriles (see p. 101) are formed by heating with P_4O_{10}, P_2S_5, and PCl_5 (see pp. 185 and 186).

6. If bromine in the presence of alkali is allowed to act upon primary amides, bromamides, $R\cdot CO\cdot NHBr$, *e.g.* $CH_3\cdot CO\cdot NHBr$, **aceto-bromamide** (colourless rectangular plates), are first formed, and these are decomposed by the alkali into

a primary amine, carbon dioxide and potassium hydroxide If less bromine is used, urea derivatives are formed, *e.g.* methyl acetyl-urea, $CH_3 \cdot NH \cdot CO \cdot NH \cdot CO \cdot CH_3$, which react with excess of alkali, yielding primary amines - in this case $CH_3 \cdot NH_2$ — containing 1 atom of carbon less than the original amide This is an excellent method for the preparation of amines from C_1 to C_5, but less valuable for those from C_6 onwards, as in the case of the higher compounds the production of amine diminishes, a nitrile being formed instead by the further action of the bromine (see below) Such nitriles $C_nH_{2n+1} \cdot CN$, in which $n > 4$, can therefore be obtained directly from the amine by the action of bromine and alkali upon it, thus -

$$C_7H_{15} \cdot CH_2 \cdot NH_2 + 2Br_2 = C_7H_{15} \cdot CH_2 \cdot NBr_2 + 2HBr$$
$$= C_7H_{15} \cdot CN + 4HBr$$

(Reversal of the *Mendius* reaction, p. 106, cf. *Hofmann*, B **15**, 407, 752, **17**, 1407, 1920, **18**, 2737)

Since these nitriles on hydrolysis yield acids containing 1 atom of carbon less than the amide originally taken, this reaction renders it possible to descend in the series successively from one acid to another (compare p. 160), *e.g.* .

$$C_6H_{13} \cdot CH_2 \cdot CO_2H \rightarrow C_6H_{13} \cdot CH_2 \cdot CO \cdot NH_2 \rightarrow C_6H_{13} \cdot CH_2 \cdot NH_2$$
$$\rightarrow C_6H_{13} \cdot CH_2 \cdot NBr_2 \rightarrow C_6H_{13} \cdot CN \rightarrow C_6H_{13} \cdot CO_2H$$

This has been done in the case of the normal acids from C_{11} to C_{17}, and it furnishes a further proof of their normal constitution.

Constitution. Most of the methods of formation and many of the properties of the amides point to the constitutional formula (I). A second formula is possible (II), in favour of which certain arguments have been adduced (B. **22**, 3273, **23**, 103; **25**, 1435):

(I) $R \cdot C\overset{O}{\underset{NH_2}{<}}$ (II) $R \cdot C\overset{OH}{\underset{NH}{<}}$

This last formula easily passes into the first by the migration of a hydrogen atom, and most of the reactions of the simple amides are explicable almost equally well by either formula. (Cf. *Titherley*, J. C. S. 1897, 468; 1901, 407.)

We thus have a single compound which appears to possess, according to its reactions, two distinct formulæ. Such a substance is usually termed a **tautomeric substance.**

On alkylation, under different conditions, it is possible to obtain two distinct types of mono-alkylated amides, viz.:

$$\text{(I) } R\cdot C\begin{matrix}O\\ NHR'\end{matrix} \quad \text{and} \quad \text{(II) } R\cdot C\begin{matrix}OR'\\ \diagdown\!\!\!

$CH_3 \cdot CCl_2 \cdot NH_2$, these are extremely unstable compounds, being converted by water into amide and hydrochloric acid, and readily giving up HCl, with formation of **imido-chlorides**, *e.g.* $CH_3 \cdot CCl{:}NH$, **acetchloroimide**. The imido-chlorides are also relatively unstable, yielding with water the amide and hydrochloric acid. When heated, they break up into nitrile and hydrochloric acid.

The alkylated amides (p. 182) also yield chloroamides, *e.g.* $CH_3 \cdot CO \cdot NH \cdot C_2H_5$ gives $CH_3 \cdot CCl_2 \cdot NH \cdot C_2H_5$, **ethyl acetchloroamide**, and $CH_3 \cdot CO \cdot NR_2$ gives $CH_3 \cdot CCl_2 \cdot NR_2$. if these still contain amido-hydrogen, they readily yield imido-chlorides, *e.g.* $CH_3 \cdot CCl{:}N \cdot C_2H_5$, **ethyl acetchloroimide**

The chlorine in these compounds is chemically active, it can be exchanged for sulphur or for an amino group.

G. Thiamides and Imido-thio-ethers

Thiamides are compounds derived from the amides by the exchange of oxygen for sulphur, *e.g.* $CH_3 \cdot CS \cdot NH_2$, **thiacetamide** (*ethane-thion-amide*), $CH_3 \cdot CS \cdot NHC_6H_5$, **thiacetanilide**. They are mostly crystalline compounds, and result from the addition of H_2S to the nitriles (*Cahours*), *e.g.*:

$$CH_3 \cdot CN + H_2S = CH_3 \cdot CS \cdot NH_2;$$

by treating acid amides with P_2S_5; from the amido-chlorides, as given above, and by the action of H_2S or CS_2 upon the amidines. Both simple and alkylated thiamides are known.

When heated alone, they yield a nitrile and sulphuretted hydrogen (compare Elimination of Water from Amides). When hydrolysed with alkalis, they yield the corresponding acid, ammonia (amine) and H_2S, thus:—

$$R \cdot CS \cdot NHR + 2H_2O = R \cdot CO \cdot OH + H_2S + NH_2 \cdot R.$$

They are rather more acid in character than the amides, and thus many of them are soluble in alkali and yield metallic derivatives. Consequently, for them, as well as for the amides, the iso-formula $R \cdot C\langle^{SH}_{NH}$ is taken into consideration. From this pseudo form $R \cdot C\langle^{SH}_{NH}$, **iso thio acid amides**, are derived a number of compounds, the **Imino-thio-ethers**, by the replacement of one or both the hydrogen atoms by alkyl groups,

acetimido-thiomethyl, $CH_3 \cdot C\langle^{S \cdot CH_3}_{NH}$, **methyl iso-thio-acetanilide**, $CH_3 \cdot C\langle^{S \cdot CH_3}_{N \cdot C_6H_5}$. They are decomposed by hydrochloric acid into esters of thiacetic acid, thus.—

$$CH_3 \cdot C(NH) \cdot SCH_3 + H_2O = CH_3 \cdot CO \cdot SCH_3 + NH_3$$

These imino-thio-ethers are prepared by the action of mercaptans upon nitriles in presence of hydrochloric acid gas (*Pinner*), and by the action of alkyl iodides upon thiamides (*Wallach*, *Bernthsen*).

$$R \cdot C\langle^{S}_{NH_2} + C_2H_5I = R \cdot C\langle^{SC_2H_5}_{NH} + HI$$

Imino-ethers, $R \cdot C\langle^{NH}_{OR'}$, which are the oxygen compounds corresponding to the above imino-thio ethers, and which are isomeric with the alkylated amides, are also known (*Pinner*). They are derived from the pseudo form of the acid amides, $R \cdot C\langle^{NH}_{OH}$, hypothetical compounds unknown in the free state, which are isomeric with the simple amides They are formed by the combination of a nitrile with an alcohol under the influence of hydrochloric acid gas, and in certain cases by alkylating amides, some of them are liquids which boil without decomposition, but others are only known in the form of salts

H. Amidines

Amidines are compounds derived from the amides, $R \cdot CO \cdot NH_2$, $R \cdot CO \cdot NHR'$, and $R \cdot CO \cdot NR'_2$, by the replacement of oxygen by the bivalent imido-residue NH or (NR).

$CH_3 \cdot C\langle^{NH}_{NH_2}$ — Acetamidine (ethane-amidine)

$CH_3 \cdot C\langle^{NC_6H_5}_{NHC_6H_5}$ — Ethenyl-diphenyl amidine

The amidines are well-defined crystalline bases, and form stable salts. Like all acyl derivatives, they are readily hydrolysed, and thus differ from the amines.

Formation.—1. By heating the amides with amines in presence of PCl_5 (*Hofmann*):

$$R \cdot CO \cdot NHR' + NH_2R' = R \cdot C(NR')(NHR') + H_2O.$$

2. By treating the imido-chlorides, thiamides, and iso-thiamides with ammonia or with primary or secondary amines (*Wallach, Bernthsen*), thus:—

$$R\cdot CS\cdot NH_2 + NH_2R' = R\cdot C(NH)(NHR') + H_2S,$$
$$R\cdot C(NH)(SR) + NH_3 = R\cdot C(NH)(NH_2) + RSH$$

3. By heating the nitriles with (primary or secondary) amine hydrochloride, this is a particularly easy method when aromatic amines are used, but not in the case of ammonium chloride (*Bernthsen*).

$$CH_3\cdot CN + NH_2\cdot R = CH_3\cdot C(NH)(NHR)$$

4. By the action of amine bases or ammonia upon imino-ethers.

Behaviour.—1. They decompose into ammonia or amine and acid when boiled with acids or alkalis (see above), and into ammonia and amide upon boiling with water.

2 The dry compounds, when heated, readily yield ammonia or amine and acid nitrile, so long as the imido-hydrogen atom has not been replaced by alkyl groups.

Amidoximes are the compounds formed by the addition of hydroxylamine to nitriles, and, from this mode of formation and from their properties, appear to be amidines in which an amido- (imido-) hydrogen atom is replaced by hydroxyl.

$$R\cdot CN + NH_2OH = R\cdot C\begin{matrix}=N\cdot OH\\ \diagdown NH_2\end{matrix}.$$

Such an amidoxime is, for instance, **isuret**, $NH_2\cdot CH:N\cdot OH$, also termed methenyl amidoxime, which is prepared from hydrocyanic acid and hydroxylamine, it is isomeric with carbamide or urea; also **ethenyl amidoxime**, $CH_3\cdot C(N\cdot OH)(NH_2)$ These compounds are hydrolysed in much the same manner as amidines.

VIII. POLYHYDRIC ALCOHOLS

A. Dihydric Alcohols or Glycols, $C_nH_{2n}(OH)_2$

The dihydric alcohols may be regarded as derived from the paraffins by the replacement of *two* hydrogen atoms by two hydroxyl groups.

As the monohydric alcohols are often compared with the hydroxides derived from the monovalent metals, we may

compare the glycols with the hydroxides derived from the bivalent metals, *e.g.* $C_2H_4(OH)_2$ with $Pb(OH)_2$. In the saturated dihydric alcohols we have the hydroxyl groups attached to a bivalent **alkylene** radical, *e.g.* C_2H_4'', C_4H_8'', &c.

In many respects they resemble the monohydric alcohols, but they possess these properties in duplicate. Just as, *e.g.*, plumbous hydroxide, $Pb(OH)_2$, can give rise to two series of salts, *e.g.* the basic chloride, $OH \cdot Pb \cdot Cl$, and the normal chloride, $PbCl_2$, so glycol, $C_2H_4(OH)_2$, can give rise to two chlorides, $OH \cdot C_2H_4 \cdot Cl$ and $C_2H_4Cl_2$, known respectively as glycol monochlorhydrin and glycol dichlorhydrin or ethylene dichloride. Similarly, with the acetates and amines derived from glycol we have—

$$\underset{\text{Mono-acetate}}{OH \cdot C_2H_4 \cdot O \cdot CO \cdot CH_3} \quad \text{and} \quad \underset{\text{Di-acetate,}}{C_2H_4(O \cdot CO \cdot CH_3)_2}$$

$$\underset{\text{Hydroxyethylamine}}{OH \cdot C_2H_4 \cdot NH_2} \quad \text{and} \quad \underset{\text{Ethylene diamine,}}{C_2H_4(NH_2)}$$

and similarly with other glycols.

The glycols, as alcohols, give rise to every class of alcoholic derivative; but when, for example, the formation of an ester such as glycollic monoacetate has taken place, this still behaves as a monohydric alcohol, yielding, *e.g.*, with a second molecule of acid, a new ester, it is therefore termed an **ester-alcohol**

It is not necessary that both the groups which replace the hydrogen or hydroxyl should be of the same nature; thus we know a mixed derivative of the composition $NH_2 \cdot C_2H_4 \cdot SO_2 \cdot OH$, which possesses at one and the same time the character of an amine and of a sulphonic acid.

The glycols are mostly thick liquids of sweetish taste, a few only being solid crystalline compounds, they dissolve readily in water and alcohol, but are only sparingly soluble in ether It will be found that the solubility of a compound in water tends to increase, and its solubility in ether to decrease, with the number of hydroxyl groups present in the molecule of the compound. Their boiling-points are much higher than those of the corresponding monohydric alcohols, just as these latter possess considerably higher boiling-points than the hydrocarbons from which they are derived.

Constitution.—As already stated, the glycols contain two hydroxyl groups in each molecule; the arguments in favour of the presence of these hydroxyl groups are exactly similar to those used in the study of the constitution of ethyl alcohol,

and are based mainly on certain methods of formation, and on the chief chemical characteristics of the compounds.

Glycols which contain two hydroxyls linked to the same carbon atom are, as a rule, incapable of existence, and are only known in derivatives (see p. 64). Instead of the glycols $CH_2(OH)_2$ and $CH_3 \cdot CH(OH)_2$, we always obtain the corresponding aldehydes, $CH_2{:}O$ and $CH_3 \cdot CH{:}O$. All glycols contain their hydroxyls attached to two different carbon atoms. Glycol itself has thus the constitution $OH \cdot CH_2 \cdot CH_2 \cdot OH$, which can be proved directly by transforming it, by means of hydrochloric acid, into glycol chlorhydrin, $CH_2Cl \cdot CH_2 \cdot OH$, and oxidizing the latter to monochloracetic acid, $CH_2Cl \cdot CO \cdot OH$. In this last compound the chlorine and hydroxyl are united to different carbon atoms, and consequently the same applies to glycol chlorhydrin and to the two hydroxyl groups of glycol. (Cf. p. 62.)

The monohydric alcohols are distinguished as primary, secondary, and tertiary. The glycols may in the same way be characterized as **di-primary** when they contain the group $CH_2 \cdot OH$ twice, as in glycol, as **primary-secondary** when they contain the group $CH_2 \cdot OH$ together with the group $CH \cdot OH$, as in propylene glycol, $CH_3 \cdot CH(OH) \cdot CH_2OH$; further as **di-secondary**, **primary-tertiary**, **secondary-tertiary**, and **di-tertiary**. The structure of a glycol is usually determined by an examination of its oxidation products. (See pp. 192, 203, *et seq.*)

Modes of Formation.—1. From the di-halogen-substituted derivatives of the paraffins, in which the two halogen atoms are attached to two different carbon atoms, *e.g.* ethylene bromide:

(*a*) By transformation into the di-acetates by means of silver or potassium acetate, and hydrolysis of the ester so produced by potash or baryta water:

$$CH_2Br \cdot CH_2Br + 2CH_3 \cdot CO \cdot OAg = CH_3 \cdot CO \cdot O \cdot CH_2 \cdot CH_2 \cdot O \cdot CO \cdot CH_3 + 2AgBr,$$

$$CH_3 \cdot CO \cdot O \cdot CH_2 \cdot CH_2 \cdot O \cdot CO \cdot CH_3 + 2KOH = OH \cdot CH_2 \cdot CH_2 \cdot OH + 2CH_3 \cdot COOK.$$

In the actual preparation of glycol from ethylene bromide, potassium acetate and alcohol (*Demole*), this saponification ensues directly upon prolonged boiling of the mixture.

(*b*) By boiling with water and lead oxide or potassium carbonate. These reagents serve to neutralize the acid as it is formed, and so the reaction is facilitated:

$$C_2H_4Br_2 + 2HOH \rightleftarrows C_2H_4(OH)_2 + 2HBr.$$

2. In the reduction of ketones to secondary alcohols, the so-called pinacones, *i.e.* di-tertiary glycols, are obtained as by-products (see pp 72 and 134), thus:—

$$\begin{matrix}CMe_2{:}O\\ CMe_2{:}O\end{matrix} + 2H = \begin{matrix}CMe_2{\cdot}OH\\ CMe_2{\cdot}OH\end{matrix} \text{ (pinacone).}$$

3 By the careful oxidation of olefines by means of very dilute $KMnO_4$ (p 45):

$$CH_2{:}CH_2 + O + H_2O = OH{\cdot}CH_2{\cdot}CH_2{\cdot}OH.$$

Behaviour —1. As in the case of the monohydric alcohols, the hydrogen of the hydroxylic groups is directly replaceable by potassium or sodium, with the formation of **alcoholates**, *e.g.* $OH{\cdot}C_2H_4{\cdot}ONa$ and $C_2H_4(ONa)_2$, **sodium** and **di-sodium glycols**

2 The metal in these compounds may be exchanged for new alkyl groups by treatment with alkyl iodide, when glycollic ethers are obtained

$$C_2H_4(ONa)_2 + 2C_2H_5I = 2NaI + \underset{\text{Glycol di-ethyl ether}}{C_2H_4(O{\cdot}C_2H_5)_2}$$

These ethers, like those of the monohydric alcohols, are stable, and cannot be hydrolysed by dilute mineral acids or alkalis

3. Acids act upon them to produce esters, which are either normal esters or ester-alcohols (see p 189).

The halogen esters of the glycols are termed chlor-, brom-, or iodhydrins, *e.g.* glycol chlorhydrin, $C_2H_4Cl(OH)$, glycol di-chlorhydrin, $C_2H_4Cl_2$, &c The ester alcohols which are formed by the action of halogen hydride may also be regarded as mono substitution products of the monohydric alcohols, which cannot be prepared by direct chlorination, *e.g.* $C_2H_4Cl(OH)$, monochlorethyl alcohol. Similarly the di-halogen esters, $CH_2Cl{\cdot}CH_2Cl$, $CH_2Br{\cdot}CH_2Br$, &c, are the di-substitution products of the paraffins, viz. ethylene dichloride and dibromide.

4. As the halogen atoms in the chlor-, brom-, and iodhydrins are readily replaceable, just as in C_2H_5Cl or C_2H_5I, these compounds may be used for the preparation of most of the other glycol derivatives; thus they yield thio-glycols with potassium hydrosulphide, amines with ammonia, sulphonic acids with sodic bisulphite, and nitriles with potassic cyanide

5. Alkalis react with the glycol monochlorhydrins, and by the elimination of HCl yield cyclic anhydrides, *e.g.* **ethylene oxide**, $\begin{matrix}CH_2\\ CH_2\end{matrix}\!\!>\!O$. It is interesting to note that these anhydrides

cannot be obtained by the elimination of water from the glycols themselves. When ethylene glycol is heated with zinc chloride at 230° water is eliminated, and the product obtained is acetaldehyde (or a polymer). This reaction is explained by assuming the intermediate formation of unsaturated alcohols which are not in themselves capable of existence, *e.g.* $CH_2{:}CH(OH)$, but which immediately undergo transformation into the isomeric aldehydes or ketones:

$$CH_2{:}CH{\cdot}OH = CH_3{\cdot}CH{:}O$$

6. As alcohols the glycols are readily oxidized. If they contain the primary alcoholic group, they can yield aldehydes and acids containing the same number of carbon atoms. If they contain a secondary alcoholic group, they yield ketones, *e.g.*:

$$CH_2OH{\cdot}CH_2OH \rightarrow CHO{\cdot}CH_2OH \rightarrow COOH{\cdot}CH_2OH \rightarrow COOH{\cdot}COOH$$

and

$$CH_3{\cdot}CH(OH){\cdot}CH_2OH \rightarrow CH_3{\cdot}CH(OH){\cdot}COOH \rightarrow CH_3{\cdot}CO{\cdot}COOH, \&c$$

Methylene- and **Ethylidene-glycols.** (See Aldehydes.)

Ethylene glycol (*glycol*), $OH{\cdot}CH_2{\cdot}CH_2{\cdot}OH$ (*Wurtz*, A **100**, 110), is prepared from ethylene bromide by means of potassium acetate in alcoholic solution (*Domole*), or of potassium carbonate in aqueous solution, as given above (A **192**, 250). For properties, see above. Its formula has been corroborated by the determination of its vapour density. Oxidizing agents transform it into glycollic acid, $OH{\cdot}CH_2{\cdot}CO{\cdot}OH$, and oxalic acid, $OH{\cdot}CO{\cdot}CO{\cdot}OH$.

Propylene glycol is known in two isomeric forms, viz.

(*a*) **Trimethylene glycol**, *β* **Propylene glycol**, *Propane* 1:3 *diol*, $OH{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH$, which is prepared from trimethylene bromide, and is a di primary glycol boiling at 216°. It is also produced by the *Schizomycetes* fermentation of glycerol (B. **14**, 2270).

(*b*) *α*-**Propylene glycol**, *Propane*-1·2-*diol*, $CH_3{\cdot}CH(OH){\cdot}CH_2{\cdot}OH$, can be prepared from propylene bromide in an analogous manner, but is more easily obtained by distilling glycerol with caustic soda. It boils at 188°. It contains an asymmetric carbon atom in the molecule, and becomes optically (−) active when fermented, *i.e.* fission fungi destroy the dextro modification more rapidly than the laevo.

Four **butylene glycols**, and various **amylene-** and **hexylene-glycols**, &c., are also known. Of these, the γ-glycols (in which the hydroxyls are in the positions 1:4, and which therefore contain the grouping $\cdot C^{1}(OH)\cdot C^{2}\cdot C^{3}\cdot C^{4}(OH)\cdot$) yield compounds of the **furane** series by the formation of anhydrides (B **22**, 2567), and therefore stand in close relation to thiophene and pyrrole.

Pinacone, Tetramethyl-ethylene glycol (2:3-*Dimethyl-butane*-2:3-*diol*), $(CH_3)_2{:}C(OH)\cdot C(OH){:}(CH_3)_2$. The hydrate, $(+ 6H_2O)$, forms large quadratic tables, in the anhydrous state it is a crystalline mass melting at 38° and boiling at 172°. When warmed with dilute sulphuric or hydrochloric acid it yields pinacoline, $CH_3\cdot CO\cdot C(CH_3)_3$, methyl tertiary-butyl ketone or 2.2-dimethyl-butan-3-one (see p. 137):

$$\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C(OH)\cdot C(OH)\!<\!\begin{matrix}CH_3\\CH_3\end{matrix} \longrightarrow CH_3\cdot CO\cdot C\!<\!\begin{matrix}CH_3\\CH_3\\CH_3\end{matrix} + H_2O$$

In this reaction an interesting intramolecular rearrangement occurs, together with the elimination of water.

Numerous other pinacones are known. They may be obtained by reducing ketones or synthetically (*Liebig*, M. **17**, 68, **19**, 16), and with acids yield the corresponding pinacolines

DERIVATIVES OF THE GLYCOLS

The **ethers**, *e.g.* $C_2H_4(OCH_3)_2$, are mostly colourless liquids with ethereal odours, and have lower boiling-points than the glycols. (Cf. Ether and Ethyl Alcohol.) They cannot be readily hydrolysed

The **esters**, *e.g.* $C_2H_4(O\cdot CO\cdot CH_3)_2$, are also mostly liquids, and are readily hydrolysed

The following esters of inorganic acids are interesting:—

Glycol chlorhydrin, $CH_2Cl\cdot CH_2\cdot OH$, obtained by passing hydrogen chloride into warm glycol, or by the addition of hypochlorous acid to ethylene, is a liquid miscible with water, and boiling at 130°, in this last respect differing from its corresponding alcohol to almost the same extent as ethyl chloride does from alcohol

Glycollic di-nitrate, $C_2H_4(NO_3)_2$, is prepared by acting on glycol with sulphuric and nitric acids:

$$C_2H_4(OH)_2 + 2NO_2\cdot OH = C_2H_4(O\cdot NO_2)_2 + 2H_2O$$

It is a yellowish liquid, insoluble in water, is readily hydro-

lysed by alkalis to glycol and nitric acid, and hence the constitution. The formation of such nitric esters, which are highly explosive, is characteristic of the polyhydric alcohols (see Nitroglycerine).

Ethylene cyanide, $CN \cdot CH_2 \cdot CH_2 \cdot CN$, obtained by the action of potassium cyanide on ethylene dibromide, is a crystalline solid, and on hydrolysis with alkalis yields $CO_2H \cdot CH_2 \cdot CH_2 \cdot CO_2H$, succinic acid, and hence may be regarded as **succinonitrile**.

Glycol monochlorhydrin with potassium cyanide yields **ethylene cyanhydrin**, or the nitrile of *β* lactic acid, $OH \cdot CH_2 \cdot CH_2 \cdot CN$. Isomeric with it is **ethylidene cyanhydrin**, $CH_3 \cdot CH(OH) \cdot CN$, the additive product of hydrocyanic acid and aldehyde (p. 126).

Ethylene oxide, C_2H_4O (*Wurtz*), obtained by distilling glycol chlorhydrin with caustic-potash solution, is a mobile liquid of ethereal odour boiling at 13·5°. It is miscible with water, and slowly converted into the glycol.

It has many of the properties of an unsaturated compound, *e.g.* with HCl it yields the chlorhydrin, with NH_3 the amino alcohol, $OH \cdot CH_2 \cdot CH_2 \cdot NH_2$, and with chlorine ethylene dichloride.

It is largely owing to the last reaction that the ring constitution, $\begin{matrix} CH_2 \\ \cdot \\ CH_2 \end{matrix}\!\!>\!O$, and not the open-chain formula, $CH_2{:}CH \cdot OH$, is given to the compound. The formation of additive compounds is accompanied by the rupture of the ring. Some of the higher homologues of ethylene oxide are much more stable, and do not yield additive compounds; this is due to the fact that the ring is more stable and therefore less easy to rupture (compare Polymethylene Compounds).

AMINES OF THE DIHYDRIC ALCOHOLS

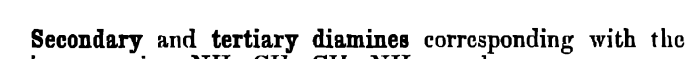
These are derived from glycols by the replacement of one or both hydroxyl groups by amino groups:

$OH \cdot CH_2 \cdot CH_2 \cdot NH_2$ and $NH_2 \cdot CH_2 \cdot CH_2 \cdot NH_2$

Hydroxy ethylamine — Ethylene diamine.

In the former case compounds are obtained which possess the properties of an amine in addition to those of an alcohol; in the latter, diamines free from oxygen, which are analogous to ethylamine, but are di-acid and not mono acid bases.

Secondary and **tertiary diamines** corresponding with the **primary amine**, $NH_2 \cdot CH_2 \cdot CH_2 \cdot NH_2$, are known, *e.g.*:



The methods by means of which these diamines can be obtained are analogous to those described for the monamines, viz.:—

1 By heating ethylene bromide, &c, with alcoholic ammonia to 100° (*Hofmann*).

$$\begin{aligned} C_2H_4Br_2 + 2NH_3 &= C_2H_4(NH_2)_2 + 2HBr; \\ C_2H_4(NH_2)_2 + C_2H_4Br_2 &= (C_2H_4)_2N_2H_2 + 2HBr; \\ (C_2H_4)_2N_2H_2 + C_2H_4Br_2 &= (C_2H_4)_3N_2 + 2HBr \end{aligned}$$

The primary, secondary, and tertiary bases, which are formed simultaneously, can be separated by fractional distillation

The hydroxy amines (or alkines, *Ladenburg*) are obtained in an analogous manner by using ethylene chlorhydrin, thus:—

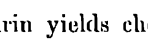
$$C_2H_4(OH)Cl + NH_3 = C_2H_4(OH)(NH_2) + HCl.$$

In this case also primary, secondary, and tertiary bases are produced at the same time, and are separated by the fractional crystallization either of their hydrochlorides or of their platinichlorides.

Ethylene chlorhydrin yields choline chloride (p. 196) with trimethylamine

2 Primary diamines are formed by the reduction of the nitriles, $C_nH_{2n}(CN)_2$, *e.g.* by adding metallic sodium to the hot alcoholic solution:

$$CN \cdot CH_2 \cdot CH_2 \cdot CN + 8H = \underset{\text{Butylene diamine}}{NH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot NH_2}$$

Ethylene diamine, $C_2H_4(NH_2)_2$, **Diethylene diamine**, $(C_2H_4)_2N_2H_2$, &c, are colourless liquids distilling without decomposition. The former boils at 123°, and has an ammoniacal odour; the latter melts at 104° and boils at 146°, and is identical with piperazine, *i.e.* hexahydro-pyrazine Hence it possesses the constitutional formula  , and has a closed-chain constitution (*Hofmann*, B. **23**, 3297).

Tetramethylene-diamine, *Butane-1:4-diamine*, *putrescine*, *butylene-diamine*, $NH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot NH_2$, is prepared according to method 2, and is also formed during the putre-

faction of flesh. As a "γ-diamine", *i.e.* the diamine of a γ-glycol, it is closely related to pyrrole, from which it is formed by the action of hydroxylamine (whereby a dioxime is first produced), and subsequent reduction (B. **22**, 1968).

Pentamethylene diamine, *cadaverine*, $NH_2 \cdot (CH_2)_5 \cdot NH_2$, is formed by the reduction of trimethylene cyanide, $CN \cdot (CH_2)_3 \cdot CN$, which on its part is prepared from trimethylene bromide, $CH_2Br \cdot CH_2 \cdot CH_2Br$, and KCN (*Ladenburg*). It is a colourless, syrupy liquid of very pronounced spermaceti and piperidine odour, solidifies in the cold, and boils at 178°–179°. It possesses especial interest, because, being a δ-diamine, it gives up ammonia and yields the cyclic base **piperidine**, $CH_2<\begin{matrix}CH_2 \cdot CH_2\\CH_2 \cdot CH_2\end{matrix}>NH$ (see this).

Many of these polyacid bases are found in decaying albumen and in corpses, and are designated **ptomaïnes** or **toxines** (cf. *e.g.* B. **19**, 2585).

Choline, *bilineurine*, *ethylol-trimethyl-ammonium hydroxide*, $OH \cdot CH_2 \cdot CH_2 \cdot NMe_3 \cdot OH$ (*Strecker*), is found in the bile (χολή, bile), brain, yolk of egg, &c., being present in these combined with fatty acids and glyceryl-phosphoric acid as lecithin. It is also found in herring brine, hops, beer, and in many fungi, &c., and is obtained by boiling sinapine with alkalis (the old name for this product was "Sinealine"). Choline is a strong, deliquescent base, and readily absorbs carbon dioxide from the air. It is not poisonous. The **chloride** has the formula $OH \cdot C_2H_4 \cdot NMe_3Cl$. Concentrated HNO_3 oxidizes choline to **muscarine**, $C_5H_{15}NO_3 = (OH)_2CH \cdot CH_2 \cdot NMe_3 \cdot OH$, an excessively poisonous base, which is present in toad-stool, *Agaricus muscarius*.

By transforming choline, by means of hydriodic acid, into its iodide, $CH_2I \cdot CH_2 \cdot NMe_3I$, and treating the latter with moist oxide of silver, and also from the putrefaction of choline, **neurine** (νεῦρον, nerve), *trimethyl-vinyl-ammonium hydroxide*, $CH_2 : CH \cdot NMe_3 \cdot OH$ (*Hofmann*), is obtained. This base, containing the unsaturated radical "vinyl", C_2H_3, is very similar to choline, and can also be prepared from brain substance; it is only known in solution, and is very poisonous. It can be re-transformed into choline. (For this, and also for derivatives, see *e.g.* A. **267**, 249; **268**.)

Another natural compound related to hydroxy ethylamine is **taurine**, $C_2H_7NSO_3$ (*Gmelin*), which is present in combination with cholic acid as **taurocholic acid** in the bile of oxen

and many other animals, also in the kidneys, lungs, &c. It crystallizes in large monoclinic prisms, is readily soluble in hot water, but insoluble in alcohol, and decomposes when strongly heated. Its constitution follows from its synthesis.

Isethionic acid, hydroxy ethyl-sulphonic acid, $OH \cdot CH_2 \cdot CH_2 \cdot SO_2 \cdot OH$, is obtained when carbyl sulphate, $C_2H_4S_2O_6$ (from C_2H_4 and SO_3), is boiled with water; its constitution follows from its properties, and also from the fact that it may be obtained by the oxidation of the hydroxymercaptan, $OH \cdot CH_2 \cdot CH_2 \cdot SH$. Isethionic acid with PCl_5 yields the chloride $CH_2Cl \cdot CH_2 \cdot SO_2Cl$, and this with water gives chloroethyl-sulphonic acid, $CH_2Cl \cdot CH_2 \cdot SO_2 \cdot OH$, which with ammonia yields taurine, its constitution must, therefore, be $NH_2 \cdot CH_2 \cdot CH_2 \cdot SO_2 \cdot OH$, **amino-ethyl-sulphonic acid**, and in accordance with this constitution it unites in itself the properties of an alcoholic amine and a sulphonic acid, and is therefore at the same time a base and an acid It forms unstable salts with alkalis, but not with acids, the groups NH_2 and SO_3H in the molecule practically neutralizing one another, so that its reaction is neutral Nitrous acid converts it into isethionic acid, a reaction analogous to the decomposition of the primary amines by this reagent As an alkyl sulphonic acid, it is not hydrolysed by boiling with alkalis and acids It is sometimes represented as a cyclic ammonium salt,

$$\begin{matrix} CH_2 \cdot NH_3 \\ | \\ CH_2 \cdot SO_3 \end{matrix}$$

B Trihydric Alcohols

The molecule of each trihydric alcohol contains three hydroxyl groups, each attached to a different carbon atom. They may be regarded as analogous to the hydroxides of tervalent metals *e.g.* $C_3H_5(OH)_3$ and $Al(OH)_3$. They can give rise to three distinct groups of derivatives according as one, two, or three of the hydroxyls react, *e.g.* chlorides—$C_3H_5Cl(OH)_2$, monochlorhydrin; $C_3H_5Cl_2 \cdot OH$, dichlorhydrin; and $C_3H_5Cl_3$, trichlorhydrin of glycerol. Similarly for acetates, amino-derivatives, &c.

Although the compound $CH(OH)_3$, **ortho-formic acid**, is not known, derivatives, *e.g.* **ethyl ortho-formate**, $CH(OEt)_3$, (p. 142), and similarly **ethyl ortho-acetate**, $CH_3 \cdot C(OEt)_3$, can readily be prepared.

Glycerine, *glycerol*, *propane*-1:2:3-*triol*, $OH \cdot CH_2 \cdot CH(OH) \cdot CH_2 \cdot OH$. (*Scheele*, 1779; formula established by *Pelouze* in 1836, and constitution by *Berthelot* and *Wurtz*.)

Synthesis.—By heating 1:2:3-trichlorpropane with water to 170°:

$$\begin{matrix} CH_2Cl \\ CHCl \\ CH_2Cl \end{matrix} + 3H \cdot OH = \begin{matrix} CH_2 \cdot OH \\ CH \cdot OH \\ CH_2 \cdot OH \end{matrix} + 3HCl.$$

The trichlorpropane is itself obtainable from isopropyl iodide (which can also be prepared synthetically) by conversion into propylene, addition of Cl_2, and heating the propylene dichloride thus formed with iodine chloride (*Friedel* and *Silva*, Bull. Soc. Chim. **20**, 98):

$$CH_3 \cdot CHI \cdot CH_3 \rightarrow CH_2 \cdot CH : CH_2 \rightarrow CH_2 \cdot CHCl \cdot CH_2Cl \rightarrow CH_2Cl \cdot CHCl \cdot CH_2Cl.$$

Glycerol is also produced when allyl alcohol is oxidized with very dilute potassium permanganate:

$$CH_2 : CH \cdot CH_2 \cdot OH \rightarrow OH \cdot CH_2 \cdot CH(OH) \cdot CH_2 \cdot OH$$

The *constitution* of glycerol follows from these syntheses and also from its relation to tartronic acid (p. 199), each of the three hydroxyls is attached to a separate carbon atom.

Preparation.—Glycerol is usually prepared by hydrolysing the natural fats and oils (especially olive oil), which are the glyceryl salts of fatty and other acids (p. 158). The hydrolysis may be effected by means of superheated steam, by heating with lime and water, or with sulphuric acid. They are thus resolved into their components, glycerol and acid, the glycerol distils over with the superheated steam, and may be purified by animal charcoal. Hydrolysis by means of an enzyme contained in castor-oil seeds is used commercially.

In the manufacture of stearic acid (p. 161) the fats are hydrolysed with sulphuric acid, when the glycerol is converted into glyceryl-sulphuric acid, $C_3H_5(OH)_2(O \cdot SO_3H)$, from which it can be obtained by boiling with water or with lime. In the preparation of plaister, by boiling fats with lead oxide and water (p. 160), an aqueous solution of glycerol is obtained together with the insoluble lead plaister.

Large quantities of glycerol are now recovered from the liquors from which the hard soaps (p. 158) have separated.

Properties.—It is a thick, colourless syrup, of specific gravity

1·27, solidifies, when strongly cooled, to crystals like those of sugar-candy, which melt at 17°. It boils at 290°, but, when impure, can be distilled without decomposition under diminished pressure only, viz. at 170° under 12 mm. It is very hygroscopic, and mixes with water and alcohol in all proportions, but is insoluble in ether.

Uses —In the manufacture of liqueurs, fruit preserves, wine, &c., for non-drying stamp colours and blacking, when mixed with glue, in book printing, as a healing ointment for external use; but especially in the manufacture of nitro-glycerine and in the colour industry.

Behaviour —1. With alkalis and other metallic hydroxides it forms **alcoholates**, which are readily decomposed again into their components

2. As a trihydric alcohol the hydrogen atoms of the OH groups can be replaced by alkyl radicals yielding **ethers**, *e.g.* **mono-ethylin**, $C_3H_5(OH)_2(OC_2H_5)$, and **triethylin**, $C_3H_5(OC_2H_5)_3$, liquids which boil without decomposition.

3. As an alcohol it forms the most various **esters** thus, with sulphuric acid, the easily saponifiable **glyceryl-sulphuric acid**, $C_3H_5(OH)_2(O\cdot SO_3H)$, with phosphoric acid, **glyceryl-phosphoric acid**, $C_3H_5(OH)_2(O\cdot PO_3H_2)$, with nitric acid, **glyceryl trinitrate**, $C_3H_5(O\cdot NO_2)_3$, with hydrochloric acid the **chlorhydrins**; and with the higher fatty acids the fats. For its behaviour with hydriodic acid, or iodine and phosphorus, see p. 60.

4. It yields compounds of a mercaptan or aminic character by exchange of OH for SH or NH_2.

5. When distilled with dehydrating agents, *e.g.* phosphorus pentoxide, or, better, anhydrous potassium hydrogen sulphate, two molecules of water are eliminated from each molecule of glycerol, and acrolein (p. 130) is formed By the indirect separation of one mol. H_2O, **glycide alcohol**, $C_3H_6O_2$, is obtained.

6. Oxidizing agents convert it, according to circumstances, either into **glyceric**, $OH\cdot CH_2\cdot CH(OH)\cdot CO_2H$, **tartronic**, $CO_2H\cdot CH(OH)\cdot CO_2H$, or **mesoxalic acid**, $CO_2H\cdot CO\cdot CO_2H$, or acids with a smaller number of carbon atoms. The formation of the three above-mentioned acids indicates that glycerol molecule must be built up of two primary and one secondary alcoholic groups, as represented in the formula already given. Halogens oxidize and do not substitute.

7. It yields normal butyl alcohol, caproic acid, and butyric acid by certain fermentations. (Cf. B. **16**, 884.)

8. It is largely used in the preparation of allyl alcohol (p. 82),

acrolein (p. 130), allyl iodide (p. 65), isopropyl iodide (p. 60), and formic acid (p. 148).

DERIVATIVES

Chlorhydrins (hydrochloric esters). **Mono-** and **dichlorhydrins** are formed by the action of hydrochloric acid on glycerol, and **trichlorhydrin** by the action of phosphorus pentachloride on the mono- or di-compounds. Each of the two first-named exists in two isomeric modifications.

α-Monochlorhydrin, *3-Chloro-propane-1·2-diol*, $CH_2(OH)\cdot CH(OH)\cdot CH_2Cl$, is formed from epichlorhydrin, $C_3H_5O\cdot Cl$, (see below), and water; **α-dichlorhydrin**, *1·3-dichloro-propane-2-ol*, $CH_2Cl\cdot CH(OH)\cdot CH_2Cl$, from epichlorhydrin and HCl, **β-monochlorhydrin**, $CH_2(OH)\cdot CHCl\cdot CH_2(OH)$, and **β-dichlorhydrin**, $CH_2Cl\cdot CHCl\cdot CH_2\cdot OH$, by the addition of hypochlorous acid to allyl alcohol or to allyl chloride

The chlorhydrins are liquids sparingly soluble in water, and readily soluble in alcohol and ether Their boiling-points are much below that of glycerol.

Glycide Compounds.—By the elimination of water from glycerol a compound is obtained which unites within itself the properties of ethylene oxide and of a monohydric alcohol, viz **glycide alcohol**,

$$\begin{matrix} OH\cdot CH_2\cdot CH\cdot OH \\ \quad\quad\quad\quad\; \dot{C}H_2\cdot OH \end{matrix} \longrightarrow \begin{matrix} OH\cdot CH_2\cdot CH \\ \quad\quad\quad\quad\; \dot{C}H_2 \end{matrix}\!\!\diagdown\!\!\diagup O,$$

which is isomeric with propionic acid.

It may be prepared by the abstraction of HCl from α-monochlorhydrin by means of baryta, just as ethylene chlorhydrin yields ethylene oxide. It is a colourless liquid, boiling at 162°, and miscible with water, alcohol, and ether. It combines with H_2O, yielding glycerol, and with HCl yielding the chlorhydrin, and, as an alcohol, forms esters (glycide esters), &c. Its hydrochloric ester is **epichlorhydrin**,

$$\begin{matrix} CH_2Cl\cdot CH \\ \quad\quad\; \dot{C}H_2 \end{matrix}\!\!\diagdown\!\!\diagup O,$$

isomeric with chlor-acetone and propionyl chloride, a mobile liquid of chloroform odour, boiling at 117°, which is formed by the elimination of HCl from either of the dichlorhydrins. Like ethylene oxide it is capable of combining with H_2O, HCl, &c.

Esters of Nitric Acid.—Mononitrin, $C_3H_5(OH)_2(O\cdot NO_2)$,

and **trinitrin** or **nitro-glycerine**, $C_3H_5(O\cdot NO_2)_3$, are known. The latter is prepared by treating glycerol with a cold mixture of concentrated nitric and sulphuric acids (B. 1899, **32**, 1444). It is a colourless oil, insoluble in water, poisonous, and of a sweet, burning, aromatic taste. Sp. gr. 1·6. M.-pt. about 11°–12°. It burns without explosion, but explodes with terrible violence when quickly heated or when struck (*Nobel's* explosive oil). When mixed with kieselguhr in the proportion of three parts to one it forms **dynamite** (*Nobel*, 1867), which is exploded by fulminate of mercury with frightful force. It is hydrolysed by alkalis and by ammonium sulphide, yielding glycerol and nitric acid, and hence its constitution as a nitrate, $C_3H_5(O\cdot NO_2)_3$, and not a nitro-derivative, *e g.* $C_3H_2(NO_2)_3(OH)_3$.

The esters derived from glycerol and the fatty acids are largely met with in vegetable and animal oils and fats. Most of these are the normal esters, *e g.* **glyceryl tripalmitate**, **tripalmitin**, $C_3H_5(O\cdot CO\cdot C_{15}H_{31})_3$, **tristearin**, &c. (see p. 158, *et seq*).

These esters can also be obtained artificially, as can also the mono- and dihydric esters, *e.g.* **monopalmitin**, $(OH)_2C_3H_5\cdot O\cdot CO\cdot C_{15}H_{31}$, and **dipalmitin**, $OH\cdot C_3H_5(O\cdot CO\cdot C_{15}H_{31})_2$.

Most are wax-like solids, and, on hydrolysis, yield as ultimate products glycerol and the fatty acid. With the normal esters this hydrolysis occurs in stages yielding the monohydroxy ester, then the dihydroxy, and finally glycerol.

C. Tetra-, Penta-, and Hexahydric Alcohols

These alcohols can react respectively with 4, 5, or 6 molecules of a monobasic acid to form neutral esters, and consequently 4, 5, or 6 alcoholic hydroxyls are to be assumed as present in their molecules.

The number of hydroxyls present in an alcohol is usually determined from the number of acetyl groups present in the ester which is formed when the alcohol is heated with acetic anhydride and anhydrous sodic acetate, thus:—

$$C_6H_8(OH)_6 + 6(CH_3\cdot CO)_2O = C_6H_8(O\cdot CO\cdot CH_3)_6 + 6CH_3\cdot CO_2H.$$

One of the simplest methods of determining the number of acetyl groups is to hydrolyse the acetate by distilling with benzene sulphonic acid in steam, and to titrate the acetic acid in the distillate with standard barium hydroxide, using phenolphthalein as indicator (*Sudborough and Thomas*, J. C. S. 1905, 1752).

The ester of any alcohol in question may also be prepared by the aid of an acid containing halogen, bromo-benzoic acid being especially suitable for this; and from the percentage of bromine found in the ester, the number of acid radicals which have entered the molecule, *i.e.* the number of hydroxyls, can be deduced.

The polyhydric alcohols are solid crystalline compounds of sweet taste Many occur as natural products, and they may be obtained by the reduction of the corresponding hydroxy aldehydes, hydroxy ketones, or hydroxy monobasic acids (mannonic acid, &c.) by sodium amalgam. (*E Fischer*, B. **22**, 2204.) Conversely, cautious oxidation by bromine water transforms them first into sugars (hydroxy aldehydes), and then into the corresponding acids. As a rule they cannot be volatilized without decomposition. Their derivatives are exactly analogous to those of glycol and glycerol

Their *constitution* follows from the generalization already repeatedly referred to, viz that not more than one hydroxyl group can be attached to the same carbon atom without the immediate separation of water, so that a tetrahydric alcohol must contain at least 4, and a hexahydric alcohol at least 6, atoms of carbon. The tetrahydric alcohol erythritol, $C_4H_6(OH)_4$, has thus the formula.

$$OH\cdot CH_2\cdot CH(OH)\cdot CH(OH)\cdot CH_2\cdot OH,$$

and mannitol, the simplest of the hexahydric alcohols, $C_6H_8(OH)_6$, the formula:

$$OH\cdot CH_2(CH\cdot OH)_4\cdot CH_2\cdot OH.$$

All the common polyhydric alcohols have a normal carbon chain, as on reduction with hydriodic acid they yield normal secondary iodides, *e.g.* erythritol yields 2-iodo-butane, $CH_3\cdot CHI\cdot CH_2\cdot CH_3$.

1. **Tetrahydric Alcohols.**—**Ortho-carbonic ether**, $C(OC_2H_5)_4$, is to be regarded as the ether of the hypothetical alcohol, $C(OH)_4$, which may be looked upon as the hydrate of carbonic acid, but is itself incapable of existence. It is a liquid of ethereal odour, boiling at 159°.

Erythritol (*Butane-tetrol*) occurs in the free state in *Protococcus vulgaris*, and combined with orsellinic acid as an ester (erythrin), in many lichens and algæ. It forms large quadratic crystals, sparingly soluble in alcohol and insoluble in ether. M.-pt. 112°; b.-pt. about 300°.

2. **Pentahydric Alcohols, Arabitol**, $OH\cdot CH_2\cdot(CH\cdot OH)_3\cdot$

$CH_2 \cdot OH$ (from arabinose by reduction). **Xylitol**, by the reduction of xylose, is stereo-isomeric; and **rhamnitol**, $OH \cdot CH_2 \cdot (CH \cdot OH)_4 \cdot CH_3$, m.-pt. 121°, from rhamnose, is homologous.

3. **Hexahydric Alcohols.**—**Mannitol**, $OH \cdot CH_2 \cdot (CH \cdot OH)_4 \cdot CH_2 \cdot OH$ (*Proust*, 1800), is found in many plants, for instance in the larch, in *Viburnum Opulus*, in celery, in the leaves of *Syringa vulgaris*, in sugar-cane, in *Agaricus integer* (of the dry substance of which it forms 20 per cent), in rye bread, and especially in the manna ash, *Fraxinus ornus*, the dried juice of which constitutes manna. It can be prepared from grape-sugar, or still better from fruit sugar, from which it only differs in composition by containing two atoms of hydrogen more in the molecule, by reduction with sodium amalgam.

It crystallizes in fine needles or rhombic prisms, and is readily soluble in cold water and boiling alcohol. It is dextro-rotatory, but a lævo rotatory and an inactive modification are also known. (See Mannonic Acid.) M.-pt 166°. When heated it is converted into its anhydrides, **mannitan**, $C_6H_{12}O_5$, and **mannide**, $C_6H_{10}O_4$. Cautious oxidation converts mannitol into a mixture of mannose, $OH \cdot CH_2(CH \cdot OH)_4 \cdot CHO$, and fructose, $OH \cdot CH_2(CH \cdot OH)_3 \cdot CO \cdot CH_2 \cdot OH$. Nitric acid oxidizes it to saccharic acid, $CO_2H \cdot (CH \cdot OH)_4 \cdot CO_2H$; hydriodic reduces it to secondary hexyl iodide, $CH_3 \cdot CHI \cdot (CH_2)_3 \cdot CH_3$ (p. 59).

The molecule of mannitol contains 4 asymmetric carbon atoms, *e.g.*:

$$OH \cdot CH_2 \cdot CH(OH) \cdot CH(OH) \cdot CH(OH) \cdot CH(OH) \cdot CH_2OH,$$

and hence a number of stereo-isomerides are known, *e.g.* *d*-, *l*-, and *r*-mannitol, *d*, *l*-, *r*-**sorbitol**, and **dulcitol**, which is optically inactive owing to the fact that its molecule is symmetrical in configuration. (See Stereochemistry of the Sugars.)

The sugars are closely related to the penta- and hexahydric alcohols, being the corresponding polyhydric aldehydes or ketones. The alcohols as a rule are not fermented by yeast, and do not reduce an alkaline cupric solution, dulcitol excepted.

OXIDATION PRODUCTS OF THE POLYHYDRIC ALCOHOLS

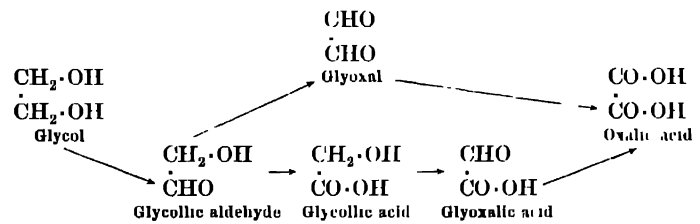
Just as the monohydric alcohols are oxidized to aldehydes, ketones, and acids so the polyhydric alcohols pass, on oxidation, into aldehydes, ketones, and polybasic acids.

Further, by this oxidation of the polyhydric alcohols we obtain not only aldehydes, ketones, and acids, but also numerous compounds which possess a double chemical character in so far as they unite in themselves the properties of more than one of these classes of compounds. These are the **hydroxy aldehydes**, which are at the same time aldehyde and alcohol, the **hydroxy ketones**, at the same time ketone and alcohol, the **hydroxy acids, aldehyde acids, ketone acids**, and **ketone aldehydes**.

An aldehyde acid, for instance, is capable, as an acid, of forming salts, esters, and amides on the one hand, and on the other, as an aldehyde, it is able to reduce an ammoniacal silver solution, to combine with $NaHSO_3$, and to react with hydroxylamine, &c.

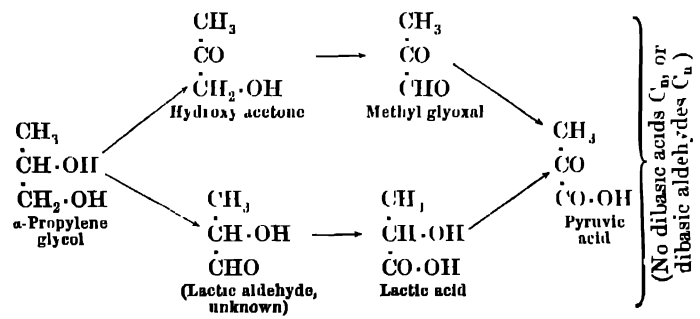
SUMMARY OF THE OXIDATION PRODUCTS

(*a*) Of the di-primary alcohols.



Possible products: Di-aldehydes, dibasic acids, hydroxy aldehydes, hydroxy acids, aldehyde acids.

(*b*) Of the hydroxy primary-secondary alcohols.



Possible products: hydroxy aldehydes, hydroxy ketones, ketone aldehydes, hydroxy acids, ketone acids.

(*c*) Of the di-secondary alcohols: hydroxy ketones, diketones. (No dibasic acids or alcohol acids, C_n.) *e.g.*:

$$\begin{array}{ccccc} CH_3\cdot CH\cdot OH & & CH_3\cdot CH\cdot OH & & CH_3\cdot CO \\ | & \rightarrow & | & \rightarrow & | \\ CH_3\cdot CH\cdot OH & & CH_3\cdot CO & & CH_3\cdot CO \end{array}$$

Di secondary butylene glycol — Dimethyl-ketol — Di-acetyl.

(*d*) The tri- and polyhydric alcohols are capable of yielding the most various products upon oxidation, especially polyhydroxy ketones, polyhydroxy acids, keto-acids, and polybasic acids.

Of all these oxidation products, the most important are the hydroxy acids, the polybasic acids, and the keto-acids. For the sake of convenience the hydroxy monobasic acids will be treated of first.

IX HYDROXY MONOBASIC ACIDS AND COMPOUNDS RELATED TO THEM

A. Monohydroxy Fatty Acids

These compounds may be regarded as monohydroxy derivatives of the fatty acids, *e.g.* $OH\cdot CH_2\cdot CO_2H$, hydroxy acetic acid, or glycollic acid, $OH\cdot CH_2\cdot CH_2\cdot CO_2H$, β-hydroxy propionic acid, or β lactic acid, &c.

They combine within themselves the **properties of a monobasic acid and of an alcohol**, and are consequently capable of forming derivatives as alcohols, as acids, and as both together.

The lowest members of the series, which are the most important, are **glycollic acid** and **lactic acid**, both syrupy liquids which solidify to crystalline masses in the desiccator, and readily give up water to form anhydrides. They cannot be volatilized without decomposition, and are readily soluble in water, and for the most part also in alcohol and ether.

Formation.—1. By the regulated oxidation of the glycols. (See Summary, p. 204.)

2 From the fatty acids, through their monohaloid substitution products, the halogen of these being easily replaced by

hydroxyl, either by means of moist oxide of silver or often by prolonged boiling with water alone:

$$CH_2Cl\cdot CO_2H + H_2O = CH_2(OH)\cdot CO_2H + HCl.$$

This reaction is conditioned by the halogen having the α-position with respect to the carboxyl (cf. pp. 169 and 170).

For a reaction of these haloid-substitution products in a different direction, see β- and γ-hydroxy acids.

3. From the aldehydes and ketones containing 1 atom of carbon less, by the preparation of their hydrocyanic acid compounds, **cyanhydrins** (see pp 126 and 135), and hydrolysis of the latter. Thus, from aldehyde is produced ethylidene cyanhydrin, and from this α-lactic acid:

$$CH_3\cdot CH(OH)(CN) + 2H_2O = CH_3\cdot CH(OH)\cdot CO_2H + NH_3.$$

Since the aldehydes and ketones are easily obtained from the corresponding alcohols, this reaction furnishes a means of preparing the acids, $C_nH_{2n}(OH)(CO_2H)$, from the alcohols, $C_nH_{2n+1}(OH)$, *i.e.* of introducing carboxyl into the latter in place of hydrogen; this is a most important synthesis.

4. From the glycollic cyanhydrins by saponification, *e.g.* β-lactic acid from ethylene cyanhydrin.

$$OH\cdot CH_2\cdot CH_2\cdot CN + 2H_2O = OH\cdot CH_2\cdot CH_2\cdot CO_2H + NH_3$$

As the cyanhydrins can be readily obtained from the glycols (p. 191), this formation of hydroxy acids represents an exchange of a hydroxyl of the glycol for carboxyl, and is analogous to the formation of acetic acid from methyl alcohol. Thus.—

$$OH\cdot CH_2\cdot CH_2\cdot OH \rightarrow OH\cdot CH_2\cdot CH_2Cl \rightarrow OH\cdot CH_2\cdot CH_2\cdot CN \rightarrow OH\cdot CH_2\cdot CH_2\cdot CO_2H$$

$$\text{and } CH_3\cdot OH \rightarrow CH_3Cl \rightarrow CH_3\cdot CN \rightarrow CH_3\cdot CO_2H$$

5. By the reduction of aldehyde acids or ketonic acids, *e.g.* lactic from pyruvic acid (p. 225). This reaction corresponds with the formation of the alcohols from the aldehydes or ketones by reduction.

6. By the action of nitrous acid upon amino acids (see Glycocoll); a reaction analogous to the formation of alcohols from amines (p. 108).

7. Hydroxy acids of the fatty series containing an equal number of carbon atoms result by *direct oxidation*, if a CH

group, *i.e.* a "tertiary" hydrogen atom, is present in the original acid (*R. Meyer*, B. **11**, 1283; **12**, 2238):

$$\underset{\text{Isobutyric acid}}{(CH_3)_2CH\cdot CO_2H} + O = \underset{\text{α-Hydroxy-isobutyric acid.}}{(CH_3)_2C(OH)\cdot CO_2H}$$

Constitution and Isomers. — As hydroxy compounds of the fatty acids, the acids of the foregoing series can exist in as many modifications as the monohaloid fatty acids. Thus there is only one glycollic acid, corresponding with monochloracetic acid, but two lactic acids—corresponding with α- and β-chloro-propionic acids—are possible, and both actually exist, they are designated as α- and β-hydroxy propionic acids:

$CH_3\cdot CHCl\cdot CO_2H$ (α-chloro-propionic acid).
$CH_3\cdot CH(OH)\cdot CO_2H$ (α-hydroxy-propionic acid or common lactic acid)
$CH_2I\cdot CH_2\cdot CO_2H$ (β-iodo-propionic acid).
$OH\cdot CH_2\cdot CH_2\cdot CO_2H$ (β-hydroxy propionic acid or β-lactic acid)

From the two butyric acids can be theoretically derived:

(*a*) From the normal acid.

$$\overset{\gamma}{CH_3}\cdot\overset{\beta}{CH_2}\cdot\overset{\alpha}{CH_2}\cdot CO_2H,$$

an α-, β-, and γ-hydroxy butyric acid.

(*b*) From isobutyric acid:

$$\begin{matrix}\beta\,CH_3\\ \beta\,CH_3\end{matrix}\!\!>\!\overset{\alpha}{C}H\cdot CO_2H,$$

an α- and β-hydroxy isobutyric acid.

Systematic Nomenclature. — $OH\cdot CH_2\cdot CH_2\cdot CO_2H$, *Propane-3-ol-1-acid*, $(CH_3)_2\cdot C(OH)\cdot CO_2H$, *2-Methyl-propane-2-ol-1-acid*; $OH\cdot CH_2\cdot CH_2\cdot CH_2\cdot CO_2H$, *Butane-4-ol-1-acid*, &c.

The constitution of these hydroxy acids can often be deduced from their methods of formation. Thus the preparation of common lactic acid from aldehyde, $CH_3\cdot CHO$, according to method 3, shows that it contains the group $CH_3\cdot CH:$, "ethylidene", it is therefore termed "ethylidene lactic acid". On the other hand, the formation of β-hydroxy propionic acid from glycol cyanhydrin, according to 4, is a proof of its containing the group $\cdot CH_2\cdot CH_2\cdot$, "ethylene"; hence the name "ethylene lactic acid".

The constitution can also frequently be deduced from a study of their oxidation products; if they can be oxidized, for instance, to dibasic acids (which contain two carboxyls),

then they must contain a primary alcohol group, $\cdot CH_2 \cdot OH$, since only such a group yields a new carboxyl on oxidation. Ethylene lactic acid is therefore a "primary" alcohol acid. Its isomer, ethylidene lactic acid, is similarly a "secondary" alcohol acid, while α-hydroxy isobutyric acid is a "tertiary" alcohol acid, *i.e.* acid and tertiary alcohol at the same time.

Behaviour.—1. The double chemical character of the hydroxy acids will be dealt with more in detail under Glycollic Acid. As acids they form salts, esters, and amides; as alcohols they yield ethers, amines, &c. Of these derivatives the alcoholic amines of the acids, the so-called amino acids, are of especial interest. (See Glycocoll, p. 211.)

2. The hydroxy acids form different kinds of anhydrides, viz.: (*a*) as alcohols (see Di-glycollic Acid); (*b*) one molecule as alcohol forms with a second molecule as acid an ester, with elimination of H_2O (see Glycollic Anhydride), (*c*) operation *b* is repeated, the first molecule acting as acid, and the second as alcohol (see Glycolide); (*d*) one molecule loses H_2O, with formation of an "intramolecular" anhydride, a so-called *lactone* (see p. 217).

3. For behaviour upon oxidation see p. 207, and also the individual compounds.

4. Just as the alcohols readily give up water, yielding olefines, so many of the hydroxy acids, especially the β-, can be transferred into unsaturated monobasic acids (See Hydracrylic Acid, p 216.)

5. When warmed with hydriodic acid, the hydroxy acids are reduced to the corresponding fatty acids, just as the alcohols are converted by this reagent into hydrocarbons.

6. When the α-hydroxy acids are warmed with dilute sulphuric acid, formic acid is produced together with the aldehyde or ketone which would give rise to the acid, according to method 3. The β-hydroxy acids, on the other hand, decompose into water and acids of the acrylic series. Thus:—

$$CH_3 \cdot CH\overset{O\,H}{\underset{CO_2H}{<}} = CH_3 \cdot CH{:}O + H \cdot CO_2H$$

$$OH \cdot CH_2 \cdot CH_2 \cdot CO_2H = CH_2{:}CH \cdot CO_2H + H_2O.$$

The α-, β-, γ-, &c, hydroxy acids also differ from each other in the facility with which they form anhydrides. (See Lactones, p. 217)

Glycollic Acid, *Hydroxy-acetic acid*, *Ethanolic acid*, $OH \cdot CH_2 \cdot CO_2H$ (*Strecker*, 1848), occurs in unripe grapes, in the leaves of the wild vine, &c.

Formation.—1. By the oxidation of glycol with dilute HNO_3 (*Wurtz*).

2. Together with glyoxal and glyoxylic acid, by the oxidation of alcohol with dilute HNO_3.

3. By the reduction of oxalic acid with $Zn + H_2SO_4$.

4. From formic aldehyde synthetically, according to method 3, p. 206.

5. It is usually prepared by boiling chloro-acetic acid with water in the presence of marble, the marble serving to neutralize the HCl formed in the reaction (A **200**, 76):

$$CH_2Cl \cdot CO_2H + H_2O \rightleftarrows OH \cdot CH_2 \cdot CO_2H + HCl$$

Properties.—It forms colourless needles or plates, is readily soluble in water, alcohol, and ether, and melts at 80°. Nitric acid oxidizes it to oxalic acid. The alkaline salts are hygroscopic, the calcium salt and the magnificent blue copper salt are sparingly soluble in water. K = 0·0152.

Derivatives.—(See table, p. 210.) As an acid, glycollic acid forms salts, esters—*e.g* **ethyl glycollate**—a chloride, **glycollyl chloride**, and **glycollamide**, all of which are readily hydrolysed, some of them even on warming with water. All these derivatives still retain their alcoholic character. If, on the other hand, glycollic acid forms derivatives as an alcohol, the properties of the alcoholic derivatives in question are combined with those of an acid, since the hydroxyl of the alcoholic group, $\cdot CH_2 \cdot OH$, enters into reaction, while the carboxyl group remains unchanged. These derivatives are either ethers, such as **ethyl-glycollic acid** (see table), or *e.g* amines, such as **glycocoll**, and, as alcoholic derivatives, they are not readily hydrolysed; or they are esters of glycollic acid, as alcohol, *e.g* **acetyl-glycollic acid**, $CH_3(O \cdot CO \cdot CH_3) \cdot CO_2H$, or **monochloracetic acid**, $CH_2Cl \cdot CO_2H$ (the hydrochloric ester of glycollic acid), and then they are of course saponifiable. These latter compounds still retain their acid character, and therefore form, on their part, esters, chlorides, and amides, which are also readily hydrolysed. The following table gives a summary of the more important derivatives of glycollic acid:—

Acid Derivatives	Alcoholic Derivatives.	Mixed Derivatives
$HO\cdot CH_2\cdot CO\cdot ONa$ Sodium glycollate.		$NaO\cdot CH_2\cdot CO\cdot ONa$ Di-sodium glycollate. Hygroscopic; decomp. by H_2O into Na salt and NaOH.
$HO\cdot CH_2\cdot CO\cdot OC_2H_5$ Ethyl glycollate Liquid, b.-pt. 160°.	$OC_2H_5\cdot CH_2\cdot CO\cdot OH$ Ethyl-glycollic acid Liquid, b -pt 206°.	$C_2H_5\cdot O\cdot CH_2\cdot CO\cdot OC_2H_5$ Ethylic ethyl-glycollate Liquid, b.-pt. 152°
$HO\cdot CH_2\cdot CO\cdot Cl$ Glycollyl chloride. Oil; decomposes on volatilizing	$CH_2Cl\cdot CO\cdot OH$ Monochloracetic acid.	$CH_2Cl\cdot COCl$ Monochloracetyl chloride Liquid, b -pt. 120°, of suffocating odour
$HO\cdot CH_2\cdot CO\cdot NH_2$ Glycollamide. Crys M -pt. 120°; does not form salts with bases.	$NH_2\cdot CH_2\cdot CO\cdot OH$ Glycocoll Crys M -pt 236°. Forms salts with acids and bases	$NH_2\cdot CH_2\cdot CO\cdot NH_2$ Glycocollamide Crys

It is easy to see that the corresponding derivatives of the first and second vertical rows are always isomeric

Anhydrides of Glycollic Acid.—1. Glycollic acid can yield different types of anhydrides (1) the elimination of one mol. of water from the alcoholic hydroxyls of two molecules of the acid produces **diglycollic acid**,

$$O\!<\!\begin{matrix}CH_2\cdot CO_2H\\ CH_2\cdot CO_2H,\end{matrix}$$

which is obtained by boiling monochloracetic acid with lime. It forms large rhombic prisms, is a dibasic acid, and, as an ether, is not saponified when boiled with alkalis, but is decomposed when heated with concentrated hydrochloric acid to 120°.

2 Diglycollic acid loses water when heated, yielding the **diglycollic anhydride**,

$$O\!<\!\begin{matrix}CH_2\cdot CO\\ CH_2\cdot CO\end{matrix}\!>\!O.$$

3. **Glycollic anhydride**, $OH\cdot CH_2\cdot CO\cdot O\cdot CH_2\cdot CO_2H$, is an ester, which is formed when glycollic acid is heated at 100°. It becomes hydrated again when boiled with water, and may be regarded as an ester derived from glycollic acid acting as an alcohol and as an acid.

4. **Glycolide**, $\begin{matrix}CH_2\cdot O\cdot CO\\ |\\ CO\cdot O\cdot CH_2\end{matrix}$, is also an ester anhydride, and is isomeric with 2 (and with fumaric acid) It is formed when sodium bromo-acetate is distilled in a vacuum Lustrous plates; m.-pt. 87°. It becomes hydrated again when boiled with water.

Glycocoll (*Amino-ethane acid*), *glycine*, *amino-acetic acid*, $NH_2\cdot CH_2\cdot CO_2H$ (*Braconnot*, 1820) This is the simplest representative of the important class of **amino acids**, so called because they are derived from the fatty acids by the exchange of a hydrogen atom of the hydrocarbon radical for an amino group, *e.g* $CH_3\cdot CO_2H$, acetic acid, $CH_2(NH_2)\cdot CO_2H$, amino-acetic acid.

Formation.—1. By the action of concentrated ammonia upon monochloracetic acid (*Heint.*, A. **122**, 261, *Kraut*, A **266**, 292):

$$CH_2Cl\cdot CO_2H + 2NH_3 = NH_2\cdot CH_2\cdot CO_2H + NH_4Cl$$

(cf. also B **23**, Ref 654) Di- and triglycollamic acids, $NH(CH_2\cdot CO_2H)_2$ and $N(CH_2\cdot CO_2H)_3$, are produced at the same time

α-Chloropropionic acid in like manner yields alanine with ammonia (see Lactic Acid). The method is a general one for the production of amino acids

2. By boiling glue with alkalis or acids

3. Together with benzoic acid, by decomposing hippuric acid, or benzoyl-glycocoll, with concentrated hydrochloric acid

$$\begin{matrix}C_6H_5\cdot CO\cdot NH\cdot CH_2\cdot CO_2H\\ +HO\ H\end{matrix} = NH_2\cdot CH_2\cdot CO_2H + C_6H_5\cdot CO_2H.$$

Properties.—Glycocoll forms large colourless rhombic prisms, readily soluble in water, but insoluble in absolute alcohol and ether. It has a sweet taste, hence the name "glue sugar" or glycocoll (γλυκύς, sweet, κόλλα, glue). It melts and decomposes at 236°. Glycocoll, like all the amino acids, possesses the properties of both an amine and an acid. It therefore forms salts with acids as well as with bases, *e.g.* **glycocoll hydrochloride**, $C_2H_5NO_2\cdot HCl$, which crystallizes in prisms, and the characteristic copper salt, **copper glycocoll**, $(C_2H_4NO_2)_2Cu + H_2O$, which crystallizes in blue needles, the latter being obtained by dissolving cupric oxide in a solution of glycocoll. Most of the other amino acids also form characteristic copper salts of this nature, which serve for their separation. Glycocoll

also yields compounds with salts, and, as an acid, forms an ethyl ester, an amide, &c. (see table, p. 210). When heated with BaO it is decomposed into methyl-amine and CO_2, while nitrous acid converts it into glycollic acid (the normal reaction of the primary amines). With ferric chloride it produces an intense red, and with copper salts a deep-blue coloration.

Ethyl amino-acetate (b.-pt. 43°/11 mm.) and nitrous acid yield the interesting **ethyl diazo-acetate**, $\begin{matrix}N\\ \|\\ N\end{matrix}\!\!>\!CH\cdot CO\cdot OC_2H_5$, from which hydrazine, $NH_2\cdot NH_2$, and its hydrate were first prepared; and from the latter the remarkable compound, hydrazoic acid, N_3H (*Curtius*, J. pr. Ch (2) **38**, 396, 172, **43**, 207, B. **24**, 3341; **29**, 759; **33**, 58). See also Di and Triazo Derivatives, Chap. LI.

Constitution (see B. **16**, 2650).—Free glycocoll may possibly be an intramolecular salt, corresponding with the formula $CH_2\!<\!\begin{matrix}NH_3\\ CO\cdot O\end{matrix}\!>$ (see Taurine, p. 197, and Betaine below).

Alkyl and Acyl Derivatives of Glycocoll:

Methyl-glycocoll or Sarcosine,	Trimethyl-glycocoll or Betaine,	Acetyl-glycocoll or Aceturic Acid,
$CH_2\cdot NHCH_3$	$CH_2\cdot N(CH_3)_3$	$CH_2\cdot NH\cdot CO\cdot CH_3$
$CO\cdot OH$	$CO\cdot O$	$CO\cdot OH$

Most of these alkyl derivatives are interesting, as they either occur as such in natural products, or may be obtained by the decomposition of certain natural compounds. Sarcosine is obtained by the decomposition of the complex natural substances creatine or caffeine. Betaine occurs in beet-root, and is present in large quantities in the molasses from beet-root sugar. It crystallizes with $1H_2O$, which it readily gives up on heating. This hydrate may possibly be $CO_2H\cdot CH_2\cdot NMe_3\cdot OH$. When heated at 293° betaine is transformed into the isomeric methyl ester of dimethylamino-acetic acid, $NMe_2\cdot CH_2\cdot CO\cdot OMe$; at higher temperatures it yields trimethylamine. It has been synthesised by the action of trimethylamine on monochloracetic acid (B. 1902, **35**, 603):

$$Cl\cdot CH_2\cdot COOH \longrightarrow (CH_3)_3N(Cl)\cdot CH_2\cdot CO\cdot OH \longrightarrow (CH_3)_3N\cdot CH_2\cdot CO.$$
$$\qquad\qquad\qquad

Lactic Acids (*Hydroxy-propionic acids*). (*Wislicenus*, A. **128**, 1; **166**, 3; **167**, 302, 346.)—As has been already mentioned, two isomeric lactic acids are theoretically possible, viz. α- and β-hydroxy-propionic acids, α- and β-lactic acids, or ethylidene- and ethylene-lactic acids, and both of these are known

The minute investigation of the different lactic acids has been of very great importance for the development of chemical theory; they were formerly held to be dibasic, and the recognition of their hydroxy-monobasic nature has materially contributed to the acceptation of the theory of the linking of atoms.

The molecule of α-hydroxy-propionic acid contains an asymmetric carbon atom,

$$CH_3 \cdot CH\!<\!\begin{matrix}OH\\CO_2H,\end{matrix}$$

and hence should exhibit exactly the same kind of isomerism as was met with in the case of active valeric acid.

In reality two optically active α-lactic acids are known, one of which is dextro (*d*), and the other lævo (*l*) rotatory. These two acids are identical in all their properties, with the exception of optical activity. A mixture (or compound) of the two in equal quantities is optically inactive, and is known as inactive (*dl*) or racemic (*r*) lactic acid.

The molecule of β-hydroxy-propionic acid does not contain an asymmetric carbon atom, and hence exists in only one modification, which is optically inactive.

Modes of Formation	Fermentation Lactic Acid	Ethylene-lactic Acid
1. By the regulated oxidation of	α-Propylene glycol, $CH_3 \cdot CH(OH) \cdot CH_2OH$.	β-Propylene glycol, $OH \cdot CH_2 \cdot CH_2 \cdot CH_2OH$
2. By the exchange of halogen for hydroxyl in	α-Chloro-propionic acid, $CH_3 \cdot CHCl \cdot CO \cdot OH$.	β-Iodo-propionic acid, $CH_2I \cdot CH_2 \cdot CO \cdot OH$.
3. By hydrolysis of	Aldehyde-cyanhydrin, $CH_3 \cdot CH(OH) \cdot CN$.	Ethylene-cyanhydrin, $OH \cdot CH_2 \cdot CH_2 \cdot CN$.
4. By action of nitrous acid upon	Alanine, $CH_3 \cdot CH(NH_2) \cdot CO \cdot OH$.	
5. By the reduction of	Pyro-racemic acid, $CH_3 \cdot CO \cdot CO \cdot OH$.	
6. By the lactic fermentation of sugar, etc.		

1. **dl-Ethylidene-lactic Acid** (*Propane-2-ol-1-acid*), *ordinary fermentation lactic acid*, $CH_3 \cdot CH \cdot (OH) \cdot CO_2H$. Discovered by *Scheele*, and recognized as hydroxy-propionic acid by *Kolbe*. Occurs in opium, sauerkraut, and in the gastric juice.

Preparation.—This depends upon the so-called **lactic fermentation** of sugars, *e g.* milk, cane- and grape-sugars, and of substances related to them, such as gum and starch; it is induced by certain species of bacteria commonly spoken of as the *lactic bacilli*. The fermentation proceeds best at a temperature of 34°–35° in a nearly neutral solution, this last condition being attained by the addition of chalk or zinc-white to the fermenting mixture. The free acid can then be liberated from the lactate of zinc by sulphuretted hydrogen. When a non-homogeneous ferment (*e.g.* decaying cheese) is used, the lactic acid at first produced is readily transformed by other organisms into butyric acid (p. 152).

Lactic acid is also produced in large quantity by heating grape- or cane-sugar with caustic-potash solution of a certain degree of concentration (B. **15**, 136). The relations of lactic acid to the sugar varieties appear, at a superficial glance, to be very simple; thus grape-sugar, $C_6H_{12}O_6$, and lactic acid, $C_3H_6O_3$, are polymers.

Lastly, the inactive acid is produced by mixing equal quantities of the two active modifications. In syntheses the latter are formed in equal amounts, and hence the inactive acid is obtained.

Properties.—When its solution is evaporated in a desiccator, a thick, non-crystallizing and hygroscopic syrup is obtained, which is miscible with water, alcohol, and ether, and which gradually loses water, yielding the solid lactic anhydride, $C_6H_{10}O_5$, before all the water of solution has been got rid of To obtain the pure acid it is necessary to distil under very low pressures, when a crystalline solid melting at 18° is obtained. K = 0 0138. When heated, it is partially converted into the anhydride, lactide, $C_6H_8O_4$, and partially into aldehyde, CO, and H_2O. Similarly it decomposes into aldehyde and formic acid when heated with dilute sulphuric acid to 130°, concentrated sulphuric giving rise to carbon monoxide instead of formic acid:

$$CH_3 \cdot CH(OH) \cdot CO_2H = CH_3 \cdot CHO + HCO_2H.$$

When oxidized, it yields acetic and carbonic acids; hydrobromic acid converts it into α-bromo-propionic acid, and boiling hydriodic acid into propionic acid itself.

The inactive acid is split up into the two active modifications by the crystallization of the strychnine salts (*Purdie* and *Walker*, J. C. S. 1892, 754), further, when green mould, *Penicillium glaucum*, is sown in a solution of the ammonium salt of the inactive acid, the lævo-acid is assimilated more rapidly than the dextro-, and the solution thus becomes optically active (*Linossier*, B. 1891, **24**, 660). A very simple resolution has been accomplished by *Purdie* (J. C. S. 1893, 1143) by crystallizing the zinc ammonium salt, $ZnC_6H_{10}O_6$, $NH_4C_3H_5O_3$, $2H_2O$. (Cf. Resolution of Racemic Acid.)

A number of well-defined salts are known, *e.g.* **Calcium lactate**, $(C_3H_5O_3)_2Ca + 5H_2O$; **zinc lactate**, $(C_3H_5O_3)_2Zn + 3H_2O$; **ferrous lactate**, $(C_3H_5O_3)_2Fe + 3H_2O$. When sodium lactate is heated with sodium, **di-sodium lactate**, $CH_3 \cdot CH(ONa) \cdot CO_2Na$, which is at the same time a salt and an alcoholate, is formed.

The *derivatives* of lactic acid are derivatives of it either as acid or as alcohol, and are perfectly analogous to those of glycollic acid (see table, p. 210). Thus **ethyl-lactic acid**, α-ethoxy-propionic acid, $CH_3 \cdot CH(OC_2H_5) \cdot CO_2H$, a thick acid liquid which boils almost without decomposition, corresponds with ethyl-glycollic acid, **ethyl lactate**, which can be distilled without decomposition, with ethyl glycollate, **lactamide**, $CH_3 \cdot CH(OH) \cdot CO \cdot NH_2$, with glycollamide; and **alanine**, $CH_3 \cdot CH(NH_2) \cdot CO \cdot OH$, with glycocoll.

By the action of PCl_5, **lactyl chloride**, $CH_3 \cdot CHCl \cdot CO \cdot Cl$ (p. 171), is formed; as the chloride of α-chloro-propionic acid it is decomposed by water, yielding the latter acid and HCl.

The following anhydrides of lactic acid are known:—

(1) **Lactylic acid** or **Lactic anhydride**, $C_6H_{10}O_5$, which is analogous to glycollic anhydride, and forms a yellow amorphous mass. (2) **Lactide**, $C_6H_8O_4$, analogous to glycolide (plates melting at 125°). (3) **Dilactic acid**, $C_6H_{10}O_5$, the alcoholic anhydride, analogous to diglycollic acid.

2. **d-Ethylidene-lactic acid**, *Sarco-lactic acid*, *para-lactic acid* (*Liebig*). This occurs in the juice of flesh, and is therefore to be found in Liebig's extract of meat. It results from certain fermentations. Its chemical properties are exactly similar to those of ordinary lactic acid; thus it readily yields lactide or aldehyde. Its salts differ to some extent, however, from those of the latter; thus, the **zinc salt**, $+ 2H_2O$, is much more easily soluble, and the **calcium salt** $+ 4H_2O$, much more sparingly soluble than the corresponding common lactates. Such differ-

ences are usually met with between *d*- and *l*-compounds on the one hand, and their *r*-isomeride on the other.

3. **l-Ethylidene-lactic acid** is obtained from the fermentation of cane-sugar by means of the *l-lactic bacillus*. Its salts correspond exactly with the salts of *d*-lactic acid. They have the same formulæ, same solubilities, &c.

4. **Ethylene-lactic acid** (*Propane-3-ol-1-acid*), *hydracrylic acid* (*Wislicenus*, A. **128**, 1), forms a syrupy mass It differs from lactic acid (*a*) by its behaviour upon oxidation, yielding carbonic and oxalic acids, and not acetic, (*b*) by not yielding an anhydride when heated, but by breaking up into water and acrylic acid, hence the name hydracrylic acid:

$$CH_2(OH)\cdot CH_2\cdot COOH = CH_2{:}CH\cdot COOH + H_2O;$$

(*c*) in solubility, and in the amount of water of crystallization of its salts (*e.g.* zinc salt, $+ 4H_2O$, very readily soluble in water; calcium salt, $+ 2H_2O$). It is not so strong an acid as α-lactic acid. K = 0·00311.

It may be synthesised from ethylene by means of the following series of reactions· (*a*) the addition of hypochlorous acid, (*b*) conversion of the chlorhydrin into the corresponding nitrile, and (*c*) hydrolysis, *e.g.*:

$$CH_2{:}CH_2 \longrightarrow OH\cdot CH_2\cdot CH_2Cl \longrightarrow OH\cdot CH_2\cdot CH_2\cdot CN \longrightarrow OH\cdot CH_2\cdot CH_2\cdot CO_2H.$$

Hydroxy-caproic Acids **Leucine** or **α-Amino-caproic acid**, $CH_3\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH(NH_2)\cdot CO_2H$, is a derivative of α-hydroxy-caproic. It forms glistening plates, and, like other amino acids, is closely related to albumen It is found in old cheese, also abundantly in the animal organism in the gastric gland, and in the shoots of the vetch and gourd, &c. It forms, along with tyrosine, a constant product of the digestion of albumen in the small intestine and of the decay of albuminous substances, and is formed when the latter are boiled with alkalis or acids. It has also been prepared synthetically. It closely resembles glycocoll, and forms a characteristic sparingly soluble blue copper salt. Leucine is dextro-rotatory. A lævo- and an inactive modification are also known (B **24**, 669).

Le Sueur (J. C. S. 1904, 827, 1905, 1888) has prepared several hydroxy derivatives of the higher fatty acids, *e.g.* α-hydroxy-margaric and α-hydroxy-stearic acids, and has found that a good yield (35–60 per cent) of an aldehyde can be obtained when the acid is heated to 240–250°. The molecule of the

aldehyde so obtained contains a carbon atom less than the molecule of the hydroxy acid, and water, formic acid, carbon monoxide, and a lactide are obtained as by-products.

LACTONES

All hydroxy acids tend to lose water under certain conditions, yielding anhydro-compounds.

The manner in which this water is eliminated is very different in the various types of hydroxy acids.

1. In the case of the α-hydroxy acids, 1 or 2 mols. of water are usually eliminated from 2 molecules of the acid, yielding compounds of the type of diglycollic acid, glycollic anhydride, &c.

2. In β hydroxy acids 1 molecule of water is usually eliminated from 1 molecule of the acid, and an α-β-unsaturated acid is formed, *e.g.*:

$CH_3 \cdot CH(OH) \cdot CH_2 \cdot CO_2H \longrightarrow CH_3 \cdot CH : CH \cdot CO_2H$ (crotonic acid).

3. In the case of γ-hydroxy acids, *e.g.* γ-hydroxy-butyric acid, $OH \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CO_2H$, 1 molecule of water is eliminated from 1 molecule of the acid, and an inner anhydride or **lactone** is formed,

$$\begin{matrix} CH_2 \cdot CH_2 \\ | \\ CH_2 \cdot CO \end{matrix} \!\!>\!\! O = \text{butyro-lactone or butanolid.}$$

The formation of such a lactone is characteristic of γ-hydroxy acids. Many of these acids are so unstable in the free state, that when mineral acid is added to their salts the lactones and not the free acids are obtained.

The "γ-lactones" are for the most part neutral liquids of faint aromatic odour, readily soluble in alcohol and ether, and distilling without decomposition. They dissolve in alkalis, yielding the salts of the corresponding hydroxy acids, and form brominated fatty acids with HBr, and amino acids or amides of γ-hydroxy acids with NH_3 (B. **23**, Ref. 234).

δ- and β-, but only a few α-lactones, from δ-, β-, and α-hydroxy acids, are also known. They show marked differences in the case with which they are formed and in their stability, the γ-lactones being the most stable. (For α-Lactones, see B. 1891, **24**, 4070; for β-, B. 1897, **30**, 1954.)

The formation of lactones by warming the isomeric unsaturated acids, $C_nH_{2n-2}O_2$ which contain the double bond in the

β-γ or γ-δ position, with HBr or with moderately concentrated H_2SO_4, is worthy of note, *e.g.*:

$$R{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CO_2H \longrightarrow R{\cdot}\underset{\diagdown\,O\,\diagup}{CH}{\cdot}CH_2{\cdot}CH_2{\cdot}CO.$$

(For details, see *Fittig* and his pupils, A. **208**, 37, 111; **216**, 26; **255**, 1, 275; **256**, 50; **268**, 110.)

The reaction is generally regarded as the addition of HBr or H_2O to the double bond, and then the elimination of the Br or OH in the γ-position with the H of the carboxyl group.

B. Polyhydric Monobasic Acids

Just as glycol on oxidation can yield the monohydroxy monobasic acid, glycollic acid, so the polyhydric alcohols on careful oxidation with nitric acid can yield polyhydroxy monobasic acids, *e.g.*:

$$OH{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2{\cdot}OH \longrightarrow OH{\cdot}CH_2{\cdot}CH(OH){\cdot}CO_2H.$$

They are usually designated according to the number of alcoholic hydroxyl groups present. This number can be determined by converting the acid, or better, its ester, into the acetyl derivative, and estimating the number of acetyl groups by analysis or by hydrolysis (p. 201).

In none of these acids do we find more than one OH group attached to the same carbon atom. All have the properties of monobasic acids and, in addition, the properties of polyhydric alcohols. Those which contain a hydroxyl group in the γ-position yield lactones.

Most of the compounds belonging to this class either crystallize badly or are gum-like. A number of these acids are formed by the cautious oxidation of the sugars or of the unsaturated acids, $C_nH_{2n-2}O_2$ (see p. 162).

I. DIHYDROXY MONOBASIC ACIDS

Glyceric acid (*Propane-2:3-diol-1-acid*), $OH{\cdot}CH_2{\cdot}CH(OH){\cdot}CO_2H$, is a syrupy liquid which is obtained by the cautious oxidation of glycerol. The molecule contains an asymmetric carbon atom, the artificial acid is optically inactive, but a *d*- and an *l*-modification are known (*Frankland*, J. C. S. 1891, 96).

Various compounds obtained from natural sources are closely related to the dihydroxy acids, viz. **serine**, α-amino-β-hydroxy-

propionic acid, obtained by boiling silk glue with dilute acids; **ornithine**, $\alpha\delta$-diamino-valeric acid; and **lysine**, $\alpha\epsilon$-diamino-caproic acid, obtained by the hydrolysis of casein.

II. TETRA- AND PENTAHYDROXY MONOBASIC ACIDS

The tetra- and pentahydroxy acids, *e g.* $OH \cdot CH_2 \cdot (CH \cdot OH)_3 \cdot CO_2H$ and $OH \cdot CH_2 \cdot (CH \cdot OH)_4 \cdot CO_2H$, are of particular importance, on account of their close connection with the simple sugars. They are obtained either by the cautious oxidation of the corresponding sugars, *e.g.* by means of bromine water: or by the reduction of the corresponding dibasic acids (saccharic acid, &c.); or, lastly, by the addition of hydrocyanic acid to the polyhydroxy aldehydes or ketones, just as lactic acid is formed from aldehyde. Conversely, the acids, in the form of their lactones, are on the one hand reconverted into the sugars by reduction with sodium amalgam; while, on the other hand, they are oxidized by nitric acid to the corresponding dibasic acids.

The acids are named according to the sugar to which they are related:

Arabinose → Arabonic Acid,
Glucose → Gluconic Acid.

(See Sugars, p. 300, &c.)

Some of the acids are known in the form of their lactones only. The phenyl-hydrazones are frequently made use of for their isolation.

A number of different acids, *e g.* mannonic, gluconic, gulonic, galactonic, and talonic acid, have been obtained by the oxidation of the hexoses (p 307) and by other methods. Investigation has shown that those acids all possess the same structural formula,

$$OH \cdot CH_2 \cdot CH(OH) \cdot CH(OH) \cdot CH(OH) \cdot CH(OH) \cdot CO_2H,$$

which is seen to contain 4 distinct asymmetric carbon atoms.

The acids are thus stereo-isomeric; their differences depend on the arrangement in space of the different radicals (cf. the Sugars).

The number of stereo-isomerides possible is the same as for the sugars (the corresponding aldo-hexoses), viz eight pairs of optically active isomerides and eight racemic compounds. Most, but not all, of these have been obtained.

Three extremely important methods have been employed (mainly by *E. Fischer*) for the preparation of these acids:—

1. Oxidation of the corresponding aldehyde (a sugar), *e.g.* ordinary glucose when carefully oxidized with chlorine- or bromine-water yields *d*-gluconic acid:

$$OH\cdot CH_2\cdot(CH\cdot OH)_4\cdot CH{:}O \longrightarrow OH\cdot CH_2\cdot(CH\cdot OH)_4\cdot CO\cdot OH.$$

2. From a stereo-isomeric acid by intramolecular transformation under the influence of high temperature, and generally in the presence of an organic base, *e.g.* *d*-gluconic heated with quinoline and water yields *d*-mannonic, galactonic → talonic.

The reaction is a reversible one, and hence the final product is a mixture of the two acids, which can be separated by the difference in solubility of certain of their salts.

3. The addition of hydrogen cyanide to a polyhydric aldehyde or ketone and subsequent hydrolysis, *e.g.*:

$$OH\cdot CH_2(CH\cdot OH)_3\cdot CHO \longrightarrow OH\cdot CH_2\cdot(CH\cdot OH)_3\cdot CH(OH)\cdot CN \longrightarrow OH\cdot CH_2\cdot(CH\cdot OH)_3\cdot CH(OH)\cdot CO_2H.$$

It is obvious that an additional asymmetric carbon atom is introduced by the addition of the HCN, and thus a mixture of two stereo-isomeric nitriles is formed, and on hydrolysis a mixture of two stereo-isomeric acids, *e.g.*:

d-Arabinose → *l*-Gluconic acid
d-Arabinose → *l*-Mannonic acid.

This reaction is somewhat similar to the addition of HCN to acetaldehyde, the main difference is that the original compound is optically active, and hence its molecule is asymmetric. By the addition of HCN two compounds are obtained, as a rule not in equal amounts, both of which are optically active, but do not stand in the relationship of object to mirror image.

This reaction has been extended, and hydroxy acids containing 7, 8, and 9 carbon atoms have thus been obtained.

C. Hydroxy Aldehydes

As examples, we have **glycollic aldehyde**, $OH\cdot CH_2\cdot CH{:}O$, **aldol**, $CH_3\cdot CH(OH)\cdot CH_2\cdot CH{:}O$ (see p. 131), and **glyceric aldehyde** $OH\cdot CH_2\cdot CH(OH)\cdot CH{:}O$. The last-named is contained in glycerose, a product obtained by oxidizing glycerol with bromine water. Alkalis convert it into a mixture of sugars, $C_6H_{12}O_6$ (see α-Acrose). (For further examples of hydroxy aldehydes and ketones, see Sugars, p. 300.)

D. Dialdehydes (cf. p. 97)

Glyoxal (*Ethane-dial*), $CHO \cdot CHO$ (*Debus*, 1856), is formed by the careful oxidation of alcohol, or better, of aldehyde; it possesses all the characteristic properties of aldehydes; one molecule of the aldehyde is capable of combining with two of hydrogen cyanide or of sodium hydrogen sulphite.

E. Diketones

1. **Diacetyl**, *Butane-dione*, *α-diketo-butane*, $CH_3 \cdot CO \cdot CO \cdot CH_3$, b.-pt. 87 –88°. This can be prepared by boiling iso-nitroso-methyl acetone, $CH_3 \cdot C(:N \cdot OH) \cdot CO \cdot CH_3$, a product obtained by the action of nitrous acid on methyl ethyl ketone, with dilute H_2SO_4, when the oximino group is replaced by oxygen. It is a yellow-green liquid, its vapour having the colour of chlorine, and an odour similar to that of quinone (*v. Pechmann*, B. **20**, 3162, **24**, 3594; *Fittig* and his pupils, A **249**, 182). Reduction converts it into dimethyl-ketol. Homologues are known (cf. B. **22**, 2115).

2 **Acetyl-acetone**, $CH_3 \cdot CO \cdot CH_2 \cdot CO \cdot CH_3$, is formed by the action of aluminic chloride upon acetyl chloride and subsequent decomposition of the aluminium compound, or better (B **22**, 1009), by the action of sodium upon a mixture of ethyl acetate and acetone (see Aceto-acetic ester synthesis, p. 224).

$$CH_3 \cdot CO \cdot OC_2H_5 + CH_3 \cdot CO \cdot CH_3 = CH_3 \cdot CO \cdot CH_2 \cdot CO \cdot CH_3 + C_2H_5OH.$$

It is a liquid which boils at 137°.

3. **Acetonyl-acetone**, *γ-diketo-hexane*, $CH_3 \cdot CO \cdot CH_2 \cdot CH_2 \cdot CO \cdot CH_3$, may be prepared from monochlor-acetone and ethyl aceto-acetate (B. **17**, 2756), also from diaceto-succinic ester (B. **22**, 168, 2100). It is a liquid of pleasant odour, and boils at 188°.

These three compounds are the simplest representatives of the *α*-, *β*-, and *γ*-diketones, or of the 1:2-, 1:3-, and 1:4-diketones, *i.e.* of those diketones whose carbonyl groups are either next to one another (*α*-position), or separated by one carbon atom (*β*-position), or separated by two (*γ*-position).

As diketones they yield mono- and dioximes, and also mono- and dihydrazones. Such dihydrazones, and also those

from the dialdehydes, are termed **osazones**, *e.g.* **diacetyl osazone.**

$$C_6H_5\cdot NH\cdot N{:}CMe\cdot CMe{:}N\cdot NH\cdot C_6H_5.$$

Osazones are also formed by the action of phenylhydrazine on polyhydroxy aldehydes or ketones, *e.g.* glucose and fructose, an atom of oxygen being at the same time taken up; they are mostly yellow in colour (cf. the phenyl-hydrazine compounds of the carbohydrates).

The diketones show the most varied behaviour on condensation. By the action of alkali on the α-diketones, they yield benzene derivatives (see Quinone); the β-diketones readily pass into pyrazole and isoxy-azole derivatives, and serve for the synthesis of derivatives of quinoline; while the γ-diketones are easily converted into derivatives of pyrrole, furane, and thiophene, and the δ-diketones into derivatives of pyridine and tetrahydrobenzene.

The constitution of the above compounds is usually deduced directly from their mode of formation, but as certain of them react as tautomeric substances (cf. Ethyl Aceto-acetate) special physical methods have also been used (cf. *W. H. Perkin*, J. C. S. 1892, 800).

F. Aldehydic Monobasic Acids

Glyoxalic acid (*Ethanal acid*), *glyoxylic acid*, $CHO\cdot CO_2H$, occurs in unripe fruits such as grapes, gooseberries, &c., and may be prepared by superheating dichloracetic acid, $CHCl_2\cdot CO_2H$, with water, 2Cl being here exchanged for 2(OH), and water being eliminated. It crystallizes in rhombic prisms, dissolves readily in water, and is volatile with steam. The acid and most of its salts contain one molecule of water of crystallization, which points to the formula $CH(OH)_2\cdot CO_2H$, analogous to that of chloral hydrate.

Glycuronic acid, $CHO\cdot[CH(OH)]_4\cdot CO_2H$. The lactone of this acid forms colourless crystals, which melt at about 175°. The acid itself is obtained from saccharic acid by reduction with sodium amalgam. It is found as a camphor compound in the urine of dogs after camphor is administered to them.

G. Monobasic Ketonic Acids

Ketonic acids are compounds which contain both a carbonyl and a carboxylic group; they react as acids, and also as ketones;

thus, besides being capable of forming salts, esters, &c., they also combine with sodium bisulphite, yield oximes with hydroxylamine hydrochloride (see p. 135), are reduced by nascent hydrogen to hydroxy acids, and so on. The most important members of this class are **pyroracemic acid**, $CH_3 \cdot CO \cdot CO_2H$, **aceto-acetic acid**, $CH_3 \cdot CO \cdot CH_2 \cdot CO_2H$, and **lævulic acid**, $CH_3 \cdot CO \cdot CH_2 \cdot CH_2 \cdot CO_2H$.

Constitution and Nomenclature.—The ketonic acids are characterized theoretically by the presence of carboxyl and of carbonyl, the latter being linked to carbon on both sides. They may be regarded either as fatty acids, in which a hydrogen atom of the alkyl group has been replaced by acyl, R·CO·, as indicated in the name aceto-acetic acid; lævulic acid is then β-aceto-propionic acid, and pyroracemic acid is aceto-formic acid; or they may be regarded as derived from the fatty acids by the replacement of the two hydrogen atoms of a CH_2· group by an atom of oxygen

In the latter case aceto-acetic acid is to be designated *β-ketobutyric acid*, or *butane-3-one-1-acid*. This last is the systematic name (Geneva Congress), the expression *one* indicates the presence of a ketonic group, and the number indicates the relative positions of the ketonic and carboxylic groups.

The *constitution* of a ketonic acid is, as a rule, easy to determine, either from its synthesis or from its transformation into the corresponding hydroxy acids of known constitution by means of nascent hydrogen

The ketonic acids are usually divided into α, β, and γ, or 1, 2, and 3 ketonic acids, according to the relative positions of the carbonyl and carboxylic groups. $CH_3 \cdot CO \cdot CO_2H$, pyroracemic or pyruvic acid, is a type of an α-acid; $CH_3 \cdot CO \cdot CH_2 \cdot CO_2H$, aceto-acetic acid, is a type of a β-acid, and $CH_3 \cdot CO \cdot CH_2 \cdot CH_2 \cdot CO_2H$, lævulic acid, is a type of a γ-acid. The α- and γ-acids are relatively stable, many can be distilled without undergoing decomposition; but the β-acids are remarkably unstable, and readily lose carbon dioxide, yielding ketones. All the ketonic acids on careful reduction yield hydroxy acids.

Modes of Formation.—1. α-Ketonic acids are formed when the acyl cyanides are hydrolysed (*Claisen* and *Shadwell*) (cf p. 179 and B. 1898, **31**, 1023):

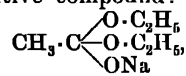
$$\underset{\text{Acetyl cyanide}}{CH_3 \cdot CO \cdot CN} + 2H_2O = \underset{\text{Pyroracemic acid.}}{CH_3 \cdot CO \cdot CO_2H} + NH_3$$

The constitution follows from this method of formation.

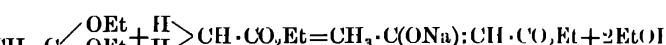
2. Aceto-acetic and other β-ketonic acids are obtained as esters by the action of sodium or sodium ethoxide on ethyl acetate and its homologues:

$$2(CH_3\cdot CO\cdot OC_2H_5) = CH_3\cdot CO\cdot CH_2\cdot CO\cdot OC_2H_5 + C_2H_5OH.$$

According to *Claisen* and *Lowman* (B. **20**, 651; **26**, 2130; **38**, 713), the ethyl acetate is first converted by the sodium ethoxide into an additive compound:



a derivative of ortho-acetic acid (p. 142), which then reacts with another molecule of ethyl acetate, thus.—



$$CH_3\cdot C(OEt):CH\cdot CO_2Et \longrightarrow CH_3\cdot CO\cdot CH_2\cdot CO_2Et.$$

From the sodium salt thus obtained, the aceto-acetic ester can be liberated by acetic acid, probably first as the enolic compound, which is immediately transformed into the ketonic.

As shown in the above formation of aceto-acetic ester, one molecule of ethyl acetate reacts with a second molecule. Many reactions of an analogous nature, in which the two reacting molecules are different, may be brought about in the same way by the aid of sodium ethoxide (*W. Wislicenus*, A. **246**, 306). Thus ethyl oxalate and ethyl acetate react in the presence of sodium ethoxide, yielding the sodio derivative of **ethyl oxal-acetate**:

$$CO_2Et\cdot CO\,OEt + H\,CH_2\cdot CO_2Et = CO_2Et\cdot CO\cdot CH_2\cdot CO_2Et + EtOH.$$

Esters also readily react with ketones, with the formation of **diketones** (*L. Claisen*):

$$\underset{\text{Ethyl acetate}}{CH_3\cdot CO\cdot OEt} + \underset{\text{Acetone}}{CH_3\cdot CO\cdot CH_3} = \underset{\text{Acetyl-acetone}}{CH_3\cdot CO\cdot CH_2\cdot CO\cdot CH_3} + EtOH$$

When ethyl formate is employed, ketonic aldehydes are not obtained, but their structural isomers, hydroxy-methylene compounds, with acetone, for example, hydroxy-methylene-acetone, thus:—

$$\underset{\text{Ethyl formate}}{H\cdot CO\cdot OC_2H_5} + \underset{\text{Acetone}}{CH_3\cdot CO\cdot CH_3} = \underset{\text{Hydroxy-methylene-acetone}}{CH(OH):CH\cdot CO\cdot CH_3} + C_2H_5\cdot OH$$

This condensation between esters, or between esters and ketones, in the presence of sodic ethoxide is usually known as *Claisen's* reaction, and is of extreme importance as a synthetical process. (For summary see B. 1905, **38**, 709.)

In all cases, according to *Claisen*, the condensation is preceded by the formation of an additive compound between the sodium ethoxide and the ester As a rule, metallic sodium and not sodium ethoxide is added to the ester (*e.g.* to ethyl acetate in the preparation of ethyl aceto-acetate), but the reaction only proceeds when the ester contains free alcohol, and can thus give rise to sodic ethoxide. Quite recently (Ber. 1905, **38**, 693) the same chemist has shown that sodamide, $Na \cdot NH_2$, may be used in place of sodic ethoxide

Michael (B. 1900, **33**, 3731, and 1905, **38**, 1922) considers that the *Claisen* condensation proceeds in a different manner, and that it may be compared with the aldol condensation. Compare also *Stoermer* and *Kippe* (B. 1905, **38**, 1953).

3. Higher homologues of aceto-acetic ester (β-ketonic acids) are easily obtained from it by the action of sodium ethoxide and alkyl halides (p. 228).

4. Ketonic acids are produced by the cautious oxidation of hydroxy acids containing the secondary alcoholic group

$$\underset{\text{Lactic acid}}{CH_3 \cdot CH(OH) \cdot CO \cdot OH} + O = \underset{\text{Pyroracemic acid}}{CH_3 \cdot CO \cdot CO \cdot OH} + H_2O$$

α-Ketonic Acids. Pyruvic or **pyroracemic acid**, $CH_3 \cdot CO \cdot CO_2H$, is a liquid which is readily soluble in water, alcohol, and ether, boils with slight decomposition at 165°–170°, and smells of acetic acid and extract of beef. It is formed by the dry distillation either of tartaric or of racemic acid, hence its name

In this decomposition carbon dioxide is probably first evolved and glyceric acid formed:

$$CO_2 H \cdot CH(OH) \cdot CH(OH) \cdot CO_2H \longrightarrow CH_2(OH) \cdot CH(OH) \cdot CO_2H.$$

This then loses water, yielding pyruvic acid.

It may also be obtained by methods 1 and 4.

Pyroracemic acid has a tendency to polymerize. Nascent hydrogen reduces it to ethylidene-lactic acid:

$$CH_3 \cdot CO \cdot CO_2H + 2H = CH_3 \cdot CH(OH) \cdot CO_2H.$$

It is a relatively strong acid owing to the negative nature

of the CO group, K = 0·56. It reacts as a ketone with phenyl-hydrazine, hydroxylamine, and hydrogen cyanide.

The **phenyl-hydrazone** crystallizes readily, melts at 192° when quickly heated, and is largely made use of in detecting the acid. The acid also resembles the ketones in the readiness with which it forms condensation products, yielding either benzene derivatives (B. **5**, 956), or—in presence of ammonia—those of pyridine.

The electrolysis of a concentrated solution of the potassium salt proceeds in the normal manner, the $CH_3 \cdot CO \cdot COO$- groups formed at the anode yield diacetyl and carbon dioxide (cf. Electrolysis of potassium-acetate solution), but secondary reactions also occur, and acetic acid is formed to a certain extent.

β-Ketonic Acids.— **Aceto-acetic acid**, $CH_3 \cdot CO \cdot CH_2 \cdot CO_2H$, is a strongly acid liquid, miscible with water, and breaking up into acetone and carbonic acid when warmed. It is prepared by the cautious hydrolysis of its ethyl ester (B. **15**, 1376, 1871) Its aqueous solution is coloured violet-red by ferric chloride. The Na- or Ca-salt is sometimes contained in urine (B. **16**, 2314). Its constitution as acetone-carboxylic acid follows from the products of decomposition.

The ethyl ester, ethyl aceto-acetate, or commonly called aceto-acetic ether, is prepared by the *Claisen* condensation method (general method 2). It is liberated from the sodium derivative by the addition of acetic acid, and purified by distillation under reduced pressure. It boils at 181°, or at 71° under 12·5 mm. pressure, is only slightly soluble in water, but readily in alcohol and ether, and has a pleasant fruity odour. Ferric chloride colours its aqueous solution violet-red. Extremely characteristic are the products to which it can give rise on hydrolysis.

1. *Normal Hydrolysis.*—As an ester, it can be hydrolysed to the corresponding acid and alcohol, viz. aceto-acetic acid and ethyl alcohol. This reaction occurs only when the ester is extremely carefully hydrolysed in the cold with dilute alkali.

2. *Ketonic Hydrolysis.*—This hydrolysis is best accomplished by the aid of dilute sulphuric acid or baryta water,

$$CH_3 \cdot CO \cdot \underset{H}{CH_2} \cdot COO \underset{OH,}{C_2H_5}$$

the products being acetone, carbon dioxide, and ethyl alcohol.

3. *Acid Hydrolysis.*—This takes place most readily when the ester is heated with concentrated alcoholic potash or soda,

$$\begin{matrix} CH_3\cdot CO\cdot CH_2\cdot COO\,C_2H_5 \\ HO.H \qquad\quad H.OH, \end{matrix}$$

the products being acetic acid and ethyl alcohol.

Ethyl aceto-acetate has been represented by the formula $CH_3\cdot CO\cdot CH_2\cdot CO_2Et$, and undoubtedly numerous arguments can be brought forward in favour of this constitution; *e.g.* it reacts with sodic-hydric sulphite, with hydrogen cyanide, and with hydroxylamine as a ketone, and hence should contain the C·CO·C group; a further argument for the ketonic constitution is to be found in the decomposition of the acid into acetone and carbon dioxide; on the other hand, with ammonia or amines it gives β-amino, or substituted β-amino crotonic acids, *e.g.* $CH_3\cdot CH(NH_2):CH\cdot CO_2H$, and with phosphorus pentachloride it yields β-chloro-crotonic acid, $CH_3\cdot CCl:CH\cdot CO_2H$. These latter reactions could be most readily explained by assuming the constitution $CH_3\cdot C(OH):CH\cdot CO_2Et$, *i.e.* ethyl β-hydroxy-crotonate for ethyl aceto-acetate. The ester is thus a typical tautomeric substance, reacting as though it possessed two distinct constitutions, and a study of the chemical properties alone will not, as a rule, permit us to settle with certainty which of the two is the more probably correct.

The following suggestions have been made to account for the tautomerism:—

(*a*) The ester is really a mixture of the two distinct compounds.

(*b*) The pure ester is unstable, and although it may have the one constitution, *e.g.* ethyl aceto-acetate or *ketonic* constitution, in the presence of various reagents it is readily transformed into the isomeric compound with the *enolic* constitution, *i.e.* ethyl β-hydroxy crotonate. This type of tautomerism is thus often spoken of as **keto-enolic tautomerism**, and is frequently met with (see Phloroglucinol, &c.). According to this view, it consists in the wandering of a hydrogen atom and a change in position of a double bond (**desmotropism**).

$$\rangle C\cdot C\cdot CH\langle \;\rightarrow\; \rangle C\cdot C(OH):C\langle$$
$$\qquad\quad \ddot{O}$$

(*c*) According to *Van Laar*, the tautomerism is due to an oscillatory hydrogen atom, which cannot be regarded as per-

manently attached to C or to O, but as continually oscillating between the two.

Physical methods have been used for elucidating the constitution of such compounds. The most important of these are the molecular refraction (*Gladstone, Bruhl*), the molecular magnetic rotation (*W. H. Perkin, Sen.*, J. C. S. 1892, 800), and the absorption of electric waves (*Drude*, B. 1897, **30**, 940). [Compare chapter on Relationship between Physical Properties and Chemical Constitution.] The conclusions arrived at from such a study are (*a*) that ethyl aceto-acetate is a mixture in chemical equilibrium of the ketonic and enolic forms, but consists mainly of the ketonic compound, and (*b*) that a rise of temperature favours the ketonic form. (See also *Baly* and *Desch*, J. C. S. 1904, 1029; 1905, 766.)

The metallic derivatives are enolic compounds.

1. **Ethyl Aceto-acetate as a Synthetical Reagent.**—One atom of hydrogen in the aceto-acetic ester molecule is readily replaceable by metals (*Geuther*; *Conrad*, A. **188**, 269) The **sodio derivative** is formed together with hydrogen on the addition of sodium, and also when an alcoholic solution of the ester is mixed with the calculated amount of sodium ethoxide in absolute alcohol:

$$CH_3\cdot CO\cdot CHNa\cdot CO_2Et \quad \text{or} \quad CH_3\cdot C(ONa):CH\cdot CO_2Et$$

This sodio derivative forms long needles or a faintly lustrous loose white mass. The **copper salt** crystallizes in bright-green needles.

The sodium is readily replaced by alkyl radicals when the sodio derivative is heated with an alkyl bromide or iodide; sodium bromide or iodide is thus formed together with alkylated aceto-acetic esters, which are of great interest in various syntheses, *e.g.*: **ethyl methylacetoacetate**, $CH_3\cdot CO\cdot CH(CH_3)\cdot CO_2C_2H_5$, and the corresponding **ethyl-** and **propyl-acetoacetic esters**, &c. In these compounds the hydrogen atom of the CH group may be again replaced by Na, and this again substituted by alkyl, with the production of dialkylated aceto-acetic esters, *e.g.*: **dimethylacetoacetic ester** or **ethyl dimethylacetoacetate**, $CH_3\cdot CO\cdot C(CH_3)_2\cdot CO_2C_2H_5$; **methylethylacetoacetic ester**, $CH_3\cdot CO\cdot C(CH_3)(C_2H_5)\cdot CO_2C_2H_5$, and so on.

These alkylated aceto-acetic esters exactly resemble the mother substance, especially in the manner in which they can be decomposed by either the "ketonic hydrolysis" or the "acid hydrolysis" (cf. p. 226). The formation of ketone

largely predominates when dilute acid is employed, and of fatty acids when concentrated alkali is used.

In the ketonic hydrolysis the alkyl groups introduced are left attached to a carbon atom of the acetone molecule, *e.g.*:

$$\begin{matrix} CH_3\cdot CO\cdot CMeEt\cdot CO_2\,Et \\ \qquad\qquad + H \qquad\quad OH \end{matrix} = EtOH + CO_2 + CH_3\cdot CO\cdot CHMeEt.$$

This affords a very general method for the synthesis of some of the higher ketones.

In the acid hydrolysis the alkyl groups remain attached to a carbon atom, which is united to a carboxylic group, *e.g.*:

$$\begin{matrix} CH_3\cdot CO\cdot CMe_2\cdot CO_2\,Et \\ + HO\;H \qquad + H\;OH \end{matrix} = CH_3\cdot CO_2H + CHMe_2\cdot CO_2H + EtOH.$$

This affords a simple method for synthesising any mono- or dialkylated acetic acid, *e.g.*: $CH_3\cdot CH_2\cdot CO_2H$, $C_2H_5\cdot CH_2\cdot CO_2H$, $(CH_3)(C_2H_5)CH\cdot CO_2H$; $(CH_3)(C_3H_7)CH\cdot CO_2H$. (Cf. Ethyl malonate synthesis, p. 237, also *Wislicenus* and his pupils, A. **186**, 161.)

2. Acyl groups may be introduced in place of alkyl radicals into aceto-acetic ester by similar methods, *e.g.* from acetyl chloride, **diaceto-acetic ester**, $(CH_3\cdot CO)_2CH\cdot CO_2C_2H_5$. The product obtained varies with the conditions. When an acyl chloride reacts with the sodio-derivative of ethyl acetoacetate the chief product is the C-acyl derivative, viz. $(CH_3\cdot CO)(R\cdot CO)CH\cdot CO_2Et$, but when the free ester is treated with an acyl chloride in the presence of pyridine the isomeric O-acyl derivative is obtained, *e.g.* $R\cdot CO\cdot O\cdot C\cdot CMe{:}CH\cdot CO_2Et$ The O derivatives, when heated or when warmed with potassium carbonate, are transformed into the isomeric C-compounds.

Ethyl chlorocarbonate and the sodio-derivative yield the O-derivative $CH_3\cdot C(O\cdot CO_2Et){:}CH\cdot CO_2Et$ together with a small amount of the C-derivative, **aceto-malonic ester**, $(CH_3\cdot CO)\cdot CH(CO_2C_2H_5)_2$; from monochloracetic ester, $CH_2Cl\cdot CO_2C_2H_5$, **aceto-succinic ester**, $CH_3\cdot CO\cdot CH(CH_2\cdot CO_2C_2H_5)(CO_2C_2H_5)$ may be similarly obtained (see Malonic and Succinic acids, and also the Synthesis of dibasic acids), &c.

3. Iodine acts upon sodio-aceto-acetic ester, yielding **diaceto-succinic ester**:

$$\begin{matrix} CH_3\cdot CO\cdot CHNa\cdot CO_2C_2H_5 \\ CH_3\cdot CO\cdot CHNa\cdot CO_2C_2H_5 \end{matrix} + I_2 = \begin{matrix} CH_3\cdot CO\cdot CH\cdot CO_2C_2H_5 \\ | \\ CH_3\cdot CO\cdot CH\cdot CO_2C_2H_5 \end{matrix} + 2NaI.$$

4. In addition to the above-mentioned simple syntheses, a number of more complex syntheses may be effected by means of ethyl acetoacetate. Many of these lead to the formation of closed-chain compounds, and will be described in connection with the various groups of ring compounds. The following may be mentioned as the more important:—

(*a*) *Hantzsch's* synthesis of pyridine derivatives, *e.g.* **ethyl dihydrocollidine dicarboxylate,**

$$NH\langle\begin{matrix}CMe{:}C(CO_2Et)\\CMe{:}C(CO_2Et)\end{matrix}\rangle CHMe,$$

by heating ethyl acetoacetate with aldehyde ammonia.

(*b*) The formation of **oxyuvitic acid** (a benzene derivative), $C_6H_2(CH_3)(OH)(CO_2H)_2$, by the action of chloroform on the sodio-derivative.

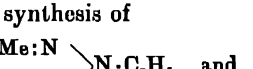
(*c*) The formation of **methyluracyl** by the condensation of ethyl acetoacetate with urea,

$$CO\langle\begin{matrix}NH_2\\NH_2\end{matrix} + \begin{matrix}EtO\cdot OC\\CH_3\cdot CO\end{matrix}\rangle CH_2 \rightarrow CO\langle\begin{matrix}NH\cdot CO\\NH\cdot C(CH_3)\end{matrix}\rangle CH$$

(See p. 287 and Synthesis of Uric Acid, p. 291.)

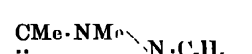
(*d*) The production of **furane** and **pyrrole derivatives** by heating ethyl diacetosuccinate (see Synthesis 3) with acids or with ammonia and amines.

(*e*) The synthesis of



Phenylmethylpyrazolone

and



Phenyldimethylpyrazolone

by the condensation of ethyl acetoacetate with phenylhydrazine and methylphenylhydrazine respectively.

Chlor- and **dichlor-aceto-acetic esters,** which are very active chemically, are produced by the replacement of the H of the methylene group by Cl. The two methylene hydrogen atoms are also replaceable by the isonitroso group, :N·OH (by the action of N_2O_3), and by the imido group, :NH (cf. A. **226**, 294; B. **28**, 2683).

Lævulic acid, $CH_3\cdot CO\cdot CH_2\cdot CH_2\cdot CO_2H$, forms crystalline plates, melts at 33°, and boils at 239°. It is formed by the action of acids upon cane-sugar, lævulose, cellulose, gum, starch, and other carbohydrates (A. **175**, 181; **206**, 207), and has also been prepared synthetically. (For its constitution, cf. A. **256**, 314.) It is employed in cotton printing and for the preparation of anti-thermine, &c.

X. DIBASIC ACIDS

Dibasic acids are those which are capable of forming two series of salts, viz. acid and normal, and likewise two series of esters, chlorides, amides, &c. They are characterized by the presence of two carboxyl groups in the molecule.

A. Saturated Dibasic Acids, $C_nH_{2n-2}O_4$, or Acids of the Oxalic Series

Name	Formula.	Melting-pt	K
Oxalic	$CO_2H \cdot CO_2H$	Sublimes 150°-160	10 0
Malonic	$CO_2H \cdot CH_2 \cdot CO_2H$	132°	0 016
Succinic	$CO_2H \cdot [CH_2]_2 \cdot CO_2H$	185	0 0065
Glutaric	$CO_2H \cdot [CH_2]_3 \cdot CO_2H$	97·5°	0 0047
Adipic	$CO_2H \cdot [CH_2]_4 \cdot CO_2H$	149	0 00371
Pimelic	$CO_2H \cdot [CH_2]_5 \cdot CO_2H$	105°	0 00323
Suberic.....	$CO_2H \cdot [CH_2]_6 \cdot CO_2H$	140°	0 00258

The above are solid crystalline compounds of strongly acid character, and most of them are readily soluble in water. When heated, they either yield an anhydride, or carbon dioxide is eliminated and a monobasic acid formed; but most of them can be volatilized *in vacuo*.

Formation.—1. By the oxidation of the di-primary glycols. (See table, p. 204)

1*a*. By the oxidation of hydroxy-acids and, generally, of many complex compounds, such as fats, fatty acids, and carbohydrates.

2. By the hydrolysis of the corresponding nitriles; thus, oxalic acid is formed from cyanogen, and succinic acid from ethylene cyanide:

$$(CN)_2 + 4H_2O = (CO_2H)_2 + 2NH_3.$$
$$CN \cdot (CH_2)_2 \cdot CN + 4H_2O = CO_2H \cdot (CH_2)_2 \cdot CO_2H + 2NH_3.$$

Since ethylene cyanide is a glycol derivative, its conversion into succinic acid represents the synthesis from a glycol of an acid containing two atoms of carbon more than itself, *i. e.* the exchange of $2(OH)$ for $2(CO_2H)$, or the indirect combination of ethylene with $2(CO_2H)$.

3. By the hydrolysis of the cyano-fatty acids (p. 170), and consequently from the halogen fatty acids also. Thus chloro- or cyano-acetic yields malonic acid, β-iodo- (or cyano-) propionic acid, common succinic acid, and α-iodo- (or cyano-) propionic acid, methyl malonic acid.

A dibasic acid can therefore be formed from each hydroxy-acid by the exchange of OH for CO_2H, or indirectly from a fatty acid by the replacement of H by CO_2H. Thus:—

$$\begin{matrix} CH_2(OH)\cdot CO_2H \\ CH_3\cdot CO_2H \end{matrix} \rightarrow CH_2Cl\cdot CO_2H \rightarrow CH_2(CN)\cdot CO_2H \rightarrow CH_2(CO_2H)_2$$

4. The homologues of malonic acid can be prepared from malonic acid itself by a reaction exactly analogous to the aceto-acetic ester synthesis (the "Malonic ester synthesis", p. 238)

The dibasic acids are also obtained by means of the aceto-acetic ester synthesis. Aceto-malonic and aceto-succinic acids, which have already been mentioned at p. 229, yield respectively malonic and succinic acids by the elimination of acetyl ("acid decomposition").

5. Higher homologues are obtainable by the electrolysis of the ethyl potassium salts (p. 234) of the simpler dibasic acids, *e.g.* adipic acid from potassium ethyl succinate.

The reaction is exactly analogous to the formation of ethane by the electrolysis of potassium acetate. For example, with potassium ethyl succinate the anions $CO_2Et\cdot\overline{C}H_2\cdot CH_2\cdot CO_2\cdot$ and kations $\overset{+}{K}$ are present When these become discharged at the electrodes during electrolysis, each $CO_2Et\cdot CH_2\cdot CH_2\cdot CO_2$ group splits up into carbon dioxide and the monovalent radical $CO_2Et\cdot CH_2\cdot CH_2\cdot$. Two such radicals then combine, yielding ethyl adipate, $CO_2Et\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CO_2Et$ The potassium formed at the cathode reacts with the water, yielding hydrogen and potassium hydroxide.

The *constitution* of the acids $C_nH_{2n-2}O_4$ is, as a rule, very easy to determine from the above-mentioned modes of formation, especially 2, 3, and 4. According to these, one has to decide between the malonic acids proper, *i.e.* malonic acid and its alkyl derivatives (p. 238), whose two carboxyl groups are both linked to one carbon atom:

$$CH_2(CO_2H)_2, \qquad R\cdot CH(CO_2H)_2, \qquad RR'C(CO_2H)_2,$$

and ordinary succinic acid and its homologues, which contain the carboxyls bound to two different carbon atoms.

The bivalent acid residues, C_2O_2 = **oxalyl**, $C_3H_2O_2$ = **malonyl**, and $C_4H_4O_2$ = **succinyl**, which are combined with the two hydroxyls, are termed the **radicals of the dibasic acids**, and are examples of bivalent acyl radicals.

Isomers.—Isomers of oxalic and malonic acids are neither theoretically possible nor actually known. We know, however, two succinic acids, viz.:

$$CO_2H\cdot CH_2\cdot CH_2\cdot CO_2H \quad \text{and} \quad CH_3\cdot CH(CO_2H)_2.$$

The former corresponds with ethylene chloride and the latter with ethylidene chloride, from which they are respectively derived by the exchange of two chlorine atoms for two carboxyls. Hence the names ethylene- and ethylidene-succinic acids, or more commonly succinic acid and methylmalonic acid.

Since ethylene cyanide can be prepared from the chloride, the above derivation of ethylene-succinic acid is also an experimental one. This is not the case, however, with the isomeric acid, since, as a rule, when several chlorine atoms are bound to the same carbon atom, as in ethylidene chloride, they cannot be exchanged for cyanogen.

Behaviour. Many of the dibasic acids, in the molecules of which the carboxyls are attached to different carbon atoms, yield intramolecular anhydrides by the elimination of a molecule of water from one of the acid. These anhydrides may be obtained either (1) by heating the acids alone, or (2) more generally by the action of phosphorus pentachloride, acetyl chloride, or carbonyl chloride upon the acids (B. **10**, 1881; **17**, 1285). They recombine slowly with water to form the free acids. This formation of anhydride is favoured by the presence of substituents in the molecule (B. **23**, 101, 620; **26**, 1925).

The elimination of water occurs most readily with succinic and glutaric acids and their substituted derivatives, in fact, with the acids containing a chain of 4 or 5 carbon atoms:

$$CO_2H\cdot\overset{|}{\underset{|}{C}}\cdot\overset{|}{\underset{|}{C}}\cdot CO_2H \quad \text{and} \quad CO_2H\cdot\overset{|}{\underset{|}{C}}\cdot\overset{|}{\underset{|}{C}}\cdot\overset{|}{\underset{|}{C}}\cdot CO_2H.$$

This is undoubtedly to be attributed to the spatial relationships of the atoms within the molecule. Assuming that the four valencies of a carbon atom are symmetrically distributed in space (*i.e.* directed towards the solid angles of a tetrahedron), then it can be readily seen by the aid of models that in acids of the above types the CO_2H groups are brought

sufficiently near to one another for water to be eliminated, and for a closed ring to be formed (compare Polymethylene Derivatives).

The derivatives of the dibasic acids, *i.e.* their esters, amides, &c, show precisely the same characteristics as the analogous derivatives of the monobasic acids, especially in the readiness with which they are hydrolysed.

DERIVATIVES OF DIBASIC ACIDS

Derivatives	Salts	Esters	Chlorides	Amides
Acid.	$\begin{matrix}CO\cdot ONa\\ CO\cdot OH\end{matrix}$ Acid sodium oxalate.	$\begin{matrix}CO\cdot OC_2H_5\\ CO\cdot OH\end{matrix}$ Ethyl-oxalic acid.	$\begin{matrix}CO\cdot Cl\\ CO\cdot O(H)\end{matrix}$ (only known in derivatives)	$\begin{matrix}CO\cdot NH_2\\ CO\cdot OH\end{matrix}$ Oxamic acid.
Neutral or normal.	$\begin{matrix}CO\cdot ONa\\ CO\cdot ONa\end{matrix}$ Neutral sodium oxalate.	$\begin{matrix}CO\cdot OC_2H_5\\ CO\cdot OC_2H_5\end{matrix}$ Ethyl oxalate.	$\begin{matrix}CO\cdot Cl\\ CO\cdot Cl\end{matrix}$ Oxalyl chloride.	$\begin{matrix}CO\cdot NH_2\\ CO\cdot NH_2\end{matrix}$ Oxamide

As in the case of the glycols, complications arise from the formation of mixed derivatives, *e.g.* partly ester and partly amide, as in the case of ethyl oxamate (p. 237), and also from the fact that many of the acids form imides. Such imides are derived from the hydrogen-ammonium salts of the acids by the elimination of two molecules of water, thus:—

$$\underset{\text{Succinic acid}}{C_2H_4\begin{matrix}CO\cdot OH\\ CO\cdot OH\end{matrix}} + NH_3 = 2H_2O + \underset{\text{Succinimide}}{C_2H_4\begin{matrix}CO\\ CO\end{matrix}NH}$$

Like the amides they are readily hydrolysed (cf. Succinimide).

Oxalic acid (*Ethane diacid*), $(CO_2H)_2$, $2H_2O$, is one of the oldest known organic acids, and occurs as its acid potassium salt in many plants, especially in *Oxalis Acetosella* (wood-sorrel), and in varieties of Rumex, and as the free acid in varieties of Boletus, as normal sodium salt in varieties of Salicornia, and as calcium salt in rhubarb root, &c.

It may be prepared by a variety of different reactions.

1. By the direct combination of carbon dioxide with sodium at 360°: $2CO_2 + Na_2 = C_2O_4Na_2$.

2. By quickly heating sodium formate to a high temperature.

$$2HCO_2Na = H_2 + C_2O_4Na_2.$$

3. It is often met with as an oxidation product of relatively complex carbon compounds, *e.g.* by the oxidation of alcohol by permanganate, and of sugar, starch, wood, &c., by nitric acid. The oxidation of cane-sugar with concentrated nitric acid is often employed for the preparation of pure oxalic acid. The crystallized acid readily separates when the liquid is cooled or evaporated.

4. On the commercial scale, oxalic acid is manufactured by the fusion of cellulose (see Carbohydrates) in the form of sawdust with a mixture of sodium and potassium hydroxides at 200°–220° in flat iron pans. The sodium and potassium oxalates are extracted with water, then precipitated as calcium oxalate, and finally converted into the acid by treatment with the requisite amount of sulphuric acid.

It crystallizes from water in large, transparent, monoclinic prisms containing two molecules of water of crystallization. They slowly effloresce in the air, and readily become anhydrous when heated at 100°. At higher temperatures the acid partly decomposes into carbon dioxide and formic acid, and partly sublimes unaltered.

The acid is readily soluble in water, moderately in alcohol, and somewhat sparingly in ether. The aqueous solution decomposes when exposed to light.

Concentrated sulphuric acid decomposes it into carbon monoxide, carbon dioxide, and water:

$$C_2H_2O_4 = CO_2 + CO + H_2O.$$

Oxalic acid is stable as regards nitric acid and chlorine, but permanganate of potash or manganese dioxide in acid solution oxidizes it to carbonic acid:

$$C_2H_2O_4 + O = 2CO_2 + H_2O.$$

It is reduced by nascent hydrogen to glycollic acid

The strength of an aqueous solution of the acid may be determined by titration with standard alkali, using phenol phthalein as indicator, or by means of standard permanganate in the presence of sulphuric acid.

Its *salts* are known as **oxalates**. The alkaline salts, both acid and normal, are readily soluble in water, the normal sodium

salt being the least so. The "**salt of sorrel**" of commerce is a mixture of C_2O_4HK and a salt, $C_2O_4HK + C_2O_4H_2 + 2H_2O$ (cf. p. 144). The **calcic salt**, $C_2O_4Ca + H_2O$ (or $3H_2O$), is insoluble in water and acetic acid, and serves for the recognition of oxalic acid. **Ferrous-potassic oxalate**, $(C_2O_4)_2FeK_2 + H_2O$, finds application in photography as a powerful reducing agent (the "oxalate developer").

Ethyl oxalate, $(CO \cdot OC_2H_5)_2$, which can be directly prepared from the anhydrous acid and ethyl alcohol without a catalytic agent, is liquid, while **methyl oxalate**, $(CO \cdot OCH_3)_2$, is a solid, crystallizing in plates which melt at 54°; both of them possess an aromatic odour, distil without decomposition, and are extremely readily hydrolysed. Partial hydrolysis, with alcoholic potash solution, produces **potassium ethyl-oxalate**, $COOK \cdot COOC_2H_5$, from which the free **ethyl-oxalic acid**, $COOH \cdot COOC_2H_5$, which is readily hydrolysed, and its chloride, **ethyl-oxalyl chloride**, $COCl \cdot COOC_2H_5$, can easily be prepared. Oxalic ester yields, with an excess of ammonia, oxamide, and with one equivalent the mixed derivative, **ammonic oxamate**, $COONH_4 \cdot CO \cdot NH_2$.

Oxalyl chloride, $(COCl)_2$, has been obtained by the action of excess of phosphorus pentachloride on ethyl oxalate. It is a liquid, b.-pt. 70°, and has a pungent odour (B **41**, 3558).

Oxamide, $NH_2 \cdot CO \cdot CO \cdot NH_2$, the normal amide of oxalic acid, is obtained, among other methods, by the distillation of ammonium oxalate, by the partial hydrolysis of cyanogen, but is most readily obtained by the addition of ammonium hydroxide solution to ethyl oxalate. It is a white crystalline powder, is readily hydrolysed, and by the abstraction of water may be converted into cyanogen. When heated it sublimes unchanged.

Oxamic acid, $NH_2 \cdot CO \cdot CO \cdot OH$, the amic acid corresponding with oxalic acid, is prepared by heating ammonium hydrogen oxalate. It is a crystalline powder, sparingly soluble in cold water, possesses acid properties, and yields salts, esters, &c. It melts and decomposes at 210°.

Ethyl oxamate, *oxamethane*, $NH_2 \cdot CO \cdot CO \cdot OC_2H_5$, is a crystalline compound, and melts at 114°–115°. The action of PCl_5 on this compound is first to form $NH_2 \cdot CCl_2 \cdot CO \cdot OC_2H_5$, **ethyl-oxamine chloride**, which readily loses hydrogen chloride yielding $NH : CCl \cdot CO \cdot OC_2H_5$ and finally $N \vdots C \cdot CO \cdot OC_2H_5$, **cyano-carbonic ester**. Corresponding with oxamide we have **dimethyl-oxamide**, $CH_3 \cdot NH \cdot CO \cdot CO \cdot NHCH_3$, and

corresponding with oxamethane, **ethyl-dimethyl-oxamate**, $(CH_3)_2N\cdot CO\cdot CO\cdot OC_2H_5$, both of which were mentioned at p. 106.

Oximide, $\begin{matrix}CO\\ \\ CO\end{matrix}\!\!>\!NH$, is prepared by the action of PCl_5 upon oxamic acid. It forms colourless prisms readily soluble in water and of neutral reaction, is quickly hydrolysed by hot water, and is transformed into oxamide by the action of ammonia (B **19**, 3228).

Cyanogen, $N\vdots C\cdot C\vdots N$, is the nitrile corresponding with oxalic acid (see p 265).

Malonic acid, *Propane diacid*, $CH_2(CO_2H)_2$, occurs in beetroot as its calcium salt, and may be obtained by the following methods:—

(1) By the oxidation of malic acid by means of chromic acid, hence its name, (2) by the hydrolysis of malonyl-urea (p. 288), (*Baeyer*), (3) by the hydrolysis of cyano-acetic acid (*Kolbe*, *Muller*, A. **131**, 348, **204**, 121):

$$CN\cdot CH_2\cdot CO_2H + 2H_2O = CH_2(CO_2H)_2 + NH_3$$

It crystallizes in large plates, dissolves readily in water, alcohol, and ether, melts at 132°, and decomposes when heated to a slightly higher temperature.

Ethyl malonate, *malonic ester*, $CH_2(CO\cdot OC_2H_5)_2$, is usually obtained by passing hydrogen chloride into a solution of cyano-acetic acid (from chloracetic acid) in absolute alcohol. It is a liquid of faint aromatic odour boiling at 198°, and having a remarkable similarity to aceto-acetic ester. Thus the hydrogen of the methylene group is replaceable by sodium, through the influence of the carbonyl groups CO, which are also bound to the methylene; and the resulting sodio-malonic ester readily exchanges the metal for alkyl when treated with an alkyl iodide. By this means the higher homologues of ethyl malonate, *e.g.* methyl-, ethyl-, propyl-, &c., malonic esters, are obtained Further, the second hydrogen atom in these can be exchanged in exactly the same manner for sodium and then for alkyl, whereby dialkyl malonic acids are formed. This so-called "malonic ester" synthesis is an important method for the preparation of the higher dibasic acids, being applicable even in complicated cases (Cf. *Conrad* and *Bischoff*, A. **204**, 121.) It is also of importance for the preparation of some of the higher fatty acids, as the substituted malonic

acids when heated above their melting-points lose carbon dioxide and yield fatty acids:

$$\begin{matrix}CH_3\\C_2H_5\end{matrix}\!\!>\!C(CO_2H)_2 \longrightarrow \begin{matrix}CH_3\\C_2H_5\end{matrix}\!\!>\!CH\cdot CO_2H.$$

When ethyl malonate is heated with its sodium compound, a derivative of phloroglucinol is formed (See this.)

Malonic anhydride, carbon suboxide, C_3O_2, O:C:C:C:O, is formed when malonic acid is heated in a suitable apparatus at 140°–150°. (*Diels* and *Wolf*, B. 1907, **40**, 355; cf. also 1906, **39**, 689; *Staudinger* and *St Bereza*, B. 1908, **41**, 4461.) The yield is only 10–12 per cent, and acetic acid and carbon dioxide are also formed. It is a colourless liquid, b.-pt. + 7°, m.-pt. − 107°, and $D_0^{0°}$ 1·11. It reacts readily with water, hydrogen chloride, dry ammonia, and aniline, yielding respectively malonic acid, malonyl chloride, malonamide, and malonanilide It is stable at low temperatures, but decomposes rapidly at 100°.

Succinic acid, *Butane diacid, ethylene-succinic acid, symmetrical ethane-dicarboxylic acid* (from *succinum* = amber), $CO_2H\cdot CH_2\cdot CH_2\cdot CO_2H$. This acid has been known for a long time, its composition was determined by *Berzelius*. It exists in amber, in various resins and lignites, in many Compositæ, in Papaveraceæ, in unripe wine grapes, urine, blood, &c.

It may be obtained by most of the general methods described on p 231, *e.g.*: 1. By the hydrolysis of ethylene cyanide This is an extremely important method, as it affords a synthesis of succinic acid and also establishes its constitution, since it can be shown that in ethylene dibromide the two bromine atoms are attached to distinct carbon atoms:

$$CH_2{:}CH_2 \longrightarrow CH_2Br\cdot CH_2Br \longrightarrow CN\cdot CH_2\cdot CH_2\cdot CN \longrightarrow CO_2H\cdot CH_2\cdot CH_2\cdot CO_2H.$$

2. From β-iodo-propionic acid by conversion first into β-cyano-propionic acid and subsequent hydrolysis.

3. By the reduction of fumaric and maleic acids, $CO_2H\cdot CH{:}CH\cdot CO_2H$.

4. By heating its hydroxy-acids, malic or tartaric, with hydriodic acid:

$$CO_2H\cdot CH(OH)\cdot CH_2\cdot CO_2H + 2HI = CO_2H\cdot CH_2\cdot CH_2\cdot CO_2H + I_2.$$

5. It may also be obtained by the fermentation of the salts of these hydroxy-acids by means of certain micro-organisms, *e.g.* certain species of bacteria.

It is also formed in small quantities as a by-product in the alcoholic fermentation of sugar, and by the oxidation of fats, fatty acids, and paraffins by means of nitric acid.

It is usually prepared from calcic malate according to 5, or by the distillation of amber.

6. It may also be synthesised from ethyl malonate. The sodio-derivative of this ester reacts not merely with alkyl iodides or bromides, but also with the esters of haloid fatty acids, *e.g.* ethyl bromoacetate.

$$(CO_2Et)_2CHNa + Br\cdot CH_2\cdot CO_2Et = NaBr + (CO_2Et)_2\cdot CH\cdot CH_2\cdot CO_2Et.$$

The product is **ethyl ethane-tricarboxylate**, and when this is hydrolysed, alcohol, carbon dioxide, and succinic acid are formed. This method is of general interest, as various substituted succinic acids may be synthesised by this method. In place of sodio-ethyl malonate, the sodio-derivatives of esters of mono-substituted malonic acids may be used, and in place of ethyl bromo-acetate the esters of other halogen fatty acids, *e.g.* ethyl iodo-propionate or ethyl bromo-valerate. It has recently been shown (*Bone* and *Sprankling*, J. C. S. 1899, 839) that better yields can be obtained by using ethyl cyano-acetate and its derivatives in place of ethyl malonate and its derivatives.

Properties. - It crystallizes in monoclinic prisms or plates with an unpleasant faintly acid taste, is readily soluble in water, melts at 185°, and boils at 235°, but is at the same time partially converted into its anhydride. (For its electrolysis, see pp 46 and 232.) Is very stable towards oxidizing agents.

Of the salts of succinic acid, the **basic ferric salt**, obtained by the addition of a ferric salt to ammonium succinate, is used in analysis for the separation of the ferric and aluminic radicals. The **calcic** salt is soluble in water.

The derivatives of succinic acid correspond closely with those of oxalic, *e.g.* **succinamic acid**, $NH_2\cdot CO\cdot CH_2\cdot CH_2\cdot CO\cdot OH$, is analogous to oxamic acid, and **succinamide**, $NH_2\cdot CO\cdot CH_2\cdot CH_2\cdot CO\cdot NH_2$, to oxamide. There also exists, as in the case of other dibasic acids, an imide, **succinimide**, $C_2H_4<\begin{matrix}CO\\CO\end{matrix}>NH$. The latter crystallizes in rhombic plates, and is formed by heating ammonium hydrogen succinate. The basic properties of the NH are so modified by the two carbonyl groups of the acid radical that the imido-hydrogen is

replaceable by metals, such as K, Ag, &c. (Cf. B. **25**, Ref. 283.) **Succinyl chloride** reacts as though it were **dichloro-butyro-lactone**, $C_2H_4<\begin{matrix}CCl_2\\CO\end{matrix}>O$. It is a colourless liquid boiling at 190°, and is obtained by the action of phosphorus pentachloride (2 mols.) on the acid, or of 1 mol. on the anhydride. In many of its properties it resembles the acid chlorides, but on reduction yields **butyro-lactone**, with benzene and aluminium chloride it yields mainly **γ-diphenyl-butyro-lactone**, $C_2H_4<\begin{matrix}CPh_2\\CO\end{matrix}>O$, and with zinc ethyl **γ-diethyl-butyro-lactone**. The chloride is probably a mixture of dichloro-butyro-lactone with a small amount of the normal chloride. **Succinic anhydride**, $C_2H_4<\begin{matrix}CO\\CO\end{matrix}>O$, is best obtained by the action of acetic anhydride on the acid. It crystallizes in glistening plates, melts at 120°, and distils without decomposition It slowly combines with water, yielding the acid, more readily with alkalis, and also with alcohols at a higher temperature, yielding the **acid esters**, *e.g.* $HO\cdot CO\cdot CH_2\cdot CH_2\cdot CO\cdot OEt$. This is the most convenient method for the preparation of acid esters The other methods sometimes employed are: (*a*) the partial hydrolysis of the neutral ester, and (*b*) the partial esterification of the acid by means of very dilute solution of hydrogen chloride in the requisite alcohol (*Bone, Sudborough*, and *Sprankling*, J. C. S. 1904, 534).

Of the higher acids the following are of interest —

Glutaric acid, *Pentane dioic acid*, $CO_2H\cdot CH_2\cdot CH_2\cdot CH_2\cdot CO_2H$ —It may be obtained from glutamic acid (p 249), and also by condensing formaldehyde with ethyl malonate in the presence of a small amount of diethylamine:

$$CH_2{:}O + 2H\cdot CH(CO_2Et)_2 = H_2O + (CO_2Et)_2\cdot CH\cdot CH_2\cdot CH(CO_2Et)_2$$

This is a further example of the readiness with which aldehydes condense with compounds containing a methylene group adjacent to carbonyl or negative groups. The product, **ethyl propane-tetracarboxylate**, on hydrolysis yields ethyl alcohol, carbon dioxide, and glutaric acid. The last crystallizes in prisms, melts at 97°, is readily soluble in water, and yields an **anhydride**, an **imide**, &c. The imide can be obtained

piperidine is oxidized with hydrogen peroxide, and when ith zinc dust yields a small amount of pyridine.

Isomeric with glutaric acid is **methyl-succinic** or **pyro-tartaric acid**, $CO_2H \cdot CHMe \cdot CH_2 \cdot CO_2H$, an acid closely resembling succinic acid, and obtained by dry distillation of tartaric acids.

The *s*-**dimethyl-** and *s*-**dibromo-succinic acids**, $CO_2H \cdot CHBr \cdot CHBr \cdot CO_2H$, occur in the same number of stereo-isomeric modifications as the tartaric acids (p. 249).

Mono- and **dibromo-succinic acids**, $C_2H_3Br(CO_2H)_2$ and $C_2H_2Br_2(CO_2H)_2$, are easily prepared, and are valuable for the syntheses of the hydroxy-succinic acids.

Sodium reacts with ethyl succinate, yielding **ethyl succinylo-succinate**, a compound related to benzene.

Isosuccinic acid, *Methyl-propane diacid, ethylidene-succinic acid*, or *methyl-malonic acid*, $CH_3 \cdot CH(CO_2H)_2$, is formed by the malonic ester synthesis, or from α-chloro- (or iodo-) propionic acid (pp 237 and 232). It is a solid, when heated decomposes into CO_2 and propionic acid, and yields no anhydride (p 231)

Relative strengths of the dibasic acids:

	K
Oxalic	10 0 (about)
Malonic	0 163
Succinic	0 0066
Glutaric	0 0047

The strengths of alkylated succinic acids are not so very different from that of succinic acid, and those of alkyl glutaric acids are of the same order as that of glutaric

B. Unsaturated Dibasic Acids

The unsaturated acids stand in the same relation to the saturated dibasic acids as acrylic acid does to propionic As dibasic acids they yield derivatives analogous to those of oxalic acid, while as unsaturated compounds each molecule possesses, in addition, the property of combining with two atoms of hydrogen or halogen, or with one molecule of halogen hydride.

Common Methods of Formation.- -1. By the elimination of water from the hydroxy dibasic-acids Thus malic acid when distilled yields water and maleic anhydride, which volatilizes, and also fumaric acid, which remains behind:

$$CO_2H \cdot CH(OH) \cdot CH_2 \cdot CO_2H \overset{\bullet}{-} H_2O = CO_2H \cdot CH{:}CH \cdot CO_2H.$$

The actual product obtained by the elimination of water

from malic acid varies considerably with the conditions of the experiment. Thus, when malic acid is maintained at a temperature of 140°–150° for some time, the chief product is fumaric acid; when the malic acid is rapidly heated at a higher temperature, maleic anhydride is largely formed

Citric acid yields, in a similar way, CO_2, H_2O, itaconic acid, $CH_2:C(CO_2H)\cdot CH_2\cdot CO_2H$, and citraconic anhydride (methyl-maleic anhydride).

2. By the separation of halogen hydride from the mono-haloid derivatives of succinic acid and its homologues, *e.g.* monobromo-succinic acid yields fumaric, thus:—

$$CO_2H\cdot CHBr\cdot CH_2\cdot CO_2H - HBr = CO_2H\cdot CH:CH\cdot CO_2H.$$

3. Fumaric acid has been prepared synthetically from acetylene di-iodide, just as succinic acid has been from ethylene dibromide.

Constitution.—The acids of this series may be regarded as dicarboxylic acids of the olefines, *e.g.* fumaric and maleic acids, $C_2H_2(CO_2H)_2$, as those of ethylene. Their mode of formation 1 corresponds exactly with the production of ethylene from alcohol, or with that of acrylic from ethylene lactic acid, while 2 agrees with that of ethylene from ethyl iodide.

Maleic acid (*cis-Butene diacid*), $CO_2H\cdot CH:CH\cdot CO_2H$, crystallizes in large prisms, possesses a grating, nauseous acid taste, and is very readily soluble in cold water It distils unchanged, excepting for partial transformation into maleic anhydride. It is conveniently prepared by heating the acetyl derivative of malic acid (see p. 247), or from fumaric acid and $POCl_3$ (A. **268**, 255).

Fumaric acid (*trans-Butene diacid*), $C_2H_2(CO_2H)_2$, crystallizes in small prisms with a strong, purely acid taste, and is almost insoluble in cold water. It does not melt, but sublimes at about 200° with formation of maleic anhydride. It occurs in *Fumaria officinalis*, various fungi, truffles, Iceland moss, &c., and is obtained from maleic acid either by prolonged heating of the latter at 130°, or by the action upon it of hydrobromic or other acids. (For its preparation, see A. **268**, 255.)

Both acids are converted into esters when their silver salts are heated with alkyl iodide, and these esters stand in very close relationship to one another, as do the free acids; thus ethyl maleate is changed into ethyl fumarate when warmed with iodine, and the latter ester is formed by saturating an alcoholic solution of maleic acid with dry hydrogen chloride.

Isomerism of Fumaric and Maleic Acids.—The isomerism of these two acids is a problem which has attracted the attention of numerous chemists. Attempts were first made to account for the difference by polymerism or structural isomerism, *e.g. Fittig* has suggested

$$CO_2H\cdot CH{:}CH\cdot CO_2H \quad \text{and} \quad CO_2H\cdot CH_2\cdot C\cdot CO_2H;$$

but isomerism of this type is impossible, since both acids when oxidized yield one or other of the tartaric acids $CO_2H\cdot CH(OH)\cdot CH(OH)\cdot CO_2H$.

Anschutz has brought forward the formulæ

$$CO_2H\cdot CH{:}CH\cdot CO_2H \quad \text{and} \quad \begin{matrix} CH\cdot CO \\ \| \\ CH\cdot C(OH)_2 \end{matrix}\!\!>\!O.$$

Such a formula as the latter is not at all probable, as in this case maleic acid, which is the stronger acid (K = 1·17, and for fumaric K = 0·093), would not possess a carboxylic, but merely a hydroxy lactone structure (*Wegscheider*, B 1903 **36**, 1543). This formula is also found to be quite untenable when the products of bromination and of oxidation are considered

The fact that the two acids are structurally identical, and must both be represented as ethylene dicarboxylic acids, is now generally recognized, and the conclusion is largely based on the following facts:—(1) Both acids when reduced with sodium amalgam yield ordinary succinic acid. (2) Both acids combine with hydrogen bromide, yielding the same bromo succinic acid. (3) Both acids combine with water at moderate temperatures, yielding the same malic acid. In most of these additive reactions the maleic acid reacts somewhat more readily than the fumaric, and is at the same time partially transformed into fumaric. (4) When carefully oxidized, the two acids yield stereo-isomeric tartaric acids, maleic being transformed into meso-tartaric, and fumaric into racemic acid. (5) Similarly, on addition of bromine they yield stereo-isomeric dibromo succinic acids.

As the two acids are structurally identical, the isomerism can only be accounted for by a different spatial relationship of the atoms within the molecule. The stereo-isomerism of these unsaturated compounds is quite distinct from that of the saturated compounds, such as lactic and tartaric acids

We are forced to assume that in saturated compounds where two C atoms are united by a single bond, there is free rotation around the axis represented by the bond; otherwise, the number of isomerides $Cabc \cdot Cdef$, or even $Caab \cdot Caab$, would be much greater than what is actually found. When, however, the two carbon atoms become united by a so-called double bond, free rotation is completely prevented, and we have the centres of gravity of the two C atoms and of the four substituents all lying in the same plane, viz. the plane of the paper, *e.g.* C_2H_4 may be represented as

$$\begin{array}{c} H \cdot C \cdot H \\ \vdots \\ H \cdot C \cdot H. \end{array}$$

No stereo-isomerism is possible with such a compound, nor yet with any compound in which the 2 radicals attached to the one carbon atom are the same, *e.g.* $CH_2{:}CCl \cdot CO_2H$, but immediately each carbon atom has 2 different radicals attached to it, isomerism is theoretically possible, *e.g.* crotonic acid, $CH_3 \cdot CH{:}CH \cdot CO_2H$, and maleic acid, $CO_2H \cdot CH{:}CH \cdot CO_2H$, viz.:

$$\begin{array}{l} CH_3 \cdot C \cdot H \\ CO_2H \cdot \ddot{C} \cdot H \end{array} \quad \text{and} \quad \begin{array}{l} CH_3 \cdot C \cdot H \\ H \cdot \ddot{C} \cdot CO_2H, \end{array}$$

$$\begin{array}{l} CO_2H \cdot C \cdot H \\ CO_2H \cdot \ddot{C} \cdot H \end{array} \quad \text{and} \quad \begin{array}{l} CO_2H \cdot C \cdot H \\ H \cdot \ddot{C} \cdot CO_2H; \end{array}$$

and similarly for oleic and elaidic acids, erucic and brassidic acids, cinnamic and allocinnamic acids and its derivatives, and also for numerous other compounds.

As the centres of gravities of the carbon atoms and of their substituents all lie in one plane, the molecules are not perfectly asymmetric, and therefore possess no optical activity, and cannot be resolved into optically active components.

The two isomerides are not so closely related to one another as *d*- and *l*-valeric acids, or as *d*- and *l*-tartaric acids; as a rule, they differ entirely as regards their ordinary physical properties, *e.g.* crystalline form, solubility, melting-point, water of crystallization, dissociation constant, &c., and in many cases considerable differences in chemical properties are met with, *e.g.* maleic acid yields an anhydride and fumaric acid does not. As a rule, one of the isomerides is less stable than the other, and under suitable conditions, *e.g.* influence of (*a*) heat,

(*b*) light, (*c*) chemical reagents, especially small amounts o halogens or halogen hydracids, the labile compound is trans formed into the stable. With certain pairs of isomerides th transformation is mutual, so that whichever of the two w start with we obtain, under the conditions enumerated above a mixture of the two in chemical equilibrium.

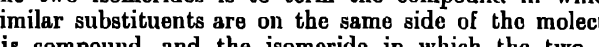
As examples of the transforming action of heat we have th following:—Fumaric → maleic; allocinnamic → cinnamic angelic → tiglic, and either chloro-fumaric, $CO_2H \cdot CCl : CH \cdot CO_2H$, or chloro-maleic acid heated separately yields a mixtur of the two. The effect of exposure to sunlight is often identica with the action of heat, but not always so, *e.g.* ethyl benzy aminocrotonate, $CH_2Ph \cdot NH \cdot \overset{CH_3}{\overset{|}{C}} : CH \cdot CO_2Et$, exists in tw stereo isomeric modifications melting at 79° and 21°, the effec of heat is to transform the higher melting ester into the lowe melting, and the effect of sunlight is the exact opposite. A examples of the influence of chemicals, we have the actio of small amounts of nitrous acid in transforming oleic int elaidic and erucic into brassidic acids. Similarly, sma amounts of bromine will transform dimethyl maleate int dimethyl fumarate.

Skraup has shown that either sulphur dioxide or hydroge sulphide alone is unable to transform maleic into fumaric, bu that a mixture of the two will bring about the transformatio The chemical reaction between the H_2S and SO_2 may be re garded as a type of detonator which starts the transformatio in the maleic acid. All chemical reactions, however, canno act in the same manner as catalysts. It has also been show that the salts of maleic acid, *e.g.* copper maleate, when decon posed by hydrogen sulphide yield fumaric acid or a mixtur of fumaric and maleic acids, although, as stated above, th sulphide itself is incapable of transforming free maleic aci into fumaric.

The exact method of transformation is not known. It ma be (*a*) that the two radicals attached to the one carbon ato actually exchange positions directly; (*b*) the two carbon aton may not be entirely unable to rotate round their comme axis, but may only be in a state of strain, and under th influence of light, heat, &c., a rotation through an angle 180° may occur; or (*c*) in the case of change brought about l chemical agents it is possible that the agent employed fir forms an additive compound and is subsequently remove

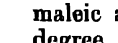
but this view has been shown to be impossible in many cases by *Anschutz*, *Fittig*, and *Michael*.

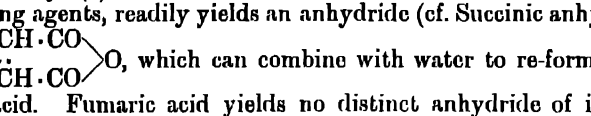
The system of nomenclature adopted to distinguish between the two isomerides is to term the compound in which two similar substituents are on the same side of the molecule the **cis** compound, and the isomeride in which the two similar radicals are on opposite sides of the molecule the **trans**:

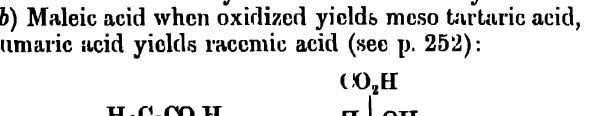


cis-Ethylene dicarboxylic acid — *trans*-Ethylene dicarboxylic acid

In cases where it has not been found possible to ascertain which of the two known compounds has the *cis* configuration and which the *trans*, the ordinary name is given to the one and the prefix *iso*, or better, *allo*, to the other, *e.g.* crotonic and isocrotonic acids, cinnamic and allocinnamic acids.

Determination of Configuration.—In the case of fumaric and maleic acids this has been accomplished with a considerable degree of certainty. The arguments used for the *cis* configuration of maleic and the *trans* configuration of fumaric are briefly: (*a*) Maleic acid when heated, or treated with dehydrating agents, readily yields an anhydride (cf. Succinic anhydride),  , which can combine with water to re-form maleic acid. Fumaric acid yields no distinct anhydride of its own. (*b*) Maleic acid when oxidized yields meso tartaric acid, whereas fumaric acid yields racemic acid (see p. 252):





The configurations of other pairs of olefine stereo-isomerides have not been determined with the same degree of certainty, and many of the methods described in text-books as being available for this purpose cannot be relied on, *e.g.* of two

stereo-isomeric α- or β-halogenated compounds, the one which has the halogen in the *cis*-position with respect to a hydrogen atom will lose halogen hydracid more readily under the influence of alkali, *e.g.*:

$$\begin{array}{l} CH_3\cdot\dot{C}\cdot Br \\ H\cdot\ddot{C}\cdot CO_2H \end{array} \quad \text{and} \quad \begin{array}{l} CH_3\cdot\dot{C}\cdot Br \\ CO_2H\cdot\ddot{C}\cdot H. \end{array}$$

In many cases it is probable that exactly the reverse holds good.

An admirable account of the stereochemistry of olefine derivatives will be found in *Werner's* "Stereochemie", 1904, pp. 179–227.

For higher homologues, see *Fittig*, B. **26**, 40.

Acetylene-dicarboxylic acid, *Butine diacid*, $CO_2H\cdot C\vdots C\cdot CO_2H$, is a type of an acetylenic acid, it is obtained by the elimination of two molecules of hydrogen bromide from one of dibromo-succinic acid. It possesses the characteristic properties of a dibasic acid, and also of an unsaturated compound, but does not yield metallic derivatives of the type of silver acetylene. It readily loses carbon dioxide, yielding propargylic acid, $CH\vdots C\cdot CO_2H$. **Diacetylene-dicarboxylic acid**, $CO_2H\cdot C\vdots C\cdot C\vdots C\cdot CO_2H$, and **tetracetylene-dicarboxylic acid**, *Decatetrine diacid*, $CO_2H\cdot C\vdots C\cdot C\vdots C\cdot C\vdots C\cdot C\vdots C\cdot CO_2H$, have been prepared by *Baeyer* (B. **18**, 678 and 2269). With increasing length of chain they show an increasing tendency to explode. (For *Baeyer's* theory of explosions, see B. **18**, 2277.)

C. Hydroxy Dibasic Acids

1. **Tartronic acid**, *Propanol diacid*, *hydroxy-malmic acid*, $OH\cdot CH\cdot(CO_2H)_2$, forms large prisms $(+\frac{1}{2}H_2O)$, and is easily soluble in water, alcohol, and ether. It cannot be distilled unchanged, since it breaks up on heating into carbon dioxide and glycolide. As hydroxy-malonic acid it may be prepared by the action of moist silver oxide on chloromalonic acid. It may also be obtained by the reduction of the corresponding ketonic acid, mesoxalic acid, $CO(CO_2H)_2$, and also by the oxidation of glycerol with permanganate.

2. **Malic acid**, *Butanol diacid*, *hydroxy-succinic acid*, $CO_2H\cdot CH_2\cdot CH(OH)\cdot CO_2H$ (*Scheele*, 1785), is very widely distributed in the vegetable kingdom, being found in unripe apples, sorb-apples, grapes, barberries, mountain-ash berries, quinces, &c.

Some of the simpler methods of formation are quite analogous to those employed in the case of hydroxy monobasic acids, *e.g.* (1) by the action of moist silver oxide on bromo-succinic acid; (2) by the reduction of tartaric or racemic acid with HI, and of oxal-acetic acid (pp. 224 and 260) with sodium-amalgam; (3) by the action of nitrous acid on the corresponding amino acid, aspartic acid; and (4) by the addition of the elements of water to fumaric or maleic acid under the influence of aqueous sodic hydroxide.

It crystallizes in hygroscopic needles, is readily soluble in water and alcohol, but only sparingly in ether. It melts at 100°, and when it is distilled, maleic anhydride passes over and fumaric acid remains in the retort (p 241). K = 0 04.

The molecule of malic acid contains an asymmetric carbon atom, and thus the acid should exist in two optically active and a racemic modification. The acid obtained from natural sources, *l*-malic acid, is lævo-rotatory in dilute solution, but the rotation diminishes as the concentration increases. With a 34-per-cent solution at 20° no optical activity is shown, and with more concentrated solutions dextro-rotation is exhibited The acid obtained synthetically is optically inactive and constitutes the racemic form, and it has been resolved into optically active modification by the usual methods (p. 254), (B. 1898, **31**, 528).

The alkali salts and the acid calcium salt of malic acid are readily soluble in water, while the normal calcium salt is only sparingly soluble.

The constitution follows from its methods of preparation, from the fact that it is readily reduced to succinic acid, and that its esters react with acetic anhydride, yielding mono-acetyl derivatives.

Amides and Amines of Malic Acid.—Like glycollic acid, malic acid forms—as an acid—amides (saponifiable), and—as an alcohol—an amine (not saponifiable). The amides are:—

Malamide, $NH_2 \cdot CO \cdot CH(OH) \cdot CH_2 \cdot CO \cdot NH_2$, crystallizing in prisms, and **malamic acid**, $CO_2H \cdot CH_2 \cdot CH(OH) \cdot CO \cdot NH_2$, the latter being only known as ethyl ester. The amino-acid, **aspartic acid**, $CO_2H \cdot CH(NH_2) \cdot CH_2 \cdot CO_2H$, unites in itself, like glycocoll, the properties of a base and of an acid, but the acid character predominates. Its acid amide, **asparagine**, $CO_2H \cdot CH(NH_2) \cdot CH_2 \cdot CO \cdot NH_2$, which is isomeric with malamide, is very widely distributed in the vegetable kingdom, being present in the young leaves of trees, in beet-root, potatoes, the shoots of peas, beans, and vetches, and in

asparagus; it was first found in the last-named vegetable in the year 1805 It forms glistening rhombic prisms ($+ H_2O$), is readily soluble in hot water, but insoluble in alcohol and ether, and yields aspartic acid when hydrolysed. It is lævo-rotatory.

A dextro-rotatory asparagine has likewise been obtained from the shoots of vetches (B. **20**, Ref 510); it possesses a sweet taste, and unites with the lævo-rotatory compound to an inactive modification. For the synthesis of the asparagines and their constitution, see *Piutti*, B **22**, Ref 241 and 243

Aspartic acid, *amino-succinic acid*, is present in beet molasses, and forms an important product of the decomposition of proteids with acids or alkalis. It has been synthesized, *e.g.* from bromo-succinic acid and ammonia, and crystallizes in small rhombic plates readily soluble in hot water. It exists in optically active modifications, which differ in taste and are convertible the one into the other (B. **20**, R. 510). Nitrous acid transforms both aspartic acid and asparagine into malic acid

Glutamic acid, *α-amino glutaric acid*, $CO_2H \cdot CH(NH_2) \cdot CH_2 \cdot CH_2 \cdot CO_2H$, and **glutamine** correspond with aspartic acid and asparagine. The former is found in beet-root and in the shoots of the vetch and gourd, while the latter is produced, together with aspartic acid and leucine, by boiling proteids with dilute sulphuric acid.

D. Dihydroxy Dibasic Acids

These acids are characterized by the presence of two hydroxyl radicals in the molecule in addition to two carboxyls.

Tartaric acid, *Butane-diol diacid*, *dihydroxy-succinic acid*, $CO_2H \cdot CH(OH) \cdot CH(OH) \cdot (CO_2H)$, exists in four distinct modifications.

1. *d* or **Dextro-tartaric acid**, m.-pt. 170°.
2. *l*- or **Lævo-tartaric acid**, *anti-tartaric acid*, m.-pt. 170°.
3. **Racemic acid**, *d-l-tartaric acid*, *para-tartaric acid*, m.-pt. 206°
4. *i*- or **Inactive tartaric acid**, *meso-tartaric acid*, m.-pt. 143°.

The constitution of these acids follows from their relationship to succinic acid, from their methods of formation, and from the fact that their esters with acetic anhydride yield *diacetyl* derivatives

Solutions of equal concentration of the two first of these

acids turn the plane of polarization of light in an equal degree, but in opposite directions. By their union the inactive racemic acid is formed, and this can, conversely, be separated into its components. The fourth tartaric acid, likewise inactive, cannot be resolved in this way.

The common tartaric acid found in nature is optically active, and is the *d*-tartaric acid, whereas the acids obtained synthetically are optically inactive, viz. racemic acid or meso-tartaric acid, or a mixture of both, *e.g* dibromo-succinic acid with moist silver oxide yields a mixture of racemic and meso-tartaric acids.

Fumaric acid when oxidized with permanganate is converted into racemic acid, and maleic acid by a similar process into meso-tartaric acid (p. 246). Glyoxal cyanhydrin (p. 221) when hydrolysed yields racemic acid, and finally, mannitol when oxidized with nitric acid yields racemic acid, and sorbitol meso-tartaric acid.

Synthesis:

$$CH_2{:}CH_2 \xrightarrow[Br_2]{} CH_2Br\cdot CH_2Br \xrightarrow[KCN]{} CN\cdot CH_2\cdot CH_2\cdot CN$$

$$\xrightarrow[\text{Hydrolysis}]{} CO_2H\cdot CH_2\cdot CH_2\cdot CO_2H \xrightarrow[Br_2]{} CO_2H\cdot CHBr\cdot CHBr\cdot CO_2H$$

$$\xrightarrow[AgOH]{} CO_2H\cdot CH(OH)\cdot CH(OH)\cdot CO_2H.$$

Stereo-isomerism of the Tartaric Acids. The isomerism of the tartaric acids is of much the same type as that discussed in the case of active valeric and of α-lactic acid. A glance at the constitutional formula for the acids shows the presence of 2 asymmetric carbon atoms; to each of these 2 atoms are attached the radicals H, OH, and CO_2H, and the remaining valency of each carbon is employed in attaching it to the other carbon atom.

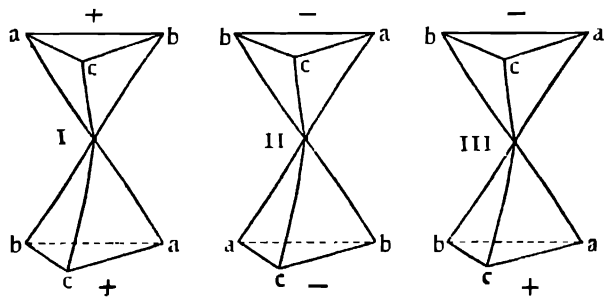
A compound of this general type, C(a, b, c)·C(a, b, c), is known as a compound containing 2 similar asymmetric carbon atoms. If one valency of each carbon is employed in uniting the 2 carbon atoms together, then the 3 radicals, a, b, c, which are attached to the remaining three valencies of a carbon atom, may be arranged in two distinct ways, viz. $\overset{a}{\underset{c}{\curvearrowright}}\overset{b}{}$, positive order, and $\overset{a}{\underset{b}{\curvearrowleft}}\overset{c}{}$, negative order.

The following combinations are thus possible:—

	+	−	+	−
	+	−	−	+
or	1	2	3	4

But Nos. 3 and 4 must be identical, as the radicals attached to the 2 asymmetric carbon atoms are identical.

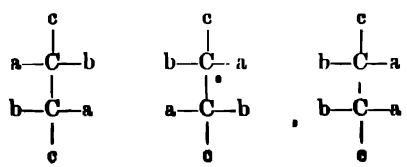
These spatial relationships may be represented:



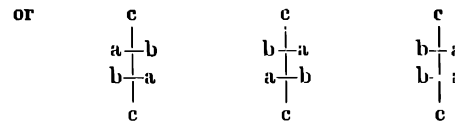
where a = H, b = OH, and c = CO_2H.

Note.—At first sight it appears as though the radicals a, b, c in the lower half of fig. 1 were arranged in the − and not the + order, as indicated. It must be remembered, however, that each part of the molecule must be looked at from the same point of view; and if we take the order of the radicals in the upper tetrahedron when arranged so that the solid angle which represents the point of attachment to the second tetrahedron is pointed down, then we must regard the second tetrahedron from the same point of view, *i.e.* we must turn the figure upside down. It is then seen that the arrangement in the lower half of the molecule is the +.

Instead of using the above cumbrous figures, it is usual to regard such models as projected upon a plane surface, and to use the projections thus obtained (*E. Fischer*, B. 1891, **24**, 2684):



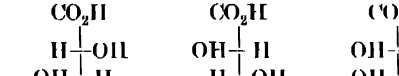
or



Note.—The manner in which these projection formulæ are obtained can be best seen by means of models.

A comparison of the three configurations at once shows that Nos. I and II are perfectly asymmetric, and are related to one another as object to mirror image, they should therefore represent the two optically active tartaric acids, and the compound of the two should represent the molecule of racemic acid. No. III has a plane of symmetry, and should therefore represent the non-resolvable, inactive acid—*meso*-tartaric acid.

The question as to whether No I represents *d*- or *l*-tartaric acid has been settled by *Fischer* (B. 1896, **29**, 1377) in favour of the *d*-acid. We thus have:



d *l* *meso*

l **Dextro-tartaric acid**, *acidum tartaricum*, is the tartaric acid found in nature It was discovered by *Scheele* in 1769 It occurs in the free state, but chiefly as acid potassium salt, in various fruits, especially in the juice of grapes, from which potassic hydric tartrate (cremor tartari) separates in crystals during fermentation. When this is boiled with chalk and chloride of calcium it is transformed into the neutral calcium salt, from which the acid is liberated on addition of H_2SO_4.

It crystallizes from water in large transparent monoclinic prisms, of a strong and purely acid taste, is readily soluble in water, also in alcohol, but almost insoluble in ether. It melts at 170°, and its aqueous solution reduces an ammoniacal silver solution upon warming. When melted, it is changed into an amorphous modification, and then into an anhydride, and when heated more strongly it carbonizes with the dissemination of a characteristic odour and formation of pyro-racemic and pyro-tartaric acids. Oxidation converts it either into dihydroxy-tartaric (p. 260) or tartronic acid, and then into formic and carbonic acids, &c. It is employed in medicine, dyeing, &c.

Normal potassic tartrate, $C_4H_4O_6K_2 + \frac{1}{2}H_2O$, forms monoclinic prisms easily soluble in water. **Acid potassic tartrate, tartar**, or cremor tartari, $C_4H_5O_6K$, small rhombic crystals of acid taste, sparingly soluble in water, is much used in dyeing, medicine, &c. Potassic sodic tartrate, **Rochelle** or **seignette salt**, $C_4H_4O_6KNa + 4H_2O$ (1672), forms magnificent rhombic prisms. **Calcic tartrate**, $C_4H_4O_6Ca + 4H_2O$, is a powder insoluble in water, but soluble in cold caustic-soda solution; on warming the solution it separates as a jelly, which redissolves upon cooling. **Potassic antimonyl-tartrate, tartar emetic**, $C_4H_4O_6(SbO)'K + \frac{1}{2}H_2O$ (see B. **15**, 1540), is obtained by heating cream of tartar (cremor tartari) with antimony oxide and water. It crystallizes in rhombic efflorescent octahedra, readily soluble in water. It is poisonous and acts as an emetic, and is used as a mordant in dyeing.

Fehling's solution is a solution of cupric sulphate mixed with alkali and Rochelle salt, and is largely used as an oxidizing agent. Thus with various carbon compounds, such as formaldehyde, glucose, fructose, &c., it readily yields a precipitate of cuprous oxide.

The **diethyl ester** is a thick oil, while the **monoethyl ester** crystallizes in prisms. **Aceto-tartaric acid** and **amides** of tartaric acid are known, and also various anhydrides. As an alcohol, it forms with nitric acid a dinitric ester, the so-called **nitro-tartaric acid**, $C_2H_2(O\cdot NO_2)_2(CO_2H)_2$, which is readily hydrolysed, yielding dihydroxy-tartaric or tartronic acid.

2. **Lævo-tartaric acid** is identical in its chemical and also in almost all its physical properties with ordinary tartaric acid, but differs from it in that its solutions turn the plane of polarization of light to the left, in a degree equal to that in which the other turns it to the right. The crystallized salts show hemihedral faces like the salts of dextro-tartaric acid, but oppositely situated (see p. 254). When equal quantities of both acids are mixed together in aqueous solution, the solution becomes warm, and we obtain,

3. **Racemic acid**, $(C_4H_6O_6)_2$, $2H_2O$, the composition of which was first established by *Berzelius*, who recognized it as being different from tartaric acid, and who developed the idea of isomerism from this first example in 1829. Racemic acid is obtained from tartar mother liquor. It differs from dextro tartaric acid in that its crystals are rhombic and efflorescent, and also less soluble in water than the former; further, the free acid is capable of precipitating a solution of calcium chloride

and is optically inactive (see below). The salts, which are termed racemates, and also the esters (B. **21**, 518), show small differences from the tartrates in the proportions of their water of crystallization, in solubility, and melting-point or boiling-point. Molecular-weight determinations of dilute aqueous solutions of racemic acid indicate that under these conditions it is completely resolved into *d*- and *l*-tartaric acids.

4. **Meso-tartaric acid**, a fourth tartaric acid, is inactive like the foregoing, but non-resolvable into the active acids. When heated with water at 170° it is partially transformed into racemic acid, which can then be resolved. It differs from racemic acid and also from the active acids in all its physical properties. It crystallizes in efflorescent rectangular plates, m.-pt. 143°. The acid-potassium salt is readily soluble in water.

Racemic Compounds. *Resolution of Racemic Compounds into their Optically Active Components.*—Racemic acid has been resolved by three distinct methods, all due to *Pasteur*, and as they are also applicable to the resolution of other racemic compounds, they are given below

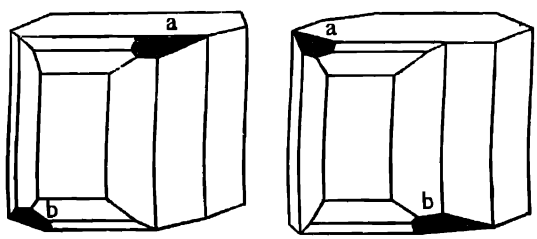
1. When a solution of sodium-ammonium racemate,

$$Na(NH_4)C_4H_4O_6, 2H_2O,$$

is evaporated, beautiful rhombic crystals having the composition $NaNH_4C_4H_4O_6, 4H_2O$ and showing hemihedral faces*

* *Hemihedral Faces.*—These are small faces which are not perfectly symmetrically situated with respect to the other crystalline faces; they occur in only half the positions where they might be expected, and thus give the crystals a non-symmetric structure.

The following figs. represent crystals of the *d*- and *l* sodic ammonic tartrates:—



The faces *a* and *b* are the hemihedral faces, and it will be noticed that the two crystals are non-superposable, but stand in the relationship of object to mirror-image.

are obtained. *Pasteur* observed that these faces were not always similarly situated, but that certain crystals were dextro-hemihedral, while others were lævo-hemihedral, so that one crystal formed the reflected image of the other. The lævo-hemihedral crystals when dissolved exhibit dextro-rotation, and *vice versa*. If now the two kinds of crystals be separated from one another mechanically, and the free acid liberated from each, this will be found to consist, not of racemic acid, but in the one case of dextro- and in the other of lævo-tartaric acid

In the process of crystallization it is essential that the temperature should be below 27°, as otherwise, in place of the enantiomorphously related crystals of sodic-ammonic *d*- and *l*-tartrates, it is found that the crystals are all alike, possess no hemihedral faces, and consist of sodic-ammonic racemate. This temperature is termed the transition point, and for each racemic compound there is a definite transition temperature. Thus for sodic-potassic racemate it is 3°, for rubidic racemate 40·4°, for ammonic-hydric malate 74°.

In the case of sodic-ammonic racemate the transition temperature may be determined by means of a dilatometer (*Van't Hoff* and *Deventer*, Zeit Phys, 1887, **1**, 173). This is a large thermometer, the bulb of which is filled with an equimolecular mixture of the two active salts and covered with oil, the level of which can be read off on the stem. As the temperature of the dilatometer is raised gradually, a considerable increase in volume is noticed at 27°, due to the change expressed by the equation:

$$NaNH_4C_4H_4O_6.4H_2O + NaNH_4C_4H_4O_6.4H_2O = (NaNH_4C_4H_4O_6)_2.2H_2O + 6H_2O.$$

Other racemic compounds have been resolved by this simple method of crystallization. In all cases the temperature employed must be below the transition temperature of the given substance, *i.e.* below the temperature at which the mixture of active components becomes transformed into the racemic compound. In this method of resolution no differences in solubility of the two components are met with, and hence no process of fractional crystallization can be employed; the two salts are deposited side by side, and must be picked out individually. The resolution of zinc ammonic lactate has already been mentioned (p. 215); further examples are sodic-potassic racemate, asparagin, and camphoric acid.

2. A very common method of resolving racemic acids is by combination with an optically active base, *e g.* an alkaloid. In the case of racemic acid itself, *Pasteur* used *l*-cinchonine. The two salts formed are (*a*) *d*-acid + *l*-base, (*b*) *l*-acid + *l*-base. As these two salts are not enantiomorphously related, *i.e.* their molecules do not stand in the relationship of object to mirror-image, they possess different solubilities, and may be separated by fractional crystallization.

The following is a list of some simple racemic compounds which have been resolved by this method; the salt named is the less soluble of the two, and crystallizes first

Acids.—Quinine: *d*-tartrate. Strychnine: *l*-lactate, *d*-methyl-succinate, *d*-methoxy-succinate, *d*-phenyldibromo-propionate. Cinchonine: *l*-tartrate, *d*-malate, *d*-mandelate. Brucine: *d*-tartrate, *l*-valerate, *l*-aspartate.

Racemic bases may be resolved by a similar process, viz. by combination with an optically active acid, *e g d*-tartaric, or even better, *d*-bromocamphor-sulphonic acid, and separating the two salts thus obtained by fractional crystallization. Thus ethyl-piperidine and conine have been resolved by *Ladenburg* by using *d*-tartaric acid (A. 1888, **247**, 85; cf. also *Pope* and *Harvey* on resolution of tetrahydro-β-naphthylamine, J C. S. 1901, 74; also *Pope* and *Peachey*, *ibid.* 1899, 1066 and 1105).

3. The third method consists in subjecting a solution of an ammonium salt of the acid to the action of some of the lower plant organisms, *e.g.* moulds, bacteria, yeasts, &c. Different organisms are required in different cases. *Pasteur* found that ordinary green mould—*Penicillium glaucum*—when grown in a solution of ammonium racemate, destroys the salt of the *d*-acid and leaves a solution of the salt of the *l*-acid. If, however, the decomposition is allowed to proceed, the *l*-salt is also destroyed, the reaction is a preferential decomposition, and, if stopped at a suitable time, practically all *d*-salt will have disappeared. It is obvious that in this method one of the active components is lost; but by using two distinct organisms in separate solutions it is sometimes possible to obtain both *d*- and *l* compounds Thus *Penicillium glaucum* grown in a solution of a salt of *d l*-mandelic acid leaves the *d*-salt, and *Saccharomyces ellipsoideus* leaves the *l*-salt.

Among other resolutions which have been effected by this method may be mentioned the destruction of *l*-lactic, *l*-mandelic, *d*-glyceric, *l*-ethoxy-succinic acids, and of *d*-methylpropyl-carbinol by *Penicillium glaucum*, and the destruction of *d*-mandelic,

l-phenyldibromo-propionic acids and of *d*-glucose, *d*-fructose, and *d*-mannose by yeast (different species).

4. *Marckwald* and *M'Kenzie* (B. 1901, **34**, 469) have suggested another method of resolution, viz. by esterifying the racemic acid with an optically active alcohol. They used *r*-mandelic acid and *l*-menthol, and found that the *d*-component of the racemic acid was esterified somewhat more rapidly than the *l*. (Cf. also *Mackenzie*, J. C. S. 1904, 378.)

5. *Ostromisslensky* (B. 1908, **41**, 3035) has shown that a mixture of *d*- and *l*-isomerides can be easily separated if a supersaturated solution of the mixture is impregnated with a crystal of a suitable active material, thus a crystal of *l*-asparagine (p. 248) immediately produces the deposition of *d*-sodium ammonium tartrate from a supersaturated solution containing the *d*- and *l*-salts. A crystal of any optically active tartrate or of any isomorphous substance will also cause a separation of one of the active sodium ammonium tartrates, the actual salt deposited depending on the activity of the crystal used, *e.g.* *d*-sodium tartrate always deposits *d*-sodium ammonium tartrate. It is not necessary that the impregnating substance should be optically active, it must, however, be isomorphous or isodimorphous. Thus a crystal of glycine can cause the deposition of *l*-asparagine from a supersaturated solution of *d-l* asparagine.

This method of resolution cannot be used when the supersaturated solution contains a definite racemic compound of the *d-l* isomerides, and can thus be used as a method for determining whether the given substance exists in solution as a *d-l* conglomerate or as a true racemic compound.

Racemisation.—When *d*-tartaric acid is heated with a small amount of water at 175° racemic acid is formed, together with a small amount of the meso acid This conversion of an optically active compound into its racemic isomeride is usually termed *racemisation*, and is to be attributed to the transformation of 50 per cent of the original active acid into its optical isomer. As further examples of racemisation, may be mentioned the heating of *d*-valeric acid with concentrated sulphuric acid and of amyl alcohol with sodium hydroxide. When valeric acid is boiled for eighty hours partial racemisation occurs, as is indicated by a slight diminution in its rotatory power. Racemisation often occurs during a chemical reaction; thus *l*-mandelic acid, $C_6H_5 \cdot CH(OH) \cdot CO_2H$, and hydrobromic acid at 50° yield not *l*-phenylbromo-acetic but

r-phenylbromo-acetic acid. (Cf. also *Easterfield*, J. C. S. 1891, 72; *Pope*, *ibid.* 1901, 81, and P. 1900, 116.)

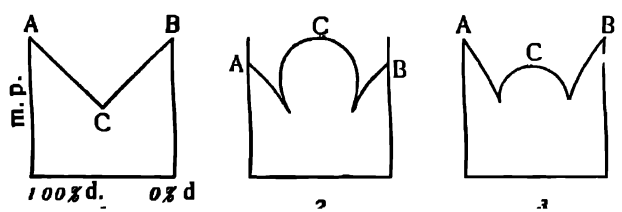
Occasionally the racemisation occurs at the ordinary temperature, and is then termed *autoracemisation*; thus *d*-phenylbromo-acetic acid when kept in benzene solution for some three years becomes quite inactive, and ethyl *d*-bromo-succinate in the course of four years diminishes in rotatory power from +40·96° to +9° (*Walden*, B. 1898, **31**, 1416).

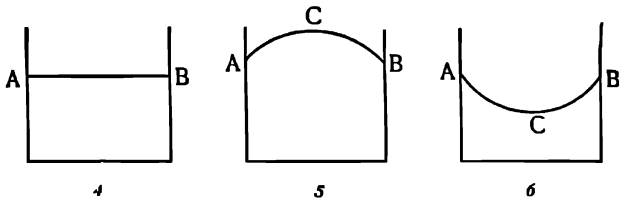
Criteria for Determining the Nature of the Racemic Compound.—The racemic substance may be one of the following.—(*a*) A definite compound of 1 molecule of the *d*-component with 1 of the *l*. (*b*) An ordinary mixture of the two in molecular proportions. (*c*) Mixed crystals, *i.e.* a solid solution of the two isomorphous antipodes without chemical combination. The first are termed racemic compounds proper, the second inactive conglomerates, and the third pseudoracemic compounds (*Kipping* and *Pope*, J. C. S. 1897, 989).

A true racemic compound cannot be recognized by molecular-weight determinations, as in the gaseous form or in solution it is usually resolved into its components. In certain cases the recognition of the substance as a racemic compound is simple, *e.g.* sodic-ammonic racemate, which crystallizes in a different crystallographic system, and contains a different amount of water of crystallization from the active isomers, and possesses a definite transition point.

When such simple criteria are of no use, *Backhuis Roozeboom* (Zeit. Phys. 1899, **28**, 494) recommends a study of the melting-point curves. These are obtained by taking the melting-points of mixtures of the compounds in different proportions, and then plotting the melting-points against the composition. The following types of curves are met with:—

Conglomerates, fig. 1. Racemic compounds, figs. 2 and 3. Mixed crystals, figs. 4, 5, and 6.





4 5 6

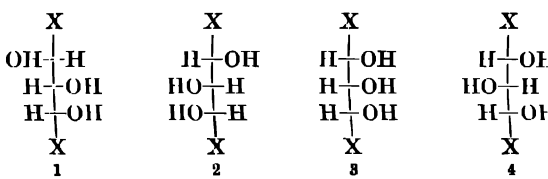
A represents the melting-point of the pure *d* compound, B that of the pure *l*, and C that of the racemic compound or mixture. These curves should be studied by aid of the Phase rule.

E. Polyhydroxy Dibasic Acids

Trihydroxy-glutaric acid, $CO_2H \cdot CH(OH) \cdot CH(OH) \cdot CH(OH) \cdot CO_2H$, and the stereo-isomeric acids—saccharic, mucic, and isosaccharic acid—$CO_2H \cdot CH(OH) \cdot CH(OH) \cdot CH(OH) \cdot CH(OH) \cdot CO_2H$, are the best-known examples

Many of these acids form lactones (p 217), the so-called lactonic acids, and some of them also double lactones (cf. *Fittig*, A. **255**, 1, *et seq.*).

Trihydroxy-glutaric acid, $CO_2H \cdot (CH \cdot OH)_3 \cdot CO_2H$, is a frequent oxidation-product of sugar varieties, *e.g.* of xylose and arabinose According to theory, four stereo-isomers should exist, and four are actually known; they may be represented by the following projection formulæ, where X = CO_2H:—



1 2 3 4

Nos. 1 and 2 are enantiomorphously related and optically active, and can form a racemic compound. Compounds 3 and 4 are inactive substances of the type of mesotartaric acid.

Saccharic acid is produced by the oxidation of cane-sugar, glucose, gulose, gulonic acid, mannitol, or starch by nitric acid, and exists in the *d*-, *l*-, and *r*-forms (see Glucoses), *d*-saccharic acid when reduced yields glycuronic acid (see p. 222). All the three varieties are deliquescent.

Mucic acid is formed by oxidizing dulcitol, the gums, muci-

lages, and milk-sugar. It is a sparingly soluble, colourless, crystalline powder. The molecule being symmetrical in structure, it is optically inactive. It is easily converted into derivatives of furane (see this).

Isosaccharic acid is obtained by the oxidation of glucosamine, $C_6H_{11}O_5(NH_2)$.

Theoretically, ten stereo-isomeric acids of the formula $CO_2H\cdot[CH\cdot OH]_4\cdot CO_2H$ are possible, most of which (*e.g.* **d-** and **i-manno-saccharic acids, talomucic acid,** &c.) have been prepared by *E. Fischer* (B. **24**, 539, 2137, 3622). For their relations to the hexoses, see the table appended to these.

F. Dibasic Ketonic Acids

Dibasic ketonic acids unite in themselves the properties of a ketone and of a dibasic acid. The following are known:—

1. **Mesoxalic acid,** $CO(CO_2H)_2$ or $C(OH)_2(CO_2H)_2$ (see p. 199), is prepared from dibromo-malonic acid, $CBr_2(CO_2H)_2$, and baryta water or oxide of silver, thus.—

$$CBr_2(CO_2H)_2 + H_2O = CO(CO_2H)_2 + 2HBr;$$

also by boiling alloxan (p. 288) with baryta water. It crystallizes in deliquescent prisms ($+H_2O$).

As a ketone it combines with $NaHSO_3$, reacts with hydroxylamine, and is reduced by nascent hydrogen to tartronic acid:

$$CO_2H\cdot CO\cdot CO_2H + 2H = CO_2H\cdot CH(OH)\cdot CO_2H.$$

Since the acid and its salts still retain a molecule of water at temperatures above 100°, this may be united in much the same manner as the water in chloral hydrate, corresponding with the formula $C(OH)_2(CO_2H)_2$, "dihydroxy-malonic acid". In fact, two modifications of the ethyl ester are known, viz. $C(OH)_2(CO_2C_2H_5)_2$ and $CO(CO_2C_2H_5)_2$.

2. **Oxal-acetic acid,** *Butanone diacid,* $CO_2H\cdot CH_2\cdot CO\cdot CO_2H$, is an acid corresponding in many respects with aceto-acetic acid. Its **ethyl ester** is prepared by the action of sodium ethoxide upon a mixture of ethyl oxalate and acetate (p. 224), and also by the action of concentrated sulphuric acid upon ethyl acetylene-dicarboxylate. It is a colourless oil, but the alcoholic solution gives an intense dark-red coloration with ferric chloride. It is of importance as a synthetical reagent, as the hydrogen atoms of the methylene group can be replaced by

sodium, and hence by various alkyl and acyl radicals (*W. Wislicenus*).

3. **Acetone-dicarboxylic acid**, *Pentanone diacid*, $CO(CH_2 \cdot CO_2H)_2$, obtained by treating citric acid with concentrated H_2SO_4, readily decomposes into acetone and $2CO_2$ (see A. **261**, 151).

4. **Dihydroxy-tartaric acid**, $CO_2H \cdot CO \cdot CO \cdot CO_2H$, or probably $CO_2H \cdot C(OH)_2 \cdot C(OH)_2 \cdot CO_2H$, is formed from pyrocatechol and nitrous acid, and by the gradual decomposition of nitro-tartaric acid. It melts at 98°. The characteristic sparingly soluble sodium salt decomposes readily into carbon dioxide and sodium tartronate

5. **Diaceto-succinic acid**, $\begin{matrix} CH_3 \cdot CO \cdot CH \cdot CO_2H \\ CH_3 \cdot CO \cdot CH \cdot CO_2H \end{matrix}$ (see p 229). The ester of this is closely related to acetonyl-acetone, the latter being readily obtainable from the former by the action of caustic-soda solution ("Ketonic decomposition", cf. B. **33**, 1219).

6. **Diacetoglutaric acid**, $CO_2H \cdot CHAc \cdot CH_2 \cdot CHAc \cdot CO_2H$. The ester of this acid is formed by condensing ethyl acetoacetate with formaldehyde in the presence of diethyl amine, and is readily converted into derivatives of tetrahydrobenzene or pyridine (*Knoevenagel*, A. **281**, 94; cf also B **31**, 1388).

Most of these ketonic acids exhibit keto enolic tautomerism, thus 5 isomerides of diacetyl-succinic acid are known (*Knorr*, A. 1899, **306**, 332).

XI. POLYBASIC ACIDS

The polybasic acids contain two or more carboxylic groups in the molecule. The tribasic acids, like phosphoric acid, can give rise to three series of salts—normal, monoacid, and di-acid. Both saturated and unsaturated acids are known, and also substituted derivatives.

A. Saturated and Unsaturated Polybasic Acids

A simple tribasic acid is **tricarballylic acid**, *symmetrical propane-tricarboxylic acid*, $CO_2H \cdot CH_2 \cdot CH(CO_2H) \cdot CH_2 \cdot CO_2H$. It occurs in unripe beet, and is prepared (*a*) by the addition of hydrogen to aconitic acid, (*b*) by heating citric acid with hydriodic acid, and (*c*) synthetically from glycerol by transforming it into the tribromhydrin, $C_3H_5Br_3$, treating this with

KCN, and hydrolysing the cyanide formed, $C_3H_5(CN)_3$. Since the three hydroxyls in glycerol are distributed among three carbon atoms, the same holds good for the carboxyls in the acid, which has, therefore, the symmetrical constitution:

$$CO_2H \cdot CH_2 \cdot CH(CO_2H) \cdot CH_2 \cdot CO_2H.$$

This acid is of importance in determining the constitution of citric acid, from which, as already seen, it can be obtained by reduction with HI. It crystallizes in rhombic prisms, is readily soluble in water, and melts at 166°.

An unsaturated tribasic acid closely related to tricarballylic acid is **aconitic acid**, $CO_2H \cdot CH : C(CO_2H) \cdot CH_2 \cdot CO_2H$, which contains two atoms of hydrogen less than tricarballylic acid. It is found in nature, in *Aconitum Napellus*, shave grass, sugar-cane, beet-root, &c., and is prepared by heating citric acid, $C_6H_8O_7$, when the elements of water are eliminated. It is a strong acid, crystallizable, readily soluble in water, melts at 191°, and is reduced by nascent hydrogen to tricarballylic acid, hence its constitution.

B. Hydroxy Polybasic Acids

Citric acid, *acidum citricum*, *hydroxy-tricarballylic acid*, $CO_2H \cdot CH_2 \cdot C(OH)(CO_2H) \cdot CH_2 \cdot CO_2H$ (*Scheele*, 1784, recognized as tribasic by *Liebig* in 1838), occurs in the free state in lemons, oranges, and red bilberries, and mixed with malic acid in gooseberries, &c., also as calcium salt in woad, potatoes, beet-root, &c. It is usually prepared from the juice of lemons by means of the lime salt It crystallizes in large rhombic prisms ($+ H_2O$), is readily soluble in water, moderately in alcohol, but only sparingly in ether. It loses its water of crystallization at 130°, melts at 153°, and breaks up at a higher temperature first into aconitic acid and water, and then into carbon dioxide, itaconic acid, citraconic anhydride, and acetone. Oxidizing agents effect a very thorough decomposition.

Calcium citrate is precipitated as a white sandy powder when a mixture of calcium chloride and alkali citrate solutions is boiled. The three series of salts are well characterized; the alkali salts are soluble in water, the others mostly insoluble. Among the derivatives may be mentioned **mono-**, **di-**, and **tri ethyl citrates** and **triethyl aceto-citrate**,

$$CO_2Et \cdot CH_2 \cdot C(O \cdot CO \cdot CH_3)(CO_2Et) \cdot CH_2 \cdot CO_2Et.$$

The formation of this last is a direct proof of the alcoholic character of citric acid The amides of citric acid are converted by concentrated H_2SO_4 into **citrazinic acid**, $C_6H_5NO_4$, a pyridine derivative (B. **17**, 2681).

The *constitution* of citric acid is arrived at (*a*) from its conversion into aconitic acid by the elimination of water, (*b*) from its reduction to tricarballylic acid, and (*c*) from its synthesis from 1 : 3 dichloroacetone, *e.g.*:

$$CH_2Cl\cdot CO\cdot CH_2Cl + HCN \rightarrow CH_2Cl\cdot C(OH)(CN)\cdot CH_2Cl \rightarrow CN\cdot CH_2\cdot C(OH)(CN)\cdot CH_2\cdot CN \rightarrow CO_2H\cdot CH_2\cdot C(OH)(CO_2H)\cdot CH_2\cdot CO_2H.$$

The acid has been synthesised by *Lawrence* (J. C. S. 1897, **71**, 457) by an application of *Reformatsky's* reaction, *i.e.* the condensation of a halogen derivative with a ketone in the presence of zinc. The substances used were ethyl bromacetate, ethyl oxalacetate, and pure zinc turnings

$$CO_2Et\cdot CH_2Br + \begin{matrix} CO\cdot CO_2Et \\ CH_2\cdot CO_2Et \end{matrix} + Zn = \begin{matrix} CO_2Et\cdot CH_2\cdot C(OZnBr)\cdot CO_2Et \\ CH_2\cdot CO_2Et. \end{matrix}$$

This condensation product reacts with water, yielding ethyl citrate, $CO_2Et\cdot CH_2\cdot C(OH)(CO_2Et)\cdot CH_2\cdot CO_2Et$, zinc oxide, and hydrogen bromide.

Citric acid is also formed when solutions of glucose are fermented by certain moulds, *e.g. Citromycetes pfefferianus* and *C. glaber* (*Wehmer*, Bull. Soc. Chim 1893 [III], **9**, 728).

Acids containing more than three carboxylic groups do not, as a rule, occur in nature, but a number of esters of such acids have been prepared by means of the aceto-acetic ester and malonic ester syntheses.

XII. CYANOGEN COMPOUNDS

Under the name of the cyanogen compounds is included a group of substances which are derivable from cyanogen, C_2N_2. Cyanogen itself is a gas of excessively poisonous properties which behaves in many respects like a halogen; and its hydrogen compound, hydrocyanic acid, HCN, is an acid re-

sembling hydrochloric acid to a certain extent. In many cyanogen compounds the monovalent group (CN) plays the part of an element; cyanogen is to be regarded as the isolated radical (CN), which, however, possesses the double formula C_2N_2, just as a molecule of chlorine (Cl_2) is made up of two atoms The cyanogen group is further capable of combining with the halogens, hydroxyl, sulphydril (SH), amidogen, &c. From the compounds so obtained numerous others are derived by the entrance of alkyl radicals in place of hydrogen Such derivatives invariably exist in two isomeric forms, sharply distinguished from one another by their properties. They are often termed normal and iso compounds, and the isomerism is of very great interest. (See table, p. 265.)

Polymeric modifications of most of those compounds also exist. The number of cyanogen compounds known is thus a very large one.

Carbon and nitrogen do not combine directly except in the presence of an alkali, and then a metallic cyanide is formed. As examples of this reaction, we have the following:—

1. When nitrogen is led over a red-hot mixture of coal and carbonate of potash, potassium cyanide, KCN, is formed, especially under a high pressure

2 Ammonium cyanide is formed when ammonia is passed over red-hot coal.

3 Potassium cyanide is formed when nitrogenous organic compounds such as leather, horn, claws, wool, blood, &c, are heated with potashes.

4. Hydrocyanic acid is formed when electric sparks are passed through a mixture of acetylene and nitrogen, and also by the action of the silent electric discharge on a mixture of cyanogen and hydrogen It is also formed (commercial method) when a carefully dried mixture of hydrogen, ammonia, and a volatile carbon compound (CO, CO_2, C_2H_2, &c) is passed over heated platinized pumice. (For further modes of formation, see p. 266 *et seq.*)

The original material for the preparation of most of the cyanogen compounds is potassium ferrocyanide, which is manufactured on the large scale and possesses the great advantage over potassium cyanide of being stable in the air and comparatively non-poisonous.

SUMMARY OF THE CYANOGEN COMPOUNDS

Relation to carbonic acid, &c. (See p. 279)	Name	Formula
Nitrile of oxalic acid,	*Cyanogen*,	N:C·C:N
Nitrile of formic acid,	*Hydrocyanic acid*, Alkyl derivatives· (*a*) Nitriles, (*b*) Isonitriles,	N:C·H R·C:N R·N:C
	Cyanogen chloride, bromide, iodide,	N:C·Cl
$CO_3H_2 + NH_3 - 2H_2O$, (Nitrile of carbonic acid, eventually Carbimide),	*Cyanic acid*, Alkyl derivatives: (*a*) Methyl cyanate, (*b*) „ isocyanate,	N:C·OH N:C·O·CH$_3$ O:C:N·CH$_3$
	Thiocyanic acid, Alkyl derivatives: (*a*) Ethyl thiocyanate, (*b*) Allyl isothiocyanate,	N:C·SH N:C·S·C$_2$H$_5$ S:C:NC$_3$H$_5$
$CO_3H_2 + 2NH_3 - 3H_2O$, (Nitrile and amide of carbonic acid, eventually Carbo-di-imide, see p. 277),	*Cyanamide*, Alkyl derivatives: (*a*) Alkyl cyanamide, (*b*) Carbo-di-imide,	N:C·NH$_2$ N:C·NH·R RN:C:NR*
The amic acid of carbonic acid,	*Carbamic acid*,	NH$_2$·CO·OH
The amide of carbonic acid,	*Urea*,	CO(NH$_2$)$_2$
	Thio-urea, Alkyl derivatives: (*a*) Alkyl-thio-ureas, (*b*) Imido-thio-carbamine compounds,	CS(NH$_2$)$_2$ NH$_2$·CS·NHR NH:C$\langle^{NH_2}_{SR}$
$CO_3H_2 + 3NH_3 - 3H_2O$, (Amidine),	*Guanidine*,	HN:C(NH$_2$)$_2$

* R = alkyl radical.

A. Cyanogen and Hydrocyanic Acid

Cyanogen, N⋮C·C⋮N, which was discovered by *Gay-Lussac* in 1815, occurs in the gases of blast-furnaces and in coal gas.

As the nitrile of oxalic acid, it may be obtained by the abstraction of the elements of water from ammonium oxalate by means of P_4O_{10}; also in the same way from the intermediate product of this reaction, oxamide:

$$NH_4O\cdot CO\cdot CO\cdot ONH_4 - 4H_2O = N{\vdots}C\cdot C{\vdots}N,$$
$$NH_2\cdot CO\cdot CO\cdot NH_2 - 2H_2O = N{\vdots}C\cdot C{\vdots}N.$$

It is usually prepared by heating dry silver cyanide, AgCN, or mercuric cyanide, $Hg(CN)_2$, strongly:

$$Hg(CN)_2 = Hg + C_2N_2;$$

or by heating a solution of cupric sulphate with potassium cyanide (B. **18**, Ref. 321).

Cyanogen is a colourless gas of a peculiar unpleasant odour resembling that of bitter almonds, and is terribly poisonous. It is easily liquefied and solidified (sp. gr 1·8 of the liquid; m.-pt. −34°; b.-pt. −21°), is soluble in 0·25 vol. of water and in even less alcohol The solutions become dark upon standing, with separation of a brown powder ("Azulmic acid"), while oxalic acid, ammonia, formic acid, hydrocyanic acid, and urea are to be found in the liquid. The formation of the oxalic acid and ammonia is due to normal hydrolysis, and that of formic acid to the hydrolysis of the hydrocyanic acid formed as an intermediate product. In presence of a minute quantity of aldehyde, oxamide is formed as the result of the addition of water. Cyanogen combines with heated potassium to KCN, and dissolves in aqueous potash to form KCN and KCNO.

Paracyanogen, $(CN)_x$, is a polymer of cyanogen. It is an amorphous brown powder which is formed as a by-product when mercuric cyanide is heated; upon further heating, it is transformed into cyanogen.

Hydrocyanic acid, *prussic acid*, CNH, was discovered about the year 1782 by *Scheele*, and investigated closely by *Gay-Lussac*.

Some of the more interesting methods of formation are the following:—

1. It is readily liberated from its salts by the action of almost any other acid, even carbonic acid; and even complex

cyanides, *e.g.* potassium ferrocyanide, when distilled with moderately dilute sulphuric acid yield hydrogen cyanide:

$$K_4Fe(CN)_6 + 5H_2SO_4 = 6HCN + FeSO_4 + 4KHSO_4.$$

The ferrous sulphate produced reacts with more ferrocyanide to form potassium ferrous ferrocyanide, $FeK_2(FeC_6N_6)$, which is not affected by dilute acids (see p. 269); consequently only half of the cyanogen present is converted into hydrocyanic acid. When concentrated sulphuric acid is employed in place of the dilute, carbon monoxide and not hydrocyanic acid is obtained.

2. As the nitrile of formic acid, it may be prepared by the action of dehydrating agents on ammonium formate or formamide:

$$H{\cdot}CO{\cdot}ONH_4 = H{\cdot}CO{\cdot}NH_2 + H_2O = HCN + 2H_2O.$$

3. Together with oil of bitter almonds, $C_6H_5{\cdot}CHO$, and grape-sugar, $C_6H_{12}O_6$, by the hydrolysis of the glucoside amygdalin under the influence of the enzyme "emulsin" (see Benzaldehyde):

$$C_{20}H_{27}O_{11}N + 2H_2O = CNH + C_7H_6O + 2C_6H_{12}O_6$$

The oil of bitter almonds and its aqueous solution (*aqua amarum amygdalarum*) — prepared from the almonds themselves consequently contain HCN.

The acid occurs in the free state in the tree *Pangium edule*, found in Java, more particularly in the seeds. It exists in the form of glucosides in various plants (C. C. 1906, ii, 1849, 1909, i, 387)

4. By the action of ammonia and chloroform on alcoholic potash under pressure. Cf. p. 103.

For other syntheses, see p. 264.

Hydrogen cyanide is a colourless liquid boiling at 25° and solidifying at −12°. Sp. gr. 0·70. It has a peculiar odour and produces an unpleasant irritation in the throat, is miscible with water, and burns with a violet flame. Like potassium cyanide, it is one of the most terrible of poisons. The best antidotes are stated to be hydrogen peroxide or small quantities of chlorine mixed with air. When absolutely pure it can be preserved unchanged, but it decomposes in presence of traces of water or ammonia, with separation of a brown mass and formation of ammonia, formic acid, oxalic acid, &c. The addition of minute quantities of mineral acids renders the aqueous solution more stable.

Liquid hydrocyanic acid is a good solvent for many salts, and has a high ionizing power. Acids (sulphuric and trichloroacetic), however, do not appear to dissociate when dissolved in the liquid.

The acid has many properties of an unsaturated compound. It is readily reduced by nascent hydrogen to methylamine. In the presence of hydrochloric acid it combines with water yielding formamide. With diazomethane (Chap. LI) it yields methyl cyanide together with methyl carbylamine. With hydrogen chloride it gives *iminoformyl chloride*, NH:CHCl, a compound of importance in the synthesis of aromatic aldehydes (A. 1906, **347**, 347); but has not been isolated. From ethyl acetate solution a product 2HCN, 3HCl = NH:CH·NH·$CHCl_2$, HCl, dichloromethyl formamidine hydrochloride is obtained. It combines directly with most aldehydes and ketones, yielding cyanhydrins (nitriles of hydroxy acids), (p. 206), and also with certain unsaturated compounds, especially in the presence of potassium cyanide, yielding saturated nitriles (*Lapworth*, J. C. S. 1903, 995; 1904, 1214; *Knoevenagel*, B. 1904, **37**, 4065); *e.g.* α-phenylcinnamo-nitrile, CHPh:CPh·CN, yields diphenylsuccinylo-nitrile, CN·CHPh·CHPh·CN.

Hydrocyanic acid is an extremely weak monobasic acid ($K = 0{\cdot}0013 \times 10^{-6}$), and its salts are decomposed even by carbonic acid. It is a typical tautomeric compound. Its reduction to an amine and its hydrolysis to formic acid are similar to the corresponding reactions of methyl cyanide, and it might be urged that these reactions favour the nitrile formula H·C:N. Both reactions are, however, compatible with the view that it has the carbylamine structure H·N:C. The salts are usually regarded as carbylamine derivatives (see derivatives of divalent carbon, Chap. L, D), and it might be argued that the free acid has a similar structure. Such an argument is, however, unsound, as numerous examples are known where salts have a structure quite different from that of the acid from which they are prepared (cf. ethyl acetoacetate and pseudo acids).

Hydrocyanic acid can be detected by converting it either into Prussian blue or into ferric thiocyanate. In the former case the solution to be tested is treated with excess of caustic soda and some ferrous and ferric salt, boiled, and acidified, when Prussian blue results; in the latter the solution is evaporated to dryness together with a little yellow sulphide

of ammonium, the residue taken up with water and ferric chloride added, when the blood-red colour of ferric thiocyanate is obtained

Trihydrocyanic acid, $(CNH)_3$, results from the polymerization of hydrocyanic acid under certain specified conditions. It forms white, acute-angled crystals, which readily yield hydrogen cyanide when heated above 180°. Its molecular weight is still unknown.

Cyanides.— The cyanides of the alkali and alkali-earth metals are soluble in water, and the solutions have a strongly alkaline reaction due to the hydrolysing action of the water (cf. Soaps, p. 159). The salts of the heavy metals, with the exception of mercuric cyanide, are insoluble in water.

Potassium cyanide, KCN, forms colourless deliquescent cubes, sparingly soluble in alcohol. The commercial product usually contains large amounts of potassium carbonate due to the action of atmospheric carbon dioxide. It is formed when potassium ferrocyanide is fused, and the product extracted with water·

$$K_4FeC_6N_6 = 4KCN + FeC_2 + N_2.$$

Large quantities are manufactured by *Bellby's* process, which consists in treating a fused mass of potassium carbonate and carbon with ammonia, the product being a molten cyanide of high strength. The pure salt can be prepared by passing hydrogen cyanide into an alcoholic solution of potassium hydroxide. It reacts with hydrogen peroxide in two different ways (cf. *Masson*, J. C. S. 1907, 1449):

1. 80 % $KCN + H_2O_2 \rightarrow KCNO + H_2O$ and
   $KCNO + 2H_2O \rightarrow NH_4 + KOH + CO_2$;
2. 20 % $KCN + 2H_2O \rightarrow NH_3 + H\cdot COOK$.

Mercuric cyanide, $Hg(CN)_2$, crystallizes in colourless prisms, is stable in the air, readily soluble in water, and excessively poisonous. Its aqueous solution is a non-conductor of the electric current, and does not give the ordinary reactions for a mercuric salt or for a cyanide (cf. B. 1908, **41**, 317). **Argentic cyanide**, AgCN, forms a white flocculent precipitate closely resembling argentic chloride in appearance, but is soluble in hot concentrated nitric acid.

Complex Cyanides.—The double cyanides, which are produced by dissolving the insoluble metallic cyanides in a solution of potassium cyanide, are divided into two classes. The

members of the one class are decomposed again on the addition of dilute mineral acids, with separation of the insoluble cyanide and formation of hydrocyanic acid, *e.g.* $KAg(CN)_2$; $K_2Ni(CN)_4$. The members of the other class are much more stable, do not evolve hydrocyanic acid, and comport themselves as salts of particular acids; to this class belong **potassium ferrocyanide**, $K_4Fe(CN)_6$, $[Fe(CN)_2, 4KCN]$, and **potassium ferricyanide**, $K_3Fe(CN)_6$, $[Fe(CN)_3, 3KCN]$. The members of this second class are often termed **complex salts**, and are the metallic salts of complex acids, *e.g.* **hydroferrocyanic acid**, $H_4FeC_6N_6$, and **hydroferricyanic acid**, $H_3FeC_6N_6$, which are formed when the salts are decomposed with mineral acids. Certain salts of the latter acid are not decomposed at all by dilute acids, for instance Prussian blue, but they are by caustic potash (which converts Prussian blue into $Fe(OH)_3$ and $K_4FeC_6N_6$).

These complex salts, as a rule, do not give the reactions characteristic of simple cyanides, *e.g.* white precipitate with silver-nitrate solution, owing to the fact that in solution they do not yield the simple cyanide ions $\bar{C}N$ but the more complex anions $\bar{F}eC_6N_6$ and $\bar{F}eC_6N_6$.

Potassium ferrocyanide, *yellow prussiate of potash*, $K_4Fe(CN)_6 + 3H_2O$, may be obtained by adding excess of potassium cyanide to a solution of ferrous sulphate, or by dissolving iron in a solution of cyanide of potassium, when hydrogen is evolved, thus:—

$$2KCN + Fe + 2H_2O = Fe(CN)_2 + 2KOH + H_2;$$
$$Fe(CN)_2 + 4KCN = K_4Fe(CN)_6.$$

The old commercial method consisted in fusing together scrap-iron, nitrogenous organic matter, and crude potassic carbonate.

It is now usually manufactured from the hydrogen cyanide present in crude coal gas or the gas from coke ovens. The spent oxide used in the purification of coal gas contains Prussian blue (ferric ferrocyanide, p. 271). The spent oxide is heated with hot milk of lime, and the Prussian blue thus transformed into calcium ferrocyanide, from which the potassium salt can be prepared.

Another method consists in passing the coal gas, before it has been subjected to dry purification, through an alkaline solution containing an iron salt. The sulphuretted hydrogen reacts with the iron salt, forming ferrous sulphide, and this

with the hydrogen cyanide and alkali (potassium carbonate) yields potassium ferrocyanide:

$$FeS + 6HCN + 2K_2CO_3 = K_4FeC_6N_6 + H_2S + 2CO_2 + 2H_2O.$$

It forms large, lemon-coloured monoclinic plates, which are stable in the air and easily soluble in water, but insoluble in alcohol. Concentrated HCl yields **hydro-ferrocyanic acid**, $H_4FeC_6N_6$, in the form of white needles. With a solution of $CuSO_4$, a red-brown precipitate of **cupric ferrocyanide**, or *Hatchett's* brown, $Cu_2FeC_6N_6$, is thrown down, and with solutions of ferrous and ferric salts the well-known characteristic precipitates (see below) Chlorine oxidizes it to

Potassium ferricyanide, *red prussiate of potash*, $K_3FeC_6N_6$, thus:—

$$2K_4FeC_6N_6 + Cl_2 = 2K_3FeC_6N_6 + 2KCl$$

This crystallizes in long, dark-red, monoclinic prisms which are readily soluble in water. The solution decomposes when kept, and acts as a strong oxidizing agent in the presence of alkali, potassium ferrocyanide being reproduced.

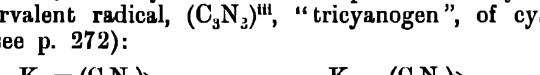
Hydro-ferricyanic acid, $H_3FeC_6N_6$, forms brown needles and is easily decomposed

FERRO- AND FERRI-CYANIDES OF IRON

	Ferrocyanides	Ferricyanides.
Ferrous salts,	Potassium-ferro-ferrocyanide, $K_2Fe^{II}(FeC_6N_6)^{IV}$, from $FeSO_4$ + $K_4FeC_6N_6$; white, becoming rapidly blue in the air from conversion into	*Turnbull's* blue, $Fe_3^{II}(FeC_6N_6)_2^{III}$, from $FeSO_4$ (excess) + $K_3FeC_6N_6$.
Ferric salts,	Potassium-ferri-ferrocyanide, $KFe^{III}(FeC_6N_6)$, or soluble Prussian blue, which is also formed from ferrous sulphate with an excess of potassic ferricyanide.	($FeCl_3$ + $K_3FeC_6N_6$ give no precipitate, but only a brown coloration.)
	Insoluble Prussian blue or *Williamson's* blue, $Fe_4^{III}(FeC_6N_6)_3^{IV}$, from $FeCl_3$ + $K_4FeC_6N_6$; blue powder with a copper glance.	

The formation of Prussian blue was first observed by *Diesbach* about the year 1700.

As regards the *constitution* of hydro-ferro- and hydro-ferricyanic acids, one may make the assumption that they contain the tervalent radical, $(C_3N_3)^{III}$, "tricyanogen", of cyanuric acid (see p. 272):



Potassium ferrocyanide — Potassium ferricyanide



Turnbull's blue

When ferrocyanide of potassium is oxidized by nitric acid, **nitro-prussic acid** is formed, the sodium salt of which, $Na_2FeC_5N_5(NO) + 2H_2O$, crystallizes in red prisms soluble in water. It forms a valuable reagent for the detection of sulphuretted hydrogen, an alkaline solution yielding with the latter a splendid but transient violet coloration.

B. Halogen Compounds of Cyanogen

Cyanogen chloride, Cl·N:C (*Berthollet*), is a colourless condensable gas of a most obnoxious pungent odour, is somewhat soluble in water, and boils at 15·5°. It is prepared by the action of chlorine upon mercuric cyanide or upon dilute aqueous hydrocyanic acid, $CNH + Cl_2 = CNCl + HCl$. It polymerizes readily to cyanuric chloride, and yields sodium chloride and cyanate with aqueous sodium hydroxide:

$$CN\cdot Cl + 2NaOH = CN\cdot ONa + ClNa + H_2O.$$

Cyanogen bromide, CNBr, forms transparent prisms, and is prepared by the action of sulphuric acid on a mixture of bromate, bromide, and cyanide of sodium:

$$HBrO_3 + 5HBr + 3HCN = 3BrCN + 3HBr + 3H_2O.$$

Cyanogen iodide, CNI, forms beautiful white prisms, smelling intensely both of cyanogen and iodine, and subliming with the utmost ease. (For constitution cf. *Chattaway* and *Wadmore*, J. C. S. 1902, 191.)

Cyanuric chloride, *trichlorocyanogen*, $(CCl)_3N_3$, is obtained from cyanogen chloride, or from hydrocyanic acid and chlorine in ethereal solution It forms beautiful white crystals of an unpleasant pungent odour, melts at 145°, and boils at

190°. Boiling water decomposes it with formation of hydrogen chloride and cyanuric acid

C. Cyanic and Cyanuric Acids

Cyanuric acid is formed when urea is heated, either alone or in a stream of chlorine gas; and when this acid is distilled, and the vapour condensed in a freezing-mixture, **cyanic acid**, CNOH, is obtained as a mobile liquid of a pungent odour.

$$C_3N_3O_3H_3 = 3CNOH$$

It is exceedingly unstable; when taken out of the freezing-mixture it changes, with explosive ebullition, into a white porcelain-like mass which consists of cyanuric acid 70 per cent, and cyamelide 30 per cent. **Potassium cyanate**, CNOK, frequently also termed potassium isocyanate, is prepared by the oxidation of an aqueous solution of potassium cyanide by means of permanganate (A. **259**, 377), or by fusing potassium cyanide or yellow prussiate of potash with PbO_2 or MnO_2 ($CNK + O = CNOK$). It crystallizes in white plates, readily soluble in water and alcohol. **Ammonium cyanate**, CNO(NH_4), forms a white crystalline mass, and is of especial interest on account of the readiness with which it changes into the isomeric urea, $CO(NH_2)_2$, (p. 281).

When these salts are decomposed with mineral acids, free cyanic acid is not formed, but its products of hydrolysis, viz. carbon dioxide and ammonia:

$$CONH + H_2O = CO_2 + NH_3.$$

This decomposition is avoided by the addition of dilute acetic acid (instead of hydrochloric), but in the latter case the cyanic acid changes into its polymer cyanuric acid, and the hydrogen-potassium salt of the latter slowly crystallizes out.

When the hydrogen atom in the cyanic acid molecule is replaced by alkyl radicals, two distinct groups of compounds are possible. The derivatives which are constituted on the type N:C·O·R are termed the *normal*, and those on the type O:C:N·R the *iso-compounds*.

Ethyl isocyanate, *cyanic ether*, O:C:N·CH_2·CH_3, obtained when potassium cyanate is distilled with ethyl iodide or potassium ethyl-sulphate, is a colourless liquid of suffocating odour, distilling at 60°, and is decomposed by water. It does

not behave as a typical ester, since when hydrolysed with acids or alkalis it yields ethylamine and carbon dioxide:

$$O{:}C{:}\,NEt + H_2O = NH_2Et + CO_2.$$

Water, which acts in a similar manner, gives rise to the more complicated urea derivatives; ammonia and amines also produce derivatives of urea, and alcohol yields derivatives of carbamic acid (see Carbonic Acid Derivatives).

The production of ethylamine as one of the products of hydrolysis is usually regarded as a strong argument in favour of the view that in the original isocyanate the ethyl group is attached to nitrogen and not to oxygen, *e.g.* O:C:N·Et. It is questionable, however, whether free cyanic acid and cyanate of potassium possess analogous constitutions, since frequent observations have shown that the normal cyanic compounds readily change into the iso- (see below); theoretical considerations indeed make it more probable that cyanic acid has the constitution N:C·OH, according to which it appears as the normal acid, with cyanogen chloride as its chloride.

Normal cyanic esters are not known (cf. A. **287**, 310)

Cyanuric acid, $C_3N_3O_3H_3$, $= (CN)_3(OH)_3$ (*Scheele*), obtained by heating urea, or by the action of water on cyanuric chloride, forms transparent prisms containing two molecules of water of crystallization. It effloresces in the air, and dissolves readily in hot water. It is a tribasic acid. The sodium salt is sparingly soluble in conc. NaOH; the ($Cu{\cdot}NH_4$) salt possesses a characteristic beautiful violet colour. Upon prolonged boiling with hydrochloric acid it is hydrolysed to CO_2 and NH_3, while phosphorus pentachloride converts it into cyanuric chloride.

Only one cyanuric acid is known, and owing to the fact that the N-methyl derivative is obtained by the action of diazo-methane is represented by the iso-structure:

$$O{:}C\begin{<}{NH\cdot CO \atop NH\cdot CO}\end{>}NH.$$

(Compare also *Hantzsch*, B. 1906, **39**, 139).

Cyanuric acid is a pseudo acid, as its salts and also chloride have the normal structure. The mercuric salt exists in two isomeric forms.

Two distinct groups of alkyl derivatives are, however, known—**normal cyanuric esters,** *e.g.* **ethyl cyanurate,**

$$EtO\cdot C\begin{<}{N - C(OEt) \atop N = C(OEt)}\end{>}N,$$

which is formed by the action of ethyl iodide on silver cyanurate at the ordinary temperature, or by the action of sodium ethoxide on cyanogen chloride or cyanuric chloride, is readily changed into an **isocyanuric ester**, *e.g.* **ethyl isocyanurate**,

$$CO\langle \begin{matrix} NEt-CO \\ NEt-CO \end{matrix} \rangle NEt.$$

These isocyanurates are often formed instead of the normal compounds if the temperature is not kept low, *e.g.* when a cyanurate is heated with potassium ethyl-sulphate. They are further formed by the polymerization of the isocyanic esters, being thus obtained as by-products in the preparation of the latter.

The constitution of the normal compounds is largely based on the fact that on hydrolysis they behave as normal esters and yield ethyl alcohol and cyanuric acid. The isocyanurates, on the other hand, usually yield primary amines, *e.g.* ethylamine, and hence presumably the alkyl group is attached to nitrogen in the isocyanurate molecule.

For mixed normal iso-esters, see *Hantzsch* and *Bauer*, B. 1905, **38**, 1005.

D. Thiocyanic Acid and its Derivatives

Nearly every oxygen derivative of cyanogen has a sulphur analogue. As examples, we have the salts of thiocyanic acid.

Potassium thiocyanate, *-sulphocyanate*, *-sulphocyanide*, *-rhodanide*, CNSK, is readily formed when potassium cyanide is fused with sulphur, or when an aqueous solution of KCN is evaporated with yellow ammonium sulphide.

It is usually prepared by fusing potassium ferrocyanide with sulphur and potashes. It forms long colourless deliquescent prisms, extremely soluble in water with absorption of much heat, and also readily soluble in hot alcohol. **Ammonium thiocyanate**, $CNS(NH_4)$, is formed when a mixture of carbon disulphide, concentrated ammonia, and alcohol (*Millon*) is heated, dithiocarbamate and trithiocarbonate of ammonia being formed as intermediate products:

$$CS_2 + NH_3 = CNSH + H_2S.$$

It forms colourless deliquescent plates, readily soluble in alcohol, and when heated to 130°–140° is partially transformed

into the isomeric thio-urea, just as ammonium cyanate is into urea. It precipitates **silver thiocyanate**, CNSAg (white), from solutions of silver salts, and is therefore employed in the titration of silver, with ferric sulphate as indicator, and it gives with ferric salts a dark blood-red coloration of **ammonium ferrithiocyanate**, $2\,Fe(CNS)_3$, $9\,NH_4CNS$, $4\,H_2O$. This last reaction is exceedingly delicate. **Mercurous thiocyanate**, HgCNS, is a white powder insoluble in water, which increases enormously in volume upon being burnt (Pharaoh's serpents). The free **thiocyanic acid**, CNSH, as obtained by decomposing the mercurous salt with hydrochloric acid, is a pale-yellow liquid of pungent odour, but when pure is a colourless solid, m.-pt. 5°. The acid and its salts appear to have the normal structure H·S·C:N. At the ordinary temperature it polymerizes to a yellow amorphous substance, and decomposes in concentrated aqueous solution, with formation of **persulphocyanic acid**, $C_2N_2S_3H_2$ (yellow crystals).

Concentrated sulphuric acid decomposes the thiocyanates with formation of carbon oxy-sulphide: $CNSH + H_2O = COS + NH_3$, sulphuretted hydrogen decomposes them into carbon disulphide and ammonia: $CNSH + H_2S = CS_2 + NH_3$.

The alkyl derivatives of thiocyanic acid exist in two distinct forms, corresponding with the normal and iso-cyanates

Normal Thiocyanates.—**Ethyl thiocyanate**, N:C·S·CH_2·CH_3, is obtained either (1) by the distillation of potassium ethyl-sulphate with potassium thiocyanate, or (2) by the action of cyanogen chloride upon ethyl mercaptide. It is a colourless liquid with a peculiar pungent odour of leeks, boils at 142°, and is almost insoluble in water. Alcoholic potash hydrolyses it in the normal manner, yielding ethyl alcohol and potassium thiocyanate; in other reactions, however, the alkyl radical remains united to sulphur, thus nascent hydrogen reduces it to mercaptan, and fuming nitric acid oxidizes it to ethyl-sulphonic acid.

These reactions, combined with its formation from a mercaptide, indicate that the ethyl group is directly attached to sulphur, viz. $C_2H_5·S·C:N$.

Allyl thiocyanate, N:C·S·C_3H_5, is a colourless liquid smelling of leeks. It boils at 161°, and when distilled is converted into the isomeric mustard oil.

The **iso-thiocyanates** are usually known as mustard oils, and are more stable than the normal thiocyanates. They contain the alkyl radical attached to nitrogen, and not to

sulphur (cf. Isocyanates), since on hydrolysis they yield primary amines, *e.g.*:

$$S{:}C{:}NEt + 2H_2O = H_2S + CO_2 + NH_2Et,$$

and also on reduction:

$$S{:}C{:}NEt + 4H = NH_2Et + CH_2S.$$

The thiomethylene formed in this last reaction immediately polymerizes to $(CH_2S)_3$. The commonest iso-thiocyanate is **allyl mustard oil**, commonly known as mustard oil, since the odour and taste of mustard seeds (*Sinapis niger*) are due to this compound. It does not exist as such in the seeds, but is formed from a glucoside, **potassium myronate**, when the seeds are pulverized and left in contact with water. The reaction is a process of fermentation, and is due to the presence of an enzyme, **myrosin**, in the seeds:

$$C_{10}H_{18}O_{10}NS_2K = C_6H_{12}O_6 + KHSO_4 + SCNC_3H_5$$

It is a liquid sparingly soluble in water and of exceedingly pungent odour, which produces blisters on the skin, and boils at 151°. It is also obtained by distilling allyl thiocyanate, owing to a molecular rearrangement, or by the action of carbon disulphide upon allylamine:

$$CS_2 + NH_2{\cdot}C_3H_5 = CS{:}N{\cdot}C_3H_5 + H_2S$$

This reaction proceeds in two stages, a dithiocarbamate, $C_3H_5NH{\cdot}CS{\cdot}SNH_3C_3H_5$, the allylamine salt of allyl-dithiocarbamic acid being first formed, and this is changed into allyl iso-thiocyanate when distilled with mercuric chloride. (See Dithiocarbamic acid, p. 296.)

Ethyl iso-thiocyanate, $C_2H_5N{:}CS$ (b.-pt. 134°), and **methyl iso-thiocyanate**, $CH_3N{:}CS$ (solid, m.-pt. 34°, b.-pt. 119°), &c., closely resemble the allyl compound, and are obtained in an analogous manner by the action of carbon disulphide upon ethylamine, methylamine, &c.

The mustard oils are also obtained by distilling alkylated thio-ureas (p. 297) with syrupy phosphoric acid (*Hofmann*, B. **15**, 985), or with concentrated hydrochloric acid.

E. Cyanamide and its Derivatives

The Amide of Cyanic Acid.—Cyanamide, $N{:}C{\cdot}NH_2$, is formed by leading cyanogen chloride into an ethereal solution

of ammonia, $CNCl + 2NH_3 = CN \cdot NH_2 + NH_4Cl$, or by the action of HgO upon thio-urea in aqueous solution ("desulphurization"), $NH_2 \cdot CS \cdot NH_2 = NC \cdot NH_2 + H_2S$.

It is a colourless crystalline hygroscopic mass, readily soluble in water, alcohol, and ether. It melts at 40°, and when heated to 150° changes into the polymeric dicyan-diamide with explosive ebullition; the same change occurs on evaporating its solution or allowing it to stand. Dilute acids cause it to take up the elements of water, with formation of urea:

$$\begin{matrix} N{:}C \cdot NH_2 \\ + H_2O \end{matrix} = CO\!<\!\begin{matrix} NH_2 \\ NH_2 \end{matrix};$$

and it combines in an analogous manner with hydrogen sulphide to thio-urea. When heated with ammonium salts, it yields salts of guanidine.

Cyanamide behaves as a weak base, forming crystalline, easily decomposable salts with acids and, at the same time, as a weak acid, yielding a sodium salt, $CN \cdot NHNa$, a lead and a silver salt, &c. The last is a yellow powder, and has the composition CN_2Ag_2.

The calcium derivative of cyanamide, $N{:}C \cdot NCa$, is manufactured for use as a fertilizer, as, in the soil, the nitrogen becomes available for the plant in the form of ammonia. It is manufactured by passing air or nitrogen over calcium carbide at about 800°–1000°,

$$CaC_2 + N_2 = CaCN_2 + C,$$

or by passing nitrogen over a mixture of lime and carbon heated to 2000°. An excess of carbon is used, and the crude product, which forms a black powder, contains 14–23 per cent of nitrogen (cf. Abs. 1904, i. 562). The presence of a small amount of calcium chloride accelerates the absorption of nitrogen by calcium carbide.

Cyanamide also gives rise to two isomeric series of alkyl derivatives.

1. **Methyl-** and **ethyl-cyanamides** are prepared from methyl and ethyl thio-urea. **Diethyl-cyanamide**, $CN_2(C_2H_5)_2$, and its homologues are obtained by the action of alkyl iodides or sulphates on crude calcium cyanamide (B. 1911, **44**, 3149). Acids hydrolyse the ethyl compound to CO_2, NH_3, and $NH(C_2H_5)_2$, hence it possesses the constitution $N{:}C \cdot N(C_2H_5)_2$:

$$N{:}C \cdot N(C_2H_5)_2 + 2H_2O = NH_3 + CO_2 + NH(C_2H_5)_2.$$

2. Other cyanamide derivatives, which are chiefly known in the aromatic series, are derived from a hypothetical isomer of cyanamide, viz. carbo-di-imide, $NH:C:NH$, for instance, **diphenyl-carbodiimide**, $CN_2(C_6H_5)_2$. Boiling with acids likewise decomposes them into CO_2 and an amine, but the latter can only be a primary one.

XIII. CARBONIC ACID DERIVATIVES

Carbonic acid is a dibasic acid, forming two series of salts, *e.g.* Na_2CO_3 and $NaHCO_3$. The acid itself, CO_3H_2, $= O:C<^{OH}_{OH}$, is unknown, but may be supposed to exist in the aqueous solution. It is the lowest hydroxy-acid $C_nH_{2n}O_n$, *i.e.* it is homologous with glycollic acid, and may be regarded as hydroxy-formic acid. As both hydroxyls are linked to the same carbon atom, the non-existence of the free hydrate is readily understood (see p. 124, &c.).

The salts of carbonic acid and several simple derivatives of carbon are usually treated of under inorganic chemistry. The esters, chlorides, and amides of carbonic acid, like the salts, form two series. The **normal** compounds, *e.g.* $CO(OC_2H_5)_2$, ethyl carbonate, $COCl_2$, carbonyl chloride, and $CO(NH_2)_2$, carbamide or urea, are well characterized, and are very similar to those of oxalic or succinic acid; the **acid** compounds, *e.g.* $OH\cdot CO\cdot OC_2H_5$, ethyl hydrogen carbonate, $OH\cdot CO\cdot Cl$, chloro-carbonic or chloroformic acid, and $OH\cdot CO\cdot NH_2$, carbamic acid, on the other hand, are unstable in the free state, but form stable salts. Many mixed derivatives are known, *e.g.* ethyl carbamate, $NH_2\cdot CO\cdot OEt$, which is an ester and an acid amide, analogous to oxamethane (p. 236); $Cl\cdot CO\cdot OC_2H_5$, ethyl chloro-carbonate, which is an ester and an acid chloride.

A. Esters

Ethyl carbonate, $CO(OC_2H_5)_2$, is formed by the action of ethyl iodide upon silver carbonate, or by the action of alcohol upon ethyl chloro-carbonate, and therefore indirectly from carbon oxy-chloride and alcohol:

$$Cl\cdot CO\cdot OC_2H_5 + C_2H_5OH = CO(OC_2H_5)_2 + HCl.$$

It is a neutral liquid of agreeable odour, lighter than water, and boils at 126°.

Analogous **methyl** and **propyl esters** are known, and also esters containing two different alkyl groups. It is a matter of no consequence which of these radicals is introduced first into the molecule, a proof of the symmetrical arrangement of the two hydroxyls.

Ethyl hydrogen carbonate, $HO \cdot CO \cdot O \cdot C_2H_5$, a type of an acid ester, corresponds exactly with ethyl hydrogen sulphate, but is much less stable, and only known in its salts. **Potassium ethyl carbonate**, $KO \cdot CO \cdot OC_2H_5$, is obtained by passing CO_2 into an alcoholic solution of potassic ethoxide: $CO_2 + KOC_2H_5 = CO_3(C_2H_5)K$. It crystallizes in glistening mother-of-pearl plates, but is decomposed by water into potassium carbonate and alcohol.

B. Chlorides of Carbonic Acid

Carbon oxy-chloride, *Carbonyl chloride*, *phosgene*, $COCl_2$ (*J. Davy*), is the true chloride of carbonic acid and is analogous to sulphuryl chloride, SO_2Cl_2. It is obtained by the direct combination of carbon monoxide and chlorine in sunlight, and also by the oxidation of chloroform by means of chromic acid. It is a colourless gas, condensing to a liquid below + 8°, of exceptionally suffocating odour, and is readily soluble in benzene or toluene. As an acid chloride it decomposes violently with water into CO_2 and HCl. It therefore transforms hydrated acids into their anhydrides, with separation of water, and converts aldehyde into ethylidene chloride. It yield urea derivatives with secondary amines of the fatty series, and carbamic chlorides with secondary amines of the aromatic (B. **20**, 783).

Chloro-carbonic acid, *Chloro-formic acid*, $Cl \cdot CO \cdot OH$, the half acid chloride of carbonic acid, is analogous to chloroxalic acid (p. 234), but is so unstable that it is unknown in the free state. Its **esters**, however, *e.g.* **ethyl chloro-carbonate**, **ethyl chloro-formate**, $Cl \cdot CO \cdot OC_2H_5$, may be prepared by the action of carbon oxy-chloride upon alcohols (*Dumas*, 1833):

$$COCl_2 + C_2H_5OH = Cl \cdot CO \cdot OC_2H_5 + HCl.$$

The ethyl ester is a volatile liquid of very pungent odour, which boils at 93°. It reacts as an acid chloride, being decom-

posed by water, and is specially fitted to effect the synthetical entrance of the carboxyl group into many compounds

The esters and acid chlorides just described are derived from ordinary carbonic acid, H_2CO_3, the analogue of metasilicic acid, H_2SiO_3. Although an ortho-carbonic acid itself, $C(OH)_4$, is unknown, certain derivatives are readily prepared **Carbon tetrachloride** may be regarded as the chloride of ortho-carbonic acid. It is much more stable than ordinary acid chlorides, and at high temperatures only is it decomposed by alkalis, yielding alkali chloride and carbonate.

The esters of ortho-carbonic acid, *e.g.* **ethyl ortho-carbonate**, $C(OC_2H_5)_4$, are readily obtained by the action of sodium alcoholates on chloropicrin (p. 97) They are colourless oils with fragrant odours. The **ethyl** ester boils at 158°, and the **propyl** at 224°. When hydrolysed, they yield an alkali carbonate and the alcohol.

C Amides of Carbonic Acid

The normal amide of carbonic acid is **urea** or **carbamide**, $NH_2 \cdot CO \cdot NH_2$, the amic acid is **carbamic acid**, $HO \cdot CO \cdot NH_2$. **Imido-carbonic acid**, $HN:C(OH)_2$, would be an imide of carbonic acid, but it is only known in its derivatives (*Sandmeyer*, B. **19**, 862).

The amidine of carbonic acid is **guanidine**. The "ortho-amide" of carbonic acid, which would possess the formula $C(NH_2)_4$, is unknown; when it might be expected, guanidine and ammonia are formed instead.

The modes of *formation* of urea and of carbamic acid are exactly analogous to those of the amides in general:

1. By the action of ammonia upon ethyl carbonate:

$$CO(OC_2H_5)_2 + 2NH_3 = CO(NH_2)_2 + 2C_2H_5 \cdot OH.$$
$$CO(OC_2H_5)_2 + NH_3 = NH_2 \cdot CO \cdot OC_2H_5 + C_2H_5OH.$$

2. By the abstraction of the elements of water from carbonate or carbamate of ammonia. Dry carbon dioxide and ammonia combine together directly to ammonium carbamate, the so-called anhydrous carbonate of ammonia, $NH_2 \cdot CO \cdot ONH_4$, which is transformed into urea when heated to 135°, or when exposed to the action of an alternating current of electricity:

$$NH_2 \cdot CO \cdot ONH_4 = CO(NH_2)_2 + H_2O.$$

3. By the action of ammonia upon carbonyl chloride and its derivatives:

$$COCl_2 + 4NH_3 = CO(NH_2)_2 + 2NH_4Cl.$$
$$CO(OC_2H_5)Cl + 2NH_3 = CO(OC_2H_5)NH_2 + NH_4Cl.$$

Carbamic acid, $NH_2 \cdot CO \cdot OH$, is known only in the form of derivatives; the *ammonium* salt, $NH_2 \cdot CO \cdot ONH_4$, forms a white mass, and dissociates at 60° into $2NH_3 + CO_2$. Its aqueous solution does not precipitate a solution of calcic chloride at the ordinary temperature, since calcic carbamate is soluble in water; but when boiled it is hydrolysed to the carbonate, and calcic carbonate is then thrown down.

Urethane, *Ethyl carbamate*, $NH_2 \cdot CO \cdot OC_2H_5$, is formed according to method 3, and by the direct union of cyanic acid with alcohol; also from urea nitrate and sodium nitrite in presence of alcohol. It forms large plates, is readily soluble in water, melts at 50°, and boils at 184°. It acts as a soporific, and on hydrolysis with alkali yields the alkali carbonate, ammonia and ethyl alcohol. One of its hydrogen atoms is replaceable by sodium. Urethane may be employed instead of cyanic acid for certain synthetic reactions (B. **23**, 1856).

Analogous **methyl** and **propyl esters** of carbamic acid are known, and are also termed urethanes.

Carbamic chloride, $NH_2 \cdot CO \cdot Cl$, obtained by the action of hydrogen chloride upon cyanic acid (*Wohler*, A. **45**, 357), and of carbonyl chloride upon ammonium chloride at 400°, forms long, compact, colourless needles of pungent odour. M.-pt. 50°, b.-pt. 61°–62°. It reacts violently with water, amines, &c., and serves for the synthesis of organic acids (see these).

Ethyl imido-dicarboxylate, $NH(CO_2C_2H_5)_2$, is the imide corresponding with the amide urethane. It may be prepared from the sodium compound of urethane and ethyl chloro-carbonate. It forms colourless crystals, melting at 50°. By the exchange of one ethoxy (OC_2H_5) group for an amido (NH_2) group, it gives rise to allophanic ester, and by the exchange of two, to biuret (see p. 289).

Urea, *Carbamide*, $CO(NH_2)_2$, was first found in urine in 1773. It is contained in the urine of mammals, birds, and some reptiles, and also in other animal fluids. An adult man produces about 30 gms. daily, and it may be regarded as the final decomposition product formed by the oxidation of the nitrogenous compounds in the organism.

It may be prepared by the action of ammonia on ethyl carbonate, ethyl carbamate, or phosgene, and synthetically by the molecular transformation of ammonium cyanate, by warming its aqueous solution or allowing it to stand (cf. pp. 1 and 273):

$$N{:}C{\cdot}ONH_4 \rightleftharpoons NH_2{\cdot}CO{\cdot}NH_2.$$

The reaction is reversible, and hence the process is never complete. When equilibrium is reached, only a very small amount of untransformed cyanate is left, and the equilibrium is practically independent of the temperature. The reaction has been shown to be a typical bimolecular one (*Walker* and *Hambly*, J. C. S. 1895, 746).

The reaction is represented as follows by *Chattaway* (P. 1911, **27**, 281):

$$NH_4{\cdot}N{:}C{:}O \longrightarrow HN{:}C{:}O + NH_3 \longrightarrow HN{:}C(OH)NH_2 \longrightarrow NH_2{\cdot}CO{\cdot}NH_2.$$

It is usually prepared by mixing a solution of potassium cyanate (from the ferrocyanide) with ammonium sulphate and evaporating the mixture (ammonium cyanate is first formed and gradually changes to urea), or by evaporating urine, adding nitric acid, and decomposing the separated and purified nitrate of urea by barium carbonate.

It is also formed by heating a solution of carbon monoxide in ammoniacal cuprous chloride:

$$CO + 2NH_3 + Cu_2Cl_2 = CO(NH_2)_2 + 2HCl + 2Cu.$$

It crystallizes in long rhombic prisms or needles, has a cooling taste, is very readily soluble in water, also in alcohol, but not in ether. It melts at 132°, sublimes *in vacuo* without decomposition, and when strongly heated yields ammonia, cyanuric acid, biuret, and ammelide. As an amide it is readily hydrolysed by boiling with alkalis or acids, or by superheating with water (cf. *Fawsitt*, J. C. S. 1904, 1581; 1905, 494):

$$CO(NH_2)_2 + H_2O = CO_2 + 2NH_3.$$

Nitrous acid reacts with it to produce carbon dioxide, nitrogen, and water:

$$CO(NH_2)_2 + 2NO_2H = CO_2 + 2N_2 + 3H_2O.$$

Sodium hypochlorite and hypobromite act in a similar manner (*Davy*, *Knop*). *Hufner's* method of estimating urea quantitatively depends upon the measurement of the nitrogen

thus obtained (J. pr. Ch., [2], **3**, 1; cf. also B. **24**, Ref. 330). Urea also reacts with bromine and alkalis in much the same manner as the lower acid amides (*Hofmann* reaction, p. 184), yielding carbon dioxide and the corresponding amine, hydrazine (C. C. 1905, i, 1227), which is best removed by the addition of benzaldehyde.

Urea reacts with an aqueous solution of chlorine, yielding the dichloro-derivative $CO(NHCl)_2$. With acids this forms nitrogen trichloride, and with ammonia it yields diurea or **paraurazine**, $CO<^{NH\cdot NH}_{NH\cdot NH}>CO$ (*Chattaway*, J. C. S. 1909, 129, 235). When warmed with alcoholic potash to 100°, urea is converted into cyanate of potassium and ammonia.

The basic character of the amino groups is greatly weakened in urea by the presence of the negative carbonyl. Among the salts of urea with acids may be mentioned **urea nitrate**, CON_2H_4, HNO_3, which crystallizes in glistening white plates, readily soluble in water, but only slightly in nitric acid; also the **chloride**, **oxalate**, and **phosphate** But like acetamide, urea also forms salts with metallic oxides, especially with mercuric oxide, *e.g.* CON_2H_4, $2HgO$, finally, it yields crystalline compounds with salts, *e.g* **urea sodium chloride**, CON_2H_4, $NaCl$, H_2O (glistening prisms), and **urea silver nitrate**, CON_2H_4, $AgNO_3$ (rhombic prisms). The precipitate which is obtained on adding mercuric nitrate to a neutral aqueous solution of urea has the formula $2CON_2H_4$, $Hg(NO_3)_2$, $3HgO$; upon its formation depends *Liebig's* method for titrating urea. (See the memoirs of *Pfluger* and *Bohland* on the subject, *e g. Pfluger*, Arch. f. Phys. **38**, 575.)

Isomeric with urea is the amidoxime, **isuret** or methane amidoxime, $NH{:}CH\cdot NH\cdot OH$, which is obtained from HCN and NH_2OH; it crystallizes in prisms (see p. 188).

Closely related to carbamide, $NH_2\cdot CO\cdot NH_2$, is **semicarbazide** or semihydrocarbazide, $NH_2\cdot CO\cdot NH\cdot NH_2$, which is the half amide and half hydrazide of carbonic acid. It may be prepared from potassium cyanate and hydrazine hydrate. It is a basic substance, melts at 96°, and is usually met with in the form of its hydrochloride. It reacts with aldehydes and ketones in much the same manner as phenyl-hydrazine, yielding condensation products known as **semicarbazones**:

$$C_6H_5\cdot CO\cdot CH_3 + NH_2\cdot NH\cdot CO\cdot NH_2 = H_2O + C_6H_5\cdot C(CH_3){:}N\cdot NH\cdot CO\cdot NH_2.$$

which crystallize well, and have well-defined melting-points (see p. 136).

Alkylated ureas are obtained by the exchange of the amido hydrogen atoms for one or more alkyl radicals.

They are produced by *Wohler's* synthetical method, viz. by the combination of cyanic acid with amines, or of cyanic esters with ammonia or amines, thus:—

$$CO{\cdot}NC_2H_5 + NH_2{\cdot}C_2H_5 = CO(NH{\cdot}C_2H_5)_2.$$

Also from amines and carbon oxy-chloride As examples may be mentioned:

Methyl urea, $CO<^{NH_2}_{NH{\cdot}CH_3}$; α-Diethyl urea, $CO<^{NH{\cdot}C_2H_5}_{NH{\cdot}C_2H_5}$

Ethyl urea, $CO<^{NH_2}_{NH{\cdot}C_2H_5}$; β-Diethyl urea, $CO<^{NH_2}_{N(C_2H_5)_2}$

Certain of them closely resemble urea, others, however, are liquid and volatilize without decomposition Their *constitution* follows very simply from the nature of the products which are formed on hydrolysis, thus α-diethyl urea breaks up into carbon dioxide and ethylamine, and the β-compound into carbon dioxide, ammonia, and diethylamine, in accordance with the generalization enunciated on p 95, that alkyl radicals which are directly united to nitrogen are not separated from it on hydrolysis.

Acyl Derivatives -- By the entrance of acyl radicals into urea, its acid derivatives or **ureides** are formed. These are formed by the action of acid chlorides or anhydrides upon urea, or by the action of phosphorus oxy-chloride upon the salts of urea with organic acids. The simple ureides correspond in many respects with acid amides or amlides, have neither distinctly acid nor basic properties, and may be hydrolysed to the acid and urea or its products of decomposition (p. 283). To this class belong **acetyl urea**, $NH_2{\cdot}CO{\cdot}NH{\cdot}CO{\cdot}CH_3$, and **allophanic acid**, $NH_2{\cdot}CO{\cdot}NH{\cdot}CO_2H$. Hydroxy-monobasic acids also form ureides, not only in virtue of their acidic nature, but as alcohol and acid at the same time, thus:—

Hydantoic acid, $CO<^{NH{\cdot}CH_2{\cdot}CO_2H}_{NH_2}$,

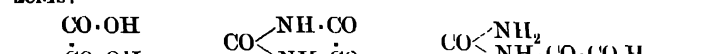
Hydantoin, $CO<^{NH{\cdot}CH_2}_{NH{\cdot}CO}$,

Lactyl urea, $CO<^{NH{\cdot}CH{\cdot}CH_3}_{NH{\cdot}CO}$.

Hydantoïn or *glycolyl urea* (needles, neutral) and **hydantoic**

acid or *glycoluric acid* (prisms), are derivatives of glycollic acid; the former on hydrolysis yields hydantoic acid, which in its turn is broken up into CO_2, NH_3, and glycocoll. They are obtained from certain uric acid derivatives (*e g.* allantoin) by the action of hydriodic acid, and also synthetically, for instance, hydantoic acid from glycocoll and cyanic acid. A **methyl-hydantoïn**, $C_3H_3(CH_3)N_2O_2$, results from the partial hydrolysis of creatinine (p. 298), NH being here replaced by O.

Just as the dibasic acids—oxalic, malonic, tartronic, and mesoxalic—yield amides with ammonia, so with urea they form compounds of an amidic nature. In such reactions either two molecules of water are eliminated, so that no carboxyl radical remains in the compound, or only one molecule is eliminated and a carboxyl group is retained In the former case the so-called **cyclic ureides** are obtained, and in the latter the **ureido-acids**, *e g.* from oxalic acid, parabanic and oxaluric acids:



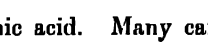
Oxalic acid — Cyclic ureide (parabanic acid) — Ureido-acid (oxaluric acid)

In an analogous manner the ureide barbituric acid, $C_4H_4N_2O_3$, is derived from malonic acid, the ureide dialuric acid, $C_4H_4N_2O_4$, from tartronic acid, and the ureide alloxan, $C_4H_2N_2O_4$, and ureido-acid alloxanic acid, $C_4H_4N_2O_5$, from mesoxalic acid.

These are solid and, for the most part, beautifully crystallizing compounds of a normal amidic character, and therefore readily hydrolysed to urea (or CO_2 and NH_3) and the respective acid. The ureido-acids may be regarded as half-hydrolysed ureides, and may be prepared from the latter in this manner. As they contain a carboxyl group, they still possess acidic properties.

The constitution of the various cyclic ureides and ureido-acids follows in most cases from the products they yield on hydrolysis, and also from their synthetical methods of formation and their relationships to one another.

Some of these ureides are obtained synthetically from urea and the requisite acid often in the presence of phosphorus oxy-chloride, *e.g.* malonyl urea (barbituric acid),



from urea and malonic acid. Many can be obtained by the

oxidation of various complex natural products, *e.g.* alloxan or parabanic acid by oxidizing uric acid with nitric acid.

Most of the ureides have the character of more or less strong acids. Since this acid character is not to be explained, as in the case of the ureido-acids, by the presence of carboxyl groups, one must assume that it depends upon reasons similar to those which apply in the case of cyanic acid and of succinimide, viz. that the replaceable hydrogen atoms are imido-hydrogen atoms, the acidic nature of which is determined by the adjacent carbonyl groups. This explains, for instance, why parabanic acid is a strong dibasic acid

Only a few of the more important among these compounds can be discussed here. The names given to the majority of them have no relationship to their constitution, and were assigned to them before the constitutions had been determined.

Parabanic acid, *Oxalyl urea*, $CO\langle^{NH\cdot CO}_{NH\cdot CO}$, is prepared by the action of nitric acid upon uric acid, and crystallizes in needles or prisms soluble in water and alcohol. The salts, *e.g.* $C_3HKN_2O_3$, $C_3Ag_2N_2O_3$, are unstable, being converted by water into salts of the monobasic **oxaluric acid**, $NH_2\cdot CO\cdot NH\cdot CO\cdot CO_2H$, which crystallize well.

A **methyl-parabanic acid**, $CO\langle^{NMe\cdot CO}_{NH-CO}$, and a **dimethyl-parabanic acid**, the so-called "**cholestrophane**", $CO\langle^{NMe\cdot CO}_{NMe\cdot CO}$, are also known. The former is prepared by the action of nitric acid upon methyl-uric acid, and crystallizes in prisms, while the latter is obtained from theine with nitric acid or chlorine water, and also by the methylation of parabanic acid, *i.e.* from the silver salt and methyl iodide. It crystallizes in plates and distils without decomposition.

Methyl-uracyl, $CO\langle^{NH\cdot C(CH_3)}_{NH\cdot CO}\rangle CH$, is produced by the action of urea upon acetoacetic ester, water and alcohol being eliminated (*Behrend*, A. **229**, 1, and p. 230). When it is treated with nitric acid, a nitro-group enters the molecule, and the methyl-group is oxidized to carboxyl, thus forming **5-nitro-uracyl-4-carboxylic acid**,

$$CO\langle^{NH\cdot C(CO_2H)}_{NH\cdot CO}\rangle C(NO_2).$$

This in its turn can give up carbon dioxide and pass into **5-nitro-uracyl**,

$$CO\langle\begin{matrix}NH\cdot CH\\NH\cdot CO\end{matrix}\rangle C(NO_2),$$

which yields upon reduction with tin and hydrochloric acid 5-amino-uracyl and **isobarbituric acid**, 5-*hydroxy-uracyl*,

$$CO\langle\begin{matrix}NH\cdot CH\\NH\cdot CO\end{matrix}\rangle C\cdot OH.$$

This last is oxidized by bromine water to **isodialuric acid**,

$$CO\langle\begin{matrix}NH\cdot C(OH)\\NH\cdot CO\end{matrix}\rangle C(OH),$$

from which uric acid may be synthesised by warming with urea and sulphuric acid (see p. 291).

Barbituric acid, *Malonyl urea*, $CO\langle\begin{matrix}NH\cdot CO\\NH\cdot CO\end{matrix}\rangle CH_2$, crystallizes in large colourless prisms ($+2H_2O$). The hydrogen atoms of the methylene group are reactive (cf. ethyl malonate), and can be replaced by bromine, $\cdot NO_2$, $:N\cdot OH$, metals, &c. The metallic radicals in their turn can be replaced by alkyl groups. The dimethyl derivative when hydrolysed yields carbon dioxide, ammonia, and dimethylmalonic acid, thus indicating that the methyl groups have replaced the methylene hydrogen atoms. The *iso*-nitroso derivative, $CO\langle\begin{matrix}NH\cdot CO\\NH\cdot CO\end{matrix}\rangle C:N\cdot OH$, **violuric acid**, can also be obtained by the action of hydroxylamine on alloxan, and on reduction yields **amino-barbituric acid** (uramil), from which pseudouric and uric acids have been synthesised (p. 291). **Diethylbarbituric acid** (*veronal*) is used as a soporific.

Dialuric acid, *Tartronyl urea*, $CO\langle\begin{matrix}NH\cdot CO\\NH\cdot CO\end{matrix}\rangle CH\cdot OH$, crystallizes in colourless needles or prisms which redden in the air. It is a strong dibasic acid, and on oxidation yields alloxantin.

Alloxan, *Mesoxalyl urea*, $CO\langle\begin{matrix}NH\cdot CO\\NH\cdot CO\end{matrix}\rangle CO$, may be prepared from uric acid by oxidation with cold HNO_3. It forms large colourless glistening rhombic prisms ($+4H_2O$), is readily soluble in water, and has strongly acidic properties. It colours the skin purple-red, and with ferrous sulphate solution produces an indigo-blue colour. It combines with $NaHSO_3$, and

readily changes into alloxantin. The corresponding ureido-acid, **alloxanic acid**, $NH_2 \cdot CO \cdot NH \cdot CO \cdot CO \cdot CO_2H$, which alloxan yields even with cold alkali, forms a radiating crystalline mass readily soluble in water. **Methyl- and dimethyl alloxan** are also known, and may be obtained by the action of nitric acid upon methyl-uric acid and caffeine respectively.

The diureide **alloxantin**, $C_8H_4O_7N_4$, stands midway in composition between tartronyl- and mesoxalyl-urea, by the combination of which it is formed. It may also be obtained by the action of H_2S on alloxan, or directly from uric acid and HNO_3. It crystallizes in small hard prisms ($+ 3H_2O$), which become red in air containing ammonia, their solution acquiring a deep-blue colour on the addition of ferric chloride and ammonia. The tetramethyl derivative, **amalic acid**, $C_8(CH_3)_4N_4O_7$, is obtained by oxidizing theine with chlorine water, and forms colourless crystals which redden the skin and whose solution is turned violet-blue by alkali. Both these compounds yield, upon oxidation, first alloxan or its dimethyl derivative, and then parabanic or dimethyl-parabanic acid. Alloxantin probably has the constitution:

$$CO\begin{<}NH\cdot CO\\NH\cdot CO\end{>}CH\cdot O\cdot C(OH)\begin{<}CO\cdot NH\\CO\cdot NH\end{>}CO$$

When heated with ammonia it is converted into **murexide**, the acid ammonium salt of **purpuric acid**, $C_8H_5N_6O_5$, which is the acid form of barbituryl iminoalloxan:

$$CO\begin{<}NH\cdot CO\\NH\cdot C(OH)\end{>}C\cdot N:C\begin{<}CO\cdot NH\\CO\cdot NH\end{>}CO$$

(J. pr. 1905, [ii], **73**, 449), which is formed when uric acid is evaporated with dilute nitric acid, and ammonia added to the residue; this constitutes the "**murexide test**" for uric acid. Murexide crystallizes in four-sided plates or prisms ($+ H_2O$) of a golden-green colour, which dissolve to a purple-red solution in water and to a blue one in potash. The free acid is incapable of existence.

Allantoïn is a diureide of glyoxylic acid, of the constitution

$$CO\begin{<}NH\cdot CH\cdot NH\cdot CO\cdot NH_2\\NH\cdot CO,\end{>}$$

and is found in the allantoic liquid of the cow, the urine of

sucking calves, &c. It forms glistening prisms, and can be synthesised from its components.

Biuret, $NH_2 \cdot CO \cdot NH \cdot CO \cdot NH_2$, is obtained by heating urea at 160°:

$$2NH_2 \cdot CO \cdot NH_2 = NH_3 + NH(CO \cdot NH_2)_2.$$

It crystallizes in white needles ($+ H_2O$), and is readily soluble in water and alcohol. The alkaline solution gives a beautiful violet-red coloration on the addition of a little cupric sulphate—the "**biuret reaction**". Biuret is also formed by the action of ammonia upon the **allophanic esters**, crystalline compounds sparingly soluble in water, which are prepared from urea and chloro-carbonic esters, thus:—

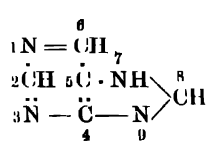
$$CO(NH_2)_2 + Cl \cdot CO_2C_2H_5 = NH_2 \cdot CO \cdot NH \cdot CO_2C_2H_5 + HCl.$$

Allophanic acid itself is not known in the free state, as it immediately breaks up into urea and carbon dioxide. Biuret may be regarded as its amide.

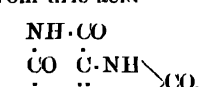
The Purine Group (*E. Fischer*, B. 1899, **32**, 435, **35**, 2564).—A number of relatively complex cyclic diureides derived from 1 molecule of hydroxy dibasic acids and 2 of urea are known. One of the most important of these is **uric acid**

The parent substance of this group of compounds is purine (*E. Fischer*, B. 1899, **32**, 449).

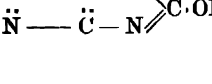
Purine.



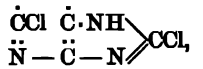
is usually obtained from uric acid:



which reacts with phosphorus oxy-chloride as the tautomeric trihydroxy purine:

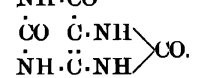


yielding the corresponding trichlorpurine:



and this on reduction yields purine itself. It is a colourless crystalline compound, melts at 216°, and is both an acid and a base. It dissolves readily in water, and is not easily oxidized. The atoms of the ring are usually numbered as indicated

Uric acid is the keto form of 2:6:8-*trihydroxy-purine*, and has the constitutional formula:

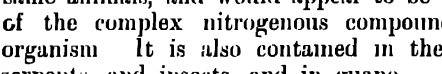


Uric acid and many other compounds containing the ·NH·CO· group, as tautomeric substances, behave in certain reactions as ketonic compounds and in other reactions as hydroxylic derivatives, *i.e.* they exhibit keto-enolic tautomerism.

It is a common constituent of the urine of most carnivorous animals, whereas that of herbivorous animals contains hippuric acid. It is also found in the blood and muscle juices of the same animals, and would appear to be the oxidation product of the complex nitrogenous compounds contained in the organism It is also contained in the excrement of birds, serpents, and insects, and in guano.

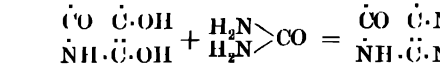
Syntheses.—1. By heating glycocoll with urea (*Horbaczewski*, B. **15**, 2678).

2. By heating isodialuric acid (p. 288) with urea and concentrated sulphuric acid (*R. Behrend* and *O. Roosen*, A. **251**, 235):



3. By heating cyano-acetic acid with urea (*Traube*, B. 1891, **24**, 3429, 1900, **33**, 3035).

4. By heating pseudouric acid with hydrochloric acid when water is eliminated (*E. Fischer*, B. 1897, **30**, 559):



The pseudo acid is obtained as the potassic salt by the condensation of amino-barbituric acid (p. 288) with potassic cyanate:

$$\begin{array}{lll} \text{NH·CO} & & \text{NH·CO} \\ \text{CO} \quad \text{CH·NH}_2 + \text{HCNO} & = & \text{CO} \quad \text{CH·NH·CO·NH}_2 \text{ (\textit{Baeyer}).} \\ \text{NH·CO} & & \text{NH·CO} \end{array}$$

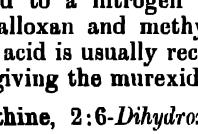
It is usually prepared from guano and the excrement of serpents, and crystallizes in small plates; is almost insoluble in water, and quite insoluble in alcohol or ether. Uric acid is a weak dibasic acid; its common salts are the acid ones, *e.g.* $C_5H_3O_3N_4K$, a powder sparingly soluble in water. The lithium and piperazine salts are somewhat more soluble, and hence are used in medicine for removing uric acid from the human system.

When the two lead salts are treated with methyl iodide, **methyl-** and **dimethyl uric acids** are obtained, both of which also are weak dibasic acids, since they still contain replaceable imido-hydrogen atoms.

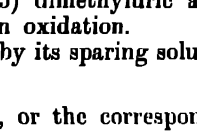
Constitution.—The constitutional formula, given above, was first proposed by *Medicus*, and afterwards proved to be correct by *E. Fischer* (A. **215**, 253). The more important arguments used were:—(1) Uric acid yields alloxan and urea when cautiously oxidized, this proving that we have to deal here with a carbonic acid derivative and a carbon chain, C·C·C; (2) uric acid contains four imido groups, since, by the introduction of four methyl groups, one after the other, four monomethyl, various di- and trimethyl, and one tetramethyl uric acids are obtained. When the tetramethyl acid is hydrolysed with concentrated hydrochloric acid all the nitrogen is eliminated as methylamine, and thus each methyl group is probably attached to a nitrogen atom; (3) dimethyluric acid yields methylalloxan and methylurea on oxidation.

Uric acid is usually recognized by its sparing solubility, and by its giving the murexide test.

Xanthine, 2:6-*Dihydroxy-purine*, or the corresponding keto form:



Xanthine

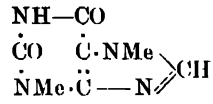


Hypoxanthine

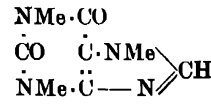
may be obtained by the reduction of uric acid with sodium amalgam, or by the action of nitrous acid on guanine (amino hypoxanthine). It is a white amorphous mass, and is both basic and acidic. The lead salt, $C_5H_2PbN_4O_2$, is converted into theobromine by methyl iodide. (Cf. B. 1897, **30**, 2235; 1900, **33**, 3035.) When oxidized it yields the same products as uric acid.

Hypoxanthine, *Sarcine*, or 6-*oxy-purine*, is sparingly soluble in water and closely resembles xanthine.

Theobromine, 3:7-*Dimethyl-xanthine*,



Theobromine



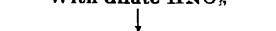
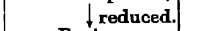
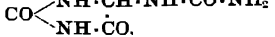
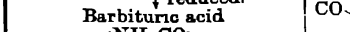
Caffeine

occurs in the beans of cacao; it is a crystalline powder of bitter taste, and is only sparingly soluble in water and alcohol. It forms salts both as a base and as an acid. The silver salt, $C_7H_7AgN_4O_2$, when treated with CH_3I, yields **caffeine** or **theine**, 1:3:7-*trimethyl-xanthine*, which occurs in tea (2–4 per cent), coffee, and various plants. (For synthesis from dimethyl urea and malonic acid, see *Fischer*, B. 1895, **28**, 3137; 1899, **32**, 435; from cyanoacetic acid, 1900, **33**, 3035.) It crystallizes (+ H_2O) in beautiful long glistening silky needles of faintly bitter taste, which are sparingly soluble in cold water and alcohol, and can be sublimed. The salts are readily decomposed by water. Chlorine oxidizes it to dimethyl alloxan and monomethyl urea. **Theophylline**, 1:3-*dimethyl-xanthine*, also occurs in tea.

Guanine, 2-*amino*-6-*oxy-purine*, or 2-*amino-hypoxanthine*, and **adenine**, 6-*amino-purine*, both contain amino-groups, and are thus basic substances. Both compounds, together with xanthine and hypoxanthine, are formed by the decomposition of the nucleic acids and other complex compounds contained in the animal system. The constitution follows largely from (1) basic properties, (2) their conversion respectively into xanthine and hypoxanthine by the aid of nitrous acid, and (3) from their oxidation products.

A summary of some of the more important ureides which can be obtained from uric acid are tabulated here:—

PRODUCTS OBTAINABLE FROM URIC ACID

1 On Oxidation			2 On Reduction	3. With PCl_5.
(*a*)	(*b*)	(*c*)		
With dilute HNO_3,	With concentrated HNO_3	In alkaline solution.	Electrolytically.	Trichloro-purine,
				
Alloxan, $CO<NH\cdot CO>CO$, $NH\cdot CO$	Parabanic acid, $CO<NH\cdot CO>$, $NH\cdot CO$	Allantoin, $CO<NH\cdot CH\cdot NH\cdot CO\cdot NH_2$, $NH\cdot CO$	$NH\cdot CH_2$, $CO\ C\cdot NH>CO$, $NH\cdot CH\cdot NH$	reduced.
reduced	with KOH	reduced.	Purone	Purine,
Dialuric acid.	Oxaluric acid.	Hydantoin,	With sodium amalgam	$N=CH$, $CH\ C\cdot NH>CH$, $N-C-N$
			Xanthine,	Xanthine, hypoxanthine, guanine, and adenine can also be obtained from trichloro-purine (B 1897, 30, 2220, 2226)
reduced.		Hydrolysed Allantoic acid,	$NH\cdot CO$, $CO\ C\cdot NH>CH$, $NH\cdot C-N$	
Barbituric acid		$CO<NH\cdot CH_2\cdot NH\cdot CO\cdot NH_2$, $NH\cdot CO_2H$.		
				
Alloxan and dialuric acid give alloxantin,				
				

D. Sulphur Derivatives of Carbonic Acid

In addition to most of the carbonic acid derivatives which have been described, there exist analogous compounds in which the oxygen is wholly or partially replaced by sulphur. Many of these again are unstable in the free state, from the fact of their being too readily hydrolysed to CO_2, COS, or CS_2, but they are known as salts, or at least as esters. The latter are often not real esters, in so far that those which contain an alkyl radical linked to sulphur do not yield the corresponding alcohols on hydrolysis, but mercaptans, in accordance with the intimate character of this linking.

Various mono-, di-, and tri-thio-derivatives of carbonic acid are known, according as 1, 2, or 3 of the oxygen atoms are replaced by sulphur.

Many of the thio-acids react as tautomeric substances, and give rise to isomeric alkyl derivatives in exactly the same manner as hydrocyanic, cyanic, and thiocyanic acids.

Thiophosgene, *Thiocarbonyl chloride*, $CSCl_2$. When chlorine is allowed to act upon carbon disulphide, there is first formed the compound $CCl_3 \cdot SCl$, which is converted into thiophosgene by $SnCl_2$. It is a red, mobile, strongly fuming liquid of sweetish taste, which attacks the mucous membrane, and boils at 73°. In its chemical behaviour it closely resembles phosgene, but is much more stable towards water than the latter, being only slowly decomposed even by hot water. With ammonia it yields ammonium thiocyanate and not thiocarbamide.

Thiocarbonic Acids.—Tri-thiocarbonic acid is made up of the constituents $CS_2 + H_2S$, so that carbon disulphide is its thio-anhydride, while the di-thiocarbonic acids contain the elements of $CS_2 + H_2O$ or of $COS + H_2S$, and the mono-acids those of $COS + H_2O$ or of $CO_2 + H_2S$. We find accordingly that CS_2 combines with Na_2S to CS_3Na_2, sodic tri-thiocarbonate, with KSC_2H_5 to $CS(SC_2H_5)SK$, with KOC_2H_5 (*i.e.* an alcoholic solution of potash) to $CS(OC_2H_5)SK$, potassium xanthate. In a similar manner COS and $CSCl_2$ combine with mercaptides and alcoholates.

Tri-thiocarbonic acid, CS_3H_2, is a brown oil, insoluble in water, and readily decomposed, and its **ethyl ester**, $S:C(SC_2H_5)_2$, a liquid boiling at 240°.

Potassium xanthate, $S:C\langle^{OC_2H_5}_{SK}$, obtained by the action of potassic ethoxide, ($KOH + C_2H_5OH$), on carbon disulphide,

crystallizes in beautiful colourless needles, very readily soluble in water, less so in alcohol. A solution of cupric sulphate throws down cupric xanthate as a yellow unstable precipitate, hence the name. It is employed in indigo printing. The free **xanthic acid**, or ethyl hydrogen dithiocarbonate, $CS(OC_2H_5)SH$, is an oil insoluble in water, and decomposes at so low a temperature as 25° into carbon disulphide and alcohol.

Thiocarbamic Acids.—Di-thiocarbamic acid, $NH_2 \cdot CS \cdot SH$, is formed as ammonic salt by the combination of CS_2 and NH_3 in alcoholic solution:

$$CS_2 + 2NH_3 = NH_2 \cdot CS \cdot SNH_4.$$

The free acid is a reddish oil which easily decomposes into thiocyanic acid and sulphuretted hydrogen.

$$NH_2 \cdot CS \cdot SH = CSNH + SH_2.$$

Carbon disulphide combines in an analogous manner with primary amines to form the aminic salts of alkylated di-thiocarbamic acids; thus ethylamine yields **ethylamine ethyl-di-thiocarbamate**, $C_2H_5NH \cdot CS \cdot SNH_3C_2H_5$. When such salts are heated above 100°, H_2S is evolved and a dialkyl-thiourea left behind, *e.g.* **diethyl-thio-urea**, $CS(NHC_2H_5)_2$, when $HgCl_2$ or $AgNO_3$ is added to their solutions, the Hg or Ag salts of the acids are precipitated, and these decompose on boiling with water into HgS or Ag_2S and the corresponding mustard oil (cf. p. 275).

$$2CS(NHC_2H_5) \cdot SAg = 2CSNC_2H_5 + Ag_2S + H_2S.$$

Secondary amines also give rise to alkylated di-thiocarbamic acids, but the latter do not yield mustard oils.

Thiocarbamide, *Thio-urea*, *sulpho-urea*, $S:C(NH_2)_2$ (*Reynolds*), is the analogue of urea, and its *modes of formation* are exactly similar to those of the latter. Thus it is formed from ammonium thiocyanate just as urea is from the cyanate.

$$N:C \cdot SNH_4 \rightleftarrows CS(NH_2)_2.$$

To effect this molecular transformation a temperature of at least 130° is required, and it is only partial, as the reaction is reversible. At 170° equilibrium is attained after 45 minutes, and the mixture then contains only 25 per cent of thiocarbamide (*Reynolds* and *Werner*, P. 1902, 207). It may also be

formed by the direct union of sulphuretted hydrogen with cyanamide:

$$CN \cdot NH_2 + SH_2 = CS(NH_2)_2.$$

Thiocarbamide crystallizes in rhombic six-sided prisms, or—if not quite pure—in long silky needles, readily soluble in water and alcohol. M.-pt. 172°. It is easily hydrolysed to CO_2, H_2S, and $2NH_3$. HgO abstracts H_2S from it, with formation of cyanamide. Cold permanganate of potash solution oxidizes it to urea. As a weak base it forms salts with acids, but at the same time it yields salts with HgO and other metallic oxides; it also combines with salts, such as AgCl, $PtCl_4$, &c. When heated with alcoholic potash to 100°, it is reconverted into (the potassium salt of) thiocyanic acid and ammonia.

Thiocarbamide gives rise to alkyl derivatives (normal and pseudo), acyl derivatives, cyclic urcides, &c., in much the same manner as urea itself.

E. Amidines of Carbonic Acid

Guanidine, or **Imino-carbamide**, $NH:C(NH_2)_2$ (*Strecker*, 1861), may be obtained by the oxidation of guanine, also by heating cyanamide with ammonium iodide, and therefore from cyanogen iodide and ammonia:

$$CN \cdot NH_2 + NH_4I = CN_3H_5, HI.$$

It is usually prepared by heating thio-urea with ammonium thiocyanate to 180°–190°, and therefore from the thiocyanate alone at this temperature (*Volhard*):

$$CS(NH_2)_2 + NH_4 \cdot CNS = \underset{\text{Guanidine isothiocyanate.}}{C(NH)(NH_2)_2, CNSH} + H_2S$$

Guanidine crystallizes well, is readily soluble in water and alcohol, deliquesces in the air, and is a sufficiently strong monoacid base to absorb carbon dioxide. **Guanidine carbonate**, $(CN_3H_5)_2, H_2CO_3$, crystallizes beautifully in quadratic prisms. The base is readily hydrolysed, at first to urea and ammonia, and finally to ammonia and carbon dioxide.

By the action of a mixture of nitric and sulphuric acids upon guanidine nitrate, **nitro-guanidine**, $NH_2 \cdot C(NH)NH \cdot NO_2$, is obtained, which is readily reduced to **amino-guanidine**, $NH_2 \cdot C(NH)NH \cdot NH_2$. The latter, when boiled with alkalis or acids, breaks up into *hydrazine*, N_2H_4, ammonia, and carbon

dioxide, and it yields with nitrous acid **diazo-guanidine**, $NH_2C(NH)NHN{:}N\cdot OH$, which in its turn is decomposed by alkalis into water, cyanamide, and *hydrazoic acid*, N_3H (*Curtius*, A. 1900, **314**, 339).

By the direct combination of cyanamide with glycocoll there is formed **glycocyamine**:

$$NH{:}C\begin{matrix}NH_2\\ NH\cdot CH_2\cdot CO_2H,\end{matrix}$$

which readily loses water with formation of **glycocyamidine**:

$$NH{:}C\begin{matrix}NH\cdot CO\\ NH\cdot CH_2\end{matrix}$$

If, instead of glycocoll, its methyl derivative, sarcosine, is used, we obtain in an analogous manner creatine and creatinine (*Volhard*):

$$NH{:}C\begin{matrix}NH_2\\ NMe\cdot CH_2\cdot CO_2H\end{matrix}$$

Creatine

$$NH{:}C\begin{matrix}NH\cdot CO\\ NMe\cdot CH_2\end{matrix}$$

Creatinine

Creatine is present in the juice of muscle, and is prepared from extract of meat (*Liebig*). It crystallizes in neutral prisms ($+ H_2O$) of a bitter taste, is moderately soluble in hot water, but only slightly in alcohol. When heated with acids it loses water and yields **creatinine**, which is an invariable constituent of urine, and which forms a characteristic double salt with zinc chloride, $2C_4H_7N_3O + ZnCl_2$. It is a strong base and much more readily soluble than creatine

Creatinine is the methyl derivative of imino-hydantoin, and as such yields, when carefully hydrolysed, ammonia and methylhydantoin.

XIV. CARBOHYDRATES

Most of the carbohydrates which occur in nature have been known for a long time. Cane-sugar was found in the sugar-beet by *Marggraf* in 1747, and dextrose in honey by *Lauber*. The transformation of starch into glucose (p. 309) was first observed by *Kirchoff* in 1811.

The name **carbohydrate** was formerly applied to certain substances which occur naturally in large quantities in the vegetable and animal kingdom, and which could be repre-

sented by the general formula $C_x(H_2O)_y$, where $x = 6$ or a multiple of 6, *e.g.* dextrose, $C_6(H_2O)_6$ or $C_6H_{12}O_6$, cane-sugar, $C_{12}(H_2O)_{11}$ or $C_{12}H_{22}O_{11}$, and starch $[C_6(H_2O)_5]_x$. In addition to these natural products, the group at the present time includes a number of compounds which have only been obtained synthetically, mainly as a result of the researches of *E. Fischer*. The number of carbon atoms in these varies considerably. Carbohydrates are now known in which the hydrogen and oxygen are not present in the proportions of 2 atoms of hydrogen to 1 of oxygen, *e.g.* rhamnose, $C_6H_{12}O_5$.

The carbohydrates are usually divided into the three following groups, according to their relative complexity:—

A. **Monosaccharoses.**—This is the simplest group of the carbohydrates, and the members are all polyhydroxy aldehydes or ketones containing from 3–9 carbon atoms The group includes the common substances arabinose, $C_5H_{10}O_5$, and the isomeric compounds, $C_6H_{12}O_6$, glucose or grape-sugar, and fructose or fruit-sugar. As a rule, the compounds are readily soluble in water, have a sweet taste, and do not crystallize very readily.

B. **Bi-** and **Trisaccharoses.**—These compounds may be regarded as anhydrides of the monoses, usually derived by the elimination of 1 molecule of water from 2 mols. of a monose, or of 2 mols. of water from 3 of a monose. It is not necessary that the 2 or 3 molecules of monose should be identical in structure, *e.g.* cane-sugar is the anhydride produced by the elimination of 1 mol. of water from 1 mol. of glucose and 1 of fructose As anhydro-derivatives they are readily hydrolysed by mineral acids, yielding the monoses, from which they may be regarded as being derived.

Most of the di- and trioses are soluble in water, crystallize very well, and also possess a sweet taste. Examples are cane-sugar, maltose, and milk-sugar.

C. **Polysacharoses** or **Polyoses.**—This group includes the complex carbohydrates, such as starch, cellulose, &c. They may be regarded as derived from the monoses by the elimination of x mols. of water from x mols. of a monose, *e.g.*:

$$xC_6H_{12}O_6 - xH_2O = (C_6H_{10}O_5)_x.$$

In conformity with such a structure they are fairly readily hydrolysed, yielding as the ultimate product a monose. As a rule, they do not dissolve in water, possess no sweet taste, and have not been obtained in a crystalline form.

A. Monosaccharoses

These are all open-chain polyhydroxy-aldehydes or ketones, *e.g.*:

$OH \cdot CH_2 \cdot CH(OH) \cdot CH(OH) \cdot CH(OH) \cdot CH{:}O$ Arabinose,
$OH \cdot CH_2 \cdot CH(OH) \cdot CH(OH) \cdot CH(OH) \cdot CO \cdot CH_2 \cdot OH$ Fructose,

and are divided into the two main groups **aldoses** and **ketoses**, according to their aldehydic or ketonic constitution. As a rule, several hydroxyl groups are present in addition to the aldehydic $\cdot C\langle^{H}_{O}$ or ketonic $>C{:}O$ group, and invariably one of these hydroxyl groups is in the α-position with respect to the aldehydic or ketonic group.

The monoses are usually divided into sub-groups, according to the number of **oxygen atoms** present in the molecule, *e.g.*:

Trioses, $OH \cdot CH_2 \cdot CH(OH) \cdot CH{:}O$ and $OH \cdot CH_2 \cdot CO \cdot CH_2 \cdot OH$,
Tetroses, $OH \cdot CH_2 \cdot (CH \cdot OH)_2 \cdot CH{:}O$;
Pentoses, $OH \cdot CH_2 \cdot (CH \cdot OH)_3 \cdot CH{:}O$ and $CH_3 \cdot (CH \cdot OH)_4 \cdot CH{:}O$;
Hexoses, $OH \cdot CH_2 \cdot (CH \cdot OH)_4 \cdot CH{:}O$ and $OH \cdot CH_2 \cdot (CH \cdot OH)_3 \cdot CO \cdot CH_2 \cdot OH$;
Heptoses, $OH \cdot CH_2 \cdot (CH \cdot OH)_5 \cdot CH{:}O$;
Octoses, $OH \cdot CH_2 \cdot (CH \cdot OH)_6 \cdot CH{:}O$;
Nonoses, $OH \cdot CH_2 \cdot (CH \cdot OH)_7 \cdot CH{:}O$.

As a rule, the molecule of any single monose contains several asymmetric carbon atoms, *e.g.* a hexose, $OH \cdot CH_2(CH \cdot OH)_4 \cdot CH{:}O$, contains 4 asymmetric carbon atoms, and hence should exist in 2^4, *i.e.* sixteen distinct optically active modifications, in addition to eight racemic forms. In most cases all the possible stereo-isomeric modifications are not known, but the number of such compounds known has been largely increased within recent years owing to the brilliant researches of *Emil Fischer* (B. 1890, **23**, 2114; 1894, **27**, 3189).

General Characteristics of Aldoses. — As aldehydes the aldoses possess most of the properties already described as characteristic of fatty aldehydes.

They are readily reduced by ordinary alkaline reducing agents, yielding polyhydric alcohols:

$$OH \cdot CH_2 \cdot (CH \cdot OH)_3 \cdot CH{:}O + 2H = OH \cdot CH_2 \cdot (CH \cdot OH)_3 \cdot CH_2 \cdot OH.$$

When oxidized, they yield first mono- and then dibasic acids, containing the same number of carbon atoms:

$$OH\cdot CH_2\cdot(CH\cdot OH)_4\cdot CH{:}O \longrightarrow OH\cdot CH_2\cdot(CH\cdot OH)_4\cdot CO\cdot OH \longrightarrow COOH\cdot(CH\cdot OH)_4\cdot COOH.$$

These reactions are of considerable importance as direct evidence of the aldehydic nature of the aldoses. The first stage of the oxidation is effected by mild oxidizing agents, such as chlorine, bromine water, silver oxide, or ammoniacal solutions of cupric salts. The last-mentioned reaction is the basis of the usual volumetric method for the estimation of glucose and other aldoses. The aldose solution is added to a given volume of a standard *Fehling's* solution (a solution containing cupric sulphate, sodic ammonic tartrate, and sodic hydroxide (p. 253)) until the blue colour just disappears on boiling. An even more exact method is to weigh the cuprous oxide (as such, as metallic copper, or as cupric oxide) formed by reducing a given volume of the sugar solution with an excess of *Fehling's* solution.

The oxidation to a dibasic acid requires somewhat stronger oxidizing agents, *e.g.* nitric acid.

Although the aldoses do not combine directly with ammonia or sodic hydric sulphite, they readily form additive compounds with hydrogen cyanide:

$$OH\cdot CH_2(CH\cdot OH)_x\cdot CH{:}O + HCN = OH\cdot CH_2(CH\cdot OH)_x\cdot CH(OH)\cdot CN.$$

This is an extremely important reaction as being the basis of a method for passing from a tetrose to a pentose, or from a pentose to a hexose (see p. 304).

They react normally with hydroxylamine, yielding **oximes**, more especially in alcoholic solution, and the oximes thus obtained may be converted into a monose containing a smaller number of oxygen atoms (p. 305).

They can also react normally with phenyl-hydrazine, yielding **phenyl-hydrazones**, which, as a rule, are sparingly soluble, colourless, crystalline compounds with definite melting-points. These are readily transformed back into the aldoses by treatment with hydrolysing agents or with benzaldehyde (A. 1895, **288**, 140). One of the most characteristic properties of monoses is the formation of **osazones** or **diphenyl-hydrazones**. This reaction may be regarded as taking place in three distinct stages:—(*a*) Formation of a phenyl-hydrazone, $X\cdot CH(OH)\cdot$

$CH:N\cdot NHPh$, in the case of an aldose, and $X\cdot C(:N\cdot NHPh)\cdot CH_2\cdot OH$ in the case of a ketose; (*b*) the oxidation of the $>CH\cdot OH$ or $\cdot CH_2\cdot OH$ group in the *α*-position with regard to the carbon atom to which the hydrazino-group is attached and the formation of a $>CO$ or $\cdot CH:O$ group, *e.g.*:

$$X\cdot CO\cdot CH:N\cdot NHPh \quad \text{and} \quad X\cdot C(:N\cdot NHPh)\cdot CH:O.$$

This oxidation occurs at the expense of the excess of phenyl-hydrazine, which becomes reduced to aniline and ammonia:

$$2H + C_6H_5NH\cdot NH_2 = C_6H_5NH_2 + NH_3.$$

(*c*) The compounds thus obtained react with a further quantity of phenyl-hydrazine, so that a second hydrazino-group is introduced, *e.g.* $X\cdot C(:N\cdot NHPh)\cdot CH:N\cdot NHPh$, and an osazone formed (*E. Fischer*). From the above formulæ it is clear that the same osazone can be obtained from a ketose and an isomeric aldose (cf. Glucose and Fructose) These osazones are usually prepared by warming a dilute acetic acid solution of phenyl-hydrazine with the sugar for an hour or more on the water-bath. The products are yellow crystalline solids with definite melting-points, they are only sparingly soluble, and are largely made use of for characterizing the various monoses Substituted phenyl-hydrazines, *e.g.* *p*-bromo phenyl-hydrazine or diphenyl-hydrazine, $NPh_2\cdot NH_2$, are often used in place of phenyl-hydrazine itself. It has been shown recently (B. 1902, **35**, 3141) that methyl-phenyl-hydrazine, $NMePh\cdot NH_2$, yields osazones with ketoses, but not with aldoses, and this difference is made use of in the separation of the two groups of compounds.

The hydroxylic nature of the aldoses can be established in various ways. Like all alcohols, they contain hydrogen atoms which can be replaced by metallic radicals. This replacement can be accomplished not only by means of metals themselves (cf. action of sodium on ethyl alcohol), but much more conveniently by means of the metallic hydroxides. The most common derivatives are the calcic, baric, or plumbous; thus from glucose, $C_6H_{12}O_6$, **calcic glucosate**, $C_6H_{11}O_6\cdot Ca\cdot OH$, is readily obtained. Many of these metallic derivatives are sparingly soluble, and are therefore made use of in the isolation of certain sugars. They are readily transformed into the original sugar when decomposed by carbon dioxide in aqueous solution.

As alcohols the aldoses also give rise to ethers; the best known are the methyl ethers of glucose, *i.e.* mixed ethers derived from the two alcohols, glucose and methyl alcohol:

$$C_6H_{12}O_6 + CH_3 \cdot OH = C_6H_{11}O_5 \cdot OCH_3 + H_2O.$$

These compounds are usually spoken of as **glucosides**, and are probably closely related to the natural glucosides (see these). They may be obtained readily by the action of dry hydrogen chloride on a methyl alcoholic solution of glucose (*E. Fischer*, B. 1894, **28**, 1151). (For constitution, see p. 310.)

The formation of **acetyl** derivatives is also a direct proof of the presence of hydroxyl radicals in the aldose molecules. Thus glucose when heated with acetic anhydride and anhydrous sodic acetate yields a **pentacetyl** or pentacetate derivative, which can be hydrolysed to acetic acid and glucose when boiled with a solution of benzene-sulphonic acid.

General Characteristics of Ketoses.—In the majority of their properties the ketoses resemble the aldoses, *e.g.* they react with hydroxylamine and phenyl-hydrazine in exactly the same manner. They form additive compounds with hydrogen cyanide, and are readily reduced to polyhydric alcohols. In certain cases the same alcohol is obtained by the reduction of a ketose and of an isomeric aldose, *e.g.* both *d*-glucose and *d*-fructose yield *d*-sorbitol on reduction.

$$\left.\begin{matrix} X \cdot CH(OH) \cdot CH{:}O \\ X \cdot CO \cdot CH_2 \cdot OH \end{matrix}\right\rangle \longrightarrow X \cdot CH(OH) \cdot CH_2 \cdot OH$$

The ketoses differ completely from the aldoses as regards their oxidation products. As ketones they cannot yield mono- or dibasic acids containing the *same number of carbon atoms*,* but always a mixture of simpler acids, *e.g.* *d*-fructose on oxidation with nitric acid yields a mixture of tartaric and glycollic acids:

$$OH \cdot CH_2 \cdot CH(OH) \cdot CH(OH) \cdot CH(\cdot OH) \cdot CO \cdot CH_2OH + 4O = CO_2H \cdot CH(OH) \cdot CH(OH) \cdot CO_2H + CO_2H \cdot CH_2OH + H_2O;$$

or when boiled with mercuric oxide it yields glycollic and trihydroxy-butyric acids:

$$OH \cdot CH_2 \cdot CH(OH) \cdot CH(OH) \cdot CH(OH) \cdot CO \cdot CH_2OH \longrightarrow OH \cdot CH_2 \cdot CH(OH) \cdot CH(OH) \cdot CO_2H + CO_2H \cdot CH_2 \cdot OH.$$

* The formation of acids containing the same number of carbon atoms is theoretically possible, since two $\cdot CH_2 \cdot OH$ groups are present, but such acids have not been obtained.

The ketoses also form metallic derivatives and acetyl derivatives.

Alcoholic Fermentation of Monosaccharoses.—Many of the natural products, *e.g.* *d*-glucose and *d*-fructose, are readily fermented by yeast (*Saccharomyces*), yielding as chief products ethyl alcohol and carbon dioxide (p. 76). This decomposition is undoubtedly due to the presence of an enzyme, *Buchner's* **zymase**, which is contained in the cells of the organism. *Fischer's* researches have shown that all monoses cannot be fermented, only certain of those containing 3 or a multiple of 3 carbon atoms. Even such monoses are not all readily fermented, *e.g.* *d*-glucose is fermented more readily than *l*-glucose, and the isomeric guloses cannot be fermented by yeast. There appears to be an intimate relationship between the configuration of the monose molecule and of the ferment (enzyme) which is capable of decomposing it. *Fischer* has compared this relationship to that of a lock and its corresponding key.

Conversion of an Aldose into an Isomeric Ketose.—This is an interesting transformation due to *E. Fischer*, and consists in converting the aldose into its osazone, which on hydrolysis with hydrochloric acid yields phenyl-hydrazine and a polyhydroxy-ketonic aldehyde, usually known as an **osone**. When the osone is reduced, the aldehydo-group is converted into a primary alcoholic radical, and a hydroxy-ketone (ketose) isomeric with the original aldose is obtained, *e.g.*

$$\begin{array}{l} X\cdot CH(OH)\cdot CH{:}O \longrightarrow X\cdot C(:N\cdot NHPh)\cdot CH{:}N\cdot NHPh \\ \qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad \downarrow \\ X\cdot CO\cdot CH_2\cdot OH \longleftarrow X\cdot CO\cdot CH{:}O. \end{array}$$

By this means *d*-glucose can be transformed into *d*-fructose.

Synthesis of a Monosaccharose from a Simpler Monosaccharose.—The aldose is converted into its cyanhydrin by means of hydrogen cyanide (*Kiliani*):

$$X\cdot CH(OH)\cdot CH(OH)\cdot CH{:}O \longrightarrow X\cdot CH(OH)\cdot CH(OH)\cdot CH\begin{matrix}OH\\ CN.\end{matrix}$$

As this reaction involves the introduction of a further asymmetric carbon atom into the molecule, two distinct optically active nitriles will be formed. As the two compounds are not related to one another as object to mirror image, they will not be optical antipodes, and will not necessarily be formed in equal amount. The mixture of cyanides is hydrolysed, the resulting hydroxy acids converted into lactones

and then reduced with sodium amalgam, when a mixture of two sugars is obtained:

$$X\cdot CH(OH)\cdot CH(OH)\cdot CH(OH)\cdot CO_2H \longrightarrow X\cdot CH\cdot CH(OH)\cdot CH(OH)\cdot CO$$
$$\text{(with O bridging the CH and the last CO)}$$
$$\downarrow$$
$$X\cdot CH(OH)\cdot CH(OH)\cdot CH(OH)\cdot CH{:}O.$$

As examples of this we have:

l-Arabinose → *l*-Mannose, *l*-Glucose.
l-Xylose → *l*-Idose, *l*-Gulose.
d-Glucose → α-Glucoheptose, β-Glucoheptose
d-Galactose → α-Galaheptose, β-Galaheptose.

By similar methods *E. Fischer* has succeeded in preparing **octoses** and **nonoses**.

Conversion of a Monosaccharose into a Simpler Monosaccharose (*Wohl*, B. 1893, **26**, 730).—The aldose is converted into its oxime, which reacts with acetic anhydride, yielding an acetylated hydroxy-nitrile, *e.g.*:

$$OH\cdot CH_2\cdot[CH\cdot OH]_4\cdot CHO \longrightarrow OH\cdot CH_2\cdot[CH\cdot OH]_4\cdot CH{:}N\cdot OH \longrightarrow OAc\cdot CH_2\cdot[CH\cdot OAc]_4\cdot CN.$$

The nitrile when treated with ammoniacal silver nitrate solution loses hydrogen cyanide and yields the acetyl derivative of a lower monose, *e.g.*:

$$OAc\cdot CH_2[CH\cdot OAc]_3\cdot CHO,$$

from which the monose itself is readily obtained.

Another method has been worked out by *Ruff* (B 1898, **31**, 1573; 1902, **35**, 2360). This consists in oxidizing the aldose to the corresponding monobasic acid, and then oxidizing the calcic salt of this with ferric acetate and hydrogen peroxide. In this way carbonic acid is split off and an aldose obtained:

$$OH\cdot CH_2\cdot(CH\cdot OH)_3\cdot CH\cdot(OH)\cdot CO\cdot OH + O = OH\cdot CH_2(CH\cdot OH)_3\cdot CH{:}O + H_2CO_3.$$

The aldose can be isolated as its phenylhydrazone, and this with benzaldehyde yields the free aldose.

Trioses.—When glycerol is oxidized with dilute nitric acid

or other oxidizing agents, a product $C_3H_6O_3$ is obtained, which has been termed **glycerose**. This has been shown to consist of the ketone, dihydroxyacetone, $OH \cdot CH_2 \cdot CO \cdot CH_2 \cdot OH$, with a small amount of the isomeric aldehyde, glyceraldehyde, $OH \cdot CH_2 \cdot CH(OH) \cdot CH:O$, and may be regarded as the simplest monose. It is a syrup, possesses most of the characteristic properties of the monoses, and when warmed with alkalis undergoes condensation and yields a hexose (α-acrose) (p. 312) which closely resembles fructose.

Tetroses, $C_4H_8O_4$.—A tetrose, **erythrose**, can be obtained by the oxidation of erythritol, $OH \cdot CH_2[CH \cdot OH]_2 \cdot CH_2 \cdot OH$, with nitric acid, and is probably a mixture of an aldose and ketose. Other tetroses can be obtained from the pentoses by the general methods described on p. 305.

Pentoses.—The pentoses are characterized by the fact that they yield furfuraldehyde or methyl-furfuraldehyde upon prolonged boiling with hydrochloric acid, water being eliminated. This reaction is largely made use of for their quantitative estimation (B. 1892, **25**, 2912; 1898, **30**, 2570). Arabinose gives furfuraldehyde itself, while its homologue, rhamnose, gives methyl-furfuraldehyde. When warmed with hydrochloric acid and phloroglucinol, cherry-red colorations are produced. The pentoses do not appear to exist free in the animal or vegetable kingdom, but are readily formed by the hydrolysis of various natural gummy carbohydrates

l-**Arabinose**, $C_5H_{10}O_5$, $= OH \cdot CH_2 \cdot [CH \cdot OH]_3 \cdot CH:O$, is produced by boiling gum-arabic, cherry gum, or beet-root chips with dilute sulphuric acid, and forms prisms which dissolve in water to a dextro-rotatory solution. It combines with hydrogen cyanide, and thus yields the nitriles of two stereo-isomeric hydroxy-caproic acids, viz. *l*-mannonic acid (*Kiliani*, B. **20**, 339, 1233) and *l*-gluconic acid (*E. Fischer*). In addition to *l*-arabinose, a *d*-arabinose and a *d-l*- or racemic arabinose are also known. They are related to one another in exactly the same manner as *l*-, *d*-, and *r*-tartaric acid. The corresponding alcohol is arabitol.

l-**Xylose**, or *Wood-sugar*, is stereo-isomeric with arabinose, and is prepared by boiling wood-gum, straw, and jute with dilute sulphuric acid, and is very similar to arabinose. (For its constitution, see B. **24**, 537.) The corresponding alcohol is xylitol. **Ribose** (B. 1891, **24**, 4214) and **Lyxose** (B. 1899, **33**, 1798) are stereo-isomeric with arabinose.

Rhamnose, or *Isodulcite*, $C_6H_{12}O_5$, $= CH_3 \cdot [CH \cdot OH]_4 \cdot CH:O$,

is obtained from several glucosides, *e.g.* quercitrin or xantho-rhamnin (yellow needles, present in French berries, *Rhamnus tinctoria*, &c.), by the action of dilute sulphuric acid. It forms colourless crystals which contain $1H_2O$, melts at 93°, and when distilled with sulphuric acid yields α-methyl-furfuraldehyde.

Several isomerides of rhamnose are known, *e.g.* **fucose** from sea-weed, **quinovose**, **rhodeose**, and **isorhamnose**.

Hexoses. — The hexoses constitute the most important group, as they contain all the more common natural monosaccharoses, *e.g.* *d*-glucose, *d*-fructose, *d*-galactose, &c. These occur in the free state in the juices of ripe fruits, and are also found combined with acids and other compounds in the ether- or ester-like compounds known as glucosides. They are also formed by the hydrolysis of more complex carbohydrates, *e.g.* cane-sugar, maltose, milk-sugar, or starch, either under the influence of mineral acids or of enzymes. They are sweet and for the most part crystalline compounds readily soluble in water, sparingly in absolute alcohol, and insoluble in ether. They possess the chemical properties of pentahydroxy-aldehydes and ketones.

Aldohexoses. — The common aldohexoses have the constitution represented by the formula:

$$OH \cdot CH_2 \cdot [CH \cdot OH]_4 \cdot CH{:}O.$$

In this formula the 4 carbon atoms contained within the brackets are asymmetric carbon atoms, and hence such a compound should exist in numerous stereo-isomeric forms. It can be shown that in this case the number of optically active isomerides theoretically possible is sixteen; of these some eleven are actually known, namely:

Aldohexose	Monobasic Acid	Dibasic Acid, $CO_2H[CH \cdot OH]_4 \cdot CO_2H$.	Alcohol.	M.-p. of Osazone
d-&*l*-Mannose	*d*-&*l*-Mannonic acid	*d*-&*l*-Mannosaccharic	*d*-&*l*-Mannitol	200°
d-&*l*-Glucose	*d*-&*l*-Gluconic acid	*d*-&*l*-Saccharic	*d*-&*l*-Sorbitol	Ibid
d-&*l*-Gulose	*d*-&*l*-Gulonic acid	*d*-&*l*-Saccharic	*d*-&*l* Sorbitol	157–159°
d-&*l*-Idose	*d*-&*l*-Idonic acid	Idosaccharic	*d*-&*l*-Iditol	193°
d-&*l*-Galactose	*d*-&*l*-Galactonic acid	ι-Mucic	ι-Dulcitol	193°
d-Talose	*d*-Talonic acid	Talomucic	*d*-Talitol	193°

All of these hexoses have to be represented by the same structural formula, and only differ as regards the spatial arrangements of the various radicals within the molecule. All are optically active in solution, and the majority form

pairs of optical antipodes, *e.g.* *d*- and *l*-glucose, which are related in exactly the same manner as *d*- and *l*-tartaric acids. The members of such a pair are identical as regards their ordinary chemical and physical properties, with the exception of their effects on polarized light, and their behaviour towards enzymes or ferments generally. As a rule, one of the two compounds exists naturally, *e.g.* *d*-glucose, and the second must be prepared by artificial means. The two are able to form a racemic compound, which differs as regards its physical properties from the active components.

The determination of the configuration of each aldohexose has been accomplished by *E. Fischer* largely from a study of the following points:—(*a*) The relationship of the aldohexose to the aldopentoses, *e.g.* *l*-arabinose can be transformed into a mixture of *l*-glucose and *l*-mannose, and hence in all three compounds the configuration of the following part of the molecule—

$$OH\cdot CH_2\cdot CH(OH)\cdot CH(OH)\cdot CH(OH)—$$

must be identical. (*b*) The nature of the dibasic acid formed on oxidation, or of the alcohol formed on reduction. When reduced, *d*-galactose yields an inactive hexahydric alcohol, viz. *i*-dulcitol, and from this it follows that in the *d*-galactose molecule the H and OH radicals must be so spatially arranged that when the $\cdot CH{:}O$ group is converted into a $CH_2\cdot OH$ group a symmetrical molecule is obtained (see formula below). (*c*) The nature of the osazone; *e.g.* *d*-glucose and *d*-mannose both give rise to the same osazone—*d*-glucosazone—and hence the spatial arrangements of the two molecules must be identical, with the exception of the part $\cdot CH(OH)\cdot CH{:}O$.

As the result of such methods, the following configurations have been arrived at for some of the commoner aldohexoses (B. 1891, **24**, 2683; 1894, **27**, 3211):—

CHO	CHO	CHO	CHO
HO·C·H	H·C·OH	H·C·OH	H·C·OH
HO·C·H	H·C·OH	HO·C·H	HO·C·H
H·C·OH	HO·C·H	H·C·OH	HO·C·H
H·C·OH	HO·C·H	H·C·OH	H·C·OH
$CH_2\cdot OH$	CH_2OH	CH_2OH	CH_2OH
d-Mannose	*l*-Mannose	*d* Glucose	*d*-Galactose.

E Fischer has suggested the following system of nomenclature. According to the Geneva Congress, the name for glucose is hexanepentolal. *Fischer* suggests that the asymmetric carbon atoms be numbered with respect to the CHO group, and that when the H is to the left and OH to the right of an asymmetric carbon atom, it is termed + and the reverse −. Thus:

d-Glucose is hexanepentolal,		+ − + +
l-Glucose	„	− + − −
d-Mannose	„	− − + +
d-Galactose	„	+ − − +
d-Gulose	„	− − + −
d-Idose	„	+ − + −
d-Talose	„	− − − +

d-Glucose, *Grape-sugar or dextrose*, $C_6H_{12}O_6 + H_2O$, occurs together with *d*-fructose in most sweet fruits, in honey, also in diabetic urine. It is prepared by the hydrolysis of more complex carbohydrates, *e.g.* sucrose or starch. The usual method, the hydrolysis of starch with dilute sulphuric acid, yields a product which contains, in addition to dextrose, dextrine and unfermentable substances. It crystallizes from water in nodular masses made up of six-sided plates which melt at 86°, and from methyl alcohol in small anhydrous prisms free from water, m.-pt. 146°. It is dextro-rotatory, $[\alpha]_D = 52{\cdot}6°$, hence the name "dextrose".

A freshly-prepared solution turns the plane of polarization almost twice as much as one which has been kept or heated to boiling, a phenomenon which is known as "bi-, multi-, or muta-rotation". (For explanation, cf. chapter on Physical Constants and Constitution.) The strength of a solution of glucose is usually determined polarimetrically from its specific rotatory power, or gravimetrically by determining the weight of cuprous oxide obtained by the reduction of *Fehling's* solution with a given volume of the solution (cf. p. 301).

d-Glucose-phenyl-hydrazone, $C_{12}H_{18}N_2O_5$, forms fine crystals which melt at 115°. Another modification melts at 144°. **d-Phenyl-glucosazone** crystallizes in sparingly soluble needles. The rotation produced by the hydrazones and osazones may be the opposite of that of the mother substance. It is an important point for the recognition of the latter. **d-Pentacetyl-glucose**, $C_6H_7O(OC_2H_3O)_5$, melts at 111°. **d-Glucosone**, $CH_2(OH)\cdot[CH(OH)]_3\cdot CO\cdot CHO$, forms a syrup which does not ferment with beer yeast, and which yields

the osazone immediately with phenyl-hydrazine. **Methyl glucoside,**

$$OH\cdot CH_2\cdot CH(OH)\cdot \underset{\llcorner\!\!-\!\!-\!\!-\!\!-O\!\!-\!\!-\!\!-\!\!-\lrcorner}{CH\cdot(CH\cdot OH)_2\cdot CH}\cdot OCH_3$$

exists in two stereo-isomeric modifications, melting at 165° and 107°. *l*-**Glucose** resembles *d*-glucose closely, excepting that it turns the plane of polarization as strongly to the left as the latter does to the right. *i*-**Glucose**, from *i*-gluconic acid, is a colourless syrup. The osazone, *i*-**glucosazone**, melts at 216°, and, apart from rotatory power, is deceptively like the *d*- and *l*-osazones.

Constitution of *d*-**Glucose.**—Its constitution as a penta-hydroxy aldehyde follows from the formation of a pentacetyl derivative, and from its oxidation first to a monobasic acid (gluconic acid) and then to a dibasic acid (saccharic acid), both of which contain the same number of carbon atoms as glucose. A proof both of its aldehydic nature and of the normal structure was afforded by *Kiliani* (B. 1886, **19**, 767), who prepared the cyanhydrin, hydrolysed this to the hexa-hydroxy-carboxylic acid, and, by reducing this with hydriodic acid and phosphorus, obtained *n*-heptylic acid:

$$OH\cdot CH_2\cdot(CH\cdot OH)_4\cdot CH{:}O \longrightarrow OH\cdot CH_2\cdot(CH\cdot OH)_4\cdot CH(OH)\cdot CN$$
$$CH_3\cdot(CH_2)_5\cdot CO_2H \longleftarrow OH\cdot CH_2\cdot(CH\cdot OH)_5\cdot CO_2H \longleftarrow$$

a product which could not have been produced if the glucose had possessed either a ketonic or an iso-chain (cf. Fructose). (For configuration, see p. 308.)

d-**Mannose** is stereo-isomeric with *d*-glucose, and is formed together with *d*-fructose by the cautious oxidation of mannitol, also by boiling the reserve cellulose of the seed of the Brazil-nut with dilute hydrochloric acid, and by reducing mannonic acid lactone with sodium amalgam. It forms a colourless amorphous mass readily soluble in water, is dextro-rotatory, $[\alpha]_D = +14{\cdot}36°$, and yields the same osazone as *d*-glucose. When treated with sodium amalgam it passes readily into *d*-mannitol. The **hydrazone** melts at 195°, and is sparingly soluble in water. *i*-**Mannose** forms a colourless syrup. The osazone is identical with that from *i*-fructose. *l*-**Mannose** is not so readily fermented as the *d*-isomeride.

d-**Galactose** is formed together with *d*-glucose by the hydrolysis of milk-sugar with dilute acid, and also from certain gums. It crystallizes in slender needles, melts at 166°, is

dextro-rotatory, $[\alpha]_D = +80{\cdot}3°$, and readily fermented. Its **pentacetyl** derivative melts at 143°, **α-methylgalactoside** at 111°, and the stereo-isomeric **β-compound** at 173°–175°.

Talose is a syrup. The phenyl-hydrazone is very readily soluble in water (difference from galactose).

Ketohexoses, $OH{\cdot}CH_2{\cdot}[CH{\cdot}OH]_3{\cdot}CO{\cdot}CH_2{\cdot}OH$, are structurally isomeric with the aldohexoses. As ketones they cannot be oxidized to acids containing the same number of carbon atoms (cf. pp. 68 and 303). The formula contains 3 asymmetric carbon atoms, and hence numerous stereo-isomerides are theoretically possible.

d-**Fructose**, *Fruit-sugar* or *lævulose*, $C_6H_{12}O_6$, is almost invariably found along with *d*-glucose in the juice of sweet fruits and also, together with the latter, in honey. It is formed along with *d*-glucose by the inversion of cane-sugar, and together with *d*-mannose by the cautious oxidation of *d*-mannitol; also from *d*-phenyl-glucosazone, and therefore indirectly from *d*-glucose. It is most easily prepared by heating inulin (p. 319) with very dilute acid (B. **23**, 2084); is somewhat difficult to obtain crystalline, and then forms hard, anhydrous, rhombic crystals melting at 95°. It is lævo-rotatory, although belonging genetically to the *d*-series. Its power of rotation is almost double that of *l*-glucose. It may be separated from *d*-glucose by means of its sparingly soluble lime compound.

Its close relationship to *d*-glucose is shown by the fact that it yields the same osazone, and on reduction yields a mixture of *d*-mannitol and *d*-sorbitol. On oxidation it yields glycollic and tartaric acids, or glycollic and trihydroxy-butyric acids. With methyl-phenyl-hydrazine it yields a colourless **osazone**. It is fermentable, but not so readily as *d*-glucose.

l-**Fructose** closely resembles *d*-fructose, but is dextro-rotatory, and as it is not readily fermented, can easily be obtained from *i*-**fructose**, which is a syrup.

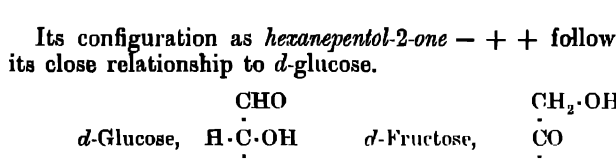
Constitution of *d*-Fructose.—The general properties point to its ketonic structure, and this was further proved by *Kiliani*, who hydrolysed the cyanhydrin, and then reduced the hydroxy-acid thus obtained with hydriodic acid and phosphorus, and obtained methyl-butyl-acetic acid:

$$OH{\cdot}CH_2{\cdot}(CH{\cdot}OH)_3{\cdot}CO{\cdot}CH_2{\cdot}OH \longrightarrow OH{\cdot}CH_2{\cdot}(CH{\cdot}OH)_3{\cdot}C\begin{cases}OH\\CN\\CH_2{\cdot}OH\end{cases}$$

$$\downarrow$$

$$CH_3(CH_2)_3{\cdot}CH\begin{cases}CH_3\\COOH\end{cases} \longleftarrow OH{\cdot}CH_2{\cdot}(CH{\cdot}OH)_3{\cdot}C\begin{cases}OH\\COOH\\CH_2OH.\end{cases}$$

Its configuration as *hexanepentol-2-one* $- + +$ follows from its close relationship to *d*-glucose.



since both yield the same osazone

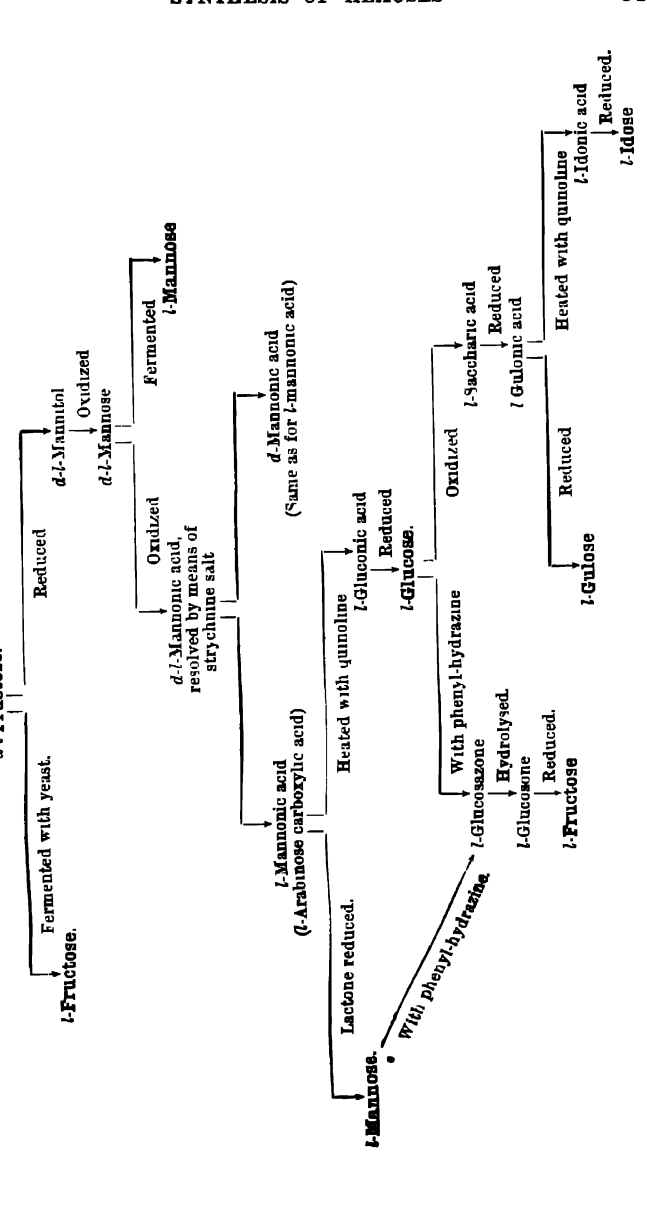
Other stereo-isomeric ketohexoses are *d*-**tagatose**, obtained by the action of potassic hydroxide solution on *d*-galactose. It melts at 124°, and yields the same osazone as *d*-galactose. *d*-**Sorbose**, obtained by oxidizing *d*-sorbitol; and *l*-**sorbose**, obtained as a by-product in the preparation of *d*-tagatose.

Synthesis of Hexoses.—*O. Loew* obtained, by the action of lime-water on formaldehyde, a substance which he termed **formose**, $C_6H_{12}O_6$, but which has since been shown to be a mixture of hexoses containing α-acrose. *Butlerow* has obtained a similar product from trioxymethylene. *Fischer* and *Tafel* (B. 1887, **20**, 1093, 3384; 1889, **22**, 97) obtained a mixture of sugars by the action of baryta water on glycerose (p. 306). Among these sugars was α-acrose, which is the starting-point for the synthesis of most other hexoses. The α-acrose is converted into its osazone, this is hydrolysed to the osone, and then reduced to the ketose, when *d*-*l*-fructose is obtained. According to *Neuberg* (B. 1902, **35**, 2626) the original α-acrose is *d*-*l*-fructose, since it reacts with methyl-phenyl-hydrazine, yielding methyl-phenyl-fructosazone. The scheme (p. 313) gives a *résumé* of the steps involved in the synthesis of the other hexoses from α-acrose.

The action of alkalis on hexoses has been studied by *Lobry de Bruyn* (B. **28**, 3078), who has shown that glucose, mannose, and fructose are partially transformed into each other under the influence of dilute alkalis:

$$\text{Glucose} \rightleftarrows \text{fructose} \rightleftarrows \text{mannose.}$$

Fructose appears to be formed as an intermediate product in the conversion of glucose into mannose. The transformation is only partial, and is accompanied by a change in rotatory power.


d-l-Fructose.
Fermented with yeast.
l-Fructose.
Reduced
d-l-Mannitol
Oxidized
d-l-Mannose
Fermented
l-Mannose
Oxidized
d-l-Mannonic acid, resolved by means of strychnine salt
d-Mannonic acid (Same as for l-mannonic acid)
l-Mannonic acid (l-Arabinose carboxylic acid)
Heated with quinoline
l-Gluconic acid
Reduced
l-Glucose.
Lactone reduced.
l-Mannose.
With phenyl-hydrazine
With phenyl-hydrazine
Oxidized
l-Saccharic acid
Reduced
l Gulonic acid
l-Glucosazone
Hydrolysed
l-Glucosone
Reduced.
l-Fructose
Heated with quinoline
l-Idonic acid
Reduced.
l-Idose
Reduced
l-Gulose

B. Di- and Trisaccharoses

This group comprises those carbohydrates which may be regarded as derived from 2 or 3 molecules of a monose by the elimination of 1 or 2 mols. of water respectively. As such anhydrides, they are all readily hydrolysed when boiled with dilute acids, yielding monoses, usually hexoses. Thus cane-sugar yields a mixture of *d*-glucose and *d*-fructose; maltose yields *d*-glucose only; milk-sugar yields *d*-glucose and *d*-galactose:

$$C_{12}H_{22}O_{11} + H_2O = 2C_6H_{12}O_6.$$

Raffinose or melitriose is a type of a trisaccharose, and on hydrolysis yields melibiose and *d*-fructose. The hydrolysis in most of these cases can not only be effected by means of acids, but also by means of enzymes, *e.g.* diastase and invertase hydrolyse cane-sugar, maltase malt-sugar, &c.

The disaccharoses are thus ethereal anhydrides of the hexoses, *e.g.* cane-sugar is *d*-glucose-*d*-fructose anhydride, and malt-sugar *d*-glucose anhydride, &c. In this anhydride formation 8 of the original 10 OH groups have remained intact, as the bioses readily yield **octacetyl** derivatives:

$$2C_6H_7O(OH)_5 = [C_6H_7O(OH)_4]_2O + H_2O.$$

The compounds possess for the most part a sweet taste, and crystallize more readily and are more stable than the monoses, but resemble the latter in solubility. They are not directly fermentable, but are readily fermented after hydrolysis to monoses. All those which occur naturally are optically active. Cane-sugar does not reduce *Fehling's* solution, but milk- and malt-sugars do.

Cane-sugar or **Sucrose**, *Saccharobiose*, $C_{12}H_{22}O_{11}$, occurs in red beet (Beta), in the sugar-cane (Saccharum), in the sugar-maple (Sorghum), and in many other plants, chiefly in the stem.

Preparation.—(*a*) From sugar-cane by expressing the juice and evaporating it until crystallization begins. (*b*) From sugar-beet by a systematic extraction of the pulp with water, *e.g.* by the "diffusion process". The impure juice is then treated with lime ("defecation"), the excess of the latter thrown down by carbon dioxide ("saturation"), and the syrup filtered through animal charcoal, and evaporated *in vacuo* to crystallization. From the mother-liquid or molasses the crystallizable sugar still present can be obtained as the sparingly

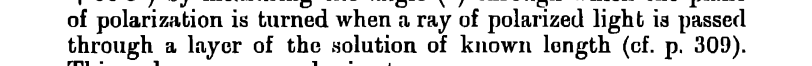
soluble strontium saccharate, $C_{12}H_{22}O_{11}$, SrO, which is then suspended in water and decomposed by carbon dioxide ("desugarizing of molasses").

Cane-sugar crystallizes in large monoclinic prisms, as is well seen in sugar-candy, and is soluble in one-third of its weight of water. It is not turned brown when heated with potash, and yields saccharates with lime and strontia, *e.g.* $C_{12}H_{22}O_{11} + CaO + 2H_2O$; $C_{12}H_{22}O_{11} + 2CaO$; $C_{12}H_{22}O_{11} + 3CaO$. Concentrated sulphuric acid produces charring (difference from *d*-glucose). Cane-sugar melts at 160°, and remains in the amorphous condition for some time after cooling (barley-sugar); when heated more strongly, it becomes brown from the formation of caramel or sugar dye, and finally chars.

The percentage of sugar in a solution of unknown strength can be determined from the specific rotatory power ($[\alpha]_D^{20°} = +66{\cdot}5°$) by measuring the angle (α) through which the plane of polarization is turned when a ray of polarized light is passed through a layer of the solution of known length (cf. p. 309). This is known as saccharimetry.

It is readily hydrolysed by acids, and this process is commonly spoken of as the **inversion** of cane-sugar, and the product as **invert sugar**. These names are due to the fact that the hydrolysis is accompanied by a change in the optical activity of the solution. The solution of cane-sugar is dextrorotatory, but after hydrolysis (or inversion) it becomes lævorotatory, as *d*-fructose is more strongly lævo- than *d*-glucose is dextro-rotatory.

Sucrose itself does not reduce *Fehling's* solution, but after inversion readily reduces. This would indicate that in the anhydride formation the aldehydic group of *d*-glucose and the ketonic group of *d*-fructose have been destroyed. The constitutional formula suggested by *E. Fischer* (B. 1893, **26**, 2405) is:



This formula readily accounts (*a*) for the formation of an octacetyl derivative (m.-pt. 67°); (*b*) for the absence of all reducing properties; (*c*) for the readiness with which it can be hydrolysed, since the two hexose molecules are united by means of an atom of oxygen; (*d*) for the non-formation of a hydrazone.

Milk-sugar or **Lactose**, *Lactobiose*, $C_{12}H_{22}O_{11} + H_2O$, occurs

in milk, and only occasionally in the vegetable kingdom. It is obtained by evaporating sweet whey. It crystallizes in hard rhombic prisms, and is much less sweet than cane-sugar, and also much less soluble in water. It is converted into "lacto-caramel" at 180°. It shows muta-rotation (p. 309), and reduces *Fehling's* solution.

Maltose or **Malt-sugar**, *Maltobiose*, $C_{12}H_{22}O_{11} + H_2O$, is formed by the action of diastase upon starch during the germination of cereals (preparation of malt). It forms a hard white crystalline mass, very similar to grape-sugar, and strongly dextro-rotatory. It reduces *Fehling's* solution, but only to about two-thirds the extent to which *d*-glucose does.

Lactose and maltose resemble one another very closely, and are probably stereo-isomeric. Since they both possess reducing properties, yield hydrazones, cyanhydrins, and can be oxidized to monobasic acids containing the same number of carbon atoms, it is obvious that they must contain an aldehydo-group, and the following structural formula has been given to both by *E. Fischer* (B. 1893, **26**, 2405):—

$$OH\cdot CH_2\cdot CH(OH)\cdot CH\cdot(CH\cdot OH)_2\cdot CH\cdot O\cdot CH_2\cdot(CH\cdot OH)_4\cdot CH{:}O.$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad \llcorner\!\!-\!\!-\!\!-

dilute acids or subjected to the action of enzymes, they are hydrolysed to mono- or di-saccharoses, generally to hexoses, *e.g.* $C_6H_{10}O_5 + H_2O = C_6H_{12}O_6$. The formation of pentoses is frequently to be noticed in this decomposition.

Like the foregoing compounds, therefore, the members of this group are to be regarded as the anhydrides of hexoses or pentoses. Consequently they still possess an alcoholic character and yield acetic and nitric esters, &c. Most of them are optically active. With dilute nitric acid they yield the same oxidation products as are obtained from the corresponding hexoses or pentoses, and iodine frequently gives characteristic colorations.

Cellulose, $(C_6H_{10}O_5)_x$, is widely distributed in nature as the membrane of plant cells, cotton, elder pith, wood, &c., consist of cellulose in a more or less pure state. It can be prepared by extracting cotton-wool or Swedish filter-paper with caustic potash, hydrochloric acid, water, alcohol, and ether successively, or by treating pine wood with sulphuric and a little nitric acid. It forms a white amorphous powder, insoluble in the ordinary reagents, but soluble in an ammoniacal solution of cupric oxide, from which it is again thrown down by acids.

When boiled with dilute sulphuric acid, it yields dextrine and *d*-glucose, while the concentrated acid converts it first into **amyloid**, an amorphous mass which is turned blue by iodine, and finally into dextrine. Parchment paper is simply unglazed paper which has been transformed superficially into amyloid by sulphuric acid.

Many cellulose derivatives are compounds of commercial importance. The nitric esters, so called nitro-celluloses, are used for a variety of purposes, and are usually prepared by the action of a mixture of nitric and sulphuric acids on the carbohydrate. The nature of the product depends largely on the concentration of the acid mixture and upon the temperature. In order to render the products stable, it is necessary to remove all traces of free acid. **Collodion**, a tetranitrate, is soluble in a mixture of alcohol and ether (1:7), and the solution is largely used for coating materials and rendering them air-tight. It is also used for the manufacture of artificial silk and in photography. When mixed with camphor (various other substitutes, such as phenolic esters, are now used) it forms ordinary celluloid. **Gun-cotton**, *pyroxiline*, is probably a hexanitrate; in appearance it resembles cotton wool, but is not so soft. It burns readily and explodes when struck or

strongly heated. It is largely used for making smokeless powders, and is often met with in the form of compressed cakes.

Practically all artificial silks are cellulose derivatives. The oldest method (*Chardonnel*) consisted in dissolving cellulose nitrates in a mixture of alcohol and ether (3:2), and forcing the solution under pressure from a copper vessel through small capillary tubes into water. The thread thus obtained was stretched to about the thickness of natural silk, and as it became hard was wound, dried, and denitrated by treatment with a reducing agent, such as ammonium sulphide or cuprous chloride and hydrochloric acid.

Other methods which are now adopted consist in (*a*) the use of cellulose acetates obtained by the action of acetyl chloride and zinc acetate or quinoline, or of acetic anhydride and a mineral acid on cellulose. The solution of the acetate is squirted into alcohol through small holes (*b*) The use of a solution of cellulose in ammoniacal cupric oxide, and forcing the solution through small holes into dilute acid (*Thiele* silk). (*c*) Use of viscose. Artificial, human, and horse hair are manufactured by similar methods The artificial silks are used for the manufacture of fabrics, and also for insulating metallic wires. **Viscose** (*Cross* and *Bevan*) is the sodium salt of cellulose xanthate. Cotton fibre is allowed to swell by treatment with sodium hydroxide solution, and is then shaken with carbon disulphide. Its solution in water forms a gelatinous mass which can be moulded. When exposed to the air it shrinks and hardens to a horn-like mass It is used as a substitute for glue, celluloid, horn, ivory, &c. When used for the manufacture of artificial silk it is necessary to purify it; this is done by acidifying with a weak acid (acetic or lactic), precipitating with alcohol or brine, and washing.

Viscoid is a mixture of viscose with clay or zinc oxide, and sets to an extremely hard mass.

Starch or **Amylum**, $(C_6H_{10}O_5)_x$, is present in all assimilating plants, being built up by the chlorophyll granules from the carbon dioxide absorbed, and is found especially in the nutriment reservoirs of the plants, *e.g.* in the grains of cereals, in perennial roots, potatoes, &c. It is converted into sugar during the transference of the sap. It forms a white velvety hygroscopic powder which consists of round or elongated granules built up of concentric layers, and insoluble in cold water. The interior of these granules consists of "granulose",

and their husk probably of cellulose. When they are warmed with water, the latter is broken open and the granulose dissolves; if the solution is moderately dilute, it can be filtered and a clear solution obtained, from which alcohol precipitates "soluble starch". Both the granules of starch and its jelly are coloured an intense blue by iodine and bright yellow by bromine, from the formation of loose additive compounds, "iodide and bromide of starch". The colour of the iodide of starch vanishes on heating, but reappears on cooling. Ordinary air-dried starch contains some 10–20 per cent of water, which can be removed by heating to 105°.

The so-called "soluble starch" is formed (*a*) when starch is heated with glycerol, (*b*) when starch is boiled with water containing sulphuric acid, (*c*) by the action of diastase or starch. Further treatment with acid converts it into dextrine and *d*-glucose, and with diastase into dextrine and maltose and isomaltose (B. 1893, **26**, 2533). Warming with very little dilute nitric acid to 110° yields dextrine.

Lichenin, or *Moss starch*, present in many lichens, *e.g.* in Iceland moss (*Cetraria islandica*), is coloured a dirty blue by iodine, and **inulin**, present in the roots of the dahlia and many composites (*Inula Helenium*), is coloured yellow by iodine and converted into *d*-fructose when boiled with water.

Glycogen, or **Animal starch**, *Liver starch*, is present, *e.g.* in the livers of the mammalia. It is a colourless amorphous powder which is turned wine-red by iodine; after the death of the animal it rapidly changes into *d*-glucose, the same conversion being effected by boiling with dilute acids, while enzymes transform it into maltose

Dextrine, or *Starch gum*, is a comprehensive name applied to intermediate products obtained in the transformation of starch into maltose and *d*-glucose. It may be prepared (*a*) by heating starch either alone or with a little nitric acid, (*b*) together with *d*-glucose by boiling starch with dilute sulphuric acid, and (*c*) together with maltose by the action of diastase on starch. The dextrines are soluble in water, and are precipitated by alcohol. They are often named according to their reaction with iodine, *e.g.* **amylo-dextrine** blue, **erythro-dextrine** red, and **achroo-dextrine** no colour. They do not reduce *Fehling's* solution even when warmed, and are not directly fermentable by yeast but only after the prolonged action of diastase, glucose being formed as an intermediate product.

Synthesis of Sugars.—The sugars are extremely important

from the point of view of plant physiology. The plant absorbs carbon dioxide and water, and with the aid of sunlight is capable, in the presence of chlorophyll, of transforming these into glucose and even more complex carbohydrates. Various speculations have been made with regard to the manner in which these complex compounds are formed. *Baeyer* has suggested that the carbon dioxide is first reduced to formaldehyde, and this then polymerizes as in *Loew's* experiments, yielding carbohydrates,

$$CO_2 \longrightarrow H\cdot C\begin{matrix}=O\\ \diagdown H\end{matrix} \longrightarrow (H_2C{:}O)_6 = C_6H_{12}O_6.$$

For many years the important link in this chain, viz. the reduction of carbon dioxide to formaldehyde, was missing; the reaction could not be accomplished in the laboratory. *Fenton* has recently shown (J. C. S. 1907, **91**, 687) that when carbon dioxide is passed into water in which sticks of magnesium are immersed, a small amount of the gas is reduced to formaldehyde, especially in the presence of ammonia or phenylhydrazine *Lob* has also found that moist carbon dioxide yields formaldehyde under the influence of the silent electric discharge (Zeit. Electrochemie, 1905, **11**, 745, 1906, **12**, 282).

Class II.—CHEMISTRY OF THE CYCLIC COMPOUNDS

XV. INTRODUCTION

The compounds which have been treated of in Sections I to XIV are derivable from the homologous hydrocarbons C_nH_{2n+2}, C_nH_{2n}, C_nH_{2n-2}, &c, by the exchange of hydrogen for halogen, hydroxyl or oxygen, amidogen, carboxyl, &c.; and since all the hydrocarbons already mentioned may also be regarded as derivatives of methane (*e.g.* $C_2H_6 = CH_3(CH_3)$ = methyl-methane, $C_3H_8 = CH_2(CH_3)_2$ = dimethyl-methane, $C_2H_4 = CH_2{:}CH_2$ = methylene-methane, $C_2H_2 = CH{:}CH$ = methine-methane, &c.), we may term the compounds which have been described in the foregoing portion of this book **methane derivatives.**

As nearly all these compounds have open-chain formulæ, they are spoken of as **open-chain compounds**, or often **aliphatic compounds.**

But in addition to this first class of organic compounds there is a second great class, viz. that of the **closed-chain compounds** The old classification was into aliphatic or methane derivatives and aromatic or benzene derivatives. The expression "aromatic" is historical, but no longer justified by facts, since compounds of agreeable as well as unpleasant odour are to be found in both classes. The members of this second class which are derivable from the hydrocarbon benzene, C_6H_6 (and also from more complicated hydrocarbons such as anthracene, naphthalene, &c., which are themselves derivatives of benzene), just as the methane derivatives are from methane, are designated benzene derivatives.

Recent investigations have led to the discovery of numerous other cyclic compounds which cannot be regarded as simple derivatives of benzene, *e.g.*:



&c.;

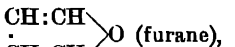
and hence the modern classification of the cyclic compounds is into:—

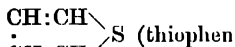
A. **Carbocyclic or Isocyclic.**—In all these compounds the ring or closed chain is composed entirely of carbon atoms. The carbocyclic compounds are usually divided into—

(i) Polymethylene derivatives or naphthenes.

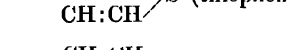
(ii) Benzene derivatives or aromatic compounds, including the allied compounds naphthalene, anthracene, &c.

B. **Heterocyclic Compounds.**—In these compounds the closed ring is formed partly of carbon atoms and partly of atoms of other elements. Well-known examples are:





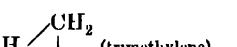




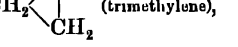
CARBOCYCLIC COMPOUNDS

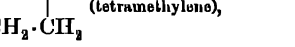
XVI. POLYMETHYLENE DERIVATIVES

The hydrocarbons from which all these compounds are derived consist of three or more methylene groups united together to form a closed ring The names for the specific hydrocarbons indicate the number of such groups, *e g.*





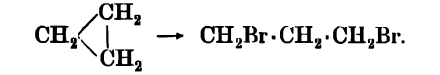




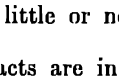
The systematic names for these compounds are **cyclo-propane, cyclo-butane,** &c., although the compounds are isomeric with the olefines, and have the same general formula, C_nH_{2n}. The above names indicate the fact that the compounds are in a sense saturated.

Relative Stability of Polymethylene Compounds.—It has been found that the majority of trimethylene derivatives are relatively unstable; to a certain extent they resemble ethylene

oxide, and are capable of forming additive products by the rupture of the ring. Thus bromine slowly transforms trimethylene under the influence of sunlight into trimethylene dibromide:

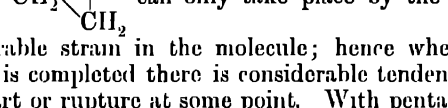


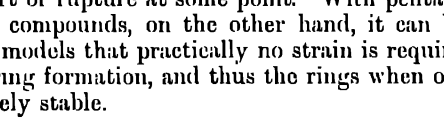
Tetramethylene derivatives are somewhat more stable, and penta- and hexa-methylene derivatives are remarkably stable and show little or no tendency towards the rupture of the molecule.

These facts are in harmony with *Baeyer's* tension theory. If the four valencies of the tetravalent carbon atom are assumed to be symmetrically distributed in space around the carbon atom, it is found that ring formation in the case of a compound  can only take place by the exercise of a considerable strain in the molecule; hence when the ring formation is completed there is considerable tendency for it to spring apart or rupture at some point. With penta- and hexa-methylene compounds, on the other hand, it can be seen by the aid of models that practically no strain is required to complete the ring formation, and thus the rings when once formed are relatively stable.

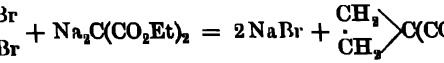
GENERAL METHODS OF FORMATION

1. By the action of sodium on dihalogen derivatives of the paraffins (*Freund*). The two halogen atoms must not be attached to the same or to adjacent carbon atoms.





2. Acids and their esters can be obtained by the condensation of ethyl sodio-malonate with ethylene dibromide and other dihalogen derivatives (*W. H. Perkin, Jun.*):



and the ester on hydrolysis yields trimethylene-dicarboxylic acid.

Ethyl acetoacetate may be substituted for ethyl malonate.

3. By the action of halogens (bromine, or preferably iodine) on the sodio-derivatives of certain esters, *e.g.* sodio-derivative of ethyl butane-tetracarboxylate (*W. H. Perkin, Jun.*):

$$\begin{matrix}CH_2\cdot CNa(CO_2Et)_2\\ CH_2\cdot CNa(CO_2Et)_2\end{matrix} + I_2 = 2NaI + \begin{matrix}CH_2\cdot C(CO_2Et)_2\\ CH_2\cdot C(CO_2Et)_2\end{matrix}$$

4. By intramolecular pinacone formation. Just as ketones on reduction yield pinacones·

$$\begin{matrix}(CH_3)_2\cdot C{:}O\\ (CH_3)_2\cdot C{:}O\end{matrix} + 2H = \begin{matrix}(CH_3)_2C\cdot OH\\ (CH_3)_2C\cdot OH\end{matrix}$$

(cf. p. 191), so certain diketones on reduction yield cyclic pinacones, *i.e.* dihydric alcohols derived from the polymethylene hydrocarbons:

$$CH_2\begin{matrix}\diagup CH_2\cdot CO\cdot CH_3\\ \diagdown CH_2\cdot CO\cdot CH_3\end{matrix} + 2H = CH_2\begin{matrix}\diagup CH_2\cdot C(OH)\cdot CH_3\\ \diagdown CH_2\cdot C(OH)\cdot CH_3\end{matrix}$$

1,2-Dimethyl 1 2-dihydroxy cyclo pentane.

5. A number of ketones derived from the polymethylenes have been obtained by the dry distillation of the calcium salts of the higher dibasic acids of the oxalic series (*J. Wislicenus*), *e.g.* calcium adipate yields keto-pentamethylene:

$$\begin{matrix}CH_2\cdot CH_2\cdot CO\cdot O\\ CH_2\cdot CH_2\cdot CO\cdot O\end{matrix}\!\!\diagdown\!\!\diagup Ca = CaCO_3 + \begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot CH_2\end{matrix}\!\!\diagdown\!\!\diagup CO,$$

and this can be reduced to pentamethylene. The constitution of the keto-derivative follows from the fact that on oxidation the ring is ruptured and glutaric acid is formed.

Keto-hexamethylene and keto-heptamethylene or suberone have been obtained by similar methods, but the yield is not so good in these two cases.

6. Hexamethylene compounds are often obtained by the reduction of benzene derivatives with sodium and alcohol:

$$CH\begin{matrix}\diagup CH{:}CH\\ \diagdown CH{:}CH\end{matrix}\!\!\diagdown CH + 6H = CH_2\begin{matrix}\diagup CH_2\cdot CH_2\\ \diagdown CH_2\cdot CH_2\end{matrix}\!\!\diagdown CH_2.$$

General Properties.—On the whole these compounds somewhat closely resemble the paraffins as regards their chemical

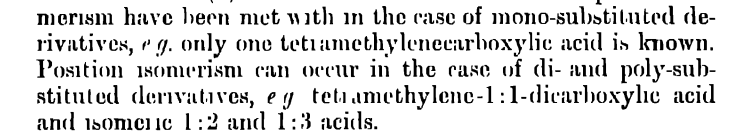
properties, hence the names cyclo-pentane for pentamethylene, cyclo-hexane, &c.

The trimethylene compounds, however, resemble the olefines, *e.g.* (*a*) they can combine with bromine to form additive compounds; (*b*) they are slowly oxidized by permanganate. In neither of these reactions do they take part so readily as the simpler olefines, and in all cases the products obtained are formed at the expense of the rupture of the ring.

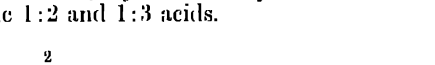
The fact that the majority of the hydrocarbons of this series resemble paraffins indicates that the formation of a closed chain does not affect to any considerable extent the properties of a compound (cf. Benzene)

In their chemical properties the compounds closely resemble the corresponding derivatives of the paraffins, *e.g.* the acids resemble to a large extent the fatty acids, yielding salts, esters, acid chlorides, amides, &c

Isomerism (*a*) **Position Isomerism.**—No examples of isomerism have been met with in the case of mono-substituted derivatives, *e.g.* only one tetramethylenecarboxylic acid is known. Position isomerism can occur in the case of di- and poly-substituted derivatives, *e.g.* tetramethylene-1:1-dicarboxylic acid and isomeric 1:2 and 1:3 acids.



1:1-Dicarboxylic acid. 1:2-Dicarboxylic acid.



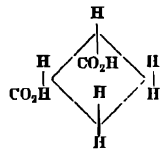
1:3-Dicarboxylic acid.

The number of isomerides possible in each case can be worked out by the student (cf. Benzene Derivatives).

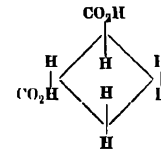
(*b*) **Stereo-isomerism**.—Certain di-substituted derivatives have been found to exist in isomeric forms which are structurally identical. These must therefore be **stereo-isomeric**. Some of the simplest examples of this stereo-isomerism are met with in the dibasic acids. For example:

Tetramethylene-1:2-dicarboxylic acid exists in two isomeric forms. In both acids the $2CO_2H$ groups are attached to the carbon atoms 1 and 2, and the only difference is in the relative spatial relationships of the groups. If the plane of the paper represents the plane in which the centres of gravity of

the four carbon atoms of the ring lie, then the possibilities are—



(I) *cis.*

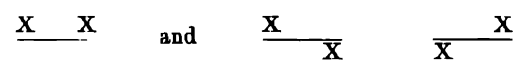


(II) *trans*

(I) That the two CO_2H groups lie in the same plane either above or below the plane of the paper (this is known as the *cis* acid), and (II) that the two CO_2H groups lie in different planes, one above and one below the plane of the paper (this is known as the *trans* acid). As a rule, the *cis* acids yield inner anhydrides, *e.g.* $C_4H_6\langle^{CO}_{CO}\rangle O$, more readily than the stereoisomeric *trans* acids, and the *cis* acids are generally transformed into the corresponding *trans* acids when heated with hydrochloric acid at 190°. (Cf. *Perkin, Jun.*, J. C. S. 1894, 572.)

A simple method of depicting these isomerides is due to *Aschan* (B. 1902, **35**, 3389).

The plane of the carbon atoms of the ring is represented by a straight line. The unsubstituted hydrogen atoms are not denoted, only those which have been replaced by substituents. It has been found that the symmetry of such projections corresponds with the symmetry of the molecules projected. For the *cis* dicarboxylic acids, for example, if CO_2H = X, we have:



(I) *cis* (II) *trans* (III)

The *cis* compound (I) is not perfectly asymmetric, whereas the *trans* compound (II) is. Corresponding with (II) is a third isomeride, which stands in the same relationship to (II) as an object to its mirror image, or as *d*- to *l*-lactic acids. Both should therefore be optically active (one *d* and the other *l* to the same extent), and should be capable of combining to yield a racemic compound. All the *trans* compounds prepared artificially are optically inactive, and are presumably therefore racemic compounds of (II) and (III), although so far very few have been resolved into optically active components.

Intermediate between the polymethylene compounds and benzene derivatives are the reduction products of benzene and its derivatives, *e.g.* di- and tetra-hydrobenzene, tetrahydrophthalic acid, &c., C_6H_8, C_6H_{10}, $C_6H_8(CO_2H)_2$. These will be discussed along with the benzene compounds, from which they are derived.

XVII. BENZENE DERIVATIVES. INTRODUCTION

Benzene is, as its formula C_6H_6 shows, a compound much poorer in hydrogen than the paraffins, containing 8 hydrogen atoms less than hexane, C_6H_{14}; in the same way all benzene derivatives are much poorer in hydrogen, *i e.* richer in carbon than the analogous methane derivatives, as is seen by comparing *e.g.* benzoic acid, $C_7H_6O_2$, with heptoic acid, $C_7H_{14}O_2$, or aniline, C_6H_7N, with ethylamine, C_2H_7N, &c

The hydrogen atoms of benzene are, like those of methane, replaceable by numerous types of radicals. By the entrance of halogens, halide substitution products are formed, by the entrance of NH_2, aromatic bases, of OH, phenols, of NO_2, nitro-compounds, and of CH_3, &c, the homologues of benzene, there are, in addition to these, aromatic alcohols, aldehydes, acids, &c.

These benzene derivatives are partly analogous in their properties to the methane derivatives of corresponding composition; in part, however, they show new and peculiar properties of their own (see pp 328 *et seq.*). One distinguishes between mono-, di-, tri-, &c, substituted benzene derivatives according as 1, 2, or more hydrogen atoms are replaced by the various radicals; thus, for instance, toluene, $C_6H_5 \cdot CH_3$, and chloro-benzene, $C_6H_5 \cdot Cl$, are mono-derivatives, dimethylbenzene, $C_6H_4(CH_3)_2$, and dichloro-benzene, $C_6H_4Cl_2$, di-derivatives, and so on. It is not necessary that the substituents should be identical, so that innumerable compounds are known containing various substituents, *e.g.* $OH \cdot C_6H_4 \cdot NO_2$, nitrophenol, $C_6H_4Br \cdot SO_3H$, bromobenzene-sulphonic acid; $CH_3 \cdot C_6H_3(NO_2)_2$, dinitro-toluene. Such compounds have usually some of the characteristics of all those mono-derivatives which result from benzene by the exchange of one hydrogen atom for one of these substituents.

All the derivatives of benzene can be converted either into benzene itself or into very closely allied compounds by *rela-*

tively simple reactions. Thus all the carboxylic acids of benzene (benzoic, phthalic, mellitic, &c.) yield benzene on distillation with lime, while other acids, such as salicylic, evolve CO_2 and yield phenol; the last-named compound is converted into benzene when distilled with zinc dust. The homologues of benzene are converted by oxidation into benzene-carboxylic acids, which yield benzene when heated with lime.

The relationship of a benzene derivative to its mother substance is therefore a very simple one.

This circumstance is one particularly worthy of note, since the atomic group C_6H_6 is already a tolerably complicated molecule in itself, and also because benzene cannot by any means be transformed into a simpler hydrocarbon containing 5, 4, or 3 carbon atoms; when oxidized, which is a matter of difficulty, it yields carbonic or similar simple organic acids.

The benzene derivatives are connected with one another by the most varied reactions. The NO_2 group is readily convertible into NH_2, and the latter is replaceable by halogen, hydrogen, and hydroxyl; the halogen is also replaceable by methyl, carboxyl, &c.

As a rule, the group of 6 carbons with the hydrogens is spoken of as the **benzene nucleus**, and all substituents are spoken of as **side chains**. Thus in $C_6H_5 \cdot \underline{CHO}$, $C_6H_4 \cdot \underline{(CH_3)_2}$, $C_6H_5 \cdot \underline{NH_2}$ the radicals underlined are the side chains.

CHARACTERISTIC PROPERTIES OF BENZENE DERIVATIVES

In many chemical properties benzene and its derivatives differ markedly from the paraffins or unsaturated open-chain hydrocarbons.

1. The aromatic hydrocarbons and their derivatives are readily attacked by concentrated nitric acid, yielding nitro-derivatives:

$$C_6H_5 \cdot H + HO \cdot NO_2 = H_2O + C_6H_5 \cdot NO_2.$$

Certain of the higher paraffins also yield nitro-derivatives when heated with nitric acid (p. 95).

2. Sulphonic acids are readily formed by the action of concentrated or fuming sulphuric acid:

$$C_6H_5 \cdot H + OH \cdot SO_2 \cdot OH = H_2O + C_6H_5 \cdot SO_2 \cdot OH.$$

This type of reaction is never met with in the aliphatic series.

3. The homologues of benzene differ from the paraffins especially as regards oxidation; while the latter are only attacked with difficulty by oxidizing agents, the former are readily converted into benzene-carboxylic acids:

$$C_6H_5 \cdot CH_3 \longrightarrow C_6H_5 \cdot CO_2H.$$

4. The halogens chlorine and bromine can react with benzene in two distinct ways: (*a*) yielding substituted derivatives, *e.g.* $C_6H_6 + Br_2 = C_6H_5Br + HBr$, or (*b*) yielding additive products, *e.g.* $C_6H_6Br_6$.

The process of substitution is the more important and the commoner of the two reactions

5. There are not wanting other distinguishing characteristics between the aromatic hydrocarbons and the paraffins. Thus the halogen compounds C_6H_5X are chemically less active, and the hydroxyl compounds, *e.g.* $C_6H_5(OH)$, are of a more acidic nature than the corresponding fatty bodies. The phenyl radical, C_6H_5, is therefore more acid or "negative" in character than the ethyl, C_2H_5 (cf *V. Meyer*, B. **20**, 534, 2944; A. **250**, 118).

6. Diazo-compounds are far more common in the aromatic series than in the aliphatic.

ISOMERIC RELATIONS

1 While several isomeric mono-derivatives are both theoretically possible and have been actually obtained from each hexane, C_6H_{14}, benzene is only capable of forming a single mono-derivative in each case; isomeric mono-derivatives of benzene are unknown *The six hydrogen atoms of benzene thus possess an equal value, or are similarly situated within the molecule.* This is not merely an empirical law, but one which has been proved experimentally.

PROOF OF THE EQUAL VALUE OF THE SIX HYDROGEN ATOMS

Let the 6 H atoms be designated as *a*, *b*, *c*, *d*, *e*, and *f* respectively.

(1) Phenol, $C_6H_5(OH)$, whose hydroxyl may have replaced the H atom *a*, may be converted into bromo-benzene, C_6H_5Br, and this latter into benzoic acid, $C_6H_5(CO_2H)$. The carboxyl in the latter has therefore also the position *a*, *i.e.* it has replaced the H atom *a*.

(2) Three hydroxy-benzoic acids, $C_6H_4(OH)(CO_2H)$, can either be prepared from benzoic acid or converted into it; their carboxyl therefore has the position *a*, and consequently their hydroxyl must replace some one of the other H atoms, be it *b*, *c*, or *d*.

(3) Each hydroxy-benzoic acid can be decomposed, yielding carbon dioxide and ordinary phenol, C_6H_5OH:

$$C_6H_4(OH)(CO_2H) = C_6H_5(OH) + CO_2$$

And since the latter compound contains the hydroxyl in position *a*, according to (1), while the hydroxyl in the hydroxy-benzoic acids replaces the H atoms *b*, *c*, and *d*, it follows that the hydrogen atoms *a*, *b*, *c*, and *d* are of equal value.

(4) Now, as will be explained on p. 331, for each H atom there are present two other pairs of symmetrical hydrogen atoms, *i.e.* pairs of which either the one or the other atom may be replaced by any given radical without different substances resulting. But the atoms of such a pair cannot both be present in the positions *a*, *b*, *c*, and *d*, as in this case three hydroxy-benzoic acids could not exist. It must therefore be the remaining H atoms *e* and *f* which are respectively in positions symmetrically situated to two of the former, and which are therefore of equal value with them, *i.e.* $e = c$, $f = b$. Since, however, $a = b = c = d$, it follows that all the 6 hydrogen atoms are of equal value (*Ladenburg*, B. 7, 1684).

2. With di-substituted derivatives of benzene it has been found that in each case three distinct isomeric forms exist. The two substituents may be alike, or they may be dissimilar, *e.g.* three dichloro-benzenes, $C_6H_4Cl_2$, three diamino-benzenes, $C_6H_4(NH_2)_2$, three dimethyl-benzenes, $C_6H_4(CH_3)_2$, three hydroxy-benzoic acids, $C_6H_4(OH)(CO_2H)$, are known. In no case have more than three such isomerides been found.

It can be shown that with respect to each H atom of benzene, *e.g.* for *a*, two pairs of other H atoms, *e.g.* *b* and *f*, *c* and *e*, are symmetrically situated, so that it makes no difference whether, after *a* is replaced, the second substituent replaces the one or the other of the symmetrically placed hydrogen atoms, say *b* or *f*. According to the above notation, therefore, $ab = af$, and $ac = ae$. On the other hand, the combinations *ab* and *ac* are not equivalent, but represent isomers; the combination *ad*, the only remaining case, represents the third isomer.

PROOFS THAT FOR EVERY H ATOM (*a*) TWO OTHER PAIRS OF SYMMETRICALLY LINKED H ATOMS EXIST

1. According to *Hubner* and *Petermann* (A. **149**, 129, cf. also *Hubner*, A. **222**, 67, 166), the (so-called meta-) bromo-benzoic acid, which is obtained by brominating benzoic acid, and whose Br atom may be in position *c* and CO_2H in position *a*, yields with nitric acid two nitrobromo-benzoic acids, $C_6H_3Br(NO_2)(CO_2H)$, the NO_2 being, say, in positions *b* and *f*. These are both reduced by nascent hydrogen to the same (so-called ortho-) amino-benzoic acid, $C_6H_4(NH_2)(CO_2H)$, the NO_2 being here changed to NH_2 and the Br replaced by H. Since the same amino-benzoic acid is formed in both cases, notwithstanding that the nitro-groups must be in the place of different H atoms, say *b* and *f*, from the fact of the two nitro-acids being dissimilar, it follows that *b* and *f* must be arranged symmetrically as regards the H atom *a*, *i.e.* *ab* = *af*.

2. In an analogous manner salicylic acid, $C_6H_4(OH)(CO_2H)$, which can be prepared from the above-mentioned amino-benzoic acid, yields two nitro-derivatives, $C_6H_3(OH)(NO_2)(CO_2H)$. If, however, the hydroxyl in these is replaced by hydrogen (a reaction which can be effected by indirect methods), the nitro-benzoic acids thus obtained, $C_6H_4(NO_2)(CO_2H)$, are identical, and therefore the H atoms which have been replaced by NO_2 are in positions symmetrical to *a*. When this nitro-benzoic acid is in its turn reduced to amino-benzoic acid, $C_6H_4(NH_2)(CO_2H)$, it is not the above (ortho-) amino-acid (where *ab* = *af*) which is obtained, but an isomer. The NO_2 groups cannot therefore here be in the positions *b* and *f*, but must replace two other H atoms which are likewise symmetric towards *a*, say *c* and *e*, *i.e.* *ac* = *ae* (*Hubner*, A. **195**, 4).

Thus two pairs of H atoms are symmetrically situated as regards the H atom *a*: *ab* = *af*; *ac* = *ae*. There remains only the third possible combination *ad*; the sixth H atom *d* is situated towards the first *a* in a position of its own, *i.e.* in one to which there is no corresponding position.

For further particulars, cf. *Ladenburg*, "Theorie der aromat. Verbindungen", Braunschweig, 1876; *Wroblewsky*, A. **168**, 153; **192**, 196; B. **8**, 573; **9**, 1055; **18**, Ref. 148. *Noelting*, B. 1904, **37**, 1015, gives a very simple proof.

It has been assumed in the considerations just detailed that when one compound is converted into another by the

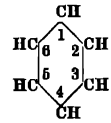
exchange of atoms or radicals (NH_2 for NO_2, H for OH), this exchange is effected without a so-called "molecular rearrangement" taking place at the same time (see p. 132) Experience has proved that this may be taken for granted in a large number of reactions which proceed with relative smoothness and at comparatively low temperatures. Those instances in which a molecular rearrangement ensues are now well known; especially is this the case in the fusion of sulphonic acids with potash (exchange of SO_3H for OH), a reaction which takes place at relatively high temperatures only, and which frequently leads to isomers of the compounds expected In other reactions which occur at high temperatures a rearrangement of the atoms in the molecule can also take place. Thus, when potassium ortho-hydroxy-benzoate is heated to 220°, the potassium salt of the para-acid is formed, the three isomeric bromo-benzene-sulphonic acids, $C_6H_4Br(SO_3H)$, and the three bromo-phenols, $C_6H_4Br(OH)$, yield only meta-dihydroxy-benzene (resorcinol), $C_6H_4(OH)_2$, when fused with potash, and not the three isomeric dihydroxy-benzenes; ortho-phenol-sulphonic acid, $C_6H_4(OH)SO_3H$, yields the para-acid when heated. Reactions of this nature probably arise from the successive taking up and splitting off of atoms or atomic groups.

CONSTITUTION OF BENZENE

The formula C_6H_6 at once indicates that benzene cannot be a saturated open-chain compound. The possibility that it is an open-chain unsaturated compound containing several double or triple bonds has been shown to be untenable, *e.g.* dipropargyl (p. 53), $CH{:}C\cdot CH_2\cdot CH_2\cdot C{:}CH$, although resembling benzene in physical properties, is quite different as regards most of its chemical properties, it combines readily with bromine, yielding additive compounds with 2, 4, 6, or 8 atoms of bromine, and it is also oxidized with the greatest readiness. Benzene combines with bromine only slowly and under specific conditions, and then yields $C_6H_6Br_6$; it is, further, extremely stable towards oxidizing agents. The equivalency of the 6 hydrogen atoms in the benzene molecule is a further strong argument against such open-chain formulæ. *Kekulé* was the first to suggest a closed-chain, cyclic, or ring formula for benzene.

In order to account for the existence of only one mono-substituted derivative, C_6H_5X, but of three isomeric di-sub-

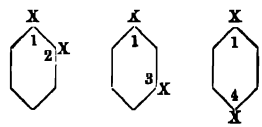
stituted derivatives, $C_6H_4X_2$, it is necessary to assume that a single hydrogen atom is attached to each carbon atom.



This formula is usually known as the benzene ring.

In the above formula the six hydrogen atoms are symmetrically placed with respect to one another, and thus in the formation of a mono-substituted derivative it is immaterial which one of the six hydrogens is replaced; only one compound, C_6H_5X, can be formed.

With di-substituted derivatives three isomerides are theoretically possible, viz.:

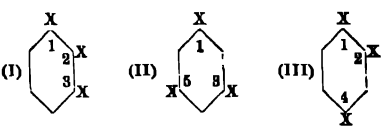


the 1:2 or ortho-compound, 1:3 or meta-compound, and the 1:4 or para-compound.

The compound 1.5 is identical with 1:3, and 1:6 is identical with 1:2. Cf. *Wohl*, B. 1910, **43**, 3171.

The hydrogen atoms in positions 2:6 form one pair of symmetrical hydrogen atoms mentioned on p 329, and those in positions 3:5 form the second pair, whereas the hydrogen in position 4 has no other hydrogen atom corresponding with it.

Similarly, three tri-substituted derivatives, $C_6H_3X_3$, are known, and only three are possible with such a ring formula, viz.:

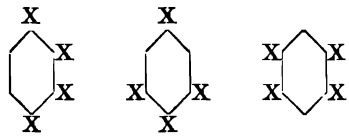


(I) 1:2:3 or adjacent tri-derivative.
(II) 1:3:5 or sym tri-derivative.
(III) 1:2:4 or unsym. tri-derivative.

Any other combination is identical with one of these, 2:4:6 = 1:3:5, and 1:4:6 = 1:2:4.

The number of isomerides is considerably increased when the three substituents are not similar, *e.g.* in a compound, $NH_2 \cdot C_6H_3Br \cdot CO_2H$.

With a tetra-substituted derivative, $C_6H_2X_4$, where all four substituents are alike, only three isomerides are possible, namely those corresponding with the *o*-, *m*-, and *p*-di-derivatives:

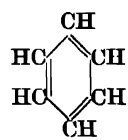


And with a penta-substituted derivative, C_6HX_5, only one form is possible.

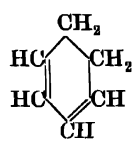
The number of isomerides actually found in each case is in perfect harmony with these theoretical deductions.

The ring formula for benzene, given above, represents each carbon atom as tervalent; the difficulty of accounting for the fourth valency can be overcome in several ways.

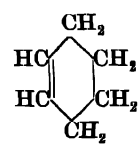
The first method, suggested by *Kekulé*, was to suppose alternate double and single bonds between the 6 carbon atoms, *e.g.*:



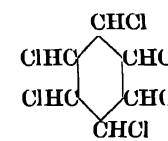
This formula is in perfect harmony with the formation of benzene from acetylene, and of trimethyl-benzene from acetone. It also largely accounts for the formation of additive compounds by benzene and its derivatives, *e.g.*:



Dihydro-benzene



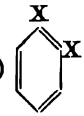
Tetrahydro-benzene

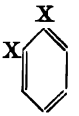


Benzene hexachloride.

Two arguments which have been brought forward against this formula are—

(*a*) Two ortho-disubstituted derivatives should be possible, namely, those represented by the formulæ:

(I) 

(II) 

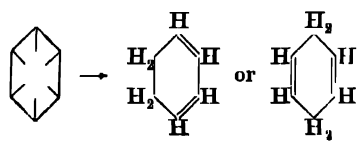
In formula (I) the 2 carbon atoms to which the substituents are attached are united by a double bond, and in formula (II) by a single bond. *Kekulé* has suggested that the single and double bonds may be continually changing, so that positions 2 and 6 are really symmetrical with respect to 1.

(*b*) The stability of benzene towards oxidizing agents has been used as an argument against such a formula containing three double bonds in the molecule. Di- and tetrahydro-benzenes—obtained by the reduction of benzene—which contain respectively two and one double bonds in their molecules, are readily oxidized, and also readily yield additive compounds with halogens. It has been suggested that the peculiar symmetrical structure of the benzene molecule may account for its stability.

(II) A second method of accounting for the fourth valency of each carbon atom is that first suggested by *Armstrong*, and afterwards developed by *Baeyer*:

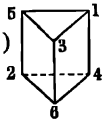
(IIA) 

It represents the fourth valency of each carbon atom as directed towards the centre of the molecule, where the 6 are kept in equilibrium. This *centric formula* for benzene represents a method of linking which is unknown in the fatty series. When reduced to dihydro-benzene, four of the six centric bonds form two double bonds.



This readily accounts for the great difference between the chemical properties of benzene and of its reduction products.

Various other formulæ have been suggested for benzene, *e.g. Ladenburg's* prism formula, *Claus's* diagonal formula, and *Dewar's* formula.

(III) 

Ladenburg

(IV) 
Claus

(V) 
Dewar

A strong objection to the prism formula and to any other three-dimension space formula is that the molecules of certain substituted derivatives would be perfectly asymmetric, and should therefore exist in optically active modifications. No benzene derivative which occurs naturally is optically active, and attempts to resolve substituted benzene derivatives, *e.g.* $C_6H(OH)(CO_2H)(CH_3)(C_3H_7)(NO_2)$, nitrothymotic acid, have been unsuccessful. *Rugheimer* (B. 1896, **29**, 1967) states, however, that he has obtained *m*-methyl-*p*-hydroxy-benzoic acid in an optically active form.

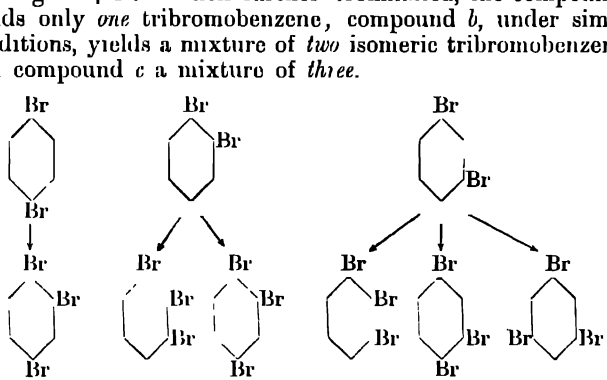
Other objections to the prism formula are (*a*) the difficulty of accounting for the reduction products of benzene, and (*b*) the fact that when benzene is oxidized by various methods no compound is met with which contains a carbon atom attached to 3 other carbon atoms, as is the case in the prism formula.

Researches upon the constitution of benzene and its derivatives by *Baeyer* (A. **245**, **251**, **256**, **258**, **269**, 176), and upon similar (and also nitrogen) ring-systems by *Bamberger* (A. **257**, 1), have shown that the nature of the groups entering the benzene molecule has an influence upon the special (fourth) linking of the atoms; so that the constitution of the ring in all benzene derivatives is not to be taken as established without further investigation because a particular formula applicable to benzene itself has been arrived at. On the contrary, *Kekulé's* formula (I) might suit for certain compounds (as has been proved by *Bueyer* for phloroglucinol [B. **24**, 2687]), and formula (IIA) for others.

Compare also A. **274**, 331; **279**, 1; B. **30**, 2975; A. **306**, 125; *Kauffmann*, Ahren's Sammlung, 1907, **12**, 79.

METHODS FOR DETERMINING WHICH OF THREE ISOMERIC COMPOUNDS IS THE ORTHO, WHICH META, AND WHICH PARA.

1. A method worked out by *Korner* (1875) for the three dibromobenzenes. One of these (*a*) is a solid melting at 89°; a second (*b*) is a liquid which boils at 224°, and when solidified melts at −1°, and the third (*c*) is a liquid boiling at 219° and melting at +1°. When further brominated, the compound *a* yields only *one* tribromobenzene, compound *b*, under similar conditions, yields a mixture of *two* isomeric tribromobenzenes; and compound *c* a mixture of *three*.



From a glance at the above formulæ, it is obvious (1) that the para- or 1·4-compound could give rise to only *one* tribromobenzene, (2) that the ortho- or 1:2-compound could give a mixture of *two* isomeric tribromobenzenes, and (3) that the meta- or 1.3-compound could give a mixture of *three* isomeric tribromobenzenes

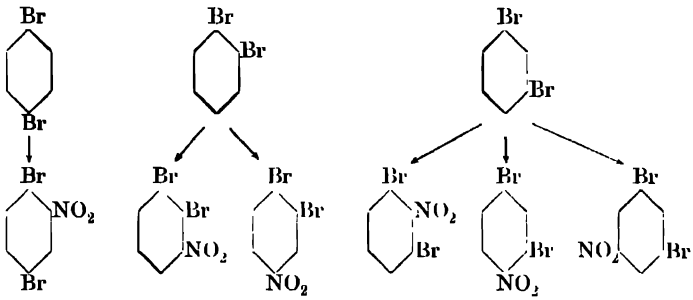
The compound melting at 89° is therefore *p*-dibromobenzene, the one boiling at 224° is the ortho-, and the one boiling at 219° and melting at +1° is the meta-compound.

Incidentally, this gives us a method for determining which of the three tribromobenzenes is the adj., which the sym., and which the unsym. A glance at the formulæ indicates that the sym.-tribr mobenzene is the one which is formed from the *m*-dibromobenzene only. The adj. is the one formed from both ortho- and meta-, and the unsym. is the one which is formed from ortho-, meta-, and para-dibromobenzenes.

Similar results are obtained by examining the nitro-dibromobenzenes obtained by nitrating the dibromobenzenes.

The *p*-compound yields only one nitro-derivative; the *o*-com-

pound yields two nitro-derivatives; the *m*-compound yields three nitro-derivatives:



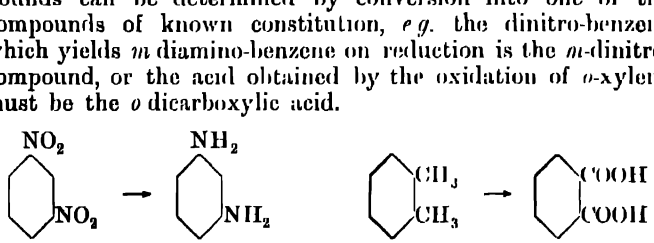
but the nitro-dibromobenzenes thus formed are all different.

Similar methods may be adopted for determining the constitutions of the three diammo-benzenes, $C_6H_4(NH_2)_2$, by determining from how many of the six diammo-benzoic acids each of the three can be obtained by elimination of carbon dioxide

The *m*-compound is the one which is formed from three distinct acids, the ortho- from two, and the para- from one only (*Griess*)

The relationships between the three xylenes, $C_6H_4(CH_3)_2$, and the six nitro-xylenes are exactly analogous to those between the three dibromobenzenes and their six nitro-derivatives.

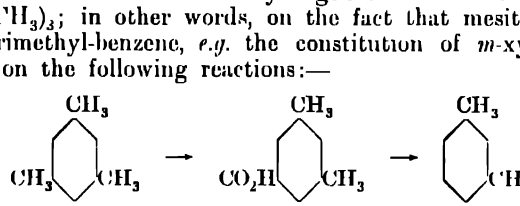
2. When the constitution of several groups of compounds, *e.g.* the dibromobenzenes, the xylenes, and the diammo-benzenes have been settled, then the constitutions of other compounds can be determined by conversion into one of the compounds of known constitution, *e.g.* the dinitro-benzene which yields *m* diamino-benzene on reduction is the *m*-dinitro-compound, or the acid obtained by the oxidation of *o*-xylene must be the *o* dicarboxylic acid.



This constitution is confirmed by the fact that this acid is the only one of the three isomeric benzene-dicarboxylic

acids which yields an inner anhydride, phthalic anhydride, $C_6H_4<\begin{matrix}CO\\CO\end{matrix}>O$, and hence the two CO_2H groups are probably attached to two adjacent carbon atoms.

3. The constitution of certain di-substituted derivatives is based on *Ladenburg's* proof (A. **179**, 174) of the equivalence of the three unsubstituted hydrogen atoms in mesitylene, $C_6H_3(CH_3)_3$; in other words, on the fact that mesitylene is sym.-trimethyl-benzene, *e.g.* the constitution of *m*-xylene is based on the following reactions:—



Ladenburg's proof is briefly as follows —Mesitylene yields a dinitro derivative, $C_6H(CH_3)_3(NO_2)_2$, in which two of the three nucleus hydrogen atoms (*a* and *b*) are replaced by nitro-groups From this we get, by the three processes of reduction, acetylation, and nitration, a dinitro-acetamino-mesitylene·

$$C_6H(CH_3)_3(\underset{a}{NO_2})(\underset{b}{NH_2}) \longrightarrow C_6H(CH_3)_3(NO_2)(NHAc)$$
$$\longrightarrow C_6(CH_3)_3(NO_2)_2(NHAc),$$

in which the third hydrogen (*c*) is replaced by NO_2; on hydrolysis, this yields $C_6(CH_3)_3(NO_2)_2(NH_2)$, and on elimination of the amino group, $C_6H(CH_3)_3(NO_2)_2$, a dinitro-mesitylene, which is identical with the original dinitro-compound started with. Hence two of the hydrogen atoms (say *b* and *c*) are similarly situated The nitro-amino-mesitylene, $C_6H(CH_3)_3(\underset{a}{NO_2})(\underset{b}{NH_2})$, in which the nitro-group is in position *a* and the amino- in position *b*, yields $C_6H_2(CH_3)_3\underset{a}{NO_2}$, and this, when reduced, acetylated, nitrated, and hydrolysed:

$$C_6H_2(CH_3)_3\underset{a}{NH_2} \longrightarrow C_6H_2(CH_3)_3\cdot\underset{a}{NHAc}$$
$$\longrightarrow C_6H(CH_3)_3(\underset{a}{NHAc})(\underset{b\text{ or }c}{NO_2}) \longrightarrow C_6H(CH_3)_3(\underset{a}{NH_2})(\underset{b\text{ or }c}{NO_2}),$$

a nitro-amino-mesitylene which is identical with the original nitro-amino-mesitylene, and hence the position *a* is similarly situated to either *b* or *c*, but in the first part of the argument it was shown that $b = c$, $\therefore a = b = c$.

Other Types of Isomerism.—1. In addition to the cases of isomerism dealt with in the preceding pages (isomerism due to the positions of the substituents in the nucleus), other types of isomerides are met with. A frequent example is the isomerism of a compound containing a substituent in the nucleus with a compound containing the same substituent in the side chain; well-known examples are $C_6H_4Cl \cdot CH_3$ and $C_6H_5 \cdot CH_2Cl$, $C_6H_4\langle\begin{matrix}CH_3\\NH_2\end{matrix}$ and $C_6H_5 \cdot CH_2 \cdot NH_2$. Isomerism of this type is usually accompanied by considerable difference in chemical properties.

2. "Side-chain isomerism" is the name given when the isomerism is confined to the side chain, *e.g.*:

$$\underset{\text{Normal-}}{C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CH_3} \text{ and } \underset{\text{and}}{C_6H_5 \cdot CH(CH_3)_2} \underset{\text{Isopropyl benzene}}{}$$

Stereo-isomerism.—When the side chain contains an asymmetric carbon atom, *e.g.* $C_6H_5 \cdot CH(OH)(CO_2H)$, mandelic acid, stereo-isomerism of the type of the active lactic acids is met with. Stereo-isomerism of the type of the crotonic acids is met with in unsaturated compounds like cinnamic acid, $C_6H_5 \cdot CH:CH \cdot CO_2H$, and stereo-isomerism analogous to that described in the case of polymethylene derivatives is met with among the reduced benzene derivatives, *e.g.* di-, tetra-, and hexahydrophthalic acid (p. 166).

OCCURRENCE OF THE BENZENE DERIVATIVES

Many benzene derivatives occur in nature, *e.g.* oil of bitter almonds, benzoic acid, salicylic acid, and hippuric acid, while others are obtained from the destructive distillation of organic substances, especially of coal.

The destructive distillation of coal yields (*a*) gases (illuminating gas); (*b*) an aqueous distillate containing ammonia and its salts, &c.; (*c*) tar; and (*d*) coke.

The various fractions obtained by distilling coal-tar contain:

(*a*) Fatty hydrocarbons in small amount.

(*b*) Aromatic hydrocarbons, the most important of which are the following:—Benzene, C_6H_6, toluene, $C_6H_5 \cdot CH_3$, and many homologues of benzene containing methyl substituents, *e.g.* mesitylene, $C_6H_3(CH_3)_3$, durene and isodurene, $C_6H_2(CH_3)_4$. More complex hydrocarbons: cinnamene, $C_6H_5CH:CH_2$; naphthalene, $C_{10}H_8$; diphenyl, $C_{12}H_{10}$; acenaphthene, $C_{12}H_{10}$;

fluorene, $C_{13}H_{10}$; anthracene, $C_{14}H_{10}$; phenanthrene, $C_{14}H_{10}$; pyrene, $C_{16}H_{10}$; chrysene, $C_{18}H_{12}$.

(*c*) Other neutral substances, *e.g.* alcohol (in very small quantity), benzonitrile, cumarone, C_8H_6O.

(*d*) Phenols: *e.g.* phenol or carbolic acid, C_6H_5OH; *o*-, *m*-, and *p*-cresol, $CH_3 \cdot C_6H_4 \cdot OH$.

(*e*) Bases: pyrrole, C_4H_5N; pyridine, C_5H_5N, and its homologues; aniline, $C_6H_5 \cdot NH_2$; quinoline, C_9H_7N, and its homologues, acridine, $C_{13}H_9N$. (See *Schultz*, "Chemie des Steinkohlentheers", Braunschweig, 1886.)

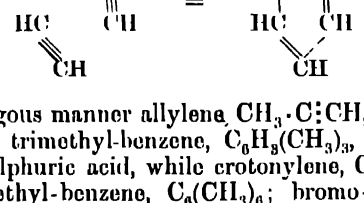
All these compounds are not present in the original coal, but are formed during the process of distillation. The compounds formed, and also their relative amounts, depend on numerous factors, *e.g.* nature of coal, temperature and pressure of distillation, kind of retort used, &c.

The presence of the hexahydro-compounds of benzene and its homologues has been proved in most natural petroleums, especially in those from the Caucasus (J. pr. Ch. (2) **45**, 561, cf p. 41).

FORMATION OF BENZENE DERIVATIVES FROM OPEN-CHAIN COMPOUNDS

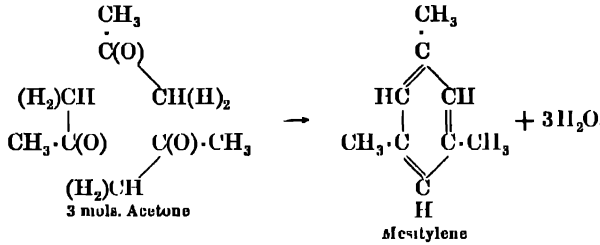
The benzene derivatives can be produced from the fatty compounds by a relatively small number of reactions only.

1. Many methane derivatives, *e.g.* alcohol, yield a mixture containing a large number of the derivatives of benzene when their vapours are led through red-hot tubes. Acetylene, C_2H_2, polymerizes at a low red heat to benzene, C_6H_6 (*Berthelot*):



In analogous manner allylene, $CH_3 \cdot C{:}CH$, yields mesitylene or 1:3·5 trimethyl-benzene, $C_6H_3(CH_3)_3$, when distilled with dilute sulphuric acid, while crotonylene, $CH_3 \cdot C{:}C \cdot CH_3$, yields hexamethyl-benzene, $C_6(CH_3)_6$; bromo-acetylene and iodo-acetylene polymerize to *s*-tribromo- and tri-iodo-benzene when exposed to light; propiolic acid, $CH{:}C \cdot CO_2H$, polymerizes to trimesic acid, $C_6H_3(CO_2H)_3$.

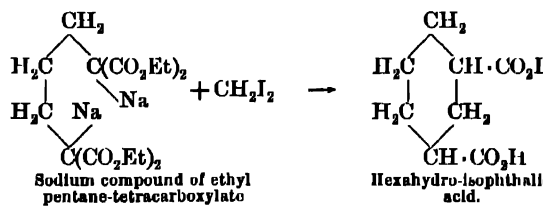
2. Ketones condense to benzene hydrocarbons when distilled with dilute sulphuric acid, *e g.* acetone yields mesitylene (*Kane*, 1838) and methylethyl ketone, triethyl-benzene:



3. Certain 1:2-diketones, aldehyde acids, and keto aldehydes are transformed in an analogous manner into benzene derivatives by suitable "condensing" agents; diacetyl, $CH_3 \cdot CO \cdot CO \cdot CH_3$, is transformed by alkalis into xylo-quinone, $C_6H_2O_2(CH_3)_2$ (B. **21**, 1411), and ethyl β-hydroxyacrylate into the ethyl ester of trimesic acid (B. **20**, 2930).

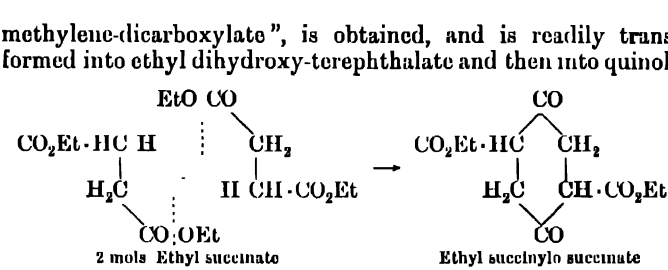
4. Certain 1:5 diketones react with hydrochloric acid, yielding reduced benzene derivatives, which can readily be transformed into benzene derivatives, *e g.* ethylidene diacetoacetic ester (from acetaldehyde and acetoacetic ester) yields dimethyl-cyclo-hexenone, $CH\langle^{CO-CH_2}_{CMe\cdot CH_2}\rangle CHMe$, the dibromide of which is converted into sym.-xylenol, $CH\langle^{C(OH):CH}_{CMe-CH}\rangle CMe$ (*Knoevenagel*).

5. By the action of methylene iodide upon the sodium compound of ethyl pentane-tetracarboxylate and subsequent hydrolysis, hexahydro-isophthalic acid is formed (*W. H. Perkin, jun.*, J. C. S. 1891, **59**, 798):



6. By the action of sodium upon ethyl succinate (*Herrmann*, **A. 211**, 306; **B. 16**, 1411), or upon ethyl bromo-acetoacetate (*Duisberg*), **ethyl succinyle-succinate**, "**ethyl diketo-hexa-**

methylene-dicarboxylate", is obtained, and is readily transformed into ethyl dihydroxy-terephthalate and then into quinol:



7. When ethyl sodio-malonate, $CHNa(CO_2Et)_2$, is heated, ethyl phloroglucinol-dicarboxylate is formed, and this on hydrolysis yields phloroglucinol. (Cf. p. 420.)

8. Hexyl iodide, $C_6H_{13}I$, is converted into hexachloro-benzene, C_6Cl_6, when heated with ICl_3, and into hexabromo-benzene, C_6Br_6, by bromine at 260°; the latter compound can also be obtained by heating CBr_4 to 300°.

9. **Mellitic acid**, $C_6(CO_2H)_6$, is produced by the oxidation of graphite or lignite by means of $KMnO_4$.

10. **Potassium carboxide**, which is formed by the action of carbon monoxide upon potassium, is the potassium compound of hexahydroxy-benzene, $C_6(OH)_6$.

THE CONVERSE TRANSFORMATION OF BENZENE DERIVATIVES INTO FATTY COMPOUNDS

1. When the vapour of benzene is passed through a red-hot tube it is partially decomposed into acetylene.

2. Benzene is oxidized by chloric acid to "**trichloro-phenomalic acid**", *i.e.* β-trichloraceto acrylic acid, $CCl_3 \cdot CO \cdot CH : CH \cdot CO_2H$ (*Kekulé* and *Strecker*, A. **223**, 170).

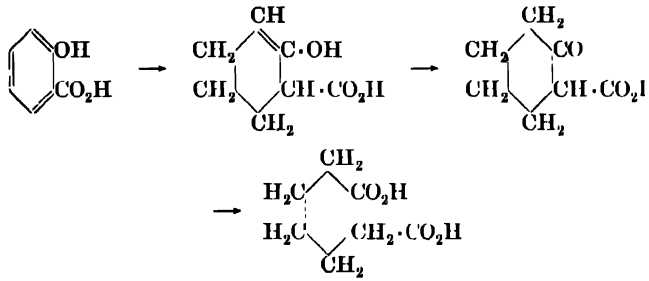
When chlorine is allowed to act upon phenol in alkaline solution, the benzene ring is broken, and the acids, $C_6H_5Cl_3O_4$, $C_6H_5ClO_4$, &c., are produced (*Hantzsch*, B. **20**, 2780). Catechol, resorcinol, and phloroglucinol are also ultimately converted into fatty compounds by treatment with chlorine and the subsequent action of alkalis, *e.g.* resorcinol (*m*-dihydroxybenzene) yields dichloro-maleic acid (B. 1894, **27**, 3364). Bromine, acting upon bromanilic acid, yields perbromo-acetone, $CBr_3 \cdot CO \cdot CBr_3$.

3. Nitrous acid converts catechol into dihydroxy-tartaric acid (see p. 260), while permanganate of potash, acting upon phenol, gives rise to inactive tartaric acid and oxalic acid (*Döbner*, B. **24**, 1753).

4. Oxidizing agents which are capable of rupturing the benzene ring yield, as a rule, carbonic, formic, and acetic acids.

5. The hexahydro-benzenes are transformed into hydrocarbons of the methane series when heated with hydriodic acid at 280° (*Berthelot*, A. **278**, 88; **302**, 5). This decomposition appears, however, to be very difficult of accomplishment.

6. When reduced with metallic sodium and amyl alcohol, *o*-hydroxy-benzoic acid is converted into pimelic acid:



XVIII. BENZENE HYDROCARBONS

A. Homologues of Benzene, C_nH_{2n-6}

The benzene hydrocarbons are for the most part colourless liquids, insoluble in water, but readily soluble in alcohol and ether (durene and penta- and hexamethyl-benzenes are crystalline). They distil without decomposition, possess a peculiar and sometimes pleasant ethereal odour, and burn with a very smoky flame. Many, especially benzene and its methyl derivatives, occur in the lower fractions from coal-tar; others are prepared synthetically by *Fittig's* or *Friedel-Crafts'* methods.

Modes of Formation.—1. *Fittig's Synthesis.*—By treating a mixture of a brominated benzene hydrocarbon and an alkyl iodide or bromide with sodium in the presence of dry ether (A. **131**, 303):

$$C_6H_5Br + CH_3I + 2Na = C_6H_5{\cdot}CH_3 + NaI + NaBr;$$
$$C_6H_4Br(C_2H_5) + C_2H_5I + 2Na = C_6H_4(C_2H_5)_2 + NaI + NaBr.$$

Formula	Name	Constitution Formula	Positions of substituents	Melting-point	Boiling-point	Specific Gravity
C_6H_6	Benzene	C_6H_6	.	5·4°	80·4°	0·874
C_7H_8	Toluene	$C_6H_5 \cdot CH_3$	.	liquid	110°	0·869
C_8H_{10}	*o*-Xylene	$C_6H_4(CH_3)_2$	1 2	−28°	142°	0·893
	m-Xylene	$C_6H_4(CH_3)_2$	1 3	−53°	139°	0·881
	p-Xylene	$C_6H_4(CH_3)_2$	1 4	+13°	138°	0·880
	Ethylbenzene	$C_6H_5 \cdot C_2H_5$	.	liquid	136°	0·883
C_9H_{12}	Hemimellithene	$C_6H_3(CH_3)_3$	1 2 3	liquid	175°	
	Pseudo-cumene	$C_6H_3(CH_3)_3$	1 2 4	liquid	169·5°	0·895
	Mesitylene	$C_6H_3(CH_3)_3$	1 3 5	liquid	165°	0·865
	o-Methylethylbenzene	$C_6H_4(CH_3)(C_2H_5)$	1 2	liquid	159°	...
	m-Methylethylbenzene	$C_6H_4(CH_3)(C_2H_5)$	1 3	liquid	159°	...
	p-Methylethylbenzene	$C_6H_4(CH_3)(C_2H_5)$	1 4	liquid	162°	.
	n-Propylbenzene	$C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CH_3$	.	liquid	159°	0·867
	Cumene	$C_6H_5 \cdot CH(CH_3)_2$	...	liquid	153°	0·866
$C_{10}H_{14}$	Durene	$C_6H_2(CH_3)_4$	1 2 4 5	80	192°	..
	Isodurene	$C_6H_2(CH_3)_4$	1 2 3 5	...	195°	.
	Metacymene	$CH_3 \cdot C_6H_4 \cdot CH(CH_3)_2$	1 3	...	175°	0·862
	Cymene	$CH_3 \cdot C_6H_4 \cdot CH(CH_3)_2$	1 4	...	175°	0·856

Jannasch synthesised *p*-xylene, durene, and isodurene by this method.

2. *Friedel* and *Crafts' Synthesis* (1877).—By the action of alkyl chlorides (bromides or iodides) on aromatic hydrocarbons in the presence of anhydrous aluminic chloride, ($AlCl_3$):

$$C_6H_6 + CH_3Cl = C_6H_5 \cdot CH_3 + HCl;$$
$$C_6H_6 + 2CH_3Cl = C_6H_4(CH_3)_2 + 2HCl, \&c.$$

This reaction is, like the preceding one, capable of very wide application; by means of it all the hydrogen atoms in benzene can be gradually replaced by methyl. The best yields are often obtained by the addition of carbon bisulphide which serves as a diluent, and also prevents the temperature rising to any appreciable extent, and thus largely avoids the decomposing or differentiating action of the chloride on the homologues first formed. At higher temperatures, for example, $C_6H_5 \cdot CH_3$ would be transformed to a large extent into C_6H_6 and $C_6H_4(CH_3)_2$ (B. 1894, **27**, 1606, 3235).

Zinc and ferric chlorides (*Nencki*, B. 1899, **32**, 2414) act in the same way as chloride of aluminium, while ethyl chloride and other haloid compounds, such as chloroform and acid chlorides, may replace methyl chloride. (See respectively triphenyl-methane and the ketones; cf. also B. **14**, 2624; **16**, 1744; Ann. de chim. et phys. [6] **1**, 419; B. **30**, 1766.) The metallic chloride forms additive compounds with the acyl chloride or alkyl derivative, *e.g.* $CH_3 \cdot COCl$, $AlCl_3$, and also with the condensation product, *e.g.* $C_6H_5 \cdot CO \cdot CH_3$, $AlCl_3$ (*Perrier*, B. 1900, **33**, 815). The reaction is a unimolecular one, except when an excess of $AlCl_3$ is used.

For a summary of the *Friedel-Crafts'* reaction, see *Steele*, J. C. S. 1903, 1470.

Alcohols also, like their haloid esters, are capable of reacting in an analogous manner in presence of $ZnCl_2$:

$$C_6H_6 + C_4H_9OH = C_6H_5 \cdot C_4H_9 + H_2O.$$

3. A method of formation somewhat analogous to the *Fittig* synthesis is the action of alkyl iodides or methyl sulphate on organo-magnesium haloids (*Grignard's* compounds) in toluene solution (*Houben*, B. 1903, **36**, 3083; 1904, **37**, 488; *Werner*, *ibid.*, 2116, 3618):

$$CH_3 \cdot C_6H_4 \cdot MgBr + C_2H_5Br = CH_3 \cdot C_6H_4 \cdot C_2H_5 + MgBr_2.$$

4. The benzene hydrocarbons are formed when their carboxylic acids are distilled with soda-lime:

$$C_6H_5 \cdot CO_2H = C_6H_6 + CO_2;$$
$$CH_3 \cdot C_6H_4 \cdot CO_2H = C_6H_5 \cdot CH_3 + CO_2.$$

5. From sulphonic acids (p. 402) by the elimination of the SO_3H group:

$$C_6H_3(CH_3)_2SO_3H + H_2O = C_6H_4(CH_3)_2 + H_2SO_4.$$

This reaction can be effected by dry distillation, by heating with concentrated hydrochloric acid to 180°, by distillation of the ammonium salt (*Caro*), or by treatment with superheated steam, *e.g.*, in presence of concentrated sulphuric acid (*Armstrong, W. Kelbe*); also by heating with concentrated phosphoric acid (B. 22, Ref. 577).

6. From the amino-compounds by transforming these into diazonium-compounds (p. 387), and boiling the latter with absolute alcohol or with an alkali stannite solution (B. 22, 587). *Griess* reaction.

7. By distillation of the phenols (or ketones) with zinc dust.

Isomers and Constitution.—The table given on p. 345 shows that the benzene hydrocarbons, from C_8H_{10} on, exist in many isomeric modifications; thus, isomeric with the three xylenes we have ethyl-benzene, with the three trimethyl-benzenes the three methylethyl-benzenes and the two propyl-benzenes, with durene, isodurene, cymene, &c.

The *constitution* of these hydrocarbons follows very simply from their modes of formation. A hydrocarbon $C_{10}H_{14}$, for instance, which is obtained from benzene and methyl chloride by the *Friedel-Crafts'* reaction, can only be a tetramethyl-benzene, another of the same molecular formula $C_{10}H_{14}$, which has been prepared from bromo-benzene, butyl bromide and sodium, must be a butyl-benzene; while a third, from *p*-bromo-toluene, normal propyl iodide and sodium, must be a *p*-propyl-toluene (*p*-methyl-*n*-propyl-benzene), &c. The synthesis therefore determines the constitution.

The groups CH_3, C_2H_5, &c., which replace hydrogen in benzene, are termed "**side chains**".

When oxidized, the hydrocarbons yield a benzene-mono-, di-, or tri-, &c., carboxylic acid, *e.g.* benzoic acid, $C_6H_5 \cdot CO_2H$, *o*-, *m*-, *p*-phthalic acid, $C_6H_4(CO_2H)_2$, according to the number of side chains present in the hydrocarbon; and a further proof of the constitution of the compound is thus afforded.

If, for example, a hydrocarbon C_9H_{12} yields a benzene-tricarboxylic acid, $C_6H_3(CO_2H)_3$, upon oxidation, it must contain three side chains, *i.e.* must be a trimethyl-benzene; should a phthalic acid, on the other hand, result, then it can only be an ethyl-toluene. Since cymene yields *p*- (or tere-) phthalic acid, $C_6H_4(CO_2H)_2$, on oxidation, its two side chains must be in the *p*-position towards one another.

The respective isomers resemble each other closely in physical properties, their boiling-points, for example, lying very near together. The ortho-derivatives often boil at about 5°, and the meta- at about 1° higher than the para-compounds; the boiling-point rises with an increasing number of methyl groups. (Cf. B. **19**, 2513.)

Behaviour.—1. The benzene hydrocarbons are, as a rule, readily nitrated and sulphonated, mono-, di-, and even tri-derivatives being all usually capable of preparation, according to the conditions. As a rule, it is only the hydrogen atoms of the benzene nucleus which are replaced, the side chains reacting as paraffin residues. Hexamethyl-benzene can thus neither be nitrated nor sulphonated. Exceptions to this generalization are met with, *e.g.* mesitylene yields a nitro-derivative, $C_6H_3(CH_3)_2 \cdot CH_2 \cdot NO_2$.

2. *Oxidation.*—Benzene itself is not readily oxidized, permanganate of potash converts it slowly into formic and oxalic acids, some benzoic acid and phthalic acid being produced at the same time. These doubtless result from some previously formed diphenyl.

The homologues of benzene, on the other hand, are readily oxidized to carboxylic acids, the benzene nucleus remaining unaltered, and each side chain—no matter how many carbon atoms it may contain—being converted, as a rule, into carboxyl.

Nitric acid allows of a successive and often a partial oxidation of individual side chains, chromic acid mixture ($K_2Cr_2O_7 + H_2SO_4$) acts more energetically, converting all the side chains in the *p*- and *m*-compounds into carboxyl, and completely destroying the *o*-compounds. The latter may be oxidized to the corresponding carboxylic acids by $KMnO_4$.

When a hydrocarbon is selectively oxidized, the longest side chain, as a rule, is most readily oxidized; thus $C_3H_7 \cdot C_6H_4 \cdot CH_3$ yields first $CO_2H \cdot C_6H_4 \cdot CH_3$, and then $C_6H_4(CO_2H)_2$.

3. *Reduction.*—The benzene hydrocarbons and most of their derivatives are capable of taking up six atoms of hydrogen.

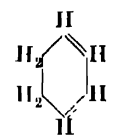
Benzene itself is only converted into hexahydro-benzene, C_6H_{12}, with difficulty, but toluene, xylene, and mesitylene combine with hydrogen more easily when they are heated with phosphonium iodide, PH_4I, at a rather high temperature, the compounds $C_7H_8 \cdot H_2$, $C_8H_{10} \cdot H_4$, and $C_9H_{12} \cdot H_6$ being formed. The two former can then be made to take up more hydrogen by energetic reaction

An interesting method of formation of C_6H_{12} is by the action of freshly reduced nickel on a mixture of hydrogen and benzene or its homologues at moderate temperatures

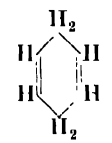
Hexahydro-benzene and its analogues, C_nH_{2n}, are colourless liquids insoluble in water, and of somewhat lower boiling-point than their mother compounds, into which they can be readily retransformed by oxidation, either by heating with sulphur or by means of fuming nitric acid, nitration also taking place in the latter case; *e.g.* hexahydro-benzene yields nitro-derivatives of benzene They are found in petroleum, especially in that from the Caucasus (*Beilstein*, *Kurbatow*), and differ from the isomeric olefines by being insoluble in sulphuric acid, and by not forming additive products with bromine (cf. B. **20**, 1850; A **234**, 89, **301**, 154).

They are identical with hexamethylene and its derivatives, and react as saturated compounds. The partially reduced benzene derivatives, on the other hand, behave more like olefines.

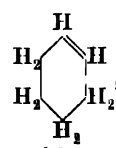
The **dihydro-benzenes**, C_6H_8, readily combine with two or four atoms of bromine, and are readily oxidized by alkaline permanganate, as might be inferred from the presence of double bonds in the molecule Two isomeric compounds, Δ 1 3-dihydro benzene and Δ 1:4-dihydro-benzene, are known:



Cyclohexa-1 3 diene



Cyclohexa 1 4-diene

Tetrahydro-benzene,  , which exists in one form

Cyclohexene

only, is readily oxidized, combines with two atoms of chlorine and bromine or with a molecule of hypochlorous acid. All are colourless, volatile liquids.

4. *Behaviour with Halogens.*—Chlorine and bromine react differently, according to the conditions. In direct sunlight they yield with benzene the additive products $C_6H_6Cl_6$ and $C_6H_6Br_6$, while in diffused daylight, especially in presence of a little iodine, $SbCl_3$ or $MoCl_5$, they give rise to the substitution products C_6H_5Cl, C_6H_5Br, &c. (For further details, and for substitution by iodine, see pp. 57 and **356**.)

5. Chromium oxychloride, CrO_2Cl_2, converts the methylated benzene hydrocarbons into aromatic aldehydes (p. 423, cf. B. **23**, 1070). (*Etard's* reaction.)

6. The numerous "condensations" which benzene, &c., can undergo with oxygenated compounds in presence of $ZnCl_2$, P_4O_{10}, or H_2SO_4, and with chlorinated compounds in presence of $AlCl_3$, are of great interest; thus benzene yields diphenyl-ethane with aldehyde and sulphuric acid, and benzophenone with benzoic acid and phosphorus pentoxide.

7. In presence of aluminic chloride, oxygen can be introduced into benzene, yielding phenol; sulphur, yielding phenyl sulphide; ethylene, yielding ethyl-benzene; carbon dioxide, yielding benzoic acid.

Benzene, C_6H_6, was discovered by *Faraday* in 1825, and detected in coal-tar by *Hofmann* in 1845. It is obtained from the portion of coal-tar which boils at 80°–85° by fractionating or freezing. It may be prepared chemically pure by distilling a mixture of benzoic acid and lime. The ordinary benzene of commerce usually contains **thiophene**, and thus gives a characteristic deep-blue coloration when shaken with a solution of isatin in concentrated sulphuric acid; but it may be freed from the impurity by repeated shaking with small quantities of sulphuric acid, which converts the thiophene into a sulphonic acid. It burns with a luminous smoky flame, and is a good solvent for resins, fats, iodine, sulphur, phosphorus, &c. When its vapour is led through a red-hot tube, diphenyl is obtained.

C_7H_8.—**Toluene**, $C_6H_5 \cdot CH_3$. Discovered in 1837. *Formation*: by the dry distillation of balsam of Tolu and of many resins. Synthesis according to *Fittig* (see above). *Preparation*: from coal-tar, in which it is found accompanied by thio-tolene. Toluene is very similar to benzene. It boils at 110°, and is still liquid at −28°. CrO_2Cl_2 converts it into benzaldehyde, and HNO_3 or CrO_3 into benzoic acid.

C_8H_{10}.—(*a*) *o*-, *m*-, and *p*-**Dimethyl-benzenes** or **Xylenes**, $C_6H_4(CH_3)_2$.—The xylene of coal-tar consists of a mixture of the three isomers, *m*-xylene being present to the extent of 70 to 85 per cent. These cannot be separated from one another by fractional distillation. *m*-Xylene is more slowly oxidized by dilute nitric acid than its isomers, and can thus be obtained with relative ease.

For the separation of these isomers by means of H_2SO_4 see B. **10**, 1010, **14**, 2625; **17**, 444; **25**, Ref 315; and for their recognition see B **19**, 2513. Benzene and toluene yield chiefly ortho-, together with a little para-xylene, when subjected to the *Friedel-Crafts* synthesis (B. **14**, 2627).

1. *o*-**Xylene**, which can be prepared synthetically from *o*-bromo-toluene, methyl iodide, and sodium, is oxidized to carbonic acid by chromic acid mixture, and to *o*-toluic acid, $C_6H_4(CH_3)CO_2H$, by dilute nitric acid; it is difficult to nitrate.

2. *m*-**Xylene** or **iso-xylene** can also be prepared from mesitylene, $C_6H_3(CH_3)_3$ [1 3 5], by oxidation to mesitylenic acid, $C_6H_3(CH_3)_2CO_2H$, and subsequent distillation with lime. Dilute nitric acid only oxidizes it at a temperature of 120°, while chromic acid mixture converts it into isophthalic acid, $C_6H_4(CO_2H)_2$. It yields **tetra-** and **hexahydro**-derivatives, C_8H_{14} and C_8H_{16}, the latter is present in Caucasian petroleum, and boils at 119°.

3 *p*-**Xylene** is prepared from *p*-bromo-toluene, or better, *p*-dibromo-benzene, methyl iodide, and sodium (B. **10**, 1356; B. **17**, 441). M.-pt. 15°. Dilute nitric acid oxidizes it to *p*-toluic acid, $C_6H_4(CH_3)CO_2H$, and terephthalic acid, $C_6H_4(CO_2H)_2$.

Dihydro-*p*-**xylene** can be prepared from ethyl succinylo-succinate. Liquid, b.-pt. 133°. It has an odour of turpentine, and is closely related to the terpenes (Cf. *Baeyer*, B. **25**, 2122.)

(*b*) **Ethyl-benzene**, $C_6H_5 \cdot C_2H_5$, is obtained from C_6H_5Br and C_2H_5Br by the *Fittig* reaction; from cinnamene, $C_6H_5CH:CH_2$, on reduction with HI; and from C_6H_6 and C_2H_5Cl by the *Friedel-Crafts* reaction. It is found in small quantity in the xylene from tar, and when oxidized yields benzoic acid.

C_9H_{12}.—(*a*) **Trimethyl-benzenes**.—1. **Mesitylene**, 1.3:5-*trimethyl-benzene*, $C_6H_3(CH_3)_3$.—This is contained in coal-tar along with the two other isomeric trimethyl-benzenes ("tar-cumene"), and can be synthesised from acetone or allylene. It is a liquid of agreeable odour. Nitric acid oxidizes the

side chains one by one, while chromic acid mixture decomposes it completely. (For *constitution*, see p. 339.)

2. **Pseudo-cumene**, 1:2:4-*trimethyl-benzene*, is separated from mesitylene, not by fractional distillation, but by taking advantage of the sparing solubility of pseudo-cumene-sulphonic acid (B. **9**, 258). Its constitution follows from its formation from bromo-*p*-xylene [1:4:2], and also from bromo-*m*-xylene [1:3:4], by the *Fittig* reaction. Nitric acid oxidizes the side chains successively.

3. **Hemellithene**, 1:2:3-*trimethyl-benzene* (see B **15**, 1853), is present in coal-tar (B. **20**, 903).

(*b*) **Propyl-benzenes.**—1. ***n*-Propyl-benzene**, $C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CH_3$, is obtained from bromo-benzene and normal propyl iodide by the *Fittig* reaction, and also from benzyl chloride, $C_6H_5 \cdot CH_2Cl$, and zinc ethyl.

2. **Isopropyl-benzene** or **Cumene**, $C_6H_5 \cdot CH(CH_3)_2$, is produced by the distillation of cumic acid, $C_6H_4(C_3H_7)(CO_2H)$, with lime; from benzene and iso- or normal propyl iodide by means of $AlCl_3$, in the latter case with molecular rearrangement (p. 132); and from benzylidene chloride, $C_6H_5 \cdot CHCl_2$, and zinc methyl, this last method furnishing proof of its constitution. On oxidation, both *n*- and iso-compounds yield benzoic acid.

$C_{10}H_{14}$. —(*a*) **Durene**, 1 : 2 : 4 : 5- or *s-tetramethyl-benzene*, $C_6H_2(CH_3)_4$, has been found in coal-tar, and can be prepared from toluene and methyl chloride by the *Friedel-Crafts* reaction, or from dibromo-*m*-xylene (from coal-tar xylene), methyl iodide, and sodium (A. **216**, 200). It is a solid, and possesses a camphor-like odour. (For its *constitution* see B. **11**, 31.) Both of its isomers are known.

(*b*) **Methyl-propyl-benzenes**, $C_6H_4(CH_3)C_3H_7$.—The most important of these is **cymene** or **isopropyl-*p*-methyl-benzene**. It is found in Roman cummin oil (*Cuminum cyminum*), in eucalyptus oil, &c., and is formed when camphor is heated with P_2S_5, or better, P_4O_{10}, also when oil of turpentine is heated with iodine, &c. It has been synthetically prepared from *p*-bromo-isopropyl-benzene, methyl iodide, and sodium; and also from *p*-bromo-toluene, *n*-propyl iodide, and sodium, the *n*-propyl- changing here into the isopropyl group. It is a liquid of agreeable odour.

Cymene was formerly regarded as *normal*-propyl-*p*-methyl-benzene, but its synthesis from *p*-brom-*iso*-propyl-benzene, methyl iodide, and sodium established its constitution as an

*iso*propyl derivative (cf *Widman*, B. **24**, 439). When oxidized, it yields either *p*-toluic acid, terephthalic acid, cumic acid, or *p*-tolyl-methyl-ketone, according to the conditions.

$C_{12}H_{18}$.—**Hexamethyl-benzene**, *Mellitene*, $C_6(CH_3)_6$, crystallizes in prisms or plates which melt at 164°. It can neither be sulphonated nor nitrated (see p. 347). $KMnO_4$ oxidizes it to mellitic acid, $C_6(CO_2H)_6$.

B. Unsaturated Benzene Hydrocarbons

The benzene hydrocarbons containing less hydrogen comport themselves, on the one hand, like benzene itself, and on the other like the unsaturated hydrocarbons of the fatty series, combining readily with hydrogen, halogen, halogen hydride, &c. They are derived from the olefines or acetylenes by the exchange of H for C_6H_5, thus $C_6H_5 \cdot CH : CH_2$, cinnamene, styrene, or phenyl-ethylene, $C_6H_5 \cdot C \vdots CH$, phenyl-acetylene. They are formed by the elimination of CO_2 from the corresponding acids, by the elimination of HBr from compounds of the type $C_6H_5 \cdot CH_2 \cdot CH_2Br$, and by the elimination of water from certain secondary and tertiary alcohols (C. R. 1901, **132**, 1182).

Cinnamene, $C_6H_5 \cdot CH : CH_2$, occurs along with other compounds in storax (*Styrax officinalis*), in the juice of the bark of *Liquidambar orientale*, and in coal-tar (being in this last case probably a degradation product of certain acids). It is formed when cinnamic acid is slowly distilled or heated with water to 200° (B. 1890, **23**, 3269). $C_6H_5 \cdot CH : CH \cdot COOH$.

It is also obtained when benzene vapour and ethylene are passed through a red-hot tube, or when α-bromo-ethyl-benzene, $C_6H_5 \cdot CH_2 \cdot CH_2Br$ (by action of bromine on ethyl benzene), is heated. It is a liquid, has a characteristic odour, and boils at 146°. It changes on keeping into the polymeric meta-styrene, an amorphous transparent mass, and yields ethyl-benzene when heated with hydriodic acid. Addition of HBr converts it into α-bromo-ethyl-benzene, $C_6H_5 \cdot CH_2 \cdot CH_2Br$. By the condensation of styrene with toluene, in presence of concentrated sulphuric acid, and on subsequent superheating, anthracene is formed (*Kramer, Spilker*, B. **23**, 3169).

Phenyl-acetylene, $C_6H_5 \cdot C \vdots CH$, is produced by the separation of CO_2 from phenyl-propiolic acid.

It is a pleasant-smelling liquid boiling at 142°, and as an acetylene derivative yields white and pale-yellow explosive

metallic compounds with solutions of silver and cuprous oxides. It combines with water to aceto-phenone, $C_6H_5 \cdot CO \cdot CH_3$, when it is dissolved in sulphuric acid, and the solution is diluted with water, or when heated with water to 300°.

XIX. HALOGEN DERIVATIVES

SUMMARY

	Cl		Br		I	
	M.-p.	B.-p.	M.-p.	B.-p.	M.-p.	B.-p.
C_6H_5Cl	−45°	132°	−31°	157°	−30°	188°
$C_6H_4Cl_2$ *o*	liq.	179°	−1°	224°	+27°	286°
m	liq.	172°	liq.	220°	+40°	285°
p	+56	173°	+87°	219°	+129°	285°
$CH_3 \cdot C_6H_4Cl$ *o*	−31°	159°	−26°	181°	liq.	211°
m	−48	162°	−40°	184°	liq	204°
p	+7·4°	162°	28°	185	+35°	211·5°
$C_6H_5 \cdot CH_2Cl$	−48°	175°	...	198	+24	decomposes
$C_6Cl_6(Br_6, I_6)$	229°	326°	above 310°		...	...

Benzene and its homologues can give rise to (A) additive compounds with bromine or chlorine, or (B) substituted derivatives.

A. Additive Compounds

These are of comparatively little importance, and are formed when the hydrocarbon is exposed for some time to chlorine or bromine vapour in bright sunlight.

Benzene hexachloride, $C_6H_6Cl_6$, exists in two stereo-isomeric modifications; the one melts at 157°, and the other sublimes at 310°. When warmed with alkali, they yield trichloro-benzene and HCl. The isomerism is probably due to the different arrangement of the halogen atoms on either side of the plane of the benzene ring in the two compounds. The **hexabromide** (*Matthews*, J. C. S. 1901, **79**, 43) melts at 212°.

B. Substituted Derivatives

Haloid substitution products in immense number are derived from the benzene hydrocarbons by the exchange of hydrogen for halogen. They are either colourless mobile liquids or

crystalline solids, insoluble in water but readily soluble in alcohol and ether, distil unchanged, and are distinguished by their peculiar odour and also, in part, by their irritant action upon the mucous membrane. They are heavier than water.

The substitution products of benzene and its homologues may be arranged in two distinct groups. In one the halogen is bound very firmly, far more so than in methyl chloride, ethyl iodide, &c.; it cannot be exchanged for OH (by means of AgOH), or for NH_2 (by NH_3), &c., but reacts with sodium (see the *Fittig* reaction, p. 344); A. **332**, 38; for an exception, see B. 1892, **25**, 1499; 1895, **28**, 2312, and magnesium (see below). All the substituted derivatives of benzene and many common derivatives of its homologues belong to this class.

In the second group, of which benzyl chloride is a good type, the halogen atoms enter into reaction as readily as do those of the haloid substitution products of the methane series.

When the members of the first group are subjected to oxidation, a process which converts side chains into carboxylic groups, chloro-derivatives of benzoic and other acids are obtained. The members of the second group, when subjected to similar treatment, yield aromatic acids which are free from halogen, *e.g.* benzoic acid, $C_6H_5 \cdot CO_2H$, phthalic acid, $C_6H_4(CO_2H)_2$. From this it follows that the halogen is present in the first case in the benzene nucleus, and in the second in the side chain. Chloro-toluene is $C_6H_4Cl \cdot CH_3$, and benzyl chloride $C_6H_5 \cdot CH_2Cl$.

When the halogen atoms replace hydrogen atoms of the benzene nucleus, the products are extremely stable, and the halogen cannot readily be removed from the molecule. On the other hand, when the halogen replaces hydrogen atoms of a side chain (methyl or ethyl groups), the compound is extremely reactive, and closely resembles the halogen derivatives of the fatty series. In this way it is always easy to arrive at the constitution of a compound from the behaviour of its halogen atoms and from its products of oxidation. Thus a compound $C_7H_6Cl_2$, which yields monochloro-benzoic acid upon oxidation, has manifestly the formula $C_6H_4Cl \cdot CH_2Cl$ (chloro-benzyl chloride).

The majority of aromatic halogen derivatives, independently of the position of the halogen in the side chain or nucleus, react in dry ethereal solution (or in benzene in presence of a little dimethyl-aniline) with dry magnesium powder, yielding organo-magnesium compounds, *e.g.* $C_6H_5 \cdot Mg \cdot Br$, phenyl-mag-

nesium bromide, $C_6H_5 \cdot CH_2 \cdot Mg \cdot Cl$, benzyl-magnesium chloride, &c. These compounds—*Grignard's* compounds—are chemically extremely active, and, like the analogous aliphatic compounds (p. 120), can be employed for the syntheses of saturated and unsaturated hydrocarbons, primary, secondary, and tertiary alcohols, thiophenols, aldehydes, ketones, acids, &c., *e.g.*:

1. $C_6H_5 \cdot Mg \cdot Br + Br \cdot C_2H_5 = MgBr_2 + C_6H_5 \cdot C_2H_5$.
2. $C_6H_5 \cdot Mg \cdot Br + O = C_6H_5 \cdot O \cdot MgBr$.
   $C_6H_5 \cdot O \cdot MgBr + H_2O = C_6H_5 \cdot OH + Br \cdot Mg \cdot OH$
3. $C_6H_5 \cdot Mg \cdot Br + CO_2 = C_6H_5 \cdot CO_2 \cdot MgBr$
   $C_6H_5 \cdot CO_2MgBr + H \cdot OH = C_6H_5 \cdot CO_2H + OH \cdot Mg \cdot Br$
4. $C_6H_5 \cdot Mg \cdot Br + C_6H_5 \cdot CO \cdot C_6H_5 = \begin{matrix} C_6H_5 \\ C_6H_5 \end{matrix} > C < \begin{matrix} OMgBr \\ C_6H_5 \end{matrix}$,

and with water $(C_6H_5)_3C \cdot OH$.

The *Grignard* compounds may also be used for converting a bromo-derivative into the corresponding iodo-compound, *e.g.*

$$C_6H_5Br \xrightarrow[Mg]{} C_6H_5 \cdot Mg \cdot Br \xrightarrow[I_2]{} C_6H_5I + MgBrI.$$

The boiling-points of the isomeric halogen substitution products differ but little from one another (cf. *o*-, *m*-, *p*-chlorobenzene and benzyl chloride).

The influence of the introduction of F, Cl, Br, or I in place of hydrogen on the boiling-point of a hydrocarbon is similar to that noted in the fatty series. Iodine raises the boiling-point to the greatest extent, and fluorine to the least.

The halogen derivatives may be nitrated, sulphonated, &c., in much the same manner as benzene itself.

Modes of Formation.—1. By the action of chlorine or bromine upon aromatic hydrocarbons there are formed, according to the conditions, either additive or substitution products, the latter class especially in presence of iodine or some other halogen carrier. The function of the halogen carrier, *e.g.* I, P, Fe, &c., is probably to form an additive compound with the halogen, *e.g.* ICl_3, PCl_5, $FeCl_3$, then to give up part or the whole of the halogen in the nascent state to the hydrocarbon, and then to be immediately converted back into the above compounds again. (Cf. p. 56, also B. **18**, 607.) Iodine only substitutes directly under the conditions detailed at p. 57. From benzene most of the chlorinated derivatives up to C_6Cl_6 can be obtained in succession; the last named compound is formed with the aid of $MoCl_5$, ICl_3, &c., at a somewhat high temperature. A hexabromo-benzene and a hexa-iodo-com-

pound also exist. In the case of toluene and its homologues the halogen enters the benzene nucleus alone if the operation is performed in the cold, with the exclusion of direct sunlight or with the addition of iodine; while if the gas is led into the boiling hydrocarbon, or if the experiment is conducted in sunlight and without addition of iodine, it goes almost exclusively into the side chain (*Beilstein, Schramm*, see also B. **13**, 1216).

2. From compounds containing oxygen (the phenols, aromatic alcohols, aldehydes, ketones, and acids), by the action of phosphorus pentachloride or bromide:

$$C_6H_5\cdot OH + PCl_5 = C_6H_5Cl + POCl_3 + HCl;$$
$$C_6H_5\cdot CH{:}O + PCl_5 = C_6H_5\cdot CHCl_2 + POCl_3.$$

3. From the primary amines. The amine is first converted into a diazonium salt (p. 385), and this is then warmed with solutions of cuprous chloride or bromide, when the corresponding chlorine or bromine compound is obtained. If the diazonium salt is warmed with potassium iodide solution, iodo-substitution products are obtained:

$$C_6H_5\cdot N(Cl){:}N = C_6H_5Cl + N_2;$$
$$C_6H_5\cdot N(Cl){:}N + KI = C_6H_5I + N_2 + KCl$$

Gattermann's modification consists in transforming the amine into the diazonium chloride, bromide, or iodide, and then decomposing this with finely-divided copper powder (*Sandmeyer*, B. **17**, 1633, 2650, *Gattermann*, B. **23**, 1218):

$$C_6H_5\cdot NI{:}N = C_6H_5I + N_2.$$

The method is largely used for the preparation of halogen derivatives of benzene homologues, especially for iodo-derivatives.

p-**Dibromo-benzene** is obtained, together with bromo-benzene, by bromination of benzene in presence of a little iron.

The **trichloro-benzene** which results by direct substitution has the (asymmetric) constitution 1:2:4. It may also be formed by the separation of 3HCl from $C_6H_6Cl_6$.

Hexachloro- and **hexabromo-benzenes** are produced by the prolonged chlorination or bromination of benzene, toluene, naphthalene, &c., and also from carbon tetrachloride and bromide, as given at p. 343. They are solid and can be distilled.

When toluene is chlorinated or brominated, as given on p. 356, the para- and ortho-compounds are formed in approximately equal quantities. *m*-Chloro-toluene is obtained from

chloro-*p*-toluidine, $C_6H_3Cl(NH_2)CH_3$ (from *p*-toluidine and Cl), according to method 3. Oxidation by HNO_3, CrO_3, or $KMnO_4$ converts them into the haloid-benzoic acids, but chromic acid mixture must only be used in the case of the *p*- and *m*-, and not in that of the *o*-compounds, as it completely disintegrates the latter.

Benzyl chloride, $C_6H_5 \cdot CH_2Cl$ (*Cannizzaro*), is prepared by chlorinating boiling toluene, and benzyl bromide in an analogous manner; the latter can be converted into benzyl iodide by potassium iodide solution. The behaviour of these compounds shows them to be the haloid esters of benzyl alcohol, $C_6H_5 \cdot CH_2 \cdot OH$, from which they may be obtained by the action of halogen hydride, or of halogen derivatives of phosphorus, and into which they are transformed by prolonged boiling with water, or better, with a solution of potassium carbonate. When boiled with potassium acetate, the chloride yields benzyl acetate, with potassium sulph-hydrate the mercaptan, and with ammonia the amine

The compounds containing halogen in the side chain irritate the mucous membrane of the nose and eyes exceedingly, and on oxidation yield benzoic acid. Benzyl chloride is used on the large scale for the preparation of oil of bitter almonds and also of certain dyes.

Benzal chloride, *Benzylidene chloride*, $C_6H_5 \cdot CHCl_2$, and **benzo-trichloride**, $C_6H_5 \cdot CCl_3$, are produced by the further chlorination of boiling toluene and also by the action of PCl_5 upon the corresponding oxygen compounds, benzaldehyde, $C_6H_5 \cdot CHO$, benzoic acid, $C_6H_5 \cdot CO_2H$, and benzoyl chloride, $C_6H_5 \cdot COCl$. They are liquids resembling benzyl chloride, and are reconverted into the original oxygen compounds by superheating with water, and into benzoic acid by oxidizing agents.

Chlorobromo-benzenes, C_6H_4ClBr, **chlor-iodo-benzenes**, and other mixed derivatives also exist in large number.

Substitution compounds of unsaturated hydrocarbons are likewise known, *e.g.* **β-bromo-styrene**, $C_6H_5 \cdot CBr:CH_2$, **α-bromo-styrene**, $C_6H_5 \cdot CH:CHBr$, &c.

Iodine Derivatives containing a Polyvalent Iodine Atom.—The iodine atom attached to the nucleus may in many cases unite with other atoms, and thus exercise a higher valency. The compounds thus obtained have but few analogues in the fatty series.

Phenyl-iodide dichloride, $C_6H_5 \cdot I:Cl_2$ (*Willgerodt*), is formed

as a yellow crystalline compound when dry chlorine is led into a chloroform solution of phenyl iodide The chlorine is loosely combined, and may be removed on warming, or by the action of potassium iodide. Alkalis transform the dichloride into **iodoso-benzene**, $C_6H_5 \cdot I{:}O$, a yellow amorphous substance which dissolves in acids, yielding salts, *e.g.* **acetate**, $C_6H_5 \cdot I(C_2H_3O_2)_2$, **nitrate**, $C_6H_5 \cdot I(O \cdot NO_2)_2$, &c. It decomposes when heated, oxidizes potassium iodide solution, and when kept or when distilled in steam is converted into phenyl iodide and **iodoxy-benzene**, $C_6H_5 \cdot IO_2$. This latter is crystalline, explodes when heated, is not basic, and resembles peroxides. It may also be prepared by oxidizing the iodoso-compound with *Caro's* reagent.

Iodonium compounds (*Hartmann* and *V. Meyer*, B **27**, 1592), *e.g.* **diphenyl-iodonium iodide**, $(C_6H_5)_2I \cdot I$, and the corresponding **hydroxide**, $(C_6H_5)_2I \cdot OH$, can be obtained when a mixture of iodoso- and iodoxy-benzene is shaken with moist silver oxide.

$$C_6H_5 \cdot I{:}O + C_6H_5 \cdot IO_2 + Ag \cdot OH = (C_6H_5)_2I \cdot OH + AgIO_3.$$

The hydroxide which is only known in solution has strongly alkaline properties The salts, which crystallize well, closely resemble the thallium salts. It is highly probable that the three valencies of the polyvalent iodine atom in these iodonium salts lie in the same plane, as, according to *Peters* and *Kipping* (J. C. S. 1902, 1350), stereo isomerides of the form RR'I·X do not appear to exist, and no resolution into optically active components can be effected.

XX NITRO-SUBSTITUTION PRODUCTS OF THE AROMATIC HYDROCARBONS

When benzene and its derivatives are treated with concentrated nitric acid, most of them are easily dissolved, with evolution of heat, and transformed into nitro-compounds which are precipitated on the addition of water. According to the conditions of the experiment and the nature of the compound to be nitrated, one or more nitro-groups enter the molecule (see, *e.g.*, phenol). The nitro-groups substitute in the nucleus, and only very seldom in the side chain (cf. p. 363).

Very often fuming nitric acid or a mixture of fuming nitric and concentrated sulphuric (or fuming sulphuric) acid is used.

The advantage of the addition of sulphuric acid is to absorb the water formed during nitration, and thus to keep the nitric acid from becoming too dilute. The stronger the acid and the higher the temperature, the larger the number of nitro-groups introduced. The homologues of benzene are, as a rule, nitrated more readily than benzene itself.

SUMMARY

		Positions of Substituents	M p	B.-p	Sp gr
$C_6H_5 \cdot NO_2$.	Nitro-benzene .		+3°	208°	1·204
$C_6H_4(NO_2)_2$ ...	*o*-Dinitro-benzene	1.2	117°	319°	
	m-Dinitro-benzene	1:3	90°	302°	
	p-Dinitro-benzene .	1 4	172°	299°	.
$C_6H_3(NO_2)_3$. ..	*s*-Trinitro-benzene	1 3 5	1·22°	†	
	as-Trinitro-benzene	1 2 4	57·5°		
$CH_3 \cdot C_6H_4 \cdot NO_2$...	*o*-Nitro-toluene	*1 2	-10·5°	218°	1·168
	m-Nitro-toluene .. .	1 3	+16°	230°	1·168
	p-Nitro-toluene	1.4	51°	234°	1·123 (54°)
$CH_3 \cdot C_6H_3 \cdot (NO_2)_2$	2 4-Dinitro-toluene .	1 2 4	70°	†	
	2.6-Dinitro-toluene	1 2 6	66°		
$(CH_3)_2 \cdot C_6H_3 \cdot NO_2$	4-Nitro-xylene	1 3 4	+2°	246	1·135
$(CH_3)_3C_6H_2 \cdot NO_2$..	Nitro-mesitylene	1.3.5 2	44°	255	

Nitro-compounds are also produced by the action of nitrous acid upon diazonium compounds in the presence of cuprous oxide (*Sandmeyer*, B **20**, 1494).

$$C_6H_5NCl{:}N + HNO_2 = C_6H_5 \cdot NO_2 + HCl + N_2,$$

and also by the oxidation of primary aromatic amines

$$C_6H_5 \cdot NH_2 \longrightarrow C_6H_5 \cdot NO_2$$

(*Bamberger*, B. 1893, **26**, 496). These reactions, however, are mainly of theoretical interest.

They cannot, however, be prepared according to mode of formation 1 for nitro-methane (p. 94), *i.e.* by the action of $AgNO_2$ on C_6H_5Cl, &c.

The nitro-compounds are, for the most part, pale-yellow liquids which distil unchanged and volatilize with water vapour; some form colourless or pale-yellow crystals; sometimes they are also of an intense yellow or red colour. Many

* The positions of CH_3 group, or groups, are always given first.

† Most of the polynitro-compounds are not volatile, but decompose when heated.

of them explode when heated They are heavier than water, and insoluble in it, but most of them are readily soluble in alcohol, ether, and glacial acetic acid.

The nitro group in most aromatic nitro-compounds is bound very firmly, as in the case of the nitro methanes, and is not exchangeable for other groups. Like the latter compounds also, they are readily reduced in acid solution to the corresponding amines; in alkaline solution they are converted into azoxy-, azo-, and hydrazo-compounds (see these), and in neutral solution into hydroxylamine derivatives

When reduced electrolytically, nitro-benzene can yield either phenyl-hydroxylamine, $C_6H_5 \cdot NH \cdot OH$, which is immediately transformed into *p* amino-phenol, $OH \cdot C_6H_4 \cdot NH_2$ (*Gattermann*, B. 1893, **26**, 1814, 1894, **27**, 1927), or it can yield aniline. Other nitro-compounds can be reduced in a similar manner. When hydrogen is passed into an alcoholic solution of nitro-benzene containing colloidal palladium, aniline is formed

Nitro-benzene, $C_6H_5(NO_2)$ (*Mitscherlich*, 1834), is formed when a mixture of sulphuric and the calculated quantity of nitric acid is added to benzene. It is a yellowish liquid with an intense odour of oil of bitter almonds, which solidifies in the cold, and melts at $+5°$.

Dinitro-benzenes, $C_6H_4(NO_2)_2$ are produced when benzene is boiled with fuming nitric acid, in this, as in all analogous cases, the two nitro groups take up the meta-position to one another, very little of the *o*- and *p*-compounds being formed, and after crystallizing from alcohol, pure *m*-dinitro-benzene is obtained in long colourless needles.

The *o*-compound crystallizes in plates and the *p*-compound in needles, both being colourless, they are prepared indirectly by eliminating NH_2 from the corresponding di-nitranilines.

When reduced, they yield first the three nitranilines, and then the phenylene-diamines (pp. 374 and 380).

o-Dinitro-benzene exchanges a nitro-group for hydroxyl when boiled with caustic soda, and for an amino-group when acted on by ammonia, yielding *o*-nitro-phenol, $C_6H_4(NO_2)(OH)$, and *o*-nitraniline, $C_6H_4(NO_2)(NH_2)$, respectively. These reactions appear to be characteristic of all compounds containing two nitro-groups in ortho-positions. The *m*-compound is oxidizable by $K_4Fe(CN)_6$ to *a*- and *β*-dinitro-phenol.

s-**Trinitro-benzene** crystallizes in colourless plates, melts at 122°, and forms additive compounds with aromatic hydro-

carbons, phenols, and especially with aromatic bases, *e.g.* aniline, naphthylamine. Most of these are well-defined crystalline compounds of red, reddish-brown, or black colour, and are readily resolved into their components by warm mineral acids (A. 1882, **215**, 344; J. C. S. 1901, 522, 1903, 1334, 1906, 583; 1910, 773).

Nitro-toluenes, $CH_3 \cdot C_6H_4 \cdot NO_2$.- When toluene is nitrated, the *p*- and *o*-compounds, with very little *m*-compound, are formed. The first is solid, crystallizing in large prisms, and the second liquid, the latter being used as a perfume under the name of "oil of mirbane"; both are employed in the colour industry. *m*-Nitro-toluene can be prepared indirectly from *m* nitro-*p*-toluidine, $C_6H_3(CH_3)(NO_2)(NH_2)$, by the elimination of the amino-group (p. 387). Further nitration gives rise to

Dinitro-toluenes, $CH_3 \cdot C_6H_3(NO_2)_2$, of the constitution $CH_3 : NO_2 : NO_2 = 1:2\ 4$ and $1 \cdot 2 \cdot 6$, the two nitro-groups being again in the *m*-position to one another in both cases. (Cf. p. 361.)

Most of these nitro-compounds are of great technical importance, on account of the readiness with which they are reduced to amines.

Trinitro-tertiary-butyl-toluene, $C_6H(CH_3)[C(CH_3)_3](NO_2)_3$, is used as "artificial musk".

Chloro- and **Bromo-nitro-benzenes.**—When chloro- or bromo-benzene is nitrated, *p*-chloro- (or bromo-) nitro-benzene is formed, together with smaller quantities of the *o*-compounds. The *m*-compounds must be prepared indirectly by replacing an amino-group in *m*-nitraniline by halogen. The *p*-derivatives have a higher melting-point than their isomers, and the *m*-compounds for the most part a higher one than the *o*-derivatives, this law frequently repeating itself in other cases also The *p*-derivatives are usually also less soluble in alcohol. The *o*- and *p*-compounds, but not the *m*-, exchange halogen for hydroxyl when boiled with potash, and for the amino-group when heated with ammonia.

In *s*-**trinitro-chloro-benzene**, $C_6H_2(NO_2)_3Cl$, and in 1-chloro-2:4-dinitro-benzene the chlorine atoms have been rendered so readily exchangeable, that the compounds behave as alkyl chlorides, or even as acid chlorides; hence the name "picryl chloride", the chloride of picric acid (p. 414), for the former compound.

o-, *m*-, and *p* **Nitro-cinnamenes**, $C_6H_4(NO_2)(C_2H_3)$, can be prepared by indirect methods. **α-Nitro-styrene**, $C_6H_5 \cdot CH:$

$CH \cdot NO_2$, which is formed by the action of nitrous acid on cinnamene, contains the nitro group in the side chain, since it can be prepared from benzoic aldehyde and nitro-methane by means of zinc chloride, thus:—

$$C_6H_5 \cdot CHO + CH_3 \cdot NO_2 = C_6H_5 \cdot CH{:}CH \cdot NO_2 + H_2O.$$

o **Nitro-phenyl-acetylene**, $NO_2 \cdot C_6H_4 \cdot C \vdots CH$, is formed when *o*-nitro-phenyl-propiolic acid is boiled with water. It crystallizes in colourless needles.

Phenyl-nitro-methane, $C_6H_5 \cdot CH_2 \cdot NO_2$, isomeric with the nitro-toluenes, is the most typical of the aromatic nitro-derivatives with a nitro-group in the side chain. It is formed by the action of nitric acid (D 1·12) on toluene under pressure, and also by the action of benzyl halides on silver nitrite (cf. Nitro-methane). It is a true nitro-derivative, and not an alkyl nitrite (benzyl nitrite, $C_6H_5 \cdot CH_2 \cdot O \cdot N{:}O$), as it is not readily hydrolysed, and when reduced yields benzylamine, $C_6H_5 \cdot CH_2 \cdot NH_2$. It exists in two distinct modifications, which are readily transformed into each other. As generally prepared, it is a colourless liquid with a characteristic odour, boils at 225°–227°, and dissolves to a certain extent in water, yielding a solution which does not give a coloration with ferric chloride. The second modification, which is a crystalline solid melting at 81°, is formed when the sodium derivative obtained from the oily compound is decomposed in the cold by hydrochloric acid. The solid modification is relatively unstable, and when kept, gradually passes over into the oily form. The solid is probably a hydroxy-compound, since (*a*) its aqueous solution gives a red-brown coloration with ferric chloride, (*b*) it reacts with phenyl-carbimide, (*c*) it reacts with PCl_5, and (*d*) with benzoyl chloride it gives dibenzhydroxamic acid,

$$C_6H_5 \cdot CO \cdot NH \cdot O \cdot COC_6H_5 \text{ (from } C_6H_5 \cdot CH{:}N \langle \begin{matrix} O \\ O \cdot CO \cdot C_6H_5 \end{matrix} \text{)}$$

The solid would thus be represented by the formula

$$C_6H_5 \cdot CH{:}NO \cdot OH \quad \text{or perhaps} \quad C_6H_5 \cdot \underset{\diagdown\!\diagup \\ O}{CH \cdot N \cdot OH},$$

an *isonitro* formula, the sodium salt by $C_6H_5 \cdot CH{:}NO \cdot ONa$, and the oil by $C_6H_5 \cdot CH_2 \cdot NO_2$. The tendency to form *iso*-nitro-compounds is also shown by certain aliphatic nitro-compounds.

The oily compound, although it gives rise to a sodium salt, is, strictly speaking, not an acid; it is what is termed a *pseudo-acid*, and before it yields a sodium salt it undergoes intramolecular rearrangement, yielding the true acid—the *iso*nitro-compound. When the sodium salt is treated with a mineral acid, the *iso*nitro-compound, or true acid, is first formed; but as this is unstable, it gradually changes over into the true nitro- or pseudo-acid form. Numerous examples of pseudo-acids, *i.e.* compounds which on formation of metallic salts undergo intramolecular rearrangement so that the original substance has a structure different from that of the salt, have been investigated by *Hantzsch* (B. 1899, **32**, 575; 1902, **35**, 210, 226, 1001; 1906, **39**, 139, 1073, &c.), who describes the following as some of the most characteristic criteria of pseudo-acids:—

1. The compound is a pseudo-acid if it *gradually* neutralizes an alkali. The pseudo-acid, as such, does not neutralize the base, but is first transformed into the isomeric true acid, which then neutralizes the alkali. If the transformation is slow, then the process of neutralization is also slow. Similarly, if when a solution of a salt of the acid is decomposed by an equivalent quantity of a mineral acid, the electrical conductivity gradually falls to that required for the metallic salt of the mineral acid, it indicates that the acid is a pseudo-acid, *e.g.* barium *iso*nitro-methane + HCl give isonitro-methane + $BaCl_2$, and then nitro-methane + $BaCl_2$. Isonitro-methane is a fairly strong acid, and hence is dissociated to an appreciable extent; as it becomes transformed into nitro-methane (the pseudo-acid) the conductivity will diminish, as nitro-methane is an extremely feeble acid—scarcely ionized.

2. If the original compound is extremely feebly acidic, and yet yields a sodium derivative which dissolves in water yielding a practically neutral solution, then the compound must be a pseudo-acid. It is a well-known fact that only sodium salts derived from comparatively strong acids, *e.g.* NaCl, Na_2SO_4, NaI, &c., dissolve in water to neutral solutions, *i.e.* are not hydrolysed by water. The sodium salts derived from feeble acids are always appreciably hydrolysed, *e.g.* Na_2CO_3, $CH_3 \cdot COONa$, &c. Hence if the sodium salt is not hydrolysed to an appreciable extent, the salt must be derived from a strong acid (the true acid), and the non- or feebly acidic compound must be the pseudo-acid.

3. If the compound in question will not yield a salt with ammonia in an anhydrous solvent, *e.g.* dry benzene, but will

do so in the presence of water, *e.g.* in moist ether, then the substance is a pseudo-acid. The formation of a salt in dry ether does not necessarily indicate that the substance is a true acid.

4. If the compound dissolves in water or in other dissociating (ionizing) media to a colourless solution, but yields a coloured solid salt or coloured ions when dissolved in alkalis, it is a pseudo-acid.

5. An abnormally high temperature coefficient for the electrical conductivity and an increase in the coefficient with rise of temperature are further indications of pseudo-acids.

Nitro-methane, bromo-nitro-methane, dibromo-nitro-methane, nitro-ethane, phenyl-nitro-methane, phenyl-bromo-nitro-methane, in addition to numerous other organic compounds, *e.g.* cyanuric acid, react as pseudo-acids

NITROSO-DERIVATIVES OF THE HYDROCARBONS

Nitroso-benzene, $C_6H_5 \cdot N:O$, an aromatic compound which contains the nitroso-group, $\cdot N:O$, in place of a benzene hydrogen atom, is produced by the action of nitrosyl chloride, $NO \cdot Cl$, upon mercury diphenyl dissolved in benzene; it is also obtained by the oxidation of diazo-benzene with alkaline permanganate, and most readily by the oxidation of phenyl-hydroxylamine with chromic acid or ferric chloride. It forms colourless plates, melts at 68°, yields green solutions, and possesses a powerful odour similar to that of cyanic acid. When reduced it yields aniline, and when oxidized nitro-benzene. It readily condenses with different compounds, *e.g.* with aniline in the presence of acetic acid to azo-benzene:

$$C_6H_5 \cdot N:O + H_2N \cdot C_6H_5 = H_2O + C_6H_5 \cdot N:N \cdot C_6H_5,$$

and with phenyl-hydroxylamine to azoxy-benzene.

Nitroso-derivatives of tertiary amines are obtained directly by the action of nitrous acid upon the latter. (See Nitroso-dimethyl-aniline, $NO \cdot C_6H_4 \cdot N(CH_3)_2$, p. 378.)

XXI. AMINO-DERIVATIVES OR ARYLAMINES*

(See Table, p. 367.)

Aniline, the simplest of the aromatic bases, may be regarded (1) as benzene in which a hydrogen atom is replaced by the amino-group ("amino-benzene"), or (2) as ammonia in which a hydrogen atom is replaced by phenyl, C_6H_5-, ("phenyl-amine"). According to the former view, amino-compounds can be derived from all the benzene hydrocarbons, and not only monamines (containing NH_2), but also diamines ($2\,NH_2$), triamines, &c.; according to the latter, the phenyl group may enter anew with the formation of secondary or tertiary amines. Secondary and tertiary amines, and even quaternary ammonium compounds, may also result from the entrance of alkyl-radicals into the above monamines, diamines, &c. Amines are also known in which the NH_2 group is attached to a carbon atom of a side chain, *e.g.* $C_6H_5 \cdot CH_2 \cdot NH_2$. These compounds differ in many respects from aniline and its homologues.

An extraordinarily large number of aromatic bases are thus theoretically possible, and also actually known. In certain respects they closely resemble the aliphatic amines, *e.g.* they form salts with acids, *e.g.* $C_6H_5NH_2$, HCl, and complex salts, *e.g.* platinichlorides and aurichlorides, $2C_6H_5NH_2$, H_2PtCl_6 and $C_6H_5NH_2$, $HAuCl_4$; they possess a basic odour, give rise to white clouds with volatile acids, and distil for the most part unchanged, &c. As a rule, however, they are weaker bases than the aliphatic amines, since the phenyl group, C_6H_5, possesses a negative character, and not—like the alphyl radicals—a positive; thus the salts of diphenylamine are decomposed even by water, and triphenylamine no longer possesses basic properties, while dimethyl-aniline has a strongly-marked basic character.

* To distinguish between monovalent alcoholic or hydrocarbon radicals of the fatty and aromatic series the following system has been suggested: – The term alkyl group comprises all such monovalent radicals whether of the aliphatic series, *e.g.* CH_3, C_2H_5, or of the aromatic, *e.g.* C_6H_5, $CH_3 \cdot C_6H_4$, $C_6H_5 \cdot CH_2$, &c. The purely aliphatic alkyl radicals are termed **alphyl** groups, and the aromatic, **aryl** (*Vorlander*, J. pr. [2], **59**, 247). Thus aniline is often spoken of as a type of the arylamines

The diamines have a more strongly basic character than the monamines, and are more readily soluble in water.

ANILINE AND ITS HOMOLOGUES

Formula	Name.	Positions of Substituents NH_2 in 1	M.-p.	B.-p.	M.-p. of Acetyl Derivative.
$C_6H_5 \cdot NH_2$.....	Aniline.....	...	−8°	183°	115°
$C_6H_4Me \cdot NH_2$..	*o*-Toluidine.....	1.2	liq.	199°	110°
	m-Toluidine...	1.3	liq.	199°	65.5°
	p-Toluidine.....	1:4	42.8°	198°	153°
$C_6H_3Me_2 \cdot NH_2$	*adj.-o*-xylidene...	1.2.3	liq.	223	134°
	unsym.-o-xylidene	1.3.4	49°	226	99°
	adj.-m-xylidene. .	1.2.6	liq.	215°	176°
	p-xylidene	1.2.5	15·5°	215°	139°
$C_6H_2Me_3 \cdot NH_2$..	Mesidine	1.2.4.6	liq.	233	216°
	Pseudo-cumidine.	1.2.4.5	68°	234°	164°
$C_6H_5 \cdot NHMe$ ...	Methyl-aniline .	..	...	192	101–102°
$C_6H_5 \cdot NMe_2$.....	Dimethyl-aniline	...	...	192	...
$C_6H_5 \cdot NHEt$.	Ethyl-aniline ...	...	..	204°	54.5°
$C_6H_5 \cdot NEt_2$.	Diethyl-aniline...	...	...	213	.
$C_6H_5 \cdot CH_2 \cdot NH_2$	Benzylamine	...	...	183°	60°

A. Primary Monamines

Isomers.—The isomerism of the aromatic is in part analogous to that of the fatty amines (p. 107), *e.g.* dimethyl-aniline is isomeric with the methyl toluidines and the xylidines. Cases of isomerism are also caused by the amino-group being present in the benzene nucleus in the one case, and in the side chain in the other. Finally, position isomerides are frequently met with, *e.g. o*-, *m*-, and *p*-toluidines, $CH_3 \cdot C_6H_4 \cdot NH_2$.

Constitution.—As already seen at pp. 108 *et seq.*, amines are very easy to characterize as primary, secondary, &c. In addition, their modes of formation, and also their behaviour, show whether the amino-group of a primary amine is present in the benzene nucleus or in the side chain.

Modes of Formation.—1. The most important mode of preparation of the primary arylamines, whether mono- or di-, &c., is the reduction of the corresponding nitro-compounds:

$$\underset{\text{Nitro-benzene}}{C_6H_5 \cdot NO_2} + 6H = 2H_2O + \underset{\text{Aniline}}{C_6H_5 \cdot NH_2}$$

$$\underset{\text{Dinitro-benzene}}{C_6H_4(NO_2)_2} + 12H = 4H_2O + \underset{\text{Phenylene-diamine}}{C_6H_4(NH_2)_2}$$

The usual method of introducing an amino-group into a benzene hydrocarbon is to first nitrate and then reduce. An interesting direct method for the introduction of the NH_2 group is by the action of ferric or aluminic chloride on a mixture of the hydrocarbon and hydroxylamine hydrochloride (B. 1901, **34**, 1778):

$$C_6H_6 + NH_2 \cdot OH = H_2O + C_6H_5 \cdot NH_2.$$

The reduction of nitro- to amino-compounds takes place most readily in acid solution, *e.g.* by the gradual addition of the former to a warm mixture of tin or stannous chloride and hydrochloric acid. On a manufacturing scale, iron and a limited amount of hydrochloric acid are used (*Béchamp*), also frequently zinc dust and hydrochloric or acetic acid. Ammonium sulphide (*Zinin*), ferrous sulphate, and baryta water, &c., also effect the reduction. (See Aniline and chapter on Reduction.)

Aniline and its homologues may also be obtained by the electrolytic reduction of nitro-compounds.

Ammonium sulphide acts more mildly than tin and hydrochloric acid, and is therefore of special value for the partial reduction of dinitro-compounds (see Nitraniline). An alcoholic solution of stannous chloride containing hydrochloric acid may also be used for this purpose (B. **19**, 2161).

Amines are also formed when nitroso-compounds and arylhydroxylamines are reduced.

2. By heating phenols with the compound of zinc chloride and ammonia, or of calcium chloride and ammonia, to 300° (*Merz*), secondary amines being formed at the same time:

$$C_6H_5 \cdot OH + H\,NH_2 = C_6H_5 \cdot NH_2 + H_2O.$$

This reaction proceeds more easily in the presence of negative groups, *e.g.* with the nitro-phenols (B **19**, 1749).

3. By distilling amino-acids with lime, sometimes by merely heating them alone:

$$NH_2 \cdot C_6H_4 \cdot CO_2H = C_6H_5 \cdot NH_2 + CO_2.$$

4. When the hydrochlorides of secondary and tertiary amines of the type of mono- and di methyl-aniline are heated in sealed tubes, the methyl groups wander from the nitrogen atom to a carbon atom of the benzene nucleus, *e.g.* methylaniline hydrochloride at 335° yields toluidine hydrochloride:

$$C_6H_5 \cdot NHCH_3, HCl = CH_3 \cdot C_6H_4 \cdot NH_2, HCl.$$

The methyl groups invariably take up the *o*- or *p*-, and not the *m*- position, with respect to the amino-group.

Similarly, the final product obtained by heating phenyltrimethylammonium iodide, $C_6H_5 \cdot NMe_3I$, is mesidine hydriodide, $C_6H_2Me_3 \cdot NH_2[NH_2 : Me_3 = 1:2:4:6^*]$. Diphenylamine hydrochloride does not behave in a similar manner

This reaction, often known as the *Hofmann* reaction, is of considerable service in obtaining the higher homologues of aniline from aniline, toluidine, &c. Aniline is readily converted into dimethyl-aniline, and when the hydrochloride of this is heated to about 300° the methyl groups wander from the side chain into the nucleus:

$$C_6H_5 \cdot NMe_2 \longrightarrow C_6H_4Me_2 \cdot NH_2$$

5 Primary amines can be obtained from acid amides by *Hofmann*'s reaction (cf p. 183), viz treatment with bromine and alkali, or from acid azides, $R \cdot CO \cdot N_3$ When boiled with alcohol the azide yields nitrogen and, by molecular rearrangement, a urethane, $R \cdot NH \cdot CO \cdot OEt$, and this on hydrolysis gives a primary amine, RNH_2

6 The aromatic amines cannot, as a rule, be obtained by heating chloro-benzene, &c, with ammonia unless there is a nitro group in the ortho- (or para) position with respect to the halogen Benzylamine, however, and all analogously constituted bases, which contain the NH_2 group in the side chain, can be obtained by the methods employed for the preparation of aliphatic amines Thus benzylamine is formed by the action of ammonia, or better, of acetamide upon benzyl chloride (the latter method gives acetyl-benzylamine, which can be readily hydrolysed)

Properties. The primary monamines are either liquid or solid crystalline bases. They are colourless when pure, but readily become brown when exposed to the air, largely owing to the presence of small amounts of impurities, and possess a weakly basic though not disagreeable odour. Aniline is somewhat soluble in water (1·31), its homologues less so.

Behaviour. 1 With acids most of them form crystalline salts, the majority of which are readily soluble in water. They do not, however, unite with very weak acids, such as

* The numbers 1:2:4:6 indicate the relative positions of the amino- and three methyl-radicals in the benzene ring.

carbonic, and they are therefore separated from their salts in the free state by sodium carbonate, and in some cases even by sodium acetate (when no acetates exist). They yield complex salts, such as **platinichlorides**, $(C_6H_5NH_2)_2, H_2PtCl_6$, **aurichlorides**, $C_6H_5NH_2, HAuCl_4$, and similar compounds with stannous, stannic, and zinc chlorides. The platinum double salts are often sparingly soluble, and therefore suited for the isolation of the bases.

All salts of the bases are readily decomposed by strong alkalis, and the free bases are regenerated. Even in aqueous solution the salts are largely split up into free acid and free base, the result is that the strength of a solution of aniline hydrochloride may be determined by titrating the hydrochloric acid present by standard alkali hydroxide, using phenolphthalein as indicator. This is not due to the fact that the salt is completely hydrolysed in aqueous solution, in reality there is a state of equilibrium represented by the equation:

$$C_6H_5\cdot NH_3Cl \rightleftarrows C_6H_5NH_2 + HCl,$$

and as the HCl is neutralized by the addition of alkali, more of the aniline salt is decomposed in order to restore the equilibrium. This continues until the whole of the salt is decomposed, and the HCl neutralized by the alkali.

The amines also form additive compounds with numerous metallic salts, *e.g.* $2C_6H_7N + ZnCl_2$, $2C_6H_7N + HgCl_2$, &c.

2. When aniline is heated with potassium or sodium, the hydrogen is replaced by metal with formation of the compounds C_6H_5NHK and $C_6H_5NK_2$. These yield di- and tri-phenylamine with bromobenzene, and decompose immediately with water.

3. The primary arylamines react with methyl iodide, benzyl chloride, &c., yielding secondary, tertiary, and even quaternary compounds:

$$\begin{aligned} C_6H_5\cdot NH_2 + CH_3I &= C_6H_5\cdot NH(CH_3), HI; \\ C_6H_5\cdot NH(CH_3) + CH_3I &= C_6H_5\cdot N(CH_3)_2, HI; \\ C_6H_5\cdot N(CH_3)_2 + CH_3I &= C_6H_5\cdot N(CH_3)_3I. \end{aligned}$$

The secondary and tertiary bases can be liberated from their hydriodides by soda, but moist oxide of silver must be used in the case of the ammonium bases (see p. 109).

4. Just as the ammonium salts of acids can eliminate water, yielding **amides**, so the aniline salts can yield **anilides**, *e.g.* aniline acetate gives acetanilide:

$$CH_3\cdot CO\cdot ONH_3C_6H_5 = CH_3\cdot CO\cdot NHC_6H_5 + H_2O.$$

These anilides may be looked upon either as acetylated amines or as phenylated amides, the formula $CH_3 \cdot CO \cdot NH \cdot C_6H_5$ corresponding with the latter view. They are in every respect analogous in their chemical behaviour to the ordinary amides, especially to the alkylated amides (p. 182), being hydrolysed to the acid and amine by alkalis, and being formed by analogous methods, *e.g.* by heating the acid, or better, its anhydride or chloride, with the amine in question, thus:—

$$\underset{\text{Toluidine}}{CH_3 \cdot C_6H_4 \cdot NH_2} + CH_3 \cdot COCl = \underset{\text{Acet-toluidide}}{CH_3 \cdot C_6H_4 \cdot NH \cdot CO \cdot CH_3} + HCl.$$

5. Aliphatic aldehydes react with the primary bases, with elimination of water, thus:—

$$CH_3 \cdot CHO + 2C_6H_5 \cdot NH_2 = \underset{\text{Ethylidene-diphenyl-diamine}}{CH_3 \cdot CH(NH \cdot C_6H_5)_2} + H_2O$$

Aromatic aldehydes, however, react as follows:—

$$C_6H_5 \cdot CHO + NH_2 \cdot C_6H_5 = C_6H_5 \cdot CH{:}N \cdot C_6H_5 + H_2O.$$

In this case an additive compound appears to be first formed, $C_6H_5 \cdot CH(OH) \cdot NH \cdot C_6H_5$, and this loses water, yielding benzylidene aniline, $C_6H_5 \cdot CH{:}N \cdot C_6H_5$.

Condensation products of this latter kind (**Schiff's bases**) can also be obtained with the fatty aldehydes, but they polymerize readily (*v. Miller, Plochl*, B **25**, 2020)

6. When warmed with chloroform and alcoholic potash, the primary bases, like those of the fatty series, yield **isonitriles** of stupefying odour. When they are warmed with carbon disulphide, **thio-ureas** are formed, and from the latter **isothiocyanates** (**mustard oils**) by treatment with phosphoric acid (cf. pp. 276 and 296).

7. Bromine and chlorine, especially in the form of sodium hypochlorite or hypobromite, react with amines, forming substituted derivatives of the type $C_6H_5 \cdot NHBr$, in which the halogen is attached to nitrogen. These compounds are extremely unstable, can only be kept at low temperatures, and the halogen atom readily passes from the side chain into the benzene nucleus:

$$C_6H_5 \cdot NHBr \longrightarrow C_6H_4Br \cdot NH_2,$$

usually into the para-position (*Chattaway* and *Orton*, J. C. S. 1899, 1046; 1900, 131, 152, 789, 797).

8. Nitrous acid converts the primary aromatic amines in acid solution into diazonium salts (p. 385), and in the absence of acids into diazo-amino-compounds (p. 392).

9. The oxidation products of the primary bases are very various, azo-benzene, nitro-benzene, *p*-amino-phenol, phenols, quinones, azo-compounds, aniline black, &c., resulting according to the conditions; a mixture of aniline and toluidine yields magenta (fuchsine) (see Triphenylmethane dyes).

10. The bases which contain the amino-group in the side chain possess, in contradistinction to the purely aromatic amines, the character of the amines of the fatty series, and cannot, therefore, be diazotized.

Aniline, amino-benzene, *Phenylamine*, $C_6H_5 \cdot NH_2$, was first obtained in 1826 by *Unverdorben* from the dry distillation of indigo, and termed by him "crystalline"; then *Runge* found it in coal-tar in 1834, and called it "cyanol". In 1841 *Fritsche* prepared it by distilling indigo with potash, and gave it the name of aniline; while in 1842 *Zinin* obtained it by the reduction of nitro-benzene, and called it "benzidam". It was accurately investigated by *A. W. Hofmann* in 1843, and he was able to show that all the above products are identical

It is present in small quantities in coal-tar and also in bone-oil.

Preparation.—Since 1864 aniline has been prepared on a manufacturing scale by reducing nitro-benzene with iron filings and a regulated quantity of hydrochloric acid, and distilling with steam after the addition of lime. The amount of hydrochloric acid actually employed is only about $\frac{1}{40}$th of that required by the equation:

$$C_6H_5 \cdot NO_2 + 3Fe + 6HCl = C_6H_5 \cdot NH_2 + 2H_2O + 3FeCl_2.$$

This is probably due to the fact that water and metallic iron, in the presence of ferrous chloride, can act as reducing agents. It is a colourless, oily, strongly refracting liquid of peculiar odour, which quickly turns yellow or brown in the air, and is finally converted into a resin. It dissolves in 31 parts of water, has no action upon litmus, and is a weaker base than ammonia, although it can displace the latter at higher temperatures. It is poisonous, burns with a smoky flame, and is a good solvent for many compounds which are otherwise not readily dissolved, *e.g.* indigo and sulphur. Aqueous solutions of the salts have a distinct acid reaction.

The *behaviour* of aniline has been investigated with the

utmost care. Oxidation in alkaline solution leads to azobenzene, while arsenic acid produces chiefly violaniline, a violet colouring-matter. A solution of free aniline is temporarily coloured violet by one of bleaching-powder, this reaction being an extremely delicate one. A solution in concentrated H_2SO_4 is first coloured red and then blue by a small grain of potassium dichromate. A solution of $K_2Cr_2O_7$ produces in an acid solution of aniline sulphate a dark-green and then a black precipitate of aniline black (*Willstatter*, B. 1907, **40**, 2665; 1910, **43**, 2976; *Green*, J. C. S. 1910, 2388; B. 1911, **44**, 2570), and ultimately quinone, $C_6H_4O_2$. A mixture of aniline and toluidine may be oxidized to magenta, mauveine, &c., and a mixture of aniline and *p*-diamines to safranines (see these). When reduced, aniline yields **amino-hexamethylene**, boiling at 134°.

Salts.- **Aniline hydrochloride**, $C_6H_5 \cdot NH_2$, HCl, forms large colourless plates which become greenish-grey in the air and distil unchanged, and **aniline sulphate**, $(C_6H_7N)_2$, H_2SO_4, beautiful white plates, sparingly soluble in water. The **platinichloride**, $(C_6H_7N)_2$, H_2PtCl_6, crystallizes in yellow plates, which are sparingly soluble.

Substitution Products—Halogen Derivatives.—Aniline is much more readily substituted by halogens than benzene, chlorine or bromine causing substitution of as many as three atoms of hydrogen, yielding *sym*-trichlor- or -tribrom-aniline, while iodine produces mono-iodoaniline. In the chlorination of aniline it is necessary to use a solvent free from water (*e.g.* chloroform or glacial acetic acid), otherwise oxidation and not substitution occurs. In bromination the simplest method is to aspirate air saturated with bromine vapour through an acid solution of aniline. In all these reactions the halogen probably first substitutes H of the NH_2 group (see p. 371). In the preparation of **monochlor-aniline**, the aniline must be "protected" by using it in the form of its acetyl derivative, acetanilide. When this is suspended in water, it is mostly transformed by chlorine into *p*-**chlor-acetanilide**, which readily yields *p*-**chlor-aniline** on hydrolysis; the latter forms colourless crystals, m.-pt. 71°, b.-pt. 231°. The *o*- and *m*-**compounds**, which are both liquid, are prepared indirectly, *e.g.* by the reduction of *o*- or *m*-chloro-nitro-benzene.

The basic character is weakened in the mono-chlor-anilines by the entrance of the halogen, this being the case particularly in the *o*-compounds. It is still more striking in *s*-**trichlor-**

aniline, $C_6H_2Cl_3(NH_2)$ (crystals, volatile without decomposition), which no longer combines with acids in presence of water. *o*- and *p* Chlor-anilines are only capable of taking up two more atoms of chlorine with the formation of trichlor-aniline: $[NH_2:Cl:Cl:Cl = 1.2.4.6]$; *m*-chlor-aniline, on the other hand, can be further chlorinated to **tetra-** and **penta-chlor-aniline.**

The bromo-derivatives of aniline closely resemble the chlor-anilines, and may be prepared by similar methods. The best-known compound is *s*-**tribrom-aniline**, which is formed by the action of bromine water on a solution of aniline hydrochloride. It crystallizes from alcohol in needles, and melts at 119°.

As an example of the methods sometimes employed for the preparation of halogen derivatives may be cited the preparation of 2:6 dibrom-aniline from sulphanilic acid, 1 amino-benzene-4-sulphonic acid. When carefully brominated, this yields the 2:6-dibromo-derivative, and when this is superheated with steam at 170° the sulphonic acid group is removed, and 2.6-**dibrom-aniline**, melting at 84°, is formed.

Nitranilines.—Aniline is likewise attacked far more violently than benzene by concentrated nitric acid, and therefore when it is wished to prepare the mono-nitro-compounds, the aniline must again be "protected", either by using its acetyl compound, or by nitrating in presence of excess of concentrated sulphuric acid. In the latter case all three nitranilines result, the *m*-compound preponderating. When acetanilide is nitrated, *p*-**nitracetanilide**, $NO_2 \cdot C_6H_4 \cdot NH \cdot CO \cdot CH_3$, and a little of the *o*-compound, are formed, and both are readily hydrolysed by potash or hydrochloric acid.

The nitranilines are further obtained by the partial reduction of the corresponding dinitro-benzenes, *e.g.* by means of ammonium sulphide, this is the method usually employed for the preparation of *m*-nitraniline. (For mechanism of the reaction, see *Cohen* and *M'Candlish*, J. C. S. 1905, 1257.)

The *o*- and *p*-compounds are also formed when *o*- and *p*-$C_6H_4Cl \cdot NO_2$, $C_6H_4Br \cdot NO_2$, $OH \cdot C_6H_4 \cdot NO_2$, or $OEt \cdot C_6H_4 \cdot NO_2$ are heated with ammonia at 180°, and conversely the *o*- and *p*-nitranilines are converted into nitro-phenols when boiled with alkalis, the former more easily than the latter, thus:—

$$C_6H_4(NO_2)(NH_2) + H \cdot OH = C_6H_4(NO_2)OH + NH_3$$

These are all further examples of the remarkable influence of nitro-groups on other substituents, *e.g.* Cl, Br, OH, NH_2,

&c., in the *o*- and *p*-, but not in the *m*-position (Cf. Picryl Chloride and Picramide.)

The three nitranilines crystallize in yellow needles or prisms, and are readily soluble in alcohol, but only very slightly in water. They melt respectively at 71°, 114°, 147°, and their **acetyl** derivatives at 92°, 142°, and 207°. The *o*- and *m*-compounds are volatile with steam, but not *p*-nitraniline. When reduced, they yield phenylene-diamines.

Di- and **trinitranilines**,

$$C_6H_3(NO_2)_2(NH_2) \quad \text{and} \quad s\text{-}C_6H_2(NO_2)_3(NH_2),$$

are likewise known; the latter, which is termed **picramide**, and which crystallizes in yellow needles, m.-pt. 188°, comports itself as the amide of picric acid, since it is readily transformed into the latter compound on hydrolysis

(For alkyl derivatives, see under Secondary and Tertiary Monamines.)

Homologues of Aniline.—Of the three **toluidines**, $CH_3 \cdot C_6H_4 \cdot NH_2$, the *o*- and *p*-compounds are obtained by the reduction of the corresponding nitro-compounds. The *o*- is liquid and the *p*- solid

***m*-Toluidine**, which is liquid, may be prepared from *m*-nitrotoluene or *m*-nitro-benzaldehyde (cf. B. **15**, 2009).

The boiling-points of the three isomeric toluidines are almost identical, but the melting-points of their acetyl compounds differ widely (see table, p. 367); these are, therefore, of value for the characterization of the toluidines. *o*-Toluidine is coloured violet by a solution of bleaching-powder, and blue by sulphuric and nitrous acids and also by ferric chloride, but not *p*-toluidine. For their conversion into fuchsine, see Triphenylmethane dyes. If during oxidation the amino-group be protected by the introduction of acetyl, the methyl radical can be oxidized to carboxyl and an acetyl derivative of aminobenzoic acid obtained. When oxidized with $KMnO_4$, the amino-compounds are transformed into azo-compounds.

(For higher homologues, see table, p. 367.)

B. Secondary Monamines

We have purely aromatic secondary amines, such as diphenylamine, $(C_6H_5)_2NH$, and mixed secondary bases, which contain both an alphyl and an aryl group, *e.g.* methylaniline. $C_6H_5 \cdot NH \cdot CH_3$.

Modes of Formation.—1. Mixed secondary amines are formed when the primary amines are heated with alphyl iodides (*Hofmann*) (see p. 105).

This reaction does not usually stop short with the introduction of one alphyl radical, but extends further with the formation of tertiary bases. In order to avoid this, the alphyl iodide, &c., may be allowed to act upon the acetylated primary bases, *e.g* acetanilide [or upon their sodium compounds (*Hepp*)], and the resulting acetyl compound hydrolysed:

$$C_6H_5\cdot NH\cdot CO\cdot CH_3 + CH_3I = C_6H_5\cdot N(CH_3)CO\cdot CH_3 + HI$$

The secondary bases are separated from the tertiary by treatment with nitrous acid (see below, under Nitrosamines)

2. The purely aromatic secondary amines are obtained when the primary arylamines are heated with their hydrochlorides.

$$C_6H_5\cdot NH_2 + C_6H_5\cdot NH_2HCl = \begin{matrix}C_6H_5\\C_6H_5\end{matrix}\!\!>\!NH, HCl + NH_3$$

Two different aryl radicals may be introduced, *e.g.* $(C_6H_5)(CH_3\cdot C_6H_4)NH$, phenyl-tolylamine.

Behaviour.—1. The mixed secondary bases have strongly-marked basic properties, while the purely aromatic are feebler bases than the primary arylamines (cf. p. 366).

2. For the migration of the alphyl group from the side chain into the nucleus, see p 369.

3. The hydrogen of the imino-group is replaceable by an alkyl or acyl radical, and also by potassium or sodium:

$$(C_6H_5)_2NH + CH_3I = HI + \underset{\text{Methyl-diphenylamine}}{(C_6H_5)_2NCH_3}$$

$$(C_6H_5)_2NH + (CH_3\cdot CO)_2O = CH_3\cdot CO_2H + \underset{\text{Acetyl-diphenylamine.}}{(C_6H_5)_2N\cdot CO\cdot CH_3}$$

4. The secondary bases give neither the isonitrile nor the "mustard oil" reaction (p. 108).

5. With nitrous acid, nitrosamines are formed (cf. p 108).

$$C_6H_5NHCH_3 + NO\cdot OH = H_2O + \underset{\text{Phenyl-methyl-nitrosamine}}{C_6H_5\cdot N(NO)\cdot CH_3}$$

These **nitrosamines** are neutral oily liquids insoluble in water, and they regenerate the secondary bases when heated with stannous chloride or with alcohol and hydrochloric acid. With mild reducing agents they yield hydrazines.

They serve for the preparation of the pure secondary bases,

since they alone are precipitated by sodium nitrite as non-basic oils from the acid solution of a mixture of primary, secondary, and tertiary bases. When such nitrosamines are digested with alcoholic hydrochloric acid, a molecular rearrangement takes place, and compounds of the nature of nitroso-dimethyl-aniline (p 378) are formed, the nitroso-group becoming attached to a carbon atom of the nucleus (*O. Fischer* and *Hepp*, B. **19**, 2991, **20**, 1247):

$$C_6H_5\cdot N(NO)\cdot CH_3 = NO\cdot C_6H_4\cdot NHCH_3$$

All nitrosamines give *Liebermann's* reaction (p. 409).

Methyl aniline, $C_6H_5\cdot NHMe$, is a colourless oil lighter than water. It is a stronger base than aniline; its **sulphate** does not crystallize, and is soluble in ether. With bleaching-powder it gives a brown coloration.

(For the oxidation of ethylaniline, see *Bamberger*, Abstr. 1902, **1**, 275.)

Diphenylamine, $NHPh_2$, crystallizes in colourless plates, melts at 54°, distils at 302°, and its solution in sulphuric acid yields an intense blue colour with a trace of nitric acid (delicate test). It is prepared by heating aniline and aniline hydrochloride at 210°–240° The **nitrosamine**, $NPh_2\cdot NO$, forms yellow plates melting at 66·5°, and the **acetyl-derivative**, $NPh_2\cdot CO\cdot CH_3$, melts at 103°. Numerous **nitro-derivatives** are known, *e.g.* $[C_6H_2(NO_2)_3]_2NH$, which is feebly acidic in properties, its ammonium salt, $C_{12}H_4(NO_2)_6N\cdot NH_4$, is the dye aurantia.

C. Tertiary Monamines

These also are either purely aromatic or mixed (alphyl-arylamines).

Modes of Formation.—1. The latter are formed when the primary or secondary bases are alkylated (cf. p. 376). Methyl bromide, iodide or sulphate are often used on the small scale, but on the manufacturing scale methyl alcohol and hydrochloric acid under pressure.

A convenient laboratory method is that due to *Noelting* (B. 1891, **24**, 563; J. C. S. 1904, **85**, 236). The primary amine is heated on the water-bath with a slight excess of the alkyl iodide and sodium carbonate solution, and in many cases an almost theoretical yield of the tertiary amine is formed. Tertiary bases are also formed when the quaternary salts are strongly heated.

2. Triphenylamine, a purely aromatic base, is formed by the action of bromobenzene upon dipotassium-aniline:

$$C_6H_5NK_2 + 2C_6H_5Br = (C_6H_5)_3N + 2KBr.$$

Behaviour.—1. Unlike the alphyl-arylamines, the purely aromatic tertiary amines are incapable of forming salts.

2. They do not yield isonitriles with $CHCl_3$, isothiocyanates with CS_2, or acyl derivatives with acid chlorides, but most of them yield quaternary compounds with methyl iodide

3. Nitrous acid reacts with the tertiary aromatic bases (which thereby differ from the tertiary bases of the fatty series), yielding coloured **nitroso-compounds** which contain the NO-group linked to the benzene nucleus:

$$C_6H_5\cdot N(CH_3)_2 + NO\cdot OH = \underset{p\text{-Nitroso-dimethyl-aniline}}{NO\cdot C_6H_4\cdot N(CH_3)_2} + H_2O.$$

Such nitroso-derivatives are, in contradistinction to the nitrosamines already mentioned, converted into diamines on reduction, and when hydrolysed yield nitroso-phenols.

4. The tertiary amines, when oxidized with hydrogen peroxide, yield unstable oxides, *e.g.* **dimethyl-phenylamine oxide**, $C_6H_5\cdot NMe_2:O$, feebly basic compounds soluble in water, and decomposed at high temperatures. (B. 1899, **32**, 346; Abstr. 1901, **1**, 200.)

5. Tertiary amines in which the three substituents are different, *e.g.* methyl-ethyl-aniline or benzyl-phenyl-hydrazine, do not exist in isomeric forms, and cannot be resolved into optically active components (*Kipping* and *Salway*, J. C. S. 1901, 438, *H. O. Jones* and *Millington*, C. C. 1904, **2**, 952). The centres of gravity of the nitrogen atom and of the three substituents would therefore appear to lie in one plane.

Dimethyl-aniline, $C_6H_5\cdot N(CH_3)_2$, is an oil of sharp basic odour, solidifying in the cold; its salts do not crystallize well. It combines with methyl iodide, even in the cold, to the compound $N(C_6H_5)(CH_3)_3I$, phenyl-trimethyl-ammonium iodide, which breaks up into its components when distilled. With nitrous acid it yields *p*-**nitroso-dimethyl-aniline**, which crystallizes in green plates, melting at 85°; the **hydrochloride** crystallizes in yellow needles. When oxidized with permanganate the nitroso-compound yields *p*-**nitro-dimethyl-aniline** (m.-pt. 162°), when reduced *p*-**amino-dimethyl-aniline**, and when hydrolysed with alkali *p*-**nitroso-phenol** (p. 412) and **dimethyl-**

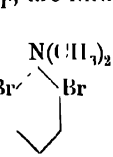
amine. (For condensations, see Malachite green, p. 483.) Bleaching-powder colours dimethyl-aniline only a pale-yellow. Dimethyl-aniline yields compounds of somewhat complex composition with acid chlorides, aldehyde, &c.; for example, tetramethyl-diamino-benzophenone or, finally, methyl violet with carbonyl chloride, leuco-malachite green with benzoic aldehyde, &c. Mild oxidizing agents, such as chloranil, convert it into methyl violet.

Diethyl-aniline boils at 213°; its **nitroso-derivative** melts at 81

Triphenyl-amine, NPh_3, melts at 127°, and yields no salts

D. The Quaternary Bases

correspond entirely with the quaternary bases of the fatty series **Trimethyl-phenyl-ammonium hydroxide**, $C_6H_5 \cdot N(CH_3)_3 \cdot OH$, for instance, is a colourless, strongly alkaline, bitter substance which breaks up into dimethyl-aniline and methyl alcohol when heated. Most of the tertiary amines, however, which contain substituents in the two ortho-positions with respect to the alphylated NH_2 group, are incapable of yielding quaternary ammonium salts, *e.g.*:



(*E. Fischer*, B. 1900, **33**, 345, 1967) This is an example of steric retardation or inhibition (cf. p. 175).

The readiness with which a given quaternary salt is formed depends to a large extent on (*a*) the order in which the radicals are introduced, (*b*) the nature of the alkyl haloid used, *e.g.* chloride bromide or iodide, the last reacting most readily, (*c*) the solvent (p. 106), and (*d*) temperature (cf. *Wedekind*, A. 1901, **318**, 90; *Jones*, B. A. Rep. 1904, 179). It has been found that in the preparation of phenyl-dimethylethyl ammonium iodide a 100-per-cent yield is obtained when methylethyl-aniline is combined with methyl iodide, but only a 15-per-cent when dimethyl-aniline is combined with ethyl iodide under similar conditions.

E. Diamines, Triamines, &c.

Polyamino-derivatives may be obtained by reducing poly-nitro-hydrocarbons or nitro-amino-compounds, *e.g.*:

$$C_6H_4(NO_2)_2 \longrightarrow C_6H_4(NH_2)_2 \text{ (phenylene-diamine).}$$

The *o*- and *p*-diamines are best obtained from the *o*- and *p*-nitro-amino-compounds. Tetramino-benzene is formed in an analogous manner by reducing dinitro-*m*-diamino-benzene.

A new amino-group can be introduced in the *p*-position into an arylamine, especially a secondary or tertiary, such as $C_6H_5 \cdot N(CH_3)_2$, by first transforming the latter into an azo-dye (*e.g.* benzene-azo-dimethyl-aniline, $C_6H_5 \cdot N:N \cdot C_6H_4 \cdot NMe$) by coupling it with benzene-diazonium chloride, and decomposing this by reduction. (See the Azo-compounds.)

Diamines are also formed by the reduction of the nitroso-compounds of tertiary amines, amino-dimethyl-aniline, $NH_2 \cdot C_6H_4 \cdot N(CH_3)_2$, from *p*-nitroso-dimethyl-aniline.

The polyamines are solid compounds which crystallize in plates and distil unchanged, and are soluble in warm water. Though originally without colour, most of them quickly become brown in the air, their instability increasing with the number of amino-groups present. In accordance with the readiness with which they are oxidized, they frequently yield characteristic colorations with ferric chloride, *e.g.* *o*-phenylene-diamine a dark-red, and 1:2:3-triamino-benzene a violet and then a brown colour.

The three isomeric groups of diamines differ materially in their behaviour: (*a*) **Ortho-diamines.**—1. Ferric chloride yields a yellowish-red crystalline precipitate of diamino-phenazine hydrochloride with a solution of *o*-phenylene-diamine.

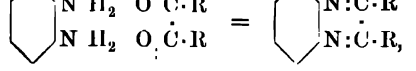
2. The mono-acyl compounds of the *o*-diamines change into derivatives of imido-azole (A. **273**, 269), the so-called "*Benz-imido-azoles*" or "*Anhydro-bases*", through the formation of intramolecular anhydrides; thus *o*-nitracetanilide, when reduced with tin and hydrochloric acid, yields methyl-benzimido-azole or phenylene-ethenyl-amidine (A. **209**, 339):

$$C_6H_4\begin{cases}NH \cdot CO \cdot CH_3 \\ NO_2\end{cases} + 3H_2 - 2H_2O = C_6H_4\begin{cases}NH \cdot CO \cdot CH_3 \\ NH_2\end{cases}$$

$$= C_6H_4\begin{cases}NH \\ N\end{cases}\!\!>C \cdot CH_3 + H_2O.$$

Compounds of this nature are also obtained by heating *o*-diamines with acids.

3. Glyoxal and many of the α-diketones yield quinoxaline and its derivatives with *o*-diamines:



and the α-ketonic alcohols react in an analogous manner, *e.g.* benzoin yields dihydro-diphenyl-quinoxaline.

4. Nitrous acid converts the *o*-diamines into the so-called "azimido-compounds", compounds which contain three atoms of nitrogen, *e.g.* *o*-phenylene-diamine into azimido-benzene = imido-azo-phenylene, $C_6H_4<\begin{matrix}NH\\N\end{matrix}>N$ (B. **9**, 219, 1524; **15**, 1878, 2195; **19**, 1757).

(*b*) **Meta-diamino-bases.**—1. These form yellow-brown dyes with nitrous acid, even when only traces of the latter are present. (See Bismarck Brown, p. 401).

2. They yield azo-dyes with benzenediazonium chloride (see Chrysoidine, p. 401.)

3. With nitroso-dimethyl-aniline, or on oxidation together with para-diamines, blue colouring-matters (indamines) are obtained, and these when boiled yield red dyes (see Toluylene red)

(*c*) **Para-diamino-compounds.** 1. When warmed with ferric chloride, or better, with $MnO_2 + H_2SO_4$, quinone, $C_6H_4O_2$ (or a homologue), is formed, and may be recognized by its odour.

2. By oxidizing para-diamines, containing one amino-group, together with a monamine or a meta-diamine, indamines are produced.

ACYL DERIVATIVES OF ARYLAMINES. ANILIDES, &c.

Practically all primary and secondary arylamines—but not tertiary react with acids, or better, acid anhydrides or acid chlorides, yielding acyl derivatives, the most characteristic of which are the **acetyl** derivatives, *e.g.* $C_6H_5\cdot NH\cdot CO\cdot CH_3$, $CH_3\cdot C_6H_4\cdot NH\cdot CO\cdot CH_3$, $(C_6H_5)_2N\cdot CO\cdot CH_3$, &c. The acyl products formed from aniline are termed **anilides** (p. 370), *e.g.* acetanilide, benzanilide, oxanilide; they are really phenylated acid amides (see p. 182 *et seq.*), and as such may be hydrolysed, although not so readily as the amides, by means of acids or alkalis, to aniline and the corresponding acid.

The dibasic acids like oxalic acid can give rise not merely to anilides, *e.g.* $C_6H_5\cdot NH\cdot CO\cdot CO\cdot NH\cdot C_6H_5$, oxanilide, but

also to half anilides, the **anilic acids**, which correspond with the amic acids, *e.g.* oxanilic acid, $C_6H_5NH \cdot CO \cdot CO \cdot OH$. These are monobasic acids, and can also be hydrolysed to their components.

Similarly, the toluidines give rise to **toluidides**, *e.g.* acetoluidide, $CH_3 \cdot C_6H_4 \cdot NH \cdot CO \cdot CH_3$, the xylidines to **xylidides**, &c.

The acetyl derivatives are frequently used for the identification of the various primary and secondary arylamines, since they crystallize well and have definite melting-points. As a rule, it is sufficient to mix the amine with a slight excess of acetic anhydride and warm for two minutes, and then to pour into water. After a short time the solid (or oily) acetyl derivative is obtained.

Formanilide, $C_6H_5 \cdot NH \cdot CH:O$, from aniline and formic acid, is worthy of note, because its sodium salt reacts according to the formula $C_6H_5 \cdot NNa \cdot CH:O$, but its silver salt according to the formula $C_6H_5 \cdot N:CH \cdot OAg$. (Cf B. **23**, 2274, Ref 659.) The latter corresponds to those isomers of the amides, the imido-hydrates and imino-ethers (p. 187).

Acetanilide, $C_6H_5 \cdot NH \cdot CO \cdot CH_3$, is most conveniently prepared by boiling aniline with glacial acetic acid for twenty-four hours. It crystallizes in beautiful white prisms which are readily soluble in hot water or alcohol, less readily in ether and benzene. It melts at 115°, and boils at 304°. In the absence of water it can form a hydrochloride, C_7H_9ON, HCl. Acetanilide is used, under the name of "antifebrine", as a medicine in cases of fever.

Thio-acetanilide, $C_6H_5 \cdot NH \cdot CS \cdot CH_3$, is formed when acetanilide is heated with P_2S_5, and from it **imido-thio-compounds, amidines**, &c., can be prepared. **Methyl-acetanilide**, $C_6H_5 \cdot N(CH_3)(C_2H_3O)$, is used as a specific against headache.

Oxanilide, $C_6H_5 \cdot NH \cdot CO \cdot CO \cdot NH \cdot C_6H_5$, is obtained when aniline oxalate is heated at 160°–180°. It melts at 252°, boils without decomposition, and is best hydrolysed by fusion with potash.

The half anilide, **oxanilic acid**, $COOH \cdot CO \cdot NH \cdot C_6H_5$, is formed when aniline oxalate is heated at 130°–140°. It melts at 149°–150°, is soluble in hot water, has the properties of a monobasic acid, and with phosphorus pentachloride yields phenyl carbimide (phenyl isocyanate):

$$C_6H_5 \cdot NH \cdot CO \cdot OH \longrightarrow C_6H_5 \cdot NH \cdot CO \cdot Cl \longrightarrow C_6H_5 \cdot N:C:O.$$

Diacyl derivatives of aniline and its homologues are also

known, *e.g.* $C_6H_5 \cdot N(CO \cdot CH_3)_2$, **diacetanilide**. This is formed, together with acetanilide, when aniline is boiled for an hour with excess of acetic anhydride, or when the amine is heated to a high temperature with acetyl chloride. The two may be separated by fractional distillation under diminished pressure. The diacetanilide crystallizes in colourless prisms, melts at 37°, and, unlike acetanilide, is readily soluble in benzene or light petroleum. On hydrolysis with dilute alkali, one acetyl group is split off more readily than the second.

The presence of one or two substituents in the *o*-position with respect to the amino-group of aniline facilitates the formation of diacetyl derivatives, *e.g.* *o* toluidine yields a diacetyl derivative more readily than aniline, and *s*-tribrom-aniline yields a diacetyl derivative with the greatest readiness (J. C. S. 1901, 533).

In nearly all those compounds of the fatty series which are amino- or imino-derivatives of alcohols, acids, or hydroxy-acids, the unreplaced ammoniacal hydrogen can be substituted indirectly either wholly or partially by phenyl. The number of these phenylated (tolylated, xylylated, &c.) compounds is thus extremely large. Among them may be mentioned **Phenyl-glycocoll**, *Phenyl-glycine*, $C_6H_5 \cdot NH \cdot CH_2 \cdot CO_2H$, from chloracetic acid and aniline; **phenyl-imino-butyric acid**, $CH_3 \cdot C(:NC_6H_5) \cdot CH_2 \cdot CO_2H$, from aniline and aceto-acetic ester; **carbanilide** or diphenyl-urea, $CO(NHC_6H_5)_2$, from aniline and carbon oxychloride (cf. p. 280); **phenyl isocyanate**, *phenyl carbimide*, $CO:N \cdot C_6H_5$, from $COCl_2$ and fused aniline hydrochloride, a sharp-smelling liquid exactly analogous to the isocyanic esters—its vapour gives rise to tears, **phenyl isothiocyanate**, $C_6H_5N:CS$ (b. pt. 222°), a liquid possessing all the characteristics of the mustard oils (p. 275); **diphenyl thiourea**, $CS(NHC_6H_5)_2$, from aniline and carbon disulphide (forms glistening plates, melting at 154°; it is decomposed into phenyl isothiocyanate and aniline when hydrolysed with concentrated HCl).

PRIMARY AMINES WITH THE AMINO-GROUP IN THE SIDE CHAIN

These compounds resemble the primary alphylamines much more closely than aniline. As an example, we have **benzylamine**, $C_6H_5 \cdot CH_2 \cdot NH_2$, the amine corresponding with benzyl alcohol; it is a colourless liquid which distils unchanged. The acetyl compound, $C_6H_5 \cdot CH_2 \cdot NH \cdot CO \cdot CH_3$,

is formed by heating benzyl chloride, $C_6H_5 \cdot CH_2Cl$, with acetamide. Benzylamine is formed, together with di- and tribenzylamines, by the action of alcoholic ammonia on benzyl chloride; it is also readily obtained by reducing the phenylhydrazone of benzaldehyde.

$$\underset{H}{C_6H_5 \cdot CH} : \underset{H_2}{N} \cdot \underset{H}{NHC_6H_5}.$$

It may also be prepared from benzyl chloride and potassium phthalimide (cf. p. 465). Its behaviour is entirely analogous to that of methylamine, as the phenyl derivative of which it is to be regarded. It dissolves in water, and the solution thus formed is alkaline. Conductivity determinations show that it is about as strong a base as ammonia, and thus differs materially from aniline.

It possesses all the characteristic properties of a primary amine, but as the NH_2 is attached to a side chain and not to the benzene nucleus it cannot be diazotized, and on treatment with nitrous acid it immediately yields benzyl alcohol

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XXII. DIAZO- AND AZO-COMPOUNDS; HYDRAZINES

A. Diazo-compounds

The primary arylamines differ characteristically from the primary alphylamines in their behaviour towards nitrous acid. The latter are converted into alcohols without the formation of intermediate products (cf. p. 108).

$$C_2H_5 \cdot NH_2 + NO \cdot OH = C_2H_5 \cdot OH + N_2 + H_2O.$$

The aromatic amines can undergo an analogous transformation; but if the temperature is kept sufficiently low, well characterized intermediate products, the so-called **diazo-compounds** or **diazonium salts**, *e.g.* benzene diazonium chloride, $C_6H_5 \cdot N_2Cl$, are obtained, which are of especial interest both scientifically and technically (cf. Azo-dyes, p. 389). They were discovered by *P. Griess* in 1860, and were carefully investigated by him (A. **121**, 257; **137**, 39).

The diazo-compounds are usually divided into (1) the diazonium salts, *e.g.* $\overset{Cl}{\overset{C_6H_5}{>}}N : N$, compounds which are analogous

to ammonium salts; (2) the true diazo-compounds, which contain the grouping $\cdot N:N\cdot$.

I. **Diazonium Compounds.**—The diazonium salts, as a rule, are not obtained in the solid state, as they themselves are of little commercial value, but are of importance as intermediate products in various decompositions.

Solutions are usually prepared by the addition of an aqueous solution of sodium nitrite to a solution of the amine in an excess of the requisite acid (*V. Meyer*). The essentials are—(1) The solution must be kept cool, at 0° or only a few degrees above, otherwise a phenol is formed and nitrogen evolved. (2) An excess of acid must be used, otherwise diazo-amino-compounds are formed (3) As a rule, it is advisable not to use an excess of nitrous acid. This is avoided by testing for free nitrous acid by means of potassium iodide starch paper.

This conversion of amino- into diazo-compounds is termed "**diazotizing**".

The crystalline salts, *e.g.* benzene-diazonium chloride, may be obtained by adding concentrated hydrochloric acid to an alcoholic solution of aniline hydrochloride, and then amyl nitrite (*Knoevenagel*). They may also be obtained by the addition of alcohol and ether to their aqueous solutions

Constitution – The N_2X group can be attached to only one carbon atom of the benzene nucleus, since (1) when the salts undergo decomposition the products formed contain groups, *e.g.* Cl, OH, CN, &c, which are attached to a single carbon atom; (2) penta-substituted anilines, *e.g.* $SO_3H\cdot C_6Br_4\cdot NH_2$, can be diazotized, hence *Griess'* formulæ, *e.g.* $C_6H_4N_2$, HCl, where the diazo-radical replaces two hydrogen atoms of the nucleus, are untenable.

For many years the constitutional formula given to these compounds was that suggested by *Kekulé*, viz $C_6H_5\cdot N:N\cdot Cl$, for the chloride, this represents them as analogous to the azo-compounds. This formula readily explains the reduction of the diazonium salts to hydrazines, $C_6H_5NH\cdot NH_2$, and their conversion into azo-dyes, *e.g.* $C_6H_5\cdot N:N\cdot C_6H_4OH$. Within the last few years a constitutional formula which was suggested by *Blomstrand* in 1875 has become generally accepted. This represents the molecule of a diazonium salt as containing a quinquevalent nitrogen atom, *e.g.* $\begin{matrix}C_6H_5\\Cl\end{matrix}\!\!>\!N:N$. The chief arguments in favour of the *Blomstrand* formula are briefly:

1. It indicates the resemblance between the diazonium and ammonium salts, as both thus contain quinquevalent nitrogen:

$$\overset{CH_3}{\underset{Cl}{}}\!\!>\!N\!:\!(CH_3)_3 \quad \text{and} \quad \overset{C_6H_5}{\underset{Cl}{}}\!\!>\!N\!:\!N.$$

The resemblance between the two groups of compounds is marked. The diazonium salts are colourless crystalline compounds readily soluble in water; those derived from strong acids, *e.g.* the chlorides, nitrates, and sulphates, are neutral in solution, cf. NH_4Cl; whereas those derived from feeble acids, *e.g.* carbonic acid, are partially hydrolysed in aqueous solution, and hence give an alkaline reaction, cf. Na_2CO_3 or $(NH_4)_2CO_3$. In addition they form sparingly soluble platinichlorides, $(C_6H_5N_2)_2PtCl_6$, and aurichlorides, $C_6H_5N_2AuCl_4$, comparable with the ammonium compounds. The aqueous solutions of the salts are ionized to much the same extent as the corresponding quaternary ammonium salts. This resemblance of the diazonium ions to the quaternary ammonium ions is further established by a comparison of migration values. The free base, benzene-diazonium hydroxide, corresponding with ammonium hydroxide, is obtained by the action of moist silver oxide on the chloride, it dissolves readily in water, yielding strongly alkaline solutions, but is very unstable, and gradually decomposes. When neutralized with acids, it yields the above-mentioned diazonium salts.

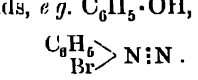
2. The conversion of aniline and its homologues into diazonium salts is rendered somewhat more simple by such a formula.

$$\overset{C_6H_5}{\underset{Cl}{}}\!\!>\!N\!\!\overset{H\ HO}{\underset{H\ \ O}{}}\!\!>\!N = 2H_2O + \overset{C_6H_5}{\underset{Cl}{}}\!\!>\!N\!:\!N$$

3. The elimination of nitrogen and the formation of monosubstituted compounds, *e.g.* $C_6H_5{\cdot}OH$, C_6H_5Br, &c., is readily explicable:

$$\overset{C_6H_5}{\underset{Br}{}}\!\!>\!N\!:\!N.$$

Cain (J. C. S. 1907, **91**, 1049) has suggested a new constitutional formula for diazonium salts, *e.g.* benzene-diazonium chloride,



It is claimed that the double linkage between nitrogen and a

carbon atom of the benzene nucleus is more in harmony with the readiness with which the nitrogen is eliminated from the molecule. It also accounts for the fact that in a *p*-diamine only one amino-group can be diazotized.

Reactions. —1. The reaction characteristic of the diazonium salts is the readiness with which nitrogen is eliminated and monovalent groups introduced into the molecule in place of the N_2X radical, and for this reason the diazonium compounds are frequently made use of in the laboratory for the preparation of various substituted benzene derivatives. As examples of this type of reaction, we have—

(*a*) *Replacement of* N_2X *by* OH.—An aqueous solution of a diazonium salt, especially one containing sulphuric acid, evolves all its nitrogen in the form of gas when warmed, and a phenol is formed:

$$\begin{matrix} C_6H_5 & (Cl) & N{:}N \\ HO & & H \end{matrix} = C_6H_5{\cdot}OH + N_2 + HCl$$

This reaction, which is of very universal application, therefore allows of the exchange of NH_2 for OH. The only exceptions appear to be those salts containing numerous negative substituents in the benzene nucleus, *e.g.* $C_6H_2Br_3{\cdot}N_2Cl$.

For the effect of light on the decomposition of solutions of diazonium salts, see *Orton*, *Coates*, and *Burdett*, P. 1905, 168.

(*b*) *Replacement by* H.—When diazonium-compounds, either in the solid state or dissolved in concentrated sulphuric acid, are heated to boiling with absolute alcohol, the diazo-group is generally replaced by hydrogen. In this reaction the alcohol gives up two hydrogen atoms, and is oxidized to aldehyde:

$$\begin{matrix} C_6H_5 & (Cl) & N{:}N \\ H & & H \end{matrix} = C_6H_6 + N_2 + HCl.$$

This affords a simple method for the replacement of NH_2 by H.

Instead of this reaction, there occurs in many cases an exchange of the diazo-group for the ethoxy-radical, $O{\cdot}C_2H_5$, with the formation of ethyl ethers of phenols; thus from chlorinated toluidines ethyl ethers of chloro-cresols are formed, and not chloro-toluenes (**B. 17**, 2703; **22**, Ref. 658; **34**, 3337).

Under certain conditions stannous chloride in alkaline solution acts in an analogous manner (B. **22**, Ref. 741), while under others it gives rise to hydrazines (p. 397). In like

manner NH_2 may be replaced by H, by first converting an amino-compound into a hydrazine, and then decomposing the latter with $CuSO_4$ (*Baeyer*, B **18**, 89).

(*c*) *Replacement by Halogen—Sandmeyer's Reaction.*—When a diazonium-compound is warmed with a concentrated solution of cuprous chloride in hydrochloric acid, the diazo-group is replaced by chlorine (*Sandmeyer*, B. **17**, 1633, **23**, 1218, 1628; A. **272**, 143) The same reaction takes place on distilling the diazonium platinichloride with soda, and sometimes on simply treating the diazo-compound itself with fuming hydrochloric acid, or with hydrochloric acid in presence of copper dust (*Gattermann*):

$$\begin{matrix} C_6H_5 \\ Cl \end{matrix}\!\!>\!N\!:\!N = C_6H_5Cl + N_2.$$

Warming with cuprous bromide yields, in the same way, a bromo-derivative (*Sandmeyer*, B. **18**, 1482), and treatment with hydriodic acid or potassium iodide an iodo-compound.

$$\begin{aligned} 2C_6H_5\cdot N_2\cdot Cl + Cu_2Br_2 &= 2C_6H_5Br + Cu_2Cl_2 + N_2, \\ C_6H_5\cdot N_2\cdot Cl + KI &= C_6H_5I + KCl + N_2. \end{aligned}$$

The amino-group may further be exchanged for bromine by boiling the diazonium perbromides (see Benzene-diazonium perbromide) with absolute alcohol

(*d*) *Replacement by* $\cdot CN$.—This is accomplished by adding the diazotized solution to a warm solution of potassium cuprous cyanide:

$$C_6H_5\cdot N_2Cl \longrightarrow C_6H_5N_2CN \longrightarrow C_6H_5\cdot CN.$$

This reaction is of importance, as the product obtained is a nitrile, and can be hydrolysed to an acid.

(*e*) Phenyl sulphide is formed by the action of hydrogen sulphide on benzene-diazonium chloride (cf. B. **15**, 1683); nitro-benzene is formed by the action of nitrous acid in presence of cuprous oxide; benzenesulphonic acid from sulphurous acid; phenyl thiocyanate from thiocyanic acid; and phenyl cyanate from cyanic acid, &c. (cf B **23** 738, 1218, 1454, 1628; **25**, 1086; **26**, 1996).

(*f*) When oxidized in alkaline solution, benzene-diazonium hydroxide yields—together with other products—nitroso-benzene (p. 365), and much **benzene-diazoic acid**, $C_6H_5\cdot N\cdot NO\cdot OH$, or its isomeride, **phenyl-nitramine**, $C_6H_5\cdot NH\cdot NO_2$ (m.-pt. 46°; explodes at 98°) (see B. **26**, 471; **27**, 584, 915).

2. When a solution of a diazonium compound reacts with a primary or secondary amine, or when nitrous acid acts upon such an amine in the absence of free mineral acid, diazo-amino-compounds are formed, and these readily change into amino-azo-compounds:

$$C_6H_5\cdot N_2Cl + NH_2\cdot C_6H_5 = HCl + \underset{\text{Diazo amino-benzene}}{C_6H_5\cdot N{:}N\cdot NH\cdot C_6H_5}$$

3. **Azo-dyes**.—The diazonium salts readily react with tertiary amines or with phenols, yielding derivatives of azo-benzene, *e.g.*:

$$C_6H_5\cdot N_2Cl + C_6H_5N(CH_3)_2 = HCl + \underset{\text{Dimethyl-amino-azobenzene}}{C_6H_5\cdot N{:}N\cdot C_6H_4\cdot N(CH_3)_2}$$

$$C_6H_5\cdot N_2Cl + C_6H_5\cdot OH = HCl + \underset{\text{Hydroxy-azobenzene}}{C_6H_5\cdot N{:}N\cdot C_6H_4\cdot OH}$$

Such derivatives possess basic or acidic properties, are usually coloured yellow, red, or brown, and are known as azo-dyes.

The formation of such an azo-dye is largely made use of as a test for a primary aromatic amine with the NH_2 in the nucleus. The amine is dissolved in acid, diazotized, and then mixed with an alkaline solution of a phenol (preferably β-naphthol), when an orange-red dye is precipitated. The process is commonly spoken of as the "coupling" up of a diazonium salt with an amine or a phenol.

It has been proposed to use diazo-compounds, sensitive to light, in photography (B **23**, 3131; **34**, 1668).

4. The diazonium salts react in alkaline solution with compounds containing the grouping $\cdot CH_2\cdot CO\cdot$, yielding azo-compounds or phenylhydrazones, *e.g.*:

$$CH_3\cdot CO\cdot CH_2\cdot CO_2Et \begin{cases} \rightarrow CH_3\cdot CO\cdot CH(CO_2Et)\cdot N{:}NC_6H_5 \\ \rightarrow CH_3\cdot CO\cdot C(CO_2Et){:}N\cdot NHC_6H_5 \end{cases}$$

Cf. B. 1888, **21**, 1697. For the azo or hydrazone constitution of such compounds, compare *Auwers* (Abstr. 1908, i, 477; 1911, i, 168, 585).

Benzene-diazonium perbromide, $C_6H_5\cdot N_2Br, Br_2$, is a dark-brown oil, solidifying to yellow crystalline plates, and is prepared by the addition of HBr or KBr and bromine water to diazonium salts. Two of its atoms of bromine are only loosely linked. Ammonia converts it into benzene-diazo-imide, which

is to be regarded as the phenyl derivative of hydrazoic acid, N_3H, thus:—

$$C_6H_5\cdot N(Br){:}N + Br_2 = C_6H_5\cdot NBr_2{:}NBr \text{ [Benzene-diazonium perbromide].}$$

$$C_6H_5\cdot NBr_2{:}NBr + NH_3 = 3HBr + C_6H_5\cdot N\langle \overset{N}{\underset{N}{\|}} \text{ [Benzene-diazo-imide].}$$

In accordance with this, dinitro-benzene-diazo-imide (from dinitro-aniline) is decomposed by alcoholic potash into dinitro-phenol and *hydrazoic acid*—a method of obtaining this latter substance by means of organic compounds (see p. 298).

II. **Diazo-compounds.**—These contain the grouping R·N:N·X, where R = an aryl radical and X an acid radical or OH or OK. When a benzene-diazonium salt is mixed with an excess of alkali, a potassium salt, **normal potassium diazo-benzene oxide**, $C_6H_5N_2OK$, is precipitated. It crystallizes in white plates, and can be quantitatively converted into benzene-diazonium chloride, it yields ethers, and on oxidation gives nitroso-benzene and benzene-diazoic acid:

$$C_6H_5\cdot N{:}N\langle \overset{O}{\underset{OH}{}} \quad \text{or} \quad C_6H_5\cdot NH\cdot NO_2.$$

The acid, $C_6H_5N_2OH$, which corresponds with the potassium salt, is not known in a pure form. When the **normal** potassium salt is heated with concentrated potash at 130°–135°, it is transformed into **potassium isodiazo-benzene oxide** (*Schraube* and *Schmidt*, B. 1894, **27**, 520). When this is acidified with acetic acid, the free **hydroxide** is obtained as a colourless oil which is very unstable.

Similar *normal* and *iso*potassium derivatives have been obtained from other diazonium salts, and it has been found that the presence of negative radicals (Br, NO_2) facilitates the formation of the iso-compound,—in fact to such an extent that certain diazonium salts, when added to an alkali, immediately yield the isodiazo-compounds. Considerable controversy has taken place regarding the constitutional formulæ of these two groups of compounds. At one time the isodiazo-oxides were regarded as derivatives of phenyl-nitrosamine, viz. $C_6H_5\cdot NK\cdot NO$, and the normal compounds as true diazo-oxides, $C_6H_5\cdot N{:}N\cdot OK$. The researches of *Hantzsch* have proved that the two compounds are very similar as regards chemical properties. For example, both "couple" with alkaline solutions of phenols, yielding azo-dyes (p. 389), but as a rule the normal more readily than the iso-compounds. Both compounds, on reduc-

tion with sodium amalgam in the presence of a large excess of alkali, yield phenyl-hydrazine, and both compounds, on oxidation in alkaline solution, yield potassium benzene-diazoate, $C_6H_5 \cdot N:NO \cdot OK$. Similarly, both compounds yield the same benzoyl derivative by the *Schotten-Baumann* method. *Hantzsch* draws the conclusion that the two compounds are structurally identical and *stereo-isomeric*. As the *n*-diazo-oxide can be synthesised by the action of hydroxylamine on nitroso-benzene in alkaline solution (B. **38**, 2056):

$$C_6H_5 \cdot N:O + H_2N \cdot OH = H_2O + C_6H_5 \cdot N:N \cdot OH,$$

it is probable that both normal and iso-compound are true diazo-derivatives, and that they are stereo-isomeric in much the same manner as the oximes (p. 138). According to *Hantzsch*, the normal compound has the *syn*- and the iso- the *anti*-configuration:



Potassium benzene *syn* diazo oxide — *anti*

as the normal compounds evolve nitrogen very readily, whereas the iso-compounds are more stable (Ber 1894, **27**, 1702; 1895, **28**, 676, 1734; **36**, 4054, **37**, 1084.)

The isodiazo-oxides can almost undoubtedly react as tautomeric compounds, viz. as nitrosamine derivatives, $C_6H_5 \cdot NK \cdot NO$, since the potassium salt yields an N-ether, $C_6H_5 \cdot NEt \cdot NO$, whereas the silver salt yields an O-ether, $C_6H_5 \cdot N:N \cdot OEt$. *Bamberger* has suggested that the normal diazo-oxides may have a diazonium constitution $C_6H_5 \cdot N(OK):N$, whereas the iso-compound has the diazo-constitution $C_6H_5 \cdot N:N \cdot OK$, but *Hantzsch* has pointed out that the diazonium hydroxides, from which the true diazonium salts are formed, must be extremely strong bases, and could not possibly therefore possess sufficiently acidic properties to give rise to stable potassium salts which are only partially hydrolysed in aqueous solution.

Certain diazo-hydroxides, $R \cdot N_2 \cdot OH$, have been isolated as colourless solids with acidic properties, the majority, however, are extremely unstable, and pass over into the isomeric nitrosamines $R \cdot NH \cdot NO$, yellow compounds with neutral properties (B. **35**, 2964; **36**, 4054; **37**, 1084).

Corresponding with the normal and isodiazo-oxides, *Hantzsch*

has discovered two groups of sulphonates and of cyanides, which he also regards as being stereo-isomeric in the same sense, *e.g.*:

$$\textit{syn}\ \begin{matrix} R\cdot N \\ NC\cdot \ddot{N} \end{matrix} \quad \text{and} \quad \begin{matrix} R\cdot N \\ \ddot{N}\cdot CN \end{matrix}\ \textit{anti}.$$

In the case of *p*-anisidine, evidence of the existence of three isomeric diazo-cyanides has been obtained. The one is colourless and is an electrolyte, and hence is regarded as the diazonium salt, $OMe\cdot C_6H_4\cdot N(CN)\vdots N$, the other two are reddish-coloured solids and non-electrolytes. The *syn*-compound is unstable, and melts at 51°, it gradually passes over into the more stable *anti*-compound, which melts at 121°.

It is probable that when a *syn* diazo-cyanide is dissolved in water it is largely transformed into the ionized diazonium cyanide:

$$\begin{matrix} R\cdot N \\ NC\cdot \ddot{N} \end{matrix} \rightarrow \begin{matrix} R\cdot \overset{+}{N} \\ \vdots\vdots \\ \ddot{N} \end{matrix} + \overset{-}{C}N.$$

Compare also *Armstrong* and *Robertson*, J. C. S. 1905, 1280, *Hantzsch*, P. 1905, 287. An account of the chemistry of diazo-compounds will be found in B. A. Rep. 1902, 181 (*G. T. Morgan*), and in *Ahrens Sammlung*, 1902, **8**, pp. 1–82 (*Hantzsch*).

B. Diazo-amino-compounds

The diazo-amino-compounds are pale-yellow crystalline substances which are stable in the air, and do not combine with acids. They are obtained by the action of a primary or secondary amine on a diazonium salt, and also when nitrous acid reacts with a free primary aromatic amine instead of with its hydrochloride, probably:

$$C_6H_5NH_2 + O{:}N\cdot OH = C_6H_5\cdot N{:}N\cdot OH + H_2O \text{ and}$$
$$C_6H_5\cdot N{:}N\cdot OH + C_6H_5NH_2 = C_6H_5\cdot N{:}N\cdot NHC_6H_5 + H_2O.$$

Diazo-amino compounds have been synthesised by the action of *Grignard* compounds on alkyl or acyl derivatives of hydrazoic acid, and decomposing the products with water:

$$RN_3 + R'MgI \rightarrow RN(MgI)\cdot N{:}NR'$$
$$RN(MgI)\cdot N{:}NR' + H_2O \rightarrow R\cdot NH\cdot N{:}N\cdot R' + MgI\cdot OH$$

In this manner not merely aromatic but aliphatic aromatic

compounds of the types $C_6H_5 \cdot NH \cdot N:N \cdot CH_3$ and $C_6H_5 \cdot CH_2 \cdot NH \cdot N:N \cdot CH_3$ have been prepared.

Reactions.—1. They are not bases, and hence do not form salts with acids.

2. They behave in much the same way as the diazo-compounds, since they are usually decomposed in the first instance into their components, a diazonium salt and an amine, the former then entering into reaction. Thus diazo-amino-benzene, for example, yields phenol and aniline when boiled with water or hydrochloric acid, while with hydrobromic acid it gives bromobenzene and aniline. These reactions are easy to recognize from the accompanying evolution of nitrogen

3. By the renewed action of nitrous acid in acid solution, they are completely transformed into diazonium salts:

$$C_6H_5 \cdot N_2 \cdot NH \cdot C_6H_5 + NO_2H + 2HCl = 2C_6H_5 \cdot N_2 \cdot Cl + 2H_2O$$

4. Most of them readily undergo molecular transformation into the isomeric amino-azo-compounds (*Kekulé*):

$$C_6H_5 \cdot N:N \cdot NH\langle \quad \rangle H \rightarrow C_6H_5 \cdot N:N\langle \quad \rangle NH_2.$$

This molecular rearrangement takes place most readily in presence of an amine hydrochloride, which acts as a catalytic agent. The amino group always takes up the para-position with regard to the azo-group ($\cdot N:N \cdot$) if this is free. If, however, this is already substituted, as in the diazo-amino-compound from *p*-toluidine, then the transformation occurs much more slowly, and the NH_2 takes up the *o*-position with respect to the $\cdot N:N \cdot$ group. The velocity of transformation has been investigated by *H Goldschmidt*, and the reaction has been shown to be unimolecular. Only a relatively small amount of aniline salt is required, and the velocity is proportional to the strength of the acid, the aniline salt of which is used (B. 1896, **29**, 1899). For similar transformations, see Benzidene (p. 395) and Azoxy-benzene (p 395)

5. The amino-hydrogen of the diazo-amino-compounds is replaceable by metallic radicals, and also by acyl groups.

Constitution.—By the action of benzene-diazonium chloride upon *p*-toluidine, "diazo-benzene-*p*-toluidide" is formed, and would appear to possess the formula:

$$C_6H_5 \cdot N:N \cdot NH \cdot C_7H_7 \quad (I).$$

But the same compound is also obtained from a mixture of *p*-toluene-diazonium chloride and aniline, a reaction which would indicate its constitution to be:

$$C_6H_5 \cdot NH \cdot N : N \cdot C_7H_7 \quad \text{(II)}.$$

It is all the more difficult to decide which of these two formulæ is the right one, from the fact that most of those "mixed diazo-amido-compounds" react as if they had both of the above constitutions. Thus, when the compound just mentioned is boiled with dilute sulphuric acid, it yields not only phenol and *p*-toluidine (according to I), but also aniline and *p*-cresol (according to II). Such diazo-amino-compounds are thus typical tautomeric substances. (Cf. *e.g.* B. **19**, 3239, **20**, 3004; **21**, 548, 1016, 2557; J. C. S. 1889, **55**, 412, 610, &c.)

Diazo-amino-benzene, $C_6H_5 \cdot N : N \cdot NHC_6H_5$ (*Griess*), is usually prepared by adding $NaNO_2$ (1 mol.) to the solution of aniline (2 mols.) in HCl (3 mols.), and saturating with sodium acetate (B. 1884, **17**, 641; 1886, **19**, 1952). It crystallizes in bright-yellow lustrous plates or prisms, is insoluble in water, but readily soluble in hot alcohol, ether, and benzene, melts at 98°, and is far more stable than the diazo-compounds.

C Azo-compounds, and Compounds intermediate between the Nitro- and Amino-compounds

While the reduction of nitro-compounds in acid solution leads to the aromatic amines, the use of alkaline reducing agents, such as sodium amalgam, zinc dust and caustic soda, and also potash and alcohol, gives rise for the most part to intermediate products, the azoxy-, azo-, and hydrazo-compounds:

$C_6H_5 \cdot NO_2$ (Nitro-benzene) — $C_6H_5 \cdot N(O) \cdot N \cdot C_6H_5$ (Azoxy-benzene) — $C_6H_5 \cdot N : N \cdot C_6H_5$ (Azo-benzene)

$C_6H_5NH \cdot NHC_6H_5$ (Hydrazo-benzene) — $C_6H_5 \cdot NH_2$; (Aniline)

and reduction in neutral solution yields phenyl-hydroxyl-amines, $C_6H_5 \cdot NH \cdot OH$.

Of these the azo-compounds are the most important.

1. AZOXY-COMPOUNDS

The azoxy-compounds are mostly yellow or red crystalline substances which are obtained by the action of alcoholic

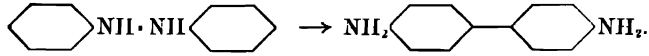
potash, and especially of potassium methoxide (B **15**, 865), upon the nitro-compounds. Many of them may also be obtained by the oxidation of azo-compounds. They are of neutral reaction, and are very readily reduced to azo-compounds.

Azoxy-benzene, $(C_6H_5)_2N_2O$ (*Zinin*), forms pale-yellow needles melting at 36°, is insoluble in water, but dissolves readily in alcohol and ether Concentrated sulphuric acid transforms it into the isomeric *p*-hydroxy-azo-benzene, $C_6H_5N:N\cdot C_6H_4\cdot OH$.

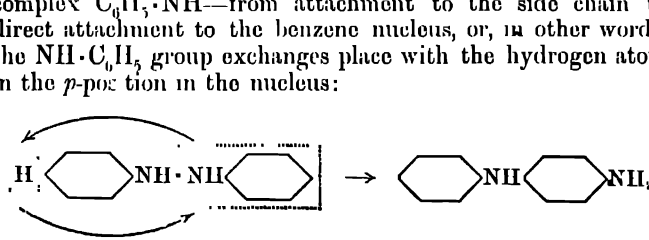
2 HYDRAZO-COMPOUNDS

These are colourless crystalline neutral compounds, and, like the azo-compounds, cannot be volatilized without decomposition, *e g* hydrazo-benzene decomposes into azo-benzene and aniline when heated They are obtained by the reduction of azo-compounds with ammonium sulphide or zinc dust and alkali, or by sodium hyposulphite. Oxidizing agents, such as ferric chloride, readily transform them into azo-compounds, a reaction which also occurs when the hydrazo-compounds are exposed to the air. Stronger reducing agents, *e.g.* sodium amalgam, convert them into amino-compounds.

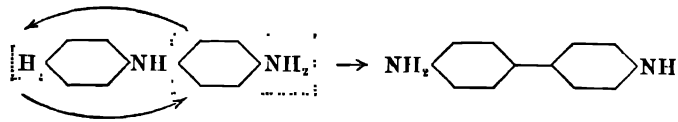
Strong acids cause them to change into the isomeric derivatives of diphenyl (p 472), thus from hydrazo-benzene and hydrochloric acid we obtain benzidine hydrochloride (the hydrochloride of *pp'*-diamino-diphenyl, p 472):



This rearrangement is typical, and is often observed in the case of aromatic compounds It may be regarded as the shifting or wandering of a radical —in this case the relatively complex $C_6H_5\cdot NH$—from attachment to the side chain to direct attachment to the benzene nucleus, or, in other words, the $NH\cdot C_6H_5$ group exchanges place with the hydrogen atom in the *p*-position in the nucleus:



The operation is repeated,



and *pp'*-diamino-diphenyl is formed

Other well-known examples of this are the transformation of methyl-aniline or dimethyl-aniline into *o*-toluidine and xylidene, and ultimately into mesidene (*Hofmann*, p. 368); the transformation of N-brominated amines or anilides, *e.g.* $C_6H_5 \cdot NBr \cdot COCH_3$ into $C_6H_4Br \cdot NH \cdot COCH_3$ (*Chattaway* and *Orton*, p. 370), of diacetylated amines, $C_6H_5 \cdot N(COCH_3)_2$, into ketonic substances, $CH_3 \cdot CO \cdot C_6H_4 \cdot NH \cdot CO \cdot CH_3$ (*Chattaway*, J. C. S. 1904, 386, 589, 1663), of phenyl-hydroxylamine into *p*-amino-phenol (p. 395), and of diazo-amino-benzene into amino-azo-benzene (p. 391).

This molecular rearrangement does not take place if the hydrogen which occupies the para-position to the imino-group is replaced by other groups. In such cases a partial rearrangement only occurs, and derivatives of diphenylamine are formed (B. **25**, 992, 1013, 1019), thus *p*-hydrazo toluene, $CH_3 \cdot C_6H_4 \cdot NH \cdot NH \cdot C_6H_4 \cdot CH_3$, yields *o*-amino-di-*p*-tolylamine, $CH_3 \cdot C_6H_4 \cdot NH \cdot C_6H_3 \langle {NH_2 \atop CH_3}$. (Cf. *Jacobson*, B. 1893, **26**, 700; 1898, **31**, 890; A. 1895, **287**, 98.)

Hydrazo-benzene, *sym.-Diphenyl-hydrazine*, $C_6H_5 \cdot NH \cdot NH \cdot C_6H_5$ (*Hofmann*), forms colourless plates of camphor-like odour, which are only slightly soluble in water, but dissolve readily in alcohol and ether, m.-pt. 131°. The imino-hydrogen atoms are replaceable by acetyl- or nitroso-groups.

3. AZO-COMPOUNDS

The azo-compounds are red or yellowish-red, crystalline, neutral substances, insoluble in water, but soluble in alcohol; some of them may be distilled without change. **Azo-benzene** itself (**benzene-azo-benzene**, $C_6H_5 \cdot N{:}N \cdot C_6H_5$) crystallizes in large red plates, melts at 68°, and distils at 293°. Oxidizing agents convert them into azoxy-, and reducing agents into hydrazo- or amino-compounds. Chlorine and bromine act as substituents.

The so-called "mixed" azo-compounds, which contain both

an alphyl and an aryl radical, are also known, *e.g* **azo-phenyl-ethyl**, $C_6H_5 \cdot N:N \cdot C_2H_5$, a bright-yellow oil (B. 1897, **30**, 793).

Modes of Formation.—1. By the cautious reduction of nitro- or azoxy-compounds, *e.g.* by means of sodium amalgam or of an alkaline solution of stannous oxide (B. **18**, 2912). 2. By distilling azoxy-benzene with iron filings. 3. By the oxidation of hydrazo-benzene. 4. By the oxidation of amino-compounds, *e.g* together with azoxy-compounds by means of $KMnO_4$:

$$2C_6H_5 \cdot NH_2 + 2O = C_6H_5 \cdot N:N \cdot C_6H_5 + 2H_2O.$$

5. By the action of nitroso- upon amino-compounds in presence of acetic acid. In this way azo-benzene is obtained from nitroso-benzene and aniline acetate:

$$C_6H_5 \cdot NO + NH_2 \cdot C_6H_5 = C_6H_5 \cdot N:N \cdot C_6H_5 + H_2O.$$

Amino- and hydroxy-derivatives of azo-benzenes are known, thus:—

$C_6H_5 \cdot N:N \cdot C_6H_4 \cdot NH_2$ — Amino azo benzene

$C_6H_5 \cdot N:N \cdot C_6H_4 \cdot OH$ — Hydroxy-azo-benzene

The former are at the same time bases and azo-compounds, and the latter azo-compounds and phenols (*i.e.* weak acids). (Cf. Azo-dyes, p. 399.)

β-Phenyl-hydroxylamine, $C_6H_5 \cdot NH \cdot OH$, is formed when nitro-benzene is reduced with zinc dust and water, more especially in the presence of a mineral salt, *e.g.* $CaCl_2$. It is a colourless crystalline substance melting at 81°, and is relatively unstable. Aqueous solutions rapidly undergo oxidation on exposure to the air, yielding azoxy-benzene, oxidizing agents generally yield nitroso-benzene. Mineral acids immediately cause molecular rearrangement into *p*-amino-phenol, $NH_2 \cdot C_6H_4 \cdot OH$ (cf. p. 394). All the arylated β-hydroxylamines corresponding with phenyl-hydroxylamine reduce *Fehling's* solution, and this affords a test for an aromatic nitro-compound. If, after warming with water and zinc dust, a solution is obtained which reduces *Fehling's* solution, the presence of a nitro-group in the original compound can be inferred.

D. Hydrazines

The aromatic hydrazines (*E. Fischer*) entirely correspond with those of the fatty series (cf. p. 111).

Phenyl-hydrazine, $C_6H_5 \cdot NH \cdot NH_2$, *s*-diphenyl-hydrazine or hydrazo-benzene, $C_6H_5 \cdot NH \cdot NH \cdot C_6H_5$; unsym.-diphenyl-

hydrazine, $(C_6H_5)_2N \cdot NH_2$, and phenylmethyl-hydrazine, $(C_6H_5)(CH_3)N \cdot NH_2$, are all known

Phenyl-hydrazine, $C_6H_5 \cdot NH \cdot NH_2$, forms a colourless crystalline mass, melting at 23° to a colourless oil, which quickly becomes brown from oxidation, and which is best distilled under reduced pressure. When kept or when heated it undergoes slow decomposition (*Chattaway*). It forms salts with mineral acids, *e.g.* the **hydrochloride**, $C_6H_5N_2H_3$, HCl (plates) Like all hydrazines, it has strong reducing power, reducing *Fehling's* solution even in the cold. It is readily destroyed by oxidation (*Chattaway*, C. N. 1911, **103**, 217), but is stable towards mild reducing agents. Energetic reducing agents convert it into aniline and ammonia. Gentle oxidation of the sulphate by means of HgO converts it into benzene-diazonium sulphate. It is *prepared*: (*a*) by reducing benzene-diazonium chloride with the calculated quantity of $SnCl_2$ and HCl.

$$C_6H_5N_2Cl + 4H = C_6H_5 \cdot NH \cdot NH_2, HCl;$$

(*b*) by reducing potassium diazo-benzene-sulphonate, $C_6H_5 \cdot N:N \cdot SO_3K$ (from $C_6H_5N_2Cl$ and K_2SO_4), with zinc dust and acetic acid to potassium phenyl-hydrazine sulphonate, $C_6H_5 \cdot NH \cdot NH \cdot SO_3K$, which is then hydrolysed to phenyl-hydrazine and sulphuric acid:

$$C_6H_5 \cdot NH \cdot NH \cdot SO_3K + HCl + H_2O = C_6H_5 \cdot NH \cdot NH_2, HCl + KHSO_4$$

Alkyl and acyl derivatives of phenyl-hydrazine are known, the former (mono-alkylated derivatives only) are obtained by the action of alkyl iodides on the base or its metallic derivatives. **Phenyl-methyl-hydrazine**, which can be obtained in this way, is largely used for differentiating ketoses and aldoses (p. 302); its constitution follows from its formation by the reduction of nitroso-methyl-aniline, $\begin{matrix} C_6H_5 \\ CH_3 \end{matrix} > N \cdot NO$. Both mono- and diacyl derivatives are known. The mono-acyl derivatives or **hydrazides** (cf. Amides, Anilides) are obtained by the action of the acid or acid anhydrides on the base; they give a violet-red coloration with sulphuric acid and dichromate of potash, and can be used for isolating acids which are readily soluble (B. **22**, 2728), *e.g.* **acetylphenyl-hydrazide**, $C_6H_5 \cdot NH \cdot NH \cdot CO \cdot CH_3$; m.-pt. 128°.

The base is an important and often an exceedingly delicate reagent for aldehydes and ketones, combining with them to hydrazones, with elimination of water (cf. pp. 127 and 135).

Most of these compounds are solid and crystalline, and are therefore eminently suited for the recognition of aldehydes and ketones. With certain sugars it yields phenyl-hydrazones, but with an excess of the base, osazones (p. 301) are formed. Diketones, keto-aldehydes, &c., also yield osazones.

With ethyl aceto-acetate, phenyl-hydrazine forms pyrazole derivatives, *e.g.* phenyl-methyl-pyrazolone, the methyl derivative of which is antipyrine (see p 230).

Diphenyl-hydrazine, $(C_6H_5)_2N \cdot NH_2$, is an oily base which boils without decomposition, and, like phenyl-hydrazine, is easily oxidized; it only reduces *Fehling's* solution, however, when warmed. It is obtained by reducing diphenyl-nitrosamine, $(C_6H_5)_2N \cdot NO$, with zinc dust and acetic acid M.-pt. 34°. Like phenyl-hydrazine, it yields characteristic hydrazones and osazones with the sugars

p-**Bromo-phenyl-hydrazone**, $C_6H_4Br \cdot NH \cdot NH_2$, and *p*-**nitro-phenyl-hydrazine** are often used in isolating ketones, &c., as the phenyl-hydrazones thus obtained crystallize well (B. 1899, **32**, 1806).

E. Azo-dyes

A number of compounds derived from azo-benzene and its homologues are largely used as dyes, under the name of azo-dyes. These compounds are either basic and contain NH_2 or $N(CH_3)_2$ groups, or are acidic and then contain either phenolic, OH, or sulphonic, $SO_2 \cdot OH$, and phenolic groups. Azo-benzene itself is a highly-coloured substance, but is not a dye. In order that a coloured substance shall be a dye, it is essential that the colour it imparts to a fabric shall not be removed by washing or treatment with soap According to *O. Witt*, when certain characteristic groups known as **chromophores**, among which are $\cdot N:N \cdot$ and NO_2, are present, the compound is coloured or is a **chromogene**, and when, in addition to the chromophore, a strongly basic (*e.g.* NH_2) or acidic group (*e.g.* $\cdot OH$ or $\cdot SO_2 \cdot OH$) is also present, we obtain a **dye**, *e.g.*:

Chromogenes	Dyes
Nitro-benzene	Nitraniline, $NO_2 \cdot C_6H_4 \cdot NH_2$;
Nitro-benzene	Picric acid, $(NO_2)_3 \cdot C_6H_2 \cdot OH$;
Azo-benzene	*p*-Hydroxy-azo-benzene, $C_6H_5 \cdot N:N \cdot C_6H_4 \cdot OH$.

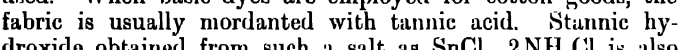
The majority of dyes, when reduced, yield colourless compounds—**leuco-compounds**—which on oxidation are converted into the original dyes.

With regard to the theory of the process of dyeing fabrics,

there are still two distinct schools. According to one, the process consists in the formation of definite compounds of the basic or acidic dye with acidic or basic constituents of the fabric dyed. According to the other, the operation is largely a physical one, and the dyed fabric may be regarded as a solid solution.

In most cases, silk and woollen—and in a few cases cotton—fabrics can be dyed by direct immersion in a solution of the dye; but, as a rule, cotton will not dye directly, but requires previous treatment with a **mordant** The object of the mordant is to deposit some substance on the fabric which will afterwards combine with or fix the dye. The chief mordants employed for acid dyes are the feeble bases aluminic, chromic, or ferric hydroxides, obtained by immersing the fabric in a solution of the metallic acetate, and then subjecting to the action of steam. The product formed by the action of the dye on the mordant is known as a **lake**, and the same dye can give rise to different-coloured lakes, according to the mordant used. When basic dyes are employed for cotton goods, the fabric is usually mordanted with tannic acid. Stannic hydroxide obtained from such a salt as $SnCl_4$, $2NH_4Cl$ is also used as a mordant.

p-**Amino-azo-benzene** is the parent substance of the dyes known as **chrysoidines** It may be obtained (1) by nitrating azo-benzene and then reducing (this indicates its constitution as an amino-derivative of azo-benzene), (2) by molecular rearrangement of diazo-amino-benzene (p. 393):

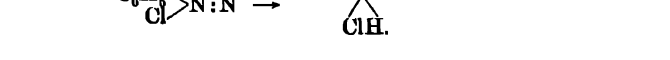


another example of the wandering of a radical from a side chain into the benzene nucleus. The amino-group occupies the *p*-position with respect to the azo-group.

Substituted amino-azo-benzenes, *e.g.* dimethyl-amino-azo-benzene, are obtained directly by the action of a diazonium salt on a tertiary amine:

$$C_6H_5N_2Cl + H\cdot C_6H_4\cdot N(CH_3)_2 = C_6H_5\cdot N{:}N\cdot C_6H_4\cdot N(CH_3)_2 + HCl.$$

Assuming the *Blomstrand* formula for the diazonium salt, the reaction is probably first additive, and then HCl is eliminated:



The azo-group always takes up the *p*-position with respect to the substituted amino-group if this position is free. If, however, the *p*-position is already substituted, a dye is not formed, or is formed very incompletely, and the *o*-position is taken up.

The chrysoidines are coloured yellow to brown, and, as they contain amino- or substituted amino-groups in the molecule, are basic, and form well-defined salts with mineral acids.

Among the simplest chrysoidines we have:—

Aniline yellow, the hydrochloride of *p*-amino-azo-benzene. It is now very little used.

Chrysoidine, or *2·4-diamino-azobenzene hydrochloride*, $C_6H_5 \cdot N:N \cdot C_6H_3(NH_2)_2$, HCl [$N_2:(NH_2)_2 = 1 \cdot 2 \cdot 4$]. It dyes silk and wool directly an orange-red colour.

Bismarck brown, or *3′:2.4-triamino-azo-benzene hydrochloride*, $NH_2 \cdot C_6H_4 \cdot N:N \cdot C_6H_3(NH_2)_2$, HCl, is obtained by diazotizing *m*-phenylenediamine and coupling the diazonium salt with a second molecule of the base.

The brown coloration obtained by the addition of a few drops of dilute nitrous acid solution to *m*-phenylenediamine is due to the formation of Bismarck brown or a related substance. The hydrochloride crystallizes in reddish-brown plates.

Many of the chrysoidine dyes are sulphonated derivatives of amino-azo-benzene As an example, we have **methyl orange**, which is the sodium salt of **helianthine** or *p*-dimethamino-azo-benzene-*p* sulphonic acid, $(CH_3)_2N \cdot C_6H_4 \cdot N:N \cdot C_6H_4 \cdot SO_2 \cdot OH$. It is largely made use of as an indicator in volumetric analysis, as it is not affected by weak acids, *e g.* carbonic, but is an extremely delicate reagent for the feeblest alkalis.

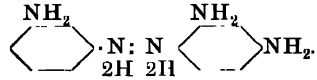
The dyes known as **tropæolines** are derivatives of *p*-hydroxy-azo-benzene. Such compounds are obtained by adding the cold diazotized solution to an *alkaline* solution of a phenol. The dye is then salted out by the addition of sodium chloride and collected. The reaction is often made use of in testing for a primary aromatic amine (p. 389), as the precipitates produced are usually coloured bright red. The azo-group invariably occupies the *p*-position with respect to the OH group, unless this is already substituted.

***p*-Hydroxy-azo-benzene** crystallizes in brick-red prisms, and is a yellowish-red dye.

Resorcin yellow, $OH \cdot SO_2 \cdot C_6H_4 \cdot N:N \cdot C_6H_3(OH)_2$, *2:4-dihydroxy-azo-benzene-4′-sulphonic acid*, obtained by coupling a

diazotized solution of sulphanilic acid with an alkaline solution of resorcinol, is known as Tropæolin O.

The *constitution* of an azo-dye can usually be determined by an examination of its decomposition products, especially the products formed by energetic reduction; *e.g.* Bismarck brown on reduction with tin and hydrochloric acid, yields a mixture of 1:3-diamino- and 1·2:4-triamino-benzene:



Bis-azo-dyes.—Certain well-known dyes, *e.g.* **Biebrich scarlet** contain two azo-groups. Such can be obtained by diazotizing an amino-derivative of azo-benzene, and then coupling it with a tertiary amine or with a phenol, and we thus obtain compounds of the type $C_6H_5\cdot N:N\cdot C_6H_4\cdot N:N\cdot C_6H_4\cdot OH$

Another type of bis-azo-compound is formed by coupling a diamine or dihydric phenol with 2 mols of a diazonium salt.

Many amino- and hydroxy-azo-derivatives react as tautomeric substances, especially those which contain an NH_2 or OH group in the ortho-position with respect to the N radical. These react as though they were quinone hydrazones or quinone-imide derivatives, *e.g.*.

$$C_6H_5\cdot N:N\cdot C_6H_4\cdot OH \longrightarrow C_6H_5NH\cdot N:C_6H_4:O,$$
$$C_6H_5\cdot N:N\cdot C_6H_4\cdot NH_2 \longrightarrow C_6H_5\cdot NH\cdot N:C_6H_4:NH$$

For a general summary compare *Auwers* (A. 1908, **360**, 11) The general conclusion drawn is that all the compounds, both para and ortho, are true hydroxy-azo-compounds

According to *Hantzsch*, many of the hydroxy-azo-compound are pseudo-acids (p. 363), *i.e.* the hydrogen compound is the quinone hydrazone; but in the formation of a salt, intramolecular rearrangement occurs, and the salt thus has a constitution quite different from that of the parent substance, *e.g.*

$$C_6H_5\cdot NH\cdot N:C_6H_4:O \longrightarrow C_6H_5\cdot N:N\cdot C_6H_4\cdot ONa.$$

F. Phosphorus Compounds, &c.; Organo-Metallic Derivatives

The phosphorus, &c., compounds of the fatty series have their analogues in corresponding compounds of the aromatic these latter have been investigated by *Michaelis* and his pupils (A. **181**, **188**, **201**, **212**, and **229**; B. **28**, 2205). fo

instance, **phenyl phosphine**, $C_6H_5 \cdot PH_2$; **phenyl phosphinic acid**, $C_6H_5PO(OH)_2$, **phosphenyl chloride**, $C_6H_5 \cdot PCl_2$, **phosphino-benzene**, $C_6H_5PO_2$, and **phospho-benzene**, $C_6H_5P:P \cdot C_6H_5$ (these two last being analogous to nitro- and to azo-benzene). Some of those compounds are solid, and they are less volatile and more stable than the corresponding aliphatic compounds. Corresponding derivatives of arsenic are also known.

Aromatic Organo-Metallic Compounds. — Mercury, tin, lead, tellurium, and magnesium yield phenyl derivatives **Mercury phenyl**, $Hg(C_6H_5)_2$, is obtained by the action of sodium amalgam of bromobenzene It is relatively stable. Numerous compounds of the type of **phenyl magnesium bromide**, $C_6H_5 \cdot Mg \cdot Br$, have been prepared, and are used as synthetical reagents (cf. p. 356).

XXIII AROMATIC SULPHONIC ACIDS

The aromatic sulphonic acids are very similar in properties to the sulphonic acids of the fatty series, but can be obtained much more readily One of the characteristic properties of benzene and its derivatives is the readiness with which they react with concentrated sulphuric acid, yielding sulphonic acids In some cases fuming sulphuric acid is used; in others sulphuryl chloride, $OH \cdot SO_2 \cdot Cl$

Benzene-sulphonic acid, $C_6H_5 \cdot SO_2 \cdot OH$ (*Mitscherlich*, 1834), is formed when benzene is heated with concentrated sulphuric acid for some hours·

$$C_6H_6 + SO_2(OH)_2 = C_6H_5 \cdot SO_2 \cdot OH + H_2O.$$

As in the case of ethyl hydrogen sulphate, advantage is taken of the solubility of its barium, calcium, or lead salt to separate it from the excess of sulphuric acid, or its sodium salt is separated by the addition of sodium chloride.

It crystallizes in small plates containing $1\frac{1}{2}H_2O$, deliquesces in the air, and is readily soluble in alcohol The **barium salt** crystallizes in glistening mother-of-pearl plates containing $1H_2O$.

It is very stable, and is not hydrolysed when boiled with alkalis or acids (cf. Ethyl hydrogen sulphate). It is, however,

decomposed into benzene and sulphuric acid when heated with hydrochloric acid at 150°, or with water vapour at a high temperature (cf. p. 347).

$$C_6H_5 \cdot SO_2 \cdot OH + H_2O = C_6H_6 + SO_2(OH)_2.$$

When fused with alkali, it yields phenol in the form of its potassium salt:

$$C_6H_5 \cdot SO_3K + 2KOH = C_6H_5 \cdot OK + SO_3K_2 + H_2O,$$

and when distilled with potassium cyanide, it yields benzonitrile:

$$C_6H_5 \cdot SO_3K + CNK = C_6H_5 \cdot CN + SO_3K_2$$

With PCl_5 the OH group present in the sulphonic acid radical is replaced by chlorine, and **benzene-sulphonic chloride** is formed:

$$C_6H_5 \cdot SO_2OH + PCl_5 = C_6H_5 \cdot SO_2Cl + POCl_3 + HCl.$$

This is an oil, insoluble in water; it melts at 14·5°, and boils at 120° (under 10 mm. pressure), as an acid chloride it is reconverted into sulphonic acid by hot water, into the corresponding esters by alcohols, and into **benzene-sulphonamide**, $C_6H_5 \cdot SO_2 \cdot NH_2$ (lustrous mother-of-pearl plates melting at 150°), by ammonia. This compound can be sublimed, and corresponds with other amides in its properties. The amido-group, however, is so affected by the strongly acidifying action of the SO_2 group that its hydrogen is replaceable by metals, and the sulphonamides consequently *dissolve in aqueous solutions of alkali hydroxides.*

The sulphonamides are largely made use of in distinguishing the various sulphonic acids. These acids themselves are difficult to purify, as a rule do not crystallize well, and have no definite melting-point. The sulphonamides, on the other hand, crystallize readily, and have sharp melting-points. The sodium salt of the acid is treated with PCl_5, and the chloride thus obtained is warmed with ammonium carbonate.

Benzene-sulphonic chloride likewise yields sulphonamides with primary and secondary amines, $C_6H_5 \cdot SO_2 \cdot NHR$ and $C_6H_5 \cdot SO_2 \cdot NRR'$, the former of these being soluble in alkali, but the latter insoluble. Tertiary amines do not, of course, give sulphonamides. This serves as the basis of a method for separating primary, secondary, and tertiary bases, especially

when β-anthraquinone sulphonic chloride is used (*Hinsberg*, B. **23**, 2962; 1900, **33**, 477, 557, 3526; **38**, 906).

When benzene-sulphonic chloride is treated with zinc dust, zinc benzenesulphinate is formed:

$$2C_6H_5\cdot SO_2Cl + 2Zn = (C_6H_5SO_2)_2Zn + ZnCl_2.$$

An alkaline sulphinate is also produced (along with phenyl disulphide as by-product) when benzene-sulphonic chloride is treated with thio-phenol in presence of alkali.

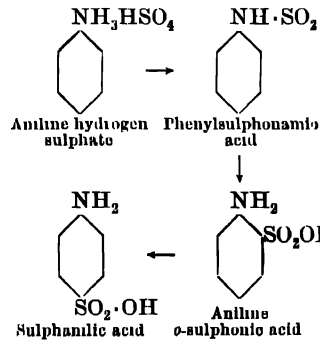
Benzene-sulphinic acid crystallizes in large glistening prisms, readily soluble in hot water, alcohol, and ether. It possesses reducing properties, and is itself converted into thio-phenol by nascent hydrogen:

$$C_6H_5\cdot SO_2H + 4H = C_6H_5SH + 2H_2O.$$

Substitution may be effected in benzene-sulphonic acid by chlorine, bromine, and the groups NO_2 and NH_2.

The **nitro-benzene-sulphonic acids**, $NO_2\cdot C_6H_4\cdot SO_3H$, are obtained by nitrating benzene-sulphonic acid or by sulphonating nitro-benzene, the *m*-compound preponderating. Reducing agents convert them into the—

Amino-benzene-sulphonic acids, $NH_2\cdot C_6H_4\cdot SO_3H$. The *p*-compound, which is termed **sulphanilic acid**, is obtained by heating aniline sulphate at 180°–200° (*Gerhardt*, 1845), also by reducing *p*-nitro-benzene-sulphonic acid. The conversion of aniline sulphate into sulphanilic acid proceeds in the following stages:—



(Cf. *Bamberger*, B. 1897, **30**, 2274.) It crystallizes in rhombic plates (+ H_2O), sparingly soluble in water, forms metallic salts,

e.g. **sodium sulphanilate**, $NH_2 \cdot C_6H_4 \cdot SO_3Na + 2H_2O$ (large plates), but does not combine with acids. The formula $C_6H_4\langle^{NH_3}_{SO_3}\rangle$ possibly expresses the constitution of sulphanilic acid. The *m*-acid, also termed **metanilic acid**, is employed in the preparation of azo-dyes, *e.g.* metanil yellow, it crystallizes in fine needles or prisms.

Diazo-benzene-sulphonic acid, $C_6H_4\langle^{N:N}_{SO_3}\rangle$ (*the anhydride of* $C_6H_4\langle^{N:N\cdot OH}_{SO_3H}\rangle$), is obtained by adding a mixture of sulphanilate and nitrite of sodium to dilute sulphuric acid. It forms colourless needles, sparingly soluble in water, shows all the reactions of the diazo-compounds, and is of great importance for the preparation of azo-dyes.

Benzene-disulphonic acids, $C_6H_4(SO_3H)_2$ (principally meta-), and **benzene-trisulphonic acids**, $C_6H_3(SO_3H)_3$, result from the energetic sulphonation of benzene with fuming sulphuric acid. The former exist, of course, in three isomeric modifications. When they are distilled with KCN, they yield the compounds $C_6H_4(CN)_2$, the nitriles of the phthalic acids, when fused with KOH, the *m*-disulphonic acid changes into resorcinol (*m* dihydroxy-benzene), $C_6H_4(OH)_2$.

Almost all the homologues of benzene, with the exception of hexamethyl-benzene, yield sulphonic acids. From toluene are obtained the *o*-, *m*-, and ***p*-toluene sulphonic acids**, $CH_3 \cdot C_6H_4 \cdot SO_3H$ (*Hollemann* and *Caland*, B 1911, **44**, 2504). Of these it is the *p*-acid which is formed in largest quantity directly; its potassium salt crystallizes beautifully.

The sulphonic acids of the three xylenes, the **xylene-sulphonic acids**, $C_6H_3(CH_3)_2SO_3H$, serve for the separation of these isomers from each other, and the power of crystallization of the salts or amides of the sulphonic acids of the higher benzene homologues is frequently made use of for the recognition and separation of these hydrocarbons.

The above instances are sufficient to show that sulphonic acids may be obtained from the most complicated aromatic compounds. This is of especial importance if the latter are dyes whose application is hindered by their insolubility in water, as in the case, *e.g.*, of indigo, amino-azo-benzene, &c. The sulphonated dyes, however, are usually inferior to their originals in colouring power and purity, *e.g.*, they do not stand the effects of light so well.

XXIV. PHENOLS

The hydroxylic derivatives of benzene and its homologues are usually divided into (*a*) phenols and (*b*) aromatic alcohols. The phenols all contain the hydroxyl group or groups directly attached to the benzene nucleus, *e.g.* $C_6H_5(OH)$, $C_6H_4(OH)_2$, whereas in the alcohols the hydroxyl group is present in a side chain, *e.g.* $C_6H_5 \cdot CH_2 \cdot OH$.

One important point of difference between the phenols and alcohols is the more pronouncedly acidic nature of the phenol. The aromatic alcohols closely resemble those of the aliphatic series, but the phenols react as feeble acids, the hydroxylic hydrogen being displaced by the action of sodium or potassium hydroxide.

The phenols are either liquid or solid compounds, and are often characterized by a peculiar odour, *e.g.* carbolic acid and thymol. Most of them can be distilled without decomposition, and all are readily soluble in alcohol or ether; some dissolve easily in water, others less readily, the solubility tending to increase with the number of hydroxyl groups present in the molecule. Many of them are antiseptics, *e.g.* phenol, creosol, and resorcinol.

The phenols are usually divided into mono-, di-, tri- or tetrahydric, according to the number of OH groups present in the molecule

Behaviour.—1. Like the alcohols, the phenols are capable of forming **ethers** such as anisole, $C_6H_5 \cdot O \cdot CH_3$, **esters**, *e.g.* phenyl acetate, $C_6H_5 \cdot O \cdot CO \cdot CH_3$, and phenyl hydrogen sulphate, $C_6H_5O \cdot SO_2 \cdot OH$, **thio-compounds**, *e.g.* thiophenol, $C_6H_5 \cdot SH$, &c.

They can only be compared with the tertiary alcohols, since they cannot, like the primary or secondary alcohols, yield acids or ketones containing an equal number of carbon atoms in the molecule upon oxidation.

2. The phenols are weak acids, and form salts known as **phenates** or **phenoxides**, *e.g.* $C_6H_5 \cdot OK$, potassium phenate or potassium phenoxide; most of the salts are readily soluble in water, and far more stable than the alcoholates, with which they correspond.

In aqueous solutions the salts are largely hydrolysed, and are decomposed by carbon dioxide, as the phenols are extremely feeble acids comparable with hydrocyanic acid (cf. *Walker*, Phys. Chem., chapter xxiv). The acid character of the

Monohydric Phenols

Formula	Name	Positions of Substituents OH in 1	Melting-point	Boiling-point	Specific Gravity
$C_6H_5 \cdot OH$	Phenol	...	42·5°	183°	1·039
$CH_3 \cdot C_6H_4 \cdot OH$	*o*-Cresol	1 2	30°	191°	1·043
	m-Cresol	1.3	4°	203°	1·035
	p-Cresol	1·4	36°	202°	1·034
$(CH_3)_2C_6H_3 \cdot OH$	adj.-*o*-Xylenol	1:2.3	73°	213°	...
	asym -*o*-Xylenol	1.3.4	65°	222°	...
	p-Xylenol	1 2:5	75°	209°	...
$(CH_3)_3C_6H_2 \cdot OH$	Pseudo-cumenol	1:2.4:5	73°	234°	...
$(CH_3)_2CH \cdot C_6H_3(CH_3)(OH)$	Carvacrol	1 2 4	0 5°	237°	0 979
	Thymol	1 3 6	50°	232°	0·982

Dihydric Phenols

$C_6H_4(OH)_2$	Catechol	1.2	104°	240°	...
	Resorcinol	1 3	119°	276°	...
	Quinol	1·4	169°	. .	.
$CH_3 \cdot C_6H_3 \cdot (OH)_2$	Orcinol	1 3 5	107°	288°	...

Trihydric Phenols

$C_6H_3(OH)_3$	Pyrogallol	1 2 3	132°	...	...
	Hydroxyquinol	1 2 4	140°	...	...
	Phloroglucinol	1·3 5	217–219°	...	...

phenols is considerably increased by the entrance of negative groups, especially NO_2, into the molecule (See Picric acid; also Abst. 1903, **1**, 754.)

3. The presence of NH_2 or OH groups in the benzene nucleus renders compounds much more reactive towards halogens, nitric acid, sulphuric acid, oxidizing agents, &c. With polyamines and aminophenols the reactivity is such that the compounds undergo spontaneous oxidation on exposure to the air. The reactivity with chlorine is so great that frequently compounds of this type cannot be chlorinated by the usual methods. *Orton* and *King* (J. C. S. 1911, 1185) have introduced a method based upon the fact that the reversible reaction

$$R{\cdot}NClAc + HCl \rightleftharpoons R{\cdot}NHAc + Cl_2$$

proceeds from left to right in the presence of glacial acetic acid, and thus by taking very dilute solutions of hydrochloric acid, *e.g.* 0·021 *N*, the concentration of the chlorine is kept so low that chloro-derivatives are obtained free from products of oxidation. Cresols can be chlorinated in the same manner. The acetyl derivative generally used is 2:4-dichloro-acetyl-chloranilide, and if the theoretical amount of this compound is used the reaction proceeds to completion, as hydrogen chloride is formed by the action of the chlorine on the amine or phenol.

4. Many phenols give characteristic colorations with ferric chloride in neutral solution, *e.g.* phenol and resorcinol violet, catechol green, and orcinol blue-violet; while pyrogallol yields a blue colour with ferrous sulphate containing a ferric salt, and a red one with ferric chloride. Bleaching-powder and iodine solution, in certain cases, also give particular coloration.

5. *Liebermann's Reaction.* - When the phenols are mixed with concentrated H_2SO_4 and a drop of nitrite solution or of a nitrosamine, they yield intensely coloured solutions which turn to a deep-blue or green when diluted and rendered alkaline with potash.

6. The sodium and potassium salts of the phenols react with CO_2 (*Kolbe*) or with $COCl_2$, with formation of aromatic hydroxy-acids, *e.g.* salicylic acid (see this).

For further methods of preparation of hydroxy-acids and aldehydes, see *Tiemann-Reimer* reaction (pp. 430 and 440).

7. The phenols couple with diazonium salts to form azo-dyes (p. 389); when heated with benzo-trichloride, $C_6H_5{\cdot}CCl_3$, they yield yellow-red dyes (see Aurin), and with phthalic acid, the phthaleins (see Phenol-phthalein).

8. When heated with zinc dust, the phenols are converted into the corresponding hydrocarbons (*Baeyer*).

9. When heated with the additive compounds of zinc chloride and ammonia or calcic chloride and ammonia, the OH is replaced by NH_2 (cf. p. 368; also B. **19**, 2901).

10. Heating with phosphorus pentachloride partially converts the phenols into chlorinated hydrocarbons, and heating with P_2S_5 into thio-phenols.

Occurrence.—Many individual phenols are found in the vegetable and animal kingdoms, and also in coal-tar.

Constitution.—The hydroxyl-groups in phenol, $C_6H_5 \cdot OH$, and in the di- and polyhydroxy-benzenes, containing six carbon atoms, are linked to the benzene nucleus. That this is also the case in the homologues of these compounds follows. (*a*) from their completely analogous reactions, (*b*) from their behaviour upon oxidation. Thus, when oxidized, *m*-cresol yields *m*-hydroxy-benzoic acid, and hence the OH is present in the benzene nucleus and not in the side chain, and must be in the *m*-position with respect to the methyl group

A. Monohydric Phenols

Modes of Formation.—1. Many phenols are formed during the destructive distillation of the more complex carbon compounds, especially of wood and coal; they are therefore present in wood- and coal-tars The latter contains more especially phenol and its homologues, cresol, &c.; the former, among other products, the methyl ethers of polyhydric phenols, *e.g.* guaiacol, $C_6H_4 \cdot (OH)(O \cdot CH_3)$, and its homologue creosol, $C_6H_3(CH_3)(OH)(O \cdot CH_3)$.

The phenols are isolated from coal-tar, &c., by shaking with sodic hydroxide solution, in which they dissolve, saturating the alkaline solution with hydrochloric acid, and purifying the precipitated phenols by fractional distillation.

2. Phenols are formed together with an alkali sulphite when salts of sulphonic acids are fused with potassic or sodic hydroxides (*Kekulé, Wurtz, Dusart*, 1867):

$$C_6H_5 \cdot SO_3K + 2KOH = C_6H_5 \cdot OK + SO_3K_2 + H_2O.$$

In the laboratory nickel or silver basins are used for this fusion, and on the large scale iron boilers, &c. The alkali salts of the phenols are formed, and the free phenols may be liberated, by the addition of mineral acid. The chlorinated

sulphonic acids and the chlorinated phenols also exchange the halogen for hydroxyl when fused with potash.

$$C_6H_4Cl(SO_3K) + 4KOH = C_6H_4(OK)_2 + SO_3K_2 + KCl + 2H_2O.$$

In certain cases intramolecular rearrangement occurs during this fusion, *e.g.* all three bromo-benzene-sulphonic acids, the ortho-, meta-, and para-, yield *m*-dihydroxy-benzene (resorcinol) when fused with potash.

3. They are formed when aqueous solutions of diazonium salts are heated (*Griess*, cf. p. 387). As a rule, a very dilute sulphuric acid solution is employed:

$$C_6H_4Cl(N_2Cl) + H_2O = C_6H_4Cl\cdot OH + N_2 + HCl.$$

4. Phenol is produced from benzene by the action of ozone or hydrogen peroxide, and also by that of the oxygen of the air in presence of caustic soda solution or of aluminium chloride. In an analogous manner di- and even trihydroxy-benzene may be obtained by fusing phenol with potash:

$$C_6H_5\cdot OH + O = C_6H_4(OH)_2.$$

5. The phenols cannot be prepared from chloro-, bromo-, or iodo-benzene in the same way as the alcohols from alkyl chlorides, bromides, or iodides, the halogen being bound too firmly to the benzene nucleus. If, however, nitro-groups are present in *o*- or *p*-positions, an exchange of this kind can be effected by heating with aqueous sodium or potassium hydroxides; trinitro-chloro-benzene indeed reacts with water alone:

$$C_6H_2Cl(NO_2)_3 + HOH = C_6H_2(OH)(NO_2)_3 + HCl.$$

Similarly, the amino-group in amino-compounds may be replaced by hydroxyl by means of boiling alkalis, provided nitro-groups are also present in certain position; thus *o*- and *p*- (not *m*-) dinitro-aniline yield dinitro-phenols, a reaction which corresponds with the saponification of the amides (cf. pp. 362 and 374).

6. Phenols are also formed when salts of the aromatic hydroxy-acids are distilled with lime, or when their silver salts are carefully heated:

$$\underset{\text{Gallic acid}}{C_6H_2(OH)_3\cdot CO_2H} = CO_2 + \underset{\text{Pyrogallol.}}{C_6H_3(OH)_3}$$

Phenol, *Carbolic acid*, *hydroxy-benzene*, C_6H_5OH, was dis-

covered in 1834 by *Runge* in coal-tar. It occurs in the urine of the herbivora and in human urine as phenyl hydrogen sulphate, also in castoreum, and in bone-oil. It forms a colourless crystalline mass consisting of long needles, melts at 42°, boils at 181°, is soluble in fifteen parts of water at 16°, and itself dissolves some water, a small percentage of the latter sufficing to liquefy the crystalline phenol. Alcohol and ether dissolve it readily. It is hygroscopic, and acquires a reddish colour in the air owing to the presence of impurities, possesses a characteristic odour and burning taste, is poisonous, acts as a splendid antiseptic, and exerts a strongly corrosive action upon the skin. As a very feeble acid it dissolves readily in caustic potash solution, but not in the carbonate Ferric chloride colours the aqueous solution violet, while a pine shaving- moistened with hydrochloric acid is turned greenish-blue by phenol.

Hexahydro-phenol, $C_6H_{11}\cdot OH$, prepared from quinitol (cyclohexane-1:4-diol) (B. **26**, 229), is a liquid with an odour resembling that of fusel oil.

Anisole, or *Phenyl methyl ether*, $C_6H_5\cdot O\cdot CH_3$, and **phenetole**, or *phenyl ethyl ether*, $C_6H_5\cdot O\cdot C_2H_5$, are best obtained by heating phenol and caustic potash with methyl or ethyl iodide in alcoholic solution:

$$C_6H_5\cdot OK + CH_3I = C_6H_5\cdot OCH_3 + KI;$$

the former is also obtained by distilling anisic acid with lime. They are liquids of ethereal odour which boil at a lower temperature than phenol, just as ether has a lower boiling-point than alcohol. They are very stable neutral compounds, which are not readily hydrolysed by acids or alkalis; when heated with HI to 140°, or with HCl to a higher temperature, or with aluminium chloride, they are decomposed, yielding phenol:

$$C_6H_5\cdot O\cdot CH_3 + HCl = C_6H_5\cdot OH + CH_3Cl.$$

Phenyl ether, *Diphenyl oxide*, $(C_6H_5)_2O$, is formed when phenol is heated with $ZnCl_2$ or $AlCl_3$, but not with H_2SO_4. It crystallizes in needles, and is not decomposed by hydriodic acid.

Esters.—Phenyl hydrogen sulphate, $C_6H_5\cdot O\cdot SO_2\cdot OH$ (cf. Ethyl hydrogen sulphate), is only capable of existence in the form of salts, being immediately hydrolysed into phenol and sulphuric acid when attempts are made to isolate it. The **potassium** salt, $C_6H_5O\cdot SO_2\cdot OK$ (plates, sparingly soluble in

water), is found in the urine of the herbivora and also in human urine after the consumption of phenol, and it may be prepared synthetically by heating potassium phenate with potassic pyro-sulphate in aqueous solution (*Baumann*). It is very stable towards alkalis, but is saponified by hydrochloric acid.

Phenyl acetate, $C_6H_5O \cdot CO \cdot CH_3$, obtained from phenol, acetic anhydride, and dry sodic acetate, is a liquid which boils at 193°, and is readily hydrolysed (cf. Ethyl acetate).

Thio-phenol, *Phenyl hydrosulphide*, $C_6H_5 \cdot SH$, is prepared from benzene-sulphonic chloride, $C_6H_5 \cdot SO_2Cl$, as given at p. 405, or by heating phenol with P_2S_5. It is a liquid of most unpleasant odour and of pronounced mercaptan character (see p. 89). It yields, for instance, a mercury compound, $(C_6H_5S)_2Hg$, crystallizing in glistening needles, and also salts with other metals. When warmed with concentrated H_2SO_4, a cherry-red and then a blue coloration is produced.

Closely related to the above are: (*a*) **phenyl sulphide**, $(C_6H_5)_2S$, which is formed by the action of benzene-diazonium chloride upon thio-phenol (B. **23**, 2469).

$$C_6H_5 \cdot N:N \cdot Cl + H \cdot S \cdot C_6H_5 = C_6H_5 \cdot S \cdot C_6H_5 + N_2 + HCl.$$

It is a liquid smelling of leeks, and is oxidizable to **phenyl sulphone**, $(C_6H_5)_2SO_2$; (*b*) **phenyl disulphide**, $(C_6H_5)_2S_2$ (glistening needles, m.-pt. 60°), which is very easily prepared by the action of iodine upon the potassium compound of thio-phenol, or by exposing an ammoniacal solution of the latter to the air. It is readily reduced to thio-phenol, and may be indirectly oxidized to **benzene-disulphoxide**, $(C_6H_5)_2S_2O_2$. (Cf. the corresponding compounds of the fatty series, p. 89, *et seq.*)

SUBSTITUTED PHENOLS

Chloro- and Bromo-phenols.—When chlorine is led into phenol, *o*- and *p*-**chloro-phenols** are formed. These, and also the *m*-compound, may be obtained by reducing and diazotizing the haloid nitro-benzenes.

Of the isomeric di-derivatives, the *p*-compounds have the highest melting-point and the *o*- the lowest; thus *o*-chloro- and bromo-phenols are liquid and the *p*-compounds solid. When fused with caustic potash they yield dihydroxy-benzenes (p. 411), often with a molecular rearrangement. The chloro

phenols have a sharp, persistent odour. All the 5 hydrogen atoms of phenol can be replaced by chlorine and bromine.

When an excess of bromine water is added to an aqueous solution of phenol, a precipitate of *s*-**tribromo-phenol** (colourless needles, melting at 92°) is obtained.

Nitroso-phenol, $OH \cdot C_6H_4 \cdot NO$, prepared from phenol and nitrous acid (*Baeyer*, B. **7**, 964), by boiling nitroso-dimethylaniline with caustic-soda solution (see p. 378), and by the action of hydroxylamine upon quinone, is identical with quinone monoxime, $O:C_6H_4:N \cdot OH$ (p. 430). It crystallizes in fine colourless needles which readily become brown, or in large greenish-brown plates, and detonates when heated.

Nitro-phenols.—A mixture of *o* and *p*-**nitro-phenols** is obtained when phenol is mixed with cold dilute nitric acid, the *p*-compound preponderates if the liquid is cold, and the ortho- if it is warm. When distilled with steam, the 1.2 compound volatilizes, while the 1:4 remains behind. *m*-**Nitro-phenol** is obtained by diazotizing *m*-nitraniline.

The *o*- and *p*-compounds can also be obtained by fusing *o*- and *p*-nitranilines with potash, and *p*-nitro-phenol has been synthesised from nitro-malonaldehyde, $NO_2 \cdot CH(CHO)_2$, and acetone (*Hull* and *Torrey*, B. 1895, **28**, 2598).

The *o*-compound crystallizes in yellow prisms, and melts at 45°, the *m*- in yellow crystals, melting at 96°, and the para- in colourless needles, melting at 114°.

The acid character of phenol is so strengthened by the entrance of the nitro-group that its salts are not decomposed by carbonic acid, but are formed from the nitro-phenols and alkali carbonate. **Sodium** *o*-**nitro-phenate**, $C_6H_4(NO_2)ONa$, crystallizes in dark red prisms, and **potassium** *p*-**nitro-phenate** in golden needles (For constitution of the salts, see chapter on Absorption Spectra.) Halogens and nitric acid readily substitute further in these mono-nitro-compounds; nitric acid yields two isomeric **dinitro-phenols**, $C_6H_3(NO_2)_2OH$, ($OH:NO_2:NO_2:NO_2 = 1:2:4$ and $1.2.6$, *i.e.* the two NO_2 groups are always in the *m*-position to one another). Further nitration in the presence of sulphuric acid gives—

Picric acid, *s-Trinitro-phenol*, $C_6H_2(NO_2)_3 \cdot OH$, ($OH:NO_2:NO_2:NO_2 = 1.2:4:6$). This compound was discovered in 1799. It may also be prepared by the direct oxidation of *s*-trinitro-benzene with $K_3FeC_6N_6$, and is produced by the action of concentrated nitric acid upon the most varied organic substances, *e.g.* silk, leather, wool, resins, and aniline.

It is a strong acid and forms beautifully crystalline salts, which explode violently when heated or struck. It crystallizes from alcohol or water in yellow plates or prisms, melting at 122°, is only sparingly soluble in water, and the aqueous solutions have a persistent deep-yellow colour. It is used for the preparation of explosives, and is also a yellow dye.

Picryl chloride, $C_6H_2(NO_2)_3Cl$ (from picric acid and PCl_5), resembles the acid chlorides (p. 362) in behaviour. Picric acid forms beautifully crystallizing additive compounds with many aromatic hydrocarbons, and also with amines and phenols

Amino-phenols are obtained by the reduction of nitro-phenols:

$C_6H_4(OH)NH_2$	$C_6H_3(OH)(NH_2)_2$	$C_6H_3(OH)(NO_2)(NH_2)$	$C_6H_3(OH)(NH_2)_3$
o-, *m-*, *p-* Amino phenols	Diamino-phenols	Nitro-amino-phenols	Triamino-phenol

In the amino-phenols (*Hofmann*, 1857) the acid character of the phenols is neutralized by the presence of the amino-group, so that they only yield salts with acids The amino-phenols themselves are relatively unstable, and readily decompose on exposure to moist air or sunlight, but the hydrochlorides are much more stable. Derivatives of these compounds, as phenols and as amines, are known. The amino-hydrogen is readily replaceable by acyl groups.

***p*-Amino-phenol**, m.-pt. 184°, obtained by the electrolysis of nitrobenzene in concentrated sulphuric acid (*Gattermann*), or by molecular rearrangement from β-phenyl-hydroxylamine, is easily oxidized to quinone, $C_6H_4O_2$, and is converted by bleaching-powder into quinone chlor-imide, $O:C_6H_4:NCl$ It is used as a photographic developer under the name of *rodinal*. *Amidol* is a salt of 2.4-diamino-phenol.

***m*-Amino-phenol** and **diethyl-*m*-amino-phenol**, $C_6H_4(OH)[N(C_2H_5)_2]$, are formed when *m*-amino-benzene-sulphonic acid or its diethyl-derivative is fused with alkali

The **anisidines**, *amino-anisoles*, *methoxy-anilines*, $CH_3O \cdot C_6H_4 \cdot NH_2$, and the **phenetidines**, $C_2H_5O \cdot C_6H_4 \cdot NH_2$, are bases similar to aniline, and are used in the colour industry (azo-dyes). The acetyl derivative, **aceto-*p*-phenetidine**, $C_2H_5O \cdot C_6H_4 \cdot NH \cdot CO \cdot CH_3$, which forms colourless crystals, is used as an anti-pyretic and as a remedy for neuralgia under the name of "*Phenacetine*". *Phenocoll* is lactyl-phenetidine

Numerous complex sulphur compounds derived from amino phenols are used as dyes (*e.g.* Primulines, Vidal-black, &c.).

Phenol-sulphonic acids, $OH \cdot C_6H_4 \cdot SO_2 \cdot OH$. — The *o*- and *p*-acids are obtained from phenol and concentrated H_2SO_4 at a moderate temperature, that is, with much greater ease than the benzene-sulphonic acids; the ortho-acid changes into the para- when its aqueous solution is heated. The two acids may be separated by means of their potassium salts. The *m*-compound can be prepared indirectly by fusing *m*-benzene-disulphonic acid with potash. All three are crystalline.

The *o*- and *m*-acids yield *o*- and *m*-dihydroxy-benzenes when fused with KOH, but the *p*-acid does not react in this way, being attacked only at temperatures over 320°, when complex products are formed. *o*-Phenol-sulphonic acid is used as an antiseptic under the name of "Aseptol" or "*Sozolic acid*"; similarly, the salts of **di-iodo-*p*-phenol-sulphonic acid**, $OH \cdot C_6H_2I_2 \cdot SO_3H$, "*Sozo-iodol*", form antiseptics resembling iodoform.

HOMOLOGUES OF PHENOL

The homologues of phenol resemble the latter very closely in most of their properties, form perfectly analogous derivatives, possess disinfecting properties, and also a peculiar odour (the cresols an unpleasant faecal-like, and the higher homologues only a faint odour).

They differ from phenol mainly by the presence of side chains which, as in the case of toluene, &c., may undergo certain transformations. Especially when they are used in the form of alkyl or acyl derivatives or acid sulphates, they can be oxidized in such a manner that the side chains (methyl groups) are transformed into carboxyl, with the production of hydroxy-carboxylic acids. The cresols themselves cannot be oxidized in this way even by chromic acid mixture, and are completely destroyed by potassic permanganate. Negative substituents, especially if they are present in the *o*-position, render such oxidation more difficult in acid, but facilitate it in alkaline solution.

All three **cresols**, $CH_3 \cdot C_6H_4 \cdot OH$, are present in coal-tar, and are also contained in the tar from pine and beech wood; they are most readily prepared from the corresponding toluidines. *o*-Cresyl hydrogen sulphate (analogous to phenyl hydrogen sulphate) is found in the urine of horses, and the *p*-compound in human urine.

***m*-Cresol** is conveniently prepared by heating thymol with phosphoric anhydride and then with potash.

p-**Cresol** is produced during the putrefaction of albumen. Its dinitro-compound is a golden-yellow dye which is used as ammonium or potassium salt under the name of **Victoria orange**.

Crude cresol is rendered soluble in water by the addition of resin soap or of oil soap; the preparations so obtained are termed *creoline* and *lysol*, and are employed as antiseptics.

Thymol, $C_{10}H_{14}O$, 1-*methyl*-4-*isopropyl*-3-*hydroxy*-*benzene*, is found together with cymene, $C_{10}H_{14}$, and thymene, $C_{10}H_{16}$, in oil of thyme, *Thymus Serpyllum*, and is used as an antiseptic.

The isomeric **carvacrol**, 1-*methyl*-4-*isopropyl*-2-*hydroxy*-*benzene*, present in *Origanum hirtum*, is prepared either by heating camphor with iodine or from its isomer, carvol, and glacial phosphoric acid.

The *constitutions* of these two phenols have been established as follows. (*a*) Both yield cymene (*p*-methyl-isopropyl-benzene) when heated with phosphorus sulphide and similar compounds. (*b*) Carvacrol, when heated with phosphorus pentoxide, yields propylene and *o*-cresol. (*c*) Thymol, when similarly treated, yields propylene and *m*-cresol.

$$C_3H_7 \cdot C_6H_3(CH_3)(OH) = C_3H_6 + OH \cdot C_6H_4 \cdot CH_3 \ (o \text{ or } m)$$

B. Dihydric Phenols

By the entrance of two hydroxyls into benzene and its homologues, the dihydric phenols are produced. These are analogous to the monohydric compounds in most of their relations, but differ from them in the same way as the dihydric alcohols from the monohydric. The methods of formation are analogous to those used for the monohydric phenols, especially by fusion of sulphonic acids and halogen derivatives with potash; instead, however, of the compound expected, an isomeride which is stable at that high temperature frequently results (see Resorcinol). The *p*-dihydroxy-compounds are characterized by their close connection with the quinones. Many of the polyhydric phenols are strong reducing agents.

Catechol, formerly called **pyrocatechin**, $C_6H_4(OH)_2$ (1:2), which was first obtained by the distillation of catechin (*Mimosa Catechu*), is present in raw beet-sugar, and is obtained when many resins or *o*-phenol-sulphonic acid are fused with potash. It crystallizes in short, white, rhombic prisms,

which can be sublimed, and dissolves readily in water, alcohol, and ether.

It is usually prepared by heating its mono-methyl ether, **guaiacol**, $C_6H_4(OH)(OCH_3)$, a constituent of beech-wood tar, with hydriodic acid (see Anisole, p. 410). Like most of the polyhydric phenols, it is very unstable in alkaline solution, which quickly becomes green and then black in the air. The aqueous solution is coloured green by ferric chloride, and then violet by ammonia (reactions of the *o*-dihydroxy-compounds). It possesses reducing properties, and precipitates silver even from a cold solution of silver nitrate. By the continued action of chlorine upon it, derivatives of pentamethylene and finally of the fatty series result (*Zincke* and *Kusten*). By boiling it with potash and potassic methyl-sulphate, it may be reconverted into guaiacol, which likewise shows the ferric chloride reaction and possesses reducing powers.

Resorcinol, or *m-Dihydroxy-benzene* (*Hlasiwetz, Barth*, 1864), is obtained when many resins (Galbanum, Asafœtida), *m*-phenol-sulphonic acid, all three bromo-benzene-sulphonic acids, or *m*- and *p*-benzene-disulphonic acids are fused with potash. The last-mentioned compounds are employed for its preparation on the technical scale. It crystallizes in rhombic prisms or plates, which quickly become brown in the air, dissolves readily in water, alcohol, and ether, and reduces an aqueous solution of silver nitrate when warmed with it, and an alkaline solution even in the cold. With ferric chloride it gives a dark-violet coloration. It acts therapeutically like carbolic acid, only more mildly.

When heated with phthalic anhydride, it is converted into fluorescein (p. 493); test for *m*-dihydroxy-benzenes), and it is therefore manufactured on the large scale. Nitrous acid or diazonium compounds transform it into azo-dyes; with the latter it can yield mono-azo-dyes or primary bis-azo-dyes (cf. p. 402) Its trinitro-derivative is **styphnic acid**, $C_6H(OH)_2(NO_2)_3$, which is formed by the action of nitric acid upon many gum resins.

Quinol, formerly called **hydroquinone**, *p-dihydroxy-benzene* (*Wohler*, 1844), may be obtained by the oxidation of quinic acid, $C_7H_{12}O_6$, by means of PbO_2, by the hydrolysis of the glucoside arbutin, and from succinylo-succinic ester (cf. p. 241), &c. It is usually prepared by the reduction of quinone with sulphurous acid, and hence the name hydroquinone. It crystallizes in monoclinic plates or hexagonal prisms, of about the same solubility as its isomers, and may be

sublimed. Ammonia colours it reddish-brown, while chromic acid, ferric chloride, and other oxidizing agents convert it into quinone or quinhydrone (p. 431). It melts at 169°, and, being a strong reducing agent, it is used as a developer in photography.

Lead acetate solution yields a white precipitate with a solution of catechol, but none with resorcinol, while quinol is only precipitated in presence of ammonia. From the observed heats of neutralization, resorcinol and quinol behave towards soda as dibasic acids, and catechol as a weak monobasic acid.

Orcinol, or *m-Dihydroxy-toluene*, (CH_3:OH:OH = 1:3:5), is found in many lichens (*Rocella tinctoria*, *Lecanora*, &c.). It is formed by the elimination of carbon dioxide from orsellinic acid, *e.g.* upon fusing extract of aloes with potash, and it can also be prepared synthetically from toluene (B. **15**, 2992). Of especial interest is its synthesis from ethyl acetone-dicarboxylate (p. 260) and sodium (B. **19**, 1446). It does not yield a fluorescein with phthalic anhydride.

Homo-catechol, $C_6H_3(CH_3)(OH)_2$, (CH_3:OH:OH = 1:3:4), deserves mention on account of its mono-methyl ether **creosol**, $CH_3 \cdot C_6H_3(OH)(O \cdot CH_3)$, occurring in beech-wood tar. Creosol is a liquid similar to guaiacol, boiling at 220°, and, as a derivative of catechol, gives a green coloration with ferric chloride.

Quinitol (*Cyclohexane-1:4-diol*), *p-dihydroxy-hexamethylene*, $C_6H_{10}(OH)_2$, a dihydroxy-derivative of reduced benzene, is obtained synthetically by the reduction of *p*-diketo-hexamethylene. It crystallizes in crusts, and has a sweet taste with a bitter after-taste; m.-pt 144°. It is the simplest representative of the inosite sugar group (p. 421).

C. Trihydric Phenols

Pyrogallol, *Pyrogallic acid* (*Scheele*, 1786), 1:2:3-*trihydroxybenzene*, is the most important of these three isomers. It is obtained, apart from synthetical reactions, by heating gallic acid, when carbon dioxide is eliminated:

$$C_6H_2(OH)_3 \cdot CO_2H = C_6H_3(OH)_3 + CO_2.$$

It crystallizes in white plates, melts at 132°, is readily soluble in water, and capable of subliming without decomposition. It is an energetic reducing agent, *e.g.* for silver salts, and is used as a developer in photography. Its alkaline solution rapidly absorbs oxygen, hence its use in gas analysis.

The aqueous solution is coloured bluish-black by a solution of ferrous sulphate containing ferric salt, and purple-red by iodine. It does not react with hydroxylamine (cf. Phloroglucinol).

Pyrogallol dimethyl ether, $C_6H_3(OH)(OCH_3)_2$ (*Hofmann*), is contained in beech-wood tar, as are likewise the dimethyl ethers of the compounds $C_6H_2(CH_3)(OH)_3$ and $C_6H_2(C_3H_7)(OH)_3$, homologous with pyrogallol.

Phloroglucinol, or 1:3:5-*Trihydroxy-benzene* (*Hlasiwetz*, 1855), is obtained by the fusion of various resins and of resorcinol with potash or soda, by the action of alkali upon the glucoside phloretin, and by fusing its dicarboxylic ester (whose synthetical formation is given on p. 439) with potash. It forms large prisms which weather in the air, melts at 218°, and sublimes without decomposition. With ferric chloride it gives a dark-violet coloration, its solutions in alkalis readily absorb carbon dioxide, and it possesses reducing properties.

Phloroglucinol is a typical example of a tautomeric compound.

In many reactions, *e.g.* (*a*) the formation of metallic derivatives, $C_6H_3(OK)_3$; of a trimethyl ether, $C_6H_3(OCH_3)_3$, which is insoluble in alkali; and of a triacetyl derivative, $C_6H_3(OAc)_3$; (*b*) its combination with phenyl-carbimide to form a tricarbaniline derivative, $C_6H_3(O\cdot CO\cdot NH\cdot C_6H_5)_3$, it reacts as a normal phenol, *i.e.* as sym. trihydroxy-benzene. On the other hand, however, in certain of its reactions it behaves as a ketone, *i.e.* as triketo-hexamethylene, $CO<\begin{matrix}CH_2\cdot CO\\CH_2\cdot CO\end{matrix}>CH_2$; thus it yields a trioxime, $C_6H_6(:N\cdot OH)_3$, and when alkylated in presence of alcoholic potash yields tetra- and hexa-alkyl derivatives, *e.g.* $C_6Me_6O_3$, $CO<\begin{matrix}CMe_2\cdot CO\\CMe_2\cdot CO\end{matrix}>CMe_2$. Its ultra-violet absorption spectrum (*Hedley*, J. C. S. 1906, 730) resembles that of other phenols.

Hydroxy-quinol, 1:2:4-*Trihydroxy-benzene*, is obtained by fusing quinol with potash. Like pyrogallol, it yields no oxime with hydroxylamine.

Hexahydroxy-benzene, $C_6(OH)_6$, forms as its potassium salt potassium carboxide, $C_6O_6K_6$, the explosive compound sometimes obtained in the manufacture of metallic potassium. It crystallizes in colourless prisms, has no definite melting-point, but decomposes at about 200°, and can be converted into its quinone.

Quercitol, $C_6H_7(OH)_5$, found in the oak, and **inosite** or **inositol**, $C_6H_6(OH)_6$, found in the muscles of the heart, are polyhydroxy-derivatives of hexamethylene. In many respects they closely resemble the aliphatic polyhydric alcohols rhamnitol and sorbitol. Quercitol melts at 235°; is optically active, and has $[\alpha]_D = +24{\cdot}16$. Inositol or hexahydroxy-cyclohexane exists in an inactive and in *d*-, *l*-, and *r*-modifications.

XXV. AROMATIC ALCOHOLS, ALDEHYDES, AND KETONES

A. Aromatic Alcohols

While the phenols remind us of the tertiary alcohols of the fatty series, although they differ from these in many points, we are acquainted with compounds which possess the alcoholic character in its entirety; they are termed aromatic alcohols. The most important of these is (primary) benzyl alcohol, $C_7H_7 \cdot OH$, which is isomeric with the cresols, this isomerism being explained by the different position of the hydroxy-group in the molecule; thus, while the cresols, like all phenols, contain the hydroxyl linked to the benzene nucleus, in benzyl alcohol it is present in the side chain:

$CH_3 \cdot C_6H_4 \cdot OH$ (cresols) $\quad C_6H_5 \cdot CH_2 \cdot OH$ (benzyl alcohol)

This follows from the formation of benzyl alcohol from benzyl chloride, $C_6H_5 \cdot CH_2Cl$ (and *vice versa*), and also from the fact that it can be oxidized to an aldehyde and an acid containing the same number of carbon atoms in the molecule as itself, these being likewise mono-derivatives of benzene:

$C_6H_5 \cdot CH_2 \cdot OH$	$C_6H_5 \cdot CHO$	$C_6H_5 \cdot CO \cdot OH$
Benzyl alcohol (Benzene-methylol)	Benzaldehyde (Benzene-methylal)	Benzoic acid (Benzene-carboxylic acid)

Benzyl alcohol may also be looked upon as methyl alcohol in which one atom of hydrogen is replaced by the group C_6H_5:

$H \cdot CH_2 \cdot OH$ (carbinol) $\quad C_6H_5 \cdot CH_2 \cdot OH$ (phenyl-carbinol),

and is therefore the simplest aromatic alcohol.

In addition to primary alcohols, *e.g.* tolyl alcohols, $CH_3 \cdot C_6H_4 \cdot CH_2OH$, β-phenyl-ethyl alcohol, $C_6H_5 \cdot CH_2 \cdot CH_2OH$,

secondary, *e.g.* α-phenyl-ethyl alcohol, or 1-*phenyl-hydroxy-ethane*, $C_6H_5 \cdot CH(OH) \cdot CH_3$, and even tertiary alcohols, *e.g.* $(C_6H_5)_3C \cdot OH$, triphenyl-carbinol, are known. Of the polyhydric alcohols, phenyl-glycerol (1-phenyl-1:2:3-trihydroxypropane) is the most important. All of these contain the hydroxyl radicals attached to carbon atoms of the side chain and not to those of the nucleus, and this is the fundamental difference between an aromatic alcohol and a phenol. The alcohols are not of the same commercial importance as the phenols, and hence have not been investigated to the same extent.

All these compounds are, as alcohols, perfectly analogous to the alcohols of the fatty series, so far as regards the formation of alcoholates, ethers, esters, mercaptans, amines, phosphines, &c. They are, however, at the same time benzene derivatives, and consequently yield chloro-, bromo-, nitro-, amino-, &c., substitution products. Unsaturated aromatic alcohols are also known, which resemble the unsaturated compounds of the fatty series to the closest extent in their chemical behaviour, but are at the same time benzene derivatives.

These remarks also apply in full degree, *mutatis mutandis*, to the aromatic aldehydes and ketones (see below).

Benzyl alcohol, $C_6H_5 \cdot CH_2 \cdot OH$, is a colourless liquid of faint aromatic odour, sparingly soluble in water, and boils at 204°. It occurs naturally in Peru and Tolu balsams as benzoic and cinnamic esters, and is formed from benzyl chloride just as alcohol is from ethyl chloride. It is usually prepared by the action of concentrated aqueous potash on benzaldehyde, whereby the one half of the aldehyde is oxidized and the remainder reduced (B. **14**, 2394):

$$2C_6H_5 \cdot CHO + KOH = C_6H_5 \cdot CH_2 \cdot OH + C_6H_5 \cdot COOK.$$

Benzyl alcohol is also formed when benzamide is reduced with sodium amalgam. This is a reaction which has been employed for the preparation of a number of substituted benzyl alcohols (*Hutchinson*, B. 1891, **24**, 173).

Phenyl-methyl-carbinol, $C_6H_5 \cdot CH(OH) \cdot CH_3$, b.-pt. 203°, can be prepared by reducing acetophenone, $C_6H_5 \cdot CO \cdot CH_3$ (p. 427), into which it is reconverted by gentle oxidation.

Numerous secondary and tertiary alcohols have been synthesized within recent years by means of *Grignard's* compounds (p. 356).

The simplest of the unsaturated alcohols is **cinnamic alco-**

("styracin") in storax. It crystallizes in glistening needles of hyacinth-like odour, yields cinnamic acid when gently oxidized, and benzoic when the oxidation is more vigorous.

B. Aromatic Aldehydes

Benzaldehyde, *Benzene-methylal*, or *oil of bitter almonds*, $C_6H_5 \cdot CHO$, was discovered in 1803 and investigated by *Liebig* and *Wohler* (A. **22**, 1). It is a colourless, strongly refracting liquid of agreeable bitter almond-oil odour. It boils at 179°, has a sp. gr. 1·05 at 15°, and is readily soluble in alcohol and ether, but only sparingly in water (1 in 30).

The modes of formation are for the most part analogous to those described under the aliphatic aldehydes (pp. 122 and 123):

(*a*) By the oxidation of the corresponding alcohol. This method, although of considerable practical importance in the aliphatic series, is of but theoretical interest in the aromatic, as the alcohols themselves are usually prepared from the aldehydes.

(*b*) By the distillation of the calcium salt of the corresponding acid, benzoic acid, with calcium formate.

(*c*) By heating the corresponding dichloride, benzal chloride, or benzylidene chloride, $C_6H_5 \cdot CHCl_2$ (from toluene), with water or sulphuric acid, or, as is done on the technical scale, with water and lime, also by heating benzyl chloride, $C_6H_5 \cdot CH_2Cl$, with water and plumbous or cupric nitrate.

This last method involves a process of hydrolysis:

$$C_6H_5 \cdot CH_2Cl \longrightarrow C_6H_5 \cdot CH_2 \cdot OH,$$

and also a process of oxidation:

$$C_6H_5 \cdot CH_2 \cdot OH \longrightarrow C_6H_5 \cdot C\!\leqslant\!{}^{H}_{O},$$

both of which are brought about by the copper nitrate solution.

(*d*) Together with dextrose and hydrocyanic acid by decomposing **amygdalin**, $C_{20}H_{27}O_{11}N$, a glucoside (see Glucosides) which occurs in bitter almonds and crystallizes in white plates, either by means of sulphuric acid or by emulsin (an enzyme likewise present in bitter almonds, cf. pp 267 and 592):

$$C_{20}H_{27}O_{11}N + 2H_2O = C_6H_5 \cdot CHO + 2C_6H_{12}O_6 + CNH.$$

(*e*) By the action of chromyl chloride, CrO_2Cl_2, upon toluene.

This is *Etard's* reaction, and is of great value for the synthesis of aldehydes and also of certain ketones from hydrocarbons. An additive compound, $C_6H_5 \cdot CH_3(CrO_2Cl_2)_2$, is first formed, and yields the aldehyde on the addition of water (B. **17**, 1462, 1700; **32**, 1050.

(*f*) By the action of *Grignard's* phenyl-magnesium bromide on ethyl orthoformate (*Bodroux*, C. R. 1904, **138**, 92 and 700), *e.g.*:

$$C_6H_5 \cdot Mg \cdot Br + CH(OEt)_3 = Mg \cdot Br \cdot OEt + C_6H_5 \cdot CH(OEt)_2$$

$$C_6H_5 \cdot CH(OEt)_2 \xrightarrow{\text{hydrolysed}} C_6H_5 \cdot CHO.$$

Gattermann and *Maffezzoli* (B. 1903, **36**, 4152) have used *Grignard's* compound with a large excess of ethyl formate at low temperatures.*

(*g*) Homologues of benzaldehyde are sometimes prepared by the elimination of carbon dioxide from substituted phenyl-glyoxylic acids:

$$C_6H_4X \cdot CO \cdot CO_2H \rightarrow C_6H_4X \cdot C\overset{H}{\underset{O}{<}},$$

a reaction which usually takes place when the glyoxylic acid is distilled.

Behaviour.—1. Its behaviour is that of an aldehyde, and in many respects it closely resembles the aliphatic aldehydes. Thus it is (*a*) easily oxidizable to the acid, and on this account reduces an ammoniacal silver solution with the production of a mirror; (*b*) reducible to the alcohol; (*c*) capable of forming a crystalline additive compound with $NaHSO_3$; (*d*) capable of combining with HCN (see Mandelic acid); (*e*) capable of reacting with hydroxylamine and phenyl-hydrazine to benzaldoxime, $C_6H_5 \cdot CH:N \cdot OH$, and benzaldehyde-phenyl-hydrazone, $C_6H_5 \cdot CH:N_2H \cdot C_6H_5$, respectively; (*f*) converted into benzylidene chloride, $C_6H_5 \cdot CHCl_2$, by the action of phosphorus pentachloride.

2. Benzaldehyde does not form an additive compound with ammonia analogous to the aldehyde-ammonias of the aliphatic series, but enters into a somewhat complex condensation, the oxygen of the aldehyde being eliminated with the hydrogen atoms of ammonia in the form of water, the complex condensation product hydrobenzamide being formed:

$$3C_6H_5 \cdot CHO + 2NH_3 = (C_6H_5 \cdot CH)_3N_2 + 3H_2O.$$

3. Benzaldehyde and its homologues can undergo poly-

* For synthetical methods see *Gattermann*, A. 1906, **347**, 347.

merization, *e.g.* when an alcoholic solution of benzaldehyde is boiled with potassium cyanide, **benzoin** is formed:

$$C_6H_5\cdot CH{:}O + C_6H_5\cdot CH{:}O = C_6H_5\cdot CH(OH)\cdot CO\cdot C_6H_5,$$

a compound which is both a secondary alcohol and a ketone.

4. A number of condensation products can be obtained from the aromatic aldehydes, and many of these are of commercial importance. The condensation usually takes place in the presence of a condensing agent, *e.g.* acetic anhydride, anhydrous zinc chloride, potassic hydroxide, sodic ethoxide, &c. Among some of the simplest of these condensations are:—

(*a*) With primary amines. The formation of benzylidene anilines (*Schiff's Bases*):

$$C_6H_5\cdot CH{:}O + H_2N\cdot C_6H_5 = H_2O + C_6H_5\cdot CH{:}N\cdot C_6H_5$$

It has been shown recently that this reaction is preceded by the formation of an additive compound, $C_6H_5\cdot CH(OH)\cdot NH\cdot C_6H_5$, which then passes into the benzylidene derivative A few such additive compounds have actually been isolated. (*Dimroth* and *Zoepritz*, B. 1902, **35**, 984.)

(*b*) With tertiary amines, *e.g.*.

$$2C_6H_5\cdot NMe_2 + C_6H_5\cdot CHO = H_2O + C_6H_5\cdot CH(C_6H_4\cdot NMe_2)_2,$$

when a substituted diamino-derivative of triphenyl-methane is produced (p 483)

(*c*) With the sodium salts of fatty acids, when unsaturated acids are formed (*Perkin's Synthesis*, pp. 441 and 442):

$$C_6H_5\cdot CHO + CH_3\cdot COONa = C_6H_5\cdot CH{:}CH\cdot CO_2Na + H_2O.$$

(*d*) With fatty aldehydes, ketones, &c.:

$$C_6H_5\cdot CH{:}O + CH_3\cdot CH{:}O = H_2O + C_6H_5\cdot CH{:}CH\cdot CHO,$$

when unsaturated aldehydes (*e.g.* cinnamic aldehyde) or ketones are formed.

5. Its reaction with alkalis (p. 422) is also different; in the fatty series aldehyde resins are formed, and with benzaldehyde a mixture of primary alcohol and the corresponding acid. This latter reaction is characteristic of aldehydes in which the CHO group is directly attached to the benzene nucleus.

6. As a benzene derivative, it can be substituted by halogens (indirectly), and can be nitrated, sulphonated, &c. (directly).

As in the case of toluene, chlorine enters the side chain at the boiling temperature, with formation of benzoyl chloride, $C_6H_5 \cdot COCl$.

Among its derivatives, the following deserve mention:—

α-Benzaldoxime, *Benz-anti-aldoxime*, $C_6H_5 \cdot CH:N \cdot OH$, is formed from benzaldehyde and hydroxylamine; it melts at 35°, and decomposes when boiled. It can be transformed by means of acids into the isomeric **β-benzaldoxime**, *benz-syn aldoxime*, which melts at 125° (for velocity, cf. *Patterson*, J C. S. 1907, 504; 1908, 1041), and in contradistinction to the isomer, readily reacts with acetic anhydride yielding benzo nitrile. The oximes are stereo-isomeric (Nitrogen-isomerism). (Cf. pp. 138 and 428.)

Benzaldehyde-phenyl-hydrazone, $C_6H_5 \cdot CH:N \cdot NHC_6H_5$ forms colourless crystals, melting at 152°. **Benzylideneazine** $CHPh:N \cdot N:CHPh$, from benzaldehyde and hydrazine sulphate, has m.-pt. 93°.

Nitro-benzaldehydes, $NO_2 \cdot C_6H_4 \cdot CHO$.—The *m*-compound is the chief product of nitration, but some 20 per cent of the *o*-compound is formed at the same time. The latter is best prepared by oxidizing *o*-nitro-cinnamic acid by $KMnO_4$ in presence of benzene; it forms long colourless needles, melting at 46°, yields indigo (p. 527) with acetone and caustic soda, and on exposure to sunlight forms *o*-nitroso-benzoic acid. It can be reduced to ***o*-amino-benzaldehyde**, $NH_2 \cdot C_6H_4 \cdot CHO$, a compound crystallizing in silvery glistening plates, m.-pt. 46° which is of value for various synthetical reactions (See Quinoline; also B. **16**, 1833.) ***m*-Amino-benzaldehyde**, which is prepared from *m*-nitro-benzaldehyde, by the reduction of its bisulphite compound, is used in the production of triphenyl methane dyes.

Cinnamic aldehyde, $C_6H_5 \cdot CH:CH \cdot CHO$, is the chief constituent of oil of cinnamon (*Persea cinnamomum*), from which it may be isolated by means of its bisulphite-compound. It is an oil of aromatic odour, boils at 246°, and is readily volatile with steam. In addition to its properties as an aldehyde, it also possesses the properties of an unsaturated compound, *e.g.* forms a dibromide. Its reaction with potassium hydrogen sulphite is characteristic. It first forms an additive compound $C_6H_5CH:CH \cdot CH(OH)(SO_3K)$, like an ordinary aldehyde, and then, as an unsaturated compound, combines with a second molecule of the sulphite, yielding $C_6H_5 \cdot CH(SO_3K) \cdot CH_2 \cdot CH(OH)(SO_3K) + 2H_2O$. (B. **24**, 1805; **31**, 3301.)

C. Aromatic Ketones

The aromatic ketones are usually divided into (1) mixed aromatic ketones, viz. those which contain both an aryl and an alphyl group, *e.g.* $C_6H_5 \cdot CO \cdot CH_3$, and (2) true aromatic or diaryl ketones, *e.g.* $C_6H_5 \cdot CO \cdot C_6H_5$.

Acetophenone, *Phenyl-methyl ketone*, $C_6H_5 \cdot CO \cdot CH_3$, is the simplest representative of the mixed aromatic ketones. It crystallizes in colourless plates, is readily soluble in water, melts at 20°, boils at 200°, and is obtained by the normal modes of preparation for ketones, *e.g.* by distilling a mixture of acetate and benzoate of calcium, as also by the *Friedel-Crafts'* synthesis (p. 346), viz. the conjoint action of acetyl chloride and aluminium chloride upon benzene. When benzene and its derivatives are converted into ketones by this method, only one acyl group is introduced as a rule, and this into the para-position with respect to any alkyl group already present. With a sym. trialkylated benzene, *e.g.* mesitylene, it has been found possible to introduce two acyl groups, *e.g* diacetyl-mesitylene, $(CH_3)_3C_6H(COCH_3)_2$ (*V. Meyer*, B. 1895, **28**, 3212; 1896, **29**, 846, 1413). When the temperature is kept low by diluting the mixture with carbon disulphide, a good yield of ketone may be obtained by the *Friedel-Crafts'* method.

Acetophenone unites in itself the properties of a ketone of the fatty series and of a benzene derivative. It yields benzoic acid and carbon dioxide when oxidized with ordinary oxidizing agents, but with cold alkaline permanganate it yields $C_6H_5 \cdot CO \cdot CO_2H$, **phenyl-glyoxylic acid** or **benzoyl-formic acid**. When warmed with halogens, it is substituted in the side chain (*e.g.* to "**phenacyl bromide**", $C_6H_5 \cdot CO \cdot CH_2Br$), and with nitric acid it is nitrated. It is used as a soporific under the name of "*Hypnone*". Its **oxime** melts at 59°, and its **phenyl-hydrazone** at 105°.

Although it combines with hydrogen cyanide to form the nitrile of α-phenyl-lactic acid, it cannot form an additive compound with sodic hydric sulphite.

Its homologues closely resemble it, but are liquid at the ordinary temperature. Acetophenone and some of its homologues can be prepared from hydrocarbons with long side chains by *Etard's* reaction (see p. 424; B. **23**, 1070; **24**, 1356). Aromatic polyketones (cf. p. 221) have also been prepared, *e.g.* **benzoyl-acetone**, $C_6H_5 \cdot CO \cdot CH_2 \cdot CO \cdot CH_3$, and **acetophenone-acetone**, $C_6H_5 \cdot CO \cdot CH_2 \cdot CH_2 \cdot CO \cdot CH_3$. The latter, like

acetonyl-acetone, is readily converted into furane, pyrrole, and thiophene derivatives (see p. 516).

Benzaldehyde condenses with acetone and acetophenone in the presence of alkalis, yielding unsaturated ketones, *e.g* **Benzylideneacetone**, $CHPh:CH\cdot CO\cdot CH_3$, m.-pt. 41°, and **benzylideneacetophenone**, *chalcone*, $CHPh\cdot CH:CH\cdot CO\cdot C_6H_5$, m.-pt 58°.

Benzophenone, *Diphenyl ketone*, $C_6H_5\cdot CO\cdot C_6H_5$, may be obtained (1) by distilling calcium benzoate, (2) by the *Friedel-Crafts'* synthesis, (3) by the oxidation of diphenylmethane, $(C_6H_5)_2CH_2$, or of diphenyl-carbinol, $(C_6H_5)_2CH\cdot OH$.

Good yields of ketones are not usually obtained by the action of *Grignard's* reagents on acid chlorides; as a rule the reaction proceeds further, and a tertiary alcohol is obtained (p. 356). An exception is found in the reaction between α-naphthyl-magnesium bromide and benzoyl chloride.

Ketones have recently (*Blaise*, C. R. 1901, **132**, 38, **133**, 299) been synthesised from *Grignard's* reagents and nitriles, *e.g.*.

$$R\cdot CN + R'\cdot Mg\cdot I = RR'C:NMgI,$$

and this with water gives.

$$R\cdot CO\cdot R' + NH_3 + I\cdot Mg\cdot OH.$$

Acid amides react in a somewhat similar manner.

Benzophenone is dimorphous, the stable modification melts at 49°, and when boiled or distilled yields the unstable modification, melting at 26°; but this gradually passes back again into the stable modification. The reaction is, however, considerably accelerated by the addition of a minute crystal of the stable compound. It yields an **oxime** melting at 140° and a **phenyl-hydrazone** melting at 105°.

When reduced with zinc dust or hydriodic acid and red phosphorus, it yields diphenylmethane.

Stereo-isomeric Oximes and Hydrazones.—The isomerism described on pp. 137 *et seq.* is more frequently met with in the aromatic than in the aliphatic series. Benzaldehyde and most of its substitution products yield two distinct oximes and most of the unsymmetrical aromatic ketones, *e.g.* *p*-chloro-benzophenone, $C_6H_4Cl\cdot CO\cdot C_6H_5$, and tolyl-phenyl-ketone, $CH_3\cdot C_6H_4\cdot CO\cdot C_6H_5$, also yield stereo-isomeric oximes of the *syn-* and *anti-* types. The one isomeride is usually readily transformed into the more stable by means of hydrochloric acid or bromine, by rise of temperature, and by exposure to light.

The following relationships of the benzaldoximes are of interest:—

Benz-*anti*-aldoxime $\xrightarrow{HCl}$ Benz-*anti*-aldoxime hydrochloride
↑ heated ↓ heated
Benz-*syn*-aldoxime $\xleftarrow{-HCl}$ Benz-*syn*-aldoxime hydrochloride.

The *syn*- or *anti*- configuration of the isomerides is determined in the case of the aldoximes by a comparison of the readiness with which water is eliminated and a nitrile formed, and in the case of the ketoximes by an examination of the products obtained by *Beckmann's* transformation (p. 139). Thus:

$C_6H_5 \cdot C(:N \cdot OH) \cdot C_6H_4 \cdot CH_3$ gives $C_6H_5 \cdot CO \cdot NH \cdot C_6H_4 \cdot CH_3$
Phenyl-*p*-tolyl-*anti*-ketoxime — Benz-*p*-toluidide

and

$C_6H_5 \cdot C(:N \cdot OH) \cdot C_6H_4 \cdot CH_3$ gives $CH_3 \cdot C_6H_4 \cdot CO \cdot NH \cdot C_6H_5$
Phenyl-*p*-tolyl *syn*-ketoxime — Anilide of *p*-toluic acid

Compare *Hantzsch*, B 1911, **44**, 1533.

D. Hydroxy or Phenolic Alcohols, Aldehydes, and Ketones

Formula	Name	Constitution
$OH \cdot C_6H_4 \cdot CH_2OH$ . .	Saligenin, or	*o*-hydroxy-benzyl alcohol.
$OCH_3 \cdot C_6H_4 \cdot CH_2OH$ . .	Anisyl alcohol, or	*p*-methoxy-benzyl alcohol.
$OH \cdot C_6H_3(OCH_3) \cdot CH_2OH$.	Vanillic alcohol, or	3-methoxy-4-hydroxy-benzyl alcohol.
$OH \cdot C_6H_3(OCH_3)(C_3H_4 \cdot OH)$.	Conferyl alcohol,	$[OCH_3 : OH = 3.4]$
$OH \cdot C_6H_4 \cdot CHO$	Salicyl-aldehyde, or	*o*-hydroxy-benzaldehyde.
$OCH_3 \cdot C_6H_4 \cdot CHO$	Anisaldehyde, or	*p*-methoxy-benzaldehyde.
$(OH)_2C_6H_3 \cdot CHO$.	Procatechuic aldehyde, or	3:4-dihydroxy-benzaldehyde.
$OH \cdot C_6H_3(OCH_3) \cdot CHO$	Vanillin, or	3-methoxy-4-hydroxy-benzaldehyde.
$CH_2O_2 : C_6H_3 \cdot CHO$	Piperonal, artificial heliotrope or	methylene-protocatechuic aldehyde.

A large number of compounds are known which possess

phenolic properties in addition to those of an alcohol, aldehyde or ketone. They are derived from the simple alcohols, &c., by the entrance of hydroxyl into the benzene nucleus.

Several of these compounds occur in nature, *e.g.* saligenin is a constituent of salicin (see the Glucosides), while salicylic aldehyde is found in Spiræa varieties and vanillin in vanilla capsules. Anisaldehyde is obtained from the oxidation of anisole (methyl phenyl ether).

An extremely interesting synthesis of hydroxy-aldehydes is by the *Tiemann-Reimer* reaction. This consists of heating a phenol with chloroform in the presence of concentrated potassium hydroxide:

$$C_6H_5\cdot OK + CHCl_3 = HCl + CHCl_2\cdot C_6H_4\cdot OK,$$

and the dichlor-derivative thus formed is hydrolysed by the alkali to $CHO\cdot C_6H_4\cdot OK$. The formyl-group $\cdot CH{:}O$ always takes up the *o*- or *p*-position with respect to the hydroxy-group, and, as a rule, the *o*- and *p*-compounds are formed together, and may often be separated by the difference in volatility of the two compounds in steam.

Vanillin crystallizes in beautiful needles, and is prepared on the large scale from **coniferin**, $C_{16}H_{22}O_8 + 2H_2O$, a compound occurring in the sap of the cambium in the Coniferæ. This is hydrolysed by acids into glucose and **coniferyl alcohol**, $C_6H_3(OH)(OCH_3)(C_3H_4\cdot OH)$, and the latter yields vanillin when oxidized (*Tiemann* and *Haarmann*); the CH_3 group is removed by heating with hydrochloric acid at 200°, with the formation of protocatechuic aldehyde. Vanillin is also found in asparagus, raw beet-sugar, and asafœtida, and it likewise results from the oxidation of olive wood, &c.

Vanillin can also be obtained synthetically from *m*-chloro-*p*-nitro-benzaldehyde (from *m*-chloro-*p*-nitro-toluene)

E. Quinones

Quinones are compounds derived from benzene and its derivatives by the replacement of two atoms of hydrogen by two of oxygen, *e.g.* $C_6H_4O_2$. As a group they are characterized by (*a*) their yellow colour, (*b*) being readily reduced to dihydric phenols, and hence often acting as oxidizing agents. They are often divided into **para-quinones**, in which the two oxygen atoms are in the *p*-position, and **ortho-quinones**, in which they are in the *o*-position.

***p*-Benzoquinone** or *Quinone*, $C_6H_4O_2$ (1838), is produced when chromic acid is added to a solution of quinol. It crystallizes in yellow needles or prisms of a characteristic pungent odour something like that of nut-shells, is sparingly soluble in water but readily in alcohol and ether, and can be sublimed; m.-pt. 116°. Corresponding with it we have a large number of higher homologues, &c. These also are solids, mostly of a yellow colour, and are volatile with steam; they are obtained by the oxidation of the corresponding dihydroxy-phenols, or of polyhydric phenols, which contain two hydroxyls in the para-position.

Quinone is also formed by the oxidation of many aniline and phenol derivatives belonging to the para-series, *e.g.* *p*-amino-phenol, sulphanilic acid, and *p*-phenol-sulphonic acid; it is usually prepared by the oxidation of aniline itself by means of chromic acid (see B. 1887, **20**, 2283). It was first obtained by distilling quinic acid with manganese dioxide and sulphuric acid. Exposure to light causes it to turn brown, and it colours the skin yellow-brown. It is readily reduced to quinol by SO_2, HI, $SnCl_2$ and HCl, &c, and can therefore act as an oxidizing agent.

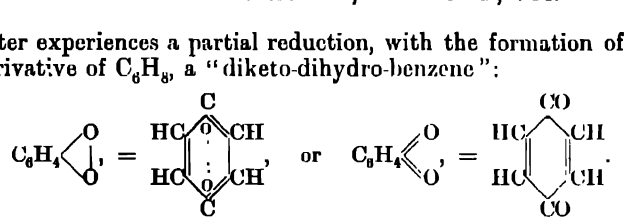
In chloroform solution it takes up two or four atoms of bromine to form a di- or tetra-bromide ($C_6H_4O_2 \cdot Br_4$). Under other conditions chlorine and bromine act upon it as substituents, while hydrochloric acid forms chloroquinol:

$$C_6H_4O_2 + HCl = C_6H_3Cl(OH)_2.$$

It yields sparingly soluble crystalline compounds with primary amines, and also coloured compounds with phenols. With quinol it forms an additive compound termed **quinhydrone**, $C_6H_4O_2 + C_6H_4(OH)_2$, this crystallizes in green prisms with a metallic lustre, and is also formed as an intermediate product in the oxidation of quinol or in the reduction of quinone. Its constitution has not been definitely settled. (Cf. *Sieg mund*, J. pr. 1911, **83**, 553; also *Knorr*, B. 1911, **44**, 1503.)

Constitution.— Quinone is derived from benzene by the exchange of two atoms of hydrogen for two of oxygen, which, from the close connection between quinone and quinol, must be in the *p*-position. The constitution of quinone may be explained either by assuming that these two oxygen atoms are linked together, as in peroxide of hydrogen, H·O·O·H, so that the benzene nucleus remains unchanged, or that the

latter experiences a partial reduction, with the formation of a derivative of C_6H_8, a "diketo-dihydro-benzene":



According to the first of these two formulæ, quinone would be a peroxide; according to the second, a ketone. In favour of the latter view (which was brought forward by *Fittig*, and is now almost universally accepted) are (1) the fact that quinone can be converted into an oxime, $C_2H_2<\begin{matrix}C(N\cdot OH)\\ -CO-\end{matrix}>C_2H_2$ (identical with nitroso-phenol, p. 414), and into a dioxime, **quinone dioxime**, $C_2H_2<\begin{matrix}C(N\cdot OH)\\ C(N\cdot OH)\end{matrix}>C_2H_2$ (B **20**, 613); (2) its power of forming additive compounds with bromine, and (3) its relations to the analogously constituted anthraquinone. (Cf. B. **18**, 568; A. **223**, 170; J. pr. Ch **42**, 161 Also chapter on Physical Properties and Constitution.)

Tetrahydro-quinone, *p-Diketo-hexamethylene* (*cyclo-hexane*-1 4-*dione*),

$$\begin{matrix}CH_2\cdot CO\cdot CH_2\\ CH_2\cdot CO\cdot CH_2\end{matrix},$$

can be prepared by hydrolysing and eliminating the carboxyl groups from succinylo-succinic ester (p 343). It crystallizes in colourless prisms, melts at 78°, and, on reduction, yields quinitol (p. 419). (Cf. B. **22**, 2168; **23**, 1272.)

Chloranil, *Tetrachloro-quinone*, $C_6Cl_4O_2$, which crystallizes in lustrous yellow plates, is obtained by chlorinating quinone and also by oxidizing many organic compounds, *e.g.* phenol, with HCl and $KClO_3$. A good yield may be obtained by chlorinating *p*-nitraniline, reducing the 2:6-dichloro-4-nitraniline thus obtained to 2:6-dichloro-*p*-phenylene-diamine, and then oxidizing and chlorinating by means of potassic chlorate and hydrochloric acid:

$$NO_2\cdot C_6H_4\cdot NH_2 \rightarrow NO_2\cdot C_6H_2Cl_2\cdot NH_2 \rightarrow C_6H_2Cl_2(NH_2)_2 \rightarrow C_6Cl_4O_2$$

(*Witt.* Abstr. 1904, **1**, 174.) When reduced, it yields the colourless tetrachloro-quinol; it also acts as an oxidizing agent, converting *e.g.* dimethylaniline into methyl-violet. A dilute

solution of potassium hydroxide transforms it into **potassium chloranilate**, $C_6Cl_2O_2(OK)_2 + H_2O$ (dark-red needles), corresponding with which there is also an analogous nitro-compound, **potassium nitranilate**, $C_6(NO_2)_2O_2(OK)_2$. The latter salt is distinguished by its sparing solubility, hence its formation may be made use of as a test for potassium compounds. (For its constitution, see B. **19**, 2398.)

Chlorine transforms chloranil and chloranilic acid into complex chloro-products of the hexa- and pentamethylene series, and finally into chlorinated fatty compounds. (For a tabular summary, see *Hantzsch*, B. **22**, 2841; cf. also B. **25**, 827, 842.)

Toluquinone, $C_6H_3(O_2)(CH_3)$, **xyloquinone**, $C_6H_2(O_2)(CH_3)_2$, **thymoquinone**, $C_6H_2(O_2)(CH_3)(C_3H_7)$, &c., are known. Several of these can be prepared synthetically by the condensation of 1·2 diketones, for instance, diacetyl yields xyloquinone under the influence of alkali (cf. B. **21**, 1411 and p. 342).

$$CH_3\cdot CO\cdot CO\cdot CH\,H_2 \\ +\ H_2\,CH\cdot CO\cdot C\,O\cdot CH_3 = \begin{matrix} CH_3\cdot C\cdot CO\cdot CH \\ \| \qquad\quad \| \\ HC\cdot CO\cdot C\cdot CH_3 \end{matrix} + 2H_2O$$

o **Benzoquinone**, $CO\langle\begin{matrix}CO\cdot CH\\ CH:CH\end{matrix}\rangle CH$, isomeric with the *p*-compound, has been recently prepared by *Willstätter* and *Pfannenstiel* (B. 1904, **37**, 4744) by the oxidation of an ethereal solution of catechol (*o*-dihydroxy-benzene) with silver oxide. It forms pale-red transparent plates, is relatively unstable, and begins to decompose at 60°–70°. It is readily reduced by sulphur dioxide to catechol, and dyes the skin brown. For two isomeric forms, cf. B. 1908, **41**, 2580, 1911, **44**, 2632.

F. Quinone Chlorimides, Quinone Aniles, and Anilino-quinones

A number of nitrogen derivatives closely related to the quinones are known. As examples, we have $C_6H_4\langle\begin{matrix}N\cdot Cl\\ O\end{matrix}\rangle$, quinone chlorimide; $C_6H_4\langle\begin{matrix}NCl\\ NCl\end{matrix}\rangle$, quinone dichlorimide; $C_6H_4\langle\begin{matrix}N\cdot OH\\ O\end{matrix}\rangle$, quinone oxime, and the corresponding dioxime; $C_6H_4\langle\begin{matrix}N\cdot C_6H_5\\ O\end{matrix}\rangle$, quinone anile, and $C_6H_4\langle\begin{matrix}N\cdot C_6H_5\\ N\cdot C_6H_5\end{matrix}\rangle$, quinone dianile.

The **quinone chlorimides** are obtained by the oxidation of the *p*-amino-phenols or *p*-phenylene-diamines with bleaching

powder, *e.g.* **quinone chlorimide**, $O:C_6H_4:NCl$, from *p*-amino-phenol hydrochloride, and **quinone dichlorimide**, $Cl\cdot N:C_6H_4:N\cdot Cl$, from *p*-phenylene-diamine hydrochloride. The first-named crystallizes in golden-yellow crystals, which are volatile with steam; when reduced it yields amino-phenol, and when boiled with water quinone; the dichorimide reacts similarly.

Quinone monoxime, obtained by the action of hydroxyl-amine hydrochloride on quinone (*H. Goldschmidt*, B. 1884, **17**, 213), is identical with the compound obtained by the action of nitrous acid on phenol, or by the hydrolysis of *p*-nitroso-dimethyl-aniline, and previously termed *p*-nitroso-phenol. It would appear to have the oxime constitution $O:C_6H_4:N\cdot OH$, as with hydroxylamine it yields the dioxime $OH\cdot N:C_6H_4:N\cdot OH$, and when alkylated yields ethers of the type $O:C_6H_4:N\cdot OR$. (Cf. also *Hartley*, J. C. S. 1904, 1016.)

Quinone monanile is obtained by oxidizing *p*-hydroxy-diphenylamine, $OH\cdot C_6H_4\cdot NH\cdot C_6H_5$, and forms fiery red crystals melting at 97°; with aniline it yields dianilino-quinone anile, $O:C_6H_2(NHPh)_2:NPh$. The dianile is obtained by oxidizing diphenyl-*p*-phenylene-diamine, $C_6H_4(NHPh)_2$, it melts at 175°–180°, and its dianilide, viz dianilino-quinone dianile, $NPh:C_6H_2(NHPh)_2:NPh$, is most readily obtained by heating *p*-nitroso-dimethyl-aniline with aniline and aniline hydrochloride. Such anilino-quinone aniles are usually termed **azophenines** (*Fischer* and *Hepp*, A. 1889, **256**, 257; 1890, **262**, 217). The important groups of aniline dyes known as **indophenols** and **indamines** are respectively hydroxy- and amino-derivatives of these aniles, *e.g.* **phenol blue** is $(CH_3)_2N\cdot C_6H_4\cdot N:C_6H_4:O$, and is obtained by oxidizing a mixture of amino-dimethyl-aniline and phenol; the corresponding α-naphthol derivative, $NMe_2\cdot C_6H_4\cdot N:C_{10}H_7:O$, is an important blue dye.

G. Pseudo-phenols. Methylene-quinones

Numerous phenolic alcohols react with halogen hydracids yielding the corresponding esters of the alcohols, *e.g.*

$$OH\cdot C_6H_3Br\cdot CH_2\cdot OH \longrightarrow OH\cdot C_6H_3Br\cdot CH_2Br,$$
$$OH\cdot C_6Br_2Me_2\cdot CH_2\cdot OH \longrightarrow OH\cdot C_6Br_2Me_2\cdot CH_2\cdot Br;$$

but the products thus obtained are insoluble in alkalis, and are characterized by the reactivity of the bromine atom in the $\cdot CH_2Br$ group. The compounds have been termed by *Auwers* **pseudo-phenols**, and they are usually regarded as *o*- or *p* quinone

derivatives, *e.g.* the two compounds mentioned above are represented as

$$O{:}C_6H_3Br{<}^{H}_{CH_2Br} \quad \text{and} \quad O{:}C_6Br_2Me_2{<}^{H}_{CH_2Br}.$$

Such compounds readily react with alkalis, losing hydrogen bromide and yielding **methylene-quinones** of the type $O{:}C_6H_3Br{:}CH_2$; the majority of these are unstable, and immediately yield condensation products which are insoluble in alkalis (cf. *Auwers*, A. **301**, 203; B. **32**, 2978; **34**, 4256; **36**, 1878, **39**, 435, *Zincke*, A. **320**, 145, **322**, 174; **329**, 1; **353**, 335, 357).

XXVI. AROMATIC ACIDS

The aromatic acids are analogous to the fatty acids in most respects. As acids they are capable of forming exactly the same kinds of derivatives as the latter, *e.g.* metallic salts, esters, chlorides, anhydrides, amides, &c.:

$C_6H_5{\cdot}CO_2H$ (benzoic acid)

$C_6H_5{\cdot}CO_2C_2H_5$ (ethyl benzoate); $(C_6H_5{\cdot}CO)_2O$ (benzoic anhydride); $C_6H_5{\cdot}CO{\cdot}Cl$ (benzoyl chloride); $C_6H_5{\cdot}CO{\cdot}NH_2$ (benzamide), &c

As benzene derivatives they yield chloro-, bromo-, iodo-, hydroxy-, nitro-, amino-, and sulphonic acid derivatives, &c., *e.g.*:

$C_6H_4Cl{\cdot}CO_2H$ (chloro-benzoic acids),
$NH_2{\cdot}C_6H_4{\cdot}CO_2H$ (amino-benzoic acids);
$OH{\cdot}SO_2{\cdot}C_6H_4{\cdot}CO_2H$ (sulpho-benzoic acids);
$OH{\cdot}C_6H_4{\cdot}CO_2H$ (hydroxy-benzoic acids);
$C_6H_5{\cdot}CH(OH){\cdot}CO_2H$ (mandelic acid); &c.

Constitution.—Corresponding with the aromatic acids there are nitriles, *e.g.* with benzoic acid, benzo-nitrile, $C_6H_5{\cdot}C{:}N$, which may also be regarded as cyanogen derivatives of the hydrocarbons (in the above case, cyano-benzene), and which, on hydrolysis, yield the acids. From this, and from their general properties, it follows that their constitution must correspond exactly with that of the fatty acids; like the latter they are characterized by the presence of carboxyl, $CO{\cdot}OH$, in the molecule. There are monobasic, di-, tri-, and up to hexabasic aromatic acids, according to the number of hydrogen atoms in the molecule which are readily replaceable by metallic radicals, *i e.* according to the number of carboxyl groups:

$C_6H_4(CO_2H)_2$	$C_6H_3(CO_2H)_3$	$C_6(CO_2H)_6$
Phthalic acids	Benzene-tri-carboxylic acids	Mellitic acid.

Numerous unsaturated aromatic acids are known. As unsaturated compounds, they readily form additive compounds with hydrogen, chlorine, hydrogen iodide, and are thereby converted into saturated acids or their substitution products. In most of these additions the benzene nucleus remains unaltered. Their constitution is therefore entirely analogous to that of the acids of the acrylic or propiolic series, they contain a side chain with a double or triple carbon bond:

$C_6H_5 \cdot CH:CH \cdot CO_2H$ (Cinnamic acid) $\qquad$ $C_6H_5 \cdot C:C \cdot CO_2H$ (Phenyl-propiolic acid.)

In addition to the aromatic acids proper, which have just been mentioned, other acids have been prepared recently, *which are derivatives either of a completely reduced or a partially reduced benzene molecule.* The acids of the former series, *e.g.* the hexa hydro-benzoic acids, have properties very similar to those of the saturated fatty acids; while those of the latter, *e.g.* the di- and tetrahydro-benzoic acids, resemble the unsaturated fatty acids. (Cf. p. 349.)

The aromatic hydroxy-acids, *e.g.* the hydroxy-benzoic acids, which are both phenols and acids, manifestly contain phenolic hydroxyl (*i.e.* hydroxyl which is linked directly to the benzene nucleus) in addition to the carboxyl group or groups, they are capable of yielding salts either as acids or as phenols, but otherwise they correspond in many points with the aliphatic hydroxy-acids.

The true aromatic hydroxy-acids, such as mandelic acid (phenyl-glycollic acid), which correspond completely with the aliphatic hydroxy-acids, manifestly contain their alcoholic hydroxyl not in the benzene nucleus, but in the side chain, as is also the case with the aromatic alcohols

Nomenclature.—One of the simplest systems of nomenclature is the designation of the aromatic acids as carboxylic acids of the original hydrocarbons in question, *e.g.* phthalic acid is benzene-1:2-dicarboxylic acid. Many names, such as xylic acid, are taken from those of the hydrocarbons into which the carboxyl has entered, while others, such as mesitylenic acid, indicate the hydrocarbons from which the acids are obtained by oxidation. An important principle as regards nomenclature depends upon the fact that aromatic acids can be derived from almost every fatty acid of any consequence by the exchange of H for C_6H_5, *e.g.*:

$CH_3 \cdot CO_2H$ (acetic acid) $\qquad$ $C_6H_5 \cdot CH_2 \cdot CO_2H$ (phenyl-acetic acid)

There thus exist phenylated acids analogous to the acids of the acetic, glycollic, succinic, malic, and tartaric series, &c. For example, atropic acid, $C_6H_5 \cdot C(CO_2H):CH_2$, may be designated α-phenyl-acrylic acid, and cinnamic acid, $C_6H_5 \cdot CH:CH \cdot CO_2H$, β-phenyl-acrylic acid.

Properties.—Most of the aromatic acids are solid crystalline substances, generally only sparingly soluble in water, and therefore precipitated by acids from solutions of their salts, but often readily soluble in alcohol and ether. The simpler among them can be distilled or sublimed without decomposition, while the more complicated, especially phenolic and polycarboxylic acids, evolve carbon dioxide when heated; *e.g.* salicylic acid, $OH \cdot C_6H_4 \cdot CO_2H$, breaks up into phenol and CO_2. The elimination of carbonic anhydride from those acids which volatilize without decomposition may be effected by heating with soda-lime; in polybasic acids the carboxyls may be successively decomposed:

$$C_6H_4(CO_2H)_2 = C_6H_5CO_2H + CO_2 = C_6H_6 + 2CO_2$$

Occurrence.—A large number of the aromatic acids are found in nature, *e.g.* in many resins and balsams, and also in the animal organism in the form of nitrogeneous derivatives such as hippuric acid (benzoyl-glycocoll), $C_6H_5 \cdot CO \cdot NH \cdot CH_2 \cdot CO_2H$.

Modes of Formation.—A. Of the **saturated** acids.—

1. By the oxidation of the corresponding primary alcohols or aldehydes, *e.g.* benzoic acid from benzyl alcohol, or from benzaldehyde.

2. One of the commonest methods of obtaining aromatic acids is by the oxidation of benzene homologues. Each alkyl group present in the nucleus of the hydrocarbon can be oxidized to a carboxylic group, whether it be long or short, *e.g.* both $C_6H_5 \cdot CH_3$ and $C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CH_3$ yield $C_6H_5 \cdot CO_2H$.

All substituted benzene homologues which contain the substituent in the side chain are similarly oxidized to non-substituted aromatic acids, *e.g.* $C_6H_5 \cdot CH_2Cl$, $C_6H_5 \cdot CH_2 \cdot NH_2$, and $C_6H_5 \cdot CH:CH \cdot CO_2H$ yield $C_6H_5 \cdot CO_2H$.

A substituted benzene homologue which contains halogen, nitro-, sulpho-, amino-, hydroxy-, &c., substituents attached to the benzene nucleus, yields a similarly substituted aromatic acid, *e.g.*:

$$C_6H_4Cl \cdot CH_3 \rightarrow C_6H_4Cl \cdot CO_2H;$$
$$(OH)_2C_6H_3 \cdot CH_3 \rightarrow (OH)_2 \cdot C_6H_3 \cdot CO_2H;$$
$$NO_2 \cdot C_6H_4 \cdot CH_2 \cdot CH_3 \rightarrow NO_2 \cdot C_6H_4 \cdot CO_2H.$$

Should there be several side chains in the molecule, they

are usually all converted directly into carboxyl by chromic acid; whereas by using dilute nitric acid, this transformation can be effected step by step, *e.g.*:

$C_6H_4(CH_3)_2$ yield first $C_6H_4(CH_3)(CO_2H)$ and then $C_6H_4(CO_2H)_2$
The xylenes — Toluic acids — Phthalic acids

Nevertheless, the three classes of isomeric benzene derivatives with two side chains comport themselves differently. The para-compounds are the most readily oxidized to acids by chromic acid mixture, and then the meta-; whereas the ortho compounds are either completely destroyed by it (p. 348), or not attacked at all. The last-named may, however, be oxidized in the normal manner by nitric acid or potassic permanganate. The entrance of a negative group or of hydroxyl into the *o*-position with respect to the alkyl radical renders the oxidation more difficult (cf. p. 416).

3. By the hydrolysis of the corresponding nitriles:

$$C_6H_5\cdot CN + 2H_2O = C_6H_5\cdot CO_2H + NH_3.$$

These nitriles, which can be prepared from the ammonium salts of the acids in the same manner as those of the fatty series, are often obtained by the following syntheses:—

(*a*) By distilling the potassic salts of the sulphonic acids with potassic cyanide or ferrocyanide (*Merz*), just as the nitriles of the fatty acids are formed from the potassium alkyl-sulphates (p. 100):

$$C_6H_5\cdot SO_3K + KCN = C_6H_5\cdot CN + SO_3K_2.$$

Nitriles cannot, as a rule, be prepared from KCN and aromatic halogen derivatives which contain the halogen attached to the nucleus (cf. p. 355); the halogen is more readily replaced by cyanogen if sulphonic acid or nitro-groups are likewise present:

$$C_6H_4Br\cdot NO_2 + KCN = CN\cdot C_6H_4\cdot NO_2 + KBr.$$

Benzyl chloride, $C_6H_5\cdot CH_2Cl$, and all the haloid hydrocarbons which are substituted in the side chain, on the other hand, react with potassic cyanide in the manner characteristic of the alphyl haloids:

$$C_6H_5\cdot CH_2Cl + KCN = KCl + \underset{\text{Benzyl cyanide.}}{C_6H_5\cdot CH_2\cdot CN}$$

(*b*) By diazotizing the primary amines and replacing the diazo-group by cyanogen, according to *Sandmeyer's* reaction

(p. 388). This reaction is frequently made use of in the preparation of substituted benzo-nitriles, *e.g.* 2·4-dibromo-benzo-nitrile, $C_6H_3Br_2CN$, and the isomeric 2:6-compound, also of tolu-nitriles, $CH_3 \cdot C_6H_4 \cdot CN$.

(*c*) By heating the mustard oils (phenyl-iso-thiocyanates, p. 276), with copper or zinc dust (*Weith*):

$$C_6H_5 \cdot N:C:S + 2Cu = C_6H_5 \cdot C{\vdots}N + Cu_2S.$$

(*d*) By the molecular transformation of the isomeric iso-nitriles at a somewhat high temperature:

$$C_6H_5 \cdot N:C \longrightarrow C_6H_5 \cdot C{\vdots}N.$$

(*e*) By eliminating the elements of water from the oximes of the aldehydes by means of acetyl chloride (pp. 137 and 429):

$$\text{Benzaldoxime, } C_6H_5 \cdot CH:N \cdot OH = C_6H_5 \cdot CN + H_2O.$$

4. By the reduction of unsaturated acids, thus hydrocinnamic by the reduction of cinnamic acid with sodium amalgam and water, or with hydrogen and finely divided Palladium·

$$C_6H_5 \cdot CH:CH \cdot CO_2H + 2H = C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CO_2H.$$

The acids obtained by this method always contain the CO_2H group attached to a side chain. Similar acids can also be obtained by the reduction of hydroxy-, bromo-, or keto acids, where the OH, Br, CO, and CO_2H are all in side chains, *e.g.*:

$$C_6H_5 \cdot CH(OH) \cdot CO_2H \longrightarrow C_6H_5 \cdot CH_2 \cdot CO_2H.$$

5 A number of syntheses of nucleus carboxylic acids can be accomplished. These may be regarded as the more or less direct introduction of the carboxylic group into the benzene nucleus, and are usually effected by means of carbonic acid derivatives. In many cases the yields are only small, and the reactions are mainly of theoretical interest.

(*a*) Benzoic acid and its homologues are produced by the action of carbon dioxide upon bromo-benzenes, &c., in presence of sodium (*Kekulé*):

$$C_6H_5Br + CO_2 + 2Na = C_6H_5 \cdot CO_2Na + NaBr.$$

(*b*) By the action of phosgene, $COCl_2$, upon benzene and its homologues in presence of $AlCl_3$ (*Friedel* and *Crafts*):

$$C_6H_6 + COCl_2 = C_6H_5 \cdot COCl + HCl.$$

Acid chlorides are first formed, but can be readily decomposed by water. By the further action of these chlorides upon benzene in presence of $AlCl_3$, ketones are formed (see Benzo-phenone). Carbonyl chloride reacts most readily with tertiary amines.

$$C_6H_5 \cdot N(CH_3)_2 + COCl_2 = (CH_3)_2N \cdot C_6H_4 \cdot COCl + HCl$$

(*c*) By the action of carbamic chloride, $Cl \cdot CO \cdot NH_2$, upon benzene (or phenol) in presence of $AlCl_3$, amides of the aromatic acids are formed, and these can be hydrolysed (*Gattermann*, B. 1899, **32**, 1116):

$$C_6H_6 + Cl \cdot CO \cdot NH_2 = C_6H_5 \cdot CO \cdot NH_2 + HCl$$

(*d*) By the action of sodium upon a mixture of a brominated benzene and ethyl chloro-carbonate (*Wurtz*); in this case the esters are first formed, but these are readily hydrolysed.

$$C_6H_5Br + Cl \cdot CO_2C_2H_5 + 2Na = C_6H_5 \cdot CO_2C_2H_5 + NaBr + NaCl$$

(*e*) The phenolic acids are formed by passing carbon dioxide over heated sodium phenates (*Kolbe*, see Salicylic acid).

$$C_6H_5 \cdot ONa + CO_2 = OH \cdot C_6H_4 \cdot CO_2Na.$$

In the case of the polyhydroxy-phenols, *e.g.* resorcinol, an acid is often formed by merely heating the phenol with a solution of ammonium carbonate or potassium bicarbonate (B **13**, 930).

(*f*) *p*-Hydroxy-acids are formed by the action of carbon tetrachloride upon phenols in alkaline solution (B. **10**, 2185; *Tiemann-Reimer* reaction; cf. p 430).

$$C_6H_5 \cdot ONa + CCl_4 = C_6H_4(OH) \cdot CCl_3 + NaCl$$
$$C_6H_4(OH) \cdot CCl_3 + 4NaOH = C_6H_4(OH) \cdot CO_2Na + 3NaCl + 2H_2O$$

(*g*) By heating the sulphonates with sodium formate (*V. Meyer*):

$$C_6H_5 \cdot SO_3Na + HCO_2Na = C_6H_5 \cdot CO_2Na + HSO_3Na.$$

(*h*) By the action of carbon dioxide on ethereal solutions of organo-magnesium compounds (*Grignard's* reagents), and subsequent treatment with acids:

$$C_6H_5 \cdot Mg \cdot Br + CO_2 \longrightarrow C_6H_5 \cdot CO_2 \cdot MgBr \longrightarrow C_6H_5 \cdot CO_2H$$

6. Syntheses by the aid of ethyl aceto-acetate and ethyl malonate.

Ethyl aceto-acetate reacts with the halide derivatives which are substituted in the side chain, *e.g.* benzyl chloride, exactly

as in the fatty series, with the formation of the more complicated ketonic acids, which again are capable of undergoing either the "acid hydrolysis" or the "ketone hydrolysis" (p. 226), *e.g.*:

$$C_6H_5\cdot CH_2Cl + CH_3\cdot CO\cdot CHNa\cdot CO_2Et = CH_3\cdot CO\cdot CH(CH_2C_6H_5)\cdot CO_2Et + NaCl$$

Benzyl-aceto-acetic ester

$$CH_3\cdot CO\cdot CH(CH_2\cdot C_6H_5)\cdot CO_2Et + 2H_2O = C_6H_5\cdot CH_2\cdot CH_2\cdot CO_2H + CH_3\cdot CO_2H + EtOH$$

β-Phenyl-propionic acid

Ethyl phloroglucinol dicarboxylate, $(OH)_3\cdot C_6H(CO_2Et)_2$, may be synthesised by heating ethyl sodio-malonate with ethyl malonate at 145° (*Moore*, J. C. S. 1904, 165).

7 Hydroxy-acids and keto-acids are formed by exactly the same methods as in the fatty series (pp. 205 and 206), *e.g.* mandelic acid by the combination of hydrogen cyanide with benzaldehyde, and hydrolysis of the nitrile thus formed (B. **14**, 239, 1965):

$$C_6H_5\cdot CHO + HCN = C_6H_5\cdot CH(OH)\cdot CN;$$

or from phenyl-chloro-acetic acid (B. **14**, 239):

$$C_6H_5\cdot CHCl\cdot CO_2H + KOH = C_6H_5\cdot CH(OH)\cdot CO_2H + KCl$$

B. The following are some of the commoner methods employed for the preparation of **unsaturated** acids:—

1 From the mono-haloid substitution products of the saturated acids by the elimination of halogen hydracid (cf. p 163); also from the corresponding nitriles, primary alcohols, &c., as in the case of the saturated compounds.

2. According to the so-called *Perkin* synthesis, by the action of aromatic aldehydes upon the sodium salts of fatty acids in the presence of a condensing agent, usually acetic anhydride. Thus, when benzaldehyde is heated with acetic anhydride and sodium acetate, cinnamic acid is formed:

$$C_6H_5\cdot CHO + CH_3\cdot CO_2Na = C_6H_5\cdot CH{:}CH\cdot CO_2Na + H_2O.$$

The acetic anhydride probably acts as a dehydrating agent in this instance, the reaction taking place between the sodium acetate and the aldehyde (cf. A. **216**, 101). Hydroxy-acids are formed as intermediate products by a reaction similar to the "aldol condensation" (p. 131); in the above case, for instance, β-phenyl-hydracrylic acid, $C_6H_5\cdot CH(OH)\cdot CH_2\cdot CO_2H$.

When the sodium salt and the anhydride of two different acids, *e.g.* sodic propionate and acetic anhydride, are used, the product varies with the conditions (B. 1901, **34**, 918), but usually consists of a mixture of two unsaturated acids.

This reaction also takes place with the hydroxy-aldehydes, with the homologues of acetic acid, and also with dibasic acids, *e.g.* malonic; but all acids employed must contain a CH_2 group in the α-position with respect to the CO_2H, *e.g.*:

$$C_6H_5\cdot CH:O + CH_3\cdot CH_2\cdot CO_2Na = H_2O + \underset{\alpha\text{-Methyl cinnamic acid}}{C_6H_5\cdot CH:C(CH_3)\cdot CO_2H}$$

It is a very general method used for the preparation of $\alpha:\beta$-unsaturated acids; in certain cases, *e.g.* α-phenyl-cinnamic acid, $C_6H_5\cdot CH:C(C_6H_5)\cdot CO_2H$, and its nitro-derivatives, two sterco-isomerides are produced corresponding with the two crotonic acids or with fumaric and maleic acid.

Unsaturated monobasic acids are also formed when aromatic aldehydes are heated with malonic acid in presence of ammonia, aniline, or other amines (*Knoevenagel*):

$$C_6H_5\cdot CH:O + H_2C(CO_2H)_2 = C_6H_5\cdot CH:C(CO_2H)_2$$
$$= C_6H_5\cdot CH:CH\cdot CO_2H + CO_2.$$

The esters of these acids are formed when aromatic aldehydes are condensed with the esters of fatty acids in the presence of sodium ethoxide (*Claisen*, B. **23**, 976; cf. *Claisen* condensation, p. 224).

3. Cinnamic acid is also formed by the action of benzal chloride upon sodium acetate (*Caro*):

$$C_6H_5\cdot CHCl_2 + CH_3\cdot CO_2H = C_6H_5\cdot CH:CH\cdot CO_2H + 2HCl.$$

4. By the action of aceto-acetic ester upon the phenols in presence of concentrated H_2SO_4, unsaturated phenolic acids or their anhydrides (B. **16**, 2119; **17**, 2191) are formed, *e.g.*:

$$C_6H_5OH + \underset{\text{(Pseudo form)}}{\overset{OHCMe:CH}{\underset{HO\cdot CO}{|}}} = \underset{\text{Methyl-cumarin}}{C_6H_4\begin{cases}CMe:CH\\ O---CO\end{cases}} + 2H_2O$$

A. Monobasic Aromatic Acids

Constitution and Isomers.—The cases of isomerism in the aromatic acids are easy to tabulate. An isomer of benzoic acid is neither theoretically possible nor actually known. Carboxylic acids of the formula $C_8H_8O_2$ may, however, be

Saturated Acids

		M.-p.	K	M.-p. of Amide.
Benzoic	$C_6H_5 \cdot CO_2H$	121°	0·0060	130°
$C_8H_8O_2$ Phenyl-acetic	$C_6H_5 \cdot CH_2 \cdot CO_2H$	76°	0·00556	154°
$C_8H_8O_2$ *o*-Toluic	$CH_3 \cdot C_6H_4 \cdot CO_2H$	105°	0·0120	139°
$C_8H_8O_2$ *m*-Toluic	Do.	111°	0·00514	
$C_8H_8O_2$ *p*-Toluic	Do	180°	0·00515	158°
$C_9H_{10}O_2$ Hydrocinnamic	$C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CO_2H$	49°	0·00227	82°
$C_9H_{10}O_2$ Hydratropic	$CH_3 \cdot CH(C_6H_5) \cdot CO_2H$	liq.	0·00425	91°
$C_9H_{10}O_2$ *o*-Tolyl-acetic	$CH_3 \cdot C_6H_4 \cdot CH_2 \cdot CO_2H$	89°		161°
$C_9H_{10}O_2$ *m*-Tolyl-acetic	Do	61°	.	141°
$C_9H_{10}O_2$ *p*-Tolyl-acetic	Do	91°	...	184°
$C_9H_{10}O_2$ *o*-Ethyl-benzoic	$C_2H_5 \cdot C_6H_4 \cdot CO_2H$	68°	...	152°
$C_9H_{10}O_2$ *m*-Ethyl-benzoic	Do.	47°	...	
$C_9H_{10}O_2$ *p*-Ethyl-benzoic	Do	112°	...	115°
$C_9H_{10}O_2$ Mesitylenic acid	$(CH_3)_2 \cdot C_6H_3 \cdot CO_2H$ (3 5 1)	166°	...	133°

Hydroxy-saturated Acids

Salicylic acid (ortho)	$OH \cdot C_6H_4 \cdot CO_2H$	155°	0·102	140°
m-Hydroxy-benzoic acid	Do	188°	0·0087	170°
p-Hydroxy-benzoic acid	Do	214°	0·00286	162°
p-Methoxy-benzoic or anisic acid	$CH_3O \cdot C_6H_4 \cdot CO_2H$	184°	0·0032	162°–163°
Mandelic acid	$C_6H_5 \cdot CH(OH) \cdot CO_2H$	118°	0·042	132°
Tropic acid	$C_6H_5 \cdot CH(CH_2 \cdot OH)CO_2H$	117°	0·0075	

Unsaturated Acids

Cinnamic acid	$C_6H_5 \cdot CH : CH \cdot CO_2H$	133°	0·00355	147°
Atropic acid	$CH_2 : C(C_6H_5) \cdot CO_2H$	106°	0·0143	
Phenyl-propiolic acid	$C_6H_5C \vdots C \cdot CO_2H$	136°	0·59	100°
Coumaric or *p*-hydroxy-cinnamic acid	$OH \cdot C_6H_4 \cdot CH \quad CH \cdot CO_2H$	206°	0·00216	.

derived from toluene by the entrance of carboxyl either into the benzene nucleus or into the side chain, thus:

$CH_3 \cdot C_6H_4 \cdot CO_2H$ — *o-m-p*-Toluic acids

$C_6H_5 \cdot CH_2 \cdot CO_2H$ — Phenyl-acetic acid

The nature of their oxidation products yields proof of their constitution, the former yielding the phthalic acids, and the latter benzoic.

Of acids $C_9H_{10}O_2$, a large number of isomers are already known (see table). Hydrocinnamic acid and hydratropic acid are phenyl-propionic acids, the former β- and the latter α-, corresponding with the lactic acids; the isomeric relations of the fatty acids thus repeat themselves here. The tolyl-acetic acids, $CH_3 \cdot C_6H_4 \cdot CH_2 \cdot CO_2H$, and the ethyl-benzoic acids, $C_2H_5 \cdot C_6H_4 \cdot CO_2H$, stand in much the same relation to each other as aceto-acetic acid, $CH_3 \cdot CO \cdot CH_2 \cdot CO_2H$, to propionyl-formic acid, $C_2H_5 \cdot CO \cdot CO_2H$, and they all yield phthalic acids when oxidized. Lastly, mesitylenic acid and its isomers are dimethyl-benzoic acids, and are oxidizable to benzene-tricarboxylic acids.

As instances of isomers among the unsaturated acids, we may take cinnamic and atropic acids (analogous to β- and α-chlor-acrylic acids, p. 168).

Further, the hydroxy-toluic acids, $C_6H_3(CH_3)(OH)(CO_2H)$, are isomeric with mandelic acid, $C_6H_5 \cdot CH(OH) \cdot CO_2H$, the former being oxidized to hydroxy-phthalic acids, $C_6H_3(OH)(CO_2H)_2$, and the latter to benzoic acid; the hydrocoumaric acids, $C_9H_{10}O_3$, are likewise isomeric with tropic acid. The first-named yield hydroxy-benzoic acids on oxidation, and the last benzoic.

Differences are apparent, *e.g.* in respect to reducibility, according as the carboxyl is linked directly to the nucleus or to a side chain; the amides of the respective acids are in the former case reduced to the corresponding alcohols, but not in the latter. (Cf. B. **24**, 173.)

1. MONOBASIC SATURATED ACIDS

Benzoic acid, $C_6H_5 \cdot CO_2H$, was discovered in gum benzoin in 1608, and prepared from urine by *Scheele* in 1785. Its composition was established by *Liebig* and *Wohler's* classical researches in 1832. It occurs in nature in gum benzoin, from which it may be obtained by sublimation ("acidum benzoicum ex resina"); also in dragon's-blood (a resin), in Peru and Tolu balsams, in castoreum, and in cranberries. It

s present in the urine of horses in combination with glycocoll .s hippuric acid, from which it may be obtained by hydrolysis vith hydrochloric acid ("acidum benzoicum ex urina"). It s obtained on the large scale ("ac. benz. ex toluole") as a)y-product in the manufacture of oil of bitter almonds from)enzyl chloride or benzal chloride. The acid may also be ormed by heating benzo-trichloride with water to a some-vhat high temperature:

$$C_6H_5\cdot CCl_3 \longrightarrow C_6H_5\cdot C(OH)_3 \longrightarrow C_6H_5\cdot CO\cdot OH.$$

Benzoic acid is also present in coal-tar. It crystallizes in olourless glistening plates or flat needles, sublimes readily, nd is volatile with steam; its vapour has a peculiar irritating)dour, and gives rise to coughing. It melts at 121°, boils at 250°, nd is readily soluble in hot water, but only sparingly in cold. When heated with lime, it is decomposed into benzene and car-)on dioxide. It is used in medicine and in the manufacture of niline blue. Some of its salts crystallize beautifully, *e.g.* **cal-:ium benzoate**, $(C_6H_5\cdot CO_2)_2Ca + 3\,H_2O$, in glistening prisms.

From the partially or wholly reduced benzene molecule here are derived (*a*) the **dihydro-benzoic acids**, $C_6H_7\cdot CO_2H$,)f which five are theoretically possible, according to the)osition of the double linkings, viz. Δ-1:3-, Δ-1:4-, Δ-1·5-, Δ-2 4-, and Δ-2:5-dihydro-benzoic acids, but only two known B. 1891, **24**, 2623, and 1893, **26**, 454); (*b*) the **tetrahydro-)enzoic acids**, $C_6H_9\cdot CO_2H$, all three of which are actually nown, viz. Δ-1-, Δ-2-, and Δ-3-tetrahydro-benzoic acids (A. 271, 231); and a **hexahydro-benzoic acid**, $C_6H_{11}\cdot CO_2H$ (*hexa-nethylene-carboxylic acid*), which is found in the petroleum from Baku, and which can also be prepared from benzoic acid.

The **Esters**, *e.g.* **methyl benzoate**, $C_6H_5\cdot CO_2CH_3$, b.-pt 199°, nd **ethyl benzoate**, $C_6H_5\cdot CO_2C_2H_5$, b.-pt. 213°, are always)repared by the catalytic method of esterification (p. 174), namely, by boiling the acid for three to four hours with a 3-per-cent solution of dry hydrogen chloride or of concentrated ulphuric acid in the requisite alcohol (*E. Fischer* and *Speier*, 3. 1895, **28**, 3252). They may also be obtained by the other general methods for the preparation of esters: (*a*) by the action)f an acid chloride on the alcohol alone, or in presence of alkali (*Schotten*, *Baumann*) or of pyridine (*Emhorn* and *Hollandt*, Abstr. 1899, **1**, 577); (*b*) by the action of an alkyl iodide on he silver salt of the acid; and (*c*) by the action of alkyl ulphates, more especially methyl sulphate, on aqueous solu-

tions of the alkali salts of the acids (*Werner* and *Seybold*, B. 1904, **37**, 3658). These esters are liquids of pleasant aromatic odour which boil for the most part without decomposition, and frequently serve for the recognition and estimation of alcohols. They may be hydrolysed in much the same manner as the aliphatic esters, although as a rule not so readily.

Benzyl benzoate, $C_6H_5 \cdot CO_2 \cdot CH_2 \cdot C_6H_5$, is present in the balsams of Peru and Tolu.

Benzoyl chloride, $C_6H_5 \cdot CO \cdot Cl$ (*Liebig* and *Wohler*), obtained by the action of phosphorus pentachloride on the acid, is the complete analogue of acetyl chloride, but more stable than the latter, since it is only slowly hydrolysed by cold water, although quickly by hot. It is a colourless liquid boiling at 198°, and has a most characteristic pungent odour It is prepared technically by chlorinating benzaldehyde.

Benzoic anhydride, $(C_6H_5 \cdot CO)_2O$ (*Gerhardt*), is exactly analogous to acetic anhydride. It crystallizes in prisms insoluble in water, boils without decomposition, and becomes hydrated on boiling with water. M.-pt. 39°.

In addition to the ordinary anhydrides or oxides, peroxides of the type **benzoyl peroxide** or **benzo-peroxide**, $C_6H_5 \cdot CO \cdot O \cdot O \cdot CO \cdot C_6H_5$, are known. They may be obtained by the action of the acid chloride on a cooled solution of sodic peroxide (B. 1900, **33**, 1575, and C. C. 1899, **2**, 396). Benzo-peroxide crystallizes from alcohol in prisms, melts at 106°–108°, is relatively stable, and is insoluble in water. When its ethereal solution is mixed with sodic ethoxide, the products formed are ethyl benzoate, and the sodic salt of **perbenzoic acid**, $C_6H_5 \cdot CO \cdot O \cdot OH$, a hygroscopic acid melting at 41°-43°. It has a strong odour resembling hypochlorous acid, is readily volatile, but decomposes violently when heated, and is a strong oxidizing agent Many aliphatic and aromatic acids yield similar derivatives.

Benzamide, $C_6H_5 \cdot CO \cdot NH_2$, corresponds with acetamide, and is prepared from benzoyl chloride and ammonia or ammonium carbonate. It forms lustrous, nacreous plates, melting at 130°, boils without decomposition, and is readily soluble in hot water.

The amido-hydrogen of benzamide may be substituted by alkyl radicals such as phenyl, &c., with the formation, *e.g.* of **benzanilide**, $C_6H_5 \cdot CO \cdot NHC_6H_5$, the anilide of benzoic acid, a compound which can be readily prepared from aniline and benzoic acid, or aniline and benzoyl chloride. It crystallizes in colourless plates, melts at 158°, distils unchanged, and is in

fact the complete analogue of acetanilide, but is much more difficult to hydrolyse, fusion with potash being one of the best methods.

Thio-benzamide, $C_6H_5 \cdot CS \cdot NH_2$, is obtained by the union of benzo-nitrile with hydrogen sulphide, or by heating benzylamine with sulphur.

Benzoyl-hydrazine, *Benzhydrazide*, $C_6H_5 \cdot CO \cdot NH \cdot NH_2$, obtained from ethyl benzoate and hydrazine hydrate, melts at 112°, and with nitrous acid yields **benzoyl-azimide**, *benzazide*, $C_6H_5 \cdot CO \cdot N\langle \overset{N}{\underset{N}{\|}}$, which yields benzoic and hydrazoic acids on hydrolysis. (Cf. *Curtius*, Abstr. 1895, **1**, 32.)

Metallic derivatives of benzamide are also known, *e.g.* **benzamide silver** *Titherley* (J. C. S. 1897, 468; 1901, 407) has shown that the silver derivative exists in two forms: a white compound, which is stable and is probably $C_6H_5 \cdot C\langle \overset{NH}{OAg}$, and an unstable orange compound, $C_6H_5 \cdot CO \cdot NHAg$. These two metallic derivatives correspond with the pseudo and normal formulæ for benzamide, viz. $C_6H_5 \cdot C\langle \overset{NH}{OH}$ and $C_6H_5 \cdot CO \cdot NH_2$. From the pseudo form are derived **imino-ethers** (cf. p. 185).

Hippuric acid, *Benzamino-acetic acid*, $C_6H_5 \cdot CO \cdot NH \cdot CH_2 \cdot CO_2H$, is an amino-derivative of benzoic acid, being derived from the latter and glycocoll (amino-acetic acid); it may be prepared by heating benzoic anhydride with glycocoll (B. **17**, 1663), and is present in the urine of horses and of other herbivora. When benzoic acid or toluene is taken internally, it is eliminated from the system in the form of hippuric acid. It crystallizes in rhombic prisms, sparingly soluble in cold water but readily in hot, decomposes when heated, and forms salts, esters, nitro-derivatives, &c. When hydrolysed with concentrated hydrochloric acid it yields glycocoll hydrochloride and benzoic acid.

Benzo-nitrile, C_6H_5CN (cf. p. 438), is an oil which smells like oil of bitter almonds, and boils at 191°. It is prepared either by the action of PCl_5 upon benzamide (p. 183), or by distilling benzoic acid with ammonium thiocyanate. It possesses all the properties of a nitrile, combining slowly with nascent hydrogen to benzylamine, readily with halogen hydrides to an imino-chloride, with amines to amidines (p. 187, cf. A. **192**, 1), with hydroxylamine to amidoximes (p. 188).

Substituted Benzoic Acids.—The hydrogen atoms of benzoic acid are replaceable by halogen with the formation *e.g.* of **chloro-benzoic acid**, $C_6H_4Cl \cdot CO_2H$. In such formation of mono-substitution products the halogen takes up the meta-position with respect to the carboxyl. Nitric acid (especially a mixture of nitric and sulphuric acids) nitrates it readily, ***m*-nitro-benzoic acid** being the chief product, together with a smaller quantity of the ortho- and a very little of the para-acid

The *o*- and *p*-halogen and nitro-compounds are usually prepared by indirect methods, *e.g.*:

$$o\text{-}CH_3 \cdot C_6H_4 \cdot NO_2 \longrightarrow CO_2H \cdot C_6H_4 \cdot NO_2$$

or $2{:}4\text{-}C_6H_3Br_2 \cdot NH_2 \longrightarrow C_6H_3Br_2 \cdot CN \longrightarrow C_6H_3Br_2 \cdot CO_2H$

In the preceding pages attention has been drawn repeatedly to the influence which a radical, already present in the benzene molecule, exerts on the position taken up by a second radical entering the molecule. As examples we have:

$C_6H_5Br \longrightarrow p\text{-}C_6H_4Br_2$; $\quad C_6H_5 \cdot OH \longrightarrow o\text{-}o\text{-}p\text{-}C_6H_2Br_3 \cdot OH$.

$C_6H_5 \cdot NO_2 \longrightarrow m\text{-}C_6H_4(NO_2)_2$; $\quad C_6H_5 \cdot NH_2 \longrightarrow o\text{-}o\text{-}p\text{-}C_6H_2Br_3 \cdot NH_2$

$C_6H_5 \cdot SO_3H \longrightarrow m\text{-}C_6H_4(SO_3H)_2$; $\quad C_6H_5 \cdot CHO \longrightarrow m\text{-}NO_2 \cdot C_6H_4 \cdot CHO$

$C_6H_5 \cdot CH_3 \longrightarrow o$- and $p\text{-}CH_3 \cdot C_6H_4 \cdot NO_2$

$C_6H_5 \cdot NH_2 \longrightarrow o$- or $p\text{-}NH_2 \cdot C_6H_4 \cdot SO_3H$.

The following broad generalizations will be found to apply to most cases.—

I. If the radical already present is Cl, Br, I, OH, NH_2, or CH_3, then, by the introduction of Cl, Br, I, NO_2, or SO_3H radicals, para- and to a certain extent ortho-compounds are formed, and only very exceptionally meta-compounds.

II. If the radical present is NO_2, SO_3H, CHO, or CO_2H, then, on chlorination, bromination, nitration, or sulphonation, meta-compounds are formed. (See *Crum Brown* and *Gibson*, J. C. S. 1892, 367. For details cf. *Obermuller*; *Hollemann*, Die Direkte Einfuhrung von Substituenten, 1910.)

In many reactions all three isomeric products have been isolated, but in very different quantities, thus at 0° benzoic acid yields 80·2 per cent of *m*-, 18·5 of *o*-, and only 1·3 of *p*-nitro-benzoic acid; at 30° nitrobenzene yields 91 per cent of *m*-, 8 of *o*-, and 1 of *p*-dinitro-benzene. It is probable that the three isomerides are also formed in other cases which have not been examined so carefully. The temperature at which the substitution occurs also appears to determine to a certain extent the relative proportions of the isomers formed.

The substituted benzoic acids closely resemble benzoic acid, and yield similar derivatives. The strengths of the different acids largely depend upon the nature of the substituents and their positions with respect to the carboxylic group.

Acid	M -p	K	Ethyl ester M -p	Ethyl ester B -p
Benzoic.	121°	0·006	...	211°
o-Methyl-benzoic	105°	0 012	...	220°
m-Methyl-benzoic....	110°	0 00514	...	225°
p-Methyl-benzoic..... ...	180°	0 00515	...	228°
o-Bromo-benzoic...	150°	0 145	...	254°
m-Bromo-benzoic.	155°	0·0137	...	259°
p-Bromo-benzoic.	251°	.	...	262°
o-Nitro-benzoic	148°	0 616	30°	...
m-Nitro-benzoic	141°	0 0345	47°	298°
p-Nitro-benzoic .. .	240°	0·0396	57°	. .
o-Amino-benzoic.....	145°	0 001	13°	267°
m-Amino-benzoic... ...	176°	0 003	.	294°
p-Amino-benzoic....	186°	0 001	89°	...

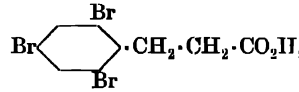
The numbers for K given in the table indicate that the introduction of negative radicals, *e.g.* NO_2, Br, &c, more especially into the ortho-position, markedly increases the strength of the acid, whereas the introduction of positive radicals, *e.g.* the amino-, more especially into ortho-positions, tends to weaken the acid (cf. p. 168).

Chemical Retardation and Influence of Substituents (cf. p. 175) —Within recent years a number of examples of the retardation or complete inhibition of chemical reactions by the presence of ortho-substituents have been discovered. One of the best known examples of this is met with in the esterification of aromatic acids by the hydrogen chloride catalytic method. *Kellas* (Zeit. Phys. Chem., 1897, **24**, 221) has shown that even one ortho-substituent, whether it be CH_3, NO_2, Br, &c, retards the formation of ester; and *V. Meyer* and *Sudborough* (B. 1894, **27**, 510, 1580, and 3146) have shown that when two such ortho-substituents are present an ester is not formed at all.* The cause of this retardation and inhibition is now generally supposed to be due to the fact that in the formation of an ester an additive compound of the acid and alcohol,

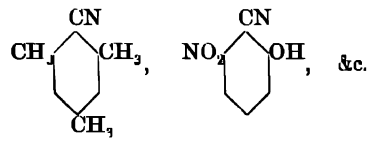
$$C_6H_5\cdot C\begin{matrix}O\\OH\end{matrix} + CH_3\cdot OH = C_6H_5\cdot C\begin{matrix}OH\\OH\\OCH_3\end{matrix} = C_6H_5\cdot C\begin{matrix}O\\OCH_3\end{matrix} + H_2O.$$

* Esters of such acids can be prepared by heating the acids with alcohol to high temperatures.

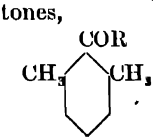
is first formed, that this compound then decomposes into the ester and water, and that the spatial arrangements are such that ortho-substituents are so close to the carboxylic group that they interfere with the formation of an additive compound, and thus retard or inhibit esterification (*Wegscheider*). In confirmation of this view we have the fact that *o*-substituents do not interfere to nearly the same extent when the carboxylic group is removed some distance, *e.g.* by the interposition of a chain of carbon atoms. The acid,



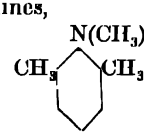
s-tribromo-hydrocinnamic acid, for example, is readily esterified under the usual conditions. Other cases of chemical retardation due to *o*-substituents have been met with in the hydrolysis of substituted benzo-nitriles; compounds like



cannot be hydrolysed to the corresponding acids by the usual methods. Di-ortho-substituted benzoyl chlorides and benzamides and benzoic esters are also remarkably stable and difficult to hydrolyse to the acids (*Sudborough, Ira Remsen*). Di-ortho-substituted ketones,



cannot be converted into oximes (*V. Meyer*), and di-ortho-substituted tertiary amines,

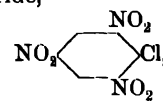


cannot yield quaternary ammonium salts (p. 379) (*E. Fischer*).

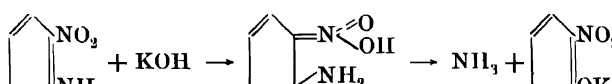
That ortho-substituents do not retard or inhibit all chemical actions is shown by the fact that esters of di-ortho-substituted

benzoic acids may be obtained by other methods, viz. the action of the alcohol on the acid chloride, and the action of alkyl iodide on the silver salt of the acid, or of methyl sulphate on an alkali salt of the acid.

In certain reactions the presence of ortho-substituents appears to favour or accelerate a chemical reaction, examples of this are to be met with in the diacetylation of arylamines (*Sudborough*, J. C. S. 1901, **79**, 533) and in the chemical reactivity of picryl chloride,



and similar compounds. The reactivity of various substituents, such as Cl, NH_2, &c, which are in the *o*- or *p*-position with respect to a nitro-group, has been noted previously (pp. 362, 374, 414). A simple explanation of this reactivity may be due to the formation of an *o*- or *p*-quinonoid additive product. Thus in the action of alkalis on *o*-nitraniline:



where the NH_2 group is replaced by OK, an ortho-quinonoid compound may be formed as indicated above, and this by the loss of ammonia would yield the potassic derivative of *o*-nitrophenol

The **amino-benzoic acids**, $NH_2 \cdot C_6H_4 \cdot CO_2H$, which are obtained by the reduction of the nitro-acids with tin and hydrochloric acid, &c., are interesting, as they are both bases and acids, *i.e.* **amphoteric**, and therefore similar to glycocoll in chemical character, they combine with hydrochloric acid, chloro-platinic acid, &c., as well as reacting with mineral bases to yield metallic salts. With regard to their constitution, cf. Glycocoll, p. 212.

With nitrous acid they yield **diazo-benzoic acids**, $C_6H_4\langle{}^{N:N}_{CO_2}\rangle$, which correspond with the diazo-benzene-sulphonic acids.

o-**Amino-benzoic acid** is also obtained from phthalimide, $C_6H_4\langle{}^{CO}_{CO}\rangle NH$, by the *Hofmann* reaction (cf. Amides, be

haviour of, par. 5), and by the oxidation of indigo with manganese dioxide and caustic soda, and is often termed **anthranilic acid**, it forms (in contradistinction to the *m*- and *p*-acids) an intramolecular anhydride, **anthranil**, $C_6H_4<\begin{matrix}CO\\NH\end{matrix}>$, and is an important intermediate product in the synthesis of indigo. The methyl ester is an important constituent of the essential oil of orange-blossom.

The **sulpho-benzoic acids**, $OH\cdot SO_2\cdot C_6H_4\cdot CO\cdot OH$, are dibasic acids. An ammonia derivative of *o*-sulpho-benzoic acid is the sweet substance "**saccharine**", $C_6H_4<\begin{matrix}SO_2\\CO\end{matrix}>NH$, *i.e.* *o*-sulpho-benzimide, or *o*-benzoyl-sulphone-imide, an imide comparable with succinimide It is a white crystalline powder, almost three hundred times as sweet as cane-sugar, and is used to some extent in place of the latter.

Acids, $C_8H_8O_2$.—1. The three **toluic acids**, $CH_3\cdot C_6H_4\cdot CO_2H$, can be prepared from the three xylenes *p*-**Toluic acid** is obtained from *p*-toluidine, by transforming it—according to the *Sandmeyer* reaction—into *p*-cyano-toluene and hydrolysing the latter (A. **258**, 9). Isomeric with them is —

2 **Phenyl-acetic acid**, *α-Toluic acid*, $C_6H_5\cdot CH_2\cdot CO_2H$ (*Cannizaro*, 1855) —This acid differs characteristically from its isomers by its behaviour upon oxidation (see p 441). It may be obtained synthetically from benzyl chloride and potassium cyanide, **benzyl cyanide**, $C_6H_5\cdot CH_2\cdot CN$ (b.-pt. 232°), being formed as intermediate product; it crystallizes in lustrous plates, melts at 76°, and boils at 262°.

It is capable of undergoing substitution either in the benzene nucleus or in the side chain. In the latter case there are formed compounds such as—

Phenyl-chloracetic acid, $C_6H_5\cdot CHCl\cdot CO_2H$, and **phenyl-amino-acetic acid**, $C_6H_5\cdot CH(NH_2)\cdot CO_2H$, compounds which possess precisely the same character as mono-chloracetic and amino-acetic acids Isomeric with phenyl-amino-acetic acid are the three **amino-phenyl-acetic acids**, $NH_2\cdot C_6H_4\cdot CH_2\cdot CO_2H$, of which the *o*-acid is interesting on account of its close relation to the indigo group It does not exist in the free state, but forms an intramolecular anhydride, oxindole (p. 522):

$$C_6H_4<\begin{matrix}NH_2\\CH_2\cdot CO_2H\end{matrix} = C_6H_4<\begin{matrix}NH\\CH_2\end{matrix}>CO + H_2O.$$

Such formation of an intramolecular anhydride is of very

frequent occurrence in ortho-amino-compounds of this kind, in contradistinction to the *m*- and *p*-compounds (see Indole). Theoretically, it may take place in the above instance in two different ways, viz. either by the elimination of a hydrogen atom of the amino-group together with OH of the carboxyl, or of both of the amino-hydrogen atoms with the oxygen atom from the carbonyl group These two cases are distinguished by *Baeyer* as "**Lactam formation**" and "**Lactim formation**". Oxindole is the lactam of *o*-amino-phenylacetic acid, isatin, $C_6H_4<\begin{matrix}NH\\CO\end{matrix}>CO$ (p. 523), the lactam of *o*-amino-phenylglyoxylic acid, $NH_2\cdot C_6H_4\cdot CO\cdot CO\cdot OH$, and carbostyril (p 156), $C_6H_4<\begin{matrix}N=C\cdot OH\\CH:CH\end{matrix}$, the lactim of *o*-amino-cinnamic acid.

Both lactams and lactims contain hydrogen which is readily replaceable, in the former case it is present in the amino-group, and in the latter in the hydroxyl.

If the compounds which result from the replacement of hydrogen by alkyl are very stable, the alkyl in them is linked to the nitrogen, and they are derivatives of the lactams; if, on the contrary, they are easily saponifiable, the alkyl is linked to oxygen, and they are ethers of the lactims. Many lactams and lactims react as tautomeric substances (cf. Isatin and chapter on Constitution and Physical Properties).

Acids, $C_9H_{10}O_2$.—1. **Dimethyl-benzoic acids**, *Xylene-carboxylic acids*, $C_6H_3Me_2\cdot CO_2H$. Of these six are possible, and four are known. **Mesitylenic acid**, $(CO_2H:CH_3:CH_3 = 1\ 3\ 5)$, is prepared by the oxidation of mesitylene. Isomeric with them are- -

2. The **Phenyl-propionic acids**

β-**Phenyl-propionic acid** or **hydrocinnamic acid**, $C_6H_5\cdot CH_2\cdot CH_2\cdot CO_2H$, is prepared by reducing cinnamic acid with sodium amalgam, or with hydrogen in presence of colloidal palladium, and is also formed during the decay of albuminous matter. It crystallizes in slender needles, m.-pt. 48°, b.-pt. 280°.

Many substitution products of this acid are known, among which may be mentioned *o*-**nitro-cinnamic acid dibromide**, $NO_2\cdot C_6H_4\cdot CHBr\cdot CHBr\cdot CO_2H$, a compound nearly related to indigo (p. 523), further, **phenyl-α-amino-propionic acid** (phenyl-alanine), $C_6H_5\cdot CH_2\cdot CH(NH_2)\cdot CO_2H$, and **phenyl-β-amino-propionic acid**, $C_6H_5\cdot CH(NH_2)\cdot CH_2\cdot CO_2H$, both of which can be prepared synthetically, the former being like-

wise produced during the decay of albumen and during the germination of *Lupinus luteus*.

o-**Amino-hydrocinnamic acid,** $C_6H_4<^{NH_2}_{C_2H_4\cdot CO_2H}$, is not stable, but is immediately transformed into its lactim, **hydrocarbostyril,** $C_6H_4<^{N\ -\ C\cdot OH}_{CH_2\cdot CH_2}$, a quinoline derivative.

Hydratropic acid, *α-Phenyl-propionic acid,* $CH_3\cdot CH(C_6H_5)\cdot CO_2H$, is obtained—as its name implies—by the addition of hydrogen to atropic acid. It is liquid and volatile with steam

2. MONOBASIC UNSATURATED ACIDS

1 **Cinnamic acid,** $C_6H_5\cdot CH:CH\cdot CO_2H$ (*Thommsdorf*, 1780), occurs in Peru and Tolu balsams and also in storax, and may be prepared as given at p. 441. It crystallizes in needles or prisms, dissolves readily in hot water, melts at 133°, and boils at 300°. When fused with potash, it is split up into benzoic and acetic acids, it also yields benzoic acid when oxidized. It yields salts, esters, &c., also additive compounds, with chlorine, bromine, hydrogen chloride, bromide, iodide, and also with hydrogen and hypochlorous acid, *e.g.* cinnamic acid dibromide (*β*-phenyl *α*-*β*-dibromo-propionic acid), $C_6H_5\cdot CHBr\cdot CHBr\cdot CO_2H$. Further, the hydrogen in the benzene nucleus may be replaced by Cl, Br, NO_2, NH_2, &c.

Cinnamic acids.—According to the ordinary stereo-chemical theory of unsaturated compounds, two cinnamic acids of the formula $C_6H_5\cdot CH:CH\cdot CO_2H$ should exist (cf. Maleic and Fumaric acids, p. 243). Two have been known for some time, viz. storax-cinnamic acid, melting at 134°, and *allo*-cinnamic acid, melting at 68°, prepared by reducing *β*-brom-allo-cinnamic acid with zinc and alcohol. But, in addition to these, several other cinnamic acids have been described (for summary see *Erlenmeyer*, Biochem. Zeitsch. 1911, **34**, 306): (*a*) *Liebermann's* iso-cinnamic acid (B. 1890, **23**, 141, 512), melting at 58°–59°; this occurs naturally together with the allo acid in cocaine alkaloids, and may also be obtained by fractionally crystallizing the brucine salt of allo-cinnamic acid (B. 1905, **38**, 2562), and decomposing with acid, or by the action of an alcoholic solution of zinc bromide on allo-cinnamic acid (B. 1905, **38**, 837). (*b*) *Erlenmeyer's* iso-cinnamic acid, melting at 37°–38°, and obtained by reducing *α*-brom-allo-cinnamic acid with zinc and alcohol (A. 1895, **287**, 1; B. 1904, **37**, 3361).

(*c*) Triclinic cinnamic acid, melting at 80°. (*d*) Hetero-cinnamic acid, m.-pt. 131°. The synthetical acid prepared by *Perkin's* method is, according to *Erlenmeyer* (Abs. 1911, i, 782), a mixture of storax- and hetero-acids, and can be separated by fractional precipitation of the sodium salt by hydrochloric acid or by fractional distillation of the ethyl ester. It is probable that the *allo-* and two *iso*-acids are trimorphous forms of the same substance (*Bulmann*, B. **42**, 182, 1443) They appear to give the same melt as shown by examination of refractive indices (*Stobbe*), and solubilities (*Meyer*), and also to give the same solutions as shown by their electrical conductivities (*Bjerrum*, B. **43**, 571), and absorption spectra (*Stobbe, ibid.*, 504). Any one of the three acids can be obtained from the melt by impregnating under suitable conditions with a crystal of the desired form, and even the solids are mutually transformable (*Stobbe*, B. **44**, 2735; *Meyer*, 2966)

According to *Ruber* and *Godschmidt* (B. **43**, 453) the hetero-acid is an impure form of the storax-acid, but this is denied by *Erlenmeyer* (Abs. 1911, i, 782), who also claims to have prepared optically active cinnamic acids (*ibid.*, 781), the molecules of which must be asymmetric. No satisfactory explanation of the existence of so many isomerides has been offered so far.

Although some six cinnamic acids are known, only two α-bromo-cinnamic acids and two β-bromo-cinnamic acids have been prepared. The α-bromo- and α-brom-allo-cinnamic acids are obtained by the elimination of hydrogen bromide from cinnamic acid dibromide:

$$C_6H_5\cdot CHBr\cdot CHBr\cdot CO_2H - HBr = C_6H_5\cdot CH{:}CBr\cdot CO_2H,$$

or its esters, and they melt respectively at 131° and 120°. The corresponding β-acids can be prepared by the addition of hydrogen bromide to phenyl-propiolic acid:

$$C_6H_5\cdot C{\equiv}C\cdot CO_2H + HBr = C_6H_5\cdot CBr{:}CH\cdot CO_2H.$$

They melt respectively at 135° and 159°. (Compare *Sudborough* and *Thompson*, J. C. S. 1903, 666, 1153, *Sudborough* and *Lloyd, ibid.*, 1898, 91; *Sudborough* and *Roberts, ibid.*, 1905, 1841; *Sudborough* and *James, ibid.*, 1906, 105; *James*, 1911, 1620.

o- and *p*-**Nitro-cinnamic acids**, $NO_2\cdot C_6H_4\cdot CH{:}CH\cdot CO_2H$, the first of which is of importance on account of its relation to indigo, are obtained by the nitration of cinnamic acid.

On reduction the former yields *o*-**amino-cinnamic acid**, which readily yields its lactim **carbostyril** (*α*-hydroxy-quinoline),

$$C_6H_4\begin{cases}CH:CH\\ N=\dot{C}\cdot OH\end{cases}$$

The radical of cinnamic acid, *i.e.* ($C_6H_5\cdot CH:CH\cdot CO—$), is termed "**cinnamyl**", and the group ($C_6H_5\cdot CH:CH—$) "**cinnamenyl**".

2. **Atropic acid**, $CH_2:C(C_6H_5)\cdot CO_2H$, is a decomposition product of atropine. It crystallizes in monoclinic plates, and can be distilled with steam It breaks up into formic and *α*-toluic acids when fused with potash.

3. (γ)-**Phenyl-isocrotonic acid**, $C_6H_5\cdot CH:CH\cdot CH_2\cdot CO_2H$, is formed when benzaldehyde is heated with sodium succinate and acetic anhydride (*W. H. Perkin, sen.*, also *Jayne*, A. **216**, 100).

$$C_6H_5\cdot CHO + CH_2(CO_2H)\cdot CH_2\cdot CO_2H - H_2O = C_6H_5\cdot CH\cdot CH(CO_2H)\cdot CH_2$$

$$\dot{O}\text{———}\dot{C}O = CO_2 + C_6H_5\cdot CH:CH\cdot CH_2\cdot CO_2H$$

It is of interest on account of its conversion into *α* naphthol (see this), $C_{10}H_7\cdot OH$, upon boiling.

4. **Phenyl-propiolic acid**, $C_6H_5\cdot C\vdots C\cdot CO_2H$ (*Glaser*, 1870), is prepared from cinnamic acid dibromide or its ethyl ester by first converting into *α*-brom-cinnamic acid by elimination of hydrogen bromide, and then into the acetylenic acid by further elimination (just as ethylene is converted by bromine into ethylene bromide, and the latter decomposed into acetylene by potash). It crystallizes in long needles, and melts at 136°–137°. When heated with water to 120°, it breaks up into CO_2 and phenyl-acetylene (p. 353). It can be reduced to hydrocinnamic acid and transformed into benzoyl-acetic acid

o-**Nitro-phenyl-propiolic acid**, $NO_2\cdot C_6H_4\cdot C\vdots C\cdot CO_2H$ (*Baeyer*), is prepared in a manner analogous to that just given, viz. by the addition of bromine to ethyl *o*-nitro-cinnamate and treatment of the resulting bromide with alcoholic potash (A. **212**, 240). It is of interest on account of its relation to indigo (see p 526). It breaks up into CO_2 and *o*-nitro-phenyl-acetylene when heated.

3 SATURATED PHENOLIC ACIDS

(For *modes of formation*, see p. 440.) These acids may also be obtained by the oxidation of the homologues of phenol

and of the hydroxy-aldehydes, which is effected, among other methods, by fusion with alkalis.

The phenolic acids form salts both as carboxylic acids and as phenols, salicylic acid, for instance, the two following classes.

$C_6H_4\langle^{OH}_{CO_2Na}$ and $C_6H_4\langle^{ONa}_{CO_2Na}$

Mono- and Di sodium salicylate

The first of these two salts is not decomposed by CO_2, while the second, as the salt of a phenol, is decomposed by it and converted into the first. The phenolic acids behave, therefore, like monobasic acids towards sodium carbonate When both of the hydrogen atoms are replaced by alkyl, there are formed compounds such as $C_2H_5O \cdot C_6H_4 \cdot CO_2C_2H_5$, which, as both ethers and esters, are only half hydrolysed when boiled with potash, *e.g.* to $C_2H_5O \cdot C_6H_4 \cdot CO_2H$, ethyl salicylic acid The ether acids thus formed possess completely the character of monobasic acids, their alphyl radical being only eliminated by hydriodic acid at a rather high temperature. (Cf. p. 412.)

The *o*-hydroxy-acids ($CO_2H:OH = 1:2$) are, in contradistinction to their isomers, volatile with steam, give a violet or blue coloration with ferric chloride, and are readily soluble in cold chloroform.

The *m*-hydroxy-acids are more stable than the *o*- and *p*-compounds, while most of the latter break up into carbon dioxide and phenols when quickly heated, or when acted on by hydrochloric acid at 220°, the former remain unaltered.

The phenolic acids are much more easily converted into halogen or nitro-substitution products than the monobasic acids, just as the phenols are far more readily attacked than the benzene hydrocarbons

Salicylic acid, *o-Hydroxy-benzoic acid* ($CO_2H:OH = 1:2$), was discovered by *Piria* in 1839 It occurs in the blossom of *Spiræa Ulmaria*, and as its methyl ester in oil of winter-green, &c. It may be obtained by the oxidation of the glucoside saligenin; by fusing coumarin, indigo, *o*-cresol, &c., with potash; by diazotizing *o*-amino-benzoic acid, &c. (see p. 387).

Preparation.—Sodium phenoxide is heated in a stream of carbon dioxide at 180°–220° (*Kolbe*, A. **113**, 125; **115**, 201, &c.), when half of the phenol distils over and basic salicylate of sodium remains behind:

$$C_6H_5 \cdot ONa + CO_2 = OH \cdot C_6H_4 \cdot CO_2Na;$$
$$OH \cdot C_6H_4 \cdot CO_2Na + C_6H_5 \cdot ONa = ONa \cdot C_6H_4 \cdot CO_2Na + C_6H_5 \cdot OH.$$

Should potassic phenoxide be used instead of the sodic compound, salicylic acid is likewise formed if the temperature be kept low (150°), but the isomeric para-hydroxy-benzoic acid at a higher temperature (220°) Mono-potassic salicylate, $C_6H_4(OH)\cdot CO_2K$, decomposes in an analogous manner at 220° into phenol and di-potassic *p*-hydroxy-benzoate.

As *Kolbe's* original method of preparation converted only 50 per cent of the phenol into salicylic acid, *Schmitt* devised the following modification:—The sodic phenoxide is heated in a closed vessel with carbon dioxide at 130°, and the compound first formed, $C_6H_5\cdot O\cdot C\leqslant^{ONa}_{O}$, sodic phenyl-carbonate, is thus transformed into mono-sodic salicylate by the exchange of the $\cdot CO\cdot ONa$ group with the ortho-hydrogen atom of the phenyl radical. (Cf. B. 1905, **38**, 1375, A. 1907, **351**, 313; C.C. 1907, ii, 48.)

Salicylic acid crystallizes in colourless four-sided monoclinic prisms, dissolves sparingly in cold water but readily in hot; it melts at 155°, can be sublimed, but is decomposed into phenol and CO_2 when heated quickly, ferric chloride colours the aqueous solution violet. It is an important antiseptic. It forms two series of salts (the basic calcium salt being insoluble in water), and two series of derivatives, viz: (1) as an acid it yields chlorides, esters, &c, and (2) as a phenol it yields ethers, &c., *e g* ethyl-salicylic acid, $C_6H_4(O\cdot C_2H_5)CO_2H$

Phenyl salicylate, $C_6H_4\leqslant^{OH}_{CO\cdot OC_6H_5}$, the ester derived from phenol and salicylic acid, and generally termed "**Salol**", is a good antiseptic, and is prepared by the action of an acid chloride such as $POCl_3$ or $COCl_2$ upon a mixture of salicylic acid and phenol, or by heating the acid itself at 220°. It forms colourless crystals. When its sodium salt is heated to 300°, it undergoes molecular transformation into the sodium salt of the isomeric **phenyl-salicylic acid**, $C_6H_5O\cdot C_6H_4\cdot CO_2Na$ (B. **21**, 501). Analogous "salols" are obtained from other phenols, *e.g.* *p*-acetylaminophenol yields *salophene*.

m-**Hydroxy-benzoic acid** is prepared by diazotizing *m*-amino-benzoic acid. It crystallizes in microscopic plates, dissolves readily in hot water, and sublimes without decomposition; ferric chloride does not colour its aqueous solution.

p-**Hydroxy-benzoic acid** forms monoclinic prisms ($+ H_2O$), and ferric chloride gives no coloration with the aqueous solution. As a phenol it yields the methyl ether, **anisic**

acid, $C_6H_4(O\cdot CH_3)\cdot CO_2H$, which can be prepared by treating *p*-hydroxy-benzoic acid with methyl alcohol, potash and methyl iodide, and saponifying the dimethyl derivative first formed; it is also formed by the oxidation of anisole. In consequence of the phenolic hydroxyl having been etherified, it resembles the monobasic and not the phenolic acids, boiling—for example—without decomposition; hydriodic and hydrochloric acids at high temperatures decompose it into *p*-hydroxy-benzoic acid and methyl iodide or chloride.

Hydro-para-coumaric acid (1:4), $OH\cdot C_6H_4\cdot CH_2\cdot CH_2\cdot CO_2H$, *β-p-hydroxy-phenyl-propionic acid*, is produced by the decay of **tyrosine**, *β-hydroxy-phenyl-alanine*, $OH\cdot C_6H_4\cdot CH_2\cdot CH(NH_2)\cdot CO_2H$, and also synthetically from *p*-nitro-cinnamic acid:

$$NO_2\cdot C_6H_4\cdot CH{:}CH\cdot CO_2H \xrightarrow[\text{reduced}]{} NH_2\cdot C_6H_4\cdot CH_2\cdot CH_2\cdot CO_2H \xrightarrow[\text{diazotized}]{} OH\cdot C_6H_4\cdot CH_2\cdot CH_2\cdot CO_2H$$

Tyrosine, which crystallizes in fine silky needles, is found in old cheese (τυρός), in the pancreatic gland, in diseased liver, in molasses, &c., and results from albumen, horn, &c., either upon boiling these with sulphuric acid or from their pancreatic digestion or their decay.

It has also been obtained synthetically, as indicated by the following series of reactions.—

$$C_6H_5\cdot CH_2\cdot CHO + HCN \longrightarrow C_6H_5\cdot CH_2\cdot CH(OH)\cdot CN + NH_3 \longrightarrow C_6H_5\cdot CH_2\cdot CH(NH_2)\cdot CN \longrightarrow C_6H_5\cdot CH_2\cdot CH(NH_2)\cdot CO_2H \longrightarrow NO_2\cdot C_6H_4\cdot CH_2\cdot CH(NH_2)\cdot CO_2H \longrightarrow OH\cdot C_6H_4\cdot CH_2\cdot CH(NH_2)\cdot CO_2H$$

(Compare also B. **32**, 3638.)

Of the numerous **polyhydroxy-phenolic acids**, the following may be mentioned:—

Protocatechuic acid, 3:4-*Dihydroxy-benzoic acid*, is obtained by fusing various resins, such as catechu, benzoin, and kino, with alkali. It may be prepared synthetically, together with the 2:3-dihydroxy-acid, by heating catechol, $C_6H_4(OH)_2$, with ammonium carbonate. It crystallizes in glistening needles or plates, and is readily soluble in water; the solution is coloured green by ferric chloride, then—after the addition of a very little sodic carbonate—blue, and finally red. Like catechol it possesses reducing properties. Its mono-methyl ether is **vanillic**

acid, or *p-hydroxy-m-methoxy-benzoic acid*, $C_6H_3(CO_2H)(O \cdot CH_3)(OH)$, which is obtained by the oxidation of vanillin (p. 430), its dimethyl ether is the **veratric acid** of sabadilla seed (*Veratrum Sabadilla*), and its methylene ether is **piperonylic acid**, $CH_2\langle{}^{O}_{O}\rangle C_6H_3 \cdot CO_2H$, which can be prepared, among other methods, by the oxidation of piperic acid (p. 464).

Gallic acid, 3:4·5-*Trihydroxy-benzoic acid*, $C_6H_2(OH)_3CO_2H$, occurs in nut-galls, in tea and many other plants, and as glucosides in several tannins. It is prepared by boiling tannin with dilute acids, or by allowing mould to form on its solution, and has also been obtained synthetically by various reactions. It crystallizes in fine silky needles ($+ H_2O$), dissolves readily in water, alcohol, and ether, and has a faintly acid and astringent taste. It evolves carbon dioxide readily when heated, yielding pyrogallol, reduces gold and silver salts, and yields a bluish-black precipitate with ferric chloride. Like pyrogallol, it is very readily oxidized in alkaline solution, with the production of a brown colour.

Gallic acid is used in the manufacture of blue-black inks. With ferrous sulphate it gives a pale-brown colour, which rapidly turns black on exposure to the air; the presence of a minute quantity of free sulphuric acid retards this oxidation, but when the acidified solution is used with ordinary paper the acid is neutralized by compounds present in the paper, and the oxidation takes place. Indigo carmine is added to the ink in order to give it a blue colour before oxidation occurs. *Dermatol* and *Airol* are bismuth derivatives.

Tannin, *Gallotanic acid*, is a colourless, amorphous, glistening mass, readily soluble in water but only slightly in alcohol, and almost insoluble in ether. It forms the chief constituent of nut-galls, and is likewise present in sumach, tea, &c. It yields gallic acid when boiled with dilute acids, and a product similar to tannin may be obtained from gallic acid by the dehydrating action of phosphorus oxychloride. The constitution is not known; it is evidently a complex compound, and appears to be optically active.

The aqueous solution is coloured dark-blue by ferric chloride. The **mercury salt** is used in medicine. Tannin has an affinity for the animal skin and for glue, and is abstracted from its solution by these substances, the skin being thus tanned or converted into leather. Numerous other tannic acids are known, and are usually named according to the plant from

which they are obtained, *e.g.* kino tannin, catechu tannin, coffee tannin, &c.

Quinic acid, which is found in quinine bark, coffee beans, &c., is a hexahydro-tetrahydroxy-benzoic acid, $C_6H_7(OH)_4CO_2H$. It crystallizes in colourless prisms and is optically active, an inactive modification being also known.

4. ALCOHOL- AND KETO-ACIDS

The monobasic aromatic alcohol-acids, which possess at one and the same time the characters of acids and of true alcohols (p. 436), contain the alcoholic hydroxyl in the side chain; this hydroxyl is consequently eliminated together with the side chain when the compound is oxidized.

In behaviour they approximate very closely to the hydroxy-acids of the fatty series, as the phenylated derivatives of which they thus appear; at the same time they yield, as phenyl derivatives, nitro-compounds, &c, although those compounds can often not be prepared directly, on account of the readiness with which the acids are oxidized. They differ from the phenolic acids in being more soluble in water, less stable, and non-volatile; as alcohols many of them give up water and yield unsaturated acids (which the phenolic acids can never do), and they can be esterified by hydrobromic acid, &c., with the formation of haloid-substitution acids, &c. Further, they are purely monobasic acids

The hydroxy-acids may be either primary, secondary, or tertiary alcohols, *e.g.* $OH\cdot CH_2\cdot C_6H_4\cdot COOH$, $C_6H_5\cdot CH(OH)\cdot COOH$, and $C_6H_5\cdot CH_2\cdot C(CH_3)(OH)\cdot COOH$. The tertiary can sometimes be prepared directly by the oxidation of such acids $C_nH_{2n-8}O_2$ as contain a tertiary hydrogen atom (:CH), by means of permanganate.

To the ketonic acids the corresponding reactions apply. As ketones they may be reduced to secondary alcohol-acids, and they further react with hydroxylamine, &c.; as acids they form salts, esters, &c.

Mandelic acid, *Phenyl-glycollic acid*, $C_6H_5\cdot CH(OH)\cdot CO_2H$ (1835), is formed by hydrolysing amygdalin with hydrochloric acid, and synthetically by the hydrolysis of benzaldehyde-cyanhydrin, $C_6H_5\cdot CH(OH)\cdot CN$ (see pp. 126 and 424). It forms glistening crystals, dissolves somewhat readily in water, and melts at 133°.

Mandelic acid possesses an asymmetric carbon atom and

exists in two optically active modifications (cf. B. **16**, 1565 and 2721), and these can form a racemic compound (para-mandelic acid) in the same manner as *d*- and *l*-tartaric acids.

The acid obtained synthetically is the racemic acid, but this can be resolved (1) by the aid of chinchonine when the chinchonine salt of the *d*-acid crystallizes first; (2) by means of green mould, "penicillium glaucum", which when grown on a solution of the ammonium salt of the acid destroys the lævo modification; (3) by partially esterifying the racemic acid with an optically active alcohol, *e.g.* *l*-menthol; the non-esterified acid is then *l*-rotatory, as the *d*-acid is somewhat more readily esterified by *l*-menthol than the *l*-acid. The method is not quantitative (*Marckuald* and *Mackenzie*, B. 1899, **32**, 2130; 1901, **34**, 469; also J. C. S. 1899, 964). The acid obtained from amygdalin is the lævo compound. It is comparable with lactic acid, $CH_3 \cdot CH(OH) \cdot CO_2H$, yielding, like the latter, formic acid (together with benzoic) when oxidized; hydriodic acid reduces it to phenyl-acetic acid, just as it does lactic acid to propionic.

***o*-Hydroxymethyl-benzoic acid**, $OH \cdot CH_2 \cdot C_6H_4 \cdot CO \cdot OH$, which is isomeric with mandelic acid, is unstable in the free state; as an ortho-compound, it readily yields the anhydride or lactone, **Phthalide**, $C_6H_4 \langle \begin{matrix} CH_2 \\ CO \end{matrix} \rangle O$, which is obtained by the reduction of phthalic anhydride or chloride. It crystallizes in needles or plates, and can be sublimed unaltered.

Tropic acid, *α-Phenyl-β-hydroxy-propionic acid*, $OH \cdot CH_2 \cdot CHPh \cdot CO_2H$ (fine prisms), is obtained together with tropine by boiling atropine with baryta water; it is reconverted into atropine when warmed with tropine and hydrochloric acid. It exists in several optically different (*d*-, *l*-, and *r*-) modifications.

Benzoyl-formic acid, *Phenyl-glyoxylic acid*, $C_6H_5 \cdot CO \cdot CO_2H$, is obtained synthetically by the hydrolysis of benzoyl cyanide, $C_6H_5 \cdot CO \cdot CN$, with cold fuming HCl (*Claisen*, 1877), and also by the cautious oxidation of mandelic acid or acetophenone. It is an oil which only solidifies slowly, and when distilled is largely decomposed into carbon monoxide and benzoic acid. It reacts similarly to isatin with benzene containing thiophene and sulphuric acid, and shows the normal reactions of the ketonic acids with $NaHSO_3$, HCN, $NH_2 \cdot OH$, &c.

***o*-Nitro-benzoyl-formic acid**, $NO_2 \cdot C_6H_4 \cdot CO \cdot CO_2H$, which can be prepared from *o*-nitro-benzoyl cyanide, yields ***o*-amino-**

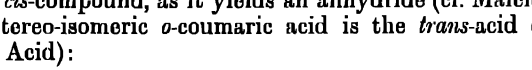
benzoyl-formic acid, *isatic acid*, $NH_2 \cdot C_6H_4 \cdot CO \cdot CO_2H$ (a white powder), upon reduction; when a solution of the latter is warmed, it yields its intramolecular anhydride (lactam), isatin, $C_6H_4 \langle \begin{matrix} NH \\ CO \end{matrix} \rangle CO$ (cf. p. 523).

Benzoyl-acetic acid, $C_6H_5 \cdot CO \cdot CH_2 \cdot CO_2H$ (*Baeyer*), is a perfect analogue of acetoacetic acid, and, like the latter, can be used for the most various syntheses. It is obtained as its ethyl ester (which is soluble in cold sodic hydroxide solution) by dissolving ethyl phenyl-propiolate in concentrated sulphuric acid and pouring the solution into water (B. **16**, 2128); or, better, by the action of sodium ethoxide upon a mixture of ethyl benzoate and acetate (*Claisen's* condensation, p. 225) (B. **20**, 651). It is crystalline, melts at 103°, and readily splits up into carbon dioxide and acetophenone, $C_6H_5 \cdot CO \cdot CH_3$; the aqueous solution is coloured a beautiful violet by ferric chloride

5. UNSATURATED MONOBASIC PHENOLIC ACIDS

Hydroxy-cinnamic or **Coumaric Acids**, $OH \cdot C_6H_4 \cdot CH{:}CH \cdot CO_2H$.—The ortho-acid is present in melilot (*Melilotus officinalis*), and can be prepared by diazotizing *o*-amino-cinnamic acid, or from salicylic aldehyde by *Perkin's* synthesis. The alcoholic solution is yellow with a green fluorescence.

Coumarin, $C_6H_4 \langle \begin{matrix} O\text{—}CO \\ CH{:}CH \end{matrix}$, is the aromatic principle of woodruff (*Asperula odorata*), and is also found in the Tonka bean and other plants. It is obtained by the elimination of water from *o*-coumaric acid by means of acetic anhydride. It crystallizes in prisms, dissolves readily in alcohol, ether, and hot water; melts at 67°, and boils at 290°. It dissolves in sodium hydroxide solution, yielding the sodium salt of **coumarinic acid**. This salt is stereo-isomeric with that of *o*-coumaric acid. The free acid itself appears to be incapable of existence, as it is immediately converted into coumarin (its anhydride), but various derivatives are known. *o*-Coumarinic acid is regarded as the *cis*-compound, as it yields an anhydride (cf. Maleic Acid). The stereo-isomeric *o*-coumaric acid is the *trans*-acid (cf. Fumaric Acid):



o-Coumaric Coumarinic acid.

3:4-**Dihydroxy-cinnamic acid**, *Caffeic acid*, $(OH)_2 \cdot C_6H_3 \cdot CH : CH \cdot CO_2H$, crystallizes in yellow prisms, and is obtained from caffetannic acid, whose mono-methyl ether is **ferulic acid** (from asafœtida); the isomeric **umbellic acid** or *p*-hydroxy-*o*-coumaric acid readily changes into the anhydride corresponding to coumarin, viz. **umbelliferone**, $C_9H_6C_3$; this last-named compound is present in varieties of Daphne.

Related to the above is **piperic acid**:

$$CH_2\langle\begin{matrix}O\\O\end{matrix}\rangle C_6H_3 \cdot CH : CH \cdot CH : CH \cdot CO_2H,$$

a decomposition product of piperine (p. 540), which crystallizes in long needles.

B. Dibasic Acids

The dibasic acids occupy exactly the same position in the aromatic series as the dibasic acids $C_nH_{2n-2}O_4$ do in the fatty. They contain two carboxyl groups; these may both be in the nucleus or in the side chain or chains, or be divided between them. They yield acid salts and normal salts, and similarly two series of esters, amides, &c. Dibasic phenolic acids can of course occur here also.

1. **Phthalic acid**, *Benzene-o-dicarboxylic acid*, $C_6H_4(CO_2H)_2$ (*Laurent*, 1836), is formed when any *o*-di-derivative of benzene, which contains two carbon side chains, is oxidized by HNO_3 or $KMnO_4$, but not by CrO_3 (cf. p. 138); it is generally formed by the oxidation of naphthalene by nitric acid, and also of anthracene derivatives. In preparing it on the large scale the naphthalene is first converted into its tetra-chlor-addition product, $C_{10}H_8Cl_4$, and then oxidized. At the present time phthalic acid is prepared on the commercial scale by oxidizing naphthalene with concentrated sulphuric acid in the presence of a small amount of mercury or mercuric sulphate at 220–300°. It crystallizes in short prisms or plates, melts at 213°, and is readily soluble in water, alcohol, and ether. When heated above its melting-point, it yields the anhydride. When heated with lime, it yields benzoic acid or benzene according to the relative amounts of acid and lime used. Chromic acid disintegrates it completely, while sodium amalgam converts it into dihydro-, tetrahydro-, and finally hexahydro-phthalic acid (see below). Its barium salt, $C_6H_4(CO_2)_2Ba$, is sparingly soluble in water. K = 0·121.

Phthalic anhydride, $C_6H_4<\begin{matrix}CO\\CO\end{matrix}>O$, crystallizes in magnificent long prisms which can be sublimed; it melts at 128°, boils at 284°, and is used in the preparation of eosin dyes (see Fluorescein).

Phthalimide, $C_6H_4<\begin{matrix}CO\\CO\end{matrix}>NH$, corresponds with succinimide in many respects. It is obtained by passing dry ammonia over heated phthalic anhydride, and readily gives rise to metallic derivatives. The *potassium salt* $C_6H_4(CO)_2NK$, obtained by the action of aqueous caustic potash on an alcoholic solution of the imide, readily reacts with alkyl iodides, yielding alkylated phthalimides, *e.g.* $C_6H_4(CO)_2NC_2H_5$, and when these are hydrolysed, primary amines, free from secondary and tertiary, are obtained, *e.g.*.

$$C_6H_4{:}(CO)_2{:}NC_2H_5 + 2H_2O = C_6H_4(CO_2H)_2 + C_2H_5NH_2$$

(*Gabriel*, B. 1887–1897). Numerous primary amines, including halogenated bases, which are difficult to prepare by other methods, have been obtained in this way. *E Fischer* (B 1901, **34**, 455) has also used the same method for the preparation of the complex amine ornithine,

$$NH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH(NH_2)\cdot CO_2H,$$

$\alpha\delta$-diamino-*n*-valeric acid The various steps are —Potassium phthalimide and trimethylene bromide yield

$$C_6H_4{:}(CO)_2{:}N\cdot CH_2\cdot CH_2\cdot CH_2Br,$$

and this on condensation with ethyl sodio-malonate gives

$$C_6H_4.(CO)_2{:}N\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH(CO_2Et)_2,$$

and on bromination and subsequent hydrolysis and loss of carbon dioxide

$$C_6H_4{:}(CO)_2{:}N\cdot CH_2\cdot CH_2\cdot CH_2\cdot CHBr\cdot CO_2H$$

is obtained. Aqueous ammonia converts this into the corresponding amino-compound, and subsequent hydrolysis gives ornithine.

The chloride, **phthalyl chloride**, which is obtained by the action of PCl_5 upon the acid or the anhydride, appears not to have the normal constitution $C_6H_4(COCl)_2$, but $C_6H_4<\begin{matrix}CCl_2\\CO\end{matrix}>O$, as it yields phthalo-phenone, $C_6H_4<\begin{matrix}C(C_6H_5)_2\\CO\end{matrix}>O$, with benzene

and aluminium chloride, and on reduction with sodium amalgam it yields phthalide, $C_6H_4<\begin{matrix}CH_2\\CO\end{matrix}>O$, the constitution of which is confirmed by its conversion on hydrolysis into *o*-hydroxy-methyl-benzoic acid (p. 462), $OH \cdot CH_2 \cdot C_6H_4 \cdot CO \cdot OH$.

2. **Isophthalic acid** (1:3), prepared from *m*-xylene, crystallizes in slender needles from hot water, in which it is only sparingly soluble; it sublimes without forming an anhydride. The barium salt is readily soluble in water $K = 0{\cdot}0287$.

Uvitic acid is 5-methyl-isophthalic acid, and may be obtained by oxidizing mesitylene.

3. **Terephthalic acid** (1:4) is obtained by the oxidation of *p*-xylene, cymene, &c., and especially of oil of turpentine or oil of cumin. It forms a powder almost insoluble in alcohol and water, and sublimes unchanged. For its preparation *p*-tolnic acid is oxidized by potassic permanganate (A. **258**, 9). The barium salt is only sparingly soluble.

A. Baeyer's researches (A. **245**, **251**, **258**, **266**, **269**, and **276**) have introduced us to a whole series of reduction products of phthalic acid, generally known as hydro-phthalic acids. The isomers among them differ from one another either by the position of the double bond in the ring (*structural isomerism*), or by the spatial arrangement of the carboxyl groups with respect to the ring (*stereo-isomerism*). This latter isomerism corresponds to a certain extent with that of fumaric and maleic acids, but more closely with that of the poly-methylene compounds (p. 325), and a distinction is therefore made here also between a *trans*- and a *cis*-form (cf. A. **245**, 130). Exactly the same applies to the hydro-terephthalic acids.

Of the **hydro-phthalic acids** (A **269**, 147) there are now known:—Five *dihydro-acids* (two of which are stereo-isomeric), four *tetrahydro-acids* (of which two again are stereo-isomeric), and two *hexahydro-acids* (which are stereo-isomers). Of the **hydro-terephthalic acids** (A **258**, 1), five *dihydro*-, three *tetrahydro*-, and two *hexahydro-acids* are known, two in each group being stereo-isomeric.

The following principles have largely served for determining the position of the double bonds in these compounds:—(1) When bromine substitutes in a carboxylic acid it takes up the *α*-position to the carboxyl (*i.e.* it is attached in the benzene nucleus to the same carbon atom to which the carboxyl is linked). (2) If two bromine atoms stand in the *ortho*-position to one another in a reduced benzene nucleus, they are elimi-

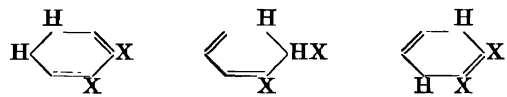
nated, without replacement, by the action of zinc dust and glacial acetic acid; whereas, if they stand in the *para*-position, they are replaced by hydrogen. (3) As in the case of the aliphatic unsaturated acids, boiling with sodic hydroxide solution often gives rise to an isomeric acid, due to the "wandering" of a double bond in the direction of a carboxyl group (p 162). (4) The stereo-isomeric modifications are also easily transformed one into the other.

The relations existing between the five known dihydro-phthalic acids may be taken as an example. When phthalic acid is reduced by sodium amalgam in presence of acetic acid, *trans*-Δ-3.5-dihydro-phthalic acid is produced, and this changes into the *cis*-Δ-3:5-acid when heated with acetic anhydride.



Trans-Δ-3:5 *Cis*-Δ-3 5

Both of these yield the Δ-2:6-dihydro-acid when warmed with alkali When the dihydrobromide of the latter acid is treated with alcoholic potash, the Δ-2.4-dihydro-acid results, and, lastly, the anhydride of this yields the anhydride of the Δ-1·4-dihydro-acid when heated:



Δ-2·6 Δ-2.4 Δ-1:4

All the dihydro-phthalic acids give anhydrides with the exception of the *trans*-Δ-3:5-acid, which in this respect comports itself like fumaric acid.

The following relationships have been established between the hydro-terephthalic acids·—

Terephthalic acid reduced with pure sodium amalgam in faintly alkaline solution gives a mixture of *cis*- and *trans*-Δ-2:5-dihydro-acids, both of which on oxidation readily yield terephthalic acid. When boiled with water both are converted into the Δ-1:5-dihydro-acid, and when boiled with caustic soda

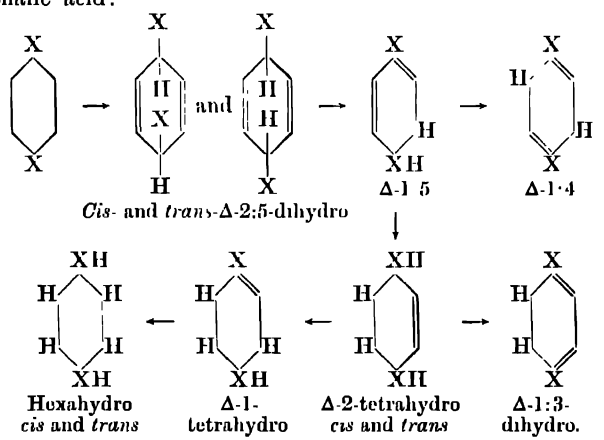
* In these formulæ X = CO_2H, Δ denotes the double bond, and the numbers refer to the carbon atoms after which the double bonds are placed. Δ-3·5 indicates two double bonds, one between carbons 3 and 4, and a second between carbons 5 and 6.

solution into the Δ-1:4-dihydro-acid. This acid is the most stable of the dihydro-acids, and is always obtained by the reduction of terephthalic acid unless great care is taken in the reduction.

When reduced with sodium amalgam the Δ-1:5-acid is converted into a mixture of *cis*- and *trans*-Δ-2-tetrahydro-acid. Both acids readily combine with bromine, which can again be removed by means of zinc dust; this dibromide, when warmed with alcoholic potash, gives the Δ-1:3-dihydro-acid, which cannot be obtained directly by the reduction of terephthalic acid.

The Δ-1-tetrahydro-acid may be obtained by warming the Δ-2-acid with sodium hydroxide solution

The Δ-1-acid yields a mixture of two stereo-isomeric dibromides (*cis* and *trans*), and these when reduced with zinc dust and acetic acid yield the *cis*- and *trans*-hexahydro-terephthalic acid:



The completely hydrogenized acids show great differences from the partially hydrogenized. Thus, hexahydro-terephthalic acid is exactly similar to a saturated acid of the fatty series; cold permanganate of potash has no effect upon it, while bromine substitutes (upon warming).

On the other hand, the partially hydrogenized acids comport themselves precisely like the unsaturated acids of the fatty series with an open chain. They are very readily oxidized by cold permanganate, and take up bromine or hydrobromic

acid until the saturation stage of the hexa-methylene ring is reached All of the hydro-acids can be transformed back into phthalic acid (A. 1894, **280**, 94).

For **hydro-isophthalic acids**, see *W. H Perkin, Jun*, and *S S Pickles*, P. 1905, 75, and *Baeyer* and *Villiger*, A. 1893, **276**, 255. Two stereo-isomeric modifications of the hexahydro-acid are also obtained synthetically from derivatives of the fatty series (*Perkin*, J. C. S. 1891, 798). This constitutes a further proof that the hexahydro-benzene-carboxylic acids are nothing more than hexa-methylene derivatives.

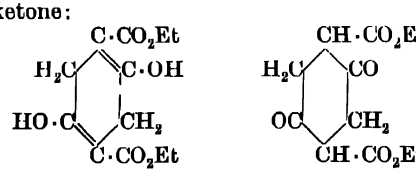
A large number of substitution products of the phthalic acids are known, *e g* **chloro-** and **bromo-phthalic acids** (which are used in the eosin industry), nitro-, amino-, hydroxy- and sulpho-phthalic acids, &c.

HYDROXY-PHTHALIC ACIDS

2 5-**Dihydroxy-terephthalic acid**, *quinol-p-dicarboxylic acid*, $C_6H_2(OH)_2(CO_2H)_2$, in which both the hydroxyls and the carboxyls are respectively in the *p*-position to one another, is obtained as its ethyl ester by the action of bromine upon succinylo-succinic ester, or of sodium ethoxide upon dibromo-acetoacetic ester. The free acid breaks up into quinol and carbon dioxide when distilled, and is converted by nascent hydrogen into succinylo-succinic acid.

Succinylo-succinic acid, *p-dihydroxy-dihydro-terephthalic acid*, $C_6H_4(OH)_2(CO_2H)_2$, is obtained as its ethyl ester by the action of sodium upon ethyl succinate (see p 312). The **ethyl ester** crystallizes in triclinic prisms which melt at 126°, and dissolves in alcohol to a bright-blue fluorescent liquid which is coloured cherry-red by ferric chloride. It contains two replaceable hydrogen atoms, being analogous to acetoacetic ester The free acid, on losing carbon dioxide, changes into tetrahydro-quinone or *p-diketo-hexamethylene*.

The ester may be represented as a dihydroxylic compound or as a diketone:



and reacts as a tautomeric substance (cf. Ethyl Acetoacetate).

C. Polybasic Acids

Benzene *s*-tricarboxylic acid or **trimesic acid**, $C_6H_3(COOH)_3$, can be obtained by the oxidation of mesitylene. The isomeric unsym. acid or **trimellitic acid** is obtained by the oxidation of colophonium, and the adjacent acid or **hemimellitic acid** is obtained by oxidizing naphthalene-1.8-dicarboxylic acid.

The benzene tetracarboxylic acids, $C_6H_2(CO_2H)_4$, **prehnitic acid** [1:2:3.4], **mellophanic acid** [1.2:3:5], and **pyromellitic acid** [1:2:4·5], are obtained by heating mellitic acid or its hexahydro-derivatives.

Mellitic acid, $C_6(CO_2H)_6$, occurs in peat as aluminium salt or honey-stone, $C_{12}Al_2O_{12} + 18H_2O$, which crystallizes in octahedra, and is also formed by the oxidation of lignite or graphite with $KMnO_4$. It forms fine silky needles of great stability, can neither be chlorinated, nitrated, nor sulphonated, but is readily reduced by sodium amalgam to **hydromellitic acid**, $C_6H_6(CO_2H)_6$, and yields benzene when distilled with lime.

As regards the esterification of these polybasic acids, it has been found that carboxylic groups which have other carboxylic groups in two ortho-positions cannot be esterified by the usual catalytic process, *e.g.* on esterification by the *Fischer-Speyer* method, hemimellitic acid and prehnitic acid yield dimethyl esters only, pyromellitic acid yields a tetramethyl ester, and mellitic acid is not acted on (*V. Meyer* and *Sudborough*, B. 1894, **27**, 3146).

XXVII. AROMATIC COMPOUNDS CONTAINING TWO OR MORE BENZENE NUCLEI. DIPHENYL GROUP

The aromatic compounds hitherto considered, with the exception of azobenzene, benzophenone, &c., contain but one benzene nucleus. In addition to these, however, a considerable number of compounds are known which contain two or more such nuclei united in a variety of ways. Such compounds are usually arranged in the following groups:—

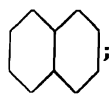
1. **Diphenyl group**; this comprises the compounds with two benzene nuclei directly united together. The parent substance of the group is diphenyl, $C_6H_5 \cdot C_6H_5$.

2. **Diphenyl-methane group**; this includes all compounds with two benzene nuclei attached to a single carbon atom. The parent substance is diphenyl-methane, $C_6H_5 \cdot CH_2 \cdot C_6H_5$.

3. **Dibenzyl** or **stilbene group**, which comprises compounds containing two benzene nuclei linked together by a chain of two or more carbon atoms, *e.g.* dibenzyl, $C_6H_5 \cdot CH_2 \cdot CH_2 \cdot C_6H_5$, and stilbene, $C_6H_5 \cdot CH : CH \cdot C_6H_5$.

4. **Triphenyl-methane group**, which contains the compounds with three benzene nuclei attached to a single carbon atom, *e.g.* triphenyl-methane, $CH(C_6H_5)_3$.

5. In addition to the above groups several extremely important groups are known which contain two or more benzene nuclei arranged in such a manner that they have two or more carbon atoms in common, *e.g.*:

Naphthalene,  ; anthracene,  ; &c.

These are usually termed compounds with condensed benzene nuclei.

DIPHENYL GROUP

Diphenyl is related to benzene in much the same manner as ethane to methane·

CH_4 and $CH_3 \cdot CH_3$ $\qquad$ C_6H_6 and $C_6H_5 \cdot C_6H_5$.

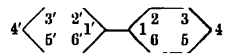
Its molecule consists of two benzene nuclei directly united Its method of synthesis by *Fittig*, by the action of sodium on an ethereal solution of monoiodo-benzene or of copper-bronze at 230° (*Ullmann*, A. **332**, 38), is analogous to the formation of ethane by the action of zinc or sodium on methyl iodide.

$$2C_6H_5I + 2Cu = C_6H_5 \cdot C_6H_5 + Cu_2I_2$$

It is also formed by passing the vapour of benzene through a red-hot tube. It is contained in coal-tar, crystallizes in large colourless plates, melts at 71°, boils at 254°, and is readily soluble in alcohol and ether.

Chromic acid oxidizes diphenyl to benzoic acid, one of the two benzene nuclei being destroyed, thus leaving only one carbon atom joined to the other benzene residue. From this and from its synthesis, the constitutional formula of diphenyl must be $C_6H_5 \cdot C_6H_5$.

Derivatives (*Schultz*, A. **207**, 311).—Like benzene, diphenyl is the mother substance of an extended series of derivatives which closely resemble the corresponding benzene derivatives in most respects. With polysubstituted derivatives the substituents are usually denoted by the following numbers, according to the position occupied:



Even the entrance of only one substituent produces isomers, since the latter may stand either in the *o*-, *m*-, or *p*-position to the point of union of the two benzene residues. The same applies in still greater degree to isomeric di-derivatives, of which *o-o*-, *p-p*-, *o-p*-, &c. compounds can exist The constitution of these is elucidated from their syntheses, from their products of oxidation, or by conversion into compounds of known constitution, thus a chloro-diphenyl, $C_{12}H_9Cl$, which yields *p*-chloro-benzoic acid when oxidized by chromic acid, is obviously *p*-chloro-diphenyl Whether all the substituents are attached to the one nucleus or are distributed between the two, can also be proved by an examination of the products of oxidation.

The substituents take up the *p*-position for choice; in di-derivatives the *p-p*- (and to a lesser extent the *o-p*-) position

Di-*p*-diamino-diphenyl, *benzidine*, $NH_2 \cdot C_6H_4 \cdot C_6H_4 \cdot NH_2$ (*Zinin*, 1845), is obtained by the reduction of *p-p*-dinitro-diphenyl (the direct nitration product of diphenyl); also, together with diphenyline, by the action of acids upon hydrazobenzene, the latter undergoing a molecular transformation (p. 395):

$$C_6H_5 \cdot NH \cdot NH \cdot C_6H_5 = NH_2 \cdot C_6H_4 \cdot C_6H_4 \cdot NH_2,$$

it is consequently formed directly from azobenzene by treating it with tin and hydrochloric acid.

Benzidine is a diacid base which crystallizes in colourless silky plates, is readily soluble in hot water or alcohol, melts at 122°, and can readily be sublimed. Its **sulphate**, $C_{12}H_{10}(NH_2)_2 \cdot SO_4H_2$, is sparingly soluble. Like its homologues (tolidine, &c.), it is of special importance in the colour industry, since, by coupling its diazonium-compound (tetrazonium-diphenyl chloride) with naphthol-sulphonic or naphthylamine-sulphonic acids, &c., colours are produced which

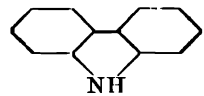
dye unmordanted cotton directly, the so-called "substantive" or cotton dyes. To this class belongs the dye **congo**,

$$(SO_3Na)(NH_2)C_{10}H_5\cdot N:N\cdot C_6H_4\cdot C_6H_4\cdot N:N\cdot C_{10}H_5(NH_2)(SO_3Na),$$

prepared by means of naphthionic acid (p. 499), and the dye **chrysamine G**, prepared with salicylic acid.

The isomeric **diphenyline**, 2·4′-diamino-diphenyl, may be obtained from 2.4′-dinitro-diphenyl, and also as a by-product in the preparation of benzidine from azobenzene. It crystallizes in needles, melting at 45°, and yields a sulphate which is readily soluble.

Carbazole,



the imide of diphenyl, is contained in coal-tar and in crude anthracene. It is formed by distilling *o*-amino-diphenyl over lime at a low red heat, or by passing the vapour of diphenylamine through red-hot tubes, just as diphenyl is obtained from benzene.

$$(C_6H_5)_2NH = (C_6H_4)_2NH + H_2.$$

It crystallizes in colourless plates sparingly soluble in cold alcohol, melts at 238°, distils unchanged, and is characterized by the readiness with which it sublimes. Concentrated sulphuric acid dissolves it to a yellow solution, and it forms an acetyl- and a nitro-compound, &c. The nitrogen in it occupies the di-ortho-position; it thus appears, like indole, to be a pyrrole derivative, and it shows, in fact, most striking analogies to the latter (B. **21**, 3299).

Benzidine-mono-, di-, &c sulphonic acids, *e.g.* $C_{12}H_6(NH_2)_2(SO_3H)_2$, are of technical importance. The **dihydroxy-diphenyls**, $C_{12}H_8(OH)_2$, of which four isomers are known, are formed (*a*) by diazotizing benzidine, (*b*) by fusing diphenyl-disulphonic acid with potash, and (*c*) by fusing phenol with potash or by oxidizing it with permanganate; in the last case hydrogen is separated and two benzene residues join together.

Diphenylene oxide, $\begin{matrix}C_6H_4\\C_6H_4\end{matrix}\!\!>\!O$, is obtained by distilling phenol with plumbous oxide; it crystallizes in plates which distil without decomposition (cf. *e.g.* B. **25**, 2745).

The **carboxylic acids** of diphenyl are obtained (1) from the

corresponding nitriles, which on their part are prepared by distilling the sulphonic acids of diphenyl with KCN, *e.g.* **di-*p*-diphenyl-dicarboxylic acid**, $C_{12}H_6(CO_2H)_2$, a white powder insoluble in water, alcohol, and ether; (2) by the oxidation of phenanthrene and similar compounds, *e.g.*, **diphenic acid**, $CO_2H \cdot C_6H_4 \cdot C_6H_4 \cdot CO_2H$, the 2:2′-dicarboxylic acid, crystallizing in needles or plates which are readily soluble in the solvents just mentioned; m.-pt. 229°. Both of these are dibasic acids, which yield diphenyl when heated with soda-lime.

The homologues of diphenyl are, like the latter, obtained by means of *Fittig's* reaction. Analogous to benzidine is ***o*-tolidine**, $C_{12}H_6(CH_3)_2(NH_2)_2$, m.-pt. 128°, whose diazo-compound unites with naphthionic acid to the red substantive dye, **benzo-purpurine 4 B**. Similarly **di-anisidine** or **dimethoxy-benzidine**, $C_{12}H_6(O \cdot CH_3)_2(NH_2)_2$, yields diazonium salts which combine with α-naphthol-α-sulphonic acid to form a blue substantive dye, **benzazurine G**.

Diphenyl may be regarded as monophenyl-benzene; the corresponding di- and triphenyl-benzenes are also known.

***p*-Diphenyl-benzene**, $C_6H_4(C_6H_5)_2$, may be obtained by the action of sodium upon a mixture of *p*-dibromo-benzene and bromo-benzene. It crystallizes in flat prisms, melts at 205°, and on oxidation yields diphenyl-monocarboxylic and terephthalic acids.

When hydrochloric acid gas is led into acetophenone, $C_6H_5 \cdot CO \cdot CH_3$, a reaction analogous to the formation of mesitylene from acetone (p. 342) ensues, and ***s*-triphenyl-benzene**, $C_6H_3(C_6H_5)_3$ (rhombic plates), is formed.

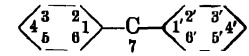
XXVIII. DIPHENYL-METHANE GROUP

Diphenyl-methane, $C_6H_5 \cdot CH_2 \cdot C_6H_5$, is derived from methane by the replacement of two hydrogen atoms by two phenyl groups, and is thus closely related to phenyl-methane or toluene, $C_6H_5 \cdot CH_3$. One important difference is that when oxidized it cannot yield an acid containing the same number of carbon atoms since it does not contain a methyl group. It can be oxidized to the secondary alcohol benzhydrol, $(C_6H_5)_2CHOH$, or the ketone benzophenone, $(C_6H_5)_2CO$. Compounds like diphenyl-ethane, $(C_6H_5)_2CH \cdot CH_3$, can yield acids.

The various derivatives are obtained by substituting one

or more of the twelve hydrogen atoms present in the diphenyl-methane molecule. If the substituent replaces any of the ten hydrogens directly attached to the benzene nuclei, a compound is formed which closely resembles the corresponding derivatives of benzene, *e.g.* $C_6H_5 \cdot CH_2 \cdot C_6H_4 \cdot NH_2$ closely resembles aniline. If, on the other hand, the substituent replaces a hydrogen atom of the methylene group, a compound with aliphatic properties is obtained, *e.g.* $(C_6H_5)_2CH \cdot OH$ closely resembles a secondary aliphatic alcohol.

The method of numbering the carbon atoms in the diphenyl-methane molecule is usually as follows:—



Formation of diphenyl-methane and its derivatives.

1. Diphenyl-methane is produced by the action of benzyl chloride upon benzene, in presence of zinc dust (*Zincke*, A. **159**, 374), or of aluminium chloride (*Friedel* and *Crafts*):

$$C_6H_5 \cdot CH_2Cl + C_6H_6 = C_6H_5 \cdot CH_2 \cdot C_6H_5 + HCl.$$

The homologues of benzene, and also the phenols and tertiary amines, may be used instead of benzene itself.

In an exactly analogous manner diphenyl-methane is obtained by the action of methylene chloride, CH_2Cl_2, upon benzene in presence of aluminium chloride:

$$CH_2Cl_2 + 2C_6H_6 = CH_2(C_6H_5)_2 + 2HCl.$$

2. Diphenyl-methane hydrocarbons are formed by the action of the aliphatic aldehydes, *e.g.* acetaldehyde or formaldehyde, upon benzene, &c., in the presence of concentrated sulphuric acid (*Baeyer*, B. **6**, 963). With formaldehyde diphenyl-methane, or with acetaldehyde diphenyl-ethane, is formed:

$$CH_3 \cdot CHO + 2C_6H_6 = CH_3 \cdot CH(C_6H_5)_2 + H_2O.$$

The acetaldehyde and formaldehyde are employed here in the form of paraldehyde and methylal. Formaldehyde itself condenses with aniline to diamino-, and with dimethyl-aniline to tetramethyl-diamino-diphenyl-methane. When aromatic aldehydes are used, triphenyl-methane derivatives are formed (p. 480).

3. Aromatic alcohols react with benzene and sulphuric acid in an analogous manner (*V. Meyer*):

$$C_6H_5 \cdot CH_2 \cdot OH + C_6H_6 = C_6H_5 \cdot CH_2 \cdot C_6H_5 + H_2O.$$

Similar reactions have also been brought about by means of ketones, aldehydo-acids, and keto-acids on the one hand, and phenol and dialkylated anilines on the other.

The true aromatic ketones of the type of benzophenone may be regarded as diphenyl-methane derivatives (see p. 428).

Diphenyl-methane, $(C_6H_5)_2CH_2$, is most conveniently prepared from benzyl chloride, benzene, and aluminic chloride. It crystallizes in colourless needles of very low melting-point (26°), is readily soluble in alcohol and ether, has a pleasant odour of oranges, and distils unaltered at 262°.

It yields nitro-, amino-, and hydroxy-derivatives. ***p*-Diamino-diphenyl-methane**, $CH_2(C_6H_4NH_2)_2$, is obtained by heating anhydro-formaldehyde-aniline, $C_6H_5 \cdot N : CH_2$, prepared from formaldehyde and aniline, with aniline and an aniline salt. It crystallizes in lustrous silvery plates, melting at 87°, and may be used for the preparation of fuchsine. Bromine at a moderate temperature reacts with the hydrocarbon yielding **diphenyl-bromo-methane**, $(C_6H_5)_2CHBr$, and when this is heated with water to 150°, it yields **benzhydrol**, *diphenyl-carbinol*, $(C_6H_5)_2CH \cdot OH$, which can also be obtained from benzophenone and sodium amalgam, or by *Grignard's* synthesis It crystallizes in glistening silky needles, melts at 68°, possesses in every respect the character of a secondary alcohol (forming esters, amines, &c.), and is readily oxidized to the corresponding ketone, benzophenone, $(C_6H_5)_2CO$ (p. 428).

αα-Diphenyl-ethane, $(C_6H_5)_2CH \cdot CH_3$ (isomeric with dibenzyl, see p. 477), is obtained by method of formation 2 (p 475). It is a liquid, boils at 286°, and is oxidized to benzophenone by chromic acid. From it is derived:

Benzilic acid, *diphenyl-glycollic acid*, $(C_6H_5)_2C(OH) \cdot CO_2H$, which is formed by a molecular transformation when benzil, $C_6H_5 \cdot CO \cdot CO \cdot C_6H_5$ (p. 479), is fused with potash. It crystallizes in needles or prisms, dissolves in concentrated sulphuric acid to a blood-red solution, and is reduced by hydriodic acid to **diphenyl-acetic acid**, $(C_6H_5)_2CH \cdot CO_2H$ (needles or plates), which may also be obtained synthetically from phenyl-bromacetic acid, $C_6H_5 \cdot CHBr \cdot CO_2H$, benzene, and zinc dust, according to mode of formation 1, p. 475.

Tolyl-phenyl-methanes, $C_6H_5 \cdot CH_2 \cdot C_6H_4 \cdot CH_3$. The *p*- and *o*-compounds are obtained from benzyl chloride and toluene.

Benzoyl-benzoic acids, benzophenone-carboxylic acids, $C_6H_5 \cdot CO \cdot C_6H_4 \cdot CO_2H$ (B. **6**, 907). Of these the *o*-acid (m.-pt. 127°) has been prepared synthetically by heating phthalic anhydride

with benzene and aluminic chloride. When heated with phosphorus pentoxide at 180°, it yields anthra-quinone, $C_6H_4\langle^{CO}_{CO}\rangle C_6H_4$; various transformations into the anthracene series have been effected in a similar manner from *o*-tolyl-phenyl-methane and the corresponding ketone.

Fluorene, *diphenylene-methane*, $\begin{matrix}C_6H_4\\C_6H_4\end{matrix}\rangle CH_2$, stands in the same relation to diphenyl-methane as carbazole (p. 473) does to diphenylamine; it is at the same time a diphenyl and a methane derivative. It is contained in coal-tar, and is produced when diphenyl-methane is led through red-hot tubes (like diphenyl from benzene), and also by passing the vapour of diphenylene-ketone over red-hot zinc dust. It crystallizes in colourless plates with a violet fluorescence, melts at 113°, and boils at 295°. The corresponding ketone, **diphenylene-ketone**, $C_{12}H_8:CO$, which crystallizes in yellow prisms melting at 84°, is obtained by heating phenanthra-quinone with lime, and is converted into **fluorenyl alcohol**, $(C_6H_4)_2:CH\cdot OH$ (colourless plates, m.-pt 153°), by nascent hydrogen, and into **diphenyl-carboxylic acid**, *o*-**phenyl-benzoic acid**, $C_6H_5\cdot C_6H_4\cdot CO_2H$, by fusion with potash.

XXIX. DIBENZYL GROUP

This group comprises the compounds containing two benzene nuclei connected by a chain of two carbon atoms. Among the most important members are:—Dibenzyl, $C_6H_5\cdot CH_2\cdot CH_2\cdot C_6H_5$; stilbene, $C_6H_5\cdot CH:CH\cdot C_6H_5$; tolane, $C_6H_5\cdot C\vdots C\cdot C_6H_5$; deoxybenzoin, $C_6H_5\cdot CH_2\cdot CO\cdot C_6H_5$; hydrobenzoin, $C_6H_5\cdot CH(OH)\cdot CH(OH)\cdot C_6H_5$; benzoin, $C_6H_5\cdot CH(OH)\cdot CO\cdot C_6H_5$; benzil, $C_6H_5\cdot CO\cdot CO\cdot C_6H_5$.

Dibenzyl is symmetrical diphenyl-ethane (for the unsymmetrical compound, see p. 476), stilbene is *s*-diphenyl-ethylene, and tolane diphenyl-acetylene.

All these compounds yield benzoic acid when oxidized.

Dibenzyl is formed when benzyl chloride is treated with metallic sodium, or by the action of benzyl chloride on benzyl magnesium chloride. It is often met with as a by-product in *Grignard's* synthesis by means of benzyl magnesium chloride.

It is isomeric with ditolyl and with tolyl-phenyl-methane; it crystallizes in needles or small plates, melts at 52°, and sublimes unchanged.

Stilbene, *s-diphenyl-ethylene*, forms monoclinic plates or prisms, melts at 125°, and also boils without decomposition. It may be prepared by the action of sodium upon benzal chloride, or by heating deoxybenzoin with sodium ethoxide, or best by the action of benzyl magnesium chloride on benzaldehyde, and possesses the full character of an olefine, giving, for instance, a dibromide, $C_6H_5 \cdot CHBr \cdot CHBr \cdot C_6H_5$, with bromine, and being converted into dibenzyl by hydriodic acid. ***p*-Diamino-stilbene**, $C_{14}H_{10}(NH_2)_2$, and its disulphonic acid (obtained by reducing *p*-nitro-toluene or its sulphonic acid in alkaline solution) are, like benzidine, mother substances of "substantive dyes" (see p. 473). Stilbene should exist in two stereo-isomeric modifications, the ordinary stilbene melting at 125° is usually regarded as the *trans* compound $\begin{matrix} H \cdot C \cdot Ph \\ \vdots \\ Ph \cdot C \cdot H \end{matrix}$. An isomeride—the *cis* compound has been described by *Otto* and *Stoffel* (B. 1897, **30**, 1799). Just as ethylene bromide yields acetylene when boiled with alcoholic potash, so stilbene dibromide yields **tolane**, which crystallizes in prisms or plates, melting at 60°. It may also be prepared by the following series of reactions:—

$$C_6H_5 \cdot CH_2 \cdot CO \cdot C_6H_5 \xrightarrow[\text{Phosphorus pentachloride}]{} C_6H_5 \cdot CH{:}CCl \cdot C_6H_5 \xrightarrow[\text{Alcoholic potash}]{} C_6H_5 \cdot C{:}C \cdot C_6H_5.$$

Tolane corresponds with acetylene in its properties in so far that it combines with chlorine to a dichloride and a tetrachloride; but it does not yield metallic derivatives, since it contains no "acetylene hydrogen" (p. 51).

When stilbene dibromide is treated with silver acetate, two di-acetates are formed; and when these are hydrolysed by alcoholic ammonia, two isomeric substances of the composition, $C_6H_5 \cdot CH(OH) \cdot CH(OH) \cdot C_6H_5$, **hydrobenzoïn** and **iso-hydrobenzoïn** or *s-diphenyl-glycol*, are produced. Both compounds are also formed by the action of sodium amalgam upon oil of bitter almonds. The former crystallizes in rhombic plates, melting at 138°, and the latter in four-sided prisms, melting at 119°, and is the more soluble of the two. The two compounds are stereo-isomeric in the same manner as meso-tartaric and racemic acid, and *Erlenmeyer. Junr.*, has been able to resolve hydrobenzoin, which corresponds with racemic acid, into

two optically active components, by separating two different kinds of hemihedral crystals (A. **198**, 115, 191; B. **30**, 1531).

The compounds **benzoïn**, **benzil**, and **deoxybenzoïn**, which have already been mentioned, are closely related to one another, as their formulæ show, and can also be prepared from benzaldehyde. When the aldehyde is boiled with an alcoholic solution of potassium cyanide it polymerises,* yielding benzoin,

$$2C_6H_5\cdot CH{:}O = C_6H_5\cdot CH(OH)\cdot CO\cdot C_6H_5,$$

which forms beautiful glistening prisms, m.-pt. 134°, nascent hydrogen reduces it to hydrobenzoin, from which it can also be obtained by oxidation. It reduces *Fehling's* solution even at the ordinary temperature, yielding benzil.

Benzil, $C_6H_5\cdot CO\cdot CO\cdot C_6H_5$, is obtained by oxidizing benzoin with nitric acid. It crystallizes in large six-sided prisms, melting at 95°. It is oxidized to benzoic acid by chromic anhydride, and reduced by nascent hydrogen—according to the conditions—either to benzoin or to deoxybenzoin. It reacts with hydroxylamine to produce:

Benzil-monoxime, $C_6H_5\cdot CO\cdot C(:N\cdot OH)\cdot C_6H_5$, and **benzil-dioxime**, $C_6H_5\cdot C(:N\cdot OH)\cdot C(:N\cdot OH)\cdot C_6H_5$, which exist in the following stereo-isomeric modifications (*Hantzsch* and *Werner*, B **23**, 11; **37**, 4295; *Dittrich*, *ibid.*, **24**, 3267):—

Monoximes:

$$\underset{\alpha\ \text{M.-pt. } 134^\circ}{C_6H_5\cdot C(\ddot{N}\cdot OH)\cdot CO\cdot C_6H_5} \xrightarrow{\text{Heated}} \underset{\gamma\ \text{M.-pt. } 113^\circ}{C_6H_5\cdot C(HO\cdot\ddot{N})\cdot CO\cdot C_6H_5}$$

Dioximes:

$$\underset{\alpha.\ \text{M.-pt } 237^\circ}{C_6H_5\cdot C(\ddot{N}\cdot OH)\cdot C(\ddot{N}\cdot OH)\cdot C_6H_5} \rightarrow \underset{\beta\ \text{M. pt } 207^\circ}{C_6H_5\cdot C(HO\cdot\ddot{N})\cdot C(\ddot{N}\cdot OH)\cdot C_6H_5} \leftarrow \underset{\gamma\ \text{M. pt } 163^\circ}{C_6H_5\cdot C(HO\cdot\ddot{N})\cdot C(HO\cdot\ddot{N})\cdot C_6H_5}$$

The configurations have been established as the result of an examination of the products obtained by the *Beckmann* transformation (A. **296**, 279; **274**, 1. Compare pp. 139 and 429).

Deoxybenzoïn, $C_6H_5\cdot CH_2\cdot CO\cdot C_6H_5$, forms large plates, melting at 55°, and may be sublimed or distilled unchanged. It can be prepared by the action of benzene and aluminium chloride upon phenyl-acetyl chloride, $C_6H_5\cdot CH_2\cdot CO\cdot Cl$, and hence its constitution, and yields di-benzyl with hydriodic acid. Deoxybenzoin can also be prepared from benzil and benzoin (B. **25**, 1728). One of its methylene hydrogen atoms

* For mechanism, cf. *Chalanay* and *Knoevenagel* (B. 1892, **25**, 295).

is readily replaceable by alkyl, just as in acetoacetic ester. The radical, $CH(C_6H_5)\cdot CO\cdot C_6H_5$, is termed "desyl"

Benzilic acid, $(C_6H_5)_2C(OH)\cdot CO_2H$ (p. 476), is produced when benzil is heated with alcoholic potash, by a peculiar molecular transformation similar to that by which pinacoline is formed (p. 193).

Compounds closely related to the dibenzyl group are those which contain two benzene nuclei united by a chain of more than two carbon atoms, *e.g.* $\alpha\gamma$-diphenyl propane, and also those compounds containing three or more benzene nuclei united by a chain of carbon atoms, *e.g.* triphenyl-ethane, tetraphenyl-ethane, &c.

XXX. TRIPHENYL-METHANE GROUP

Triphenyl-methane, $CH(C_6H_5)_3$, is the compound obtained as the result of the entrance of three phenyl groups into the methane molecule; among its homologues are tolyl diphenyl-methane, $(C_6H_5)_2CH\cdot C_6H_4\cdot CH_3$, ditolyl-phenyl-methane, $C_6H_5\cdot CH(C_6H_4\cdot CH_3)_2$, &c.

These hydrocarbons are of especial interest as being the mother substances of an extensive series of dyes, the amino-, hydroxy-, and carboxy-derivatives of triphenyl-methane are the leuco-bases obtained from such dyes as rosaniline, aurine, malachite green, &c.

Their *formation* is effected in a manner analogous to that of the diphenyl-methane derivatives, *i.e.* by the aid of zinc dust or aluminic chloride when chlorine compounds are used, or by the aid of phosphoric anhydride when oxygen compounds are employed.

Thus, triphenyl-methane may be obtained (*a*) from benzal chloride and benzene in the presence of aluminic chloride,

$$C_6H_5\cdot CHCl_2 + 2C_6H_6 = CH(C_6H_5)_3 + 2HCl,$$

or from benzaldehyde, benzene, and zinc chloride; (*b*) from chloroform and benzene in presence of aluminic chloride,

$$3C_6H_6 + CHCl_3 = CH(C_6H_5)_3 + 3HCl;$$

(*c*) from benzhydrol and benzene in the presence of phosphoric anhydride,

$$(C_6H_5)_2CH\cdot OH + C_6H_6 = (C_6H_5)_2CH\cdot(C_6H_5) + H_2O.$$

Derivatives of triphenyl-methane may be obtained by similar methods, *e.g* the leuco-base of bitter-almond-oil green, tetramethyl-diamino-triphenyl-methane (cf p 483), may be prepared by the condensation of benzaldehyde and dimethyl-aniline:

$$C_6H_5\cdot CHO + 2C_6H_5\cdot N(CH_3)_2 = C_6H_5\cdot CH:[C_6H_4\cdot N(CH_3)_2]_2 + H_2O.$$

When other amines or even phenols are used, a series of allied compounds (which are often dyes) is obtained, the separation of water being facilitated by the addition of zinc chloride, concentrated sulphuric acid, or anhydrous oxalic acid

Triphenyl-methane, $CH(C_6H_5)_3$ (*Kekulé* and *Franchimont*, B. **5**, 906) This compound may be prepared from chloroform and benzene by the *Friedel-Crafts* reaction (cf A. **194**, 152), diphenyl-methane being produced at the same time, also by eliminating the amino-groups from *p*-leucaniline, $C_{19}H_{13}(NH_2)_3$, and most readily by reducing triphenyl-carbinol with zinc dust and acetic acid It crystallizes in colourless prisms, m -pt 93°, b -pt 359°, and dissolves readily in hot alcohol, ether, and benzene.

It crystallizes from benzene with one molecule of "benzene of crystallization", which is also the case with many triphenyl-methane derivatives When triphenyl-methane is treated with bromine in a solution of carbon bisulphide, the methane hydrogen atom is exchanged for bromine with the formation of **triphenyl-methyl bromide**, $(C_6H_5)_3\cdot CBr$, which, when boiled with water, yields **triphenyl-carbinol**, $(C_6H_5)_3C\cdot OH$ This crystallizes in glistening prisms, melts at 159°, and can be sublimed unchanged, it may also be prepared directly by oxidizing a solution of triphenyl-methane in glacial acetic acid with chromic acid, or synthetically by the action of *Grignard's* phenyl magnesium bromide on benzophenone or ethyl benzoate

$$(C_6H_5)_2CO \longrightarrow (C_6H_5)_3C\cdot OMgBr \longrightarrow (C_6H_5)_3C\cdot OH.$$

A number of homologues of triphenyl-methane have been prepared by this last method (*Homben*, B 1903, **36**, 3087).

Fuming nitric acid converts triphenyl-methane into **trinitro-triphenyl-methane**, $(C_6H_4\cdot NO_2)_3\cdot CH$ (yellow scales), which can then be oxidized by chromic acid to **trinitro-triphenyl-carbinol**, $(C_6H_4\cdot NO_2)_3C\cdot OH$. The latter gives para-rosaniline, $(C_6H_4\cdot NH_2)_3C\cdot OH$, when reduced with zinc dust and glacial acetic acid

Homologous with triphenyl-methane are the **tolyl-diphenyl-**

methanes, $(C_6H_5)_2CH \cdot C_6H_4 \cdot CH_3$. From these also dyes are derived, especially from ***m*-tolyl-diphenyl-methane** (in which the CH_3 occupies the meta-position with regard to the methane carbon atom), which can be prepared by diazotizing ordinary leucaniline, it crystallizes in small prisms and melts at 59·5°.

TRIPHENYL-METHANE DYES

Of the derivatives of triphenyl-methane and of tolyl-diphenyl-methane, those are especially interesting which contain amino-, hydroxy-, or carboxy-groups. The entrance of three amino- or hydroxy-groups converts them into the leuco-compounds of dyes, some of which latter are of great value. Two amino-groups suffice for the full development of the dye character only when the amino-hydrogen atoms are replaced by alkyl radicals, one amino-group being insufficient for this (see under *p*-amino-triphenyl-methane).

The following are the chief groups of triphenyl-methane dyes:—

1. Those derived from diamino-triphenyl-methane. The malachite-green group.
2. Those derived from triamino-triphenyl-methane. The rosaniline group.
3. Those derived from trihydroxy-triphenyl-methane. The aurine group.
4. Those derived from triphenyl-methane-carboxylic acid. The eosin group.

Leuco-bases or **leuco-compounds** of dyes (p. 399) are the colourless compounds formed by the reduction of the dyes, usually by the addition of two atoms of hydrogen. When oxidized they are converted back into the dyes.

All the dyes of the triphenyl-methane group, and also indigo, methylene blue, safranine, &c., are capable of yielding such leuco-compounds, generally on reduction with zinc and hydrochloric acid, stannous chloride, or ammonium sulphide.

The oxidation of the leuco-compounds is often quickly effected by the oxygen of the air (*e.g.* in the cases of indigo white and of leuco-methylene blue), in the triphenyl-methane group it is slower and frequently more complicated. Leuco-malachite green is readily oxidized to the corresponding colour-base when treated with lead peroxide in acid solution, and leucaniline when warmed with chloranil in alcoholic solution, or when its hydrochloride is heated either alone or

with a concentrated solution of arsenic acid, or with metallic hydroxides such as ferric hydroxide.

The leuco-bases of the triphenyl-methane dyes are derivatives of triphenyl-methane or its homologues, the corresponding dye-bases obtained by oxidizing the leuco-bases are derivatives of triphenyl-carbinol or its homologues, and the dyes themselves are salts obtained by the elimination of water from the dye-base and an acid. The relationships between the three groups of compounds—leuco-base, dye-base, and dyes—are indicated in the following scheme:

$$\text{Leuco-base} \underset{\text{reduced}}{\overset{\text{oxidized}}{\rightleftarrows}} \text{dye-base} \underset{\text{alkali}}{\overset{\text{acid}}{\rightleftarrows}} \text{dye.}$$

As an example:

$$CH(C_6H_4\cdot NH_2)_3 \xrightarrow[+O]{} OH\cdot C(C_6H_4\cdot NH_2)_3 \xrightarrow[-H_2O]{+HCl} C\begin{cases}(C_6H_4\cdot NH_2)_2\\ C_6H_3\cdot NH\cdot HCl\end{cases}$$

1. AMINO- AND DIAMINO- TRIPHENYL-METHANE GROUP

***p*-Amino-triphenyl-methane** can be synthesized either by the condensation of *p*-nitro-benzaldehyde with benzene and subsequent reduction, or from benzhydrol and aniline. It forms large prisms, and melts at 84°. The corresponding carbinol is colourless and with acids yields red salts, but these cannot dye animal fibres.

***p*-Diamino-triphenyl-methane**, $C_6H_5\cdot CH(C_6H_4\cdot NH_2)_2$, is prepared by the action of zinc chloride or of fuming hydrochloric acid upon a mixture of benzaldehyde and aniline sulphate or chloride:

$$C_6H_5\cdot CHO + 2C_6H_5NH_2 = C_6H_5\cdot CH(C_6H_4\cdot NH_2)_2 + H_2O.$$

It crystallizes in prisms, and the colourless salts yield an unstable blue-violet dye, benzal violet, when oxidized. Methylation converts the base into.

Tetramethyl-di-*p*-amino-triphenyl-methane, *leuco-malachite green*, $C_6H_5\cdot CH[C_6H_4\cdot N(CH_3)_2]_2$, which is prepared on the technical scale by heating benzaldehyde and dimethyl-aniline with zinc chloride or concentrated sulphuric acid (*O. Fischer*, A. **206**, 103). It forms colourless plates or prisms. As a diacid base it yields colourless salts, which are slowly converted by the air, but immediately by other oxidizing agents, such as lead dioxide and sulphuric acid, into the salts of **tetramethyl-diamino-triphenyl-carbinol**, $C_6H_5\cdot C(OH)[C_6H_4N(CH_3)_2]_2$.

The free base is obtained by precipitating the salts with alkali. It crystallizes in colourless needles and dissolves in cold acid to a colourless solution; upon warming, however, the intense green coloration of the salts is produced. (For an explanation of this, see p. 486.)

The double salt with zinc chloride, $(C_{23}H_{25}N_2Cl)_2$, $2ZnCl_2$, $2H_2O$, or the oxalate, $(C_{23}H_{25}N_2)_2$, $3H_2C_2O_4$, of this base is the valuable dye **bitter-almond-oil green**, *malachite green* or *Victoria green*, which forms green plates, readily soluble in water This can also be prepared directly by heating benzo-trichloride with dimethyl-aniline and zinc chloride (*Doebner*). **Brilliant green** is the corresponding tetraethyl compound.

The sulphonic acid of the diethyl-dibenzyl-diamino-triphenyl-carbinol is **acid green**

2. ROSANILINE GROUP

Fuchsine or magenta was first obtained in 1856 by *Natanson*, who noticed the formation of a red substance, in addition to that of aniline hydrochloride and ethylene-aniline, when ethylene chloride was allowed to act upon aniline at a temperature of 200° (A. **98**, 297) It was prepared shortly afterwards by *A. W. Hofmann*, by the action of carbon tetrachloride upon aniline, and was first manufactured on the technical scale in 1859. *Hofmann's* scientific researches on this subject date from 1861 The chemical constitution was made clear by *Emil* and *Otto Fischer* in 1878 (A **194**, 242). (Cf also *Caro* and *Graebe*, B. **11**, 1116.)

The rosaniline dyes are derived partly from triphenyl-methane and partly from *m*-tolyl diphenyl-methane; in the former case they are often designated para-compounds (*e.g.* "para-rosaniline", because it is prepared from aniline and para-toluidine, "para-rosolic acid").

Para-leucaniline, *triamino-triphenyl-methane*, $CH(C_6H_4\cdot NH_2)_3$, and **leucaniline**, *triamino-diphenyl-tolyl-methane*, $CH_3\cdot C_6H_3(NH_2)\cdot CH(C_6H_4\cdot NH_2)_2$, are formed by the reduction of the corresponding trinitro-compounds and also of the corresponding dye-bases, para-rosaniline and rosaniline; the first named likewise by the reduction of *p*-nitro-diamino-triphenyl-methane. The free leuco-bases are precipitated by ammonia from solutions of their salts as white or reddish flocculent masses, and crystallize in colourless needles or plates; they melt at 203° and 100° respectively. As triacid bases they form colourless crystalline salts.

Para-rosaniline, $OH \cdot C(C_6H_4NH_2)_3$, and **rosaniline**, $OH \cdot C{\leq}{}^{(C_6H_4 \cdot NH_2)_2}_{C_6H_3Me \cdot NH_2}$, are the bases of the fuchsine dyes. They are obtained by precipitating solutions of their salts with alkalis, and crystallize from hot water or alcohol in colourless needles or plates, which become red in the air. Both are tri-acid bases, stronger than ammonia. As they yield tri-diazonium salts on treatment with nitrous acid, they must contain three primary amino-groups. The diazonium compounds readily yield the corresponding hydroxylic dyes, aurine and rosolic acid (p 490), when boiled with water.

Constitution.—The relations between the rosanilines and triphenyl methane were made clear by *Emil* and *Otto Fischer*, who transformed leucaniline into diphenyl-tolyl-methane by diazotizing and decomposing with alcohol. In a similar manner, para-leucaniline was converted into triphenyl-methane. The two leuco-bases are, therefore, undoubtedly triamino-derivatives of diphenyl-*p*-tolyl-methane and of triphenyl-methane respectively. The dye-bases, which differ from the leuco-bases by one atom of oxygen, are the corresponding carbinol derivatives, *i.e.* rosaniline is triamino-diphenyl-*p*-tolyl-carbinol, and para-rosaniline triamino-triphenyl-carbinol.

That the three amino-groups are distributed equally among the three benzene nuclei is clear from the synthesis of para-leucaniline by means of *p*-nitro-benzaldehyde. *p*-Nitro-benzaldehyde, aniline, and sulphuric acid yield *p*-nitro-diamino-triphenyl-methane, $NO_2 \cdot C_6H_4 \cdot CH(C_6H_4 \cdot NH_2)_2$, which, when reduced, yields para-leucaniline. We have, therefore, the following formulæ:

$$CH{\leq}{}^{C_6H_4 \cdot NH_2}_{C_6H_4 \cdot NH_2}{}_{C_6H_4 \cdot NH_2}$$

Para-leucaniline.

$$C(OH){\leq}{}^{C_6H_4 \cdot NH_2}_{C_6H_4 \cdot NH_2}{}_{C_6H_3(CH_3) \cdot NH_2}$$

Rosaniline

It can be shown that each amino-group occupies the *p*-position with respect to the methane carbon atom. Diamino-triphenyl-methane can be synthesized from benzaldehyde and aniline in the presence of a dehydrating agent. When diazotized and warmed with water, the corresponding dihydroxy-triphenyl-methane is formed, and this, when fused with potash, yields *p*-dihydroxy-benzophenone.

$$C_6H_5 \cdot CH(C_6H_4NH_2)_2 \longrightarrow C_6H_5 \cdot CH(C_6H_4 \cdot OH)_2 \longrightarrow CO(C_6H_4 \cdot OH)_2$$

In this last compound the *p*-positions of the hydroxy-groups

have been established, and hence the original amino-groups must also have occupied the *p*-positions, unless intramolecular rearrangement has occurred.

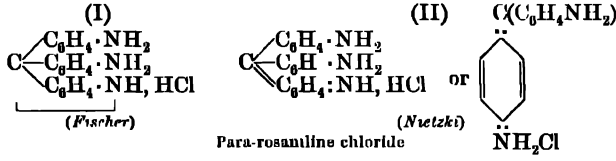
When *p*-nitro-benzaldehyde is condensed with aniline, *p*-nitro-diamino-triphenyl-methane is formed, and the nitro-group must be in the *p*-position, and by analogy with the previous reaction the two amino-groups are also in *p*-positions, and as this compound on reduction yields para-leucaniline it follows that all three amino-groups occupy *p*-positions—a conclusion which is supported by the fact that para-leucaniline can also be transformed into *p*-dihydroxy-benzophenone.

The salts of rosaniline and para-rosaniline, **fuchsine**, $C_{20}H_{20}N_3Cl$, **rosaniline nitrate**, $C_{20}H_{20}N_3(NO_3)$, **rosaniline acetate**, $C_{20}H_{20}N_3(C_2H_3O_2)$, **para-fuchsine**, $C_{19}H_{18}N_3Cl$, &c, are the actual dyes. While they possess a magnificent fuchsine-red colour in solution, and have intense colouring power (dyeing wool and silk without a mordant), their crystals are of a brilliant metallic green with cantharides lustre, *i.e.* of nearly the complementary colour. They are fairly soluble in hot water and alcohol.

In the formation of the salts, water is eliminated:

$$C(OH)(C_6H_4\cdot NH_2)_3 + HCl = C_{19}H_{17}N_3, HCl + H_2O.$$

In the dyes there is therefore present a peculiar nitrogen-carbon linking (see formula I), which is reminiscent of the older quinone formula; but the simpler constitution (formula II), which corresponds with the newer quinone formula, is now more generally accepted, and is usually termed the quinonoid formula:



Para-rosaniline chloride

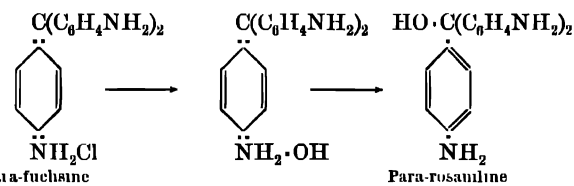
An analogous separation of water is also observed in the formation of salts of the malachite green base, but this only takes place upon warming, as is proved by the fact that it dissolves without colour in cold acids, and that the intense coloration of the salts first becomes apparent after warming the solution.

In addition to the above salts there also exist acid ones, *e.g.* $C_{20}H_{20}N_3Cl + 3HCl$ (which yields a yellow-brown solution,

not a fuchsine-coloured one); these dissociate into the neutral salts and free acid upon the addition of much water. The formation of such acid salts is readily accounted for by the quinonoid formula.

Rosenstiel has suggested the constitution $Cl \cdot C(C_6H_4NH_2)_3$ for para-fuchsine, according to which the salt is the chloride (ester) of a tertiary alcohol. Such a constitution, according to *Hantzsch* and *Osswald* (B. 1900, **33**, 278), is not in harmony with known facts.

Assuming the quinonoid structure II for para-fuchsine, then the conversion into para-rosaniline under the influence of alkalis should be preceded by the formation of an unstable quaternary ammonium hydroxide, which becomes transformed into the carbinol compound, para-rosaniline.



Para-fuchsine Para-rosaniline

Hantzsch and *Osswald*, by means of electrical conductivity determinations (B. 1900, **33**, 278), have been able to indicate the presence of such an ammonium derivative in the solution which is formed when the dye is brought into contact with an equivalent of alkali. This compound is coloured in contradistinction to the carbinol base, is very strongly basic and therefore strongly ionized, and is gradually transformed into the insoluble carbinol base. Para-rosaniline and the dye-bases generally are pseudo-bases corresponding in many respects with the pseudo-acids (p. 363).

Formerly in the manufacture of magenta, a mixture of aniline with *o*- and *p*-toluidine was oxidized by syrupy arsenic acid, stannic chloride or mercuric chloride or nitrate, &c.; in the modern method, a mixture of nitro-benzene with aniline and toluidine is heated with iron filings and hydrochloric acid (*Coupier*). Nitro-toluene may also be employed instead of nitro-benzene. If *o*-toluidine is present in the mixture of aniline and *p*-toluidine to be oxidized, rosaniline is formed, and if it is absent, para-rosaniline. When pure aniline is oxidized alone, it yields no fuchsine at all, but products of the nature of indulin. This is explained by the fact that for the

formation of fuchsine a carbon atom is required which shall serve to link the benzene nuclei together, a so-called "methane-carbon"; in the action of carbon tetrachloride upon aniline, this carbon originates from the tetrachloride, and in the oxidation of a mixture of aniline and *p*-toluidine, from the methyl group of the latter, as is shown in the following scheme:

$$NH_2 \cdot C_6H_4 \cdot CH_3 + 2C_6H_5NH_2 \longrightarrow NH_2 \cdot C_6H_4 \cdot C \lesssim \begin{matrix} C_6H_4 \cdot NH_2 \\ C_6H_4 : NH_2Cl. \end{matrix}$$

Para-rosaniline and rosamline are also formed by heating *p*-diamino-diphenyl-methane (p. 476) with aniline and *o*-toluidine respectively, in presence of an oxidizing agent (B. **25**, 302).

When rosaniline is heated with hydrochloric or hydriodic acid to 200°, it is split up into aniline and toluidines, when superheated with water, para-rosaniline yields *p*-dihydroxy-benzophenone, ammonia, and phenol. When boiled with hydrochloric acid, rosaniline breaks up into *p*-diamino-benzophenone and *o*-toluidine (B. **16**, 1928; **19**, 107, **22**, 988). A solution of fuchsine is decolorized by sulphurous acid, an additive-product, fuchsine-sulphurous acid, being formed. This solution, *Schiff's* reagent, is a delicate reagent for aldehydes, which colour it violet-red (see p. 127, B. **21**, Ref. 149, &c.).

Derivatives of Rosaniline

1. **Methylated rosanilines** (*Hofmann*, *Lauth*).—The red colour of para-rosaniline and of rosaniline is changed into violet by the entrance of methyl or ethyl groups, the intensity of the latter colour increasing with an increasing number of these groups. The salts of **hexamethyl-para-rosaniline** have a magnificent bluish-violet shade. In the manufacture of these "**methyl-violets**" one may either (1) methylate rosaniline (by means of CH_3Cl or CH_3I); or (2) oxidize, instead of aniline, a methylated aniline such as dimethyl-aniline by means of cupric salts, whereby para-rosaniline derivatives result; or (3) allow phosgene to act upon dimethyl-aniline (or the latter to act upon the tetramethyl-diamino-benzophenone at first produced) (cf. B. **17**, Ref. 339):

$$COCl_2 + 3C_6H_5 \cdot N(CH_3)_2 = C(OH)[C_6H_4 \cdot N(CH_3)_2]_3 + 2HCl.$$

In the last case hexamethyl-violet, termed "**crystal violet**" on account of the beauty of its crystals, is formed, while the

ıethyl-violets prepared by methods (1) and (2) are mixtures of exa-, penta-, and tetramethyl-rosanilines and are amorphous.

The hydrochloride of the hexamethyl dye has the constitution:

$$C\!\left\langle \begin{matrix}[C_6H_4\cdot N(CH_3)_2]_2 \\ C_6H_4\cdot N(CH_3)_2\cdot Cl\end{matrix}\right. \quad \text{or} \quad C\!\left\langle \begin{matrix}[C_6H_4\cdot N(CH_3)_2]_2 \\ C_6H_4{:}N(CH_3)_2\cdot Cl.\end{matrix}\right.$$

An interesting synthesis of this compound is by the action of he magnesium derivative of *p*-bromo-dimethyl-aniline on tetra-ıethyl-diamino-benzophenone and subsequent treatment with ydrochloric acid (cf. Synthesis of Tertiary Alcohols, p. 356)

The hexamethyl-carbinol no longer contains an amino-ydrogen atom, in consequence of which any further methyl hloride or iodide cannot effect an exchange of hydrogen for lkyl, but can only form an additive compound, a quaternary mmonium salt. Such addition causes a change of colour from iolet to green; thus the compound

$$(CH_3)_2NCl{:}C_6H_4{:}C\!\left\langle \begin{matrix}C_6H_4\cdot N(CH_3)_2 \\ C_6H_4\cdot NCl(CH_3)_3\end{matrix}\right.$$

s the dye **methyl green** or *light green*. **Ethyl green** (ethyl-examethyl rosaniline) is formed by the action of ethyl bro-ıide on methyl violet

Various **ethyl violets** are known corresponding with the ıethyl violets. The hexa-substituted rosanilines, which con-ain benzyl as well as methyl or ethyl groups, are similar to rystal violet; their sulphonic acids form useful dyes, *e.g.* **acid iolet.**

2. **Phenylated rosanilines.** By the successive entrance of henyl-groups into rosaniline, there are formed in the first ıstance violet dyes, which change to blue when three phenyl roups have entered. **Triphenyl-fuchsine** or "**aniline blue**" s a beautiful blue dye, insoluble in water but soluble in lcohol. It is prepared by heating rosaniline with aniline in resence of benzoic acid, when ammonia is eliminated; or by he oxidation of phenylated aniline, *i.e.* diphenylamine, *e.g.* by ıeans of oxalic acid. The latter supplies the "methane carbon tom", and the beautiful "diphenylamine blue" or **spirit blue** hich is formed is a para-rosaniline derivative. Formic alde-yde can also supply the methane carbon atom.

Dyes insoluble in water are converted into soluble sulphonic cids. Such acids are **Nicholson's blue, water blue,** and **light** lue. **Patent blue, new patent blue,** are disulphonic acids.

3. TRIHYDROXY-TRIPHENYL-METHANE, $CH(C_6H_4 \cdot OH)_3$, OR THE AURINE GROUP

The hydroxy-analogues of para-rosaniline and rosaniline are **aurine**, $C_{19}H_{14}O_3$, and **rosolic acid**, $C_{20}H_{16}O_3$:

$$(OH \cdot C_6H_4)_2C \cdot C_6H_4 \cdot O \quad \text{or} \quad (OH \cdot C_6H_4)_2 \cdot C : C_6H_4 : O$$
(Aurine.)

These likewise possess the dye character, but, instead of being basic, they are acid dyes (phenol dyes); they are of far less value than the basic dyes which have been already described.

They are formed when the diazonium derivatives of para-rosaniline or rosaniline are boiled with water (*Caro* and *Wanklyn*, 1866):

$$OH \cdot C(C_6H_4N_2SO_4H)_3 + 3H_2O = OH \cdot C(C_6H_4 \cdot OH)_3 + 3N_2 + 3H_2SO_4;$$
$$OH \cdot C(C_6H_4 \cdot OH)_3 = (OH \cdot C_6H_4)_2C : C_6H_4 : O + H_2O.$$

The carbinol which must be produced here in the first instance is incapable of existence, and loses water. The constitutional formulæ just given follow from this close relation to the rosanilines.

Aurine is also obtained by heating phenol with oxalic and sulphuric acids to 130°–150° (*Kolbe* and *Schmitt*, 1859), the oxalic acid yielding the "methane carbon atom"; rosolic acid results in an analogous manner from a mixture of phenol and cresol with arsenic and sulphuric acids. Phenol by itself yields no rosolic acid upon oxidation.

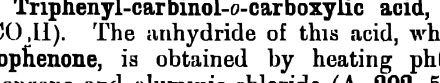
Aurine and rosolic acid crystallize in beautiful green needles or prisms with a metallic lustre, dissolve in alkalis with a fuchsine-red colour, and are thrown down again from this solution by acids. The alkaline salts are decidedly unstable, aurine being but a weak phenol; at the same time it possesses a slightly basic character. An ammonium salt is known which crystallizes in dark-red needles with a blue lustre. Upon reduction there are formed the leuco-compounds **leucaurine**, $CH(C_6H_4 \cdot OH)_3$, and **leuco-rosolic acid**, $OH \cdot C_6H_3Me \cdot CH(C_6H_4 \cdot OH)_2$, both of which crystallize in colourless needles of phenolic character. Superheating with water transforms aurine into *p*-dihydroxy-benzophenone, $CO(C_6H_4 \cdot OH)_2$, and phenol; superheating with ammonia, into para-rosaniline.

4. TRIPHENYL-METHANE-CARBOXYLIC-ACID, OR THE EOSIN GROUP

(Cf. *Baeyer*, A. **183**, 1; **202**, 36)

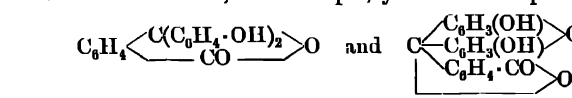
Triphenyl-methane-carboxylic acid, $CH(C_6H_5)_2(C_6H_4 \cdot CO_2H)$, obtained by the reduction of phthalophenone (see below), crystallizes in colourless needles melting at 162° and yields triphenyl-methane by the elimination of carbon dioxide.

Triphenyl-carbinol-*o*-carboxylic acid, $OH \cdot C(C_6H_5)_2(C_6H_4 \cdot CO_2H)$. The anhydride of this acid, which is termed **phthalophenone**, is obtained by heating phthalyl chloride with benzene and aluminic chloride (A. **202**, 50), and forms plates, melting at 115°. The acid itself is incapable of existence, but its salts are obtained by dissolving the anhydride in alkalis. Phthalophenone is on the one hand a triphenyl-methane derivative and on the other a derivative of phthalic acid; in accordance with the constitutional formula:



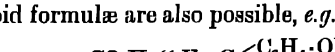
it is to be regarded as diphenyl-phthalide (Phthalide, p. 462).

Phthalophenone is the mother substance of a large series of dyes, which are derived from it by the entrance either of hydroxyl or of amino-groups. They are prepared by the action of phenols upon phthalic anhydride, and are termed *Phthaleins*. Phenol and resorcinol, for example, yield the compounds:



Phenol-phthalein Fluorescein

Quinonoid formulæ are also possible, *e.g.* for phenol-phthalein,



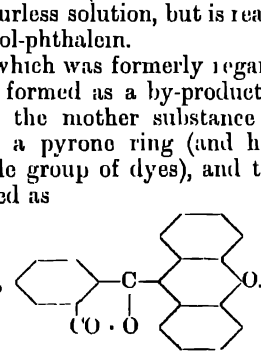
Free phenol-phthalein, which is colourless, probably has the lactone formula, and its coloured salts the quinonoid structure. Phenol-phthalein would then be a *pseudo-acid* (p. 364).

See also *H. Meyer*, M. 1899, **20**, 337; *R. Meyer* and *Spendler*, B. **36**, 2949; **38**, 1318; *Green* and *A. G. Perkin*, J. C. S. 1904, 398; *Green* and *King*, B. **39**, 2365; **40**, 3724; *Stieglitz*, J. A. C. S. **25**, 1112; *Acree*, Am. C. J. **39**, 528, 771; **42**, 115.

In the case of fluorescein a molecule of water is split off from two hydroxyls of the two resorcinol residues. Phthaleins of this kind (being hydroxy-phthalophenones) are converted by reduction into the hydroxy-derivatives of triphenyl-methane-carboxylic acid, which are termed "*Phthalines*"; *e.g.* phenol-phthalein into dihydroxy-triphenyl-methane-carboxylic acid (*i.e.* phenol-phthaline), $CH\lessdot^{(C_6H_4\cdot OH)_2}_{C_6H_4\cdot CO_2H}$. The phthalines are colourless, and are to be looked upon as leuco-compounds of the phthaleins. The phthaleins include among themselves many dyes which are of technical value, *e.g.* the eosins (*Caro, Baeyer*, 1871).

Phenol-phthaleïn is prepared by heating phthalic anhydride with phenol and sulphuric acid, or better, stannic chloride (or oxalic acid), to 115°–120°. It may also be obtained by nitrating diphenyl-phthalide, reducing the two substituting nitro-groups, and replacing the amino-groups thus formed by hydroxyl in the usual manner (A. **202**, 68) It crystallizes from alcohol in colourless crusts; is nearly insoluble in water, but dissolves in dilute alkalis with a beautiful red colour which vanishes again on neutralization with acids, it is thus a valuable indicator. With very concentrated alkalis (KOH) phenol-phthalein yields colourless solutions probably containing metallic salts of a non-quinonoid structure. The *p*-positions of the two hydroxy-groups have been proved by conversion into *p*-dihydroxy-benzophenone. It yields a **di-acetyl** derivative melting at 143° and an **oxime** melting at 212°. It is reduced by potash and zinc dust to **phenol-phthaline** (colourless needles), which dissolves in alkali to a colourless solution, but is readily reoxidized in this solution to phenol-phthalein.

Fluorane, $C_{20}H_{12}O_3$, which was formerly regarded as phenol-phthalein anhydride, is formed as a by-product in the phenol-phthalein melt, and is the mother substance of fluorescein. Both probably contain a pyrone ring (and hence the name **Pyronines** for the whole group of dyes), and the constitution of fluorane is represented as

Fluorane, 

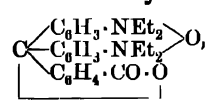
(Cf. *R. Meyer*, B. 1892, **25**, 1385, 2118; 1893, **26**, 1271.)

Fluoresceïn, *Dihydroxy-fluorane* or *resorcinol-phthalein*, $C_{20}H_{12}O_5 + H_2O$, is prepared by heating phthalic anhydride and resorcinol at 200°. It forms a dark-red crystalline powder, and dissolves in alcohol with a yellow-red colour, and in alkalis with a red colour and splendid green fluorescence. It is reducible to the phthaline "Fluorescein", and with bromine yields red crystals of tetrabromo-fluorescein, the potassium salt of which, $C_{20}H_6Br_4O_5K_2$, is the magnificent dye **eosin**. Fluorescing dyes are likewise formed in an analogous manner from all the derivatives of 1 3-dihydroxy-benzene, in which position 5 is unoccupied, and the reaction is often made use of on the one hand for testing for *m*-dihydroxy-derivatives, and on the other for phthalic anhydride or succinic anhydride.

Instead of phthalic acid itself, chlorinated or brominated, &c, phthalic acids may be employed, so that, by gradually increasing the amount of halogen present, a whole series of yellow-red to violet-red eosins can be prepared, *e.g.* tetrabromo-di-iodo-eosin; these are known under the names of Erythrosin, Rose de Bengale, Phloxin, &c. It is worthy of note that many other dibasic acids (*e.g.* succinic) and also benzoic acid are capable of yielding fluorescing compounds.

Gallein, $C_{20}H_{12}O_7$, is the dye obtained from pyrogallol and phthalic anhydride.

The **rhodamines** are dyes closely allied to fluorescein. They are obtained by the condensation of phthalic anhydride and *p*-alkylated-amino-phenols in presence of sulphuric acid They contain the pyrone ring, and may be regarded as fluorescein in which the two hydroxyl groups have been replaced by tertiary amino-groups. **Tetra-ethyl rhodamine,**



is colourless, and has basic properties. The salts, *e.g.* sulphate, are red dyes, and probably possess a quinonoid structure.

Tetraphenyl-methane, $C(C_6H_5)_4$.—Many attempts to obtain this compound were made, but without success, until *Gomberg* (B. 1897, **30**, 1897) succeeded in preparing it from triphenyl-bromo-methane. With phenyl-hydrazine this yields $CPh_3 \cdot NH \cdot NHPh$, triphenylmethane-hydrazobenzene, which gives the corresponding azo-compound when oxidized, $CPh_3 \cdot N:NPh$,

and when this is heated nitrogen is evolved and tetraphenyl methane is formed. It is more readily prepared by the action of magnesium phenyl bromide on triphenyl-chloro-methane (B. 1906, **39**, 1462). It forms colourless crystals, m.-pt 282°.

XXXI. COMPOUNDS WITH CONDENSED BENZENE NUCLEI. NAPHTHALENE GROUP

The higher fractions of coal tar contain hydrocarbons of high molecular weight, especially naphthalene, $C_{10}H_8$, anthracene, $C_{14}H_{10}$, and its isomeride phenanthrene. The first-named is found in the fraction between 180°–200°, and the two latter in that between 340°–360°.

These compounds are of more complex composition than benzene, the molecule of naphthalene differing from that of the latter by C_4H_2, and those of anthracene and phenanthrene from that of naphthalene by the same increment. They closely resemble benzene as regards behaviour, and give rise to types of derivatives similar to those of benzene itself.

They undoubtedly contain benzene nuclei, as anthracene yields benzoic acid upon oxidation, naphthalene phthalic acid, and phenanthrene diphenic acid. From their modes of formation and behaviour it follows that in the building up of their molecules the benzene residues combine together in such a manner that 2 or (2 × 2) adjacent carbon atoms are common to both (cf. pp. 496 and 506).

NAPHTHALENE GROUP

Naphthalene, $C_{10}H_8$, was discovered by *Garden* in 1820. It is contained in coal-tar and crystallizes from the fraction which distils over between 180°–200°. These crystals are pressed to free them from oily impurities, and can then be further purified by treatment with small amounts of concentrated sulphuric acid and subsequent sublimation.

It is also formed when various carbon compounds are subjected to a red heat; thus, together with benzene, styrene, &c., by passing the vapours of methane, ethylene, acetylene, alcohol, acetic acid, &c., through red-hot tubes. Its presence in coal-tar may be due to some similar cause.

The constitutional formula (p. 496) is largely based on the following syntheses:—

1. **By the action of *o*-xylylene bromide upon the sodium compound of the symmetrical ethane-tetracarboxylic ester, ethyl tetrahydronaphthalene-tetracarboxylate** is formed:

$$C_6H_4\begin{<}{CH_2Br}{CH_2Br}+\begin{matrix}Na\cdot C(CO_2Et)_2\\ Na\cdot C(CO_2Et)_2\end{matrix}=C_6H_4\begin{<}{CH_2\cdot C(CO_2Et)_2}{CH_2\cdot C(CO_2Et)_2}+2NaBr;$$

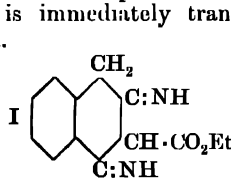
and from this, naphthalene may be obtained by hydrolysis, the elimination of the carboxyl groups and subsequent oxidation (*Baeyer* and *Perkin*, B. **17**, 448).

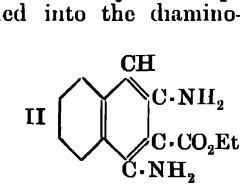
2. α-Naphthol, $C_{10}H_7\cdot OH$, is produced by the elimination of water from γ-phenyl-isocrotonic acid (*Fittig* and *Erdmann*, B. **16**, 43; see p. 456), and yields naphthalene when heated with zinc dust.

3. *J. F. Thorpe* (P. 1905, **21**, 305) has succeeded in synthesising a number of naphthalene derivatives by means of ethyl sodio-cyano-acetate, *e.g.* ethyl 1:3-diamino-naphthalene-2-carboxylate from ethyl sodio-cyano-acetate and benzyl cyanide.

$$C_6H_5\cdot CH_2\cdot CN + CO_2Et\cdot CH_2\cdot CN \longrightarrow C_6H_5\cdot CH_2\cdot C(:NH)\cdot CH(CO_2Et)CN,$$

and this with sulphuric acid yields the bicyclic compound I, which is immediately transformed into the diamino-derivative II.

I 

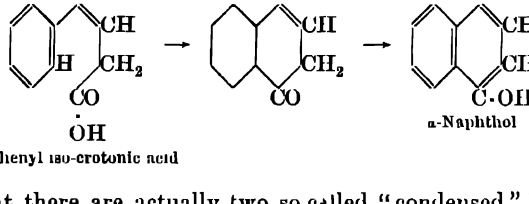
II 

The same compound may be synthesised from ethyl sodio-cyano-acetate by the following stages (J. C. S. 1907, **91**, 578). Condensed with *o*-toluyl chloride, $CH_3\cdot C_6H_4\cdot CO\cdot Cl$, it yields ethyl cyano-*o*-toluyl-acetate, $CH_3\cdot C_6H_4\cdot CO\cdot CH(CN)CO_2Et$, and this when heated with ammonium acetate gives the corresponding imino-derivative, $CH_3\cdot C_6H_4\cdot C(:NH)\cdot CH(CN)CO_2Et$, ethyl β-imino-α-cyano-β-*o*-tolyl-propionate, which reacts with acids giving compound I.

1:4-Naphthalene-diamines have been prepared by similar methods, using derivatives of phenyl-butyric acid (J. C. S. 1907, **91**, 1004).

Constitution.—That naphthalene contains a benzene nucleus, in which two hydrogen atoms occupying the ortho-position are replaced by the group $(C_4H_4)''$, follows not only from its oxidation to phthalic acid, but also from its formation from

o-xylylene bromide. And that the four carbon atoms of this group are linked to one another without branching is shown by the formation of α-naphthol.



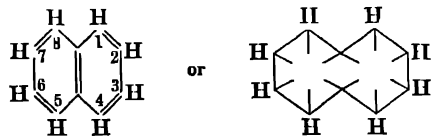
γ-Phenyl iso-crotonic acid

α-Naphthol

That there are actually two so-called "condensed" benzene nuclei present in the naphthalene molecule is a necessary consequence of the fact that phthalic acid or its derivatives ensue on the breaking up of the compound, not only from one but from both of the rings.

For instance, α-nitro-naphthalene (p 499) on oxidation yields nitro-phthalic acid, $C_6H_3(NO_2)(CO_2H)_2$, consequently the benzene ring to which the nitro-group is linked remains intact. But, on reducing the nitro-naphthalene to amino-naphthalene and oxidizing the latter, no amino-phthalic acid nor any oxidation product of it is obtained, but phthalic acid itself, a proof that this time the benzene nucleus to which the amino-group is attached has been destroyed, and that the other has remained intact (*Graebe*, 1880, for an analogous proof by him, see **A. 149**, 20).

Naphthalene therefore receives the constitutional formula (*Erlenmeyer*, 1866):



There is the same difficulty in deciding between the double bond *Kekulé* formula and the centric formula as in the case of benzene.

The above constitutional formula is in complete harmony with the number of isomeric forms in which naphthalene derivatives occur, and also with the formation of additive compounds with hydrogen or chlorine. (Cf. *Bamberger*, A. **257**, 1; B. 1891, **24**, 2054.)

This union of two benzene nuclei is accompanied by a modification of their properties, so that naphthalene and its derivatives differ characteristically from benzene in many respects. Such differences show themselves, for instance, between the naphthylamines and aniline, the naphthols and phenol; and also especially in the greater readiness with which the naphthalene derivatives are reduced, the latter taking up as many as four atoms of hydrogen easily

After such addition the reduced nucleus is found to have entirely lost the characteristics of a benzene nucleus, and to have become similar in properties to an alphyl radical, whereas the non-reduced nucleus assumes the character of a benzene nucleus in its entirety (*Bamberger*). (See the Tetrahydro-derivatives of the Naphthylamines and Naphthols, pp 500 and 502)

Properties — Naphthalene crystallizes in glistening plates, is insoluble in water, sparingly soluble in cold alcohol and ligroin, but dissolves readily in hot alcohol and ether; it melts at 80° and boils at 218°. It has a characteristic tarry smell, and is distinguished by the ease with which it sublimes and volatilizes with steam

With picric acid it yields an additive compound, $C_{10}H_8$, $OH \cdot C_6H_2(NO_2)_3$, crystallizing in yellow needles and melting at 149° It takes up hydrogen far more readily than benzene does, yielding **di-** and **tetrahydronaphthalenes**, $C_{10}H_{10}$ and $C_{10}H_{12}$, both of these are liquids of pungent odour which regenerate naphthalene again when heated. By the powerful action of hydriodic acid and phosphorus, the second benzene nucleus can also be made to take up hydrogen, so that a **hexahydro-**, $C_{10}H_{14}$, and finally a **dekahydronaphthalene**, $C_{10}H_{18}$, are formed. It also yields additive products with chlorine more readily than benzene does, *e.g.* **naphthalene dichloride**, $C_{10}H_8 \cdot Cl_2$, and **-tetrachloride**, $C_{10}H_8 \cdot Cl_4$ (m -pt. 182°), the latter is oxidized to phthalic acid more easily than naphthalene itself, hence that acid is sometimes prepared from it on the large scale

Naphthalene is principally used for the preparation of phthalic acid (for eosin, indigo, &c.), and of naphthylamines and naphthols (for azo-dyes), also for the carburation of illuminating gas. It is a powerful antiseptic, and is employed therapeutically.

NAPHTHALENE DERIVATIVES

The number of substitution products in the case of naphthalene is greater than with benzene.

The mono-derivatives invariably exist in two isomeric forms, the α- and β-compounds, e.g.:

$C_{10}H_7Cl$ (α- and β-chloro-naphthalene).
$C_{10}H_7NH_2$ (α- and β-naphthylamine).
$C_{10}H_7OH$ (α- and β-naphthol).
$C_{10}H_7CH_3$ (α- and β-methyl-naphthalene).

As in the case of the benzene compounds, the existence of two series of mono-derivatives has not only been established empirically, but it has also been proved (in a manner similar to that given on p 329, *et seq.*) that in the naphthalene molecule two sets of hydrogen atoms (the α and β, α = 1, 4, 5, 8; β = 2, 3, 6, 7) have an equal value as regards one another, but the atoms of the one set differ from those of the other, so that the α- and the β-positions occur severally four times, *i.e.* twice in each benzene nucleus (*Atterberg*).

The above constitutional formula for naphthalene satisfies these conditions, since, according to it, the positions 1, 4, 5, and 8 are severally equal and also the positions 2, 3, 6, and 7, but not the positions 1 and 2. The conception that in the α-compounds the position 1, 4, 5, or 8 is occupied is due to *Laubermann* (A. **183**, 225), *Reverdin* and *Noelting* (B. **13**, 36), and *Fittig* and *Erdmann* (cf. the formation of α-naphthol given above).

With regard to the di-derivatives of naphthalene, a considerable number of isomerides of a good many are known; according to the naphthalene formula, ten are theoretically possible in each case when the two substituents are the same, and fourteen when they are different. The ten possible isomerides are 1:2, 1:3, 1·4, 1 5, 1:6, 1:7, 1:8, 2.3, 2:6, and 2 7. All other combinations are identical with one of these ten. According to *Armstrong* and *Wynne* ten dichloro- and fourteen trichloro-naphthalenes are actually known. (See also B. 1900, **33**, 1910, 2131.)

The position 1:8 is termed the "*peri*-" position, it resembles the ortho- position to some extent, *e.g. peri*-naphthalene-dicarboxylic acid like an *o*-dicarboxylic acid yields an anhydride.

The **homologues** of naphthalene are of comparatively small importance, and are usually prepared by *Fittig's* or by *Friedel* and *Crafts'* synthesis. Most of them are liquids, and on oxidation yield acids resembling benzoic acid.

α-Bromo-naphthalene can be prepared directly by brominating naphthalene, and is partially converted into the β-compound

when heated with aluminium chloride. Its bromine atom is somewhat more readily exchangeable than that of bromobenzene, but cannot be eliminated by boiling with alkalis. Interesting methods of formation of the halogen derivatives are by heating the hydroxy-, nitro-, or sulphonic acid derivatives with phosphorus pentachloride.

α-Nitro-naphthalene, $C_{10}H_7 \cdot NO_2$ (*Laurent*, 1835), is formed by the direct nitration of naphthalene. It crystallizes in yellow prisms, melts at 61°, boils without decomposition, and readily yields 1·5 and 1:8 di- and various tri- and tetra-nitronaphthalenes upon further nitration. On reduction it is converted into α-naphthylamine. The position of the nitro-group has been established by conversion of this compound into α-naphthol.

The isomeric **β-nitro-naphthalene** can be obtained indirectly by diazotizing β-naphthylamine, and acting on the product with sodium nitrite in presence of cuprous oxide (B **20**, 1494, **36**, 4157), it crystallizes in bright yellow needles melting at 79°.

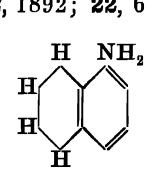
α-Naphthylamine, $C_{10}H_7 \cdot NH_2$ (*Zinin*), forms colourless needles or prisms, melts at 50°, boils at 300°, and is readily soluble in alcohol. It can be obtained by reducing the α-nitro-compound, and also readily by heating α-naphthol with the double compound of calcium chloride and ammonia, while aniline can only be prepared from phenol in a similar manner with difficulty $C_{10}H_7 \cdot OH + NH_3 = C_{10}H_7 \cdot NH_2 + H_2O$.

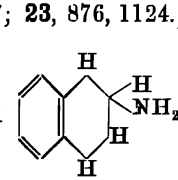
It possesses a disagreeable faecal-like odour, sublimes readily, and turns brown in the air. Certain oxidizing agents, such as ferric chloride, produce a blue precipitate with solutions of its salts, while others give rise to a red oxidation product; chromic anhydride oxidizes it to α-naphthaquinone. In other respects it resembles aniline, for differences, see B **23**, 1124. Its hydrochloride is only sparingly soluble in water.

The isomeric **β-naphthylamine**, $C_{10}H_7 \cdot NH_2$ (*Liebermann*, 1876), is most conveniently prepared by heating β-naphthol either in a stream of ammonia or with the double compound of zinc chloride and ammonia. It is now generally prepared by the action of ammonium hydroxide and sulphite on β naphthol (C. C. 1901, **1**, 349). Naphthyl ammonium sulphite is formed as an intermediate product and reacts with the ammonia, yielding naphthylamine and ammonium sulphite. This reaction is frequently used for transforming derivatives of α and β naphthol into corresponding amino-compounds. The reaction is reversible and can be used for replacing NH_2 by OH.

β-Naphthylamine crystallizes in nacreous plates, melts at 112°, boils at 294°, and has no odour. It is more stable than α-naphthylamine, and is not coloured by oxidizing agents.

Both of these naphthylamines can be converted into tetrahydro-compounds by the action of sodium and amyl alcohol (*i.e.* nascent hydrogen) upon them. The **tetrahydro-α-naphthylamine** resembles its mother substance closely in most of its properties, *e.g.* it can be diazotized and has entirely assumed the character of aniline; the hydrogen atoms have entered the nucleus which does not contain the amino-group. It is termed *aromatic* or "*ar*"-tetrahydro-α-naphthylamine. (Formula I.) **Tetrahydro-β-naphthylamine**, on the other hand, is not diazotized by nitrous acid, but transformed into a very stable nitrite. Here it is the benzene nucleus containing the amino-group which has become reduced; the compound has assumed the properties of an amine of the fatty series, and is termed *alicyclic* or "*ac*"-tetrahydro-β-naphthylamine. (Formula II.) The α-compound is oxidizable to adipic acid (p. 231), and the β-compound to *o*-hydrocinnamo-carboxylic acid, $C_6H_4{<}^{CH_2\cdot CH_2\cdot CO_2H}_{CO_2H}$. (Cf. *Bamberger* and others, B. **21**, 847, 1112, 1892; **22**, 625, 767; **23**, 876, 1124.)

I 

II 

An **ac-tetrahydro-α-** and an **ar-tetrahydro-β-naphthylamine** have also been prepared.

From both naphthylamines there are derived, as in the benzene series, **methyl-** and **dimethyl-naphthylamines**, **phenyl-α-** and **-β-naphthylamines** (which are of technical importance), **nitro-naphthylamines**, diamino-naphthalenes or **naphthylene-diamines**, $C_{10}H_6(NH_2)_2$, **diazonium-compounds** (which are in every respect analogous to the diazonium salts of benzene, especially in the formation of azo-dyes, many of which are of great technical importance), **diazo-amino-compounds**, &c.

The **diazo-amino-naphthalene**, $C_{10}H_7\cdot N:N\cdot NH\cdot C_{10}H_7$, which is formed by the action of nitrous acid upon α-naphthylamine, readily undergoes a molecular transformation (like the corresponding benzene compound) into **amino-azo-naphthalene**,

$C_{10}H_7 \cdot N : N \cdot C_{10}H_6 \cdot NH_2$. This latter compound crystallizes in brownish-red needles with a green metallic lustre, and can be diazotized, its diazo-compound yielding **α-azo-naphthalene**, $C_{10}H_7 \cdot N : N \cdot C_{10}H_7$ (red to steel-blue glistening prisms), when boiled with alcohol. This last can either not be prepared at all or only with great difficulty by the methods which hold good for azo-benzene.

A mixture of **naphthalene α- and β-sulphonic acids**, $C_{10}H_7 \cdot SO_2 \cdot OH$, is obtained by warming naphthalene to 80° with concentrated sulphuric acid. They may be separated by aid of their calcic or baric salts, as the β-sulphonates are less soluble than the α-salts. The α-acid is transformed into the β-acid when heated with concentrated sulphuric acid, and hence the chief product obtained by sulphonating naphthalene at 160° is the β-acid. The sulphonic acid radicals in these compounds may be readily replaced by hydroxyl or cyanogen by the usual methods.

Naphthalene-disulphonic acids, $C_{10}H_6(SO_3H)_2$.—Two isomeric β-β-acids (2:6 and 2:7) are formed when naphthalene is heated with concentrated sulphuric acid at 160°–200°, while an α-α-acid (1:5) is obtained with chloro-sulphonic acid, SO_3HCl, in the cold, and the α-β-acid (1:6) from the β-mono-sulphonic acid in a similar manner.

Naphthylamine-mono-sulphonic acids, $NH_2 \cdot C_{10}H_6 \cdot SO_2 \cdot OH$.—Thirteen isomers of these are known (7 α- and 6 β-). **Naphthionic acid** ($NH_2 : SO_3H = 1 : 4$) is obtained by the sulphonation of α-naphthylamine; it is employed in the preparation of azo-dyes, as are also several of its isomers and various **naphthylamine-disulphonic acids**. These last are obtained (*a*) directly from α- or β-naphthylamine, or (*b*) by nitrating the naphthalene-sulphonic acids and then reducing the nitro- to an amino-group.

α- and β-Naphthols, $C_{10}H_7 \cdot OH$, which are present in coal-tar, can be easily prepared, not only from the naphthalene-sulphonic acids as above, but also by diazotizing the naphthylamines. They crystallize in glistening plates, have a phenolic odour, and dissolve readily in alcohol and ether but only sparingly in hot water. α-Naphthol (*Griess*, 1866) melts at 95° and boils at 282°, while β-naphthol (*Schaffer*, 1869) melts at 122° and boils at 288°; both of them are readily volatile at ordinary temperatures. They possess a phenolic character but nevertheless resemble the alcohols of the benzene series more than the phenols, their hydroxy-groups being much more reactive

than those of the latter, *e.g.* they can be readily replaced by amino-groups (see above). β-Naphthol is an antiseptic.

ar-Tetrahydro-α-naphthol, $C_{10}H_7 \cdot H_4 \cdot (OH)$, obtained by reducing α-naphthol, has the character of a pure phenol, and not that of α-naphthol. A mixture of **ar-** and **ac-tetrahydro-β-naphthols** is obtained from β-naphthol, the *ar*-compound corresponds with phenol and the *ac*-compound with alcohol.

Ferric chloride oxidizes α- and β-naphthols, with production of violet and greenish colorations respectively, to **di-naphthols**, $C_{20}H_{12}(OH)_2$, which correspond with the dihydroxy-diphenyls (p. 473), and are derivatives of di-naphthyls (p 504). The cautious oxidation of α-naphthol yields ***o*-cinnamo-carboxylic acid**, $CO_2H \cdot C_6H_4 \cdot CH:CH \cdot CO_2H$, and that of β-naphthol, *o*-carboxy-phenyl-glyoxylic acid, $CO_2H \cdot C_6H_4 \cdot CO \cdot CO_2H$.

The naphthols yield alkyl and acyl derivatives. The ethers are formed by the action of an alcohol and hydrogen chloride on the naphthols. **β-Naphthyl-methyl-ether**, $C_{10}H_7 \cdot O \cdot CH_3$, is the *nerolin* used as a perfume.

From the naphthols, as from the phenols, there are derived **nitro-, dinitro-, trinitro-**, and **amino-compounds**, &c. The calcium salt of **dinitro-α-naphthol**, $C_{10}H_5(NO_2)_2 \cdot OH$, is known as *Martius'* yellow or naphthalene yellow, and its sulphonic acid, **naphthol yellow S** or *fast yellow*, is a valuable dye

Amino-naphthols, $C_{10}H_6(NH_2)(OH)$, are obtained by the reduction of nitro-naphthols, like the amino-phenols they are readily oxidized in the air ($NH_2:OH$ in the α-compound = 1:4, in the β-compound = 1:2)

A number of **naphthol-mono-, -di-**, &c., **sulphonic acids** are known, also amino-naphthol-sulphonic acids, which are of great technical value. Among these may be mentioned **1:4-naphthol-sulphonic acid** (*Nevile* and *Winther*), from naphthionic acid, the 2:8-acid, the 2:6-acid, the **β-naphthol-disulphonic acids R** (2:3:6) or "R-salt", and **G** (2·6·8) or "G-salt". 1-Amino-8-naphthol-3:6-disulphonic acid = H acid.

Sodium **1-amino-2-naphthol-6-sulphonate** is used as a photographic developer under the name of *Eikonogen*.

Azo-dyes.—A series of very important azo dyes (see also under Benzidine, p. 472) are produced by the action of diazonium compounds, and of diazo-naphthalene-sulphonic acids upon the naphthylamines and naphthols, and especially upon the sulphonic acids of these, *e.g.*:

Benzene-azo-α-naphthylamine, $C_6H_5 \cdot N:N \cdot C_{10}H_6 \cdot NH_2$;

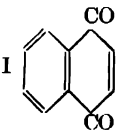
Orange II, $SO_3Na \cdot C_6H_4 \cdot N:N \cdot C_{10}H_6 \cdot OH[\beta]$;

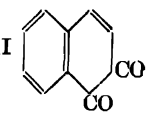
Ponceau 2 R, from diazotized xylidine and "R-salt"; **Fast Red C** ("*Echtroth*"), $SO_3Na \cdot C_{10}H_6 \cdot N:N \cdot C_{10}H_5(OH)(SO_3Na)$, from naphthionic acid and 1-naphthol-4-sulphonic acid, **Biebrich Scarlet**, $SO_3Na \cdot C_6H_4 \cdot N:N \cdot C_6H_4 \cdot N:N \cdot C_{10}H_6(OH)$, from amino-azo-benzene-sulphonic acid and β-naphthol; **Brilliant Black**, $(SO_3Na)_2C_{10}H_5 \cdot N:N \cdot C_{10}H_6 \cdot N:N \cdot C_{10}H_4(OH)(SO_3Na)_2$, from naphthylamine-disulphonic acid, α-naphthylamine, and "R-salt"; **Palatin Black**, $SO_3Na \cdot C_6H_4 \cdot N_2 \cdot C_{10}H_3(N_2C_{10}H_7)(NH_2)(OH)(SO_3Na)$, from diazobenzenesulphonic acid, α-azonaphthalene, and 1-amino-8-naphthol-4-sulphonic acid.

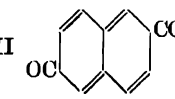
Quinones of the Naphthalene Series.—Three isomeric quinones, $C_{10}H_6O_2$, are known, two correspond with para and ortho benzoquinones

α-Naphthaquinone may be obtained by the oxidation of naphthalene, α-naphthylamine, 1-amino-4-naphthol, 1.4-dihydroxy-naphthalene, and of various derivatives of naphthalene containing substituents in the α-positions, by chromic acid. It crystallizes in yellow rhombic plates, melts at 125°, and is the complete analogue of ordinary quinone, having a similar odour and being volatile with steam. It can be reduced to 1:4-dihydroxy-naphthalene by sulphurous acid, and can yield a dioxime, hence its constitution as a para- or 1·4-quinone. (Formula I.)

β-Naphthaquinone (II) has no odour and is not volatile, being thus more like phenanthraquinone It can be obtained by the oxidation of 1-amino-2-naphthol, and when reduced with sulphurous acid yields 1 2-dihydroxy-naphthalene, hence its constitution as a 1 2 or orthoquinone. It decomposes at 115° without melting and crystallizes in red needles:

I 

II 

III 

2:6-Naphthaquinone (III), isomeric with the α- and β-compounds, forms odourless, non-volatile, yellowish-red prisms, and is a strong oxidizing agent.

Hydroxy-naphthaquinones are known; the common one is 2-hydroxy-α-naphthaquinone; **juglone** is the isomeric 5-hydroxy-compound, and occurs in nut shells; **naphthazarine**, "alizarin black", is a valuable dye which is prepared by acting upon α-dinitro-naphthalene with zinc and sulphuric acid,

comports itself like the alizarin dyes; it is the "alizarin" of the naphthalene series.

Carboxylic Acids.—The **naphthoic acids**, $C_{10}H_7 \cdot CO_2H$, can be obtained by saponifying the cyano-naphthalenes and also by the other synthetical methods given for the acids of the benzoic series. They crystallize in fine needles sparingly soluble in hot water, and break up into naphthalene and carbon dioxide when distilled with lime From them are derived the **hydroxy-naphthoic acids**, $C_{10}H_6(OH)(CO_2H)$, which are related to salicylic acid or its isomers. Among the **naphthalene-dicarboxylic acids**, $C_{10}H_6(CO_2H)_2$, which are known may be mentioned **naphthalic acid**, (1:8), which at a somewhat high temperature yields an anhydride similar to phthalic anhydride.

Phenyl-naphthalene, $C_{10}H_7(C_6H_5)$, has also been prepared, it is a compound built up of a naphthalene and of a benzene nucleus, and is therefore analogous to diphenyl, $C_6H_5 \cdot C_6H_5$. The same applies to·

Di-naphthyl, $C_{10}H_7 \cdot C_{10}H_7$, which yields derivatives (*e.g.* the di-naphthols, see p 502) analogous to those of diphenyl. The three modifications which are theoretically possible, namely, the α-α-, β-β-, and α-β-compounds, are known.

Another derivative of naphthalene is **acenaphthene**, $C_{12}H_{10}$, $= C_{10}H_6 \begin{smallmatrix} CH_2 \\ | \\ CH_2 \end{smallmatrix}$ (1·8), which is found in coal-tar. It crystallizes in colourless prisms, melts at 95°, boils at 277°, and yields naphthalic acid on oxidation.

XXXII. THE ANTHRACENE AND PHENANTHRENE GROUPS

A. Anthracene

Anthracene, $C_{14}H_{10}$ (*Dumas* and *Laurent*, 1832, *Fritzsche*, 1857), is formed, together with benzene and naphthalene, by the destructive distillation of coal and, generally, by the pyrogenous reactions which give rise to these products, *e.g.* by passing CH_4, C_2H_6, C_2H_2, the vapour of alcohol, &c., through red-hot tubes.

Although coal-tar contains only some 0·25–0·45 per cent of anthracene, it is the chief source from which this hydrocarbon

is obtained. The fraction of coal-tar distilling above 270° and known as anthracene oil yields, on further distillation and digesting with solvent naphtha, a solid mass known as 50-per-cent anthracene, which is then distilled with one-third of of its weight of potassium carbonate. This serves to remove carbazole (p. 473), which yields a non-volatile potassium derivative $C_6H_4\diagdown\diagup C_6H_4\rangle NK$, and the distillate consists of anthracene and phenanthrene The phenanthrene is removed by extraction with carbon disulphide, and the anthracene crystallized from benzene.

The following are some of the more important methods by means of which the hydrocarbon has been synthesised, and they throw considerable light upon its constitution:—

1. By heating *o*-tolyl phenyl ketone with zinc dust (B. **7**, 17):

$$C_6H_4\langle\begin{matrix}CO\\CH_3\end{matrix}\rangle C_6H_5 = C_6H_4\langle\begin{matrix}CH\\|\\CH\end{matrix}\rangle C_6H_4 + H_2O.$$

2 Together with dibenzyl, by heating benzyl chloride with water at 200° (B. **7**, 276):

$$4C_6H_5\cdot CH_2Cl = C_{14}H_{10} + C_{14}H_{14} + 4HCl.$$

3 From *o*-bromo-benzyl bromide and sodium in ethereal solution dihydro-anthracene is at first formed, and this is converted by oxidation (which is partly spontaneous during the above reaction) into anthracene (B. **12**, 1965):

$$C_6H_4\langle\begin{matrix}Br\\CH_2Br\end{matrix} + \begin{matrix}BrCH_2\\Br\end{matrix}\rangle C_6H_4 + 4Na = C_6H_4\langle\begin{matrix}CH_2\\CH_2\end{matrix}\rangle C_6H_4 + 4NaBr;$$

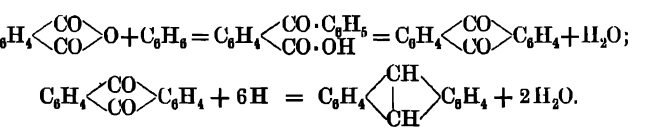
$$C_6H_4\langle\begin{matrix}CH_2\\CH_2\end{matrix}\rangle C_6H_4 - H_2 = C_6H_4\langle\begin{matrix}CH\\|\\CH\end{matrix}\rangle C_6H_4.$$

4. By heating benzene with symmetrical tetrabromo-ethane and aluminic chloride (*Anschutz*, B. **16**, 623):

$$C_6H_6 + \begin{matrix}BrCHBr\\|\\BrCHBr\end{matrix} + C_6H_6 = C_6H_4\langle\begin{matrix}CH\\|\\CH\end{matrix}\rangle C_6H_4 + 4HBr.$$

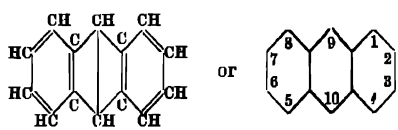
5. When phthalic anhydride is heated with benzene and aluminic chloride, *o*-benzoyl-benzoic acid is formed, and this when heated with phosphoric anhydride yields anthraquinone

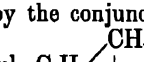
(*Behr* and *v. Dorp*, B. **7**, 578), which on reduction with zinc dust gives anthracene:



6. When a mixture of *m*-xylene and styrene is treated with concentrated sulphuric acid, there is formed *α-tolyl-β-phenyl-propane*, $CH_3 \cdot C_6H_4 \cdot CH_2 \cdot CH\langle^{C_6H_5}_{CH_3}$, which decomposes almost quantitatively into methane, hydrogen, and methyl-anthracene when strongly heated (B. **23**, 3272).

Constitution.—From mode of formation 5, the anthracene molecule is seen to contain two benzene nuclei, C_6H_4, joined together by a middle group, C_2H_2. The carbon atoms of this middle group are likewise linked together, as is seen from mode of formation 4, and take up the *o*-position with regard to each other on one or other of the benzene nuclei (on one nucleus according to methods of formation 1 and 5, and on the other according to method 3; for further proofs of this, see *e.g. v. Pechmann*, B. **12**, 2124). The constitution of anthracene is thus the following (*Graebe* and *Liebermann*, A. Suppl. **7**, 313):



The two carbon atoms of the middle group thus form a new hexagon-ring with the carbon atoms of the benzene nuclei to which they are linked, so that anthracene may also be looked upon as being built up by the conjunction of three benzene nuclei. Besides the formula  , the "quinoid" formula  has also to be taken into consideration (*Armstrong*, P. 1890, 101; *Kehrmann*, B. 1894, **21**, 3348).

Properties and Behaviour.—Anthracene crystallizes in colourless plates which show a magnificent blue fluorescence. It is

insoluble in water and dissolves only sparingly in alcohol and ether, but readily in hot benzene. It melts at 213°, boils above 351°, and with picric acid yields an additive compound which crystallizes in beautiful red needles melting at 138°.

Anthracene is transformed by sunlight into the polymeric **para-anthracene**, $(C_{14}H_{10})_2$. When reduced with hydriodic acid and phosphorus it takes up, in the first instance, two atoms of hydrogen, with the formation of 9:10-**dihydro-anthracene**,

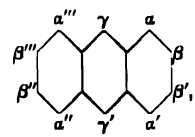
$$C_6H_4\begin{<}CH_2\\CH_2\end{>}C_6H_4$$

(see p. 505, mode of formation 3). This crystallizes in colourless plates, melts at 107°, and is readily soluble in alcohol It sublimes readily and distils without decomposition, but yields anthracene at a red heat or when warmed with concentrated sulphuric acid.

Further addition of hydrogen yields the hydrides $C_{14}H_{16}$ and, finally, $C_{14}H_{24}$.

DERIVATIVES OF ANTHRACENE

Theoretically three isomeric mono-derivatives are possible in each case, viz., the α-, β-, and γ-compounds:



since in the graphical formula given on the preceding page, $1 = 4 = 5 = 8 = \alpha$, $2 = 3 = 6 = 7 = \beta$, and $9 = 10 = \gamma$. The observed facts are in complete accordance with this.

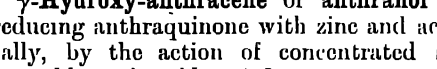
The position of the substituting group can usually be determined either by an examination of the oxidation products, *e.g.* if it be in the γ-position it will be eliminated and anthraquinone formed; or it is arrived at from the synthesis of the compound, *e.g.* in the case of alizarin, the formation of which from catechol and phthalic acid shows that its two hydroxyls are contained in one and the same benzene nucleus.

The number of di-substituted derivatives is large, for example, when both substituents are alike, 15 isomerides are theoretically possible.

Numerous derivatives of anthracene are known, *e.g.* halogen-, nitro-, amino-, and sulphonic acid derivatives.

Hydroxy-anthracenes.— The α- and β-compounds are termed α- and β-**anthrols**; they are obtained by fusing the corresponding sulphonic acids with alkali, and in their properties closely resemble phenols and naphthols.

γ-**Hydroxy-anthracene** or **anthranol** may be obtained by reducing anthraquinone with zinc and acetic acid, or synthetically, by the action of concentrated sulphuric acid on *o*-benzyl-benzoic acid at 80°:



It is readily oxidized to anthraquinone, and with hydroxylamine yields anthraquinone oxime.

Anthraquinone, $C_{14}H_8O_2$ (*Laurent*, 1834), is readily obtained by oxidizing anthracene with chromic acid mixture (which is the method followed on the large scale), or with chromic anhydride and glacial acetic acid, and is also produced when calcium benzoate is distilled.

It crystallizes in yellow prisms or needles soluble in hot benzene, melts at 285°, sublimes with great readiness, and is exceedingly stable as regards oxidizing agents. Hydriodic acid at 150° reduces it either to anthracene or its dihydride, while fusion with potash converts it into benzoic acid. It possesses more of a ketonic than of a quinonic character (*Zincke, Fittig*), as it is not reduced by sulphurous acid, and gives an oxime with hydroxylamine.

It yields mono- and dibromo-, nitro- and sulphonic-acid derivatives. **Anthraquinone β-mono-sulphonic acid** crystallizes in yellow plates, and is formed by the action of sulphuric acid under normal conditions, but in the presence of mercury salts the isomeric α-acid is obtained, of the **disulphonic acids** two are formed directly from anthraquinone, and two may be prepared by the oxidation of the corresponding anthracene-disulphonic acids.

Fusion of the sulphonic acids with potash does not generally yield the analogous hydroxy-compounds in theoretical quantity, oxygen being usually absorbed from the air at the same time; thus the mono-sulphonic acids yield mono- and dihydroxy-, and the di-sulphonic acids di- and trihydroxy-anthraquinones. In practical working the theoretical amount of chlorate of

potash required is added to the "melt". Prolonged fusion with potash tends to form hydroxy-benzoic acids.

Various **hydroxy-anthraquinones** can also be prepared by the synthetical mode of formation 5, p. 505, viz., from phthalic anhydride and the mono- or dihydroxy-benzenes (*Baeyer* and *Caro*, B. **7**, 792; **8**, 152), *e.g.*:

$$C_6H_4\langle\begin{matrix}CO\\CO\end{matrix}\rangle O + C_6H_4(OH)_2 = C_6H_4\langle\begin{matrix}CO\\CO\end{matrix}\rangle C_6H_2(OH)_2 + H_2O;$$

phenol yields by this method the two hydroxy-anthraquinones (yellow needles), catechol yields alizarin, quinol yields quinizarin, and so on. The hydroxy-derivatives are further produced by fusing chloro- and bromo-anthraquinones with potash, while *m*-hydroxy-benzoic acid can be converted directly by sulphuric acid into anthraflavic acid, water being eliminated. Cf. A **240**, 245.

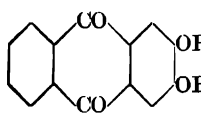
Alizarin, 1 2-**dihydroxy-anthraquinone**, $C_{14}H_8O_4$, is the most important constituent of the beautiful red dye of the madder root (*Rubia tinctorum*), which has been known for ages, being present in the latter as the readily decomposable glucoside, Ruberythric acid, $C_{26}H_{28}O_{14}$; in addition to alizarin, madder also contains purpurin. It is manufactured on the large scale by fusing anthraquinone-β-sulphonic acid with potassic hydroxide and chlorate (*Graebe* and *Liebermann*, *Caro*, *Perkin*, B. **3**, 359; A. **160**, 130).

It crystallizes in magnificent red prisms or needles of a glassy lustre, melts at 289°, and can be sublimed; it dissolves readily in alcohol and ether, only sparingly in hot water, but, as a phenol, very readily in alkalis to a violet-red solution. It yields insoluble coloured compounds—the so-called "**lakes**"—with metallic oxides, the alumina and tin lakes being of a magnificent red colour, iron lake violet-black, and lime lake blue. In the Turkey Red manufacture, for instance, the materials to be dyed are previously mordanted with acetate of alumina or with "ricinoleic-sulphuric acid".

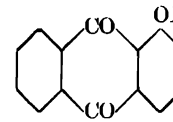
Its constitutional formula is based on the following considerations:—(*a*) Its conversion into anthracene when heated with zinc dust (*Graebe* and *Liebermann*, B. 1868, **1**, 49; A. Sup. **7**, 297); (*b*) its formation by fusing dibromo-anthraquinone or anthraquinone-sulphonic acid with potash; (*c*) its synthesis from phthalic anhydride and catechol.

All these indicate that it is a dihydroxy-anthraquinone

with the two hydroxy-groups in the *o*-positions with respect to one another:



2 3 or



1:2.

The fact that two isomeric mono-nitro-derivatives (with the nitro-group in the same nucleus as the two hydroxy-groups) have been prepared is a proof of the positions 1:2 for the hydroxy-groups.

Anthrarobin, *dihydroxy-anthranol*, $C_6H_4\begin{<}{C(OH)}{CH_2}{>}C_6H_2(OH)_2$, obtained from alizarin, ammonia, and zinc dust, is a yellowish-white powder which yields alizarin on oxidation; on account of its reducing properties it is used in skin diseases

Nitric peroxide converts alizarin into **β-nitro-alizarin** or alizarin orange, $C_{14}H_7(NO_2)O_4$, a yellowish-red dye, and this with glycerol and sulphuric acid (the *Skraup* reaction, p 542), yields **alizarin blue**, $C_{17}H_9NO_4$ (see Quinoline), a valuable blue dye which is converted by fuming sulphuric acid into **alizarin green**.

Purpurin, 1:2.4-*trihydroxy-*, **anthrapurpurin**, 1 2 7-*trihydroxy-*, and **flavopurpurin**, 1 2 6-*trihydroxy-anthraquinone*, are also valuable dyes which are manufactured on a large scale, the same applies to the isomeric compound **anthragallol**, 1 2:3-*trihydroxy-anthraquinone*, or "anthracene brown", which is prepared by acting on a mixture of gallic and benzoic acids with concentrated sulphuric acid.

Tetra-, penta-, and hexa-hydroxyanthraquinones are also used as dyes. (B. 1890, **23**, 3739; J. pr. **43**, 237, 246.) **Alizarin bordeaux** is a 1:2·5:8-tetrahydroxy- and **alizarin-cyanine** 1:2:4:5:8-pentahydroxy anthraquinone

According to *v. Kostanecki* the colouring power of these compounds is connected with the presence of two hydroxyls in the ortho-position to one another.

For **Indanthrene** dyes see **B. 36**, 3410.

B. Phenanthrene

Phenanthrene (*Fittig* and *Ostermeyer*, 1872, A. **166**, 361), which is isomeric with anthracene, accompanies this hydrocarbon in coal-tar. It crystallizes in colourless glistening

plates, dissolves in alcohol more readily than anthracene (yielding a blue fluorescent solution), melts at 99°, and boils at 340°. It may be separated from anthracene by partial oxidation and subsequent distillation, as the latter is more readily attacked. Oxidizing agents convert it into diphenic acid (p. 474). Its **picrate** crystallizes in yellow needles melting at 145°.

It may also be obtained:—1. By leading the vapour of toluene, stilbene, dibenzyl or *o*-ditolyl through a red-hot tube, thus:

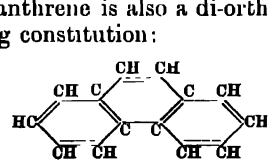
$$o\text{-ditolyl, } \begin{matrix} C_6H_4\cdot CH_3 \\ C_6H_4\cdot CH_3 \end{matrix} = \begin{matrix} C_6H_4\cdot CH \\ C_6H_4\cdot CH \end{matrix} + 2H_2.$$

2. Together with anthracene from *o*-bromo-benzyl bromide and sodium.

3. A recent synthesis by *Pschorr* (B. 1896, **29**, 496; **32**, 162, 176; **33**, 496) is from *o*-nitro-benzaldehyde. This with sodic phenyl-acetate and acetic anhydride (*Perkin's* synthesis, p. 441) yields α-phenyl-*o*-nitro-cinnamic acid, $NO_2\cdot C_6H_4\cdot CH{:}CPh\cdot CO_2H$. When this is reduced, diazotized, and treated with copper powder, β-phenanthrene-carboxylic acid is formed, $\begin{matrix} C_6H_4\cdot CH \\ C_6H_4\cdot C\cdot CO_2H \end{matrix}$, and when carbon dioxide is eliminated this yields phenanthrene Numerous phenanthrene derivatives have been synthesised in a similar manner. (See also *Rabe*, B. 1898, **31**, 1896.)

The formation of phenanthrene from *o*-ditolyl, and its oxidation to diphenic acid, $\begin{matrix} C_6H_4\cdot CO_2H \\ C_6H_4\cdot CO_2H \end{matrix}$, show that it is a diphenyl derivative, and that it contains a carbon atom linked to each benzene nucleus; this carbon atom is joined to the corresponding one by a double bond, as is shown, *e.g.*, by its formation from stilbene, $\begin{matrix} C_6H_5\cdot CH \\ C_6H_5\cdot CH \end{matrix}$, a reaction completely analogous to the preparation of diphenyl from benzene. Since diphenic acid is a di-ortho-diphenyl-dicarboxylic acid (*Schultz*, **A. 196**, 1; **203**, 95), phenanthrene is also a di-ortho-derivative and possesses the following constitution:

$\begin{matrix} C_6H_4\cdot CH \\ C_6H_4\cdot CH \end{matrix}$ or

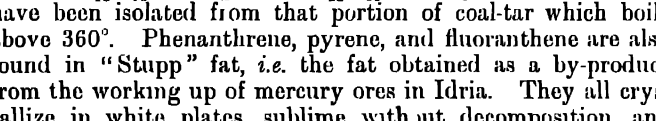


According to the above formula, the two CH-groups form a new hexagon ring with the carbon atoms of the two benzene nuclei to which they are linked, so that phenanthrene—like anthracene—may be looked upon as the product of the coalition of three benzene nuclei, or of one naphthalene and one benzene nucleus.

Additive and substitution products of phenanthrene are also known, *e.g.* a tetrahydride, nitro-, amino-, cyano-, and hydroxy-compounds, and sulphonic and carboxylic acids **Phenanthrol**, $C_{14}H_9(OH)$, is a hydroxy-phenanthrene, and **phenanthrene-quinol**, $C_{14}H_8(OH)_2$, a dihydroxy-compound; when oxidized the latter yields **phenanthraquinone**, $\begin{matrix} C_6H_4\cdot CO \\ C_6H_4\cdot CO \end{matrix}$, which may also be prepared directly from phenanthrene and chromic acid It crystallizes in odourless, orange needles, melts at 200°, distils unchanged, and is not volatile in steam. Phenanthraquinone possesses the character of a diketone, reacting with hydroxylamine, sodium bisulphite, &c, but it can be reduced to the corresponding quinol by sulphurous acid. It gives a bluish-green coloration with toluene containing thio-tolene, glacial acetic acid, and sulphuric acid, and when the mixture is diluted and extracted with ether the latter becomes violet-coloured; this is the *Laubenheimer* reaction (B **17**, 1338).

C. Complex Hydrocarbons

Fluoranthene, $C_{15}H_{10}$, **pyrene**, $C_{10}H_{10}$, **chrysene**, $C_{18}H_{12}$, **retene**, $C_{18}H_{18}$, and **picene**, $C_{22}H_{14}$, are hydrocarbons which have been isolated from that portion of coal-tar which boils above 360°. Phenanthrene, pyrene, and fluoranthene are also found in "Stupp" fat, *i.e.* the fat obtained as a by-product from the working up of mercury ores in Idria. They all crystallize in white plates, sublime without decomposition, and when oxidized are converted into the corresponding ketones. Their constitution is expressed by the following formulæ.



(Cf. A. **240**, 147; **284**, 52; **351**, 218; B. **26**, 1745; B. **36**, 4200.)

HETEROCYCLIC COMPOUNDS

XXXIII. INTRODUCTION

The third great division of carbon derivatives consists of the *Heterocyclic Compounds*. These, like the carbocyclic compounds, contain a closed chain or ring, but differ from the latter by the presence in the actual ring of atoms of elements other than carbon (cf. formulæ, p 514). The number of such compounds is enormous, although the number of elements usually associated with carbon in rings is comparatively small. The more common elements are oxygen and sulphur, but more especially nitrogen.

A number of these compounds have been already mentioned, among the oxygen compounds are ethylene oxide, glycolide, phthalic anhydride, and among the nitrogen compounds succinimide, phthalimide, and lactams.

The compounds are divided into groups according to the number of atoms constituting the ring, thus three-membered rings, *e.g.* ethylene oxide, four-membered rings, *e.g.* betaine, five-membered rings, *e.g.* thiophene; six-membered rings, *e.g.* pyridine, &c As in the carbocyclic series, the most important and also the most stable are the five- and six-membered rings. A further division of these groups can be made according to the *number* of atoms other than carbon present Thus in the five-membered ring compounds we can have the following sub-groups: 4C + 1N, 3C + 2N; 2C + 3N; termed respectively the monazole, di- and tri-azole sub-groups.

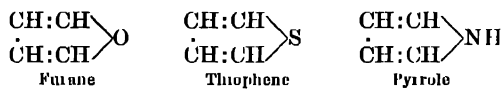
The stability of the compounds and their general chemical characteristics depend to a large extent on the saturated or unsaturated nature of the rings Compounds like thiophene, pyrrole and pyridine are stable and closely resemble benzene—they possess general aromatic properties. Like benzene they can be reduced, the two former can each take up two or four atoms of hydrogen, and pyridine two, four or six. These reduction products no longer have aromatic properties. It is interesting to note that although the five-membered heterocyclic unsaturated compounds resemble benzene, the unsaturated carbocyclic compound cyclopentadiene does not.

Some of the common heterocyclic compounds contain condensed nuclei, *i.e.* the two condensed rings have two carbon atoms in common. A well-known example of condensed

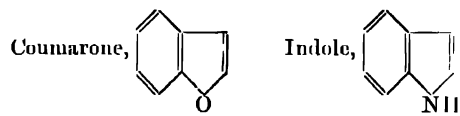
heterocyclic rings is met with in purine and its derivatives (p. 290). Examples of compounds containing a benzene nucleus condensed with a heterocyclic ring are met with in quinoline, coumarone and indole (see below).

Compounds with condensed nuclei behave very differently on oxidation. Certain of them have the heterocyclic ring ruptured, and thus yield ortho-derivatives of the carbon ring, others, again, have the carbon ring ruptured, and yield ortho-acids of the heterocyclic ring. The compounds dealt with in the following sections will be grouped as follows:

1. Five-membered heterocyclic compounds containing 4C + 1O, S or N atoms, or the **furane** group, *e.g.*:

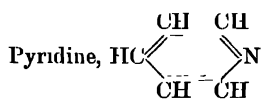


2. Compounds formed by the condensation of these rings with a benzene nucleus, *e.g.*:

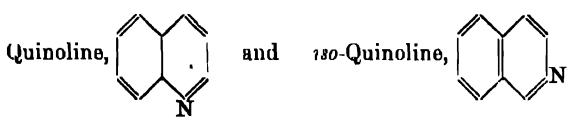


3. Five-membered heterocyclic compounds containing three carbon atoms, *e.g.* pyrazole and thiazole group

4. Six-membered heterocyclic compounds or **pyridine** group, *e.g.*:

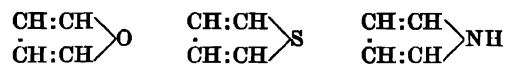


5. The compounds formed by the condensation of a benzene and pyridine ring, *e.g.*:



6. Six-membered heterocyclic compounds, with not more than four carbon atoms in the ring.

XXXIV. FURANE GROUP

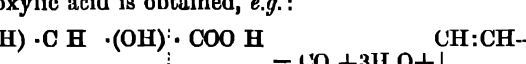


Furane Thiophene Pyrrole.

From these compounds a whole series of derivatives are obtained by the substitution of hydrogen by halogen, and also by the entrance of the groups $\cdot CH_3$, $\cdot CH_2OH$, $\cdot CHO$, $\cdot CO_2H$, &c. In their properties furane, thiophene, and pyrrole remind one of benzene. Thiophene, in particular, is delusively like the latter, *e.g.* in odour and boiling-point, and its various derivatives often show a marvellous similarity in their chemical and physical relations to the corresponding derivatives of benzene.

Furane, pyrrole, and thiophene also resemble one another in many respects. All three boil at relatively low temperatures ($+32°$, 131°, 84°), are either insoluble or only sparingly soluble in water, but readily in alcohol and ether, and show many analogous colour reactions. Thus pyrrole and thiophene and their derivatives give, for the most part, an intense violet to blue coloration when mixed with isatin and concentrated sulphuric acid, and a cherry-red or violet coloration with phenanthraquinone and glacial acetic or sulphuric acid. The vapour of pyrrole colours a pine shaving which has been moistened with hydrochloric acid carmine red (πυῤῥός, fiery-red), while furaldehyde vapour colours it an emerald green, the latter likewise colours a piece of paper moistened with xylidine- or anilineacetate red. Furane is converted by mineral acids, *e.g.* hydrochloric acid, into an insoluble amorphous powder, and pyrrole into an insoluble amorphous brown-red powder, "pyrrole-red" (with evolution of ammonia), while thiophene remains unaltered; the derivatives show a similar behaviour. Pyrrole is distinguished from the two other compounds by having feebly basic properties.

Derivatives of all three compounds may be obtained from mucic acid, $CO_2H\cdot(CH\cdot OH)_4\cdot CO_2H$ (p. 259). When distilled, mucic acid yields pyromucic acid or furane-α-carboxylic acid; when its ammonium salt is distilled, pyrrole is formed; and when free mucic acid is heated with barium sulphide, thiophene α-carboxylic acid is obtained, *e.g.*:



A very general method for the formation of derivatives of this group is from γ-diketones, *e.g.* acetonyl-acetone, $CH_3 \cdot CO \cdot CH_2 \cdot CH_2 \cdot CO \cdot CH_3$ (p. 221; also p. 230). When this compound is heated with phosphorus pentoxide or zinc chloride, dimethyl-furane is formed; with phosphorus pentasulphide, dimethyl-thiophene; with alcoholic ammonia, dimethyl-pyrrole (B. **18**, 58, 367; **20**, 1074).

This behaviour would indicate that the acetonyl-acetone reacts as the tautomeric compound:

$$CH_3 \cdot C(OH):CH \cdot CH:C(OH) \cdot CH_3 \quad \text{or} \quad \begin{matrix} CH:C(CH_3)(OH) \\ CH:C(CH_3)(OH) \end{matrix};$$

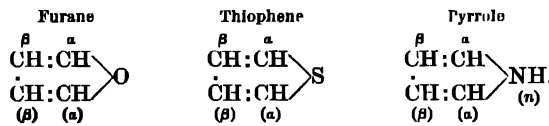
upon this assumption the formation of dimethyl-furane appears simply as that of an anhydride, that of dimethyl-pyrrole as an exchange of 2(OH) for NH (imide formation), and that of dimethyl-thiophene as the formation of a sulphide, *i.e.* exchange of 2(OH) for S, according to the following equations:

$$\begin{matrix} CH:C(CH_3) \cdot OH \\ CH:C(CH_3) \cdot OH \end{matrix} = \begin{matrix} CH:C(CH_3) \\ CH:C(CH_3) \end{matrix}\!\!>\!O + H_2O$$

$$H_2S + \begin{matrix} CH:C(CH_3) \cdot OH \\ CH:C(CH_3) \cdot OH \end{matrix} = \begin{matrix} CH:C(CH_3) \\ CH:C(CH_3) \end{matrix}\!\!>\!S + 2H_2O$$

$$NH_3 + \begin{matrix} CH:C(CH_3) \cdot OH \\ CH:C(CH_3) \cdot OH \end{matrix} = \begin{matrix} CH:C(CH_3) \\ CH:C(CH_3) \end{matrix}\!\!>\!NH + 2H_2O.$$

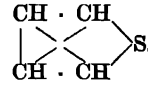
From the above reactions the *constitutional formulæ* for the three compounds would be:



These formulæ receive corroboration from the frequently observed fact that the substances are capable of yielding additive compounds with bromine or hydrogen (see Pyrroline). According to the above formulæ, two isomeric mono-substituted derivatives of furane and thiophene are possible: (1) one in which the hydrogen atom (α) which stands nearest to the oxygen, sulphur, or nitrogen atom, and (2) one in which a quasi-middle hydrogen atom (β) is substituted. As a matter

of fact, two such isomers have been observed in many cases, *e.g.* two thiophenic acids. These form mixed crystals, the crystals having a homogeneous appearance although they contain both acids (*V. Meyer*, A. **236**, 200). In the case of pyrrole, on the other hand, three kinds of derivatives (*α*-, *β*-, and *n*-) are both possible and known.

An examination of the molecular refraction of thiophene and also of its heat of combustion (B. 1885, **18**, 1832) point to the presence of only one double bond in the thiophene molecule. The formula $\begin{matrix}CH\cdot CH\\ \cdot\cdot\quad\cdot\\ CH\cdot CH\end{matrix}\!\!>\!S$ has been suggested, and this is quite in harmony with the production of substituted maleic acids by the oxidation of thiophene derivatives. Probably the simplest explanation is that the thiophene molecule contains centric bonds, and should be represented as:



Furane or **furfurane** is a colourless mobile liquid, boiling at 32°, and with an odour resembling that of chloroform. It is present in pine-wood tar, in the first runnings from ordinary wood tar, &c., and is obtained by the distillation of sugar with lime, or by distilling barium pyromucate. *α*-**Methyl-furane** or *sylvane* is likewise present in pine-wood tar, and in the products of distillation of sugar with lime. It boils at 65°. *αα*-**Dimethyl-furane** is obtained from sugar and lime, and also from acetonyl-acetone (p. 516). It is a colourless mobile liquid of a characteristic odour, and boils at 94°. Concentrated acids convert it into a resin; it can be transformed back into acetonyl-acetone.

Furol, *α-furaldehyde* or *furfuraldehyde*, $C_4H_3O\cdot CHO$ (*Dobereiner*), is obtained when pentoses, *e.g.* arabinose and xylose, are distilled with concentrated hydrochloric acid:

$$C_5H_{10}O_5 - 3H_2O = C_5H_4O_2.$$

The yield is quantitative, and the method is made use of for determining the amounts of pentoses present in various substances.

It may also be obtained by distilling bran, wood, sugar, or various carbohydrates with moderately concentrated sulphuric

acid. It is a colourless oil of agreeable odour, turns brown in the air, and boils at 162°.

It possesses all the properties of an aldehyde, and can yield condensation products in much the same manner as benzaldehyde (p. 424): *e.g.* **furoïn**, $C_4H_3O \cdot CH(OH) \cdot CO \cdot C_4H_3O$, corresponding with benzoin; **furalmalonic acid**, $C_4H_3O \cdot CH : C(CO_2H)_2$, corresponding with benzalmalonic acid; and **furylacrylic** and *allo*-**furylacrylic acid**, $C_4H_3O \cdot CH : CH \cdot CO_2H$, corresponding with cinnamic and *allo*-cinnamic acids.

Pyromucic acid, $C_4H_3O \cdot CO_2H$.—Furane-α-carboxylic acid crystallizes in needles or plates similar to those of benzoic acid, and melts at 132°; it sublimes easily, is readily soluble in hot water and alcohol, and decolorizes alkaline permanganate almost instantaneously.

Pyrrole is a constituent of coal-tar (*Runge*) and of bone-oil (*Anderson*); it boils at 131°, and possesses, like many of its homologues, a chloroform odour. It is a secondary base, and its imino-hydrogen is replaceable by metals and alkyl, or acyl radicals.

In addition to the methods of formation mentioned on p. 516, it may also be obtained by heating succinimide (p 239) with zinc dust, or from acetylene and ammonia at a red heat.

When pyrrole is acted upon by hydroxylamine the ring is broken, and the dioxime of succinic-aldehyde, $\begin{matrix} CH_2 \cdot CH : N \cdot OH \\ CH_2 \cdot CH : N \cdot OH \end{matrix}$, is formed; this yields tetramethylene-diamine upon reduction (B. **22**, 1968). Dimethyl-pyrrole in a similar manner yields acetonyl-acetone-dioxime.

n-**Potassium-pyrrole**, C_4H_4NK, which is obtained from pyrrole and potassium or solid potassic hydroxide, is a colourless compound which is decomposed by water. A number of *n*-alkyl and acyl derivatives may be prepared by the aid of this potassium compound, but most of them are relatively unstable, and when heated are transformed into the isomeric α-alkyl or acyl compounds. A most interesting reaction is the conversion of pyrrole into pyridine (p. 533) by means of sodium methoxide and chloroform or methylene iodide. By the action of iodine and alkali, substitution takes place with the formation of **tetra-iodo-pyrrole** or **iodole**, $C_4I_4(NH)$, which crystallizes in yellow plates, and is used as an antiseptic in place of iodoform.

Zinc and glacial acetic acid convert pyrrole into **pyrroline**,

$\begin{matrix}CH{:}CH\\ \dot{C}H_2\cdot CH_2\end{matrix}\!\!>\!NH$, or more probably $\begin{matrix}CH\cdot CH_2\\ \dot{C}H\cdot CH_2\end{matrix}\!\!>\!NH$ (B. 1901, **34**, 3954), a colourless liquid boiling at 91° and also a strong secondary base; when this latter is heated with hydriodic acid, it is further reduced to **pyrrolidine**, $\begin{matrix}CH_2\cdot CH_2\\ \dot{C}H_2\cdot CH_2\end{matrix}\!\!>\!NH$, a colourless, strongly alkaline base resembling piperidine, and boiling at 86°. It is also formed by the action of sodium on an alcoholic solution of succinimide, and is obtained synthetically by heating δ-chloro-butylamine with alkali, and by treating ethylene cyanide with sodium and alcohol, thus:

$$\begin{matrix}CH_2\cdot CN\\ \dot{C}H_2\cdot CN\end{matrix} + 4H_2 = \begin{matrix}CH_2\cdot CH_2\cdot NH_2\\ \dot{C}H_2\cdot CH_2\cdot NH_2\end{matrix} = \begin{matrix}CH_2\cdot CH_2\\ \dot{C}H_2\cdot CH_2\end{matrix}\!\!>\!NH + NH_3,$$

it is consequently designated **tetramethylene-imine** (*Ladenburg*, B. **19**, 782; **20**, 442).

The red colouring matter of blood yields pyrrole derivatives as some of its products of decomposition, and pyrrolidine derivatives, especially pyrrolidine-carboxylic acid (proline), are decomposition products of albumen.

Thiophene (*V. Meyer*, B. **16**, 1465, &c) is present in coal-tar, being invariably found in benzene (up to 0·5 per cent); the same applies to its homologues thiotolene (methyl-thiophene), and thioxene (dimethyl-thiophene), which accompany toluene and xylene, &c. Its boiling-point (84°) is almost the same as that of benzene (80·4°), from which it is extracted by repeatedly shaking with small quantities of concentrated sulphuric acid, which transforms the thiophene into a soluble sulphonic acid (B. **17**, 2641, 2852). It is also attacked more readily than benzene by other reagents, such as halogens.

Thiophene is also obtained synthetically by leading the vapour of ethyl sulphide through a red-hot tube (*Kekulé*), and in small quantity by heating crotonic acid, *n*-butyric acid, paraldehyde, &c., with phosphorus pentasulphide.

Stilbene (p. 478) and sulphur yield **tetraphenylthiophene**, *thionessal*, m.-pt. 183°.

The preparation and properties of the thiophene derivatives are almost identical with those of the corresponding benzene compounds. Thus nitric acid acts on thiophene to produce a **nitro-thiophene**, analogous to nitro-benzene, which can in its turn be reduced to amino-thiophene; the latter is, however, much less stable than the corresponding amino-benzene.

The boiling-points of thiophene compounds and their corresponding benzene derivatives are almost identical.

The homologues can be obtained by *Fittig's* synthesis, the α-compounds from 1:4-diketones, and the β-derivatives from mono- or di-substituted succinic acids and phosphorus pentasulphide.

Thiophene-sulphonic acid, $OH \cdot SO_2 \cdot C_4H_3S$, decomposes into thiophene and sulphuric acid when superheated with water, and does not yield a phenol on fusion with potash.

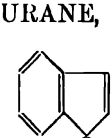
Hydroxythiotolene, $C_4H_2S(CH_3)(OH)$, the phenol of thiotolene, is formed by heating lævulic acid with P_2S_5 (B. **19**, 553).

A mixture of the α- and β-monocarboxylic acids when crystallized slowly from water yields **mixed crystals**, which cannot be resolved into their components.

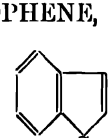
The blue coloration which is formed when benzene containing thiophene is shaken with isatin and concentrated sulphuric acid, is due to the formation of the blue colouring matter "**Indophenin**", $C_{12}H_7ONS$.

(Cf. *V. Meyer's* "Die Thiophengruppe", Braunschweig, 1888.)

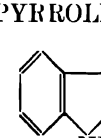
XXXV. COMPOUNDS FORMED BY THE CONDENSATION OF A BENZENE NUCLEUS WITH A FURANE, THIOPHENE, OR PYRROLE RING



Coumarone

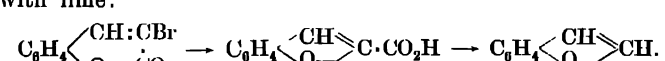


Benzo-thiophene



Indole

Coumarone closely resembles pseudo-cumene. It occurs in coal-tar, and may be isolated as its **picrate**. It is usually obtained from bromocoumarin; this with alcoholic potash yields coumarilic acid which gives coumarone when distilled with lime:



It is a colourless liquid distilling at 170°; yields a **dibromide** and a **dihydro**-derivative, thus indicating the presence of a double bond. Numerous derivatives are known.

Benzo-thiophene, *Thionaphthene*, melts at 31°, boils at 221°, and has an odour resembling naphthalene.

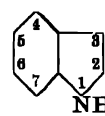
INDOLE GROUP

Indole (*Baeyer*, 1868) is the most important compound in this group, as it is the parent substance of indigo. As a derivative of pyrrole it possesses feebly basic properties. It is obtained by distilling oxindole with zinc dust; by heating *o*-nitro-cinnamic acid with potash and iron filings; by the action of sodic ethoxide upon *o*-amino-β-chloro-styrene (B. **17**, 1067)·

$$C_6H_4\langle\begin{matrix}NH_2\\CH:CHCl\end{matrix} + NaO\cdot C_2H_5 = C_6H_4\langle\begin{matrix}NH\\CH\end{matrix}\rangle CH + NaCl + C_2H_5OH;$$

by the pancreatic fermentation of albumen; together with skatole by fusing albumen with potash; and by passing the vapours of various anilines, *e.g.* diethyl-*o*-toluidine, through red-hot tubes, &c. It occurs in the essential oil of jasmine flowers, crystallizes in plates, melts at 52°, volatilizes readily with steam, and usually has a peculiar fæcal-like odour, although in the pure state and diluted it is stated to have a fragrant odour. It is feebly basic, colours a pine shaving which has been moistened with hydrochloric acid cherry-red, with nitrous acid gives a red precipitate, which consists partly of the so-called nitroso-indole, $[C_8H_6N(NO)]_2$ (a delicate reaction; see B. **22**, 1976), and yields acetyl-indole when acetylated. These last reactions show that indole contains an imino-group. When oxidized with ozone it yields indigo.

The system of numbering the substituents in the indole molecule is as follows:



The 1-substituted derivatives are sometimes termed *n*-derivatives, *e.g.* *n*-methyl-indole, $C_6H_4\langle\begin{matrix}NMe\\CH\end{matrix}\rangle CH$.

Various derivatives may be obtained synthetically by the condensation of the aromatic primary or secondary hydrazines either with pyroracemic acid or with certain ketones or aldehydes, and treatment of the resulting hydrazones with dilute hydrochloric acid or zinc chloride, when ammonia is eliminated

(*E. Fischer*, A. **236**, 116; **242**, 372); thus acetone-phenyl-hydrazone, $C_6H_5 \cdot NH \cdot N : C<^{CH_3}_{CH_3}$, yields α-methyl-indole, $C_6H_4<^{NH}_{CH}>C \cdot CH_3$, propaldehyde-phenyl-hydrazone yields skatole, and phenacyl bromide and aniline yield α-phenyl-indole. See also B. **25**, 2860.

Skatole, 3-*methyl-indole*, $C_6H_4<^{NH}_{CMe}>CH$, is found in fæces, and is produced, together with indole, *e.g.*, by the decay of albumen, or by fusing it with potash. It crystallizes in colourless plates of a strong fæcal odour and melts at 95°. Nitrous acid does not colour it red. It takes up two atoms of hydrogen to form a hydro-compound. Acids, aldehydes, &c., are also known.

Dioxindole, $C_6H_4<^{CH(OH)}_{NH}>CO$, or the lactam of *o*-amino-mandelic acid, $NH_2 \cdot C_6H_4 \cdot CH(OH) \cdot CO_2H$, is obtained by the reduction of isatin (into which it is again easily oxidized) with zinc dust and hydrochloric acid, or by the oxidation of oxindole. It crystallizes in colourless prisms, melts at 180°, and possesses both basic and acid properties (two hydrogen atoms being replaceable); it also forms a nitroso-compound, an N-acetyl derivative, &c.

Oxindole, $C_6H_4<^{NH}_{CH_2}>CO$, the lactam of *o*-amino-phenyl-acetic acid, is formed by the reduction of *o*-nitro-phenyl-acetic acid (p. 452); also by that of dioxindole with tin and hydrochloric acid. It crystallizes in colourless needles, melts at 120°, is readily oxidized to dioxindole, and therefore possesses feebly reducing properties. Oxindole is amphoteric, dissolving both in alkalis and in hydrochloric acid. Baryta water at a somewhat high temperature transforms it into barium *o*-amino-phenyl-acetate. The imino-hydrogen is exchangeable for ethyl, acetyl, the nitroso-group, &c.

Isomeric with oxindole is **indoxyl**, $C_6H_4<^{C(OH)}_{NH}>CH$, which is obtained by the elimination of carbon dioxide from indoxylic acid, a product formed from phenyl-glycocoll (p. 452), also by fusing indigo with potash. It is often present in the urine of the carnivora as potassium indoxyl-sulphate or urine-indican, $C_8H_6N \cdot O \cdot (SO_3K)$. It forms yellow crystals, melting at 85°, is moderately soluble in water with yellow fluorescence, and

not volatile with steam. It is very unstable, quickly becoming resinous, and is readily transformed into indigo when its alkaline solution is exposed to the air, or when ferric chloride is added to its solution in hydrochloric acid.

It yields a **nitroso-compound**, $C_6H_4\langle^{N(NO)}_{C(OH)}\rangle CH$, of the same character as the nitrosamines, and therefore it contains an imino-group; further, its relation to indoxyl-sulphuric acid shows that it contains an alcoholic hydroxy-group, and thus its constitution follows.

Potassium indoxyl-sulphate is prepared synthetically by warming indoxyl with potassium pyrosulphate; it crystallizes in glistening plates and is hydrolysed when warmed with acids.

Ethyl-indoxyl is obtained from indoxyl by the exchange of the hydroxylic hydrogen for C_2H_5. Derivatives of the hypothetical **pseudo-indoxyl**, $C_6H_4\langle^{NH}_{CO}\rangle CH_2$, are also known, some of them being convertible into indigo derivatives (*e.g.* diethyl-indigo).

Indoxylic acid, $C_6H_4\langle^{NH}_{C(OH)}\rangle C \cdot CO_2H$, the carboxylic acid of indoxyl, forms white crystals, is oxidized to indigo by ferric chloride, and breaks up into indoxyl and carbon dioxide when fused. It is obtained from its ester, **ethyl indoxylate**, by fusing with soda. The latter compound crystallizes in stout prisms, melts at 120°, and may be obtained, among other methods, by the reduction of ethyl *o*-nitro-phenyl-propiolate with ammonium sulphide.

Isatin, $C_6H_4\langle^{CO}_{NH}\rangle CO$, the lactam of *o*-amino-benzoyl-formic acid (p. 463), is readily prepared by oxidizing indigo or indoxyl with nitric acid (*Erdmann* and *Laurent*, 1841; cf. also B. 17, 976). It may also be obtained by the oxidation of dioxindole or of oxindole (indirectly).

The following are among some of the most important methods by means of which isatin has been synthesised:—

(*a*) When *o*-nitro-phenyl-glyoxylic acid (*o*-nitro-benzoyl-formic acid, p. 462) is reduced, the corresponding amino-acid is obtained; but this immediately loses water, yielding a lactam or lactim:

$$C_6H_4\langle^{CO\cdot CO\cdot OH}_{NH_2} \rightarrow C_6H_4\langle^{CO}_{NH}\rangle CO \text{ or } C_6H_4\langle^{CO}_{N=}\rangle C\cdot OH.$$

(*b*) *o*-Nitro-phenylacetic acid when reduced yields the lactam, oxindole, $C_6H_4<^{CH_2}_{NH}>CO$, and this with nitrous acid gives the iso-nitroso-oxindole, $C_6H_4<^{C(:N\cdot OH)}_{NH}>CO$, which on reduction is converted into amino-oxindole, and this on oxidation with ferric chloride yields isatin.

(*c*) *Sandmeyer* has worked out the following synthesis:—Aniline and carbon disulphide readily yield thio-carbanilide, $CS(NHC_6H_5)_2$, which, on boiling with potassium cyanide, white-lead, and water, yields hydrocyano-carbo-diphenyl-imide, $C_6H_5\cdot N:C(CN)\cdot NHC_6H_5$. With ammonium sulphide this latter yields $^{NH_2\cdot CS}_{C_6H_5\cdot N}>C\cdot NHC_6H_5$, which is converted by concentrated sulphuric acid into α-isatin-anilide, $C_6H_4<^{CO}_{N=}>C\cdot NHC_6H_5$, and this may be hydrolysed by dilute acids to isatin and aniline (C.C. 1900, **2**, 928).

(*d*) *o*-Nitrophenyl-propiolic acid (p. 456) may be synthesised, and when this is warmed with alkalis it undergoes molecular rearrangement and yields **isatogenic acid**, which by elimination of carbon dioxide forms isatin:

$$C_6H_4<^{C\equiv C\cdot CO_2H}_{NO_2} \longrightarrow C_6H_4<^{CO\cdot C\cdot CO_2H}_{N-O} \longrightarrow C_6H_4<^{CO}_{NH}>CO.$$

Isatin crystallizes in reddish-yellow monoclinic prisms, which are only sparingly soluble in cold water, but more readily in hot water and in alcohol to a brownish-red solution. It dissolves in potassium hydroxide solution, yielding the potassium derivative, $C_6H_4<^{CO}_{N=}>C\cdot OK$, which is readily hydrolysed to potassium *o*-amino-phenyl-glyoxylate when boiled with water. **Isatin chloride**, $C_6H_4<^{CO}_{N=}>C\cdot Cl$, is obtained when isatin is heated with phosphorus pentachloride, and on reduction with zinc dust and acetic acid yields indigo.

Two isomeric methyl ethers are known:

$C_6H_4<^{CO}_{N=}>C\cdot OCH_3$ and $C_6H_4<^{CO}_{N(CH_3)}>CO$

O-methyl isatin — N-methyl isatin or pseudo-methyl isatin

The O-ether is obtained by converting the potassic-isatin into the silver compound, and then heating this with methyl

iodide. It is a colourless solid melting at 102°, and on hydrolysis yields isatin or *o*-amino-phenyl-glyoxylic acid.

The N-ether may be obtained by the action of sodic hypobromite on N-methyl-indole. Its constitution follows from its method of formation, and also from the fact that on hydrolysis it yields *o*-methylamino-phenyl-glyoxylic acid, $C_6H_4<^{CO\cdot CO_2H}_{NHCH_3}$.

The constitution of isatin itself for some years was a matter of dispute; from its method of formation it must be either the lactam or lactim of *o*-amino-phenyl-glyoxylic acid. Certain of its methods of formation and of its reactions, *e.g.* with alkalis or phosphorus pentachloride, point to the lactim formula, whereas others would indicate the lactam constitution—isatin is thus a typical tautomeric compound. *Hartley* and *Dobbie* (J. C. S. 1899, 647) assign to it the lactam constitution. The ultra-violet absorption of alcoholic solutions of isatin is almost identical with that of the N-methyl ether, and quite different from that of the O-methyl ether, and hence the N-methyl ether and the parent substance have similar formulæ. Isatin is thus a pseudo-acid, since the hydrogen compound itself is the ketonic substance, $C_6H_4<^{NH}_{CO}>CO$; but its sodic derivative is the enolic compound, $C_6H_4<^{N}_{CO}>C\cdot ONa$.

INDIGO AND RELATED COMPOUNDS

Indole or benzo-pyrrole	$C_6H_4<^{CH}_{NH}>CH$.
Indoxyl or hydroxy-indole	$C_6H_4<^{C(OH)}_{NH}>CH$.
Oxindole or *o*-amino-phenyl-acetic acid lactam	$C_6H_4<^{CH_2}_{NH}>CO$.
Dioxindole or *o*-amino-mandelic acid lactam	$C_6H_4<^{CH(OH)}_{NH}>CO$.
Isatin or *o*-amino-phenyl-glyoxylic acid lactam	$C_6H_4<^{CO}_{NH}>CO$.
Indigo	$C_6H_4<^{CO}_{NH}>C:C<^{CO}_{NH}>C_6H_4$.

Indigo, which is obtained from the indigo plant (*Indigofera tinctoria*), and from woad (*Isatis tinctoria*), has been known for thousands of years as a valuable blue dye, especially for woollen fabrics. In addition to indigo-blue (indigotin),

commercial indigo contains indigo-gelatine, indigo-brown, and indigo-red, all of which can be extracted from it by solvents. The colouring matter is not present as such in the indigo plant, but as the glucoside of indoxyl "**Indican**", from which it can be prepared either by dilute acids or certain enzymes and subsequent oxidation with atmospheric oxygen.

It forms a dark-blue coppery and shimmering powder or, after sublimation, copper-red prisms, insoluble in most solvents (including the alkalis and dilute acids), but dissolving to a blue solution in hot aniline and to a red one in paraffin, from either of which it may be crystallized. Its vapour is dark-red. The formula $C_{16}H_{10}O_2N_2$ is confirmed by its vapour density. It is converted by reducing agents, such as ferrous sulphate and caustic soda solution or grape-sugar and soda, into the leuco-compound, **indigo-white**, $C_{16}H_{12}O_2N_2$, a white crystalline powder soluble in alcohol and ether, also in alkalis (as a phenol); the alkaline solution quickly becomes oxidized by the oxygen of the air, with the separation of a blue film of indigo. It yields an acetyl compound which crystallizes in colourless needles.

Warm concentrated or fuming sulphuric acid dissolves indigo to **indigo-monosulphonic** and **disulphonic acids**, the former of which (termed phœnicin-sulphonic acid) is sparingly soluble in water, but the latter readily so; the sodium disulphonate is the **indigo-carmine** of commerce. Nitric acid oxidizes indigo to isatin, while distillation with potash yields aniline, and heating with manganese dioxide and a solution of potash, anthranilic acid.

Indigo has been prepared synthetically by numerous methods. The following are among the most important:—

1. By the reduction of isatin chloride with zinc dust and acetic acid:

$$2C_6H_4\langle\begin{matrix}CO\\N\end{matrix}\rangle CCl + 4H = C_6H_4\langle\begin{matrix}CO\\NH\end{matrix}\rangle C{:}C\langle\begin{matrix}CO\\NH\end{matrix}\rangle C_6H_4 + 2HCl.$$

The syntheses of isatin already described (pp. 523 and 554) are thus syntheses of indigo.

2. By warming *o*-nitro-phenyl-propiolic acid with grape-sugar in alkaline solution (*Baeyer*, 1880):

$$2NO_2\cdot C_6H_4C{:}C\cdot CO_2H + 4H = C_{16}H_{10}N_2O_2 + 2CO_2 + 2H_2O.$$

3. *Baeyer* and *Drewson* (1882) started with toluene, and on nitration obtained a mixture of *o*- and *p*-nitro-toluenes. The

o-compound was oxidized by manganese dioxide and sulphuric acid to *o*-nitro-benzaldehyde, and this was then condensed with acetone, yielding *o*-nitro-phenyl-lactyl methyl ketone,

$$NO_2 \cdot C_6H_4 \cdot CH(OH) \cdot CH_2 \cdot CO \cdot CH_3;$$

which when warmed with alkalis gave indigo and water. The yield was good, but the method was of no great practical importance, as the amount of toluene is limited, and no use could be found for the *p*-nitro-toluene obtained as a by-product.

4. In 1890 *Heumann* obtained **phenyl-glycocoll** by the condensation of aniline with chloracetic acid·

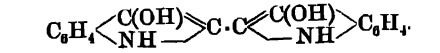
$$C_6H_5 \cdot NH\ H + Cl \cdot CH_2 \cdot CO_2H \longrightarrow C_6H_5 \cdot NH \cdot CH_2 \cdot CO_2H,$$

and when this was fused with alkali, indigo-white was obtained.

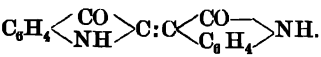
A modified form of *Heumann's* synthesis consists in condensing anthranilic acid (p. 452) with chloracetic acid, when phenyl-glycocoll-*o*-carboxylic acid is obtained, and this on fusion with alkali yields indoxyl, which oxidizes in the air to indigo-blue. The yield is good, and this method is now employed on a manufacturing scale by the "Badische Anilin Fabrik" for the production of artificial indigo, as anthranilic acid can be obtained cheaply; the general method is by oxidation of naphthalene by mercury and sulphuric acid to phthalic acid, the conversion of this into phthalic anhydride, and then into phthalimide by the aid of ammonia. The phthalimide with alkali and chlorine yields anthranilic acid—*o*-amino-benzoic acid (*Hofmann* reaction, p. 184).

Homologues of indigo are produced in an analogous manner and its sulpho-acids by the action of fuming sulphuric acid upon phenyl-glycocoll.

Indigo-blue is one of the best of the blue dyes, on account of its "fastness" to light, alkalis, acids, and soaps. As indigo blue itself is insoluble, its "leuco" compound indigo-white is usually employed, the fabric being immersed in an alkaline solution of this, and then exposed to the air, when oxidation to indigo-blue takes place. Indigo-blue is usually reduced to indigo-white by means of calcium hyposulphite. The indigo white is a colourless solid with phenolic properties, and probably has the constitution represented by the formula—



Indirubin, *Indigo-purpurin*, is an isomeride of indigo-blue, and can be obtained synthetically by the condensation of isatin and indoxyl in alkaline alcoholic solution:



It is also obtained, together with indigo-blue, by the reduction of isatin chloride. It crystallizes from aniline in chocolate-brown needles, and on oxidation yields isatin.

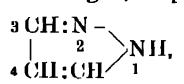
(For history and manufacture of indigo, see *J. Ind.* 1901, 239, 332, 551, 802; J. C. S. 1905, 974.)

XXXVI. PYRAZOLE GROUP, ETC.

1. PYRAZOLE GROUP

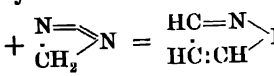
This comprises compounds with a five-membered ring containing three carbon and two nitrogen, sulphur, or oxygen atoms.

Pyrazole,



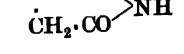
...retically derivable from pyrrole in the same way as ...idine is from benzene, *i.e.* by the exchange of CH for N. The positions three and five appear to be identical unless the H of the NH is replaced by alkyl groups.

It is a weak base of great stability, crystallizing in colourless needles; it melts at 70°, boils at 185°, and possesses aromatic properties (B. 1895, **28**, 714) Its simplest synthesis is by the union of acetylene and diazo-methane:



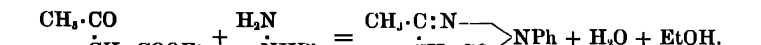
(*Von Pechmann*, B. 1897, **31**, 2950). (For other syntheses, see B. **23**, 1103; A. **273**, 214.)

Pyrazoline, $C_3H_6N_2$, and **pyrazolidine**, $C_3H_8N_2$, are derived theoretically from pyrazole by the addition of hydrogen. By the exchange of two atoms of hydrogen for one of oxygen, the formula of pyrazole changes into that of **pyrazolone**,



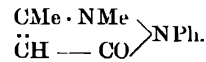
(an oil, b.-pt. 77°; see B, **25**, 3441), and by the entrance of phenyl and methyl into this latter we get:

1-Phenyl-3-methyl-pyrazolone, which is obtained by the action of phenylhydrazine on ethyl acetoacetate (p. 230):



This crystallizes in compact prisms, melts at 127°, and boils without decomposition. As a weak base it dissolves in acids, and is also soluble in alkalis; it further contains the chemically-active methylene group. When it is heated with methyl iodide and methyl alcohol it yields:

1-Phenyl-2·3-dimethyl-pyrazolone or **antipyrine,** $C_{11}H_{12}N_2O$, which is also produced by the action of ethyl acetoacetate upon methyl-phenyl-hydrazine, and which therefore possesses the constitutional formula (*L. Knorr*, A. **238**, 137),

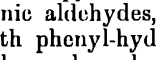


It crystallizes in small colourless plates melting at 113°. The aqueous solution is coloured red by ferric chloride and blue-green by nitrous acid. Antipyrine is an excellent febrifuge. β-Ketonic acids, β-ketonic aldehydes, β-diketones also yield pyrazole derivatives with phenyl-hydrazine.

Isomeric with pyrazole is glyoxaline (p 530), in which the two atoms of N are separated by a C atom.

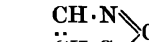
2. THIAZOLE GROUP

Thiazole,

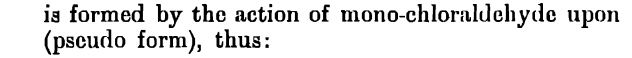


is derived from thiophene in the same way as pyridine is from benzene, by the exchange of CH for N, and closely resembles —along with its derivatives—the bases of the pyridine series in properties. It is obtained from amino-thiazole (see below) by the exchange of the amino-group for hydrogen, in a similar manner to the conversion of aniline into benzene. It is a colourless liquid, boiling at 117°, hardly distinguishable from pyridine; as a base it forms salts, but it is scarcely affected by concentrated sulphuric acid, &c. (*Hantzsch, Popp*, A. **250**, 273).

Amino-thiazole,

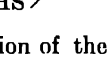


is formed by the action of mono-chloraldehyde upon thio-urea (pseudo form), thus:

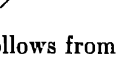


The constitution of the thiazoles follows from this and similar modes of formation Amino-thiazole is a base of perfect "aromatic" character, like that of aniline. (Cf. *Hantzsch* and his pupils, A. **249**, 1, 7, 31; **250**, 257; **265**, 108)

As further types of five-membered rings, may be cited:

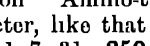
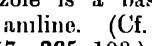


Imidazole or glyoxalin



Oxazole,

which are related to thiazole as pyrrole and furane are to thiophene.

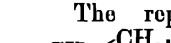
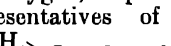
Triazole,  and **tetrazole,** 

are examples of five-membered rings extremely rich in nitrogen. (Cf. B. **25**, 225, 1411; **26**, 2392.)

The foregoing constitutional formulæ with their double linkings correspond with *Kekulé's* benzene formula But formulæ with diagonal (centric) linkings analogous to the centric benzene formula (p. 334) have been introduced recently. (Cf. *Bamberger*, B. **24**, 1758; A. **273**, 373; also A. **249**, 1; **262**, 265; B. **21**, Ref. 888, **24**, 3485; **27**, 3077; **28**, 1501.)

XXXVII. SIX-MEMBERED HETEROCYCLIC RINGS

Ring compounds closely related to pyrrole, thiophene, and furane, but containing six atoms in the ring (viz five carbon atoms + one oxygen, sulphur, or nitrogen atom), are known.

The representatives of these are: **δ - valerolactone,**  **glutaric anhydride,** 

(p. 240), and more especially the **pyrones**, *e.g.* γ-pyrone, $CO<^{CH:CH}_{CH:CH}>O$.

Of the nitrogen compounds, **pyridine**, $CH<^{CH\cdot CH}_{CH:CH}>N$, and **piperidine**, $CH_2<^{CH_2\cdot CH_2}_{CH_2\cdot CH_2}>NH$, are of great importance. The derivatives of the sulphur compound, **penthiophene**, $CH_2<^{CH:CH}_{CH:CH}>S$, are of but little importance.

Six-membered rings containing two nitrogen atoms are the diazines, $C_4H_4N_2$, the ortho compound is *pyridazine*, the meta *pyrimidine*, and the para *pyrazine*. The compound, $NH<^{CH_2\cdot CH_2}_{CH_2\cdot CH_2}>O$, is *morpholin*. Six-membered rings containing three and four nitrogen atoms are termed respectively triazines and tetrazines (Cf triazole and tetrazole, p 530)

A Pyrones

γ-Pyrone, a solid, m.-pt 32·5° and b.-pt 315°, is obtained when its dicarboxylic acid, chelidonic acid (p. 533), is heated **αα-dimethyl-γ-pyrone**, $CO<^{CH:CMe}_{CH:CMe}>O$, may be synthesised from cupric ethyl aceto-acetate and carbonyl chloride.

$$CO<^{Cl}_{Cl} + Cu<^{CH(CO_2Et)\cdot CO\cdot CH_3}_{CH(CO_2Et)\cdot CO\cdot CH_3} = CuCl_2 + CO<^{CH(CO_2Et)\cdot CO\cdot CH_3}_{CH(CO_2Et)\cdot CO\cdot CH_3}$$

On hydrolysis with sulphuric acid the ester yields the free acid, which loses carbon dioxide, yielding.

$$CO<^{CH_2\cdot CO\cdot CH_3}_{CH_2\cdot CO\cdot CH_3} \text{ or } CO<^{CH:C(OH)CH_3}_{CH:C(OH)\cdot CH_3}$$

which immediately loses water, yielding dimethyl-γ-pyrone:

$$CO<^{CH:C(CH_3)}_{CH:C(CH_3)}>O.$$

(For a modified formula, see *Collie*, J. C. S. 1904, 971.) *Collie* and *Tickle* (J. C. S. 1899, 710) have shown that this compound can form definite salts with acids, *e.g.* the hydrochloride, $C_7H_8O_2$, HCl, and oxalate. The addition of the acid undoubtedly occurs at the oxygen atom, since the salts are relatively unstable and are completely hydrolysed in dilute aqueous solution. The oxygen atom in these salts, therefore,

probably functionates as a tetravalent atom, $\begin{matrix}\cdot C\\ \cdot C\end{matrix}\!\!>\!O\!<\!\!\begin{matrix}H\\ Cl\end{matrix}$, and the salts are termed **oxonium salts** on account of their similarity to ammonium salts. Numerous other compounds have since been obtained, which tend to show that the oxygen atom can frequently functionate in this manner, *e.g.* numerous oxygen compounds, esters, ethers, ketones, acids, aldehydes yield definite crystalline compounds with anhydrous metallic salts, *e.g.* $MgBr_2$ or $AlCl_3$ (*Walker*, J. C. S. 1904, 1106, similar oxygen compounds also form well-defined crystalline salts with complex acids, *e.g.* ferrocyanic acid (*Baeyer* and *Villiger*, B. 1901, **34**, 2679, 3612; 1902, **35**, 1201); and lastly, the additive compound of organo-magnesium derivatives with ether are probably of the type, $\begin{matrix}C_2H_5\\ C_2H_5\end{matrix}\!\!>\!O\!<\!\!\begin{matrix}MgCH_3\\ I\end{matrix}$. Solutions of the oxonium salts have exactly the properties we should expect. Since the salt is derived from a very feeble base (solutions of dimethyl-pyrone are very feeble conductors) and a relatively strong acid, the solution should be highly hydrolysed, and should give a strongly acid reaction. That the hydrolysis is not complete in the case of a moderately concentrated solution of the picrate has been shown by *Walden* (B. 1901, **34**, 4191), who compared the partition coefficient of picric acid between water and benzene both with and without the addition of dimethyl-pyrone, and found that the ratio $\frac{\text{concentration of benzene solution}}{\text{concentration of aqueous solution}}$ is less when the pyrone is present.

Other methods which have also led to the conclusion that a certain amount of salt exists in solution are (*a*) depression of the freezing-point of aqueous solutions. If no compound exists in an aqueous hydrochloric acid solution, then the depression caused would be the sum of the depressions produced by the known amounts of dimethyl-pyrone and hydrochloric acid present. The actual value obtained is less than this sum (*Walden*). (*b*) A determination of the electrical conductivity. If no compound is formed, the conductivity should be the same as the conductivity of a solution of pure hydrochloric acid of the same concentration; but if any appreciable amount of a salt is formed in solution this will give rise to a certain number of $\overset{+}{C_7H_8O_2H}$ and $\bar{Cl}$, *i.e.* the number of hydrions will be less than in a solution of pure hydrochloric acid of the same

concentration, and hence the electrical conductivity will be considerably reduced. It has actually been found that the conductivity is less, and that it tends to decrease as the solution becomes more concentrated.

γ-Pyrone-dicarboxylic acid, or chelidonic acid, occurs in the greater celandine (*Chelidonium majus*), and may be synthesised by *Claisen's* method (p. 224). Acetone and ethyl oxalate readily condense, yielding the ester of acetone-dioxalic acid or xantho-chelidonic acid:

$$CO\langle{}^{CH_3}_{CH_3} + {}^{CO_2Et\cdot CO_2Et}_{CO_2Et\cdot CO_2Et} = CO\langle{}^{CH:C(CO_2Et)OH}_{CH:C(CO_2Et)OH} + 2\,EtOH,$$

which immediately loses water, yielding ethyl chelidonate, and this on careful hydrolysis yields chelidonic acid:

$$CO\langle{}^{CH:C(CO_2H)}_{CH:C(CO_2H)}\rangle O.$$

The salts of this acid are colourless, but when it is warmed with an excess of alkali yellow salts of xantho-chelidonic acid are formed, thus indicating the readiness with which the ring is ruptured.

B. Pyridine

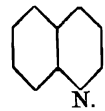
Pyridine, C_5H_5N, may be compared with benzene in many points:

1. It is even more stable than benzene, and does not yield substituted derivatives so readily with such reagents as sulphuric and nitric acids or the halogens. Sulphonic acids are obtained at very high temperatures only; nitro-pyridines are as yet unknown, as are also iodo-pyridines; while chloro- and bromo-pyridines have so far only been prepared in small number. Neither pyridine nor its carboxylic acids are affected by nitric acid, chromic acid, or permanganate of potash.

2. The behaviour of its derivatives is on the whole very like that of the derivatives of benzene. Thus its homologues (and also quinoline, &c.) are transformed into pyridine-carboxylic acids when oxidized, and these acids yield pyridine when distilled with lime, just as benzoic acid yields benzene.

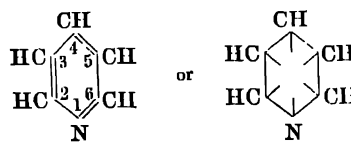
3. The isomeric relations are also precisely analogous to those of the benzene derivatives. Thus the number of the isomeric mono-derivatives of pyridine is the same as that of the isomeric bi-derivatives of benzene, viz., three; and the number of the bi-derivatives of pyridine, containing the same substituents, the same as that of the benzene derivatives C_6H_3XXX', viz., six.

4. Just as two benzene nuclei can form naphthalene, so can a benzene and a pyridine form the compound quinoline:



5. The products of reduction are likewise analogous. Pyridine like benzene yields a hexahydro-derivative, $C_5H_{11}N$, only somewhat more readily; this is known as piperidine. Quinoline yields a tetrahydro-derivative, $C_9H_{11}N$, more readily than naphthalene, and acridine readily yields a dihydro-derivative, $C_{13}H_{11}N$, which is analogous to anthracene dihydride In these latter compounds further combination with hydrogen may take place, but there is likewise a tendency to the reproduction of the original bases.

We are therefore forced to the conclusion that pyridine has a ring constitution similar to that of benzene, and is to be represented as.



In contradistinction to the neutral benzene hydrocarbons, pyridine and its homologues are strong bases, most of them having a pungent odour; pyridine is readily soluble in water, but quinoline only slightly so. They distil or sublime without decomposition, and form salts, those with hydrochloric and sulphuric acids are for the most part readily soluble, while those with chromic acid or hydro-ferrocyanic acid, though often characteristic, are usually only sparingly soluble; they also form double salts with the chlorides of platinum, gold, and mercury, most of which are sparingly soluble, *e.g.* $(C_5H_5N)_2H_2PtCl_6$.

The bases are tertiary, and hence cannot be acetylated; they combine, however, with alkyl iodides, yielding quaternary ammonium salts, *e.g.* pyridine and methyl iodide yield C_5H_5N, CH_3I, **methyl-pyridonium iodide.**

Pyridine and some of its homologues are present in coal-tar, and are therefore constituents of the lower boiling fractions. They may be extracted from these by shaking with dilute

sulphuric acid, in which they dissolve It is also present in tobacco smoke. A number of pyridine bases are present in bone-oil or Dippel's oil, a product obtained by the dry distillation of bones from which the fat has not been extracted

Mixtures of pyridine bases can readily be obtained from this source. Certain alkaloids (p. 557) yield pyridine or its derivatives when distilled alone or with alkalis, *e.g.* chinchonine when distilled with potash yields a dimethyl-pyridine or lutidine. Pure pyridine may be obtained by distilling its carboxylic acid with lime

Among the more interesting methods by means of which pyridine and its derivatives have been synthesised are the following.—

1. When pentamethylene-diamine hydrochloride is strongly heated it yields piperidine, and when this is oxidized with concentrated sulphuric acid at 300° pyridine is formed (*Ladenburg*):

$$CH_2\langle\begin{matrix}CH_2\cdot CH_2\cdot NH\ H\cdot HCl\\ CH_2\cdot CH_2\cdot\ NH_2\end{matrix} \longrightarrow CH_2\langle\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot CH_2\end{matrix}\rangle NH$$

$$\longrightarrow CH\langle\begin{matrix}CH:CH\\ CH\cdot CH\end{matrix}\rangle N.$$

A method very similar to this, which can be employed at much lower temperatures, is the elimination of hydrogen chloride from 5-chloroamylamine, $CH_2Cl\cdot(CH_2)_3\cdot CH_2\cdot NH_2$. This elimination occurs when an aqueous solution of the base is heated on the water-bath; ring formation takes place, and piperidine hydrochloride is formed (*Gabriel*). These two methods are of great importance in deciding the constitution of piperidine, and therefore indirectly that of pyridine.

2. The ammonia derivatives of various unsaturated aldehydes yield pyridine homologues when distilled (p 130), *e.g.* β-methyl-pyridine is obtained from acrolein ammonia, and collidine from croton-aldehyde ammonia (*Baeyer*, A. **155**, 283, 297).

3. When ethyl acetoacetate is warmed with aldehyde-ammonia, the ester of "Dihydro-collidine-dicarboxylic acid", *i.e.* ethyl trimethyl-dihydro-pyridine-dicarboxylate is produced (*Hantzsch*) (cf. p. 230):

$$\begin{matrix}CO_2Et\cdot CH_2\\ MeCO\end{matrix} + \begin{matrix}O\cdot CHMe\\ NH_3\end{matrix} + \begin{matrix}CH_2\cdot CO_2Et\\ COMe\end{matrix}$$

$$= 3H_2O + \begin{matrix}CO_2Et\cdot C-CHMe-C\cdot CO_2Et\\ \quad\quad\quad\

This loses its two "hydro"-hydrogen atoms when acted on by nitrous acid, and yields ethyl collidine-dicarboxylate, $C_5N(CH_3)_3(CO_2Et)_2$, from which collidine may be obtained by hydrolysis and elimination of carbon dioxide.

If, instead of aldehyde-ammonia, the ammonia compounds of other aldehydes are used, homologous bases of the type $C_5H_2N(CH_3)_2(C_nH_{2n+1})$ are formed.

In the above reaction a molecule of the acetoacetic ester may be replaced by one of an aldehyde, when the mono-carboxylic esters of dialkylated pyridines are formed, thus.

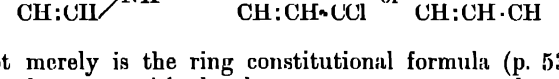
$$C_6H_{10}O_3 + 2CH_3\cdot CHO + NH_3 = C_5H_2NH_2(CH_3)_2\cdot CO_2Et + 3H_2O.$$

This is a very important synthetical method (*Hantzsch*, A. **215**, 1, &c.).

Two methods of obtaining pyridine derivatives, which indicate the relationship of pyridine to quinoline and pyrrole, are:

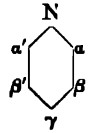
(*a*) The conversion of quinoline into quinolinic acid or pyridine $a\beta$-dicarboxylic acid (p. 544).

(*b*) The conversion of potassium-pyrrole into chloro-pyridine when heated with chloroform, or into pyridine when heated with methylene-chloride:



Not merely is the ring constitutional formula (p. 534) in perfect harmony with the characteristic properties of pyridine and its derivatives, and also with certain of the synthetical methods of formation, but this formula receives additional support from a study of the number of isomeric forms in which pyridine derivatives occur.

Three isomeric mono-substituted derivatives of pyridine are known in each case. They are designated as a-, β-, and γ-derivatives of pyridine, as is shown in the following graphic formula:



or as 2-, 3-, or 4-derivatives according to the numbering on p. 534.

In order to determine the position of any given group, it is sought to exchange it for carboxyl; should picolinic acid result, the group occupies the α-position, and should nicotinic or *iso*-nicotinic, then it fills the β- or γ-position respectively, since in these acids the α-, β-, and γ-positions of the carboxyl have been determined by special means. (See M. **1**, 800; **4**, 436, 453, 595; B. **17**, 1518; **18**, 2967; **19**, 2432.)

Di-derivatives of pyridine containing the same substituent twice can exist theoretically in six isomeric forms. As a matter of fact the six dicarboxylic acids are known (αα'-, αβ-, αγ-, αβ'-, βγ-, and ββ'- (see p. 538).

The isomerism of picoline, C_6H_7N, with aniline, $C_6H_5 \cdot NH_2$, which repeats itself in their homologues, is also worthy of notice.

Pyridine, C_5H_5N (*Anderson*, 1851), may be prepared from bone-oil, and can be obtained pure by heating its carboxylic acid with lime; the ferrocyanide is especially applicable for its purification, on account of its sparing solubility in cold water. It is also found in the ammonia of commerce. Pyridine is a liquid of very characteristic odour, miscible with water, and boiling at 115°. It is used as a remedy for asthma, and also in Germany for mixing with spirit of wine in order to render the latter duty-free. When sodium is added to its hot alcoholic solution, or when solutions of its salts are electrolysed, hydrogen is taken up and piperidine, $C_5H_{11}N$, formed (*Ladenburg* and *Roth*, B. **17**, 513).

When heated strongly with hydriodic acid, pyridine is converted into normal pentane.

The ammonium iodides, *e.g.* C_5H_5N, CH_3I, give a characteristic pungent odour when heated with potash, a fact which may be made use of as a test for pyridine bases; it depends upon the formation of alkylated dihydro-pyridines, *e.g.* **dihydro-methyl-pyridine**, $C_5H_6 \cdot N(CH_3)$ (*Hofmann*, B. **14**, 1497).

Pyridine is polymerized by the action of metallic sodium to **dipyridine**, $C_{10}H_{10}N_2$ (an oil, b.-pt. 286°–290°), with the simultaneous production of *p*-**dipyridyl**, $C_5H_4N \cdot C_5H_4N$ (long needles, m.-pt. 114°), a compound corresponding to diphenyl (p. 471); both of these yield iso-nicotinic acid when oxidized. An isomeric *m*-**dipyridyl** has also been prepared, which gives nicotinic acid when oxidized.

Pyridine can be brominated but not nitrated; it can also be sulphonated with the formation of β-pyridine-sulphonic acid, $C_5H_4N \cdot (SO_3H)$, which with potassium cyanide yields **β-cyano-**

pyridine, $C_5H_4N \cdot CN$, or by fusion with potash, β-hydroxy-pyridine.

The three **hydroxy-pyridines**, $C_5H_4N(OH)$ (α-, β-, γ-), are best prepared by the elimination of carbon dioxide from the respective hydroxy-pyridine-carboxylic acids. The melting-points are respectively: α, 107°; β, 124°, γ, 148°. They possess the character of phenols, and are coloured red or yellow by ferric chloride. As in the case of phloroglucinol, so here also there is a tertiary as well as a secondary form to be taken into account, the former reminding one of the lactams and the latter of the lactims; for instance, γ-hydroxy-pyridine may either have the "phenol" formula $C_2H_2\langle^{C(OH)}_{N=}\rangle C_2H_2$ or the "pyridone" formula $C_2H_2\langle^{CO}_{NH}\rangle C_2H_2$, the latter of the two representing a keto-dihydro-pyridine. The two methyl ethers, methoxy-pyridine and methyl-pyridone, which result from these two forms by the exchange of H (of the OH or NH respectively) for CH_3, are both known, and differ considerably in properties (M. **6**, 307, 320; B. **24**, 3144).

Homologues of Pyridine (cf. *Ladenburg*, A. **247**, 1) — **Methyl-pyridines** or **picolines**, $C_5H_4N(CH_3)$. All the three picolines are contained in bone-oil, and probably also in coal-tar. The β-compound is obtained from acrolein-ammonia (p. 130), and also when strychnine is heated with lime, or when trimethylene-diamine hydrochloride is distilled. They are liquids of unpleasant, piercing odour resembling that of pyridine, and they yield α-, β-, or γ-pyridine-carboxylic acid when oxidized. The boiling-points are: α, 129°; β, 142°; γ, 142°–144°.

Ethyl-pyridines, $C_5H_4N(C_2H_5)$, are also known.

Propyl- and **isopropyl pyridines**, $C_5H_4N(C_3H_7)$, have been carefully investigated on account of their relation to coniine. They are prepared by heating pyridine with the alkyl iodides. **Conyrine**, $C_8H_{11}N$ (liquid, b.-pt. 166°–168°), which is formed when coniine, $C_8H_{17}N$, is heated with zinc dust, and which yields coniine again when treated with hydriodic acid, is α-normal-propyl-pyridine.

α-Allyl-pyridine, $C_5H_4N(C_3H_5)$, is produced when α-picoline is heated with aldehyde:

$$C_5H_4N \cdot CH_3 + OHC \cdot CH_3 = C_5H_4N \cdot CH{:}CH \cdot CH_3 + H_2O.$$

Reduction transforms it into inactive coniine (b.-pt. 189°–190°).

Dimethyl-pyridines or Lutidines, $C_5H_3N(CH_3)_2$.—The presence of three lutidines has been proved in bone-oil and coal-tar (B. **21**, 1006; **29**, 2996). $\alpha\gamma$-Lutidine boils at 157°, the $\alpha\alpha'$-compound at 142°, and the $\beta\gamma$-compound at 164°.

The **trimethyl-pyridines** or **collidines**, $C_5H_2N(CH_3)_3$, are isomeric with the propyl-pyridines. Some of them are present in bone-oil, and can be prepared from cinchonine by distilling the latter with caustic potash (p. 560). The $\alpha\alpha'\gamma$-collidine, which is obtained from the condensation product of ethyl acetoacetate and aldehyde ammonia (p. 230), boils at 171°–172°.

Pyridine-carboxylic Acids (*Weber*, A. 1887, **241**, 1).—The **pyridine-mono-carboxylic acids**, $C_5H_4N(CO_2H)$, are formed by the oxidation of all mono-alkyl derivatives of pyridine, *i.e.* from methyl-, propyl-, phenyl-, &c., pyridines; also from the pyridine-dicarboxylic acids by the decomposition of one of the carboxyl groups, just as benzoic may be got from phthalic acid The carboxyl which is in closest proximity to the nitrogen is the first to be eliminated. Nicotinic acid is also produced by the oxidation of nicotine. The acids unite in themselves the characters of the basic pyridine and of an acid, and are therefore comparable with glycocoll. They yield salts with HCl, &c., and double salts with $HgCl_2$, $PtCl_4$, &c.; on the other hand, they form metallic salts as acids, those with copper being frequently made use of for the separation of the acids.

(For *constitution*, see *Skraup* and *Cobenzl*, M. 1883, **4**, 436.)

The α-acid is **picolinic acid**, and forms needles melting at 135°.

The β-acid is **nicotinic acid**, and melts at 231°.

The γ-acid is **iso-nicotinic acid**, and melts at 309° in a sealed tube.

It is noteworthy that all three acids (and also the $\beta\gamma$-dicarboxylic acid) readily yield up their nitrogen as ammonia when acted upon by sodium amalgam, being thereby transformed into unsaturated acids of the fatty series (*Weidel*, M. 1890, **11**, 501).

The constitution of nicotinic acid follows from its relationship to quinoline. Quinoline on oxidation yields pyridine $\alpha\beta$-dicarboxylic acid, the constitution of which follows from the constitution of quinoline. When heated, the dibasic acid loses carbon dioxide, yielding a monobasic acid which is not identical with picolinic acid (which can be shown to be the α-acid), and therefore it must be pyridine β-carboxylic acid.

Pyridine-dicarboxylic acids, $C_5H_3N(CO_2H)_2$

α-β-	= **Quinolinic acid**	M.-pt. 190°.
α-γ-	= **Lutidinic acid**	M.-pt. 235°.
α-α'-	= *Dipicolinic acid.*	M.-pt. 226°.
α-β'-	= *Iso-cinchomeronic acid.*	M.-pt. 236°.
β-β'-	= *Dinicotinic acid.*	M.-pt. 323°.
β-γ-	= *Cinchomeronic acid.*	M.-pt. 266°.

Quinolinic acid, which crystallizes in short glistening prisms, is the analogue of phthalic acid, and is obtained by the oxidation of quinoline, just as phthalic acid from naphthalene; cinchomeronic and iso-cinchomeronic acids are obtained by the oxidation of cinchonine and quinine.

Hydro-pyridines.—According to theory, hexa-, tetra-, and dihydro-pyridines may exist. The first of these receive the generic name of "piperidines", *e.g.* pipecoline, $C_5H_{10}N(CH_3)$, lupetidine, $C_5H_9N(CH_3)_2$, and copellidine, $C_5H_8N(CH_3)_3$; while the tetrahydro-compounds are termed "piperideins".

Piperidine, $C_5H_{11}N$ (*Wertheim*, *Rochleder*, 1850), is a colourless liquid of peculiar odour, slightly resembling that of pepper, and of strongly basic properties yielding crystalline salts. It dissolves readily in water and alcohol, and boils at 106°.

It occurs in pepper in combination with piperic acid, $C_{12}H_{10}O_4$ (p. 464), in the form of the alkaloid **piperine**, $C_{18}H_{18}NO_3 = C_5H_{10}N \cdot C_{12}H_9O_3$, *i.e.* piperyl-piperidine, which crystallizes in prisms, melting at 129°; from this latter it may be prepared by boiling with alkali.

(For its formation from pyridine and from pentamethylene-diamine, see pp. 196, 535, 537.)

Piperidine is a secondary amine; its imino-hydrogen is replaceable by alkyl and acyl radicals. When its vapour, mixed with that of alcohol, is led over zinc dust, homologous (ethylated) piperidines are formed.

When methylated, piperidine yields, as a secondary base, in the first instance, tertiary *n*-**methyl-piperidine**, $C_5H_{10}N(CH_3)$, and then with a further quantity of methyl iodide an ammonium iodide, **dimethylpiperidonium iodide**. The corresponding hydroxide does not decompose in the usual manner when distilled, but yields water and an aliphatic base, "dimethyl-piperidine", $C_7H_{15}N$ or $CH_2:CH \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot NMe_2$.

The latter forms a quaternary iodide, the hydroxide of which, when distilled, gives trimethylamine and piperylene, $CHMe:CH \cdot CN:CH_2$ (exhaustive methylation. For further examples, see Chap. on Alkaloids).

XXXVIII. QUINOLINE AND ACRIDINE GROUPS

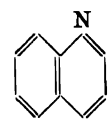
A. Quinoline Group

The quinoline group comprises the compounds formed by the condensation of a benzene nucleus with a heterocyclic six-membered ring. The best-known examples are:

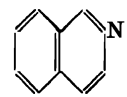
Chromone (benzene + pyrone rings),



Quinoline (benzene + pyridine),



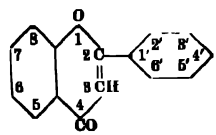
Iso-quinoline (benzene + pyridine),



1. CHROMONE GROUP

Chromone.—Chromone itself melts at 59° (*Ruhemann* and *Stapleton*, J. C. S. 1900, 1185), and the phenyl derivative, **flavone**, $C_6H_4\langle^{O—C\cdot C_6H_5}_{CO\cdot CH}$, is the parent substance of a number of yellow dyes which occur in the vegetable kingdom. Most of these dyes are hydroxylic derivatives of flavone, and occur in nature in the form of glucosides.

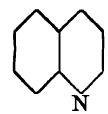
As examples we have **Chrysin** (dihydroxy-flavone), **Luteolin** (5:7:3′:4′-tetrahydroxy-flavone, *Kostanecki*, Abstr. 1901, **1**, 92, 335), **Quercitin** (3:5:7:3′:4′-pentahydroxy-flavone, *Herzig*, M. 1885, **6**, 872), **Rhamnetin** (3:5.3′:4′-tetrahydroxy-7-methoxy-flavone), and **Rhamnazin** (3:5:4′-trihydroxy-7:3′-dimethoxy-flavone, *Perkin* and *Allison*, J. C. S. 1902, 469).



The constitution of these compounds is often arrived at by an examination of the products formed by the action of alcoholic potash on the compound, or, more readily, by aspirating air through the dilute alkaline solution; under these conditions rhamnetin yields protocatechuic acid, 3:4-dihydroxybenzoic acid (p. 459), and phloroglucinol monomethyl ether.

2. QUINOLINE AND ITS DERIVATIVES

Quinoline,



bears the same relationship to naphthalene that pyridine does to benzene, its molecule consisting of condensed benzene and pyridine nuclei. It occurs, together with derivatives, in both coal-tar and bone-oil, and may be obtained by heating certain alkaloids with potash, *e.g.* cinchonine yields quinoline itself (*Gerhardt*, 1842), and quinine gives methoxy-quinoline.

Among the various syntheses of quinoline and its derivatives the following may be noted.—

1. The first synthesis, which was accomplished by *Koenigs*, was by the oxidation of allyl-aniline by passing its vapour over heated lead oxide:

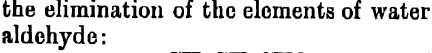
$$C_6H_5\cdot NH\cdot CH_2\cdot CH{:}CH_2 + 2O = C_6H_4\begin{cases} CH{:}CH \\ N{=}\dot{C}H \end{cases} + 2H_2O$$

2. One of the usual methods employed for the preparation of pure quinoline is by *Skraup's* synthesis (B **14**, 1002). In this process aniline is heated with glycerol and sulphuric acid in presence of nitro-benzene or arsenic acid:

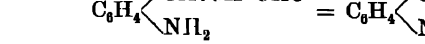
$$C_6H_4\begin{cases} H \\ NH_2 \end{cases} + \begin{matrix} OH\cdot CH_2\cdot CH\cdot OH \\ \dot{C}H_2\cdot OH \end{matrix} + O = C_6H_4\begin{cases} CH{:}CH \\ N{=}\dot{C}H \end{cases} + 4H_2O$$

The nitro-benzene simply acts as an oxidizing agent. The formation of acrolein as an intermediate product is to be assumed here, the latter combining in the first instance with aniline to acrolein-aniline, $C_6H_5\cdot N{:}CH\cdot CH{:}CH_2$. The homologues and analogues of aniline yield homologues and analogues of quinoline by corresponding reactions, when naphthylamine is used, the more complicated naphtho-quinolines are formed.

3. *Baeyer* and *Drewson* (B. **16**, 2207) obtained quinoline by the elimination of the elements of water from *o*-amino-cinnamic aldehyde:

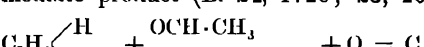


If *o*-amino-cinnamic acid is used, carbostyril (*α*-hydroxy-quinoline, p. 546) is obtained (*Baeyer*):



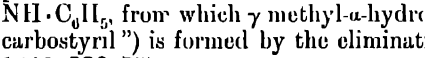
4. When aniline is heated with aldehyde (paraldehyde) and hydrochloric acid, *α*-methyl-quinoline (quinaldine) is obtained (*Doebner* and *v. Miller*).

In this reaction ethylidene-aniline is formed as an intermediate product (B. **24**, 1720, **25**, 2072):

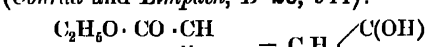


Here, again, various other primary arylamines may be used instead of aniline, and other aldehydes (B. **18**, 3361) or ketones (*e. g.* B. **19**, 1394) instead of paraldehyde.

5. Aniline and acetoacetic acid combine together at temperatures above 110° to aceto-acetanilide, $CH_3 \cdot CO \cdot CH_2 \cdot CO \cdot NH \cdot C_6H_5$, from which γ methyl-α-hydroxy-quinoline ("methyl-carbostyril") is formed by the elimination of water (*Knorr*, A. 1886, **236**, 75):



Aniline can also react with acetoacetic ester below 100°, yielding **ethyl β-phenyl-amino-crotonate**, $C_6H_5 \cdot NH \cdot C(CH_3) : CH \cdot CO_2C_2H_5$, which yields γ-hydroxy-quinaldine when heated (*Conrad* and *Limpach*, B **20**, 944):



β-Diketones and other compounds closely related to aceto-acetic ester also condense with aniline. In place of β-diketones, mixtures of ketones and aldehydes, or mixtures of aldehydes which would yield β-diketones or β-ketonic aldehydes if condensed together (*C. Beyer*, B. **20**, 1767), can be

employed. With acetyl-acetone we obtain $\alpha\gamma$-dimethyl-quinoline (B. 1899, **32**, 3228):

$$C_6H_5\cdot NH_2 + \begin{matrix}CH_3\cdot CO\cdot CH_2\\ \dot{C}O\cdot CH_3\end{matrix} = C_6H_4\begin{matrix}\diagup C(CH_3):CH\\ \diagdown N = \dot{C}\cdot CH_3\end{matrix} + 2H_2O.$$

These reactions are nearly allied to those already spoken of under 4.

6. *o*-Amino-benzaldehyde condenses with aldehydes and ketones under the influence of dilute caustic soda solution, yielding quinoline derivatives (*Friedlander*, B. **15**, 2574, **16**, 1833; **25**, 1752). With aldehyde quinoline itself results, and with acetone quinaldine:

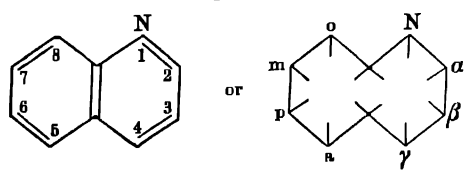
$$C_6H_4\begin{matrix}\diagup CHO\\ \diagdown NH_2\end{matrix} + \begin{matrix}CH_2\cdot R\\ \dot{C}O\cdot R'\end{matrix} = C_6H_4\begin{matrix}\diagup CH:C\cdot R\\ \diagdown N=\dot{C}\cdot R'\end{matrix} + 2H_2O$$

Acetophenone, acetoacetic ester, malonic ester, diketones, &c., also react in a similar way.

Constitution.—The above modes of formation (especially 3 and 6) show that quinoline is an ortho-di-substituted-derivative of benzene, and that it contains its nitrogen linked directly to the benzene nucleus, they also show that the three carbon atoms, which enter the complex, form a new hexagon (*pyridine*) ring with this nitrogen and with two carbon atoms of the benzene ring. The latter point also follows from the oxidation of quinoline to pyridine-dicarboxylic acid (*Hoogewerff* and *van Dorp*):

$$\underset{\text{Quinoline}}{C_6H_4\begin{matrix}\diagup CH:CH\\ \diagdown N=\dot{C}H\end{matrix}} + 9O = \underset{\text{Quinolinic acid}}{\begin{matrix}CO_2H\cdot C\cdot CH:CH\\ CO_2H\cdot \ddot{C}\cdot\ N\ :\dot{C}H\end{matrix}} + 2CO_2 + H_2O$$

We have thus the following constitutional formula:



according to which quinoline is constituted in a manner perfectly analogous to naphthalene, and may be regarded as derived from the latter by the exchange of CH for N, or as formed by the "condensation" of a pyridine and a benzene nucleus.

When quinoline derivatives are oxidized, the benzene ring is usually more readily ruptured than the pyridine one, *e.g.* quinoline yields pyridine-dicarboxylic acid (p. 540). α-Methyl-quinoline gives, on the other hand, *o*-acetyl-amino-benzoic acid when oxidized:

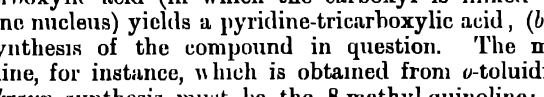
$$C_6H_4\begin{cases}CH{:}CH\\ N{=}\dot{C}\cdot CH_3\end{cases} + 5O = C_6H_4\begin{cases}CO\cdot OH\\ NH\cdot CO\cdot CH_3\end{cases} + CO_2$$

(For laws governing the oxidation of quinoline derivatives, see *W. v. Miller*, B **23**, 2252; **24**, 1900; M. 1891, **12**, 304.)

The pyridine nucleus of quinoline takes up hydrogen more readily than the benzene one; thus quinoline is easily converted, even by tin and hydrochloric acid, into tetrahydro-quinoline. It can be further reduced to the deca-hydride, but only with difficulty

The three hydrogen atoms of the pyridine nucleus, counting from the N, are designated as α-, β-, and γ-, and the four hydrogen atoms of the benzene nucleus as *o*-, *m*-, *p*-, and *a*- (ana-) hydrogen atoms, or more commonly the numbering shown above is adopted, the nitrogen atom being numbered 1 and the carbon atoms consecutively 2, 3, &c., up to 8. As no two hydrogen atoms are symmetrically situated in the molecule, seven mono-substituted derivatives of quinoline are in each case theoretically possible. As a matter of fact, all seven quinoline-monocarboxylic acids have been prepared.

The position of the substituents follows: (*a*) from the nature of the oxidation products, *e.g.* B-quinoline-carboxylic acid (*i.e.* an acid in which the carboxyl is attached to the benzene nucleus) yields a pyridine-dicarboxylic acid, while a Py-quinoline-carboxylic acid (in which the carboxyl is linked to the pyridine nucleus) yields a pyridine-tricarboxylic acid, (*b*) from the synthesis of the compound in question. The methyl-quinoline, for instance, which is obtained from *o*-toluidine by the *Skraup* synthesis must be the 8-methyl-quinoline:



whilst *m*-toluidine must yield a 7- or 5-, and *p*-toluidine a 6-methyl-quinoline.

Quinoline (*Runge*, 1834) is a colourless strongly refracting liquid of a peculiar and very characteristic odour. It boils at

239°, is a mono-acid base, forms a sparingly soluble dichromate, $(C_9H_7N)_2, H_2Cr_2O_7$, and is used as an antifebrile. As a tertiary base it yields **quinolonium** salts (*Roser*, A. 1893, **272**, 221).

Nascent hydrogen transforms it first into **dihydro-quinoline**, C_9H_9N, which melts at 161°, and then into **tetrahydro-quinoline**, $C_9H_{11}N$, $= C_6H_4\begin{cases}CH_2\cdot CH_2\\ NH\cdot CH_2\end{cases}$, a liquid boiling at 245°. Since both of these yield nitrosamines and can be alkylated, they are secondary bases. The tetrahydro-compound exerts a stronger antifebrile action than the mother substance, especially in the form of its ethyl derivative, **cairolin** (B. **16**, 739).

Quinoline decahydride, $C_{10}H_{17}N$, is obtained when strong reducing agents are employed. It forms crystals of a narcotic, coniine-like odour, melts at 48°, and boils at 204°.

Halogen derivatives of quinoline and nitro-quinolines have been prepared by the *Skraup* reaction, &c.; and, from the reduction of the latter, amino-quinolines, $C_9H_6N(NH_2)$. The quinoline-sulphonic acids yield cyano-quinolines with potassium cyanide, and hydroxy-quinolines when fused with potash.

1-Hydroxy-quinoline, *carbostyril*, is a quinoline hydroxylated in the pyridine nucleus (see p 543, mode of formation 3). It crystallizes in colourless needles, melts at 198°, and is soluble in alkali, from which it is again thrown down by carbonic acid. Its constitution follows from its formation from *o*-amino-cinnamic acid (p. 456).

Quinaldine, *2-methyl-quinoline*, $C_{10}H_9N$, is contained in coal-tar. It is a colourless liquid of quinoline odour, and boils at 246°. When oxidized with chromic acid it yields a quinoline derivative, with permanganate a pyridine-tricarboxylic acid.

The hydrogen of the methyl group readily enters into reaction; quinaldine reacts with phthalic anhydride to produce a beautiful yellow dye, **quinoline-yellow**, $C_{10}H_7N(CO)_2C_6H_4$ (B. **16**, 2602). A mixture of quinoline and quinaldine is transformed into the (unstable) blue dyes, the **cyanines**, when alkylated and treated with caustic potash. These are used as sensitizers for photographic plates.

Quinoline-carboxylic Acids.—All the seven quinoline mono-carboxylic acids, which are possible according to theory, are known. Quinoline-benz-carboxylic acids are those which contain the carboxyl group in the benzene nucleus.

Cinchoninic acid, *quinoline-4-carboxylic acid*, $C_9H_6N(CO_2H)$, which is obtained by the oxidation of cinchonine with per

manganate of potash, crystallizes in needles or prisms and melts at 254°. From it is derived **quinic acid**, *6-methoxy-quinoline-4-carboxylic acid*, $C_9H_5N(OCH_3)\cdot CO_2H$, which is obtained by oxidizing quinine with chromic acid; it forms yellow prisms, melting at 280°.

Quinoline-2·3-dicarboxylic acid, or *acridinic acid*, is formed by the oxidation of acridine.

3. ISO-QUINOLINE

Iso-quinoline, an isomer of quinoline, occurs along with the latter in coal-tar (B. **18**, Ref. 384). It is a solid, melts at 23°, and boils at 240°. Since oxidation converts it into cinchomeronic acid on the one hand and phthalic acid on the other, it possesses the constitution:

$$C_6H_4\begin{cases}CH:N\\ CH:CH.\end{cases}$$

Its constitution also follows from its synthesis* from homophthalic acid, $C_6H_4\begin{cases}CH_2\cdot CO_2H\\ CO_2H\end{cases}$, in which the substituents are in the *o*-position. This may be converted into its imide, $C_6H_4\begin{cases}CH_2\cdot CO\\ CO-NH\end{cases}$, by heating the ammonium salt. This imide with phosphorus oxychloride reacts as the tautomeride, $C_6H_4\begin{cases}CH=C(OH)\\ C(OH):N\end{cases}$, and yields the corresponding dichloro-iso-quinoline, which is reduced by hydriodic acid and red phosphorus to iso-quinoline.

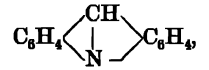
B. The Acridine Group

Acridine, $C_{13}H_9N$ (*Graebe* and *Caro*), is a basic constituent of the crude anthracene of coal-tar, and also of crude diphenylamine. It crystallizes in colourless needles, may be sublimed, and is characterized by an intensely irritating action upon the epidermis and the mucous membrane, and also by the greenish-blue fluorescence shown by dilute solutions of its salts.

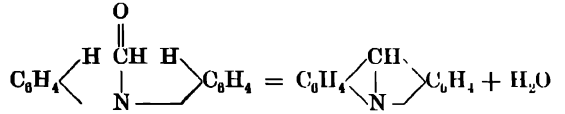
Acridine stands in the same relationship to anthracene that pyridine does to benzene or quinoline to naphthalene. It may

* For synthesis from β-naphthaquinone see B. **25**, 1138, 1493; **27**, 198; and for synthesis from benzylaminoacetaldehyde hydrochloride and sulphuric acid see *E. Fischer*, B. **26**, 764.

be regarded as anthracene in which one of the CH-groups of the middle ring is replaced by N. This constitutional formula:



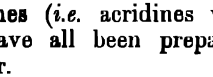
is based (*a*) upon the oxidation of acridine to quinoline-2:3-dicarboxylic acid, and to pyridine tetracarboxylic acid—the *p*-union between C and N becomes ruptured during the oxidation, (*b*) upon its synthesis from diphenylamine and formic acid, or formyl-diphenylamine, $(C_6H_5)_2N \cdot CHO$, with zinc chloride (*Bernthsen*, A. **224**, 1):



It is also obtained when the vapour of *o*-tolyl-aniline is passed through a red-hot tube.

Acridine is a tertiary base, and as such combines with alkyl iodides, yielding **acridonium iodides**. It is a much feebler base than quinoline, and on reduction readily forms a dihydro-derivative, which is not basic.

Methyl- and **butyl-acridines**, **phenyl-acridine**,



and **naphtho-acridines** (*i.e.* acridines which contain $C_{10}H_6$ instead of C_6H_4) have all been prepared synthetically in an analogous manner.

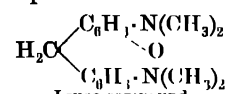
Diamino-dimethyl-acridine, *acridine yellow*, $C_{13}H_5(CH_3)_2(NH_2)_2N$, a yellow basic dye, is formed by condensing formic aldehyde with *m*-toluylene-diamine, splitting off ammonia, and oxidizing the leuco-base produced.

The **chrysaniline** or *phosphin* of commerce, a beautiful yellow dye, is *diamino-phenyl-acridine*, $C_{19}H_{11}N(NH_2)_2$, since it yields phenyl-acridine when its diazo-compound is boiled with alcohol.

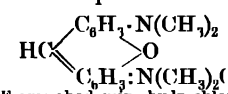
Acridine is therefore, like anthracene, a chromogene.

The oxygen analogue of dihydro-acridine, $C_6H_6\langle\begin{smallmatrix}CH_2\\NH\end{smallmatrix}\rangle C_6H_4$, is **diphenylene-methane oxide**, $C_6H_4\langle\begin{smallmatrix}CH_2\\O\end{smallmatrix}\rangle C_6H_4$, which can

be prepared synthetically and also by distilling euxanthone over zinc dust. It crystallizes in plates, and melts at 98·5°. It is on the one hand the mother substance of **xanthone**, $C_6H_4<\begin{matrix}CO\\O\end{matrix}>C_6H_4$, and its derivative **euxanthone** or *dihydroxyxanthone*, $OH\cdot C_6H_3<\begin{matrix}CO\\O\end{matrix}>C_6H_3\cdot OH$, and on the other hand, of the rhodamines and fluoresceins (p 493). Its **tetramethyldiamino**-derivative results from the condensation of formic aldehyde with dimethyl-*m*-amino-phenol to tetramethyldiamino-dihydroxy-diphenyl-methane and subsequent elimination of water (ring formation), and is the leuco-compound of **formo-rhodamine** or *pyronine*, $C_{17}H_{19}N_2OCl$, into which it passes upon oxidation and production of quinoid linking, thus:



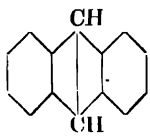
Leuco compound



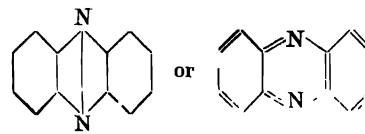
Formo-rhodamine hydrochloride

XXXIX SIX-MEMBERED HETEROCYCLIC COMPOUNDS WITH NOT MORE THAN FOUR CARBON ATOMS IN RING. AZINES, ETC.

A number of six-membered heterocyclic compounds, containing four carbon and two other atoms, are known, *e.g* **paroxazine**, with 4C, 1O, and 1N, the O and N in the *p*-position. A derivative of this is **morpholine**, $O<\begin{matrix}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{matrix}>NH$. Similarly, **thiazines** (4C, 1S, 1N) and **diazines** (4C, 2N) are known, and these are the parent substances of numerous important dyes. The majority of these dyes are not simple derivatives of oxazines, thiazines, or diazines, but are derived from condensed benzene and oxazine, or benzene and diazene nuclei, and may be compared with anthracene. For example, **phenazine** is anthracene in which two CH-groups have been replaced by two N-radicals:

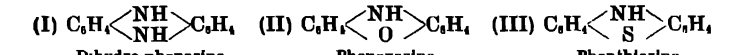


Anthracene



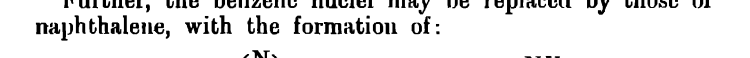
Phenazine

dihydro-phenazine corresponds with dihydro-anthracene, and phenoxazine with dihydro-anthracene in which one CH_2 has been replaced by O and another by NH, *e.g.*:



Dihydro-phenazine — Phenoxazine — Phenthiazine (thio-diphenylamine)

Further, the benzene nuclei may be replaced by those of naphthalene, with the formation of:

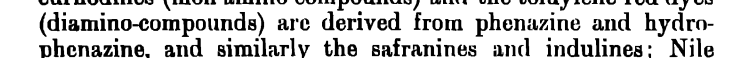


Naphthazine — Naphtho-phenoxazine

The compounds (I–III) of the type of dihydro-anthracene are the leuco-compounds of dyes when they contain an amino- (alkyl-amino-) or hydroxy-group in the *para*-position to the nitrogen. The dyes themselves are obtained from these by oxidation (*i.e.* elimination of hydrogen), so that they are derived from amino- or hydroxy-phenazines. In this way the eurhodines (mon-amino-compounds) and the toluylene red dyes (diamino-compounds) are derived from phenazine and hydrophenazine, and similarly the safranines and indulines; Nile blue is derived from naphtho-phenoxazine; and the thionine dyes from phenthiazine.

THE DIAZINES

The three simple diazines are:



Pyridazine — Pyrimidine — Pyrazine.

Pyridazine is a colourless liquid, b.-pt. 208°, is miscible with water, has an odour of pyridine, and forms soluble salts. (Preparation, cf. B. **28**, 451.)

Pyrimidine can be obtained from barbituric acid and from methyluracil (p. 287); it forms colourless crystals, m.-pt. 22° and b.-pt. 124°. The pyrimidine ring is met with in uric acid and in most purine derivatives (cf. B. **34**, 3248).

Pyrazine forms colourless prisms, m.-pt. 47°, b.-pt. 118°, and is basic (J. pr. [ii], **51**, 449). **Dimethylpyrazine**, *Ketin*, is present in crude amyl alcohol, and can be obtained by the reduction of isonitrosoacetone or by condensation of amino-

acetone. **Tetraphenylpyrazine** is readily obtained from benzoin.

Of the compounds formed by the union of a benzene and a diazine nucleus the most important is **quinoxaline**, $C_6H_4\langle\begin{matrix}N:CH\\N:CH\end{matrix}$, which is obtained from *o*-phenylene-diamine and glyoxal. Substituted quinoxalines are formed by condensing α-diketones, α-ketonic acids, &c., with *o*-phenylene-diamines. Of more importance is the group of compounds containing two benzene nuclei condensed with one diazine ring, *e.g.* phenazine

Phenazine, or *azo-phenylene* (p. 549), is obtained by the distillation of barium azo-benzoate, or by leading the vapour of aniline through red-hot tubes; also from nitrobenzene, aniline, and sodium hydroxide at 140°, or by the oxidation of its hydro-compound (see below). It crystallizes in beautiful, long, bright-yellow needles melting at 171°, and can be readily sublimed. It is only sparingly soluble in alcohol, but readily in ether, and also dissolves in concentrated sulphuric acid to a red solution; the alcoholic solution yields a green precipitate on the addition of stannous chloride. When reduced with ammonium sulphide it yields the colourless hydro-compound, **dihydro-phenazine**, $C_{12}H_{10}O_2$, which may be obtained synthetically by heating catechol with *o*-phenylene-diamine:

$$C_6H_4\langle\begin{matrix}OH\\OH\end{matrix} + \begin{matrix}NH_2\\NH_2\end{matrix}\rangle C_6H_4 = C_6H_4\langle\begin{matrix}NH\\NH\end{matrix}\rangle C_6H_4 + 2H_2O.$$

The entrance of hydroxy- or amino-groups into these azines converts them into dyes In accordance with modern views of the quinonoid structure of dyes these derivatives are usually given ortho or para quinonoid formulæ:

$$\text{Para, } C_6H_4\langle\begin{matrix}N=\\NH\end{matrix}\rangle C_6H_3{:}NH; \quad \text{ortho, } C_6H_4\langle\begin{matrix}N\\N\end{matrix}\rangle C_6H_3{\cdot}NH_2,$$

and similarly for hydroxy derivatives.

The amino-compounds are usually termed **Eurhodines**, and may be obtained by condensing arylamines with *o*-amino-azo-compounds.

Eurhodine, *amino-naphtho-toluzine*,

$$CH_3{\cdot}C_6H_3\langle\begin{matrix}N_2\\\end{matrix}\rangle C_{10}H_5{\cdot}NH_2 \text{ or } CH_3{\cdot}C_6H_3\langle\begin{matrix}N_2H\\\end{matrix}\rangle C_{10}H_5{:}NH,$$

obtained from α-naphthylamine and *o* amino azo-toluene, forms lustrous golden crystals and yields scarlet salts (B. **19**, 441

21, 2418; **24**, 1337). When heated with concentrated hydrochloric acid it is converted into the basic and at the same time phenolic compound **eurhodol**,

$$HO\cdot C_{10}H_5\langle N_2\rangle C_6H_3\cdot CH_3 \quad \textbf{or} \quad CH_3\cdot C_6H_3\langle N_2H\rangle C_{10}H_5{:}O$$

(cf. B. **24**, 1337).

***o*-Diamino-phenazine**, $C_{12}H_6N_3(NH_2)_2$, is obtained by the oxidation of *o*-phenylene-diamine with ferric chloride (B. **22**, 355), and is the parent substance of the important dyes of the **toluylene red** group. When a mixture of *p*-phenylene-diamine and *m*-toluylene-diamine is oxidized in the cold, the beautiful blue compound, toluylene blue, an indamine (p. 434), is formed, which is further oxidized to toluylene red, diamino-tolu-phenazine, when boiled.

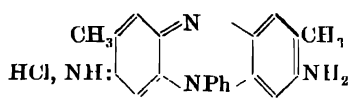
$$NH_2\cdot C_6H_4\cdot NH_2 + NH_2\cdot C_6H_3Me\cdot NH_2 + 2O = NH_2\cdot C_6H_4\cdot N{:}C_6H_2Me(NH_2){:}NH + 2H_2O$$

$$NH_2\cdot C_6H_4\cdot N{:}C_6H_2Me(NH_2){:}NH + O = NH_2\cdot C_6H_3\langle \overset{N}{N}\rangle C_6H_2Me\cdot NH_2 + H_2O$$

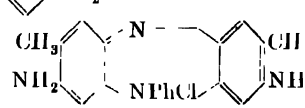
This diamino-tolu-phenazine is the simplest of the toluylene reds, and its constitution follows from the fact that when diazotized it yields methyl-phenazine. Analogous dyes are *neutral red*, the hydrochloride of dimethyl-diamino-tolu-phenazine, $NMe_2\cdot C_6H_3\langle N_2\rangle C_6H_2MeNH_2$, HCl, and *neutral violet*, dimethyl-diamino-phenazine hydrochloride. The leuco-compounds are the corresponding derivatives of dihydrophenazine.

The group of dyes known as the safranines are related to toluylene red. They are amongst the oldest of the aniline dyes, and include *mauve*, the first dye prepared by *W. H. Perkin, Senr.*, in 1856. The simplest member of this group is pheno-safranine, $NH{:}C_6H_3\langle \overset{N}{NPh}\rangle C_6H_3\cdot NH_2$, which is of historical interest only. The dye *safranine* is the hydrochloride of dimethyphenosafranine.

I.



II.



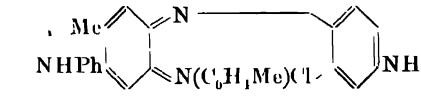
I. represents the compound with a paraquinonoid, and II. with an orthoquinonoid structure.

The commercial product is usually a mixture of this with a homologue containing the *o*-tolyl group in place of the Ph. The method of manufacture consists in the oxidation of molecular proportions of *p*-toluylene-diamine and *o*-toluidine to the corresponding indamine, and then the condensation of this with *o*-toluidine to give the tolu-safranine. It can be used for cotton mordanted with tannin, and gives red colours.

The safranines are beautiful crystalline compounds of a metallic green lustre, readily soluble in water, and dye yellowish-red, red, and violet. The solution in concentrated sulphuric acid is green, becoming blue, violet, and finally red on dilution with water. Reduction gives rise to leuco-compounds, which are diamino-compounds of the as yet unknown substance $C_6H_4<\begin{matrix}NH\text{——}\\N(C_6H_5)\end{matrix}>C_6H_4$ (B. **19**, 2690, 3017, 3121; **29**, 361, 1442, 1870, &c.), treatment with nitrous acid and alcohol yields phenyl-phenazonium chloride. The safranines are therefore diamino-compounds of phenyl-phenazonium chloride:

$$C_6H_4<\begin{matrix}N\text{——}\\N(C_6H_5)Cl\end{matrix}>C_6H_4$$

Numerous other safranines are manufactured. *Methylene violet* is asymmetric dimethyl-safranine chloride, *safranine*, MN, is a dimethyl tolyl-safranine chloride, and *amethyst violet*, tetramethyl safranine chloride. *Perkin's mauve* has the formula



The **aposafranines** are analogous to the safranines, but contain only one amino- or substituted amino-group, and at least one naphthalene residue in place of a benzene ring. They are divided into *Rosindulines* and *Isorosindulines*. The former contain the amino group attached to the naphthalene ring and give red shades, the latter contain the amino group attached to a benzene ring and give blue or green shades.

Safranines can be diazotized and coupled with alkaline solutions of β-naphthol. *Indon blue* is the hydrochloride of safranine-azo-naphthol, $C_{20}H_{16}N_3 \cdot N:N \cdot C_{10}H_6OH$, HCl.

PHENOXAZINES AND PHENTHIAZINES

Phenoxazine (p. 550) is obtained by heating catechol with *o*-aminophenol, and crystallizes in plates. The leuco-compound of *nile blue* is a diethyldiamino-naphthaphenoxazin. The dye itself, $NH{:}C_{10}H_5\langle^{N}_{O}\rangle C_6H_4\cdot NEt_2$, HCl, obtained by heating the nitroso-derivative of diethyl-*m*-aminophenol with *α*-naphthylamine, is a brilliant green-blue basic dye

Methylene blue, $NMe_2\ C_6H_3\langle^{N}_{S}\rangle C_6H_3{:}NMe_2Cl$, a valuable blue dye for wool, is formed by the action of ferric chloride on amino-dimethylaniline and carbon disulphide. With nitrous acid it yields methylene green.

For constitution cf. *Kehrmann*, B. **39**, 911, *Hantzsch*, *ibid* 1365

XL. ALKALOIDS

The group of alkaloids at one time comprised the whole of the nitrogenous basic compounds present in plants or derived from the various plant tissues by distillation. Thus methylamine, betaine, asparagine, caffeine, and the opium alkaloids were all grouped together, but as their constitutional formulæ were established they were grouped with the compounds to which they were closely related, *e g* methylamine with the primary aliphatic amines, betaine with the alkyl derivatives of glycocoll, and caffeine with the uric acid or purine derivatives. The name is now largely restricted to the nitrogenous basic plant constituents which can be regarded as derived from pyridine, quinoline, or iso-quinoline, and to those of unknown constitution.

They form an extremely important group of compounds on account of their physiological properties, and they constitute the active principles of the common vegetable drugs and poisons.

With a single exception they occur exclusively in dicotyledons, and as a rule do not exist in the free state, but combined with organic acids in the form of salts Such acids are malic (p. 217), citric (p. 261), and tannic (p. 160); quinic acid usually accompanies the alkaloids of opium.

A few of the alkaloids are built up of carbon, hydrogen, and

nitrogen, *e.g.* coniine, nicotine. Such compounds as a rule are liquids and are readily volatile, the majority, on the other hand, contain in addition oxygen, and then are usually crystalline and non-volatile. All are optically active, and as a rule lævo-rotatory. A few like coniine are secondary bases, but the majority are tertiary, and a few quaternary ammonium compounds.

The following reagents as a rule precipitate the alkaloids in the form of complex derivatives from solutions of their salts, viz tannin, phosphomolybdic acid, a potassium iodide solution of iodine, and also potassium mercuric iodide. They are further characterized by their bitter astringent taste and by their poisonous properties. Each individual alkaloid gives characteristic colour reactions.

The alkaloids are usually extracted from plant tissues by lixiviating the finely-divided tissue with acidified water. The extract is then rendered alkaline with ammonia and the free alkaloid separated by filtration, or, if it is at all readily soluble, by extraction with chloroform.

For relationship between constitution and physiological properties see *P. May*, "The Chemistry of Synthetic Drugs", London, 1911.

The structural formula for an alkaloid is usually determined by a study of its more important chemical reactions and of its degradation products. Among the reactions generally studied are:—

1. Determination of the number of free hydroxyl groups by acetylation (cf. p. 201). Thus morphine can be shown to contain two, codeine one, and papaverine none

2. Determination of methoxy groups by *Zeisel's* method or *Perkin's* modification. Papaverine contains four such groups narcotine three and codeine one.

3. Study of the action of hydrolysing agents Esters are hydrolysed, but most other types of linking are resistent to such agents. Narcotine (p. 561) yields opianic acid and hydrocotarnine, and is presumably an ester derived from these two compounds. Similarly, atropine (p. 565) on hydrolysis yields tropic acid and tropine. As the products of hydrolysis are simpler than the original alkaloid, the elucidation of their constitutions is less difficult.

4. Examination of the products of oxidation. Thus codeine contains a secondary alcoholic group, as on oxidation it yields a ketone, codeinone, containing the same number of carbon

atoms. Conine when oxidized yields picolinic acid, and must thus be an α-substituted derivative of pyridine. Cinchonine yields quinoline-γ-carboxylic acid.

5. Determination of the primary, secondary, tertiary, or quaternary nature of the base.

6 Study of the degradation products obtained by exhaustive methylation. As an example of this method the simple secondary amine piperidine may be taken. When methylated by means of methyl iodide it yields first the tertiary amine, methylpiperidine, and finally the quaternary ammonium iodide, dimethylpiperidonium iodide. This with moist silver oxide yields the quaternary base, which on distillation decomposes into water and an unsaturated aliphatic tertiary amine:

$$CH_2\begin{matrix}<\\<\end{matrix}\begin{matrix}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{matrix}\begin{matrix}>\\>\end{matrix}NMe_2\cdot OH$$
$$= H_2O + CH_2{:}CH\cdot CH_2\cdot CH_2\cdot CH_2\cdot NMe_2$$

When methylated and treated with silver oxide this unsaturated base yields a quaternary hydroxide, which splits up into water, trimethylamine, and $\Delta^{\alpha\delta}$ pentadiene when distilled.

$$CH_2{:}CH\cdot CH_2\cdot CH_2\cdot CH_2\cdot NMe_3\cdot OH$$
$$= H_2O + NMe_3 + CH_2{:}CH\cdot CH_2\cdot CH{:}CH_2$$

7 An examination of the products obtained by fusing the alkaloid with potash or by distilling it with zinc dust. Thus morphine and zinc dust yield phenanthrene together with other products, and hence the molecule of morphine probably contains a phenanthrene ring. Papaverine, when fused with potash, yields dimethoxy-iso-quinoline and 3 4-dimethoxy-toluene, and hence papaverine is probably an iso-quinoline derivative. The processes of fusion with potash and distillation with zinc dust require high temperatures, and as molecular rearrangements occur much more readily at high than at low temperatures, the conclusions drawn from a study of the products formed during such processes should be accepted with a certain amount of reserve unless supported by other evidence.

The alkaloids can be grouped according to their origin, *e.g.* the opium alkaloids, bases from solanine, &c., or according to the heterocyclic ring which they contain. The latter method is adopted here, and we thus have the pyridine, quinoline, *iso*-quinoline, and phenanthrene groups.

A. Alkaloids derived from Pyridine

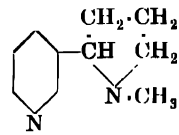
Coniine, dextro-rotatory *α-normal-propyl-piperidine*, $C_5H_{10}N(C_3H_7)$, is the poisonous principle of hemlock (*Conium maculatum*). It is a colourless dextro-rotatory liquid of stupefying odour, sparingly soluble in water, and boils at 167°. Hydriodic acid at a high temperature reduces it to normal octane, while nitric acid oxidizes it to butyric acid, and potassium permanganate to picolinic acid (hence the α-position).

Ladenburg has prepared it synthetically by reducing α-allyl-pyridine (p. 538) in alcoholic solution by means of sodium (*B.* **19**, 2578):

$$C_5H_4N(C_3H_5) + 8H = C_5H_{10}N(C_3H_7).$$

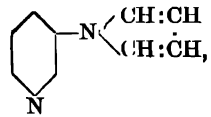
The pyridine ring is reduced to a piperidine ring, and at the same time the unsaturated allyl side-chain is reduced to a *n*-propyl group The α-carbon atom is an asymmetric carbon atom, *i e.* it is attached to four different monovalent radicals, and the whole molecule is asymmetric The synthetical product is optically inactive, and thus differs from the natural product, but it has been resolved by fractional crystallization of the *d*-tartrate into dextro-coniine and a lævo-coniine. The relations of these two bases to one another and to the inactive modification are the same as that of dextro- to lævo-tartaric acid and to racemic acid.

Nicotine, $C_{10}H_{14}N_2$, is the poisonous constituent of the tobacco plant, in which it exists in combination with malic and citric acids. It is a colourless, oily liquid soluble in water, and is lævo-rotatory. It rapidly oxidizes in contact with the air, and boils at 247°. It is a di-tertiary base, and therefore readily combines with methyl iodide. On oxidation with permanganate it yields nicotinic acid, and hence must be a β-pyridine derivative. It has been synthesised recently by *Pictet* (C. R. 1903, **137**, 860), and been shown to be α-pyridyl-N-methyl-pyrrolidine·

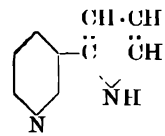


The method of synthesis is as follows:—Nicotinic acid is transformed first into its ethyl ester, and then into the amide,

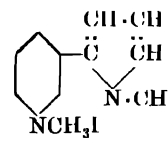
this with bromine and alkali (*Hofmann's* reaction, pp. 107, 183) gives β-amino-pyridine, and when the salt of this base with mucic acid (p. 259) is distilled, N-pyridyl-pyrrole,



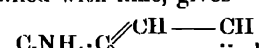
is formed. When the vapour of this compound is passed through a heated tube, it is transformed into the isomeric α-pyridyl-pyrrole,



This forms a potassic derivative which with methyl iodide yields



and this, when distilled with lime, gives



α-pyridyl-N-methyl-pyrrol, which can be converted into α-pyridyl-N-methyl-pyrrolidine (*i*-nicotine) by the addition of hydrogen. The racemic alkaloid thus obtained may be resolved into its optically active components by the aid of *d*-tartaric acid when *l*-nicotine-*d*-tartrate crystallizes out first

B. Bases derived from Quinoline

Among these are the alkaloids contained in the barks of certain species of **Cinchona**.

(*a*) **Quinine**, $C_{20}H_{24}O_2N_2 + 3H_2O$, a diacid base of intensely bitter taste and alkaline reaction, of which the sulphate and chloride are universally used as febrifuges. It crystallizes in prisms or silky glistening needles, melts at 177° when anhydrous, is sparingly soluble in water, and is lævo-rotatory.

The quinine salts in dilute solution are characterized by a magnificent blue fluorescence.

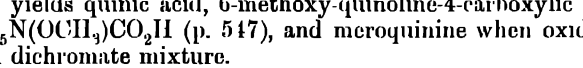
As a base quinine is a tertiary diamine, but it contains in addition—as its reactions show—one hydroxy-, one methoxy-group and an ethylene linking, and seems to be built up of two different ring systems, in accordance with the following formula:

$$(CH_3O)\cdot C_9H_6N\cdot C_{10}H_{15}(OH)N.$$

The first of these represents the radical of a 6-methoxy-quinoline, and this compound is obtained when quinine is fused with potash. The second system probably possesses a ring similar to that of tropine, since it yields as decomposition products sometimes a pyridine derivative (*e.g.* β-ethyl-pyridine on fusion with alkali), and sometimes benzene derivatives containing no nitrogen (*e.g.* a phenolic compound, $C_{10}H_{12}OH$, together with ammonia, on successive treatment with phosphorus pentachloride, potash, and hydrobromic acid).

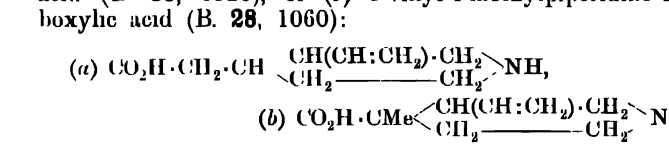
It yields quinic acid, 6-methoxy-quinoline-4-carboxylic acid, $C_9H_5N(OCH_3)CO_2H$ (p. 547), and meroquinine when oxidized with dichromate mixture.

Meroquinine appears to be either (*a*) 3-vinylpiperidyl-acetic acid (B **30**, 1326), or (*b*) 3-vinyl-4-methylpiperidine-4-carboxylic acid (B. **28**, 1060):



as it yields *loiponic acid*, piperidine-3:4-dicarboxylic acid, when oxidized with permanganate.

The formulæ suggested for quinine are therefore either



where X represents the 6-methoxy-quinoline residue attached to the CH_2 group in position 4.

Quinine is a valuable drug in cases of malaria; numerous

substitutes are now employed, especially derivatives of quinine which are free from bitter taste.

Various esters are used, e.g *aristoquinine* is diquinine carbonate, *euquinine* is ethyl quinine carbonate, and *saloquinine* is quinine salicylate.

(*b*) **Cinchonine**, $C_{19}H_{22}ON_2$, is similar to quinine, but without the methoxy group in the quinoline nucleus. It crystallizes in colourless prisms, sublimes readily, and is not so active a febrifuge as quinine When oxidized with dichromate and sulphuric acid it yields cinchoninic (quinoline-4-carboxylic) acid and meroquinine, with permanganate it yields cinchotenine and carbonic acid. Cinchotenine no longer combines with hydrogen chloride, and in the oxidation the double linking present in cinchonine has been removed and a carboxylic group introduced. When treated with PCl_5 and then with alcoholic potash, cinchonine loses a molecule of water, yielding *cinchene*, $C_{19}H_{20}N_2$, which can be hydrolysed by 25 per cent phosphoric acid to lepidine (4-methyl-quinoline) and meroquinine.

(*c*) **Conchinine**, $C_{20}H_{24}O_2N_2$, and **Cinchonidine**, $C_{19}H_{22}ON_2$, are probably stereoisomeric with quinine and cinchonine respectively, and are milder in their action

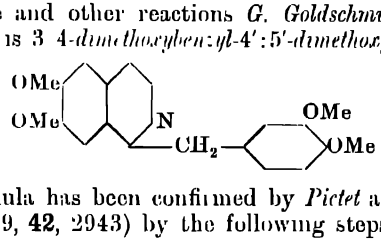
These are but a few of the numerous alkaloids present in these barks. In addition, organic acids (*e.g* quinic and quinotannic) and neutral substances are also present

C Bases derived from *Iso*-Quinoline

(*a*) **Papaverine**, $C_{20}H_{21}O_4N$, is found (1 %) together with narcotine, narceine, laudanosine, laudanine, and the morphine alkaloids in opium, the solid obtained by drying the juices extracted from the seed vessels of *Papaver somniferum*. In addition to some twenty alkaloids, many of which are present in only small quantities, opium also contains fats, resins, sugars, albumins, &c. The alkaloid crystallizes in prisms, m.-pt. 147°, and is optically inactive. It has hypnotic properties, but not to the same extent as morphine It is a tertiary base, and all four oxygen atoms are present as methoxy groups, and when hydrolysed with hydriodic acid the corresponding tetrahydroxy-derivative, *papaveroline*, $C_{16}H_{13}O_4N$, is formed. When oxidized with permanganate it yields first *papaveraldine*, $C_{20}H_{19}O_5N$, and finally dimethoxy-isoquinoline-carboxylic acid and α-carbocinchomeronic acid (pyridine-1·2:3-

carboxylic acid). When fused with potash it takes up two hydrogen atoms, and yields 4:5-dimethoxy-iso-quinoline and 3:4-dimethoxytoluene

From these and other reactions *G. Goldschmidt* concluded that the base is 3 4-*dimethoxybenzyl*-4':5'-*dimethoxy-iso-quinoline*



and this formula has been confirmed by *Pictet* and *Gan's* synthesis (B. 1909, **42**, 2943) by the following steps:—

1. $C_6H_4(OMe)_2$ (Veratrole or 1 2 dimethoxybenzene) $\xrightarrow{}$ ($C_6H_3(OMe)_2$ Friedel-Crafts') $\rightarrow$ $C_6H_3(OMe)_2\cdot CO\cdot CH_3$ Acetoveratrone

$\rightarrow$ $C_6H_3(OMe)_2\cdot CO\cdot CH{:}N\cdot OH$ (Amyl nitrite; Isonitrosoacetoveratrone)

$\rightarrow$ ($SnCl_2$) $C_6H_3(OMe)_2\cdot CO\cdot CH_2\cdot NH_2HCl$ Amino acetoveratrone hydrochloride

2 $CHO\cdot C_6H_3(OMe)OH$ (Vanillin) $\xrightarrow{}$ (methylated) $CHO\cdot C_6H_3(OMe)_2$ Methylvanillin

$\rightarrow$ (HCN) $C_6H_3(OMe)_2\cdot CH(OH)\cdot CN \rightarrow$ (hydrolysis) $C_6H_3(OMe)_2\cdot CH(OH)\cdot CO_2H$

$\rightarrow$ (HI) $C_6H_3(OH)_2\cdot CH_2\cdot CO_2H$ Homoprotocatechuic acid $\rightarrow$ (methylated) $C_6H_3(OMe)_2\cdot CH_2\cdot CO_2H$ Homoveratric acid

$\rightarrow$ $C_6H_3(OMe)_2\cdot CH_2\cdot COCl$ Homoveratroyl chloride

3 Amino-acetoveratrone hydrochloride and homoveratroyl chloride condense in the presence of cold potassium hydroxide, yielding $(OMe)_2C_6H_3\cdot CO\cdot CH_2\cdot NH\cdot CO\cdot CH_2\cdot C_6H_3(OMe)_2$, this can be reduced to the corresponding secondary alcohol which reacts with dehydrating agents, losing two molecules of water and forming 3':4' dimethoxybenzyl-4:5-dimethoxy-iso-quinoline, which is identical with papaverine.

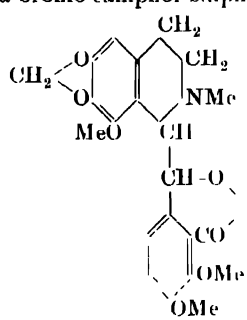
(*b*) **Laudanosine**, $C_{21}H_{27}O_4N$, crystallizes in needles, m.-pt 89°, and is dextro rotatory. It has been shown by *Pictet* and *Athanescu* (B. **33**, 2346) to be an N-methyl-tetra-hydropapaverine, and has been synthesised by *Pictet* and *Finkelstein* (C. R. 1909, **148**, 295).

(*c*) **Narcotine**, $C_{22}H_{23}O_7N$, occurs in opium (6 per cent), crystallizes in colourless needles, m.-pt. 176°, and is lævo-rotatory. It is a feeble tertiary base, and its salts are readily hydrolysed by water. It contains three methoxy groups, and

when hydrolysed by dilute acids or alkalis, yields opianic acid and hydro-cotarnine. When reduced it yields meconine and hydro-cotarnine, and when oxidized yields opianic acid and cotarnine, and when heated with alkalis at 220° yields methylamines, thus indicating that the N-atom is methylated.

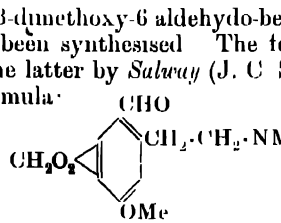
The racemic compound has been synthesised in small quantities (*Perkin* and *Robinson*, J. C. S. 1911, 776) by boiling an alcoholic solution of cotarnine and meconine, and has been resolved by means of *d*-bromo-camphor-sulphonic acid

Narcotine,

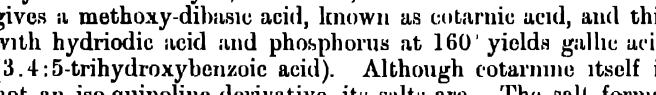


Both opianic (2.3-dimethoxy-6 aldehydo-benzoic acid) acid and cotarnine have been synthesised. The former by *Fritsch* (A. **301**, 351) and the latter by *Salway* (J. C. S. 1910, 1208).

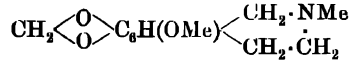
The structural formula:



was deduced by *Roser* for cotarnine by a study of its degradation products. When methylated and decomposed by alkalis it yields an aldehyde, cotarnone, which on further oxidation gives a methoxy-dibasic acid, known as cotarnic acid, and this with hydriodic acid and phosphorus at 160° yields gallic acid (3.4:5-trihydroxybenzoic acid). Although cotarnine itself is not an iso-quinoline derivative, its salts are. The salt formation is accompanied by a closing of the ring (cf. *Dobbie*, *Lauder*, and *Tinkler*, J. C. S. 1903, 598):



Hydro-cotarnine is also a reduced iso-quinoline derivative:

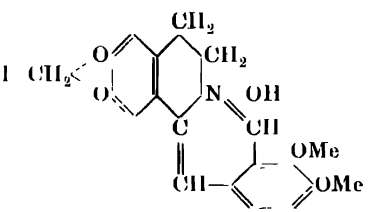


The steps in the synthesis of cotarnine are: Myristic aldehyde (3-methoxy-4.5-methylenedioxy-benzaldehyde) → 3-methoxy-4·5-methylenedioxy-cinnamic acid —(Perkin's synthesis)→ corresponding dihydro acid → acid amide —(red)→ β-3-methoxy-4·5-methylenedioxy-phenylethylamine —(−CO)→ phenacetyl-derivative of amine → 8-methoxy-6 7-methylenedioxy-1-benzyl-3.4-dihydro-iso-quinoline → 1-benzylhydrocotarnine —(Methochloride with tin and HCl)→ cotarnine.

(*d*) **Hydrastine**, $C_{21}H_{21}O_6N$, occurs in the roots of *Hydrastis canadensis*, and differs from narcotine by having no methoxy group in the iso-quinoline ring. When oxidized it yields opianic acid and hydrastinine, which is the analogue of cotarnine. (Synthesis, cf. *Freund*, B **20**, 2403.)

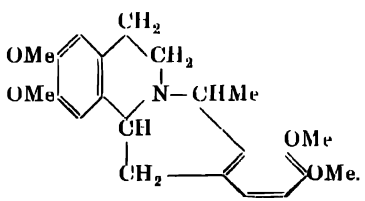
(*e*) **Berberine**, $C_{20}H_{17}O_4N$, H_2O, is the chief alkaloid present in *Hydrastis*, but has not marked physiological properties. The probable structural formula is I (*Perkin* and *Robinson*, J. C. S. 1910, 305).

I



(*f*) **Corydaline**, $C_{22}H_{27}O_4N$, from *Corydalis cava*, crystallizes in prisms, m.-pt 134·5°, and contains four methoxy groups. The structural formula suggested by *Dobbie* and *Lauder* (J. C. S. 1903, 605) is II.

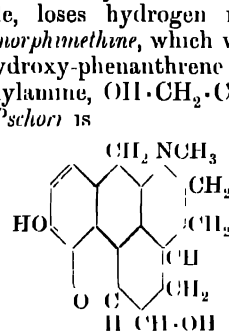
II



D. The Morphine Group of Bases

The three alkaloids morphine, codeine, and thebaine are characterized by containing a phenanthrene nucleus in addition to a nitrogen ring. They are all present in opium.

(*a*) **Morphine**, $C_{17}H_{19}O_3N$, constitutes on the average 10 per cent of opium. It crystallizes in small prisms ($+H_2O$), melting and decomposing at 230°, has a bitter taste, and is a valuable soporific. It is a mono-acid tertiary base, containing two hydroxyl groups, one of which is phenolic and the second alcoholic. When distilled with zinc dust it yields phenanthrene together with pyrrole, pyridine, and trimethylamine. Further proof of the presence of the phenanthrene nucleus has been afforded by the process of exhaustive methylation. With methyl iodide it yields codeine methiodide, formed by the methylation of the phenolic hydroxyl group and addition of methyl iodide to the tertiary N-atom. This product, with potassium hydroxide, loses hydrogen iodide and yields a tertiary base, *methylmorphimethine*, which with acetic anhydride gives 3-methoxy-4-hydroxy-phenanthrene (methylmorphol) and hydroxyethyldimethylamine, $OH \cdot CH_2 \cdot CH_2 \cdot NMe_2$. The formula suggested by *Pschorr* is



(*b*) **Codeine**, $C_{18}H_{21}O_3N$, is a methyl derivative of morphine, and can be obtained from the latter by methylation of its phenolic group. When oxidized it yields the ketone *codeinone*, and this with acetic anhydride yields hydroxyethyl-methyl amine and 3-methoxy-4.6-dihydroxy-phenanthrene.

(*c*) **Thebaine** is morphine in which both phenolic and alcoholic hydroxyls are methylated.

Numerous alkyl derivatives of morphine are manufactured and used as drugs in place of codeine. *Dionine* is ethylmorphine hydrochloride, *peronine* is benzylmorphine hydrochloride, *heroin* is diacetylmorphine.

For synthetical products allied to morphine see *Knorr*, A. **301**, 1; **307**, 171, 187; B. **32**, 732.

E. Strychnine Bases

Strychnos nux vomica and certain other beans contain:

(*a*) **Strychnine**, $C_{21}H_{22}O_2N_2$. This is excessively poisonous, produces tetanic spasms, crystallizes in four-sided prisms, and yields quinoline and indole when fused with potash, β-picoline when distilled with lime, and carbazole when heated with zinc dust. It is a mono-acid tertiary base, and melts at 284°. (For suggested formula see *Perkin* and *Robinson*, J. C. S. 1910, 305.)

(*b*) **Brucine**, $C_{23}H_{26}O_4N_2$, $4H_2O$, which crystallizes in prisms, and is converted into homologues of pyridine on fusion with potash.

F. Solanine and Coca Bases

Atropine and hyoscyamine are isomeric bases of the formula $C_{17}H_{23}O_3N$, which can be respectively prepared from *Atropa Belladonna* (Deadly Nightshade) and *Datura Stramonium*, and which are remarkable for their mydriatic action (power of dilating the pupil of the eye).

Atropine crystallizes in colourless prisms or needles melting at 115°, possesses an extremely bitter taste, is optically inactive, and is hydrolysed by baryta water to *dl*-tropic acid (α-phenyl-β-hydroxy-propionic acid, $C_6H_5 \cdot CH(CO_2H) \cdot CH_2OH$, p. 462) and tropine, $C_8H_{15}ON$, and is therefore the tropic ester of tropine. The alkaloid can be synthesised by evaporating a dilute hydrochloric acid solution of tropine and tropic acid. A complete synthesis of atropine has been accomplished, as both tropic acid and tropine have been synthesised.

When optically active (*d*- and *l*-) tropic acids are used, a dextro- and a lævo-rotatory atropine result (B. **22**, 2590). And if, instead of tropic acid itself, other organic acids are employed, homologous bases, the "**tropeïnes**", are obtained, thus mandelic acid yields **homatropine**, $C_{16}H_{21}NO_3$, which exerts like atropine a mydriatic action, although a less lasting one (*Ladenburg*, A. **217**, 82, *Jowett* and *Pyman*, J. C. S. 1909, 1090).

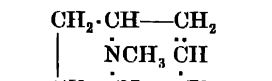
Tropine itself is a cycloheptanol with a nitrogen bridge:

$$\begin{array}{l} CH_2 \cdot CH\text{---}CH_2 \\ \quad\quad | \quad\quad\quad\quad \\ \quad\quad NCH_3 \; CH \cdot OH \\ \quad\quad | \quad\quad\quad\quad \\ CH_2 \cdot CH\text{---}CH_2 \end{array}$$

(*Willstatter*, B. 1898, **31**, 1538, 2498, 2655). For synthesis cf. *Willstatter*, A. 1901, **317**, 307.

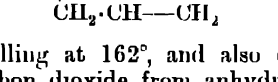
It is a tertiary base, crystallizes in plates, m.-pt. 62°, and b.-pt. 220°.

On oxidation it yields the ketone **tropinone**, and then **tropinic acid**, or *N-methyl-pyrrolidine-α-carboxylic-α'-acetic acid*. Concentrated hydrochloric acid converts it into **tropidine**,



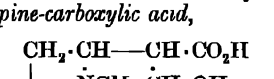
an oily base distilling at 162°, and also obtainable by the elimination of carbon dioxide from anhydro-ecgonine.

Ecgonine, or *tropine-carboxylic acid*,



crystallizes with one molecule of water, and may be obtained by the hydrolysis of products contained in coca leaves. It melts at 198°, and is lævo-rotatory; and on warming with alkalis, gives iso-ecgonine, which is dextro-rotatory. As an alcohol it forms a benzoyl derivative, and as an acid a methyl ester. (See Cocaine.)

Cocaine, or *benzoyl-l-ecgonine methyl ester*,



is the active constituent of the coca leaf (*Erythroxylon coca*), it melts at 98°, is lævo-rotatory, and is used in surgery for deadening pain. It has been synthesised by the action of benzoic anhydride and methyl iodide on ecgonine (B. 1885, **18**, 2953).

Hyoscyamine, which crystallizes in needles or plates, melting at 109°, resembles atropine closely, and is readily transformed into the latter under the influence of various alkalis (*Will*, B. **21**, 1725, 2777). In contact with water it is slowly hydrolysed to *l*-tropic acid and inactive tropine. Atropine is racemic hyoscyamine.

Various substitutes for cocaine have been recommended, as its solutions do not keep well. *Willstatter* (B. **29**, 1575, 2216) obtained an isomeride of ecgonine by the addition of HCN to tropinone (p. 566) and subsequent hydrolysis, and from this

α-cocaine was obtained by benzoylation and esterification. α-Cocaine contains both CO_2Me and COPh groups attached to the same carbon atom. **α-Eucaine** is a cheap substitute for cocaine prepared from triacetonamine, $NH<\begin{matrix}CMe_2\cdot CH_2\\CMe_2\cdot CH_2\end{matrix}>CO$ (p. 134), by addition of HCN, hydrolysis, benzoylation of the hydroxy-acid thus formed, and final methylation of the imino and carboxylic groups. Its structure is:

$$NMe<\begin{matrix}CMe_2\cdot CH_2\\CMe_2\cdot CH_2\end{matrix}>C(CO_2Me)\cdot O\cdot COPh$$

β-Eucaine has the formula:

$$NH<\begin{matrix}CMe_2 \quad CH_2\\CHMe\cdot CH_2\end{matrix}>CH\cdot O\cdot COPh$$

(*Harries*, B. **29**, 2730).

XLI. TERPENES AND CAMPHORS

For history of terpenes see *Tilden*, Science Progress, 1911, **6**, 46 Cf *Wallach's* "Terpene und Camphor", 1909.

Ethereal Oils.—Many plants, especially varieties of Coniferæ and of Citrus, contain, in their blossoms and fruits, oily substances to which they owe their peculiar fragrance or odour, and which can be obtained from them by distillation in steam or by pressure. These oils, "ethereal oils", were formerly grouped together in a special class, but now they are recognized as being more or less heterogeneous; thus oil of bitter almonds is benzoic aldehyde, and Roman oil of cumin is a mixture of cymene and cumic aldehyde, &c. Many of these ethereal oils contain unsaturated hydrocarbons, which are usually termed **terpenes**. The common hydrocarbons met with have the general formula $C_{10}H_{16}$, and are spoken of as terpenes proper, but, in addition to these, hydrocarbons, represented by the formula C_5H_8 and known as **hemiterpenes**, exist The commonest of these is **isoprene**, obtained by distilling caoutchouc. Hydrocarbons represented by the formula $C_{15}H_{24}$ are termed sesquiterpenes, and the more complex hydrocarbons, $(C_5H_8)_n$, polyterpenes. Certain ethereal oils consist chiefly of such hydrocarbons, *e.g.* turpentine, oil of citron, orange oil, and oil of thyme. Other oils contain appreciable amounts of oxygenated compounds, mainly of an alcoholic or ketonic character,

e.g. camphor and menthone, $C_{10}H_{16}O$, pulegone, &c. Many of these terpenes and ketones are reduced benzene derivatives, *e.g.* limonene, menthone; others again are more complex ring compounds, *e.g.* pinene and camphor. In addition to these two groups of compounds a third group has been discovered within recent years, namely, open chain olefinic alcohols, aldehydes, or ketones, *e.g.* citronellal, geraniol, linalool.

The terpenes are widely distributed in the vegetable kingdom, especially in the Coniferæ (*Pinus*, *Picea*, *Abies*, &c.), in the varieties of Citrus, &c. The products which are isolated in the first instance from the individual plants, and which according to their source are designated terpene, citrene (from oil of citron), hesperidene (from oil of orange), thymene (from thyme, carvene (from oil of cumin), eucalyptene, olibene, &c., have for the most part the formula $C_{10}H_{16}$, and approximately equal boiling-points (160°–190°); they are not, however, chemical individuals, but mixtures of isomeric compounds

With the exception of camphene they are all liquid, but it is hardly possible to separate them completely by fractional distillation (see table, p. 578, for boiling-points) The terpenes can, however, be obtained chemically pure from crystalline derivatives Quite recently, numerous compounds belonging to this class have been synthesised.

For simplicity the terpenes and allied oxygen compounds (camphors) may be divided into the following groups:—

A. Open-chain olefinic compounds.

B. Monocyclic terpenes (mainly reduced benzene derivatives).

C Complex cyclic terpenes

Practically all the compounds dealt with in these three divisions could have been discussed under the aliphatic and cyclic compounds. A clearer view, however, of their relationships is obtained by bringing them together under the general heading of terpenes and camphors.

A. Open-chain Olefinic Terpenes and Camphors

Isoprene, the best-known hemiterpene, is a diolefine represented by the constitutional formula, $CH_2:CMe\cdot CH:CH_2$, 2-methyl-$\Delta^{1,3}$-butadiene. It is a colourless liquid, b.-pt. 37°, is formed by the dry distillation of rubber, or by decomposing turpentine at a dull red heat (cf. *Staudinger*, B. **44**, 2212). At 300° it undergoes polymerization to diisoprene (probably

dipentene), and is transformed into products analogous to rubber when treated with concentrated hydrochloric acid, when kept for some time or when exposed to sunlight in the presence of traces of acid. Two syntheses of isoprene are of interest.

(*a*) From methyl-pyrrolidine by exhaustive methylation (*Euler*, J. pr. [ii], **57**, 132).

$$CH_2\text{—}CH_2 > NH \xrightarrow[\text{methylated}]{} CH_2\text{—}CH_2 > NMe_2I$$
$$CHMe\cdot CH_2 \qquad\qquad CHMe\cdot CH_2$$
$$\xrightarrow[\text{KOH}]{} CH_2{:}CH\cdot CHMe\cdot CH_2\cdot NMe_2$$
$$\xrightarrow[\text{methylated}]{} CH_2{:}CH\cdot CHMe\cdot CH_2\cdot NMe_3I$$
$$\xrightarrow[\text{KOH}]{} CH_2{:}CH\cdot CMe{:}CH_2 + NMe_3 + HI.$$

(*b*) From dimethyl-allene by the addition of two molecules of hydrogen bromide and subsequent elimination of the same (*Ipatieff*, *ibid.* **55**, 4):

$$CMe_2{:}C{:}CH_2 \longrightarrow CMe_2Br\cdot CH_2\cdot CH_2Br \longrightarrow CH_2{:}CMe\cdot CH{:}CH_2.$$

It has been suggested that indiarubber should be synthesised from isoprene, but the cost of the isoprene has so far interfered with the adoption of this method on the commercial scale.

Practically all the natural products belonging to this group contain oxygen and are either aldehydes or alcohols.

Citronellal, $CH_2:CMe\cdot CH_2\cdot CH_2\cdot CH_2\cdot CHMe\cdot CH_2\cdot CHO$, is an example of an olefine aldehyde, it is present in citronella oil and also in lemon-grass oil, together with citral and geraniol. It has b.-pt 205°–208°. Its aldehydic nature is proved by the readiness with which it is reduced to a primary alcohol, citronellol, and oxidized to a monobasic acid, citronellic acid, containing the same number of carbon atoms. By oxidizing its dimethyl-acetal, *Harries* and *Schauwecker* (B. **34**, 1498, 2981) obtained a dihydroxy-derivative, thus proving the presence of an olefine linking; and on further oxidation with chromic anhydride they obtained the acetal of a keto-aldehyde containing nine carbon atoms, thus proving that the double bond is between the 'ast and last but one carbon atoms with respect to the aldehyde group:

$$CH_2{:}CMe(CH_2)_3\cdot CHMe\cdot CH_2\cdot CHO + 4O$$
$$= CO_2 + H_2O + O{:}CMe(CH_2)_3\cdot CHMe\cdot CH_2\cdot CHO.$$

The positions of the methyl groups are proved by the rela-

tionship of the aldehyde to isopulegol, into which it is transformed when kept for some time, or more quickly when heated with acetic anhydride at 180°:

$$CHMe\langle^{CH_2\cdot CH_2}_{CH_2\cdot CHO}\rangle CH_2\cdot CMe{:}CH_2$$
$$\longrightarrow CHMe\langle^{CH_2\cdot CH_2}_{CH_2\cdot CH(OH)}\rangle CH\cdot CMe{:}CH_2.$$

The constitution of pulegol follows from the fact that when oxidized it yields isopulegone, and this with baryta is transformed into pulegone by the wandering of an olefine linking.

$$\text{Pulegone} = CHMe\langle^{CH_2\cdot CH_2}_{CH_2\cdot CO}\rangle C{:}CMe_2.$$

An interesting reaction of citronellal is its oxidation in alkaline solution with permanganate, when it yields acetone and β-methyladipic acid, a result which would lead to the conclusion that the double bond is in position 5:6 with respect to the CHO group.

The only manner of reconciling this reaction with the reactions already given is the assumption that in the oxidation in alkaline solution a wandering of the double bond occurs:

$$CH_2{:}CMe\cdot(CH_2)_3\cdot CHMe\cdot CH_2\cdot CHO$$
$$\longrightarrow CMe_2{:}CH(CH_2)_2\cdot CHMe\cdot CH_2\cdot CHO.$$

Citral or **geranial**, $C_{10}H_{16}O$, occurs in both oil of lemons and of oranges, and may also be obtained by the oxidation of geraniol. Lemon-grass oil contains 70–80 per cent. It is a colourless oil, and distils at 110°–112° under 12 mm. pressure Its constitution is represented as:

$$CMe_2{:}CH\cdot CH_2\cdot CH_2\cdot CMe{:}CH\cdot CHO.$$

Its aldehydic nature follows from its reduction to **geraniol**, and its oxidation to an acid containing the same number of carbon atoms, namely, **geranic** acid. Its unsaturated character and the positions of the double bonds within the molecule follow from its general properties, but more especially (*a*) from its products of oxidation, viz. acetone, lævulic acid, and carbon dioxide:

$$CMe_2{:}CH\cdot CH_2\cdot CH_2\cdot CMe{:}CH\cdot CHO$$
$$\longrightarrow Me_2CO + CO_2H\cdot CH_2\cdot CH_2\cdot COMe + 2CO_2;$$

(*b*) from its conversion into methyl-heptenone and acetaldehyde by means of potassium carbonate:

$$CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CMe{:}CH{\cdot}CHO = CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}COMe + CH_3{\cdot}CHO.$$
$$+ \quad OH_2$$

When heated with potassium hydrogen sulphate, citral is converted into *p*-cymene.

Both citral and geranic acid have been synthesised by *Barbier* and *Bouveault* (C. R. 1896, **122**, 393) 1-Methyl-Δ^1-heptenone reacts with metallic zinc and iodo-acetic acid (*Reformatsky* reaction), yielding the compound:

$$CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}C\begin{cases}CH_2{\cdot}CO_2H\\OZnI\\CH_3\end{cases}$$

With dilute acid this yields the hydroxy-acid:

$$CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CMe(OH){\cdot}CH_2{\cdot}CO_2H,$$

and when this is distilled with acetic anhydride, water is eliminated and geranic acid formed.

Geranic acid, when reduced in the form of its ethyl ester with sodium and amyl alcohol, yields *i*-rhodinic acid

$$CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CHMe{\cdot}CH_2{\cdot}CO_2H,$$

which is structurally isomeric with citronellic acid, and when ethyl rhodinate is reduced with sodium and alcohol, the corresponding primary alcohol, **rhodinol**, is formed.

Citral occurs in two stereoisomeric forms, termed *a*- and *b*-citrals. They are both inactive, and the isomerism is of the same type as that met with in the crotonic acids and fumaric and maleic acids (p. 243).

Geraniol, $C_{10}H_{18}O$, is the alcohol corresponding with citral, and is the chief constituent (90 per cent) of Indian geranium oil, which is largely used for adulterating rose oil. Its constitution follows from its relationship to citral and geranic acid, into which it is readily oxidized.

By reducing citral with alcohol and sodium amalgam, two stereoisomeric alcohols, geraniol and nerol, are obtained, and both yield citral when reoxidized. Both alcohols yield terpineol by the action of acetic acid containing 1 to 2 per cent of sulphuric acid, but nerol reacts about nine times as readily as geraniol. The formation of terpineol can be accounted for by the addition and withdrawal of water. The two alcohols

are structurally identical, and are represented by the two stereochemical formulæ.

I. $CMe_2{:}CH{\cdot}(CH_2)_2{\cdot}C(CH_2{\cdot}OH){=}CH{\cdot}CH_3$ (Geraniol)

II. $CMe_2{:}CH{\cdot}(CH_2){\cdot}C(CH_3){=}CH{\cdot}CH_2{\cdot}OH$ (Nerol)

as No. II would lose water more readily than No I to form a six-membered ring. It is probable that citral *a* corresponds with geraniol, and citral *b* with nerol.

Linalool or **coriandrol** is isomeric with geraniol, into which it is readily transformed by the action of dilute organic acids. It occurs as linalyl acetate in lavender, sage, and coriander oils. It is optically active, reacts as a tertiary alcohol, and hence is structurally- and not stereo-isomeric with geraniol. Its reactions agree best with the formula:

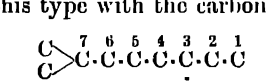
$$CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CMe(OH){\cdot}CH{:}CH_2,$$

and its conversion into geraniol probably depends upon the addition and subsequent removal of water, the glycol,

$$CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CMe(OH){\cdot}CH_2{\cdot}CH_2{\cdot}OH,$$

being formed as the intermediate product. *l*-Linalool reacts with acetic anhydride, yielding nerol, geraniol, and *d*-terpineol.

Compounds of this type with the carbon system



are readily transformed into derivatives of *p*-cymene by union between carbon atoms numbers 1 and 6 (cf. p 571), or into tetrahydrobenzene derivatives by union of numbers 2 and 7 (cf. Ionone, p 589; also conversion of citral into α- and β-cyclo-citrals, cyclic βγ and αβ unsaturated aldehydes).

B. Monocyclic Terpenes and Camphors

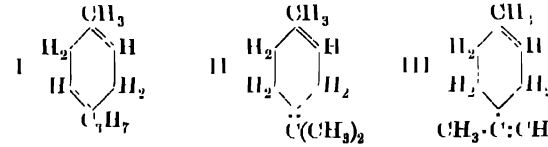
I. Terpenes.—These compounds are to be regarded as hydro-derivatives of cymene (p. 352). Their close relationship to cymene can be shown in very different ways: *e.g.* (*a*) the hydrocarbon **terpinene** when heated with iodine is transformed into *p*-cymene, *i.e.* *p*-methyl-isopropyl benzene; (*b*) the ketone

carvone when heated with mineral acids yields carvacrol, *i.e.* 1-methyl-2-hydroxy-4-isopropyl benzene (p. 417), (*c*) on oxidation many terpenes yield terephthalic acid, (*d*) when brominated and then reduced many monocyclic terpenes yield benzene hydrocarbons (B. 1898, **31**, 2068).

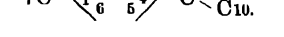
The unsaturated nature of these compounds follows from the readiness with which they form additive compounds, they yield **dihydrochlorides**, $C_{10}H_{18}Cl_2$, **tetrabromides**, $C_{10}H_{16}Br_4$, **nitroso-chlorides**, $C_{10}H_{16}(NOCl)_2$, **nitrosites**, $C_{10}H_{16}(NO)(NO_2)$, and **nitrosates**, $C_{10}H_{16}N_2O_4$. These compounds are of considerable importance, as most of them are well-defined crystalline compounds with definite melting-points, and can therefore be made use of in separating and identifying the various liquid terpenes The nitroso-chlorides were first prepared by *Tilden* (J. C S. 1877, 554), by the direct action of nitrosyl chloride, but are now usually obtained by *Wallach's* method, viz by the action of a mixture of ethyl nitrite, acetic and hydrochloric acids on the hydrocarbon. The nitrosites are usually obtained by the action of sodium nitrite and acetic acid on the hydrocarbon, and the nitrosates by the direct addition of nitric peroxide or by the action of amyl nitrite and concentrated nitric acid.

An interesting group of compounds are the **nitrolamines**, obtained by the action of amines (piperidine or benzylamine) on the nitroso-chlorides. They contain the NHR-group in place of the chlorine of the nitroso-chlorides Such compounds crystallize well, and can be used for identifying the various terpenes.

All these reactions point to the presence (*a*) of a six-membered carbon ring in the monocyclic terpenes; (*b*) to the presence of two side chains, usually in *p* positions, one consisting of the CH_3 group, and the second containing the grouping $-C<^{C}_{C}$; (*c*) to the presence of two double bonds in the molecule. These may be both in the carbon ring, or one in the ring and one in a side chain, *e.g.*.



Fourteen such isomerides are theoretically possible. The carbon atoms are usually numbered as follows:



The saturated compound $C_{10}H_{20}$, viz. *p*-methyl-isopropyl-hexamethylene, is called **terpane***, and the compounds $C_{10}H_{16}$ are **terpadienes** I is Δ-1 4-terpadiene, II is Δ-1.4 (8)-terpadiene, and III Δ-1 8 (9)-terpadiene.

The double linking in No. II between a carbon atom in the ring and a carbon of a side chain is termed a *semicyclic* linking. Such an unsaturated linking is quite stable under the influence of heat, but in the presence of acids it wanders into the nucleus, *e.g.* $\Delta^{4(8)}$ *p*-menthene is readily transformed into Δ^{3} *p*-menthene.

A few of the terpenes contain the methyl- and isopropyl-groups in the meta positions, *e.g.* sylvestrene; such compounds are termed *m*-terpadienes.

The nitroso-chlorides are frequently colourless, and then appear to be bimolecular, some give blue solutions containing the monomolecular form Compounds with a semicyclic linking $>C:CR_2$ yield unimolecular blue nitroso-chlorides volatile with steam. The blue compounds are true nitroso-compounds. When the NO-group becomes attached to $>CH$ it usually passes over into the isonitro-group $>C:N\cdot OH$, and the compound becomes colourless.

The following hydrocarbons belong to this group:—

Dipentene, Δ-1:8 (9)-**terpadiene** or **inactive limonene** (see formula III; for constitution cf. B. 1895, **28**, 2145; 1898, **31**, 1402; 1900, **33**, 1457). It occurs together with cineol in *Oleum cinæ*, and is prepared by heating pinene, camphene, sylvestrene, or limonene to 250°–270° for several hours, and also by the abstraction of hydrogen chloride from its dihydrochloride. It is further produced from pinene under the influence of dilute alcoholic sulphuric acid, from terpin hydrate and terpineol by the elimination of water, by the polymerization of isoprene, and, together with the latter substance, on distilling caoutchouc. Its formation from isoprene, $CH_2:C(CH_3)\cdot CH:CH_2$, by heating at 300° is a synthesis, since isoprene has been synthesised (p. 569). It is a liquid of pleasant odour like that of oil

* The name **menthane** is sometimes used for this hydrocarbon and **menthadienes** for the terpadienes.

of citron, boils at 175°–176°, and is more stable than pinene, although it can still be transformed into terpinene by acids. It readily forms dipentene dihydrochloride with hydrochloric acid, and with bromine a crystalline tetrabromide melting at 125°. Its (inactive) nitroso-chloride yields, by the elimination of hydrogen chloride, the so called **nitroso-dipentene** (inactive carvoxime), melting at 93°.

d-**Limonene**, *hesperidene*, *citrene*, or *carvene* The oil of the orange rind consists almost entirely of dextro-limonene, which is also the chief constituent of carvene, oil of dill, oil of erigeron, &c., oil of citron consists mainly of *d*-limonene and pinene It boils at 175°, and forms a dextro-rotatory tetrabromide, $C_{10}H_{16}Br_4$, which melts at 104° The dextro- and lævo-tetrabromides are identical, except that their crystals are the mirror images of one another. Dextro-limonene is very readily racemized to dipentene.

l-**Limonene** is present together with lævo-pinene in the oil of fir cones.

l- and *d*-limonenes yield nitroso-chlorides, $C_{10}H_{16}NOCl$, of corresponding rotatory powers, and, on the elimination of hydrogen chloride from these, *l* and *d*-**nitroso-limonenes**, $C_{10}H_{15}NO$, which are identical with the carvoxmes

The conversion of geraniol into dipentene is of considerable interest (*Tiemann* and *Schmidt*, B 1895, **28**, 2137)·

$$(CH_3)_2C{:}CH\cdot CH_2\cdot CH_2\cdot C(CH_3){:}CH\cdot CH_2OH$$

Geraniol

$$\dashrightarrow (CH_3)_2C(OH)\cdot CH_2\cdot CH_2\cdot CH_2\cdot C(CH_3)(OH)\cdot CH_2\cdot CH_2OH \quad (+ 2H_2O)$$

Terpin hydrate

$$\dashrightarrow (CH_3)_2(OH)C\cdot CH\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot CH_2\end{matrix}C(OH)(CH_3) \quad (- H_2O)$$

Terpin

$$\longrightarrow CH_3\cdot C\begin{matrix}CH_2\cdot CH_2\\ CH_2=\end{matrix}CH\begin{matrix}-CH_2\cdot CH_2\\ -CH_2\cdot CH=\end{matrix}C\cdot CH_3 \quad (- 2H_2O)$$

Dipentene

Dipentene readily combines with hydrogen chloride, yielding a **dihydrochloride**, $C_{10}H_{18}Cl_2$, which melts at 50°. The same compound is also formed by the action of hydrogen chloride on limonene or on pinene, and when left in contact with aqueous alcohol yields terpin hydrate, $C_{10}H_{19}(OH)_3$ (cf formula above), in the form of large rhombic crystals melting at 117°

Terpinene, probably Δ-1:3-*terpadiene*, is one of the most stable of the terpenes. It may be obtained by the action of alcoholic sulphuric acid on dipentene, or on other compounds

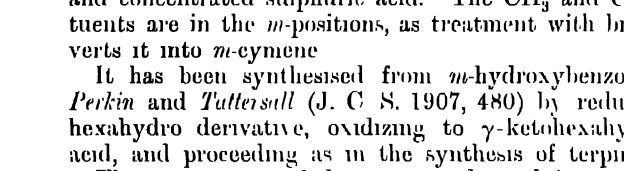
which yield dipentene as an intermediate product, *e.g.* by shaking pinene with concentrated sulphuric acid, or by boiling terpin hydrate with dilute sulphuric acid. It boils at 179°–181°, is optically inactive, and most of its derivatives are oils, with the exception of the nitrosite, which melts at 155°.

Terpinolene, Δ-1:4 (8)-*terpadiene*, is formed when terpineol is boiled for a short time with oxalic acid solution. It boils at 183°–185°, and is readily transformed by acids into terpinene. It forms a blue nitroso-chloride.

Sylvestrene, *Carvestrene*, Δ-1:8 (9)-*m-terpadiene*, b.-pt. 175°, is the chief dextro-rotatory constituent of Swedish and Russian oil of turpentine. It is one of the most stable of the terpenes, and gives a magnificent blue coloration with acetic anhydride and concentrated sulphuric acid. The CH_3 and C_3H_7 substituents are in the *m*-positions, as treatment with bromine converts it into *m*-cymene.

It has been synthesised from *m*-hydroxybenzoic acid by *Perkin* and *Tattersall* (J. C. S. 1907, 480) by reducing to its hexahydro derivative, oxidizing to γ-ketohexahydrobenzoic acid, and proceeding as in the synthesis of terpineol.

The constitution of dipentene is derived from its relationship to terpineol (p. 579), from which it is obtained by the elimination of water. If molecular rearrangement does not occur during this reaction, it is clear that dipentene must have a constitutional formula corresponding with I or II.



Formula I is not asymmetric, and therefore cannot represent the molecules of *d*- and *l*-limonenes and of dipentene; formula II, on the other hand, contains an asymmetric carbon atom, the one indicated by an asterisk, the molecule is asymmetric, and can form *d*-, *l*-, and *r*-modifications.

The correctness of formula II is confirmed by a study of some of the reactions of dipentene.

Dipentene forms a nitroso-chloride (colourless), and this with alkalis gives the oxime of carvone. The oxime when hydrolysed yields carvone, and this on reduction yields dihydrocarveol, a secondary alcohol formed by the addition of two

atoms of hydrogen to one of the ethylene linkings and two atoms of hydrogen to the carbonyl group. Dihydrocarveol, when oxidized yields a ketonic alcohol, $CH_3 \cdot C_6H_9(OH) \cdot CO \cdot CH_3$, proving the presence of the $\cdot C(CH_3):CH_2$ group in dihydrocarveol, carvone, and dipentene.

Terpinolene is also formed from terpineol by the elimination of water, and should therefore be represented by formula No. I, a formula which is in harmony with the inactivity of the hydrocarbon. The stable terpinene most probably contains conjugate double bonds, and as it is formed from terpinoline by the action of acids it is probably Δ-1 3-terpadiene.

Phellandrene.—Three isomeric phellandrenes exist in nature, *d*-α-phellandrene in oil of bitter fennel and in elemi oil, *l*-α-phellandrene in Australian eucalyptus oil (*Eucalyptus amygdalina*), and *d*-β-phellandrene in water dropwort (*Phellandrium aquaticum*). The *d*- and *l*-α-phellandrenes are optical antipodes, and are both Δ-1:5-*terpadienes*. The b.-pt. is 62°/12 mm. It is transformed into terpinene by the action of acids, and its dibromide with alkalis yields cymene. This constitution follows from the fact that nitro-α-phellandrene, when carefully reduced, yields active carvotanacetone, Δ-5-terpene-2-one, and has been confirmed by the synthesis of α-phellandrene from 4-isopropyl-Δ2-hexenone (A. **359**, 285):

$$C_3H_7 \cdot CH\langle \begin{matrix} CH_2 \cdot CH_2 \\ CH:CH \end{matrix} \rangle CO \xrightarrow[\text{Grignard}]{} C_3H_7 \cdot CH\langle \begin{matrix} CH_2 \cdot CH_2 \\ CH:CH \end{matrix} \rangle CMe \cdot OH \xrightarrow[\text{dehydrated}]{} C_3H_7 \cdot CH\langle \begin{matrix} CH_2 \cdot CH \\ CH:CH \end{matrix} \rangle CMe,$$

and also by its synthesis from carvone (p. 579).

Carvone $\xrightarrow{HBr}$ carvone hydrobromide $\xrightarrow[\text{reduced}]{}$ Δ6-terpen-2-one $\xrightarrow{PCl_5}$ 6-chloro-Δ-1:5-terpadiene $\xrightarrow[\text{reduced}]{}$ α-phellandrene.

β-Phellandrene is Δ-2:1 (7)-*terpadiene*. It has boiling-point 57°/11 mm., yields two nitrosites, melting-point 97° and 102°. Its constitution is based on the fact that it is oxidized by atmospheric oxygen to 4-isopropyl-Δ-2-hexenone (A. **343**, 29), and on its synthesis from carvone (J. pr. [ii], **72**, 193; **75**, 141).

Carvone $\xrightarrow[\text{reduced}]{}$ carvomenthol (terpane-2-ol) $\xrightarrow[\text{dehydrated}]{}$ Δ-1-terpene $\xrightarrow{\text{bromine}}$ terpenedibromide $\xrightarrow[\text{alc. potash}]{}$ β-phellandrene

Menthene, obtained from menthol by the elimination of water, is Δ-3-terpene; when oxidized it yields a glycol, which on further oxidation gives β-methyladipic acid:

$$CHMe\langle\begin{matrix}CH_2\cdot CH\\ CH_2\cdot CH_2\end{matrix}\rangle C\cdot C_3H_7 \rightarrow CHMe\langle\begin{matrix}CH_2\cdot CO_2H\\ CH_2\cdot CH_2\cdot CO_2H.\end{matrix}$$

It has been synthesised by *Wallach* (B. **39**, 2504) by condensing 1-methylcyclohexan-4-one with ethyl α-bromoisobutyrate and zinc, hydrolysing and eliminating CO_2 and water.

A synthetical **terpene** or **dihydro-cymene** boiling at 174° has been prepared from succinylo-succinic ester (pp. 342, 469) (B. **26**, 233). It shows the complete terpene character, has a turpentine odour, becomes resinous on exposure to the air, decolorizes permanganate at once, and takes up bromine.

SUMMARY OF DERIVATIVES

	Boiling-point	Tetra-bromide M.-p.	Dihydro-chloride M.-p.	Nitrosite M.-p.
Limonene..	175°	104°	50°	. .
Dipentene....	175°	125°	50°	...
Terpinolene...	183°–185°	116°	. .	...
Terpinene.. ..	179°–181°	oil	oil	153°
Phellandrene	171°–172°	oil	oil	105°
Sylvestrene ..	175°	135°	72°	

II **Camphor Compounds.—Alcohols and Ketones**

Menthol, 3-*terpanol*, mint camphor, $C_{10}H_{20}O$:

$$CH_3\cdot CH\langle\begin{matrix}CH_2\cdot CH(OH)\\ CH_2 \text{——} CH_2\end{matrix}\rangle CH\cdot CH(CH_3)_2$$

The *l*-modification is the chief constituent of oil of peppermint. It melts at 43°, has a strong odour of peppermint, and is used as an antiseptic and anæsthetic. When heated with copper sulphate it yields cymene, when reduced with hydriodic acid, hexahydrocymene, and on oxidation with permanganate it yields β-methyladipic acid, and several fatty acids. As the formula contains three asymmetric carbon atoms, several stereo-isomerides are possible.

The corresponding ketone **menthone**, 3-*terpanone*, $C_{10}H_{18}O$, is obtained when the alcohol is oxidized with dichromate (*Beckmann*, A. 1891, **262**, 31), and also occurs in oil of peppermint. It boils at 207°, and has the characteristic properties

of a ketone; its **semicarbazone** melts at 184°. It is readily converted into thymol (1-methyl-3-hydroxy-4-isopropyl-benzene) by bromination and elimination of hydrogen bromide, and when oxidized yields β-methyladipic acid. Hence follows the constitution, which is supported by its synthesis by the distillation of calcium β-methyl-α'-isopropylpimelate (*Kotz* and *Schuarz*, A. **357**, 206):

$$\begin{matrix} CH_2\cdot CHMe\cdot CH_2\cdot COO \\ CH_2\cdot CH(C_3H_7)\cdot COO \end{matrix}\!\!>\!Ca \;\rightarrow\; \begin{matrix} CH_2\cdot CHMe - CH_2 \\ CH_2\cdot CH(C_3H_7)\cdot CO \end{matrix}$$

An unsaturated ketone—**pulegone**, Δ-4 (8)-*terpene*-3-*one*, may be obtained from oil of pennyroyal. It is isomeric with ordinary camphor, and on reduction yields menthone Its constitution follows from the fact that when heated with water it yields acetone and methylcyclohexanone

Isomeric with menthol is **carvomenthol** or *terpane*-2-*ol*.

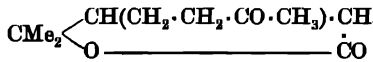
Carvone, Δ-6:8 (9)-*terpadiene*-2-*one*, is the chief constituent of oil of carraway seeds, and is widely distributed in the vegetable kingdom. It is a liquid, distils at 228°, exists in *d*-and *l*-modifications, and has the properties of an unsaturated ketone (cf. A. 1897, **297**, 122). With hydroxylamine it yields carvoxime, which is identical with nitroso-limonene When heated with phosphoric acid carvone is isomerized to carvacrol.

Terpineol, Δ-1-*terpen*-8-*ol*, does not occur in large quantities naturally, but is obtained readily from natural products, *e.g.* by the action of dilute potash on limonene hydrochloride, or by the hydration of pinene hydrate. It has m.-pt 37°, b.-pt. 218°, and $[\alpha]_D - 106°$. When treated with dilute acids it can give dipentene, terpinolene, terpinene, terpin hydrate, cineol or cymene, according to the conditions Its constitution is of importance, as those of several terpenes are deduced from that of terpineol. The constitution is based on (1) examination of its decomposition products, (2) its synthesis.

By means of dilute permanganate two hydroxyls are added to the double bond, and 1·2:8-trihydroxyterpane (trihydroxyhexahydro-*p*-cymene) is formed, and this on further oxidation yields a ketolactone, homoterpenylic methyl ketone, which can be oxidized to acetic and terpenylic acids. The constitution of the latter has been proved to be:

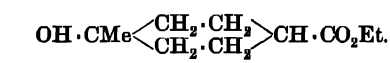
$$CMe_2\!<\!\begin{matrix} CH(CH_2\cdot CO_2H)\cdot CH_2 \\ O \text{———} CO \end{matrix}$$

from its method of synthesis (*Simonsen*, J. C. S. 1907, 184). This gives the formula:

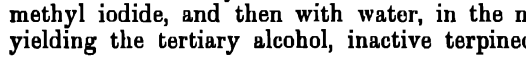


for homoterpenylic methyl ketone, and proves the 1:2:8-positions of the three hydroxyl groups in the first oxidation product, and the Δ-1-position of the ethylene linking and position 8 of the hydroxyl group in terpineol.

Its synthesis (*Perkin*, J. C. S. 1904, 654) is from δ-keto-hexahydrobenzoic acid (δ-keto-cyclohexane-carboxylic acid). The ester of this acid reacts with magnesium methyl iodide, and then with water, yielding:



By the action of fuming hydrobromic acid the hydroxyl is replaced by bromine, and then by the action of pyridine hydrogen bromide is eliminated and Δ-3-tetrahydro-*p*-toluic acid is formed. The ethyl ester of this acid reacts with magnesium methyl iodide, and then with water, in the normal manner, yielding the tertiary alcohol, inactive terpineol:



and by the elimination of water from this alcohol dipentene was obtained.

This method of synthesis has been extended by *Perkin* and his students to a large number of cases, and they have obtained alcohols and unsaturated hydrocarbons analogous to the natural products, but which, so far, have not been obtained naturally. From Δ-1-tetrahydro-*p*-toluic acid, Δ-3-*p*-terpen-8-ol, and Δ-1:8 (9) terpadiene. From hexahydro-*o*-toluic acid, compounds similar to terpineol and dipentene were obtained, but with the substituents in *o*-positions. From hexahydrobenzoic acid a compound was obtained analogous to dipentene, but without the methyl substituent in position 1. By using optically active Δ-1-tetrahydro-*p*-toluic acid, an active alcohol and terpene were synthesised. (Compare J. C. S. 1905, 639, 655, 661, 1067, 1083; 1906, 832, 839; 1908, 573, 1871, 1876; 1910, 2129, 2147; 1911, 118, 518, 526, 727, 741.)

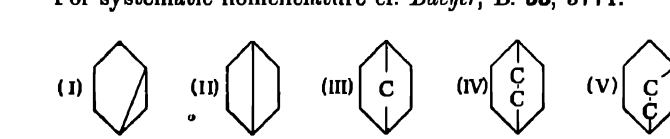
Terpin, *p-terpa*-1:8-*diol*, has been synthesised by the action

of magnesium methyl iodide on both carbonyl groups of ethyl cyclohexanone-4-carboxylate (*Kay* and *Perkin*, J. C. S. 1907, 372), and is also formed by boiling terpineol with dilute sulphuric acid. It exists in two stereoisomeric modifications, *cis* and *trans*. The *cis* is the common form, and combines with water to give **terpin hydrate**, $C_{10}H_{22}O_3$, which forms well-developed crystals, m.-pt. 116°. When dehydrated the terpins yield terpinene, terpinolene, terpineol, and **cineol**; the latter is an inner anhydride (ether) formed by the elimination of water from the two hydroxyl groups.

C. Complex Cyclic Terpenes and Camphors

The compounds belonging to this group are bicyclic, *i.e.* the molecule is built up of two rings. Benzene or reduced benzene derivatives containing a diagonal linking in the *m*- or *p*-position (examples I and II) are bicyclic, also the compounds which can be regarded as derived from a single ring by the introduction of a *bridge* consisting of one or more carbon atoms (examples III, IV, and V).

For systematic nomenclature cf. *Baeyer*, B. **33**, 3771.



I. **Terpenes.**—**Pinene**, $C_{10}H_{16}$, is the chief constituent of German and American oil of turpentine, oil of juniper, eucalyptus, oil of sage, &c. It forms, together with sylvestrene and dipentene, Russian and Swedish turpentine oil.

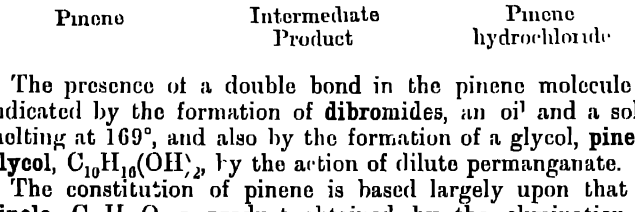
Oil of turpentine is obtained by distilling turpentine, the resin of pines, with steam, colophonium (fiddle resin) remaining behind. It is a colourless, strongly refracting liquid of characteristic odour, almost insoluble in water, but readily soluble in alcohol and ether. It dissolves resins and caoutchouc (being therefore used for the preparation of oil paints, lakes), also sulphur, phosphorus, &c. Pinene absorbs oxygen from the air with the formation of ozone and production of resin, minute quantities of formic acid, cymene, &c., being formed at the same time. Dilute nitric acid gives rise either to terephthalic acid in addition to fatty acids, or—under other conditions—to terpenylic acid (p. 579), $C_8H_{12}O_4$ (which belongs

to the fatty series). Heating with iodine transforms it into cymene, the action being violent. It acts as an antiseptic, and arrests the secretions (*e.g.* that of the kidneys).

It exists in three stereoisomeric modifications: *d*-pinene or australene occurs in large quantities in German, Russian, and Swedish oils; *l*-pinene or terebenthene in French turpentine oil; *d-l*-pinene is obtained by heating pinene nitroso-chloride with aniline:

	$[\alpha]_D^{20°}$	B.-pt.	$d_{4°}^{20°}$
d.....	+45°	156°	0·858
l.....	−43·4°	156°	0·858
d-l.....	0°	156°	0·858

Pinene has all the characteristic properties of an unsaturated compound. It forms a **nitroso-chloride** $(C_{10}H_{16}, NOCl)_2$, colourless crystals melting at 103°, which is used for isolating pinene from mixtures; also a **hydrochloride**, $C_{10}H_{17}Cl$, a white crystalline solid melting at 131°, with a camphor-like odour, hence the name "artificial camphor". This is insoluble in water, but readily soluble in alcohol, and if hydrogen chloride is eliminated by weak alkali, *e.g.* by heating it with soap or with silver acetate, camphene is obtained. It is identical with bornyl chloride, and on oxidation yields camphoric and apocamphoric acid. It is probable that by conversion into the hydrochloride an intramolecular rearrangement has taken place, as indicated by the following formulæ.

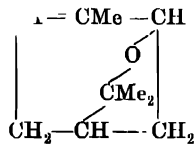


Pinene — Intermediate Product — Pinene hydrochloride

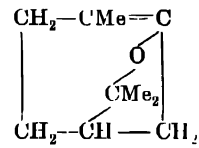
The presence of a double bond in the pinene molecule is indicated by the formation of **dibromides**, an oil and a solid melting at 169°, and also by the formation of a glycol, **pinene glycol**, $C_{10}H_{16}(OH)_2$, by the action of dilute permanganate.

The constitution of pinene is based largely upon that of **pinole**, $C_{10}H_{16}O$, a product obtained by the elimination of water from **soberol**, $C_{10}H_{16}(OH)_2$, which is formed when pinene is left exposed to sunlight in contact with air and water. With

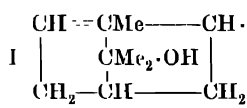
ate, pinole, which is an unsaturated ether, $C_{10}H_{16}O(OH)_2$, and this on further oxidation with nitric alcohol, **sobrerythritol**, $C_{10}H_{16}(OH)_4$, is converted to terpenylic acid. Pinole presumably on grouping of carbon atoms as terpenylic acid should be either:



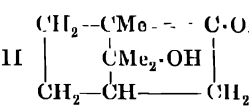
or



Sobrerol would then be



or



but since sobrerol on further oxidation yields a tetrahydric alcohol and not a dihydroxy-ketone, formula I is correct, and the formula on p 582 follows for pinene (*Wagner*).

When boiled with dilute acids pinene yields terpineol or its esters, such a transformation is explicable if the assumption is made that the four-membered ring is unstable, and that a rupture between the CMe_2 and upper CH-group occurs. A similar rupture, accompanied by the wandering of a chlorine atom, occurs in the transformation of pinene nitroso-chloride into hydrochlorocarvoxime under the influence of hydrochloric acid.

When pinene is oxidized with permanganate the double linking is broken and a monobasic ketonic acid, **pinonic acid**,

$$CO_2H \cdot CH_2 \cdot CH\langle \begin{matrix} CMe_2 \\ CH_2 \end{matrix} \rangle CH \cdot CO \cdot CH_3,$$

is formed, and this on further oxidation yields the dibasic acid **pinic acid**,

$$CO_2H \cdot CH_2 \cdot CH\langle \begin{matrix} CMe_2 \\ CH_2 \end{matrix} \rangle CH \cdot CO_2H,$$

from which **norpinic acid**, 1:1-*dimethyl-cyclobutane*-2:4-*dicarboxylic acid*, can be obtained (*Baeyer*, B. 29, 1907), indicating that the four-membered ring is stable in the presence of

oxidizing agents, although readily ruptured by hydrolysing agents, *e.g.* pinonic acid yields when hydrolysed a lactone, homoterpenylic methyl ketone (cf. p. 580).

$$OH\cdot CO\cdot CH_2\cdot CH\langle{}^{CMe_2}_{CH_2}\rangle CH\cdot CO\cdot CH_3$$
$$\rightarrow OH\cdot CO\cdot CH_2\cdot CH\langle{}^{CMe_2OH}_{CH_2\cdot CH_2\cdot CO\cdot CH_3}$$
$$\rightarrow O\langle{}^{CMe_2}_{CO\cdot CH_2}\rangle CH\cdot CH_2\cdot CH_2\cdot CO\cdot CH_3$$

The only reactions of pinene difficult to account for by means of *Wagner's* formula are its oxidation to isoketocamphoric acid, isocamphoronic acid, and terebic acid (*Tiemann* and *Semmler*, B. **29**, 529, 3027; *Perkin*, Proc 1900, 214)

Bornylene is obtained by the action of alkalis on bornyl iodide (from pinene and hydrogen iodide), and as it is readily oxidized to camphoric acid it is represented by formula I.

The corresponding saturated hydrocarbon **camphane**, $C_{10}H_{16}$, the parent substance of the camphor group, is obtained by reducing bornyl iodide. It melts at 154°, and is optically inactive, its molecule should therefore be symmetrical

I $CH_2\cdot CMe\cdot CH$ / CMe_2 / $CH_2\cdot CH{=}CH$ — Bornylene

II $CH_2\cdot CMe\cdot CO$ / CMe_2 / $CH_2\cdot CH{-}CH_2$ — Camphor

III $CH_2\cdot CMe\cdot CO_2H$ / CMe_2 / $CH_2\cdot CH{-}CO_2H$ — Camphoric acid

Camphene, *d* and *l*, is a solid, m.-pt. 50°. It can be obtained from pinene by combining with hydrogen chloride, forming bornyl chloride, and then removing hydrogen chloride by means of alkalis For some years it was represented by formula I, but it does not yield camphoric acid when oxidized. *Harries* and *Palmer* (B. 1910, **43**, 1432) have shown that it forms an ozonide when its acetic-acid solution is saturated with ozone, and that this when warmed yields a mixture of camphenilone (30 per cent) (IV),

IV $CMe_2\cdot CH\cdot CH_2$ / CH_2 / $CO{-}CH\cdot CH_2$

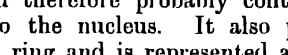
V $CMe_2\cdot CH\cdot CH_2$ / O CH_2 / $CO{-}CH\cdot CH_2$

VI $CMe_2\cdot CH\cdot CH_2$ / CH_2 / $CH_2{:}C{-}CH\cdot CH_2$

and *d*-hydroxy-camphenilic acid lactone (50 per cent) (V), and they therefore suggest formula VI for camphene. The for-

mation of camphene from bornyl chloride must thus involve molecular rearrangements.

Sabinene occurs in marjoram oil; it has b.-pt. 163°–165° and $[\alpha]_D$ + 80°. It forms a hydrochloride and a nitroso-chloride; when oxidized it yields a ketone by the replacement of CH_2 by O, and therefore probably contains a methylene group attached to the nucleus. It also probably contains a three-membered ring and is represented as



The tri-ring is readily ruptured, as sabinene and its derivatives can be transformed into terpinene and related hydroxy compounds. α and β Thujenes, $C_{10}H_{16}$ (*Tschugaeff*, B. **34**, 2279; **37**, 1481), also contain a tri-ring and a double linking in positions 1 and 3 respectively.

II. **Camphors.**—The most important variety of camphor is:

Common or **Japan camphor**, $C_{10}H_{16}O$, which is found in the camphor tree (*Laurus camphora*), and can be obtained from the latter by distillation in steam. It forms colourless, transparent, glistening prisms of characteristic odour. It melts at 175°, boils at 204°, has a sp. gr. 0·985, and can be sublimed readily. It is dextro-rotatory in alcoholic solution, the amount of rotation varying with the source of the camphor. When distilled with phosphoric anhydride it yields cymene; zinc chloride at high temperatures also transforms camphor into cymene, though in the latter case the reaction is less simple:

$$C_{10}H_{16}O = C_{10}H_{14} + H_2O.$$

When heated with iodine it yields carvacrol, *i.e.* hydroxy-cymene (p. 417), just as oil of turpentine yields cymene. Nitric acid oxidizes it to the dibasic **camphoric acid**, $C_8H_{14}(CO_2H)_2$, which somewhat resembles phthalic acid (see B. **23**, 218), and then to **camphoronic acid**, unsym. trimethyl-carballylic acid, &c. Camphor reacts with hydroxylamine to produce **camphor-oxime**, $C_{10}H_{16}(NOH)$, and therefore contains a carbonyl group, and with nitrous acid to produce **isonitroso-camphor**, $C_{10}H_{14}O{:}N{\cdot}OH$, and thus contains the group $\cdot CH_2 \cdot CO$. The oxime by the loss of water is converted into the **cyanide**, $C_9H_{15}{\cdot}CN$, which yields **campholenic acid**, $C_9H_{15}{\cdot}CO_2H$, on

saponification, and **camphylamine**, $C_9H_{15}(CH_2 \cdot NH_2)$, on reduction (B. **21**, 1125).

A considerable amount of attention has been devoted by various chemists to the question of the constitution of camphor (*Lapworth*, B. A Report, 1900, 299). At first, great importance was attached to the readiness with which camphor can be transformed into benzene derivatives, *e.g.* cymene and carvacrol, and attempts were made to represent it as a simple six-carbon ring compound, *e.g. Kekulé.*

$$CMe_2 \cdot CH\begin{matrix}\diagup CH_2 \cdot CO \\ \diagdown CH_2 \cdot CH\end{matrix}\diagdown\!\!\diagup CMe,$$

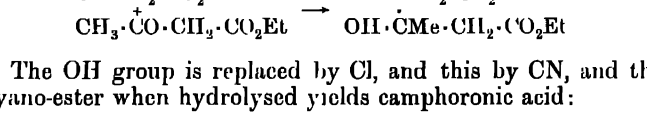
whereas others represented it as a bridged six-carbon ring. In 1893 *Bredt* suggested the formula II (p 584), which is now generally accepted, and which has been confirmed recently by the synthesis of camphoric acid *Bredt* drew especial attention to the oxidation products of camphor, namely camphoric, camphoronic, and trimethyl-succinic acid previously obtained by *Koenigs* He showed that camphoronic acid when heated gave trimethyl-succinic, isobutyric, and carbonic acids and carbon, and suggested the formula $CO_2H \cdot CH_2 \cdot CMe(CO_2H) \cdot CMe_2 \cdot CO_2H$, viz. α-α-β-trimethyl-carballylic acid, a constitution which has since been confirmed by *W H Perkin* and *Thorpe's* synthesis (J C. S. 1897, 1169). This consists in condensing ethyl acetoacetate and ethyl α-bromo-isobutyrate by means of zinc to ethyl β-hydroxy α-α-β-trimethyl glutarate·

$$\begin{matrix} CBrMe_2 \cdot CO_2Et \\ CH_3 \cdot \dot{C}O \cdot CH_2 \cdot CO_2Et \end{matrix} \longrightarrow \begin{matrix} CMe_2 \cdot CO_2Et \\ OH \cdot \dot{C}Me \cdot CH_2 \cdot CO_2Et \end{matrix}$$

The OH group is replaced by Cl, and this by CN, and the cyano-ester when hydrolysed yields camphoronic acid:

$$\begin{matrix} CMe_2 \cdot CO_2Et \\ CN \cdot \dot{C}Me \cdot CH_2 \cdot CO_2Et \end{matrix} \longrightarrow \begin{matrix} CMe_2 \cdot CO_2H \\ CO_2H \cdot \dot{C}Me \cdot CH_2 \cdot CO_2H. \end{matrix}$$

The relationship between camphor and its oxidation products is thus simple, as shown by the following scheme:—



Camphoric acid has been synthesised by *Komppa* (B. 1901, **34**, 2472, 1903, **36**, 4332) Ethyl oxalate and ethyl $\beta\beta$-dimethyl-glutarate condense in the presence of sodic ethoxide, yielding diketo-apocamphorate:

$$\begin{matrix}CO\cdot OEt\\ CO\cdot OEt\end{matrix} + \begin{matrix}H\cdot CH\cdot CO_2Et\\ CMe_2\\ H\cdot CH\cdot CO_2Et\end{matrix} = 2EtOH + \begin{matrix}CO\cdot CH\cdot CO_2Et\\ |\quad CMe_2\\ CO\cdot CH\cdot CO_2Et.\end{matrix}$$

This is methylated by means of sodium and methyl iodide, and the ethyl ester of diketo-camphoric acid thus obtained,

$$\begin{matrix}CO\cdot CH\cdot CO_2Et\\ |\quad CMe_2\\ CO\cdot CMe\cdot CO_2Et,\end{matrix}$$

may be reduced with sodium amalgam to dihydroxy-camphoric acid, and this, in its turn, with phosphorus and hydriodic acid to dehydro-camphoric acid,

$$\begin{matrix}CH\cdot CH\cdot CO_2Et\\ \|\quad CMe_2\\ CH\cdot CMe\cdot CO_2Et,\end{matrix}$$

which combines with hydrogen bromide; and the β-bromo-camphoric acid thus obtained, when reduced with zinc and acetic acid, yields the racemic modification of camphoric acid.

Camphor can be synthesised from camphoric acid by the following series of reactions (*Haller*, C. R. 1896, **122**, 446):

$$C_8H_{14}\!<\!\begin{matrix}CO\\ CO\end{matrix}\!>\!O \xrightarrow[\text{reduced}]{} C_8H_{14}\!<\!\begin{matrix}CO\\ CH_2\end{matrix}\!>\!O \xrightarrow{KCN} C_6H_4\!<\!\begin{matrix}COOK\\ CH_2\cdot CN\end{matrix}$$

Camphoric anhydride — Camphorlide — Homocamphoric nitrile

$$\xrightarrow[\text{hydrolysed}]{} C_8H_{14}\!<\!\begin{matrix}COOH\\ CH_2\cdot COOH\end{matrix} \xrightarrow[\text{distilled}]{\text{Ca salt}} C_8H_{14}\!<\!\begin{matrix}CO\\ CH_2\end{matrix}$$

Homocamphoric acid — Camphor

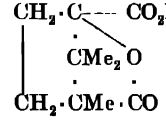
Considerable amounts of camphor are manufactured from pinene by the following series of reactions:

$$\text{Pinene} \xrightarrow[HCl]{} \text{Bornyl chloride} \xrightarrow[\text{acetate}]{\text{Metallic}} \text{Isobornyl acetate} \xrightarrow[\text{hydrolysed}]{} \text{Isoborneol} \xrightarrow[\text{oxidised}]{} \text{Camphor.}$$

(Cf. *Houssemann*, Sci. Progress, No. 9.)

Camphoric acid is an unsymmetrical dibasic acid, as it gives two isomeric monomethyl esters and two amic acids. One carboxylic acid is probably attached to a tertiary and the other to a secondary carbon atom, as the acid yields a single *mono*bromo substituted derivative when subjected to the *Hell-Volhard-Zelinsky* method of bromination. The derivatives are known respectively as α and β (or ortho and allo), the α-methyl ester, for example, contains the group $>CH\cdot CO_2Me$, and the β-methyl ester the group $>C\cdot CO_2Me$. As isonitroso-camphor—$C(:NOH)\cdot CO$—when warmed with hydrochloric acid yields α-camphoramic acid, $>CH\cdot CO\cdot NH_2$, it follows that the methylene group of camphor corresponds with the α-carboxylic group in camphoric acid.

Camphoric acid exists in four optically active and two racemic modifications, the latter known respectively as *r*-camphoric and *r*-isocamphoric acids. This points to the presence of two asymmetric carbon atoms in the molecule of the acid, as indicated in the formula. Camphor, on the other hand, exists in two active and one racemic form only. When *d*-camphoric acid is racemized the product is not *r*-camphoric acid, but a mixture of the original acid with *l*-iso-camphoric acid. This is due to the fact that only one asymmetric carbon atom is concerned in the racemization. In the oxidation of camphoric acid to camphoronic acid, **camphanic acid**, the lactone of α-hydroxy-camphoric acid is formed as an intermediate product, its constitution follows from the fact that it is formed by boiling bromo-camphoric anhydride with water.



Camphanic acid.

Various **chloro-**, **bromo-**, **nitro-**, and **amino-camphors** are known.

Borneol or **Borneo camphor**, $C_{10}H_{17}\cdot OH$, occurs in nature (in *Dryobalanops camphora*), and is produced by the action of nascent hydrogen upon Japan camphor:

$$C_{10}H_{16}O + 2H = C_{10}H_{18}O.$$

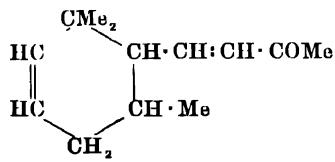
It resembles the latter, but has at the same time an odour

of pepper. It crystallizes in hexagonal plates, melts at 208°, boils at 212°, and when oxidized yields in the first instance camphor. Borneol possesses the character of a secondary alcohol, yielding esters, and with PCl_5 yields **bornyl chloride**, $C_{10}H_{17}Cl$ (m.-pt. 148°), which is identical with pinene hydrochloride; bornyl chloride yields camphene when warmed with alkalis.

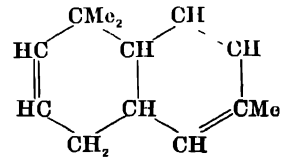
D. Compounds related to Terpenes

Irone—a methyl ketone, $C_{13}H_{20}O$—is the odoriferous principle of the iris root, and also probably of the violet. When boiled with hydriodic acid it yields the hydrocarbon **irene**, $C_{13}H_{18}$.

The formulæ suggested for these compounds are:



Irone



Irene

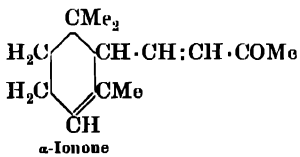
(cf. *Tiemann* and *Krüger*, B. **26**, 2675). These chemists have synthesised two isomerides of irone, which they term α- and β-**ionones**

These also possess the odour of violets, and are employed at the present time for the manufacture of violet essence

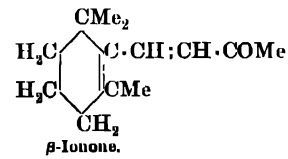
The synthesis consists in the condensation of citral (p. 570) with acetone to form the unsaturated ketone pseudo-ionone.

$$CMe_2{:}CH\cdot CH_2\cdot CH_2\cdot CMe{:}CH\cdot CH\ O + H_2\ CH\cdot COMe$$
$$= CMe_2{:}CH\cdot CH_2\cdot CH_2\cdot CMe{:}CH\cdot CH{:}CH\cdot COMe,$$

which is transformed into the ring compounds α- and β-ionones when boiled with sulphuric acid:

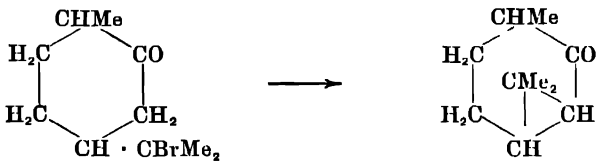


α-Ionone

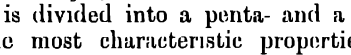


β-Ionone.

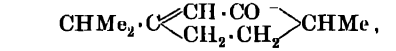
Carone, $C_{10}H_{16}O$, is one of the most important ring ketones of the terpene series, and is formed when dihydrocarvone hydrobromide, 8-bromoterpane-2-one, is treated with alcoholic potash (*Baeyer*, B. 1896, **29**, 5 and 2796).



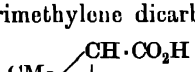
It is a colourless oil with an odour of camphor and peppermint, and boils at 210°, but is, at the same time, partially transformed into the isomeric carvenone. The molecule, according to *Baeyer*, contains a six-carbon ring with a bridge, so that it is divided into a penta- and a tri-methylene ring. One of the most characteristic properties is the readiness with which the bridge is broken and derivatives of *p*- or *m*-terpane are produced Thus when heated it yields carvenone or Δ-3-*p*-terpene-2-one,



with hydrobromic acid it yields 8-bromoterpane-2-one, and with sulphuric acid 8-hydroxy-terpane-2-one,



When oxidized, carone yields a dibasic acid, **caronic acid** (*cis* and *trans* modifications), which *Baeyer* suggested was dimethyl-trimethylene dicarboxylic acid,



a conclusion which has been confirmed by *Perkin's* synthesis (J. C. S. 1899, 48). In this synthesis ethyl dimethylacrylate, $CMe_2{:}CH\cdot CO_2Et$, is condensed with ethyl sodic malonate (or ethyl sodio-cyanoacetate), and the product, ethyl dimethyl-propane-tricarboxylat-, $(CO_2Et)_2CH\cdot CMe_2\cdot CH_2\cdot CO_2Et$, when hydrolysed and heated at 200°, yields *ββ*-dimethyl glutaric acid, $CO_2H\cdot CH_2\cdot CMe_2\cdot CH_2\cdot CO_2H$. The α-bromo-derivative of the ethyl ester of this acid, $CO_2Et\cdot CHBr\cdot CMe_2\cdot CH_2\cdot CO_2Et$,

yields *cis* and *trans* caronic acids when heated with alcoholic potash:



XLII. RESINS; GLUCOSIDES

A. Resins

Many organic compounds, the terpenes in particular, possess the property of becoming "resinified" by oxidation in the air or under the influence of chemical reagents, *i.e.* of being converted into substances very similar to the resins which occur in nature. These natural resins are solid, amorphous, and generally vitreous brittle masses of conchoidal fracture, insoluble in water and acids, but soluble in alcohol, ether, and oil of turpentine. They are found naturally in abundance, partly also as balsams, *i.e.* dissolved in terpenes or ethereal oils, from which they can be separated by distilling in steam. The resins dissolve in alkalis to form compounds of the nature of soap (resin soaps), being again precipitated from the aqueous solutions of these on the addition of acids; most resins must therefore consist of a mixture of somewhat complicated acids (the so-called resin-acids).

Abietic acid, $C_{19}H_{28}O_2$, has been isolated from colophonium (the residue from the distillation of turpentine); it crystallizes in small plates, melts at 153°, and is soluble in hot alcohol. **Pimaric acid**, $C_{20}H_{30}O_2$, has been prepared from galipot resin (*Pinus maritima*) in a similar way. It melts at 144°–146°, and closely resembles abietic acid.

The resins show their relation to the aromatic compounds by their conversion into hydrocarbons of the benzene or naphthalene series when distilled with zinc dust, and by the formation of di- and trihydroxy-benzenes when they are fused with potash.

In addition to **colophonium**, there may be mentioned among other resins **shellac** (from East Indian Ficus varieties), and **amber**, a fossil resin which contains succinic acid in addition to resin-acids and a volatile oil.

The resins are largely used for the manufacture of lacs, varnishes, &c.

B. Glucosides

Glucoside is the name given to a number of complex organic compounds which occur in vegetable tissues. They are all characterized by the fact that on hydrolysis with acids, alkalis, or enzymes, a sugar—usually *d*-glucose—is formed. They are therefore to be regarded as anhydro-compounds of *d*-glucose or some other sugar with various organic compounds

In addition to these natural glucosides, the constitutions of which are unknown, *E. Fischer* has prepared artificially simpler glucosides, of the type of α- and β-methyl-glucosides (p. 310), by the action of methyl alcohol and hydrogen chloride on glucose. These are probably stereoisomeric compounds

$$OCH_3\cdot CH[CH\cdot OH]_2\cdot CH\cdot CH(OH)\cdot CH_2\cdot OH$$
$$\qquad\qquad\quad \llcorner\!\!-\!\!-\ O\ -\!\!-\!\!-\!\!-

to saligenin (*o*-hydroxy-benzyl alcohol) and dextrose, **populin** or *benzoyl-salicin*, $C_{10}H_{22}O_8$ (in varieties of Populus), can be prepared artificially from benzoyl chloride and salicin.

Arbutin, $C_{12}H_{16}O_7$, and **methyl-arbutin**, $C_{13}H_{18}O_7$, present in the leaves of the bear-berry, &c., yield glucose and quinol or methyl-quinol respectively Methyl-arbutin has been synthesised by *Michael* (B. 1881, **14**, 2097) from acetochloroglucose and quinol methyl ether.

Hesperidin, $C_{22}H_{26}O_{12}$, which is contained in unripe oranges, &c, can be decomposed into glucose, hesperetic acid (isomeric with ferulic acid, p. 464), and phloroglucinol.

Phloridzin, $C_{21}H_{24}O_{10}$, found in the bark of fruit-trees, yields grape-sugar and **phloretin**, $C_{15}H_{14}O_5$ (B 1895, **28**, 1393), and this latter, in its turn, phloretic acid and phloroglucinol (p. 420) Both induce glycosuria (*i.e* a functional derangement of the liver, giving rise to temporary diabetes) in animals.

Aesculin, $C_{15}H_{16}O_9$, present in the bark of the horse-chestnut, is decomposed by acids into grape-sugar and Aesculetin (dihydroxy-coumarine), $C_9H_6O_4$.

Digitonin, **digitalin**, and **digitaleïn** are three glucosides which, together with **digitoxin** (the most important constituent from a pharmacological point of view), are present in the digitalis of commerce (cf. B. **24**, 339; **25**, Ref 680, **31**, 2154).

Coniferin, $C_{16}H_{22}O_8 + 2H_2O$, contained in the cambium sap of the Coniferæ, yields glucose and conteryl alcohol on hydrolysis, and serves for the preparation of vanillin (p. 430).

Indican (p. 526) is indoxyl glucoside.

Syringin, the glucoside of Syringa, is a methoxy-conteryl

Myronic acid, $C_{10}H_{17}O_9NS_2$, is present as potassium salt (*Sinigrin*), $C_{10}H_{16}KO_9NS_2$, H_2O (glistening needles), in black mustard seed. It is hydrolysed by baryta water, or by myrosin, an enzyme present in mustard seed, to grape-sugar, potassium bisulphate, and allyl isothiocyanate (p. 277).

(For list of natural glucosides cf. *Armstrong*, "Simple Carbohydrates and Glucosides", p. 80.)

XLIII. ALBUMINS, PHYSIOLOGICAL CHEMISTRY

An extended description of the substances (other than those already mentioned) which are found in the animal organism, and which are therefore of importance for physiological chemistry,

will not be attempted here, since they are for the most part better known from a physiological than from a chemical point of view. Only the albumins and some of the substances which are produced during metabolic processes will be dealt with.

Albumins

For an account of the modern views of the chemistry of albumins see *A. Kossel* (B. 1901, **34**, 3214; *E. Fischer*, B. 1906, **39**, 530).

The albumins make up the chief part of the organism, being present partly in the soluble and partly in the solid state; they are found in protoplasm and in all the nutritive fluids of the body. In the tissues of green plants the albumins are synthesised in quite unknown ways from simple substances like carbon dioxide, water, ammonium nitrate and sulphate. (Cf *Meldola*, J C S 1906, 719) The majority of albumins are insoluble in water, but dissolve in dilute saline solutions. Their presence in the juices of the animal organism is probably due to saline and other substances In solution they are opalescent, lævo-rotatory, and do not diffuse through parchment paper, *i.e.* are colloids, but they are thrown down when the solution is warmed, or upon the addition of strong mineral acids, of many metallic salts [*e.g.* copper sulphate, basic lead acetate, and mercuric chloride], of alcohol, tannic acid, acetic acid together with a little potassium ferrocyanide, picric acid, or phosphotungstic acid. They are insoluble in alcohol or ether, and their solutions are usually precipitated ("salted out") by the addition of ammonium sulphate, and mixtures of different albumins can often be fractionally precipitated by gradually increasing the concentration of the ammonium sulphate. This concentration is definite for each albumin, as is also its temperature of coagulation. Proteins can also be coagulated by treatment with absolute alcohol or with boiling water. After coagulation all albumins become insoluble in neutral solvents, but dissolve in alkalis or acids, yielding **metaproteins**, which are also formed by boiling the uncoagulated albumins with acetic acid or alkali. When boiled: (*a*) with nitric acid, they are coloured yellow (the xantho-protein reaction); (*b*) with a solution of mercuric nitrate containing nitrous acid (*Millon's reagent*), red, (*c*) with caustic soda solution and a very little cupric sulphate, violet.

Many of the albumins have been prepared pure, although

this is a very difficult operation. With the exception of the crystalline albumin which occurs in hemp, castor-oil, and pumpkin seeds (B. **15**, 953), and the recently isolated crystalline egg albumin and serum albumin (B. **24**, Ref. 469, **25**, Ref 173), they do not crystallize

The different albumins vary only slightly among themselves in percentage composition, they contain·

C = 52·7 to 54 5 p c ; H = 6 9 to 7 3 p c ; N = 15 4 to 17 6 p c.; O = 20 9 to 23 5 p.c., and S = 0 8 to 5 0 p c.

It is impossible at present to construct a formula from these numbers, and even approximate molecular weights have not been determined.

The fact that albumin contains sulphur is worthy of note, though the mode in which it is combined in the molecule is unknown, warming with a dilute alkaline solution is sufficient to eliminate it partially, *e g.* when white of egg is boiled with an alkaline solution of lead oxide, sulphide of lead is precipitated (the test for sulphur in albumin).

Albumin preparations usually leave a very considerable amount of ash, *i e* inorganic salts, on incineration It is not yet certain in how far this mineral matter forms an integral constituent of these substances, but the properties of "egg albumin free from ash" are materially different from those of ordinary albumin (B **25**, 204).

Although the constitution of no single albumin has been determined, a considerable amount of work has been done in this direction, more especially by an examination of the simpler products obtained when the albumins are (*a*) oxidized, (*b*) hydrolysed, and (*c*) fermented by micro-organisms

(*a*) The products obtained on oxidation consist largely of volatile fatty acids, their aldehydes, ketones, and nitriles, together with hydrogen cyanide and benzoic acid.

(*b*) The usual hydrolytic agents used are (1) baryta water, (2) hydriodic acid, (3) concentrated hydrochloric acid, and (4) sulphuric acid (25 per cent). The last of these appears to be the best, as it produces less complex decomposition, *e.g.* less ammonia and more amino-acids. The most marked feature of the products thus obtained is the predominance of amino-acids.

The list of compounds which have been isolated from the hydrolytic products is as follows. (i) Ammonia; (ii) carbamide; (iii) diamino-acids; (iv) monamino-acids; (v) pyr-

rolidine-2-carboxylic acid (proline), $HN\langle \begin{matrix} CH_2 \text{———} CH_2 \\ CH(CO_2H)\cdot CH_2 \end{matrix}$, and its hydroxy derivative (oxyproline), (vi) furaldehyde (p. 517); (vii) histidine (iminazole-alanine), $C_6H_9O_2N_3$; (viii) arginine, or δ-guanino-α-amino valeric acid, $NH_2\cdot C(:NH)\cdot NH\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH(NH_2)\cdot CO_2H$, which has been synthesised from ornithine (p. 465) and cyanamide (p. 277), (ix) tryptophan (indol-alanine); (x) tyrosine (p. 459).

Of the diamino-acids the following are the more important: Diamino-acetic acid from casein, αδ-diamino-valeric acid or ornithine, αε-diamino-*n*-caproic acid or lysine

Of the monamino-acids: Glycocoll, and derivatives such as skatolglycocoll, α-amino-propionic acid or alanine, α-amino-isobutylacetic acid or leucine, α-amino-isovaleric acid or valine, α-amino-succinic or aspartic acid, α-amino-glutaric or glutamic acid, phenylalanine or β-phenyl-α-amino-propionic acid, $CH_2Ph\cdot CH(NH_2)\cdot CO_2H$, α-amino-α-hydroxy-propionic acid or serine, α-amino-α-thiolactic acid or cystein, and the corresponding disulphide or cystin, β-hydroxy-phenyl-α-amino-propionic acid.

Certain albumins also yield carbohydrates, more especially amino-sugars, *e.g.* glucosamine, $C_6H_{11}O_5\cdot NH_2$ (B. 1895, **28**, 3082).

A simple method for the separation and isolation of many of these amino-acids from the products of hydrolysis is due to *E. Fischer*. He converts the acids into esters by the hydrogen-chloride method, and then separates these by fractional distillation under reduced pressure.

A few simple proteins yield only a single amino-derivative; thus both **salmine** and **clupeine**, obtained respectively from the testicles of the salmon and herring, yield very little besides histidine. As a rule, the more complex proteins yield a considerable number of amino-compounds, the number of such compounds and also their relative proportions varying with the protein.

A glance at the list of above products indicates that the albumin molecule is largely built up of aliphatic groups. The carboxylic groups present in the hydrolytic products are probably not present in the original molecule, and it is highly probable that most of the amino-groups are not present as such, but are employed in uniting the various radicals together, since only some 10 per cent of the total nitrogen in

albumin is eliminated as such on treatment with nitrous acid; in other words, the amino-group of one molecule reacts with the carboxylic group of another, yielding compounds with the group, ·CO·NH·, characteristic of acid amides. *Emil Fischer* and others have synthesised complex compounds of this type by the gradual condensation of amino-acids. Although none of the proteins has been so far synthesised, the products—**the polypeptides**—exhibit considerable analogy to the peptones.

The following general methods are used for the synthesis of polypeptides:—

1. The chloride of a halogenated fatty acid is condensed with the ester of an amino-acid, the resulting ester hydrolysed, and the halogen then replaced by an amino-group by means of ammonia:

$$CH_3\cdot CHBr\cdot COCl + NH_2\cdot CH_2\cdot CO_2Et \rightarrow CH_3\cdot CHBr\cdot CO\cdot NH\cdot CH_2\cdot CO_2Et \rightarrow \underset{\text{Alanylglycine}}{CH_3\cdot CH(NH_2)\cdot CO\cdot NH\cdot CH_2\cdot CO_2H}$$

2. The dipeptide thus obtained can be converted into its acid chloride, and this condensed with a molecule of an ester of an amino-acid, *e.g.* glycine ester, yielding the compound $CH_3\cdot CH(NH_2)\cdot CO\cdot NH\cdot CH_2\cdot CO\cdot NH\cdot CH_2\cdot CO_2C_2H_5$, which on careful hydrolysis yields the corresponding acid—**alanylglycylglycine**—an example of a tripeptide. The operations can be repeated, and in this way compounds containing 18 amino-acid residues have been synthesised, one of which has a molecular weight 1213.

As the amino-acids obtained by hydrolysing natural proteins are optically active, *Fischer* used optically active acids and esters in his synthetical operations, the optically active acid being obtained by resolving its racemic benzoyl derivative by means of active bases and then removing the benzoyl group.

3. A modification of the above synthesis consists in converting an amino-acid into its acid chloride by means of acetyl chloride and phosphorus pentachloride, and then condensing this chloride with a molecule of an amino-acid.

4. Glycylglycine can be obtained by heating ethylglycine when the anhydride diketopiperazine, $NH\langle\begin{matrix}CO\cdot CH_2\\CH_2\cdot CO\end{matrix}\rangle NH$, is formed, and hydrolysing this with dilute alkali.

A few polypeptides, *e.g.* tetrapeptides, have been isolated from the hydrolytic products of certain proteins.

Kutscher has shown that many albumins can combine together to give complex substances, and it is probable that many natural albumins are complexes formed by union of simpler molecules.

(*c*) The putrefaction of albumins gives rise not only to amino-acids, but also to other aromatic and fatty acids (*e.g.* butyric acid, phenyl-acetic acid), indole, skatole, and cresol; further, to the alkaloid-like **ptomaïnes** (the toxines or poisonous alkaloids produced in dead bodies), of which tetramethylene-diamine, or "putrescine", and pentamethylene-diamine, or "cadaverine", B. **19**, 2585, have been isolated (cf. p 196). For a compilation of the ptomaines, see *Brieger*, Archiv. f. patholog Anatomie, **115**, 483

Albuminous matters undergo change when acted upon by the juices of the stomach at a temperature of 30°–40°, the enzyme pepsin converting them in the first instance into **anti-** and **hemi-albumoses**, both of which then pass into peptone; trypsin, an enzyme of the pancreas, likewise gives rise to the two above albumoses, but then transforms the anti-compound into peptone and the hemi-compound into leucine, tyrosine, aspartic acid and glutamic acid (the pancreatic digestion; for details, see *Kuhne*, B **17**, Ref 79) The peptones are readily soluble in water, diffuse quickly through vegetable parchment, and they are neither coagulated upon heating nor by most of the reagents which coagulate albumin, *e.g.* ammonium sulphate, whereas the albumoses are precipitated by this reagent. These reactions indicate that the albumoses are intermediate between the albumins proper and the simple decomposition products already mentioned, and that the peptones are intermediate between the same decomposition products and the albumoses Both albumoses and peptone possess acidic and basic properties, and may be esterified by means of alcohol and hydric chloride, hence they probably contain carboxylic groups.

The different albumoses, *e.g.* hetero- and proto-albumoses, must differ considerably as regards constitution, as the former yields glycocoll, much arginine, but little histidine, and very little tyrosine and indole on hydrolysis, whereas the latter yields no glycocoll, equal amount of arginine and histidine, and much tyrosine and indole.

Other methods adopted are to introduce chemical substances into the animal system intravenously or *per os*, and then to examine in what form the compound is excreted from the

system; as examples, bromobenzene is excreted as bromophenyl-mercapturic acid, and various terpene derivatives are excreted in combination with glycuronic acid.

When soluble salts of iron are allowed to act upon white of egg and upon peptone, **iron albuminate** and **iron peptonate** are respectively produced, these being employed in medicine as iron preparations for internal use under the names of *liquor ferri albuminati* and *peptonati*.

The following scheme of nomenclature for proteins is accepted by most English-speaking chemical and physiological societies:—

1 **Protamines.**—The simplest proteins, they include **salmine, sturine,** &c, isolated from fish testicles.

2. **Histones**.—These are somewhat more complex than the protamines. They can be precipitated by ammonia.

3 **Albumins,** *e.g.* egg albumin, serum albumin from blood and nutritive fluids, and lact-albumin from milk. These are crystalline, dissolve in water, and are not precipitated by common salt. They coagulate at 70°–75°.

4. **Globulins** are insoluble in water but dissolve in dilute salt solution. They can be salted out by means of magnesium sulphate. Examples: **Globulin** from the crystalline lens of the eye, **fibrinogen** from blood, **fibrin** from clotted blood, and **myosin** from the plasma of living muscle, are globulin derivatives.

5. **Gluteins** are proteins of vegetable origin. They are soluble in alkalis, and are closely allied to the globulins.

6. **Gliadins**.—Vegetable proteins, soluble in alcohol.

7 **Phospho-proteins,** *e.g.* caseinogen, the principal protein of milk; casein obtained from caseinogen by the action of rennet. They are acidic and do not coagulate.

8. **Sclero-proteins**.—Mainly insoluble proteins, which form the skeletal parts of tissues, *e.g.* gelatin from cartilages, chondrin, elastin from ligaments, and keratin from hoofs, nails, hair, &c. Sponge and coral contain similar substances.

9. **Conjugated proteins** consist of compounds containing a protein molecule united to some other group.

(*a*) **Nucleo-proteins** are important constituents of the cell nucleus, *e.g.* of pus cells, blood corpuscles, and yeast cells. They are insoluble in water or acids, but dissolve in alkalis, and contain combined phosphoric acid. On hydrolysis they yield albumin and nucleic acid, and on further hydrolysis the nuclein bases, viz. adenine, hypoxanthine, guanine, and xanthine (p. 292).

Certain varieties of nuclein are free from sulphur, while others contain it; the latter group yield tyrosine when decomposed The product which is obtained when the albumin of hens' eggs is coagulated by meta-phosphoric acid resembles nuclein.

Nucleic acid may also be transformed into nuclein bases by various enzymes present in the different organs of the animal system. Recent work renders it highly probable that at least three distinct enzymes take part in such transformations: (*a*) an oxidase; (*b*) adenase, which transforms adenine into hypoxanthine and xanthine, (*c*) guanase, which transforms guanine into xanthine.

(*b*) **Chromo-proteins** or **Hæmoglobins**.—**Hæmoglobin** is the colouring matter of the red blood corpuscles. It can be decomposed into globin and hæmatin (see below). Hæmoglobin combines very readily with oxygen, *e.g.* in the lungs, to **oxy-hæmoglobin**, which yields up its oxygen again, not only in the organism, but also in a vacuum and when exposed to the action of reducing agents, *e.g.* ammonium sulphide. With carbon monoxide it combines to the compound, **carbon monoxide-hæmoglobin**. All three compounds can be obtained crystallized in the cold, and they possess characteristic absorption spectra. **Hæmin**, $C_{31}H_{32}O_4N_4FeCl$, is obtained in the form of characteristic microscopic, reddish-brown crystals by the action of glacial acetic acid and some common salt upon oxy-hæmoglobin; this is a delicate test for the presence of blood. **Hæmatin**, a dark-brown powder containing 8 per cent of iron, is obtained by the spontaneous decomposition of hæmoglobin, or by the action of alkalis on hæmin, and contains OH in place of the Cl atom of hæmin (cf. *Piloty* and *Eppinger*, A. **377**, 341).

(*c*) **Gluco-proteins**.—The **mucins** yield albumin and carbohydrate on hydrolysis; they are insoluble in water, but possess acidic properties. The percentage of nitrogen is less than in the ordinary albumins.

10. **Protein derivatives**, or the products of protein hydrolysis.

(*a*) **Meta-proteins**.—This includes the substances previously known as alkali-albumins and acid-albumins. (*b*) **Proteoses**, including albumoses, globuloses, and gelatoses. (*c*) **Peptones** (cf. p. 598). (*d*) **Polypeptides** (cf. p. 597).

XLIV. REDUCTION

Reduction is the name usually given to a reaction in which oxygen is withdrawn from or hydrogen added to a compound; in certain cases both of these processes occur. Numerous cases of reduction have been mentioned in the preceding chapters, as examples:

$(C_6H_5)_2 \cdot N_2O$, azoxy-benzene, $\longrightarrow (C_6H_5)_2N_2$, azo-benzene (p. 397);
$(CH_3)_2 \cdot CO$, acetone, $\longrightarrow (CH_3)_2 \cdot CH \cdot OH$, *iso*-propyl alcohol (p. 72);
$C_6H_5 \cdot NO_2$, nitro-benzene, $\longrightarrow C_6H_5NH_2$, aniline (p. 372).

As the reaction is so general, a more detailed discussion of it is given in this chapter.

In addition to the above reactions, viz. withdrawal of oxygen or addition of hydrogen, the process previously referred to as inverse substitution (p. 33)—the replacement of halogen by hydrogen, *e.g.* $C_2H_5I \longrightarrow C_2H_6$—is usually regarded as a type of reduction.

A. **Nascent Hydrogen.**—Of the numerous methods that can be employed for reduction, one of the commonest is by means of nascent hydrogen, *i.e.* hydrogen generated in the presence of the substance to be reduced. The fact that the majority of these reductions cannot be effected by means of ordinary gaseous hydrogen, but can be readily attained by the use of hydrogen at its moment of formation, is used as an argument in favour of the view that nascent hydrogen consists of the free atoms. As nascent hydrogen can be produced in a variety of ways, it follows that reductions by this method can be conducted under very varying conditions; and it is of extreme importance to note that the conditions are a prime factor in determining the nature of the product. It has already been pointed out that the reduction of nitro-benzene can give rise to azoxy-benzene, azo-benzene, phenyl-hydroxylamine, or aniline, according to the conditions under which the reaction occurs, and similar phenomena have been mentioned in the case of the reduction of terephthalic acid (p. 468).

Reductions by means of nascent hydrogen may take place in acid, alkaline, or neutral solution, and this affords a simple method of classification for these reactions.

(*a*) **Reduction in Acid Solution.**—Almost any combination of acid and metal which gives rise to nascent hydrogen may be employed for this purpose; but the usual combinations are

tin and hydrochloric acid, zinc and hydrochloric acid, zinc and acetic acid, zinc dust and acetic acid, iron and acetic acid.

The usual method employed in the laboratory for the reduction of nitro-compounds to the corresponding amino-compounds (see Aniline) is by means of tin and hydrochloric acid. The metal is first converted into stannous, and then into stannic chloride:

$$\begin{aligned} Sn + 2HCl &= SnCl_2 + 2H; \\ SnCl_2 + 2HCl &= SnCl_4 + 2H; \\ C_6H_5NO_2 + 6H &= C_6H_5\cdot NH_2 + 2H_2O; \\ \text{or } C_6H_4(NO_2)_2 + 12H &= C_6H_4(NH_2)_2 + 4H_2O. \end{aligned}$$

The method has certain objectionable features which render it unsuitable for use on the manufacturing scale. Among these may be mentioned (*a*) need for large excess of concentrated acid, and the fact that this acid will subsequently have to be neutralized. (*b*) The strong acid is liable to react with the reduction product, yielding halogenated amines. The introduction of the halogen into the benzene nucleus probably occurs in the following manner:—

$$C_6H_5\cdot NO_2 \rightarrow C_6H_5\cdot NH\cdot OH \rightarrow C_6H_5\cdot NHCl \rightarrow Cl\cdot C_6H_4\cdot NH_2$$

(*Bamberger*) Such chlorinated amines are always liable to be formed when concentrated hydrochloric acid is used in combination with a metal for the reduction of nitro-compounds. (*c*) The reduced compound often combines with the stannic chloride to form a double salt, *e.g.* $C_6H_5\cdot NH_2$, HCl, $SnCl_4$, and certain of these are somewhat difficult to decompose.

Aliphatic nitro-derivatives may also be reduced to amines by this method, except in cases where two nitro groups are attached to the same carbon atom, when a ketone is formed. Other examples are the conversion of cyclic derivatives into hydro-derivatives, *e.g.* *p*-hydroxy-quinoline to tetrahydro-*p*-hydroxy-quinoline, and of sulphonic chlorides, $R\cdot SO_2\cdot Cl$, into thio-phenols, $R\cdot SH$.

In many cases tin-foil is stated to be preferable to granulated tin, as it exposes a larger surface, and occasionally alcoholic solutions of the hydrogen chloride are used in place of aqueous. Stannous chloride and hydrochloric acid occasionally give better yields than tin and acid; thus nitromethane is reduced to methyl-hydroxylamine, and the method has been recommended for the estimation of nitro-groups. An excess of standard stannous chloride solution is used, and

the excess titrated after the reduction is complete, each nitro-group requiring 3 gram molecules of stannous chloride.

Stannous chloride is sometimes used without the addition of free acid; thus *Witt*, by reducing amino-azo-benzene with alcoholic stannous chloride, obtained aniline and *p*-phenylene-diamine:

$$C_6H_5\cdot N{:}N\cdot C_6H_4\cdot NH_2 + 4H = C_6H_5\cdot NH_2 + NH_2\cdot C_6H_4\cdot NH_2$$

(Compare also *Jacobson*, A 1895, **287**, 100.)

Most of the objections referred to in connection with the reduction of nitro-derivatives by means of tin and hydrochloric acid may be avoided by using iron and acetic acid or dilute hydrochloric acid. This method is usually adopted on the manufacturing scale, as only a small amount of acid, some one-fortieth of that indicated by the equation,

$$C_6H_5NO_2 + 3Fe + 6HCl = C_6H_5\cdot NH_2 + 3FeCl_2 + 2H_2O,$$

is required The reason for this may be that the ferrous chloride reacts with the aniline and water, yielding ferrous hydroxide and aniline hydrochloride:

$$FeCl_2 + 2C_6H_5NH_2 + 2H_2O = Fe(OH)_2 + 2C_6H_5NH_2,HCl$$

The hydrochloride then reacts with more iron, producing ferrous chloride and nascent hydrogen, which can reduce more of the nitro-compound.

The iron method possesses further advantages, as the reduction can be regulated much more readily than in the case of tin and acid. Thus *p*-nitro-acetanilide reduced by the iron method gives the corresponding amino-compound, $NH_2\cdot C_6H_4\cdot NH\cdot CO\cdot CH_3$, whereas with tin and hydrochloric acid hydrolysis and reduction both occur, and the product is *p*-phenylene-diamine.

Iron and acid may also be employed for the reduction of aromatic polynitro-compounds to amino-nitro-derivatives:

$$C_6H_4(NO_2)_2 \longrightarrow NH_2\cdot C_6H_4\cdot NO_2,$$

but such a reduction is almost impossible with tin and acid.

Zinc, as granulated zinc, or more frequently as zinc dust, is also used in conjunction with acids, usually hydrochloric or acetic. When concentrated hydrochloric is employed, chlorine is apt to enter the benzene ring (cf. p. 602); with glacial acetic acid (*Kraffts*, B. 1883, **16**, 1715) acetyl derivatives are formed occasionally instead of the simple reduction products. For

example, when aldehydes are reduced, alkyl acetates and not alcohols are formed:

$$R{\cdot}CHO + 2H + CH_3{\cdot}CO_2H = R{\cdot}CH_2{\cdot}O{\cdot}CO{\cdot}CH_3 + H_2O,$$

and when nitro-derivatives are reduced, acetylated amines are obtained. Although aliphatic ketones cannot be reduced by this method, all ketones containing one or two benzene nuclei directly attached to the carbonyl group are readily reduced to pinacones (p. 191). Hydroxy-derivatives of anthraquinone may also be reduced in a similar manner, one or more of the hydroxy-groups being replaced by hydrogen, and aliphatic nitro-derivatives, such as nitro-guanidine, $NH{:}C(NH_2){\cdot}NH{\cdot}NO_2$, may be reduced to the corresponding amino-compounds

A transformation occasionally effected by means of zinc dust and glacial acetic acid is the removal of two atoms of halogen and the conversion of a saturated compound into an olefine, *e.g.* tetramethyl-ethylene dibromide into tetramethyl-ethylene:

$$CMe_2Br{\cdot}CMe_2Br + 2H = 2HBr + CMe_2{:}CMe_2.$$

All peroxides (p. 181) are readily reduced by this method, *e.g.* diethyl-peroxide, Et_2O_2, to ethyl alcohol (or ethyl acetate).

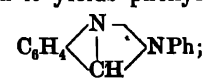
Dilute acetic acid is frequently used with zinc dust. This is the usual method adopted for the reduction of osones to ketoses (*Fischer*) (p. 304):

$$R{\cdot}CO{\cdot}CHO + 2H = R{\cdot}CO{\cdot}CH_2{\cdot}OH.$$

It is also extremely useful in the preparation of hydrazines from nitrosamines and nitramines, *e.g. Fischer* (A. 1886, **236**, 198) obtained methyl-phenyl-hydrazine, $NPhMe{\cdot}NH_2$, by the reduction of methyl-phenyl-nitrosamine, $NPhMe{\cdot}NO$. Other reducing agents, *e.g.* metal and concentrated hydrochloric acid, stannous chloride, zinc dust and alkali, are all liable to carry the reduction a stage further and yield a mixture of ammonia and amine:

$$NPhMe{\cdot}NH_2 + 2H = NHPhMe + NH_3.$$

An extremely interesting example of the influence of the reducing agent and the method of reduction on the nature of the final product is met with in the case of nitro-benzyl-phenyl-nitrosamine, $NO_2{\cdot}C_6H_4{\cdot}CH_2{\cdot}NPh{\cdot}NO$. With tin and hydrochloric acid it yields phenyl-indazole,



with sodium amalgam in alkaline solution, *o*-amino-benzyl-aniline, $NH_2 \cdot C_6H_4 \cdot CH_2 \cdot NHPh$, and ammonia; and with zinc dust and glacial acetic acid, *o*-amino-benzyl-phenyl-hydrazine, $NH_2 \cdot C_6H_4 \cdot CH_2 \cdot NPh \cdot NH_2$. (*Busch*, B. 1894, **27**, 2899.)

With zinc dust and dilute sulphuric acid the reaction is somewhat slower than with acetic acid; with these reagents sulphonic chlorides may be transformed into thio-phenols, or the reaction may proceed a stage further and the sulphur be completely removed.

Zinc dust and concentrated sulphuric acid are occasionally used for the reduction of nitro-compounds, and in all cases the product is an amino-hydroxy- and not a simple amino-derivative:

$$C_6H_5 \cdot NO_2 \longrightarrow p\text{-}NH_2 \cdot C_6H_4 \cdot OH,$$
$$NO_2 \cdot C_6H_4 \cdot CO_2H \longrightarrow NH_2 \cdot C_6H_3(OH) \cdot CO_2H.$$

Lassar-Cohn attributes this to the oxidizing action of the concentrated sulphuric acid, whereas it is probable that reduction to a phenyl-hydroxylamine first occurs; and this, in the presence of the concentrated acid, undergoes intra-molecular rearrangement, yielding the amino-phenol (cf. p. 397):

$$C_6H_5 \cdot NO_2 \longrightarrow C_6H_5 \cdot NH \cdot OH \longrightarrow OH \cdot C_6H_4 \cdot NH_2$$

When zinc or zinc dust and any acid are added to the nitrate of an aromatic amine, a diazonium salt is formed:

$$C_6H_5 \cdot NH_2, HNO_3 + Zn + 3HCl = ZnCl_2 + C_6H_5N_2Cl + 3H_2O.$$

Sodium amalgam is sometimes used as a reducing agent in the presence of acid, thus with acetic acid it is used for the reduction of hydrazones to primary amines:

$$R_1R_2 \cdot C{:}N \cdot NHPh \longrightarrow R_1R_2CH \cdot NH_2.$$

Reductions by means of sodium amalgam and dilute sulphuric acid have been largely used by *E. Fischer* in his synthetical work on the sugars, since the lactones of hydroxy-acids when reduced in this way at 0° yield aldoses (pp. 304, 305):

$$X \cdot CH \cdot CH(OH) \cdot CH(OH) \cdot CO \longrightarrow X \cdot CH(OH) \cdot CH(OH) \cdot CH(OH) \cdot CH{:}O.$$
$$\qquad\qquad\qquad

who, in his earlier experiments, used the acid alone; but when he found that the liberated iodine interfered with the reduction by giving rise to iodo-derivatives or by oxidizing, he added red phosphorus or sometimes phosphonium iodide. The function of the phosphorus is to combine with the iodine immediately it is liberated from the hydrogen iodide, and thus form phosphorus tri-iodide, which is then decomposed by the water present, yielding hydrogen iodide and phosphorous acid. Phosphonium iodide is often formed as a by-product in these reductions. It has been shown that with hydriodic acid alone practically all oxygen compounds are reduced to saturated hydrocarbons at a temperature of 275°, the reduction being conducted in sealed tubes, *e.g.* glycerol yields propane. Amines are also transformed into paraffins, *e.g.* methylamine yields methane.

When hydriodic acid and phosphorus are used, the reduction can either take place in open vessels, *e.g.* a flask with reflux condenser, or in sealed tubes if a higher temperature is required As examples of the former we have the following:—$CHI_3 \rightarrow CH_2I_2$; anthraquinone → dihydro-anthracene, benzilic acid, $OH \cdot CPh_2 \cdot CO_2H$ → diphenyl-acetic acid, $CHPh_2 \cdot CO_2H$, trihydroxy-glutaric acid, $CO_2H \cdot [CH \cdot OH]_2 \cdot CO_2H$ → glutaric acid, mixed ketones, *e.g.* $C_6H_5 \cdot CO \cdot CH_3$ → hydrocarbons.

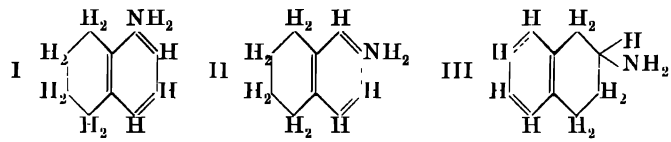
As examples of the latter we have the conversion of fatty acids, from $C_8H_{17} \cdot CO_2H$ upwards, into paraffin-hydrocarbons, the reduction of anthracene to hydro-anthracenes, and of hydroxy-hexamethylene carboxylic acid, $OH \cdot C_6H_{10} \cdot CO_2H$, to hexahydro-benzoic acid, $C_6H_{11} \cdot CO_2H$.

It is interesting to note that hydriodic acid is not a good reducing agent for nitro-compounds, as a rule it leaves the nitro-group intact, *e.g.* nitro-benzene-sulphonic chloride, $NO_2 \cdot C_6H_4 \cdot SO_2Cl$, yields first $NO_2 \cdot C_6H_4 \cdot SO \cdot SO \cdot C_6H_4 \cdot NO_2$, and ultimately *m*-dinitro-diphenyl-disulphide, $NO_2 \cdot C_6H_4 \cdot S \cdot S \cdot C_6H_4 \cdot NO_2$.

(*b*) **Nascent Hydrogen in Alkaline Solution.**—There are various methods of reducing with nascent hydrogen in alkaline solution; one of the commonest is the addition of metallic sodium, in the form of wire or thin strips, to boiling ethyl alcohol; as a rule it is necessary to use absolute alcohol, as the presence of water diminishes the yields. As examples, we have the reduction of nitriles to primary amines, $R \cdot CN \rightarrow R \cdot CH_2 \cdot NH_2$ (p. 106), of esters to alcohols (p. 72), of naphthalene to dihydro-naphthalene, of pyridine to piperidine (p. 537),

although quinoline is not so readily converted by this process into tetrahydro-quinoline, and lastly, of various benzene derivatives, *e.g.* *m*-hydroxy-benzoic acids into corresponding hexahydro-derivatives, *i.e.* derivatives of hexamethylene. When a higher temperature is required than can be attained with ethyl alcohol, boiling amyl alcohol is used (*Bamberger*) By this method naphthalene and its derivatives may be converted into their tetrahydro-compounds, *e.g.* the naphthols, $C_{10}H_7 \cdot OH$, into tetrahydro-naphthols, $C_{10}H_{11} \cdot OH$

It is interesting to note that the chief reduction product obtained from α-naphthylamine is *ar*-tetrahydro-α-naphthylamine (I), and from β-naphthylamine a mixture of *a*- and *ar*-tetrahydro derivatives (II and III):



Similarly phenanthrene is reduced to its tetrahydro-derivative, anthracene to its dihydro-compound, and the benzene carboxylic acids to di-, tetra-, or hexahydro derivatives, according to the temperature and other conditions of reduction (cf. p. 467); with sodium and boiling amyl alcohol, benzoic acid yields mainly $C_6H_{11} \cdot CO_2H$. In a few cases, when substituted benzoic acids are reduced by this method, a rupture of the ring occurs and an aliphatic acid is formed One of the best-known examples is the reduction of salicylic acid to pimelic acid (p 314); in this case it may be assumed that a tetrahydro-salicylic acid is first formed, and that by the addition of the elements of water this is converted into pimelic acid:

$$CH\begin{matrix}<\\>\end{matrix}\begin{matrix}CH \cdot C(CO_2H)\\CH : CH\end{matrix}\Big\rangle C \cdot OH \rightarrow CH_2\begin{matrix}<\\>\end{matrix}\begin{matrix}CH_2 \cdot C(CO_2H)\\CH_2 \cdot CH_2\end{matrix}\Big\rangle C \cdot OH$$

$$\rightarrow CH_2\begin{matrix}<\\>\end{matrix}\begin{matrix}CH_2 \cdot CH_2 \cdot CO_2H\\CH_2 \cdot CH_2 \cdot CO_2H\end{matrix}$$

Although aniline cannot be converted into its hydro-derivatives by this method, aniline-*o*-sulphonic acid yields a hexahydro-derivative In place of alcohol moist ether is sometimes used in conjunction with sodium. This is generally accomplished by adding the metal to ether floating on water, or better, on a solution of sodic bicarbonate. Dibenzyl ketone can thus be reduced to dibenzyl-carbinol, mesityl oxide to

methyl-isobutyl-carbinol, and acid chlorides, $R \cdot COCl$, to the corresponding alcohols, $R \cdot CH_2 \cdot OH$.

Sodium amalgam may be used in place of sodium itself, as a rule in combination with water, the amalgam is added gradually and the mixture kept agitated, and a small amount of alcohol is added, if necessary, to prevent frothing. By this method, benzene and its derivatives may be reduced to di- and tetrahydro-compounds. Many olefine derivatives are reduced to saturated compounds, *e.g.* cinnamic acid, $C_6H_5 \cdot CH:CH \cdot CO_2H$, to phenyl-propionic acid, $C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CO_2H$, and ketones to secondary alcohols Alcohol is occasionally a better medium than water, and by this method azo- may be reduced to hydrazo-compounds (p. 395), and benzaldehyde and its substituted derivatives into benzyl alcohols.

In many instances the alkali formed by the action of the metal on water or alcohol has a deleterious action on the products of reduction, and it becomes necessary to neutralize the alkali as far as possible. This may be effected by the occasional addition of mineral acid, but is most readily accomplished by *Aschan's* method of leading carbon dioxide through the liquid as the reduction proceeds, and in this way converting the sodium hydroxide into bicarbonate as fast as formed It is the method often used in the reduction of phthalic acids, &c, and may also be employed for converting naphthalene and resorcinol into their dihydro-derivatives, and benzoic acid into its tetrahydro-compound.

Zinc and alkali are often used to reduce aromatic ketones to secondary alcohols, *e.g.* $(C_6H_5)_2CO \rightarrow (C_6H_5)_2CH \cdot OH$; whereas when zinc and acetic acid are used, the corresponding pinacones, $(C_6H_5)_2C(OH) \cdot C(OH)(C_6H_5)_2$, are formed Alkali, especially sodic hydroxide, may be used with zinc dust, the usual method being to keep the alkali and substance well stirred, and to add the zinc dust gradually. As examples we have: Anthraquinone → anthranol; fatty diazo-compounds → hydrazo-compounds; *o*-nitraniline → *o*-phenylene-diamine. Further examples are the dehalogenating of aromatic compounds and the preparation of azoxy- and azo-compounds (p. 397).

(*c*) **Nascent Hydrogen in Neutral Solution.**—Many reductions take place most readily in the absence of free acid or free alkali, and may be effected by the following reagents:—(i) Zinc filings or granulated zinc and alcohol, *e.g.* β-bromo-allo-cinnamic acid → allo-cinnamic acid (p. 454); (ii) *Gladstone-Tribe* couple, in the reduction of alkyl haloids to paraffins (p. 33); (iii) mix-

ture of zinc and iron, in the presence of certain metallic salts, *e.g.* acetone → isopropyl alcohol; (iv) zinc dust and water (or alcohol), which may be used for reducing azo-dyes to mixtures of amines, *e.g.* chrysoidine, $NPh:N\cdot C_6H_3(NH_2)_2$, to aniline and triamino-benzene, and also for reducing aromatic nitro-compounds to the corresponding hydroxylamines, *e.g.* $C_6H_5\cdot NO_2 \rightarrow C_6H_5\cdot NH\cdot OH$, a reaction which proceeds extremely readily in the presence of ammonic chloride solution. The same reagents are extremely useful in converting sulphonic chlorides into sulphinic acids, $C_6H_5\cdot SO_2Cl \rightarrow C_6H_5\cdot SO_2H$. (v) Aluminium amalgam (*Cohen* and *Ormandy*, B.A. Report, 1889, 550) is also a useful neutral reducing agent in the presence of water; by this method nitro-derivatives are readily transformed into hydroxylamines, and ketones to secondary alcohols.

B. Among other chemical methods we may mention **heating with metals**. Thus azo-benzene is formed when azoxy-benzene is heated with metallic iron, anthracene when alizarin is heated with zinc dust, and pyrrole when succinimide is heated with the same reagent. In all these cases the metal abstracts oxygen and is converted into an oxide. It is a method frequently adopted when dealing with unknown complex substances and it is desired to know from what simpler compounds they are derived.

Alcohol alone, as in the conversion of diazonium salts into hydrocarbons

$$C_6H_5N_2Cl + CH_3\cdot CH_2\cdot OH = C_6H_6 + N_2 + HCl + CH_3\cdot CHO$$

(p. 387).

Sodium ethoxide, or often alcoholic potash, for the reduction of nitro-compounds to azoxy- or azo-compounds (*De Bruyn*), and also for reduction of deoxy-benzoin and other aromatic ketones to secondary alcohols, *e.g.* hydroxy-dibenzyl:

$$C_6H_5\cdot CO\cdot CH_2\cdot C_6H_5 \rightarrow C_6H_5\cdot CH(OH)\cdot CH_2\cdot C_6H_5$$

(J. C. S. 1895, 604).

Sodium stannite, obtained by adding an excess of sodium hydroxide to stannous chloride, is employed for preparing azo-compounds from nitrated hydrocarbons, for the reduction of diazonium salts to hydrocarbons, *e.g.* benzene from benzene diazonium chloride. An interesting reduction is the conversion of *p*-nitro-benzyl chloride into dinitro-dibenzyl:

$$2NO_2\cdot C_6H_4\cdot CH_2Cl \rightarrow NO_2\cdot C_6H_4\cdot CH_2\cdot CH_2\cdot C_6H_4\cdot NO_2,$$

as the nitro-groups are left intact.

Hydrogen sulphide, or more frequently **ammonium sulphide**, in alcoholic solution (*Cohen* and *M'Candlish*, J. C. S. 1905, 1257), is made use of for the reduction of nitro- and nitroso-derivatives to amines, and is especially useful when several nitro-groups are present and it is required to reduce only one, *e.g.* m-$C_6H_4(NO_2)_2 \rightarrow m$-$NO_2 \cdot C_6H_4 \cdot NH_2$, $C_6H_2Me(NO_2)_3 \rightarrow NH_2 \cdot C_6H_2Me(NO_2)_2$, &c.; also o-nitro-cinnamic acid $\rightarrow$ α-hydroxy-quinoline or carbostyril (p. 546) In many cases sulphur-derivatives are formed instead of simpler reduction products, especially with ketones or aldehydes

Sulphurous acid is used in reducing quinones to quinols, *e g.*:

$$C_6H_4O_2 + H_2SO_3 + H_2O = C_6H_4(OH)_2 + H_2SO_4;$$

and **sodium hyposulphite**, $Na_2S_2O_4$, is an extremely useful reagent for preparing leuco-compounds from dyes.

C. **Catalytic Reduction**, or reduction by means of hydrogen in presence of finely-divided metals. The catalytic action of finely-divided substances, especially platinum black, in the combination of sulphur dioxide and oxygen, or hydrogen and oxygen, or in the decomposition of hydrogen peroxide, is well known. In a similar manner, numerous carbon compounds, when mixed with excess of gaseous hydrogen and passed over a layer of platinum black at a moderate temperature, undergo complete reduction.

The action of other metals in a fine state of division has been investigated in recent years (1897–1911) by *Sabatier* and *Senderens*. They find that nickel, cobalt, copper, and iron can act in somewhat the same manner as platinum black, and that of these nickel is the most efficient. It is necessary that the metal shall be in an extremely fine state of division, and this is accomplished by reducing the metallic oxide in a current of hydrogen at a temperature of about 300°. The substance to be reduced is usually vaporized, mixed with excess of hydrogen, and passed over the metal heated to a temperature which varies somewhat with the different substances, but usually lies between 160° and 250°. A few grams of the metal are usually sufficient, and it retains its activity for a long time. The finely-divided metal appears to transform the hydrogen into an active condition comparable with what is usually termed the nascent state.

Of the numerous reductions which have been accomplished by this process, we may mention the following:—Carbon monoxide at 200° and carbon dioxide at 300° are reduced to

methane and water. Ethylene, propylene, β-hexene, α-octene, &c., are quantitatively reduced to the corresponding paraffins. Acetylene at 150° and α-heptine at 170° yield ethane and heptane respectively. Aromatic hydrocarbons, *e.g.* benzene, toluene, xylene, cymene, at 180° yield their hexahydro-derivatives. Ethyl-benzene reacts in a somewhat curious manner; it appears to be first reduced to its hexahydro-derivative, $C_6H_{11}\cdot C_2H_5$, but this is partially reduced to $C_6H_{11}\cdot CH_3$ and CH_4. Similarly phenyl-acetylene, $C_6H_5\cdot C:CH$, yields a mixture of ethyl-cyclohexane, methyl-cyclohexane, and methane. The terpenes—limonene, sylvestrene, terpinene, menthene—all yield *p*-methyl-isopropyl-cyclohexane. Pinene yields a dihydro-derivative and naphthalene a tetrahydro-compound, and this with more hydrogen, dekahydro-naphthalene, $C_{10}H_{18}$ (*Leroux*).

Aliphatic nitriles at 180°–200° yield primary amines, and finally secondary and tertiary amines and ammonia

$$R\cdot CN \longrightarrow R\cdot CH_2\cdot NH_2;\quad 2R\cdot CH_2\cdot NH_2 \longrightarrow (R\cdot CH_2)_2NH + NH_3.$$

Aromatic nitriles yield ammonia and an aromatic hydrocarbon:

$$C_6H_5CN + 3H_2 = C_6H_5\cdot CH_3 + NH_3$$

Aromatic chloro-derivatives are readily dehalogenized at temperatures above 270°:

$$C_6H_5Cl \longrightarrow C_6H_6,$$

and similarly for polychloro-derivatives. The presence of CH_3, OH, and NH_2 groups appear to facilitate reduction:

$$Cl\cdot C_6H_4\cdot NO_2 \longrightarrow C_6H_5\cdot NH_2, HCl.$$

Aliphatic nitro-compounds at 150°–180° yield the corresponding primary amines, but at higher temperatures paraffins and ammonia. Aromatic nitro-compounds are best reduced in presence of copper at 300°–400°; in this manner nitrobenzene yields aniline and α-nitro-naphthalene α-naphthylamine; whereas, when nickel is used, α-nitro-naphthalene yields ammonia and tetrahydro-naphthalene.

Phenol, *o*-cresol, thymol, and carvacrol at 170°–180° are reduced to their hexahydro-derivatives as are also methyl- and ethyl-anilines. Aniline at 190° also yields its hexahydro-derivative, cyclohexylamine, $C_6H_{11}\cdot NH_2$, but at the same time dicyclohexylamine, $(C_6H_{11})_2NH$, and cyclohexyl-aniline, $C_6H_{11}\cdot NH\cdot C_6H_5$, are produced.

At moderate temperatures (130°–160°) polyhydric phenols yield corresponding hexahydro-derivatives.

Alcohols are formed by the reduction of aldehydes and ketones at temperatures slightly above their boiling-points, *e.g.*:

$$(C_2H_5)_2CO \longrightarrow (C_2H_5)_2CH \cdot OH.$$

Olefine derivatives are readily transformed into the corresponding saturated compounds at moderate temperatures, and compounds of the aromatic series, *e.g.* cinnamic acid, can be reduced to saturated compounds without the benzene nucleus being affected. Unsaturated ketones, *e.g.* mesityl oxide and phorone, can be reduced to the corresponding saturated ketones. Diketones yield various products: thus diacetyl at 140°–150° yields a mixture of hydroxyketone and glycol; acetonylacetone yields the anhydride of the corresponding glycol; benzil, benzoin, and benzoylacetone yield the corresponding hydrocarbons. Lævulic acid yields valerolactone, quinones yield quinols, and carbylamines, alkyl isocyanates, and oximes yield mixtures of amines, mainly secondary. (*Sabatier* and *Senderens*, Annales, 1905 [viii], **4**, 319; *Sabatier* and *Maihle*, ibid. 1909, **16**, 70; *Sabatier*, B. 1911, **44**, 1984.)

Recent experiments have shown that finely divided palladium or platinum can bring about the reduction of various carbon compounds at moderately low temperatures. *Paal* and *Gerum* (B. 1907, **40**, 2209) show that when hydrogen is passed through an alcoholic solution of nitrobenzene mixed with a small amount of colloidal platinum, a 50-per-cent yield of aniline can be obtained at temperatures between 65° and 85°. They also show (B. 1908, **41**, 2273; 1909, **42**, 1553, 2244, 3930) that unsaturated acids and esters, *e.g.* fumaric acid, maleic acid, cinnamic acid, and methyl cinnamate can be reduced to their saturated analogues by passing hydrogen into their alcoholic solutions at the ordinary temperature, provided small amounts of colloidal platinum or palladium, or even of palladium black, are present. They have used the method for converting unsaturated oils (oleic acid derivatives) into saturated glycerides. (Cf. also *Willstatter* and *Mayer*, ibid. 1475, 2199.) The most effective reagent appears to be colloidal palladium. On this reaction *Fokin* (Abs. 1908, ii, 637) suggests a method for determining the "**hydrogen value**" of unsaturated acids by ascertaining the volume hydrogen absorbed by an alcoholic solution of a known weight of the

unsaturated compound when well shaken with the gas in the presence of molecular platinum. *A. Skita* prepares the colloidal palladium by the addition of *gummi arabicum* to a slightly acidified solution of palladous chloride, and shows that unsaturated ketones are converted into saturated, that citral yields citronellal and citronellol, and that many alkaloids take up hydrogen (B. **42**, 1627; **44**, 2862).

The reduction proceeds most rapidly when the hydrogen is under an increased pressure of 0·25 to 1 atmosphere (*Skita* and *Ritter*, B. 1910, **43**, 3393) By this method unsaturated ketones are reduced to saturated without the carbonyl group being affected:—*d*-pulegone → *d*-menthone, mesityl oxide → methyl-isobutyl ketone. An exception is met with in phorone (p. 137), which yields di-isobutyl carbinol. If, however, a smaller pressure is used the reduction stops at the formation of the saturated ketone, valerone. Similarly in the other cases, if the pressure of the hydrogen is increased, a saturated secondary alcohol is obtained. Cyclic ketones and aromatic aldehydes can be reduced to alcohols, using a pressure of 5 atmospheres. *Skita* (B. **44**, 2862, and Chem Zeit., 1911, **35**, 1098) shows that in many cases a solution of palladous chloride in hydrochloric acid can be used, instead of the colloidal metal, with equally good results.

Ipatieff (B. **34**, 596, 3579, **35**, 1047, 1057, **36**, 1990, 2003, 2011, 2016; **37**, 2961, 2986; **40**, 1270, 1281, 1827, **41**, 991, 993, 996, 1001; **42**, 2089, 2092, 2097) has studied the reduction by numerous carbon compounds with hydrogen under pressures of 100–120 atmospheres in the presence of various catalysers.

A special iron or gun-metal bomb has been constructed for this purpose, and can be heated to the required temperature in an electric furnace. Of the catalytic agents investigated, namely, iron, nickel, copper, aluminium, nickelous and nickelic oxide (Ni_2O_3), the last named was found to be the most effective, and only 2–3 grm. were required for 20–30 grm. of the substance to be reduced. The oxide may be used a second time, but afterwards is less active, analysis of the recovered oxide indicates that only a comparatively small amount of reduction to metallic nickel has taken place. In most cases the best temperature is 230°–260°. Under such conditions, acetone yields pure isopropyl-alcohol; phenol, hexahydrophenol; diphenyl, dicyclohexyl; naphthalene, tetra- or deka-hydronaphthalene; dibenzyl, dicyclohexylethane; α- and β-

naphthols, α- and β-dekahydronaphthols, and similarly for sodium β-naphthioate; benzophenone, diphenylmethane; sodium benzoate, sodium hexahydrobenzoate (60 per cent yield of pure acid); aniline, hexahydroaniline (50 per cent yield); diphenylamine, dicyclohexylamine $(C_6H_{11})_2NH$; quinoline, dekahydroquinoline; anthracene, perhydroanthracene, $C_{14}H_{24}$; phenanthrene, perhydrophenanthrene, $C_{14}H_{24}$; acenaphthene, dekahydroacenaphthene. In the last-mentioned reactions it is necessary to repeat the reduction three times in order to obtain the perhydro-derivatives. Olefines are reduced to paraffin derivatives.

It is claimed that this method is much better and yields purer products than *Sabatier* and *Senderens'* method of reducing with hydrogen at atmospheric pressure and in the presence of finely divided nickel.

D. **Electrolytic Reduction**.—Within recent years, numerous reductions have been effected by electrolytic methods. The basis of all these methods is the fact that when an electric current is passed through an aqueous solution of an acid or an alkali, using metal electrodes, hydrogen in the nascent state is produced at the cathode or negative terminal. The actual products formed are dependent not merely on the substances reduced, but also upon the conditions, among the most important of which we may mention: (*a*) nature and concentration of solvent, *e.g.* dilute or concentrated acid, alkaline or neutral solvent, (*b*) strength of current or the current density, *i.e.* the intensity of the current per square decimetre of electrode, (*c*) the materials of which the electrodes are made, due to the difference of potential at which the hydrogen ions are discharged (as a rule platinum, mercury or lead electrodes are used), and (*d*) the temperature.

The method has been mainly used for the reduction of aromatic nitro-compounds, of ketones, and of unsaturated acids.

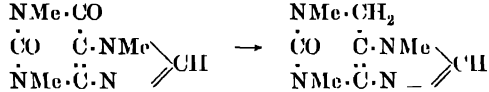
In many cases the reduction is carried out in a double cell provided with a diaphragm. (*a*) The cathode solution is placed in an ordinary unglazed porous cell, and this is introduced into a beaker which serves as the anode compartment; or (*b*) two glazed pots with small perforations are used, and the small annular space between these is packed with asbestos paper. If necessary the liquid can be agitated by using a rotating cathode.

The reduction of nitro-benzene may be cited as one of the best examples which show the effect of conditions on the nature of the product:

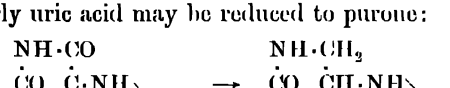
NITRO-BENZENE IN THE CATHODE COMPARTMENT

Cathode compartment	Anode compartment	Electrodes	Current density in amperes	Voltage	Temperature	Time in ampere hours	Product
Alcohol + twice its weight of 25-per-cent sulphuric acid	25-per-cent sulphuric acid	Lead	4–5	3·7–4	65°–80°	35	Aniline
Concentrated sulphuric acid + little water	Concentrated sulphuric in porous cell	Platinum	5–6	7–8	75°–80°		*p*-Amino-phenol
3-per-cent sodic hydroxide	15-per-cent sodic sulphate with very little sulphuric acid	Anode lead Cathode nickel	5–6	6–8		22	Azoxy-benzene
70-per-cent ethyl alcohol with sodic acetate	Cold saturated sodic carbonate solution in porous cell	Anode platinum Cathode nickel	6–8	8–9		30	Azo-benzene
70-per-cent ethyl alcohol with sodic acetate	Cold saturated sodic carbonate solution in porous cell	Anode platinum Cathode nickel	First 6–8 then 2–3	8–9		35	Hydrazo-benzene
Concentrated hydrochloric acid	20-per-cent sulphuric acid	Platinum	1·5–2	5–6·5		50	*o*- and *p*-chloranilines

In the reduction of ketonic compounds, *Tafel* (B 1900, **33**, 2209) has shown that the best effects are obtained by using *pure* lead electrodes, as the hydrogen ions are thus discharged at a higher potential than when other metals are employed, and by employing in the cathode compartment 30–60 per cent sulphuric acid; with stronger acid, reduction of the acid occurs and sulphur is deposited. It is also essential that the current density shall be as low as possible. (For preparation of cells, see *Tafel.*) Acetone when reduced under such conditions, using mercury as cathode, yields isopropyl alcohol; but under similar conditions with a lead cathode it yields a mixture of isopropyl alcohol and pinacone. Camphor may be reduced to borneol (p. 568), and caffeine to deoxy-caffeine:



Similarly uric acid may be reduced to purone:



Further, acetanilide, $C_6H_5 \cdot NH \cdot CO \cdot CH_3$, may be reduced to ethyl-aniline, $C_6H_5 \cdot NH \cdot CH_2 \cdot CH_3$; pyridine to piperidine, using lead cathodes, aconitic acid to tricarballylic acid and cinnamic to hydrocinnamic acid, by using mercury cathodes.

The esters of oxalic, malonic, acetoacetic, benzoic, and phthalic acids, when reduced electrolytically, yield ethers, *e.g.*:

Ethyl benzoate → benzyl-ethyl ether.

XLV. OXIDATION

Oxidation includes not only those processes in which oxygen is added to a compound, *e.g.* conversion of an aldehyde, $R \cdot CH:O$, into an acid, $R \cdot CO \cdot OH$, but also processes in which hydrogen is withdrawn from a compound, *e.g.* transformation of a primary alcohol, $R \cdot CH_2 \cdot OH$, into an aldehyde, $R \cdot CH:O$. In certain cases both processes can occur, *e.g.* oxidation of aniline, $C_6H_5NH_2$, to nitroso-benzene, $C_6H_5 \cdot NO$.

Most of the oxidizing agents employed are substances rich in oxygen, *e.g.* potassic dichromate or permanganate, nitric acid, chromic anhydride, peroxides, &c. During the oxidation, although the organic compound is oxidized, the oxidizing substance is reduced, *e g.* nitric acid gives up part of its oxygen to the substance to be oxidized, and itself becomes reduced to nitrous acid or to various oxides of nitrogen.

Oxygen itself is sometimes made use of as an oxidizing agent, but usually in the presence of a catalyser, *e.g.* finely-divided metals such as platinum black or one of the enzymes known as oxydases. Processes of oxidation, like those of reduction, depend not merely upon the substances to be oxidized, but also on the oxidizing agent selected, and on such conditions as the acid, alkaline, or neutral nature of the solvent, temperature, and concentration. Examples of this have previously been cited among the aromatic hydrocarbons Thus *m*-xylene is not acted upon by dilute nitric acid, but with chromic anhydride yields isophthalic acid. A very good example is aniline:

Aniline with

Manganese dioxide and sulphuric acid	→	ammonia and little quinone;
Dichromate mixture	→	quinone;
Alkaline permanganate	→	azo-benzene and ammonia,
Acidified permanganate	→	aniline black,
Neutral permanganate	→	nitro-benzene and azo-benzene,
Bleaching-powder	→	nitro-benzene;
Hypochlorous acid	→	*p*-amino-phenol.

Compounds of similar constitution are not always oxidized in the same manner; thus, to oxidize *p*-nitro-toluene or *p*-nitro-cinnamic acid the best reagent is dichromate mixture, but for the isomeric *o*-compounds, dilute nitric acid or permanganate are recommended. The inhibiting influence of halogen and other negative radicals in the *o*-position with regard to the alkyl group, on the oxidation of such hydrocarbons by means of acid oxidizing agents, has already been referred to (p. 436), and also the fact that the final product of oxidation of a benzene homologue depends on the number and positions of the side chains, and not on their length, each yielding ultimately a CO_2H group.

When a compound like cymene, $CH_3 \cdot C_6H_4 \cdot C_3H_7$, is selectively oxidized, it is usually the longer side chain which is first affected; and it has been found possible, in a few cases, to carry the oxidation to a stage where a long side chain has

become only partially oxidized, *e.g.* aceto-mesitylene, $C_6H_2Me_3 \cdot CO \cdot CH_3$, to mesityl-glyoxylic acid, $C_6H_2Me_3 \cdot CO \cdot CO_2H$, *m*-butyl toluene, $CH_3 \cdot C_6H_4 \cdot C_4H_9$, by nitric acid at 180°, to *m*-methyl-phenyl-propionic acid, $CH_3 \cdot C_6H_4 \cdot CH_2 \cdot CH_2 \cdot CO_2H$.

Cohen and *Miller* (J. C. S. 1904, **174**, 1622) find that compounds containing chlorine or bromine in the meta-position with regard to a methyl group are least readily oxidized by nitric acid, those with similar substituents in the para-position most readily, and those with *o*-chloro- and bromo-substituents are intermediate.

In certain cases of oxidation, labile groups are present which have to be protected from the oxidizing agent; two such groups are the amino- and aldehydo-groups. An amino- or imino-group can often be protected from undergoing oxidation by transformation into the acetylated group ·NHAc or :NAc, or even better, into a nitroso-derivative, :N·NO. The further oxidation of an aldehydo- to a carboxylic group can often be prevented by the addition of some substance to the oxidizing mixture which will yield a sparingly soluble compound with the aldehyde, such compounds are a primary aryl-amine, which forms a compound of the type of benzylidene-aniline, $C_6H_5 \cdot CH : NC_6H_5$, sodic hydric sulphite, or calcium naphthionate, the calcium salt of 1-amino-naphthalene-4-sulphonic acid. From the additive compound to which the last salt gives rise, the aldehyde may be obtained by distillation in steam

A. Potassium Permanganate.—This is the commonest and one of the most useful oxidizing agents, as it may be used in neutral, alkaline, or acid solution Other permanganates are also employed, *e g* the calcium and barium salts, especially for the oxidation of complex proteins.

(*a*) **Alkaline Solution.**—Even when no alkali is added at the beginning, the solution becomes alkaline during the reaction. The permanganate, a derivative of Mn_2O_7, becomes reduced to hydrated MnO_2, and thus each molecule of permanganate, $K_2Mn_2O_8$, can yield *three* atoms of nascent oxygen.

$$K_2Mn_2O_8 + H_2O = 2MnO_2 + 2KOH + 3O.$$

When the product formed is an acid, this remains dissolved in the alkaline liquid, and may often be obtained by the addition of mineral acid after the manganese dioxide has been removed by filtration. In this manner, numerous benzene hydrocarbons and their derivatives can be oxidized to

the corresponding acids, *e.g.* *p*-chloro-toluene to *p*-chloro benzoic acid, naphthalene to phthalonic acid, $o\text{-}CO_2H\cdot C_6H_4\cdot CO\cdot CO_2H$. Other examples are the conversion of *o*-nitrophenol into dinitro-dihydroxy-diphenyl, $NO_2\cdot(OH)C_6H_3\cdot C_6H_3(OH)\cdot NO_2$, and of uric acid into allantoin (p 294).

The oxidation of olefine derivatives by two per cent permanganate (*Fittig*) is of extreme interest. Two hydroxyl groups are invariably added, and a glycol derivative formed, thus cinnamic acid, $C_6H_5\cdot CH:CH\cdot CO_2H$, yields phenyl-glyceric acid, $C_6H_5\cdot CH(OH)\cdot CH(OH)\cdot CO_2H$. When a stronger permanganate solution or a more powerful oxidizing agent is used, the unsaturated compound is ruptured at the point of the double bond, and a mixture of less complex acids or ketones formed

An excess of alkali is often added to the permanganate before use. Under these conditions *o*-toluic acid yields phthalic acid, and the method is largely made use of for oxidizing *o*-substituted derivatives of toluene, &c When the solution is dilute and the temperature is kept at 0°, the oxidation is mild, and can stop at the formation of a glyoxylic acid, *e.g.*:

$$C_6H_2Me_3\cdot CO\cdot CH_3 \rightarrow C_6H_2Me_3\cdot CO\cdot CO_2H;$$

otherwise a substituted benzoic acid—in this case $C_6H_2Me_3\cdot CO_2H$—is always formed. Substituted cinnamic acids, by this method, can be converted into corresponding benzoic acids, *e.g.*.

$$NO_2(OH)C_6H_3\cdot CH:CH\cdot CO_2H \text{ to } NO_2(OH)C_6H_3\cdot CO_2H.$$

Similarly, hydrocarbons of the type of triphenyl-methane, $CHPh_3$, can be oxidized to carbinols, *e.g.* $CPh_3\cdot OH$, and compounds of the type of diphenyl methane, CH_2Ph_2, to ketones, $CPh_2\cdot CO$.

(*b*) **Neutral Solution.**—In a few cases it is necessary to keep the solution neutral from beginning to end, and this is accomplished by the addition of an excess of magnesic sulphate, which yields insoluble magnesic hydroxide with the caustic potash produced during the oxidation. When aceto-toluidide, $CH_3\cdot C_6H_4\cdot NH\cdot CO\cdot CH_3$, is thus oxidized, an 80-per-cent yield of acetanthranilic acid. $CO_2H\cdot C_6H_4\cdot NH\cdot CO\cdot CH_3$, is formed, whereas in the presence of alkali the yield is only some 30 per cent.

(*c*) **Acid Solution.**—Acetic or sulphuric acid is used, and the acid is added gradually with the permanganate. The

method is of use for the preparation of very stable compounds only, as the majority are completely decomposed by these reagents. The reaction is quite different from that in alkaline solution, the permanganate (a derivative of Mn_2O_7) is reduced to a manganous salt (derived from MnO), and thus each molecule of permanganate gives rise to *five* atoms of available oxygen:

$$K_2Mn_2O_8 + 3H_2SO_4 = 2MnSO_4 + K_2SO_4 + 3H_2O + 5O.$$

Sulphides or hydrosulphides in both the aliphatic and aromatic series may be oxidized to sulphonic acids, a reaction which is useful for the preparation of certain naphthalenesulphonic acids which cannot be obtained by direct sulphonation. *o*-Iodo-benzoic acid may be oxidized to *o*-iodoso-benzoic acid, tetrabromo-*p*-xylene to tetrabromo-terephthalic acid, and primary alcohols to aldehydes.

B. **Chromic Acid Derivatives.**—**Chromic anhydride**, CrO_3, is often used as an oxidizing agent when dissolved in glacial acetic acid, two molecules of the anhydride yielding three atoms of oxygen, $2CrO_3 = Cr_2O_3 + 3O$. Usually only the theoretical amount required for the oxidation is used, and this is gradually run in from a dropping funnel. Quinoline homologues are oxidized to quinoline carboxylic acids, and aromatic alcohols to aldehydes, if a primary amine is present to form a *Schiff's* base (p. 425). Even benzene homologues may be oxidized to aldehydes in the presence of acetic anhydride, as the acetyl derivatives thus formed are stable.

Chromyl chloride, CrO_2Cl_2, the chloride of chromic acid, is used for oxidizing benzene hydrocarbons to aldehydes (*Etard's* reaction, p. 424). The usual method is to dissolve the hydrocarbon and chromyl chloride separately in carbon disulphide, and to run in the chloride solution until the red colour persists, and then to decompose with water. A precipitate of a double compound, *e.g.* $C_6H_5 \cdot CH_3$, $2CrO_2Cl_2$, is first produced, and this is decomposed by water according to the equation:

$$3[C_6H_5CH_3, 2CrO_2Cl_2] = 3C_6H_5CHO + 4CrCl_3 + 2H_2CrO_4 + H_2O.$$

The usual method of using chromic acid is in the form of a mixture of a **dichromate** and **sulphuric acid**, which react according to the equation:

$$K_2Cr_2O_7 + 4H_2SO_4 = K_2SO_4 + Cr_2(SO_4)_3 + 4H_2O + 3O,$$

each molecule of dichromate yielding three atoms of available

oxygen. Sometimes potassic dichromate is used, but more frequently the sodic salt, as it is cheaper and more readily soluble in water. As a rule, the dichromate mixture is added gradually to the oxidizable substance. It is the common method of preparing aldehydes from alcohols (see Acetaldehyde, p. 128), and also from aromatic hydrocarbons, as there is not the same tendency for the ·CHO group to be further oxidized as when permanganate is employed. Complex alcohols may also be oxidized to ketones or aldehydes, *e.g.* menthol to menthone (p. 578). Many compounds, such as hydroxy-acids, ketones, ketonic acids, &c., are ruptured by chromic acid mixture, and acids or ketones containing a smaller number of carbon atoms are formed.

This is the oxidizing agent usually employed for the preparation of quinones, *e.g.* from aniline, and as a rule the temperature should be kept at about 0°. According to *Bamberger*, the following series of reactions occur:

$$C_6H_5\cdot NH_2 \longrightarrow C_6H_5\cdot NH\cdot OH \longrightarrow p\text{-}OH\cdot C_6H_4\cdot NH_2 \longrightarrow O{:}C_6H_4{:}O$$

C. **Nitric Acid.**—Examples of the complete oxidizing action of fuming nitric acid are met with in the ordinary *Carius* method for estimating halogens or sulphur. One of the chief drawbacks of nitric acid is, that in addition to being an oxidizing agent, it is also a nitrating agent, and the products of oxidation, even when dilute acid is used, contain smaller or larger amounts of nitro-derivatives. By means of dilute nitric acid many benzene homologues are oxidized to carboxylic acids, but the process is slow; thus pentamethyl benzene dissolved in benzene requires sixty hours' boiling to oxidize it to tetramethyl-benzoic acid, and slightly longer time is required to oxidize 2·6-chloro-nitro-toluene to the corresponding acid. An interesting oxidation is that of *m*-butyl-toluene to *m*-methyl-phenyl-propionic acid, and a somewhat complex oxidation is that of camphor to camphoronic acid (p. 586). *Krafft* (B. 1889, **21**, 2735) introduced the use of concentrated nitric acid (sp. gr. 1·5) for oxidizing purposes. The admixture was effected at 0°–10°, the temperature gradually raised to 50°, and the product poured into water. This is a very good method for oxidizing compounds which are already nitrated, as in other cases nitro-derivatives are very liable to be formed. Dinitroxylene is oxidized in this way to dinitrophthalic acid. Sulphoxides, *e.g.* Et_2SO, may be oxidized to sulphones, Et_2SO_2, iodo-benzoic acid to

iodoso-benzoic acid, cane-sugar to oxalic acid, &c. The method adopted in oxidizing glycerol to glyceric acid is to allow the aqueous solution of the glycerol to float on concentrated nitric acid.

A mixture of concentrated nitric and sulphuric acids, which is an extremely good nitrating agent, may be used for oxidizing purposes, *e.g.* *o*-nitro-benzyl alcohol to the corresponding aldehyde, of *p*-nitro-cinnamic acid to *p*-nitro-benzaldehyde, and of *s*-trinitro-toluene to *s*-trinitro-benzoic acid.

D. **Sulphuric Acid.**—One of the oldest examples of the oxidizing action of concentrated sulphuric acid is the conversion of ethyl mercaptan, C_2H_5SH, to ethyl disulphide, $(C_2H_5)_2S_2$, and another that of piperidine to pyridine. *Schmidt* introduced the use of fuming sulphuric acid (60 or 70 per cent SO_3) at low temperatures for converting alizarin and other hydroxy-derivatives of anthraquinone into tri- to hexahydroxy-derivatives, many of which are important dyes. The hydroxy-groups form an ester with the sulphuric acid, but this is readily hydrolysed when boiled with dilute acid. Concentrated sulphuric acid may also be used for the preparation of the same compounds, and the yields are largely increased by the addition of boric acid, this being probably due to the fact that boric esters are formed, which prevent the removal of the hydroxy-groups when once introduced.

An oxidizing action of commercial importance is the conversion of naphthalene into phthalic acid by means of concentrated sulphuric acid and a small amount of mercuric sulphate at a temperature above 300°.

E. **Peroxides.**—The peroxides mainly employed are MnO_2, PbO_2, and occasionally H_2O_2. **Lead peroxide** is frequently used in the form of a paste with acetic acid, one of the earliest oxidations with this reagent being that of uric acid to allantoin (p. 294). Characteristic oxidations are (i) that of α-hydroxy-acids to aldehydo-acids, with one less carbon atom (p. 305), *e.g.*:

$$CO_2H\cdot CH(OH)\cdot CH_2\cdot CO_2H \longrightarrow CO_2 + O{:}CH\cdot CH_2\cdot CO_2H;$$

(ii) of alkyl acetates to aldehydes, *e.g.*:

$$o\text{-}NO_2\cdot C_6H_4\cdot CH_2\cdot O\cdot CO\cdot CH_3 \text{ to } o\text{-}NO_2\cdot C_6H_4\cdot CH{:}O;$$

(iii) of triphenyl-methane-derivatives to the corresponding carbinols, the salts of which are dyes, *e.g.*:

$$(NMe_2\cdot C_6H_4)_3CH \longrightarrow (NMe_2\cdot C_6H_4)_3C(OH);$$

and (iv) of amino-hydroxy-derivatives of anthraquinone to the corresponding polyhydroxy-derivatives, the NH_2 being replaced by OH, a reaction which does not occur when the amino-group is acetylated. **Manganese dioxide** alone, or in the presence of sulphuric acid, may be used for converting CH_3 groups in benzene homologues into aldehydo-groups. The mixture is kept stirred, and an excess of hydrocarbon is always present. Benzaldehyde, *o*-chloro-benzaldehyde, *p*-nitro-benzaldehyde, terephthalic aldehyde, &c., have been prepared by this method. A remarkable oxidation is that of benzene to benzoic acid by means of the peroxide and sulphuric acid. Hydroxy-acids are often ruptured by these reagents, *e.g.* lactic acid, $CH_3 \cdot CH(OH) \cdot CO_2H$, yields aldehyde and carbonic acid This is the basis of a method for estimating the strength of solutions of lactic acid by determining the amount of aldehyde formed. The same reagents are also used for the oxidation of alkaloids, and for the conversion of the leuco-bases of triphenyl-methane dyes into the dye salts, *e.g.* *p*-leucaniline into *p*-rosaniline. **Hydrogen peroxide** is often used in the presence of potassium hydroxide for the preparation of organic peroxides, *e.g.* diethyl-peroxide, Et_2O_2, benzoyl-peroxide, $(C_6H_5CO)_2O_2$. Piperidine, when oxidized with three per cent peroxide solution, yields glutaric acid owing to the rupture of the ring Benzene, with the peroxide, yields a certain amount of phenol. Azo-compounds are converted into corresponding azoxy-derivatives, and phenols into dihydric phenols or quinones Fatty acids are converted into ketones, $R \cdot CH_2 \cdot CO \cdot OH \longrightarrow R \cdot CH_2 \cdot CO \cdot CH_2R$ (*Dakin*, Am. C. J. 1910, **44**, 41).

Fenton and others (J. C. S. 1894, 899; 1895, 48, 774; 1899, 1) have made use of hydrogen peroxide in the presence of small amounts of ferrous salts; by this method the following reactions have been effected:

Glycollic acid, $OH \cdot CH_2 \cdot CO_2H$,	$\longrightarrow$	glyoxylic acid, $CHO \cdot CO_2H$;
Lactic acid, $CH_3 \cdot CH(OH) \cdot CO_2H$,	$\longrightarrow$	pyruvic acid, $CH_3 \cdot CO \cdot CO_2H$,
Tartronic acid, $OH \cdot CH(CO_2H)_2$,	$\longrightarrow$	mesoxalic acid, $CO(CO_2H)_2$;
Glyceric acid, $OH \cdot CH_2 \cdot CH(OH) \cdot CO_2H$,	$\longrightarrow$	hydroxy-pyruvic acid, $OH \cdot CH_2 \cdot CO \cdot CO_2H$;
Tartaric acid, $CO_2H \cdot CH(OH) \cdot CH(OH) \cdot CO_2H$,	$\longrightarrow$	dihydroxy-maleic acid, $CO_2H \cdot C(OH) : C(OH) \cdot CO_2H$;
Polyhydric alcohols,	$\longrightarrow$	aldoses

F. **Oxygen** itself can often be used for oxidation, generally in the presence of platinum black or platinized asbestos. *Dennstedt's* method for estimating carbon and hydrogen in organic

compounds is based on this. Many aldehydes, when exposed to moist air, are transformed into acids; thus specimens of benzaldehyde which have been kept for some time contain appreciable amounts of benzoic acid Cinnamic alcohol may be oxidized to cinnamaldehyde, glycerol to glyceraldehyde, and methyl alcohol to formaldehyde in presence of slightly oxidized copper. Alkaline solutions of polyhydroxylic phenols are readily oxidized (see Pyrogallol), and a similar solution of gallic acid yields the yellow dye galloflavin. *Glock* has shown that methane and air, when repeatedly passed over heated metallic copper at 600°, yield methyl alcohol and formaldehyde, and that ethane and air yield ethyl alcohol, acetaldehyde, and acetic acid. [Compare also *Bone's* experiments (pp 36 and 37).] Ozone may also be used as an oxidizing agent, it is employed commercially for refining oils, &c. (cf. J. Ind. 1898, 1101) *C. Harries* (A. 1905, **343**, 311; 1910, **374**, 288) has examined the action of ozone on various types of carbon compounds, mainly in glacial acetic acid solution. Methane, ethyl alcohol, &c, are oxidized to aldehydes and acids, hydrogen peroxide also being formed. Saturated aldehydes and, to a certain extent, ketones yield labile peroxides of the type, $R \cdot CH : O : O$. Most unsaturated hydrocarbons and alcohols combine with ozone, yielding ozonides, *e.g.* $C_2H_4+O_3$, *ethylene ozonide*. The structure of such compounds is usually represented as follows, *e.g.*

$$O\begin{matrix}\diagup O\cdot CH_2 \\ \diagdown O\cdot CH\cdot CH_2\cdot OH\end{matrix}\text{, allyl alcohol ozonide,}$$

and for each ethylene linking one molecule of ozone is added. Many compounds combine with more than this amount of ozone, yielding **oxozonides**, *e.g.* propylene yields a product, $C_3H_6+O_4$, which are not readily transformed into normal ozonides. They are regarded as derived from the hypothetical O_4. Unsaturated carbonyl derivatives, *e.g.* acids, aldehydes, and ketones, also combine with ozone, yielding ozonides; they can, however, combine with a fourth atom of oxygen, yielding **perozonides**, which are decomposed by water, yielding the ozonide and hydrogen peroxide. The three atoms of the ozonide are regarded as attached to the two carbon atoms of the ethylene linking, whilst the fourth atom is attached to the carbonyl group. Oleic acid perozonide is represented as:

$$CH_3\cdot[CH_2]_7\cdot CH\cdot CH\cdot[CH_2]_7\cdot C:O:O$$
$$\dot{O}\cdot O\cdot\dot{O} \qquad\qquad \dot{O}H$$

The ozonides are decomposed when gently heated, or when the solutions in glacial acetic acid are warmed. Oleic acid ozonide decomposes into the four products.

$$\underset{\text{I Nonaldehyde}}{CH_3\cdot[CH_2]_7\cdot CH:O} + \underset{\text{II}}{O\!<\!CH\cdot[CH_2]_7\cdot CO_2H}$$

and $\underset{\substack{\text{III Nonaldehyde}\\ \text{peroxide}}}{CH_3\cdot[CH_2]_7\cdot CH\!<\!\overset{O}{\underset{O}{\cdot}}}$ + $\underset{\text{IV Azelaic acid semi-aldehyde}}{CHO\cdot[CH_2]_7\cdot CO_2H}$,

Some of these products are readily oxidized, *e.g.* nonaldehyde yields the corresponding acid, and the semialdehyde yields azelaic. At the same time the aldehyde peroxides are transformed into the isomeric carboxylic acids, so that appreciable amounts of nonylic and azelaic acids are always found in the final decomposition products. The nonaldehyde peroxide formed in this way is isomeric, and not identical with the peroxide obtained by the direct action of ozone on the aldehyde. It is more stable, has m.-pt. 73°, and is represented by formula III.

Such decompositions of ozonides can be used for determining the position of the ethylene linking in the molecule of the original compound, and also for the preparation of certain aldehydes, aldehydic acids, and dialdehydes.

Benzene yields a highly explosive triozonide, $C_6H_6O_9$.

G. **Other Oxidizing Agents.**—**Chlorine** and **bromine** are generally used in alkaline solution, *i.e.* in the form of hypochlorite or hypobromite. As examples, we have the well-known *Hofmann* reaction, the conversion of amides, and imides such as succinimide and phthalimide, into amines or nitriles (pp. 183 and 184); also the oxidation of reduced benzene derivatives back to the original benzene compound. An interesting oxidation is that of benzylidene-acetone to cinnamic acid with four per cent. sodium hypobromite:

$$C_6H_5\cdot CH:CH\cdot CO\cdot CH_3 + 3NaBrO = C_6H_5CH:CH\cdot CO_2Na + CHBr_3 + 2NaOH,$$

and of potassium cyanide to cyanate by hypochlorite. Bromine water itself is frequently used for the oxidation of sugars, *e.g.*

of an aldose to the corresponding monobasic acid; thus glycerose to glyceric acid, glucose to gluconic acid.

Less common oxidizing agents are **potassic ferricyanide**, which is reduced to the ferrocyanide:

$$2K_3FeC_6N_6 + 2KOH = 2K_4FeC_6N_6 + H_2O + O.$$

s-Trinitro-benzene may be oxidized by this reagent to picric acid, phenyl-acetylene to diphenyl-diacetylene, $CPh{:}C{\cdot}C{:}CPh$, nitroso- to nitro-derivatives, quinone-dioxime to dinitroso-benzene, benzene-diazo-oxides to salts of benzene-diazoic acid, $C_6H_5{\cdot}N{:}NO{\cdot}OH$, and nitro-toluenes to nitro-benzoic acids. **Ferric chloride**:

$$2FeCl_3 + H_2O = 2FeCl_2 + 2HCl + O,$$

may be used for oxidizing hydroxylamine derivatives to nitroso-compounds, *e.g.*:

$$C_6H_4Br{\cdot}NH{\cdot}OH \longrightarrow C_6H_4Br{\cdot}NO;$$

quinols to quinones, and naphthols to dinaphthols:

$$OH{\cdot}C_{10}H_6{\cdot}C_{10}H_6{\cdot}OH.$$

Silver oxide oxidizes glycerol to glycollic acid, and generally aldehydes to acids, and *o*-dihydroxy-benzene to *o*-benzoquinone. **Mercuric oxide**, usually with alkali, *e.g.* barium hydroxide, is used for oxidizing fructose to trihydroxy-butyric acid and glycollic acid, and glucose to gluconic acid. It also oxidizes unsym. diethyl-hydrazine to tetraethyl-tetrazone, $NEt_2{\cdot}N{:}N{\cdot}NEt_2$, and sym. diethyl-hydrazine to mercury-diethyl, nitrogen, and water. **Nitro-benzene** is used as an oxidizing agent in the manufacture of magenta (p. 487), and also in the *Skraup* synthesis of quinoline (p. 542). **Potassium persulphate**, mixed with concentrated sulphuric acid, is known as *Caro's* reagent or sulphomono-per-acid, and can oxidize salicylic acid to 2:5-dihydroxy benzoic acid. It is also used for oxidizing various terpene derivatives, and readily oxidizes aromatic primary amines to nitroso-derivatives, *e.g.*:

$$C_6H_5NH_2 \longrightarrow C_6H_5NO.$$

H. **Electrolytic Oxidation.**—Organic compounds may be oxidized by means of the oxygen formed at the anode of an electrolytic cell. The method is not so general in application as electrolytic reduction, as it is extremely difficult to stop the reaction at the right point. Even when the theoretical

amount of oxygen has been formed, it is often found that part of the compound is unacted on, and part has been completely oxidized. The following are fairly typical examples:—

Purpuro-gallin is formed by the electrolysis of a solution of pyrogallol in sodium sulphate solution, using a rotating platinum anode of 2 sq. dm. The reaction is complete after 6–8 hours with a C.D. of 1·5–2 ampères and an E.M.F. of 4·3–4·5 volts.

Anthraquinone may be prepared by oxidizing an emulsion of anthracene, water, and sulphuric acid, using a rotating lead cathode, and a leaden vessel as anode. The best yields are obtained when an oxygen carrier, *e.g.* manganese sulphate, is employed with a temperature of 75°–90°, a C.D. of 1–2 ampères, and an E.M.F. of 2·8–3·5 volts.

Numerous azo-dyes have been obtained electrolytically; thus, **Orange II**, or *β-naphthol-azobenzene-sulphonic acid*, $OH \cdot SO_2 \cdot C_6H_4 \cdot N:N \cdot C_{10}H_6 \cdot OH$ (p. 502), is produced from an aqueous solution containing sodic sulphamilate, β-naphthol, and sodic nitrite. The cathodes of nickel or platinum wire are placed in two separate cathodic compartments consisting of small porous cells and containing sodic hydroxide solution. The rotating anode is of platinum; and a C.D. of 8–12 ampères, an E.M.F. of 15–18 volts, and as low a temperature as possible, give the best results. The homologues of benzene, when oxidized with platinum electrodes in the presence of sulphuric acid and acetone, yield aldehydes, *e.g.* toluene → benzaldehyde, *o*-xylene → *o*-toluic aldehyde, but the yields, as a rule, are not good. Ortho-substituents of a negative character tend to inhibit such oxidations. Acetic acid solutions of *p*- and *o*-nitro-toluenes yield the corresponding nitro-benzyl alcohols, whereas the *m*-compound yields *m*-nitro-benzaldehyde. Benzyl sulphide yields benzylsulphoxide, benzyldisulphoxide, or tribenzylsulphonium sulphate according to conditions.

XLVI. STEREO-CHEMISTRY OF SULPHUR, SELENION, TIN, AND NITROGEN COMPOUNDS

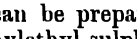
Attention has already (pp. 154 and 213) been drawn to the fact that a compound containing an asymmetric carbon atom, Ca, b, c, d, exists in two optically active isomerides which can unite to form a racemic compound. The researches of *Pope* and others within the past few years have proved that compounds containing other quadravalent atoms, such as

S, Se, and Sn, attached to four different univalent radicals, also exist in optically active isomeric forms.

A. **Sulphur Compounds** (*Pope* and *Peachey*, J. C. S. 1900, 1072).—The sulphur compounds selected were derivatives of **methylethylthetine bromide**:

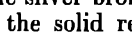


a product which can be prepared by the addition of bromo-acetic acid to methylethyl sulphide. The bromide was mixed with the theoretical amount of silver *d*-camphor-sulphonate in aqueous solution, the silver bromide removed, the filtrate evaporated at 40°, and the solid residue crystallized some 40–50 times from a mixture of absolute alcohol and dry ether. The sparingly soluble *d*-**methylethylthetine** *d*-**camphor-sulphonate**,



melts at 118°–120°, and has a molecular rotation $[M]_D^*$ = +68°. The rotation for the camphor-sulphonate ion is +51·7°, and this gives a rotation of +16·3° for the thetine ion. A very similar value has been obtained by repeatedly crystallizing the *d*-**bromo-camphor-sulphonate**. The corresponding **platinichloride**, $(SMeEtCl\cdot CH_2\cdot CO_2H)_2$, $PtCl_4$, has a molecular rotation +30·2°.

Smiles (J. C. S. 1900, 1174) has obtained **methylethylphenacylsulphine bromide**:



(from methylethyl sulphide and bromo-acetophenone) in optically active modifications by a similar process.

B. **Selenion Compounds** have been resolved by *Pope* and *Neville* (J. C. S. 1902, 1552). The compound used was **methylethylselenetine bromide**, $SeMeEtBr\cdot CH_2\cdot CO_2H$, obtained from methylethyl selenide and bromo-acetic acid; the corresponding *d*-bromo-camphor-sulphonate was repeatedly crystallized from alcohol, and the least soluble fraction melted at 168°, and had $[M]_D$ = +330·8, which gives a rotation of +60·8 for the methylethylselenetine ion.

The corresponding salt of the *l*-base + *d*-acid was isolated; it melted at 151°, and had $[M]_D$ = +209·6, which gives a value of −60·4 for the *l*-selenetine ion. The **platinichloride**

* For meaning of this, see p. 627.

had a molecular rotation $+55°$, but the **mercuri-iodide**, $SeMeEtI \cdot CH_2 \cdot CO_2H$, HgI_2, was optically inactive.

C. **Tin Compounds** (*Pope* and *Peachey*, P. 1900, 42, and 116).—A compound containing an asymmetric tin atom was prepared by the following series of reactions:

$$\begin{aligned} 2SnMe_3I + ZnEt_2 &= 2SnMe_3Et + ZnI_2; \\ SnMe_3Et + I_2 &= SnMe_2EtI + MeI; \\ 2SnMe_2EtI + ZnPr_2 &= 2SnMe_2EtPr + ZnI_2; \\ SnMe_2EtPr + I_2 &= SnMeEtPrI + MeI. \end{aligned}$$

The **methylethylpropyl-tin iodide** (a liquid boiling at 270°) was converted into the *d*-camphor-sulphonate by means of silver *d*-camphor-sulphonate, and after the removal of the silver iodide the solution was evaporated, when crystals of ***d*-methylethyl-*n*-propyl-tin *d*-camphor-sulphonate**, $SnMeEtPr \cdot O \cdot SO_2 \cdot C_{10}H_{15}O$, melting at 125°–126°, were obtained. In aqueous solution, $[M]_D = +95°$, which gives a value for the univalent ion, SnMeEtPr, of about $+45°$. When the mother liquor from the above-mentioned crystals is evaporated, a further quantity of the same compound is obtained, and the operation can be continued until all the water has been expelled. No trace of *l*-methylethylpropyl-tin *d*-camphor-sulphonate can be isolated. *Pope* and *Peachey* attribute this to the conversion of the *l*-base into the *d*-base by continued racemization (p. 257), in the following manner:—The solution of the racemic base with the *d*-acid deposits a portion of its *d*-base as the sparingly soluble salt *d*-base + *d*-acid; the excess of *l*- over *d*-base remaining in the solution racemizes as evaporation proceeds, a further quantity of *d*-base separates as salt, and racemization of the residue again proceeds.

A *d*-methylethyl-*n*-propyl-tin iodide with $[\alpha]_D + 23°$ in ethereal solution has been prepared from the camphor-sulphonate.

The resolution of tin compounds has also been accomplished by means of the *d*-bromo-camphor-sulphonate. If the aqueous solution of *d*-methylethyl-*n*-propyl-tin *d*-bromo-camphor-sulphonate is heated at 100° in a sealed tube for two hours, racemization proceeds, and the rotation $[M]_D + 272°$ is that due to bromo-camphor-sulphonate ion only.

D. **Silicon Compounds.**—Silicon is the element most closely allied to carbon, and hence numerous attempts have been made to prepare optically active silicon compounds containing an asymmetric silicon atom.

It is only recently, however, that these experiments have met with success. *Kipping* (J. C. S. 1907, **91**, 209) has prepared the compound

$$\begin{matrix} C_2H_5 \\ C_6H_5 \end{matrix}\!\!>\!Si\!<\!\begin{matrix} C_3H_7 \\ CH_2\cdot C_6H_5 \end{matrix}$$

ethylpropylbenzylphenylsilicane, by the following series of reactions:—

$$\begin{aligned} SiCl_4 + MgEtBr &= SiEtCl_3 + MgClBr \\ SiEtCl_3 + MgPhBr &= SiEtPhCl_2 + MgClBr \\ SiEtPhCl_2 + MgPrBr &= SiEtPhPrCl + MgClBr \\ SiEtPhPrCl + MgBzCl &= SiEtPhPrBz + MgCl_2 \end{aligned}$$

This hydrocarbon when sulphonated gives rise to benzene and a sulphonic acid:

$$SO_3H\cdot C_6H_4\cdot CH_2\cdot SiEtPr\cdot O\cdot SiEtPr\cdot CH_2\cdot C_6H_4\cdot SO_3H,$$

sulphobenzylethylpropylsilicyl oxide. As the formula indicates, this compound contains two similar asymmetric silicon atoms, and should presumably exist in the same number of isomeric modifications as tartaric acid (p. 249). One of the acids isolated by *Kipping* has been shown to be a *d-l*-compound, and its salt with the active base, *d*-methylhydrindamine can be resolved into its optically active components when repeatedly crystallized from acetone or aqueous methyl alcohol. The two acids have extremely low rotatory powers, *e.g.* $[\alpha]_D$ $\pm$ 3° to 4°. Similar active compounds containing an isobutyl in place of the propyl group have been obtained, they have $[\alpha]_D \pm 10{\cdot}5°$. And still more recently compounds containing a single asymmetric silicon atom have been isolated, *e.g.* **ethylpropyldibenzylsilicanemonosulphonic acid,**

$$CH_2Ph\cdot SiEtPr\cdot CH_2\cdot C_6H_4\cdot SO_3H,$$

which can be resolved into active components by means of brucine. Most of the active silicon derivatives are characterized by the close similarity between the active and racemic forms and by the low rotatory powers, so that it is difficult to say, in certain cases, whether resolution has been effected or not.

Pope and *Peachey* conclude that all the elements of Group IV of the Periodic Classification, namely C, Si, Ti, Ge, Zr, Sr, Ce, Pb, Th, also probably O, S, Se, Te, should in a similar manner give rise to optical activity in their asymmetric derivatives.

E. Nitrogen Compounds (*H. O. Jones*, B.A. Rep. 1904, 169).—(i) *Tervalent Nitrogen Compounds.*—No optical activity has been met with in compounds of the type N a, b, c, and all attempts to resolve such compounds have proved fruitless. *Jones* and *Millington* (C. C. 1904, **2**, 952) have attempted to resolve benzyl-phenyl-hydrazine by means of *d*-camphor-sulphonic acid, and to resolve methylethylaniline-sulphonic acid by means of brucine. Other chemists (*Krafft, Behrend* and *Konig, Ladenburg*) have attempted to resolve benzyl-ethyl-amine, *p*-tolyl-hydrazine, β-benzyl-hydroxylamine, methyl-aniline, and tetra-hydroquinoline by means of *d*-tartaric acid.

Kipping and *Salway* (J. C. S. 1904, 438) have adopted the method of treating a secondary amine with a racemic acid chloride, namely *d-l*-benzylmethylacetyl chloride, $CHMeB_2 \cdot COCl$, and examining the substituted acid amide formed. With a true *d-l*-base, the following compounds should be formed: *d*B *d*A, *l*B *l*A, *d*B *l*A, *l*B *d*A, of which 1 and 2 form an enantiomorphously related pair, and 3 and 4 a similar pair. Thus the complete product would be a mixture of two racemic substituted acid amides. Experiments conducted with methyl-aniline, *p*-toluidine, phenyl-hydrazine, and benzyl-aniline gave a homogeneous product in each case Similarly, when *p*-toluidine and benzyl-aniline are condensed with *d*-methyl-benzylacetyl chloride, no indication of the formation of isomerides is met with.

A pair of compounds, $C_6H_4Me_2 \cdot NH \cdot CHMe \cdot CH_2 \cdot CHO$, containing tervalent nitrogen and stated to be stereoisomeric, have been shown by *Jones* and *White* (J. C. S. 1910, 632) to be structurally isomeric.

The general conclusion to be drawn is, that the centres of gravity of the three radicals, and also of the nitrogen atom itself, lie in a single plane, and the whole arrangement is the most symmetrically possible one. (Cf. Oximes, pp. 138, 429.)

(ii) *Quinquevalent Nitrogen Compounds.*—(For formation, see pp. 105, 379.) The most interesting type of compound is that in which all five radicals are different, *e.g.* N a, b, c, d, X. These compounds are quaternary ammonium salts, in which four of the radicals are alkyl groups, and the fifth an acid group. No cases of inactive isomerides have been met with. An example described by *Wedekind*, viz. methylallylphenyl-benzylammonium iodide, has recently been shown by *H. O. Jones* (J. C. S. 1905, 1721) to be non-existent.

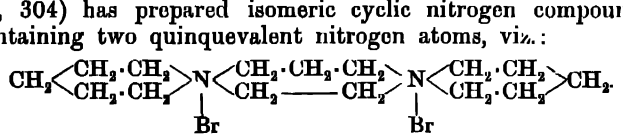
The only known examples of stereoisomerides are the

optically active modifications in which compounds of the type **methylethylpropylisobutylammonium chloride**, $N(CH_3)(C_2H_5)(C_3H_7)(C_4H_9)Cl$, exist. This type of compound is always obtained in an inactive form when synthesised in the laboratory by the addition of an alkyl haloid to a tertiary amine. In 1891 *Le Bel* claimed to have obtained a *lævo*-modification by means of *penicillium glaucum* (green mould), and in 1899 he confirmed this result. In the same year *Pope* and *Peachey* (J. C. S. 1899, 1127) obtained a resolution of *Wedekind's* benzylphenylallylmethylammonium iodide by the aid of silver *d*-camphor-sulphonate.

When the mixture of **benzylphenylallylmethylammonium *d*-camphor-sulphonates** is crystallized from acetone, a sparingly soluble fraction is obtained, and this, when treated with potassium iodide, yields an optically active iodide, $N(C_7H_7)(C_6H_5)(C_3H_5)(CH_3)I$, with $[M]_D + 192°$.

H. O. Jones (J. C. S. 1903, 1418; 1904, 223) has resolved phenylbenzylmethylethylammonium iodide and phenylmethylethylallylammonium iodide by means of silver *d*-bromo-camphor-sulphonate. *Jones* has observed that many of these salts show a tendency to undergo racemization, and during the fractional crystallization of the salts it is advisable to keep the temperature as low as possible. Auto-racemization (p. 257) occurs when the cold chloroform solutions are kept in the dark, a phenomenon also observed by *Pope* and *Harvey* (J. C. S. 1901, 828) with other optically active ammonium salts, and probably due to a partial dissociation of the quaternary ammonium salt into tertiary amine and alkyl iodide and subsequent recombination. (For other optically active ammonium salts, see *Wedekind*, B. 1905, **38**, 1838; *Thomas* and *Jones*, J. C. S. 1906, 280.)

Quinquevalent nitrogen derivatives of the type Na_2bcX, *e.g.* phenylallyldimethylammonium iodide, phenyldipropylmethylammonium iodide, &c., do not exist in isomeric modifications, and attempts to resolve such compounds into optically active components have given negative results (J. C. S. 1897, 522; 1903, 1141, 1406; 1904, 412). *Aschan* (Zeit. phys. 1903, **46**, 304) has prepared isomeric cyclic nitrogen compounds containing two quinquevalent nitrogen atoms, viz.:



The one compound is formed by the union of ethylene-di-

peridide with trimethylene bromide, and the other by the combination of trimethylene-dipcridide with ethylene bromide. This isomerism can be accounted for if the bromine atoms and the central ring lie in one plane and the other rings in a plane at right angles to the first.

A similar compound containing one nitrogen atom,

$$C_6H_4\begin{<}CH_2\\CH_2\end{>}N(Br)\begin{<}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{>}CH_2,$$

has been shown by *Scholz* (B. **43**, 2121) to exist in two optically active forms.

Methylethylaniline oxide, NMeEtO, has been resolved into active modifications by means of bromocamphorsulphonic acid. The base itself, probably $NMeEt(OH)_2$, has $[\alpha]_D - 25°$. The compound

$$I\cdot NMeEtPh\cdot CH_2\cdot CH_2\cdot CH_2\cdot NMeEtPhI,$$

containing two similar asymmetric nitrogen atoms, like tartaric acid, exists in two inactive forms, but so far neither has been resolved into active components. When an asymmetric nitrogen atom is introduced into a compound already containing an asymmetric carbon atom, two stereoisomerides are formed, just as two products are formed when a new asymmetric carbon atom is introduced into an active compound.

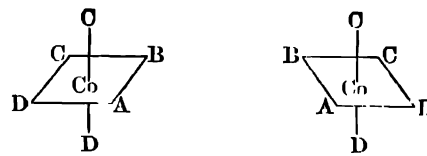
One of the simplest spatial arrangements of the radicals attached to a quinquevalent nitrogen atom is that suggested by *Bischoff* and accepted by *Jones*. The nitrogen atom is supposed to be situated at the centre of a pyramid on a rectangular base, and the five radicals at the five solid angles, the four alkyl groups occupying the four angles of the base, and the acid radical occupying the angle at the apex. Since the three radicals in a tertiary amine all lie in one place, it follows that in the conversion of a tertiary amine into a quaternary ammonium salt a change of "valency direction" occurs.

The equilibrium positions of the radicals in the tervalent nitrogen compound are disturbed, and new positions must be found, which for any four alkyl groups must be determined jointly by the forces between these radicals and the nitrogen atom, and the mutual forces exerted by the groups on one another; consequently there will be some definite spatial arrangement around the nitrogen atom. The fifth group, which is always different in character from the other four, will always bear approximately the same relation to each of

these four groups, in other words, it occupies the apex of the pyramid, and it is improbable that it should ever take the place of an alkyl group at the base of the pyramid. The relative positions of the four alkyl radicals at the base of the pyramid is fixed by the forces exerted by these radicals on one another.

F. **Phosphorus Compounds.**—*Meisenheimer* and *Lachtenstadt* (B 1911, **44**, 356) have obtained methylethylphenylphosphine oxide, O:PMeEtPh, in optically active forms The base was prepared by combining methyl iodide with ethyldiphenylphosphine, liberating the base with moist silver oxide and then distilling, and was resolved by means of *d*-bromocamphorsulphonic acid. The base has $[\alpha]_D + 33{\cdot}8$ in benzene solution. Somewhat similar experiments of *Caven* (J. C. S. 1902, 1362) and *Ephraim* (B. 1911, **44**, 631) have given negative results.

G. **Cobalt Compounds.**—*Werner* (B 1911, **44**, 1887, 2445, 3272, 3279) has obtained optically active derivatives of cobalt. It is pointed out that compounds like CoA_3BCD, $CoABC_2D_2$ or $CoABC_4$ should exist in optically active isomerides, provided the cobalt atoms occupy the centre of an octahedron and the six radicals are situated at the solid angles, *e g.*:



Such active isomerides have been isolated in the case of 1-chloro(or bromo)-2-ammine-diethylenediamine-cobaltic salts, $[CoBrNH_3en_2]Br_2$, where C_2 and D_2 are replaced by divalent ethylenediamine radicals ($\dot{N}H_2 \cdot CH_2 \cdot CH_2 \cdot \dot{N}H_2$:). The resolution was effected by means of *d*-bromocamphorsulphonic acid, and the active salts obtained were quite stable. Similar cases of isomerism have been met with in the case of chromium derivatives (*Werner*, ibid., 3132, cf. also A. **386**, 1). For stereoisomeric platinum-derivatives, see *Kirmreuther*, B. **44**, 3115.

H. **Carbon Compounds, with Semicyclic Double Linkings.**—Many years ago van't Hoff predicted that compounds of the allene type, $\overset{a}{\underset{b}{>}}C:C:C\overset{a}{\underset{b}{<}}$, should exist in optically active modifications. Attempts by *Lapworth* and *Wechsler* (J. C. S. 1910, 38) to obtain such compounds in optically active forms have not met with success. *Perkin* and *Pope* (J. C. S. 1908,

1075; 1909, 1789; 1911, 1510), however, have succeeded in resolving 1-methylcyclohexylidene-4-acetic acid,

$$CHMe\begin{<}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{>}C{:}CH\cdot CO_2H,$$

into optically active components by means of its brucine salt. The two forms have m.-pt. 52·5°–53° and $[\alpha]_D \pm 81°$ in ethyl alcohol. This resolution is of interest, as the formula does not contain an asymmetric carbon atom, although the molecule as a whole is asymmetric. By the addition of bromine to the *d*- and *l*-acids, it has been found possible to obtain four optically active dibromides.

An example of somewhat the same type is met with in the oxime of cyclohexan-1-one-4-carboxylic acid,

$$CO_2H\cdot CH\begin{<}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{>}C{:}N\cdot OH,$$

which has been resolved by *Mills* and *Bain* (J. C. S. 1910, 1866) into active forms by means of morphine or quinine. Two active sodium salts were obtained, but when acidified with hydrochloric acid an inactive acid was formed.

This resolution is used as a strong argument in favour of *Hantzsch* and *Werner's* view (p. 138) that when a tervalent nitrogen atom is attached by a double linking to carbon the three valencies of the nitrogen do not lie in a single plane. If all three valencies were in the same plane the formula for the oxime would contain a plane of symmetry and should not be resolvable.

Azobenzene (p. 396) also appears to exist in two stereoisomeric forms (*Goldschmidt*, J. A. C. S. 1910, **32**, 1294), viz red prisms, m.-pt. 68°, and orange-red needles, m.-pt. 25°, which are represented by *anti* and *syn* configurations.

XLVII. RELATIONSHIPS BETWEEN PHYSICAL PROPERTIES AND CHEMICAL CONSTITUTION

A. Boiling-point. — Attention has been repeatedly drawn to the fact that in any homologous series the boiling-point tends to increase with the number of carbon atoms present (see pp. 31, 66, 141).

In the majority of cases the increase in boiling-point for each additional CH_2 is not constant, but tends to decrease with increasing molecular weight (*e.g.* fatty acids, and especially the paraffin hydrocarbons and alkyl haloids).

In the case of the ethyl esters of the normal fatty acids the increase is fairly constant, and is about 21° for a CH_2 group (*Kopp*, 1842), *e.g.*:

		Difference.
Ethyl formate	54·5°	→ 22·5°
Ethyl acetate	77°	→ 21°
Ethyl propionate	98°	→ 22°
Ethyl butyrate	120°	→ 24·5°
Ethyl valerate	144·5°	→ 22·5°
Ethyl hexoate	167°	→ 21°
Ethyl heptoate	188°	→ 20°
Ethyl octoate	208°	→ 20°
Ethyl nonoate	228°	

With the alkyl chlorides the difference between methyl and ethyl chlorides is 35°, and this difference diminishes by 2° for each subsequent homologue, so that the difference between heptyl and octyl chlorides is only 23° (*Schorlemmer*).

Attempts have been made to find a general law for the diminution of the difference in boiling-point with increase in molecular complexity. *Goldstein* suggested the formula

$$\frac{n-1}{n}\,380 + (n-1)\,19 - 340\,9^{\circ}$$

for the boiling-points of the normal hydrocarbons, where n = the number of carbon atoms; this gives good results up to $C_{12}H_{26}$, but not beyond. (Compare also *Mills*, Phil. Mag. [5], **17**, 180.)

A comparison of isomeric substances shows that the boiling-points can vary considerably, even when the isomerides belong to the same series, *e.g.* the amyl alcohols:

$CH_3(CH_2)_3\cdot CH_2\cdot OH$, 137°;
$(CH_3)_2CH\cdot CH_2\cdot CH_2\cdot OH$, 131·6°;
$CH_3\cdot CH_2\cdot CH(CH_3)\cdot CH_2\cdot OH$, 128°;
$CH_3(CH_2)_2\cdot CH(CH_3)OH$, 118·5°;
$CH_3\cdot CH_2\cdot CH(OH)\cdot CH_2\cdot CH_3$, 116·5°;
$(CH_3)_2CH\cdot(CH_3)\cdot OH$, 112·5°.

In all such cases the normal compound has the highest boiling-point, and the more branched the carbon chain

becomes, the lower is the boiling-point. Generally there is a difference of 7° between the boiling-points of a pair of isomeric compounds of the type $CH_3 \cdot CH_2 \cdot CH_2 \cdot X$ and $(CH_3)_2 \cdot CH \cdot X$. According to *Menschutkin*, in a group of isomeric alcohols, amines, or amides, the boiling-point falls as the side chain approaches the hydroxy- or amino-substituent.

A comparison of isomeric esters, *e.g.*:

n-Butyl acetate, $CH_3 \cdot CO \cdot OC_4H_9$, 124°;
n-Propyl propionate, $CH_3 \cdot CH_2 \cdot CO \cdot O \cdot C_3H_7$, 122·4°;
Ethyl *n*-butyrate, $CH_3 \cdot CH_2 \cdot CH_2 \cdot CO \cdot O \cdot C_2H_5$, 121°;
Methyl *n*-valerate, $CH_3 \cdot (CH_2)_3 \cdot CO \cdot OCH_3$, 127°,

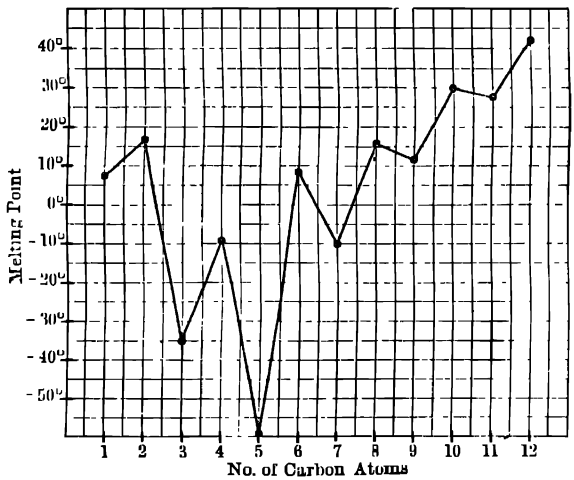
shows that the boiling-point is lower the nearer the oxygen atoms are to the middle of the carbon chain.

A remarkable feature is the relatively high boiling-points of hydroxylic compounds when compared with their isomerides or with closely related compounds. As an example, the *n*-acid isomeric with the last-mentioned group of esters, namely *n*-hexoic acid, boils at 205°. A similar relationship can be shown by the comparison of an alcohol with the ethers isomeric with it. Similarly, a comparison of the boiling-points of the ethyl-derivatives, C_2H_6, $C_2H_5 \cdot OH$, C_2H_5Cl, C_2H_5Br, $C_2H_5NH_2$, $C_2H_5 \cdot OEt$, $C_2H_5 \cdot CN$, indicates the enormous effect of the hydroxyl group on the boiling-point, or, again, a comparison of the boiling-point of an acid with those of its chloride, esters, anhydride, or nitrile

The effect of the introduction of halogen atoms has already been referred to (p. 56). The introduction of an atom of chlorine for hydrogen often raises the boiling-point some 60°, an atom of bromine about 84°, and an atom of iodine 110°, and the introduction of a second or third chlorine atom further raises the boiling-point, but not to the same extent

Extremely interesting is the fact that a saturated compound and its ethylene analogue have very nearly the same boiling-points (cf. propyl and allyl alcohols, both 97°; C_7H_{16} and C_7H_{14}, both 99°; propionic acid, 140·7°, and acrylic acid, 140°), although they differ considerably as regards most of their other physical characteristics. Further, methyl ketones, acetyl esters, and corresponding acid chlorides boil at very nearly the same temperature, *e.g.* acetone, methyl acetate, and acetyl chloride at 55°–56°; propyl methyl ketone, methyl butyrate, and butyryl chloride at 101°–105° (*Schroder*, B. 1883, **16**, 1312).

B. **Melting-point.**—Although, on the whole, in any homologous series the melting-points of the solid members tend to rise with increase in molecular complexity, in many series an alternating rise and fall is met with, the members containing an even number of carbon atoms melting at relatively higher temperatures than those with an odd number. This is the case with the higher fatty acids, as is readily seen when the melting-points are plotted against the number of carbon atoms.



Many other series show a similar relationship, *e.g.* succinic acid and its homologues, where the melting-points are:

C_4, 180°, C_5, 97°; C_6, 148°; C_7, 103°; C_8, 140°; C_9, 106°; C_{10}, 127°

(Compare also *Beach*, Zeit. phys. 1904, **50**, 43.) In the case of a group of closely related isomeric compounds it is found that the melting-point tends to rise with the number of side chains or branches, *e.g.* $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot OH$ is a liquid, and $C(CH_3)_3 \cdot OH$ melts at 25°; or again, glutaric acid melts at 97°, methyl-succinic at 112°, and dimethyl-malonic at 117°. The conversion of an acid into an ester always produces a lowering of the melting-point, and the methyl ester always has the highest melting-point of any of the esters derived from a given acid; in fact, in many cases the methyl esters

are solids, and the ethyl and higher esters liquids at the ordinary temperature.

In the aromatic series it is found that of the isomeric *o*-, *m*-, and *p*-compounds the para- has the highest melting-point. *G. Schultz* (A. 1881, **207**, 362) has also shown that in the group of compounds,

Nitro → azoxy → azo → hydrazo → amine,

the melting-point increases up to the azo-compound, and then falls again to the amine. According to *Franchimont* (Rec. 1897, **16**, 126), the melting-point of an organic compound is invariably raised when two hydrogen atoms attached to the same carbon are replaced by oxygen, or when a hydrogen atom is replaced by hydroxyl; cf. $C_6H_5 \cdot CH_2 \cdot OH$ and $C_6H_5 \cdot CO \cdot OH$, or C_6H_4 and $C_6H_5 \cdot OH$.

C. **Molecular Volume.**—The relationships between specific gravity and chemical constitution are not so marked as in the case of other physical properties Attention has already been drawn to the fact that in a homologous series the specific gravity either decreases with an increase in the number of carbon atoms, and tends to reach a minimum value (p 141), or increases with the number of carbon atoms and tends to attain a maximum (p. 31)

More interesting results have been obtained by an examination of molecular volumes, *i.e.* the quantity $\frac{\text{molecular weight}}{\text{specific gravity}}$. *Kopp* (1842) determined the molecular volumes of a number of carbon compounds, and came to the conclusion that in the case of closely related compounds the same difference in composition corresponds with a similar difference in molecular volume, *e.g.*:

		Mol volume	Difference
Alcohols,	$CH_3 \cdot OH$	42 2	
	$C_2H_5 \cdot OH$	62 2	→ 20
	$C_3H_7 \cdot OH$	81 34	→ 19 14
	$C_4H_9 \cdot OH$	101 58	→ 20 24
Fatty acids,	$H \cdot CO_2H$	41 4	
	$CH_3 \cdot CO_2H$	63 7	→ 22 3
	$C_2H_5 \cdot CO_2H$	85 4	→ 21·7
	$C_3H_7 \cdot CO_2H$	107 1	→ 21·7

and further, that isomeric liquids have the same molecular volumes, *e.g.* acetic acid 63 7, and methyl formate 63·4; propionic acid 85·4, ethyl formate 85·3, and methyl acetate 84·8.

The replacement of an atom of oxygen or an atom of carbon by two atoms of hydrogen does not appear to alter the molecular volume to any considerable extent:

Methyl alcohol, CH_4O ...	42·1	Amyl alcohol, $C_5H_{12}O$	124 0
Formic acid, CH_2O_2.....	41 4	Ether, $C_4H_{10}O$	106 0
Benzyl alcohol, C_7H_8O ...	123 7	Butyric acid, $C_4H_8O_2$	107 1

The difference due to a CH_2 group is roughly 22, and since the atomic volume of carbon is twice the atomic volume of hydrogen, it follows that the atomic volume of carbon = 11 and of hydrogen = 5·5. *Kopp* also indicated that the atomic volume of a polyvalent element, *e.g.* oxygen, is not a constant quantity, but varies according to the manner in which the oxygen atom is united to the other atoms in the molecule. Thus in the form of a carbonyl group, $>C{:}O$, the atomic volume of oxygen is 12·2 (carbonyl oxygen), but in the form of $>C\cdot O\cdot C<$ or $>C\cdot O\cdot H$ (oxidic oxygen) it has the value 7·8. Similarly, *Schiff* has shown that the carbon atom can have different values according as it is united to another carbon atom by a single, double, or triple bond. Thus each double bond causes an increase of four units in the molecular volume. By means of these atomic volumes it is possible to calculate the molecular volume of any simple carbon compound, *e.g.* ethyl formate, $H\cdot CO\cdot O\cdot CH_2\cdot CH_3$,

$$\left.\begin{array}{rcl} 3\,C & = & 33 \\ 6\,H & = & 33 \\ 1\,O: & = & 12\,2 \\ 1\,O\cdot & = & 7\,8 \end{array}\right\} = 86\,0,$$

and the value actually obtained by experiment is 85–86. Although such generalizations as those mentioned are of considerable theoretical importance, the method is not one which has been used to any great extent for determining the constitution of chemical compounds (compare molecular refraction and molecular magnetic rotation). This is partly due to the fact that the specific gravity, and hence the molecular volume, varies with the temperature. At first, *Kopp* made all his determinations at 0°, but obtained better results by taking the specific gravity at the boiling-point of the liquid. It is not necessary to actually make the determination at the boiling-point, but to determine the specific gravity

at a lower temperature, and then to correct for the coefficient of expansion as determined by the dilatometer In reality, the determinations should be made at temperatures when the liquids are all in an exactly comparable condition, viz. at the critical point (compare Zeit. phys 1890, **6**, 578). More recent determinations of molecular volumes by *T. E. Thorpe* (J. C. S. 1880, 327) indicate that isomeric compounds have not always the same molecular volumes, and that the differences amount to several units per cent, but that elements such as chlorine and bromine in the liquid state have the same atomic volumes as in their organic compounds (compare also *Lossen*, A. 1883, **214**, 138; *Horstmann*, B. 1885, **20**, 766; *Schiff*, A. 1884, **220**, 71, *Zahnder*, A 1883, **214**, 138).

D. **Molecular Refraction.**—It has been shown that the molecular refraction, like the molecular volume, is to a large extent an additive property, *i.e.* the molecular refraction is the sum of the atomic refractions of the atoms present in the molecule, but, in addition, that it is to a certain extent constitutive; thus the oxygen atom has distinct atomic refractions according to whether it is in the carbonyl or oxidic state of combination.

The refractive index itself, $n = \frac{\text{sine of angle of incidence}}{\text{sine of angle of refraction}}$, does not lend itself to the study of generalizations, but, according to *Gladstone* and *Dale* (1858), such generalizations are found when the specific refractory power, $\frac{n-1}{d}$ (where d = specific gravity), is employed. This specific refraction varies but little with the temperature, thus with water:

t	0°	10°	20°	90°	100°
Specific refraction ...	0 3338	0 3338	0 3336	0 3321	0 3323

and is not largely affected by the presence of other substances A second formula for the specific refractive power has been introduced by *Lorentz* and *Lorenz*, viz. $\frac{n^2-1}{(n^2+2)d}$; this has the advantage that the value appears to be independent of the physical state of the compound.

	t	*Lorentz-Lorenz* Gas	*Lorentz-Lorenz* Liquid.	*Gladstone-Dale* Gas	*Gladstone-Dale* Liquid
Water.....	10°	0·2068	0·2062	0·3101	0·3338
Carbon disulphide.....	10°	0 2898	0·2805	0·4347	0 4977
Chloroform.....	10°	0 1796	0·1790	0·2691	0 3000

When the refractive powers of different substances are compared, it is usual to employ the molecular refractive powers rather than the specific refractions. The molecular refraction is the product of the specific refraction into the molecular weight; according to *Gladstone* $\frac{M(n-1)}{d}$, and according to *Lorentz–Lorenz* $\frac{M(n^2-1)}{d(n^2+2)}$.

As the refractive index differs with light of different wavelengths, it is necessary to determine the value of n for monochromatic light, and to indicate the special light employed; generally determinations are made for the D line in the sodium, or the α line in the hydrogen spectrum, and are carried out in hollow prisms containing the liquid and provided with sides of plate glass.

Landolt examined the molecular refractions of the members of several homologous series, and came to the conclusion that the molecular refraction is an additive quantity, and that similar changes in composition induce similar changes in the molecular refractive power.

Alcohols	$\frac{M(n-1)}{d}$	Diff	Acids	$\frac{M(n-1)}{d}$	Diff
$CH_3 \cdot OH$.....	13 17	→ 7 53	$H \cdot CO_2H$... .	13 91	→ 7 20
$C_2H_5 \cdot OH$. .	20 70	→ 7 60	$CH_3 \cdot CO_2H$	21 11	→ 7 46
$C_3H_7 \cdot OH$	28 30	→ 7 81	$C_2H_5 \cdot CO_2H$	28 57	→ 7 65
$C_4H_9 \cdot OH$.	36 11	→ 7·27	$C_3H_7 \cdot CO_2H$	36 22	→ 7 83
$C_5H_{11} \cdot OH$....	43 38		$C_4H_9 \cdot CO_2H$	41 05	

and similarly for various groups of esters, the mean value for the CH_2 group being 7 6 units By methods similar to those described under molecular volumes, values were obtained for the atomic refractive powers of the elements for the α line, *e.g.* C = 5, H = 1 3, O = 3, Cl = 9 79, Br = 15 34, &c. The values thus obtained for the halogens are practically identical with those determined for the elements in the free state. The molecular refraction of any simple carbon compound can be calculated by adding together the atomic refractions of the constituent elements. Thus, for ethyl alcohol, C_2H_6O, the calculated molecular refraction is $2 \times 5 + 6 \times 1{\cdot}3 + 3 = 20{\cdot}8$, and that actually found experimentally is 20·7.

According to *Landolt*, the molecular refraction is purely additive, and thus isomeric compounds should possess identical molecular refractive powers. This is largely true in certain

cases, *e.g.* the compounds $C_3H_6O_2$—propionic acid, 28·57; methyl acetate, 29·36; and ethyl formate, 29·18.

In a series of investigations begun in 1878 (A. 1879, **200**, 139; 1880, **203**, 1 and 255) *Bruhl* has examined the influence of atomic grouping on the molecular refraction, and has been able to show that the property is not purely additive, but to a certain extent constitutive Thus a comparison of the experimental and calculated values for unsaturated and the corresponding saturated compounds at once exhibits anomalies:

	$\frac{M(n-1)}{d}$ for α-line.		
	Observed.	Calculated	Difference
Allyl alcohol, C_3H_6O.....	27 88	25 8	2 08
Propyl alcohol, C_3H_8O.....	28 60	28·4	0·2

Similarly in other unsaturated compounds it is found that a double bond between two carbon atoms usually increases the molecular refraction by about two units (mean value 2 15), and a triple bond by 1·95 unit.

Other polyvalent elements have atomic refractions which vary with their state of combination; thus oxygen in carbonyl compounds has the value 3·4 in hydroxy-derivatives, and in ethers the value 2·8. The following is a list of some of the more important atomic refractions used by *Gladstone* and by *Bruhl*·

	Gladstone	*Bruhl* (*L*-*L* formula)
Carbon in saturated compounds..	5·0	2 365
Hydrogen	1 3	1 103
Carbonyl oxygen in $>C{:}O$.	3 4	2·328
Ether oxygen in $>C\cdot O\cdot C<$.....	2 8	1·655
Hydroxylic oxygen in $>C\cdot O\cdot H$..	2·8	1·506
Chlorine	9 9	6 014
Bromine	15 3	8 863
Iodine..	24 5	13·808
Ethylene bond	2·1	1 836
Acetylene bond.	1·95	2 22
Sulphur in C:S	16 0	...
Sulphur in C·S·H.....	14 1	...
Nitrogen in compounds $>C\cdot N<$	...	2·76

Bruhl has employed the molecular refraction for the investigation of certain tautomeric substances, *e.g.* ethyl acetoacetate.

The observed value for the α line is 31·89, and the values calculated for the ketonic and enolic formulæ respectively, 31·53 and 32·55

$CH_3 \cdot CO \cdot CH_2 \cdot CO \cdot OC_2H_5$		$CH_3 \cdot C(OH):CH \cdot CO \cdot OC_2H_5$	
6C	= 14·190	6C	= 14 190
10H	= 11 03	1 ethylene bond	= 1 836
2O (carbonyl)	= 4 656	10H	= 11·03
1O (ether)	= 1·655	1O (carbonyl)	= 2 328
	31·531	1O (ether)	= 1·655
		1O (hydroxyl)	= 1 506
			32 545

The conclusion to be drawn from these numbers is that the ethyl acetoacetate at the ordinary temperature consists mainly of the ketonic form, but probably contains a small amount of the enolic. *Brühl* also tests the purity of numerous compounds prepared by him, by means of molecular refraction and dispersion determinations in place of ordinary combustions. *Perkin* and *Gladstone* have examined the molecular refractive powers of several di- and triketonic substances Thus, for acetylacetone at 11°, using the formula $\frac{n-1}{d}M$ for the α line, the value 45 17 was obtained, and this decreased to 44 14 at 99·3°. The ketonic formula requires 42·2, the mono-enolic 43·7, and the di-enolic 45 2. At 11° the diketone undoubtedly consists mainly of the dihydroxylic compound $CH_3 \cdot C(OH):C:C(OH) \cdot CH_3$, and at the higher temperature, probably of a mixture of the mono- and dihydroxylic forms.

Schaum has also used the method to show that reagents like sodic ethoxide or piperidine have no enolizing or ketonizing actions on ethyl acetoacetate, as in presence of both these compounds the molecular refraction is 32 for the sodium line Compounds which have a strong dispersive power do not appear to lend themselves to the calculation of molecular rotation in the manner just described.

E. **Molecular Magnetic Rotation.**—This is quite distinct from the ordinary optical activity exhibited by substances with asymmetric molecules, and is common to practically all substances when they are examined by means of a polarimeter in a strong magnetic field. The tube containing the liquid to be examined is placed end on between the two poles of an electro-magnet, these poles being pierced in order that the ob-

server may take readings, and the apparatus is often jacketed in order that the temperature may be kept constant. (For new form of apparatus, see J. C. S. 1906, 608.) When the magnetic field is changed, it is found that the amount of rotation remains the same but changes sign, and in each determination several positive and several negative readings are made. The rotations of all substances are compared with water under the same conditions, and thus the molecular magnetic rotation is $\frac{M a l_1 d_1}{18 a_1 l d}$, where M is the molecular weight of the substance, a its observed rotation using a column of liquid l cm. long, and d the specific gravity of the liquid; 18 is the molecular weight of water, a_1 its observed rotation, d_1 its density, and l_1 the length of column used. As a rule $l = l_1$ and $d_1 = 1$ (approx.). An examination of different homologous series by *W. H. Perkin, Sen.*, showed that for an increase of CH_2 in the molecule there is usually an increase of 1·023 units in the molecular magnetic rotation. At first, *Perkin* attempted to obtain atomic magnetic rotations for each element in the same manner as already described for atomic volumes and atomic refractions; the values so obtained gave good results with several distinct series, but could not be applied generally. The method of using **series constants** was then adopted. The molecular magnetic rotation r of a compound may be represented as:

$$r = C + n1{\cdot}023.$$

Where C is a constant which varies with different homologous series, n is the number of carbon atoms present.

A few of the constants are:

n-Paraffins	0 513	Higher esters.....	0 337
iso-Paraffins.....	0 631	Aldehydes....	0·263
n-Alcohols.	0 699	Alkyl chlorides. ..	1 988
iso-Alcohols	0 841	Alkyl bromides.	3 816
n-Fatty acids. . ..	0 391	Alkyl iodides..	8 011
Alkyl acetates . .	0 370		

If in any series it is required to calculate the molecular magnetic rotation of a member, this is readily accomplished by adding $n \times 1\ 023$ to the series constant; thus for *n*-nononic acid we have

$$0{\cdot}391 + 9 \times 1{\cdot}023 = 9{\cdot}598,$$

and the value actually found by experiment is 9·600.

There is usually a definite relationship between the values for an unsaturated compound and its saturated analogue, *e.g.*:

		Diff			Diff
Ethyl crotonate...	7·589	1·112	Ethyl oleate.....	21·909	1·112
Ethyl butyrate....	6·477		Ethyl stearate...	20 797	

With allyl compounds the difference is not so great; thus the difference between allyl alcohol, 4·682, and propyl alcohol, 3 768, is only 0·914, and similarly for other allyl compounds.

These facts have been used as arguments in the determination of the constitution of undecylenic acid (J. C. S. 1886, 205). The difference in molecular magnetic rotation between undecylenic acid, $C_{10}H_{19}\cdot CO_2H$, and undecylic acid, $C_{10}H_{21}\cdot CO_2H$, is 0·897, and similarly for the esters the difference is 0 890. It is argued that this difference approximates to 0 91, the usual difference between an allyl compound and the corresponding saturated derivative, and hence undecylenic acid is presumably an allyl derivative with the formula $CH_2{:}CH[CH_2]_8\cdot CO_2H$

The molecular magnetic rotation of a complex compound can be calculated by taking as the series constant the mean of the series constants of the various groups of compounds which it represents. Thus ethyl lactate, $CH_3\cdot CH(OH)\cdot CO_2C_2H_5$, possesses the groupings characteristic of an ethyl ester and also of a secondary alcohol, the series constants for these are:

Ethyl ester = 0·337; secondary alcohol = 0·844. Mean = 0 590

The series constant for ethyl lactate and homologues is thus 0·590, and the molecular magnetic rotation of the lactate

$$5 \times 1{\cdot}023 + 0\ 590 = 5{\cdot}705,$$

which agrees very well with the experimental value, 5·720. The values of their molecular magnetic rotations have been used by *Perkin* in discussions on the constitutions of certain tautomeric compounds, especially those of the keto-enolic type.

In the case of ethyl acetoacetate, the molecular magnetic rotation for the ketonic form may be calculated as follows:

Series constant for alkyl acetate.....	0·370
Series constant for ketone.....	0 375
Mean.....	0 372

Molecular rotation = $6 \times 1\ 023 + 0\ 372 = 6\ 510$.

For the enolic form—ethyl β-hydroxy-crotonate, $CH_3\cdot C(OH)$:

$CH \cdot CO_2C_2H_5$—the molecular rotation may be calculated by the two following methods:

1. Molecular rotation of ethyl crotonate	7·589
OH replacing H as in alcohol	0 194
Molecular rotation of ethyl hydroxy-crotonate	7 783
2. Molecular rotation for ethyl β-hydroxy-butyrate .	6 737
Difference between unsaturated and corresponding saturated compound	1 112
Molecular rotation for ethyl hydroxy-crotonate.....	7 849

The experimental value actually found for ethyl acetoacetate at the ordinary temperature is 6 501, and this indicates that, at this temperature, the ester consists essentially of the keto-form. Some general conclusions drawn by *Perkin* are:—

(i) That monoketonic compounds and keto-esters, which react as tautomeric substances, as a rule, have the ketonic and not the enolic structure, except when a number of negative groups, such as phenyl and carboxethyl, $\cdot CO_2C_2H_5$, are present. These have an enolizing tendency, as shown in ethyl benzoyl-acetate, $C_6H_5 \cdot CO \cdot CH_2 \cdot CO_2C_2H_5$, which, according to *Perkin*, is a mixture of some 75 per cent of the keto- and 25 per cent enolic compound

(ii) Acetylacetone at 17° consists of a mixture of some 80 per cent of the hydroxy-ketone, $CH_3 \cdot CO \cdot CH{:}C(OH) \cdot CH_3$, and some 20 per cent of the dienolic form, $CH_3 \cdot C(OH){:}C{:}C(OH) \cdot CH_3$. If alkyl radicals replace the hydrogen atoms of the methylene group of acetylacetone, the tendency to form the enolic form is less marked, whereas the introduction of negative groups, $\cdot CO_2Et$, increases the tendency.

(iii) Rise of temperature favours ketonization.

(For full details, see J. C. S. 1884, 421; 1886, 205, 777; 1887, 362, 808; 1888, 561, 695; 1889, 680, 1891, 981, 1892, 800, 1893, 488, 1894, 402, 815; 1895, 255; 1896, 1025; 1900, 267; 1902, 177, 292.)

F. **Absorption Spectra.**—*Ostwald* (Zeit. phys 1892, **9**, 579) has studied the absorption spectra of groups of closely related coloured compounds, *e.g.* a series of *soluble* metallic permanganates, various salts of fluorescein, eosin, and rosolic acid, and has been able to show that, in dilute solutions, the absorption spectrum of a salt is the sum of the spectra of the ions; thus all the permanganates gave practically the same absorption due to the $\bar{Mn}_2\bar{O}_8$ ion.

Hartley and others have carried out numerous investigations on ultra-violet absorption spectra of carbon compounds, and extremely important relationships have been established. (For references, see B. A. Reports mentioned in Preface.) *Hartley* photographed the spark spectrum of an alloy of tin, lead, cadmium, and bismuth after it had passed through a solution of the substance under examination. It was found that practically all open-chain and even the closed-chain polymethylene compounds give no distinct selective absorption; they are remarkably transparent to ultra-violet rays. Numerous exceptions, *e.g.* ethyl acetoacetate derivatives, ketones, and practically all ketonic compounds, whether open-chain or cyclic, have since been met with (*Baly* and *Desch*, J. C. S. 1901, 1039). In any given series, *e.g.* the alcohols, it is usually found that each increment of CH_2 produces a slight increase in the absorption of the more refrangible rays.

Benzene derivatives, naphthalene, anthracene, phenanthrene, and their derivatives, also pyridine, quinoline, dimethylpyrazin, $N<\begin{matrix}CMe\cdot CH\\ CH:CMe\end{matrix}>N$, in alcoholic or aqueous solutions, exhibit, in many cases, distinct **absorption bands**. Most of the terpenes, furane, thiophene and pyrrole derivatives, piperidene and reduced benzene derivatives, resemble the aliphatic compounds.

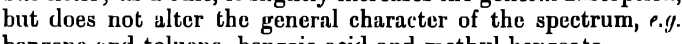
In all cases *Hartley* examined the absorption for solutions of very different concentrations, always increasing the dilution until complete transmission was obtained. He also used layers of the given solutions of different lengths, and then plotted the results in the form of curves, putting the oscillation frequencies (reciprocal of wave-lengths) as abscissæ, and equivalent thicknesses of solution as ordinates. Thus with two solutions, one ·01 N and the second ·001 N, and using layers of each 30, 20, 15, 10, 5 mm thick, the equivalent thicknesses are 300, 200, 150, 100, 50, 30, 20, 15, 10, and 5, and these numbers are used in the plotting. *Baly* and *Desch* have used the iron arc spectrum and a glass cell with quartz ends for containing the solution, so arranged that the length of the column of liquid can easily be varied. They also plot the oscillation frequencies against the logarithms of the relative thicknesses of liquid. It is claimed that from the absorption curves so plotted it is very much easier to compare the relative persistence of the absorption bands.

Hartley examined a number of isomeric benzene derivatives, *e.g.* xylenes, cresols, and dihydroxy-benzenes, and found that

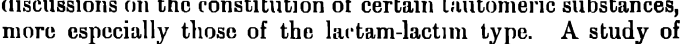
the oscillation frequency of the extreme rays transmitted follows the order ortho → meta → para, *i.e.* the para-compounds exhibit the greatest absorption. The same generalization does not hold for other groups of compounds, *e.g.* the hydroxy-benzoic acids.

A most important fact is that the introduction of a methyl group for a hydrogen atom affects the absorption spectrum but little; as a rule, it slightly increases the general absorption, but does not alter the general character of the spectrum, *e.g.* benzene and toluene, benzoic acid and methyl benzoate.

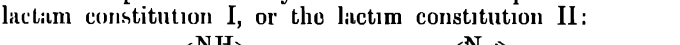
This fact has been largely used by *Hantzsch* and *Dobbie* in discussions on the constitution of certain tautomeric substances, more especially those of the lactam-lactim type. A study of the general chemical properties of isatin (p. 523) does not render it possible to say whether this compound has the lactam constitution I, or the lactim constitution II:



Isatin gives rise to the two distinct methyl ethers: (*a*) methyl-isatin, III, a solid melting at 101°, readily hydrolysed, and obtained by the action of methyl iodide on silver isatin; (*b*) pseudo-methyl-isatin, IV, a solid melting at 134°, not readily hydrolysed, and prepared by heating methyl-dibromo-oxindole with water:



An examination of the absorption curves of the three compounds, isatin, methyl-isatin, and pseudo-methyl-isatin (J. C. S. 1899, 640), shows that the curves for isatin and the pseudo-ether are practically identical, both possessing two bands of similar intensity and differing considerably from that of methyl-isatin, which consists of a single band. There can be no question but that isatin itself has a constitution similar to that of the pseudo-methyl ether; and since the reactions of this prove beyond doubt that it is a nitrogen and not an oxygen ether, isatin must have the lactam constitution represented by formula I. Similarly carbostyril (p. 541), by a comparison of its absorption curve with that of its two methyl ethers, can be shown to possess the lactam constitution I and not the lactim constitution II:



and *o*-oxycarbanil, obtained by fusing *o*-amino-phenol hydrochloride with carbamide, has an absorption spectrum practically identical with that of its N-ethyl ether, and hence has the lactam constitution $C_6H_4\langle^{NH}_{O}\rangle CO$.

Hartley and *Dobbie* (J. C. S. 1900, 498) have also examined the absorption spectra of the three dibenzoyl-succinates obtained by *Knorr*. According to the latter, the α-compound has the enolic constitution I, whereas the two solid β- and γ-compounds are stereo-isomeric ketones with constitution II:

$$\text{I}\quad \begin{matrix} OH\cdot CPh{:}C\cdot CO_2Et \\ OH\cdot CPh{:}C\cdot CO_2Et \end{matrix} \qquad \text{II}\quad \begin{matrix} COPh\cdot CH\cdot CO_2Et \\ COPh\cdot CH\cdot CO_2Et \end{matrix}$$

In accord with this view is the fact that the β- and γ-compounds give practically the same spectrum, which differs, however, considerably from that of the α-compound. The transformation of the α- into a mixture of the β- and γ-compounds can readily be followed by examining alcoholic solutions at different intervals of time, at the end of three hours, considerable change has taken place, and at the end of three weeks the ketonization is practically complete.

Baly and *Desch* have found that although ethyl acetoacetate in dilute solution, and its two ethyl derivatives, $CH_3\cdot CO\cdot CHEt\cdot CO_2Et$ and $CH_3\cdot C(OEt){:}CH\cdot CO_2Et$, give no selective but only general absorption, the metallic derivatives, *e.g.* ethyl sodio-acetoacetate, have distinct banded absorption spectra, and that even the addition of a small amount of alkali to ethyl acetoacetate produces a banded spectrum. Acetylacetone itself and its aluminium, beryllium, and thorium derivatives all give banded ultra-violet absorption spectra. Since neither the C- nor the O-ethyl derivative of ethyl acetoacetate produces selective absorption, it would appear that the characteristic band in open-chain compounds cannot be due to either the ketonic or the enolic constitution, and *Baly* and *Desch* draw the conclusion that these absorption bands are only produced by compounds which are in an actual state of change, for example, passing alternately from the ketonic to the enolic form; in all cases valency changes (desmotropism), and in particular cases, *e.g.* keto-enolic compounds, a wandering of a labile atom (tautomerism) occur. Within certain limits the same type of valency change produces an ultra-violet absorption band in the same position, although the

compounds undergoing change may contain elements of very different atomic weights, *e.g.* hydrogen, sodium, aluminium, thorium; the vibrations in the molecule which synchronize with the oscillation frequency of the rays absorbed cannot, therefore, be the vibration of the labile atoms themselves, but may be due to the change of linking (J. C. S. 1905, 768), *i.e.* according to the electronic theory to the vibrations of the valency electrons. The persistence of the band over a definite range of concentration is taken as a measure of the relative number of molecules which are actually undergoing change.

The absorption bands characteristic of simple benzene derivatives may be accounted for in a somewhat similar manner (J. C. S. 1904, 1029, 1905, 1331). In the case of simple benzene derivatives, especially hydrocarbons, seven distinct bands are visible, due to seven distinct valency changes. (Compare also J. C. S. 1906, 514, 983; 1907, 449, 1122, 1908, 1906; 1910, 571, 1337, 1194.)

Baly and *Stewart* (ibid. 1906, 489, 502, 618) have examined the absorption curves of various ketones and quinones. Their results with fairly concentrated solutions show that the ketones which show the most persistent absorption bands are those which are most reactive from a chemical point of view, *e.g.* react most readily with sodium hydrogen sulphite or with hydroxylamine. In these cases also, the bands are attributed to actual valency changes (desmotropism) going on in the molecules of the substances. With β-diketones and monoketones the change is between the keto- and enolic forms.

It is well known that the entrance of substituents into the acetone molecule tends to diminish its reactivity, a phenomenon which for several years has been attributed to steric hindrance (pp. 175, 449). *Baly* and *Stewart* object to this view, since it does not account for the increased reactivity of ethyl acetoacetate as compared with acetone, or more especially with methylethyl ketone. The relative reactivities of the three compounds are indicated by the following numbers: Methylethyl ketone, 22·5; acetone, 39·7; ethyl acetoacetate, 47·0, which give the percentage amount of each compound transformed into its bisulphite derivative after twenty minutes.

The ordinary theory of steric hindrance would lead us to expect that ethyl acetoacetate would be less reactive than acetone, since it contains the relatively large substituent $\cdot CO_2Et$. Since ketones, when arranged according to their reactivities, and according to the persistence of their absorp-

tion bands, follow the same order, there would appear to be a simple relationship between the two properties; and according to *Baly* and *Stewart* both are due to the same cause, namely, the extent to which tautomeric or desmotropic change occurs in the molecule. In the case of the keto-enolic compounds,

$$R\cdot CO\cdot CH_2R' \rightleftharpoons R\cdot C(OH):CHR',$$

the carbonyl group is supposed to be in a specially reactive state during the change—in fact, to be in a condition comparable with what is usually termed the *nascent state* in the case of the elements. The introduction of substituents, as a rule, lessens the amount of tautomeric change occurring in the molecule, and thus lessens its chemical reactivity. The introduction of the carbethoxy-group, however, tends to increase the desmotropism, as is shown by a comparison of the absorption curves of concentrated solutions of acetone and of ethyl acetoacetate, and thus the chemical activity of the ketone is increased and not diminished by the introduction of the $\cdot CO_2Et$ group.

The enormous reactivity of ethyl pyruvate and its very persistent absorption bands are accounted for by a dynamic change of the type

$$CH_3\cdot\overset{\cdot\cdot}{C}\cdot\overset{\cdot\cdot}{C}\cdot OEt \rightleftharpoons CH_3\cdot C:C\cdot OEt$$
$$\qquad\quad \overset{\cdot\cdot}{O}\ \overset{\cdot\cdot}{O} \qquad\qquad\quad \dot{O}\cdot\dot{O}$$

Quinones also give characteristic absorption bands which are attributed to the change:

$$\begin{matrix} CH:CH \\ C\cdot O \\ \\ CH\cdot CH \end{matrix}\!\!\begin{matrix} \diagdown \\ \\ \diagup \end{matrix}\!\!\begin{matrix} \\ ——— \\ \\ \end{matrix}\!\!\begin{matrix} \diagup \\ \\ \diagdown \end{matrix}\!\!\begin{matrix} CH:CH \\ O\cdot C \\ \\ CH\cdot CH \end{matrix} \rightleftharpoons O:C\begin{matrix} \diagup \\ \\ \diagdown \end{matrix}\!\!\begin{matrix} CH:CH \\ \\ CH:CH \end{matrix}\!\!\begin{matrix} \diagdown \\ \\ \diagup \end{matrix}\!\!C:C.$$

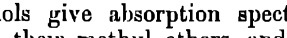
The introduction of substituents into the quinone molecule renders the absorption bands less persistent, and also lessens the chemical reactivity of the compound.

An examination of the absorption curves of the nitranilines, where there are persistent bands in the visible part of the spectrum closely resembling those of quinone, leads *Baly, Edwards,* and *Stewart* (J. C. S. 1906, 513) to the conclusion that the free amines have a quinonoid structure,

$$HN:C\begin{matrix} \diagup \\ \\ \diagdown \end{matrix}\!\!\begin{matrix} CH:CH \\ \\ CH:CH \end{matrix}\!\!\begin{matrix} \diagdown \\ \\ \diagup \end{matrix}\!\!C:N\begin{matrix} \diagup \\ \\ \diagdown \end{matrix}\!\!\begin{matrix} O \\ \\ OH \end{matrix},$$

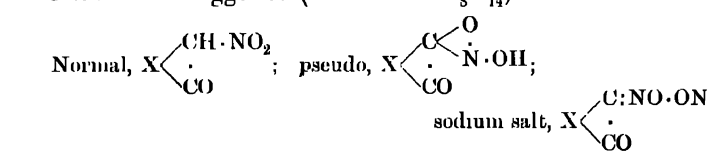
and that tautomeric change of the same type as that described under the quinones occurs. Their hydrochlorides, on the other hand, have the ordinary benzenoid constitution, $NO_2 \cdot C_6H_4 \cdot NH_2$, HCl.

The nitro-phenols give absorption spectra which closely resemble those of their methyl ethers, and would appear to have the benzenoid formula $NO_2 \cdot C_6H_4 \cdot OH$. The sodium salts, on the other hand, give absorption curves which closely resemble those for the nitranilines, and would thus be represented by the quinoid formula,

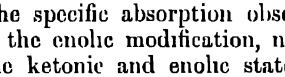


which would be capable of tautomeric change in much the same manner as quinone.

According to *Lowry* and *Desch* (J. C. S. 1909, 807), intramolecular change is not always accompanied by selective absorption. The conversion of normal nitrocamphor into the pseudo-isomeride, a reaction which can be studied quantitatively (p. 657), is not accompanied by any characteristic absorption bands, but such bands make their appearance when an alkali is added, and the addition of an excess of alkali does not produce increased absorption. The absorption cannot be due to tautomeric change, as in the presence of the alkali the nitrocamphor exists as a stable sodium salt. The following formulæ are suggested (where X = C_5H_{14}):



Hantzsch (B **43**, 1549), as the result of spectroscopic investigations of ethyl acetoacetate and its derivatives, draws the conclusion that the specific absorption observed in solutions cannot be due to the enolic modification, nor yet to an oscillation between the ketonic and enolic states, but to an isomeric aci-form in which the latent valencies of two oxygen atoms are operative, *e.g.*:



The fact that an increase in the amount of alkali produces an

increase in the selective absorption is attributed to the fact that an excess of alkali prevents the hydrolysis of the sodium salt to the enol and sodium hydroxide.

The absorption bands of various vapours, *e.g.* benzene, pyridine, furane, and thiophene derivatives, have been studied by *Hartley* (Phil. Trans. 1908, A. **208**, 475) and *Purvis* (J. C. S. 1910, 692, 1035, 1546, 1648; 1911, 2318), who show that in the form of vapour these compounds give absorption spectra which are much more complex than those of their solutions.

The conclusion that ethyl acetoacetate is an equilibrium mixture of the ketonic and enolic modifications—a conclusion based mainly on the study of physical properties—has been confirmed quite recently by other methods. Of these, the following are the more important.

1. *Knorr* (B. 1911, **44**, 1138) has shown that, by cooling to $-78°$ a solution of the ordinary ester in alcohol and ether in an apparatus specially designed to exclude moisture and to maintain a high vacuum, the ketonic form separates as well-defined needles or prisms, m.-pt. $-39°$ and b.-pt. $39°$–$40°$/2 mm. It does not give a coloration with ferric chloride, and does not react with bromine solution. Even at the ordinary temperature it takes several weeks before the equilibrium mixture is again formed. The practically pure enol is obtained by suspending the sodium derivative in light petroleum cooled to $-78°$ in a special apparatus, and passing in hydrogen chloride just insufficient for complete decomposition. The solution when filtered and evaporated at -78 yields the enolic ester as a colourless oil, which gives an intense coloration with ferric chloride. At the ordinary temperature it requires ten to fourteen days to again form the equilibrium mixture, but at $100°$ the change is completed in one minute. By comparing the refractive index of the ordinary ester with the values for mixtures of known concentration, it has been calculated that the equilibrium mixture contains 2 per cent of the enol.

2. By means of experiments made with compounds which exist in stable keto and enolic forms, *K. H. Meyer* (A **380**, 212; B. **44**, 2718) shows that the unsaturated hydroxylic modification reacts instantaneously with an alcoholic solution of bromine, yielding an unstable dibromide, which immediately gives off hydrogen bromide and forms the bromo-ketone. The best method for estimating the amount of enol is to add an excess of the alcoholic bromine solution, to remove the excess by means of β-naphthol, and then to determine the

amount of bromo-ketone by adding potassium iodide solution, and titrating the liberated iodine by means of standard thiosulphate:

$$—CO·CHBr— \rightarrow —CI(OH)·CHBr— \rightarrow —CI(OH)·CHI— \rightarrow —C(OH):CH + I_2.$$

In this way it has been shown that the ordinary ethyl acetoacetate contains about 7 per cent of the enol, and the same results are obtained when freshly prepared solutions in various solvents are examined; but such solutions when kept undergo change, *e.g.* a hexane solution when kept for forty-eight hours at 18° contains nearly equal amounts of keto and enolic modifications. A rise in temperature also tends to favour the formation of the ketonic form. In a similar manner acetylacetone has been shown to contain 80 per cent of enol.

3 *Knorr* and *Schubert* (B 1911, **44**, 2772) use a colorimetric method for estimating enols in allelotropic mixtures, a method which is based on the reaction between the enol and ferric chloride,

$$RH + FeCl_3 = FeRCl_2 + HCl,$$

where R is the enolic residue. The comparison is made with standard solutions prepared by mixing solutions of the pure enol with one of sublimed ferric chloride in molecular proportions

G. **Anomalous Electric Absorption.**—*P. Drude* (B. 1897, **30**, 941) has found that numerous organic compounds containing hydroxyl groups are capable of absorbing electric waves of high frequency (about 400 million per second), although they are not good conductors; whereas ordinary non-conductors show no such absorption The phenomenon is termed by *Drude* "**anomalous electric absorption**", and, with the exception of water, all liquid hydroxyl derivatives display this anomalous absorption. The presence of hydroxyl groups cannot always be inferred from the exhibition of anomalous absorption, as a few compounds which contain no hydroxyl groups possess the property to a slight extent.

Drude himself applied the method to the examination of certain keto-enolic tautomeric substances. Ethyl acetoacetate itself absorbs but slightly, and is thus presumably mainly the [illegible]form.

Ethyl benzoylacetate and ethyl oxalacetate absorb strongly, and should thus contain considerable percentages of the enols.

H. **Optical Activity.**—Attention has already been drawn to the fact that compounds, the molecules of which are asymmetric, are, when in the liquid or dissolved state, optically active, *i.e.* able to rotate the plane of polarization (p. 154) either to the right (dextro-rotatory) or to the left (lævo-rotatory). The specific rotatory power $[\alpha]$ of a liquid is obtained by dividing the observed rotation by the length of the column of liquid used and by the specific gravity of the liquid $[\alpha] = \frac{a}{l \times d}$, and the molecular rotation is the product of the specific rotatory power into the molecular weight (M).

For a solution:

$$[\alpha] = \frac{100a}{l \times c} = \frac{100a}{l \times p \times d} = \frac{100a \times v}{l \times g},$$

where c = concentration or number of grams of the active compound in 100 c.c. of solution, d = specific gravity of the solution, p = per cent of active substance in the solution, and g = number of grams of active substance in v c.c. of solution. The specific rotatory power of a solution may often be increased enormously by the introduction of an inorganic salt; some of the most effective are boric acid and alkali molybdates and tungstates. As a rule, the nature of the monochromatic light, *e.g.* sodium light, is indicated, also the temperature and the nature of the solvent, *e.g.* $[\alpha]_D^{15°}$, where D indicates that the number refers to sodium light and that the determination was made at 15°. Various attempts have been made to deduce general conclusions bearing upon the amount of rotation and the constitution of the compound. *Guye* (C. R. **110**, 714) has attempted to connect the degree of asymmetry of the molecule of a compound C a, b, c, d with the masses of the four radicals present and the distance of the centre of gravity of the molecules from the centre of the tetrahedron (C. R. 1896, 1309; 1898, **181**, 307). The researches of *P. F. Frankland* and others (J. C. S. 1899, 337, 347, 493, &c.) have shown that *Guye's* conclusions are not of general application.

Patterson (J. C. S. 1901, 167, 477; 1902, 1097, 1134; 1904, 765, 1116, 1153; 1905, 122, 313) has made a careful investigation of the influence of solvent, temperature, &c., on the optical activity of various substances. He finds that *dilute* solutions of ethyl tartrate in water, or in methyl, ethyl, or propyl alcohol, possess a higher specific rotation than the pure ester itself, that the specific rotation increases with dilution

until a concentration of 10 grams in 100 grams of solvent is reached, and then the rotation remains practically constant. The highest values are always obtained with aqueous solutions, and the other solutions follow in the order—methyl, ethyl, *n*-propyl, isobutyl, and sec-octyl alcohol.

The effect of increase of temperature upon corresponding solutions varies somewhat. In water the coefficient is negative for dilute solutions, but in the various alcoholic solutions it is positive, as it is also for the pure ester.

According to *Patterson* the change in specific rotation with solvent or temperature is not to be attributed to association, but rather to the internal pressure of the solvents (compare Abst. 1900, **2**, 329).

Walden has also conducted numerous investigations on optically active compounds, and concludes that there is a relationship of a qualitative nature only between the optical activity of a substance in a given solution and its molecular weight in that solution. (For a summary of work on optical activity see *Walden*, B. 1905, **38**, 345–409).

The polarimetric method has been used by *Lowry* (J. C. S. 1899, **75**, 211) for a quantitative study of the tautomerism or dynamic isomerism of the nitro- and bromo-nitro-camphors.

Each of these compounds appears to exist in two distinct forms, one of which contains the nitro-group, $>CH\cdot N\lessdot^{O}_{O}$, and the other the isonitro-group, $>C{:}NO\cdot OH$. Ordinary crystalline nitro-camphor, melting at 102°, is regarded as consisting of the normal form, its homogeneity being vouched for by the constancy of its initial specific rotatory power ($[\alpha]_D = -124°$ in 5-per-cent benzene solution), and by its well-defined crystalline form. When dissolved the nitro-compound at once begins to change into the pseudo form, and this change is accompanied by an alteration in the rotatory power; with the 5-per-cent benzene solution the specific rotatory power has fallen to −104° at the end of four days, and then remains stationary. This solution represents a mixture of the normal and pseudo-compounds in dynamic equilibrium, and assuming that the pseudo-compound, which so far has not been obtained in a pure form, has a specific rotatory power +180° in benzene solution, then the solution, with a rotation of −104°, contains some 93 per cent of the normal and 7 per cent of the pseudo form.

The velocity of the transformation, normal → pseudo, is increased by rise of temperature, by increase in concentration, and by the addition of traces of alkalis

Both the normal and pseudo forms of π-bromo-nitro-camphor have been isolated (*Lapworth* and *Kipping*, J. C. S. 1896, 304). The compound, melting at 142°, when dissolved in benzene, gives an initial specific rotatory power +188°, which changes to −38° in a 3·33-per-cent benzene solution, and appears to be the pseudo form. The compound melting at 108° shows a change in rotatory power from −51° to −38°, and appears to be the normal compound. When either of the two pure compounds is dissolved in benzene, tautomeric change occurs, and a mixture of the two compounds in dynamic equilibrium is obtained. From the specific rotatory power of this solution, viz. −38°, it follows that it contains some 5·5 per cent of pseudo-compound for 94·5 of the normal.

The change in rotation of an optically active solution is usually known as **mutarotation** (p. 309), and is a property exhibited by various optically active compounds, especially sugars, *e.g.* glucose, galactose, xylose, milk-sugar, and maltose, and certain hydroxy-acids and their lactones, *e.g.* anhydrous lactic acid

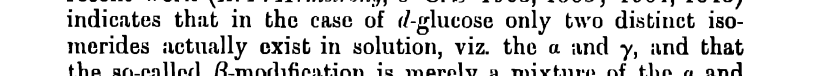
In all cases the rotation changes when the solution is kept; with glucose, for example, the value decreases to half, with milk-sugar the values are as 1·6 : 1, with galactose 1·46 : 1, and with xylose 4·67 : 1. The rotatory powers of maltose and lactic acid solutions increase when kept.

All acids and alkalis appear to facilitate the conversion, and in the order of their degree of ionization. Common salt, alcohol, and various organic compounds, on the other hand, tend to retard the transformation.

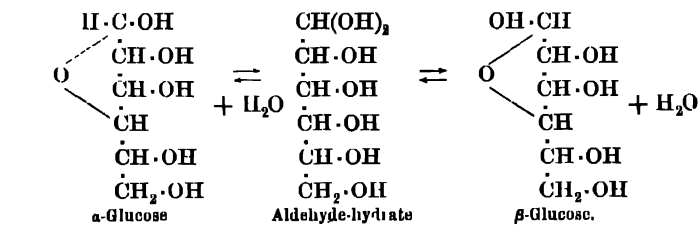
Various theories have been brought forward in order to account for the phenomenon. The first of these assumed the presence of complex molecules, *e.g.* $(C_6H_{12}O_6)_x$, in the freshly-prepared solution, and the gradual decomposition of these into the simpler molecules, $C_6H_{12}O_6$, thus producing a lowering of the rotatory power. The assumption of the presence of complex molecules was rendered untenable as soon as it was shown that the molecular weight, as determined by the cryoscopic method, is the same in the freshly-prepared and the old solution. The second explanation was that, after solution, water is either withdrawn from or added on to the original molecular aggregates. The latest theory is that the different

rotations are due to different isomeric substances present in the two solutions, and that a gradual change in rotation accompanies the conversion of the one isomeride into the other.

Tanret (1895) claimed to have isolated three distinct modifications of *d*-glucose, which had the respective specific rotatory powers $\alpha = +105°$, $\beta = +52{\cdot}5$, and $\gamma = +22{\cdot}5$ More recent work (*E. F. Armstrong*, J. C. S. 1903, 1305; 1904, 1043) indicates that in the case of *d*-glucose only two distinct isomerides actually exist in solution, viz. the α and γ, and that the so-called β-modification is merely a mixture of the α and γ in chemical equilibrium. The α- and γ-modifications are represented as stereo-isomeric, and correspond in structure with the α- and β-methyl-glucosides (p. 310), since these glucosides, when hydrolysed with enzymes, have rotatory powers of the order of those of the α- and γ-glucoses, and the addition of an alkali to the products of hydrolysis produces the same change as with the α- and γ-sugars They are therefore now termed α- and β-glucoses, and may be represented by the configurations:



(Compare also *Behrend* and *Roth*, A. 1904, **331**, 359, and *Lowry*, J. C. S. 1904, 1551). *Lowry* concludes that in an ordinary solution of glucose, in addition to the α- and β-modifications, small amounts of the aldehyde or aldehyde-hydrate are also present. This accounts for the aldehydic properties of glucose solutions, and also affords an explanation of the conversion of the α- into the β-glucose.



(For *resumé*, see *Lowry*, B. A. Rep. 1904, 193.)

Asymmetric Synthesis.—It has already been stated that the product formed by the synthesis of a compound containing an asymmetric carbon atom from symmetrical compounds is always a mixture or compound of the *d*- and *l*-modifications in equal amounts, and a single active modification can only be obtained by the resolution of this racemic compound or mixture. Numerous attempts have been made to carry out an asymmetric synthesis, *i.e.* according to *Marckwald* (B. 1904, **37**, 1368), to obtain artificially an optically active compound from a symmetrical substance by the employment of an active product but without the use of an analytical process (such, for example, as those involved in the usual separation of racemic mixtures). A synthesis suggested by *E. Fischer* was as follows.—By the cyanhydrin reaction mentioned on p. 304 it is possible to transform an optically active monose containing C_n into a mixture of two active sugars containing C_{n+1}. The amounts of the two active compounds vary considerably in different cases, and with *d*-mannose only one *d*-mannoheptose can be isolated. Similarly the *d*-mannoheptose yields only one mannooctose, and this only one nonose. If it were possible by some method to decompose this *d*-manno-nonose so as to regenerate *d*-mannose then the other product would be an active glyceric aldehyde·

Mannononose, $CHO\cdot CH(OH)\cdot CH(OH)-CH(OH)\cdot[CH\cdot OH]_4\cdot CH_2OH$

→ glyceric aldehyde, $CHO\cdot CH(OH)\cdot CH_2\cdot OH$ and $CHO\cdot[CH\cdot OH]_4\cdot CH_2\cdot OH$.

Cohen and *Whiteley* (J. C. S. 1901, 1305), starting with cinnamic acid, prepared active amyl and menthyl esters, to which they added bromine and then attempted to obtain an active cinnamic acid dibromide, $C_6H_5\cdot CHBr\cdot CHBr\cdot CO_2H$, by the hydrolysis of the esters, but without success. The hydrolysis of the products obtained by reducing the active amyl and menthyl esters of mesaconic, α-methylcinnamic, and pyruvic acids gave rise to inactive acids. Similar negative results were obtained by *Kipping* (P. 1900, 226). *A. M'Kenzie* (J. C. S. 1904, 1250; 1905, 1373; 1906, 365) has succeeded in accomplishing several asymmetric syntheses. Thus when *l*-menthyl pyruvate, $CH_3\cdot CO\cdot CO\cdot OC_{10}H_{19}$, is reduced by aluminium amalgam, a mixture of unequal amounts of *l*-menthyl *d*-lactate and *l*-menthyl *l*-lactate is formed. When this mixture is hydrolysed by an excess of alcoholic potassic hydroxide and the *l*-menthol removed, a dextro-rotatory potassic salt containing

an excess of *l*-lactate over *d*-lactate is produced; this mixture, when acidified, becomes lævo-rotatory, and the asymmetric synthesis of *l*-lactic acid is thus accomplished. If *l*-menthyl benzoylformate, $C_6H_5 \cdot CO \cdot CO_2 \cdot C_{10}H_{19}$, is treated in exactly the same manner, the final product is *r*-mandelic acid, due, probably, to the racemizing effect of the alkali. A second asymmetric synthesis has been accomplished by *M'Kenzie* by means of *Grignard's* reaction. Thus *l*-menthyl benzoylformate and magnesium methyl iodide yield the additive compound $CMePh(O \cdot MgI)(CO_2C_{10}H_{19})$, which is converted by dilute acids into the *l*-menthyl phenylmethylglycollate $CMePh(OH)(CO_2C_{10}H_{19})$, from which, on hydrolysis with alcoholic potassium hydroxide, a lævo-rotatory potassium phenylmethylglycollate, $CMePh(OH)(CO_2K)$, was obtained. Thus

$$\underset{\text{Inactive}}{C_6H_5 \cdot CO \cdot CO_2H} \longrightarrow \underset{\text{Active}}{C_6H_5 \cdot CO \cdot CO_2C_{10}H_{19}} \longrightarrow \underset{\text{Active}}{C_6H_5 \cdot C(CH_3)(OH)(CO_2C_{10}H_{19})}$$

$$\longrightarrow \underset{\text{Active}}{C_6H_5 \cdot C(CH_3)(OH)(CO_2H)}$$

Similar active acids have been obtained by using other *Grignard* reagents in conjunction with *l*-menthyl benzoylformate.

For a further asymmetric synthesis, see *Marckwald*, B. 1904, **37**, 349.

The Walden Inversion.—In a chemical reaction in which one radical is displaced by another, it is usually assumed that the group introduced takes the place of the radical removed, unless reasons to the contrary can be adduced. When an optically active compound is used we should expect the product formed to correspond in configuration with the original substance. That this is not always true follows from the fact that during certain reactions racemization occurs, and the product obtained is optically inactive (cf. p. 257). Even more remarkable than this is the phenomenon known as Walden's inversion. An example of this is met with in the conversion of *l*-chloro-succinic acid into the *d*-isomeride by the following series of reactions:

$$\underset{}{l\text{-Chloro-acid}} \xrightarrow[\text{Moist } Ag_2O]{} \underset{}{l\text{-malic acid}} \xrightarrow[PCl_5]{} \underset{}{d\text{-chloro-acid.}}$$

It is not possible to say which of the two reactions is normal and which abnormal, as although the malic acid may be lævo-rotatory, its configuration may correspond with that of the *d*-chloro-acid and not with that of the *l*-acid.

Walden (B. **32**, 1833) carried out a remarkable series of

experiments on the reaction between *l*-chloro- and *l*-bromo-succinic acids and various alkalis. He found that the hydroxides of potassium, rubidium, and ammonium gave practically pure *d*-malic acid, moist silver oxide gave the pure *l*-malic acid; and the hydroxides of sodium, barium, lead, and lithium gave mixtures in which the *d*-acid preponderated, whereas oxides of mercury and palladium gave mixtures in which the *l*-acid was in excess. The conclusion was drawn that the reaction with potassium hydroxide is normal, and that inversion occurs when silver oxide is used.

Interesting cases are those in which a complete cycle is involved, *e.g.*:

1. *l*-Chloro-succinic acid $\xrightarrow{\text{Moist } Ag_2O}$ *l*-malic acid
   $\uparrow PCl_5$ $\downarrow PCl_5$
   d-malic acid $\xleftarrow{\text{Moist } Ag_2O}$ *d*-chloro-succinic acid.

2. *d*-Alanine $\xrightarrow{NOBr}$ *l*-bromo-propionic acid
   $\uparrow NH_3$ $\downarrow NH_3$
   d-bromo-propionic acid $\xleftarrow{NOBr}$ *l*-alanine.

3. *d*-$C_6H_5\cdot CH(OH)\cdot CO_2H$ $\xleftarrow{HNO_2}$ *l*-$C_6H_5\cdot CH(NH_2)\cdot CO_2H$
   $\downarrow PCl_5$ $\uparrow NH_3$
   l-$C_6H_5\cdot CHCl\cdot CO_2H$ *d*-$C_6H_5\cdot CHCl\cdot CO_2H$
   $\downarrow NH_3$ $\uparrow PCl_5$
   d-$C_6H_5\cdot CH(NH_2)\cdot CO_2H$ $\xrightarrow{HNO_2}$ *l*-$C_6H_5\cdot CH(OH)\cdot CO_2H$

In some of these cases it is possible to determine in which of the different reactions inversion occurs; thus in Example No. 2 the reaction with nitrosyl bromide is abnormal and not that with ammonia, as *E. Fischer* has shown that under very varying conditions ammonia always gives the same product. With NOBr *d*-alanine gives *l*-bromo acid, but the ester of *d*-alanine reacts with NOBr, giving *d*-bromo-propionic acid. *l*-Valin (amino-isovaleric acid), with NOBr gives the *l*-bromo acid, and this with ammonia yields *l*-valin.

Practically all the inversions mentioned above occur when the asymmetric carbon atom has a carboxyl group attached to it. Experiments made by *E. Fischer* and *Scheibler*, with compounds in which the asymmetric atom is in the β-position with respect to the carboxylic group, prove that inversion does not take place:

$$l\text{-}CH_2\cdot CH(OH)\cdot CH_2\cdot CO_2H \underset{Ag_2O}{\overset{PCl_5}{\rightleftharpoons}} d\text{-}CH_2\cdot CH(OH)\cdot CH_2\cdot CO_2H,$$

and similar results are obtained when the methyl esters are used. The same holds good in the case of β-hydroxy-β-phenyl-propionic acid (*M'Kenzie* and *Humphreys*). There are, however, several exceptions, *e.g.*:

1. *Fischer:*

$$\begin{array}{ccc} d\text{-}\beta\text{-Amino-butyric acid} & \xrightarrow[HNO_2]{} & l\text{-}\beta\text{-hydroxy-butyric acid} \\ \downarrow NOCl & & \\ l\text{-}\beta\text{-chloro-butyric acid} & \xrightarrow[Water]{} & d\text{-}\beta\text{-hydroxy-butyric acid.} \end{array}$$

2. *M'Kenzie and Barrow:*

$$\begin{array}{ccc} d\text{-}\beta\text{-Hydroxy-}\beta\text{-phenyl-propionic acid} & & \\ \xrightarrow[SOCl_2]{} & d\text{-}\beta\text{-chloro-}\beta\text{-phenyl-propionic acid} & \\ & \downarrow \text{Water} & \\ & l\text{-}\beta\text{-hydroxy-}\beta\text{-phenyl-propionic acid.} & \end{array}$$

Frequently phosphorus pentachloride and thionyl chloride react differently, *e.g.*:

$$\begin{array}{lcl} l\text{-Mandelic acid or ester} & \xrightarrow{PCl_5} & d\text{-chloro acid or ester} \\ l\text{-mandelic acid or ester} & \xrightarrow[SOCl_2]{} & l\text{-chloro acid or ester.} \end{array}$$

In connection with this the following cycles are of interest.

$$\begin{array}{ccc} l\text{-Mandelic acid} & \longrightarrow & d\text{-chloro acid} \\ \uparrow NaOH & PCl_5 & \downarrow NaOH \\ l\text{-chloro acid} & \longleftarrow & d\text{-mandelic acid} \\ & PCl_5 & \end{array}$$

$$\begin{array}{ccc} l\text{-Mandelic acid} & \longrightarrow & l\text{-chloro acid} \\ \downarrow Ag_2CO_3 + water & SOCl_2 & \downarrow Ag_2CO_3 + water \\ d\text{-chloro acid} & \longleftarrow & d\text{-mandelic acid.} \\ & SOCl_2 & \end{array}$$

In the case of β-hydroxy-β-phenyl-propionic acid it has been shown that the reaction with thionyl chloride is normal, since the chloro ester derived from the *l*-hydroxy ester is transformed back into *l*-hydroxy acid when warmed with water and marble.

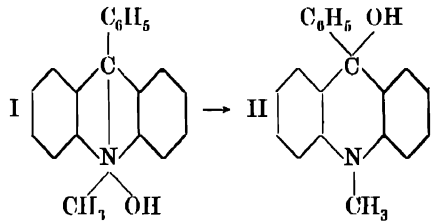
(For details see *Walden*, B. **28**, 2772; **29**, 133; **30**, 3146. *E. Fischer* and students, B. **41**, 889, 2891; **42**, 1219; **43**, 2020; A. **381**, 123; **383**, 337; **386**, 374. *Werner*, A. **386**, 65. *M'Kenzie* and others, J. C. S. 1908, 811; 1909, 777; 1910, 121, 1016, 1355, 2564; 1911, 1910, 1912, 390. *Bulmann*, A. **1912**, **388**, 330.)

I. **Electrical Conductivity.**—Attention has previously (p. 161) been drawn to the fact that the degree of ionization, α, of an acid in solutions of given concentration, v, may be determined by a comparison of the electrical conductivity, λ (reciprocal of resistance), at that dilution with the conductivity at infinite dilution when ionization would be complete, *i.e.* $\alpha = \frac{\lambda}{\mu\infty}$. From *Ostwald's* dilution law, based on the law of mass action, it follows that $\frac{\alpha^2}{v(1-\alpha)}$ is a constant $= k$, where v = number of litres of solution containing one equivalent of acid. This constant k (or $100k = K$) is known as the **dissociation constant**, and is used as a measure of the strength of all feeble acids. The effect of the introduction of strongly negative groups into the acid molecule on this constant has been referred to (pp. 168, 447), and the influence of strongly positive groups, *e.g.* NH_2, is equally marked. Thus benzoic acid = 0·006, *o*-amino-benzoic = 0·0009, *m*-amino-benzoic = 0·0010, and *p*-amino-benzoic = 0·008.

Hantzsch has used the electrical conductivity method in the diagnosis of pseudo-acids and bases. Thus with certain nitro-compounds the ordinary compound $R \cdot CH_2 \cdot NO_2$ is a pseudo-acid and the isonitro-compound $R \cdot CH : NO \cdot OH$ is a true acid, and all the salts are derived from the latter. These salts, as a rule, are but little hydrolysed, as the isonitro-compounds are relatively strong acids. A solution of such a salt will thus contain the metallic ions and the isonitro-ion $R \cdot CH : NO \cdot O^-$. When this solution is mixed with an equivalent quantity of hydrochloric acid the ions present are $\overset{+}{Na}$, $\overset{-}{Cl}$, $R \cdot CH : NO \cdot O^-$, and $\overset{+}{H}$. In the majority of cases there is a considerable tendency for the strongly acidic and hence strongly ionized isonitro-compound (true acid) to become transformed into the ordinary nitro-compound (pseudo-acid). As this is practically a non-electrolyte, it follows that as this transformation occurs the conductivity of the solution will gradually diminish until it attains the value of a sodium chloride solution of the given concentration. Thus with sodium *p*-bromophenylnitromethane, $C_6H_4Br \cdot CH : NO \cdot ONa$, at 25°, and $v = 256$, after mixing with an equivalent of hydrochloric acid, the conductivity, $\mu = 151{\cdot}4$ after 1·5 minute, and after 45 minutes a constant value $\mu = 129{\cdot}5$ was obtained. This approximates to the value $\mu_{256} = 114{\cdot}4$

for sodic chloride, and the difference may be due to secondary changes.

Similar results have been obtained with pseudo-bases. The true base, methyl-phenyl-acridonium hydroxide (I), which is first liberated when salts of the base are decomposed with alkali, is readily transformed into the pseudo-base with the carbinol formula (II):



which is practically a non-electrolyte. When a solution of the chloride of the base is neutralized with an equivalent of sodic hydroxide, the solution has a maximum conductivity which gradually diminishes until the value for a solution of sodic chloride of the given concentration is practically reached Similarly with the sulphate and an equivalent quantity of barium hydroxide; at 0° and $v = 256$, the initial conductivity was $\mu = 119\cdot2$, but after 15 hours it had fallen to $\mu = 1\cdot7$ (due to small amounts of dissolved baric sulphate). Phenomena of this kind, which are termed by *Hantzsch* "slow neutralization", are largely used to denote tautomeric change, *i.e.* the change from a true acid to a pseudo-acid or from a true base to a pseudo-base (cf. p. 485) during the conversion of the salt into the acid or base.

The study of other physical properties such as **Internal Viscosity** (Zeit. phys. 1887, **1**, 285, 293; 1888, **2**, 744; compare also *Dunstan*, J. C. S. 1907, 1728; 1908, 1815, 1919; 1909, 1556; 1910, 1935), **Heat of Combustion** (*Stohmann*, Zeit. phys. 1890, **6**, 334; 1892, **10**, 410), **Capillary Constants** (*Schiff*, A. 1884, **223**, 47), **Magnetic Susceptibility** (*Pascal*, Bull. 1909. 1110, 1910, 17, 45; 1911, 6, 79, 134, 177, 336, 809, 868) indicate that here also there are similar relationships between constitution and physical properties.

XLVIII. FERMENTATION AND ENZYME ACTION

A. **Alcoholic Fermentation.**—*Lavoisier*, 1789, was the first to recognize that alcoholic fermentation consists essentially in the decomposition of a sugar into alcohol and carbon dioxide; and *Gay-Lussac*, 1810, drew attention to the fact that the presence of air appeared to be essential for fermentation and putrefaction to take place. The fact that brewers' yeast is a low form of plant life was discovered independently by *Cagniard-Latour*, *Theodor Schwann*, and *Kutzing*, 1837 By microscopical examination they observed the growth of the organism, and showed that it could be destroyed by heat or by certain poisons. These results were not accepted by *Berzelius*, *Liebig*, and others, who still regarded yeast as a chemical substance without life. According to *Berzelius* the yeast acted as a contact substance which decomposes the sugar without undergoing change itself; whereas *Liebig* regarded the ferment as an extremely susceptible substance, which undergoes a change of the nature of decay, and suggested that the decomposition of the sugar was a type of sympathetic reaction induced by the change of the ferment. In 1857 *Pasteur* began his researches on fermentations. He was able to show that in other cases of fermentation, such as the lactic fermentation of milk, micro-organisms are present. He was further able to show that during alcoholic fermentation the yeast grows and multiplies, and was led to the conclusion that fermentation is a physiological process accompanying the life of the yeast.

In his own words: "I am of opinion that alcoholic fermentation never occurs without simultaneous organization, development, multiplication of cells, or the continued life of cells already formed". This conclusion harmonized with the facts already known that boiled liquids could be kept from fermenting by heating or filtering through cotton wool the air admitted to the liquid.

It was *Pasteur* who proved that only 95 per cent of the glucose is accounted for as carbon dioxide and alcohol; he was able to isolate glycerol and succinic acid from the final products.

As early as 1858 *M. Traube* expressed the view that all fermentations produced by living organisms are ultimately due to ferments, which are definite chemical substances manufactured in the cells of the organism. These ferments he re-

garded as analogous to proteins *Traube's* conclusions have been verified in the case of alcoholic fermentation by *Buchner's* isolation of "zymase" from yeast (see p. 77). Buchner's yeast juice, when quite free from yeast cells, can ferment solutions of glucose, fructose, sucrose, and maltose; and the fermenting power is not destroyed by the addition of chloroform, benzene, or sodium arsenite, antiseptics which inhibit the action of living cells, by filtration through a Berkefeld filter, by evaporation to dryness at 30°–35°, or by precipitation with alcohol. The fermenting power is, however, completely destroyed by heating to 50°, or by the addition of powerful antiseptics. The activity of the juice diminishes in the course of time, as a digestive enzyme is also present which gradually decomposes the zymase. Both in rate of fermentation and in the total fermentation produced, the extract or juice is much less efficient than the equivalent amount of living yeast, and glycerol is formed as a by-product when the extract is used. During fermentation a portion of the sugar is converted into a compound of less reducing power which is not fermented, but which yields sugar when hydrolysed with acids. Permanent preparations containing zymase can be obtained by evaporating the juice to a syrup at 20°–25°, drying at 35°, and then exposing to sulphuric acid in a vacuum desiccator. Such a powder when dry retains its activity for twelve months, and can be heated at 85° for eight hours without any serious loss of fermenting power Another preparation can be obtained by bringing the juice into 10 volumes of acetone, centrifuging, washing the precipitate with acetone and then with ether, and drying over sulphuric acid. An important medicinal preparation known as *zymin* is manufactured by stirring moist yeast with acetone, filtering and draining at the pump, again mixing with acetone and draining. The product is then roughly powdered, kneaded with ether, filtered, drained, and spread on filter paper or porous plates, and finally dried at 45° for twenty-four hours. This product is quite incapable of growth or reproduction, but produces fermentation and is much more active than yeast extract.

The researches of *Harden* and *Young* (Abs. 1905, ii. 109; 1906, i. 470) indicate that the activity of yeast juice or extract is due to an enzyme and a co-enzyme, which can be separated by filtration or dialysis through a Martin gelatin filter; the residue contains the enzyme, and the filtrate or dialysate the co-enzyme. Neither by itself can induce fer-

mentation, but a mixture of the two is equal in activity to the original juice. The co-enzyme is dialysable, and is not destroyed by boiling, but disappears from yeast juice during fermentation, or when the juice is allowed to undergo autolysis. It cannot be a protein, and its nature has not yet been determined. It is decomposed by acid or alkaline hydrolysing agents, by repeatedly boiling the extract, and also by the lipase of castor-oil seeds. In the case of other fermentations brought about by enzymes, *e.g.* lipase, it has been clearly demonstrated that both enzyme and co-enzyme are necessary, and also that the co-enzyme is a metallic salt of the complex taurochloric acid (p. 196). *Harden* and *Young* (Abs. 1908, i. 590) have also shown that phosphates added to a mixture of glucose and yeast juice produce both an initial acceleration and also an increased total fermentation. An optimum concentration of phosphate exists which produces a maximum initial rate of fermentation; an increase beyond this optimum diminishes the rate. The reaction between the glucose and phosphate is represented by the following equations:—

$$2C_6H_{12}O_6 + 2Na_2HPO_4 = 2CO_2 + 2C_2H_6O + C_6H_{10}O_4(PO_4Na_2)_2 + 2H_2O$$

and $$C_6H_{10}O_4(PO_4Na_2)_2 + 2H_2O = C_6H_{12}O_6 + 2Na_2HPO_4.$$

According to the second of these, the glucose phosphate is hydrolysed by the water and yields sodium phosphate, which can then react with a further quantity of glucose. These conclusions are supported by the following facts. Careful experiments have shown that during the period of increased fermentation the amounts of alcohol and carbon dioxide produced exceed those which would have been formed in the absence of added phosphate by a quantity exactly equivalent to the phosphate added in the ratio $C_2H_6O:Na_2HPO_4$. (Compare also *Iwanoff*, Abs. 1909, **1**, 752.) It has been proved that the metallic phosphate is not the co-enzyme already mentioned, as the filtered enzyme and phosphate are not capable of inducing fermentation in the absence of the filtrate. Fermentation does not proceed in the absence of phosphate although both enzyme and co-enzyme are present, and although arsenates and arsenites have accelerating actions on the rate of fermentation they cannot be used in place of the phosphate. The function of the arsenate or arsenite appears to be t act as accelerators in the decomposition of the glucose phosphate. *Slator* finds that phosphates have not an accelerating effect

when living yeast cells are employed. He has estimated (J. C. S. 1906, **89**, 128; 1908, **93**, 217) the amounts of carbon dioxide evolved during given periods of time when yeast itself is used, and finds that the rate of fermentation is exactly proportional to the amounts of yeast present, and is almost independent of the concentration of the glucose. A yeast which can ferment glucose does not necessarily ferment isomeric sugar, *e.g.* galactose, it is probable that different enzymes are required for the different sugars.

The fermentation of glucose undoubtedly consists of a whole series of chemical reactions, at present we know the substances we start with and the final products obtained. Several suggestions have been made with regard to the nature of some of the intermediate products. *Buchner* and *Meisenheimer* (B. 1905, **38**, 620) have suggested that lactic acid (p. 213) is first formed by the action of zymase on glucose, and that a second enzyme, lactacidase, then decomposes the lactic acid into ethyl alcohol and carbon dioxide. A serious objection to this view is that lactic acid itself is only very slowly fermented by yeast (*Slator*).

Another suggestion is that dihydroxy-acetone, $CO(CH_2 \cdot OH)_2$, is an intermediate product, and it has been proved that this compound can be fermented by yeast (*Buchner* and *Meisenheimer*, B. **43**, 1773; *Lebedeu*, **44**, 2932), compare also *Franzen* and *Steppuhn*, ibid., 2915

Of the by-products mentioned on p. 76, glycerol is formed from the sugar, as *Buchner* and *Meisenheimer* have shown that it is also formed when yeast extract or zymin acts on sugar solutions. The fusel oil and succinic acid, on the other hand, do not owe their origin to the sugar, but to other products present in the mixture undergoing alcoholic fermentation. The researches of *F. Ehrlich* (1904–1910) prove that the alcohols and also the aldehydes present in ordinary fusel oil are derived from the amino-acids formed by the hydrolysis of proteins. Thus isoamyl alcohol, one of the chief constituents of fusel oil, is closely related to leucine, α-amino isohexoic acid, and active amyl alcohol to isoleucine, α-amino-β-methyl-valeric acid, both of which are formed by the hydrolysis of proteins, and according to *Ehrlich* both these acids are transformed into the corresponding amyl alcohols under the influence of pure yeast cultures, in the presence of sugar:

$$(CH_3)_2CH \cdot CH_2 \cdot CH(NH_2) \cdot CO_2H + H_2O \rightarrow (CH_3)_2CH \cdot CH_2 \cdot CH_2 \cdot OH + CO_2 + NH_3.$$

These changes, although brought about by yeast, do not occur when zymin or yeast extract is used. Other amino acids undergo a similar decomposition. tyrosine (p. 459) yields *p*-hydroxy-phenyl-ethyl-alcohol, tyrosol, $OH \cdot C_6H_4 \cdot CH_2 \cdot CH_2 \cdot OH$, and phenyl-alanine (p. 453) gives phenyl-ethyl alcohol.

The ammonia is not found at the end of the reaction, as it is used up by the organism for the purpose of building up new protein molecules. If appreciable amounts of simple nitrogenous substances, such as ammonium salts, are originally present in the fermenting liquor, the organism uses these in preference to decomposing the amino-acids, and *Ehrlich* has found it possible to increase or diminish the amounts of fusel oil formed, by diminishing or increasing the amounts of ammonium salts present at the beginning of the fermentation. Practically all amino-acids formed by the hydrolysis of proteins can undergo similar decomposition by yeast, but only in the presence of sugar. The succinic acid found as a by-product in alcoholic fermentation is probably formed in a similar manner from glutamic acid.

According to *Neuberg* and *Fromherz* (1911), ketonic acids are probably formed as intermediate products in the fermentation of amino-acids to alcohols, and *Neuberg* has been able to show that many α-ketonic acids, *e.g.* pyruvic, $CH_3 \cdot CO \cdot CO_2H$, and oxalacetic, $CO_2H \cdot CH_2 \cdot CO \cdot CO_2H$, are readily decomposed by yeast even in the absence of sugar, yielding carbon dioxide and aldehyde:

$$CH_3 \cdot CO \cdot CO_2H \longrightarrow CH_3 \cdot CHO + CO_2$$

With a 1-per-cent solution of pyruvic acid the decomposition is almost as rapid as with a sugar solution. The decomposition is probably due to an enzyme, termed "carboxylase" by *Neuberg*.

For fermentations induced by organisms other than yeasts, see pp. 150, 152, 214. According to *Harden* (J. C. S. 1901, 610), *Bacillus coli communis* ferments glucose, fructose, or mannitol, yielding lactic, succinic, and acetic acids, alcohol, formic acid, carbon dioxide, and hydrogen. The main reaction can be represented by the equation:

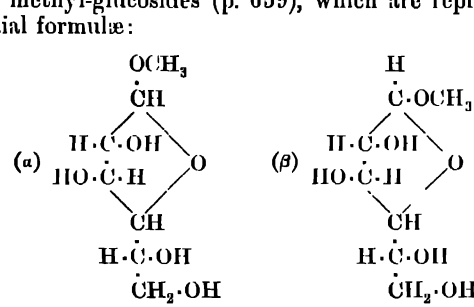
$$2C_6H_{12}O_6 + H_2O = 2C_3H_6O_3 + C_2H_4O_2 + C_2H_6O + 2CO_2 + 2H_2.$$

With glucose the weight of lactic acid is practically 50 per cent of the sugar, and the alcohol and acetic acid are formed in equal amounts. The alcohol probably comes from the

group $CH_2(OH)\cdot CH(OH)$, and as this group occurs twice in the molecule of mannitol the yield of alcohol is much greater when this compound is used. The lactic acid is probably derived from the $CH(OH)\cdot CH(OH)\cdot CH(OH)$ grouping. *B. typhosus* yields similar products, except that it gives formic acid instead of carbon dioxide and hydrogen (Abs 1906, II, 380).

B. **Enzyme Action**.—Attention has been drawn several times (pp. 76, 77, 423) to the fact that chemical decompositions can be brought about by certain complex organic substances found in animal and plant tissues. Such substances are termed *unorganized ferments* or *enzymes*. The great majority act as catalysts in processes of hydrolyses, *e.g.* invertase which hydrolyses cane sugar, amylase which hydrolyses starch, emulsin (p. 423), myrosin (p. 593), pepsin and trypsin (p. 598), lipases which hydrolyse esters, but in addition there are enzymes which bring about oxidation, viz the *oxiduses*, enzymes which bring about complex reactions, *e.g.* zymases. The enzymes are unstable nitrogenous compounds of colloidal nature, but not necessarily proteins. They act as catalysts, in the majority of cases as positive, but in a few as negative. The catalytic nature is shown by the fact that the rate of reaction is directly proportional to the concentration of the enzyme, but that the total decomposition is independent of the amount of enzyme, provided sufficient time is allowed, and provided the enzyme does not undergo decomposition. They are sensitive to high temperatures, *e.g.* when heated to below 100° their activity is completely destroyed; they are, however, resistant towards certain antiseptics which destroy protoplasm and kill fermenting organisms. Strong antiseptics, such as formaldehyde, tend to destroy enzymes. Enzymes are often precipitated from their colloidal solutions by the addition of alcohol or acetone, but such products are not pure; in many cases they consist of a mixture of enzymes, and in this way the study of their reactions is complicated. The modern system of nomenclature is to name the enzymes according to the compounds they hydrolyse, *e.g.* maltase, sucrase (= invertase), amylase (= diastase), &c. The nature of the products formed varies not merely with the substance used, but also with the enzyme, thus the trisaccharose, raffinose, if hydrolysed by acids, yields galactose, fructose, and glucose; the same carbohydrate with diastase yields melibiose and fructose, and with emulsin galactose and sucrose. The

action of enzymes is essentially selective, and in this respect differs from the hydrolysing action of alkalis or acids. Thus esters, amides, carbohydrates, glucosides, &c., are all hydrolysed by hydrochloric acid, whereas esters, but not carbohydrates, can be hydrolysed by lipases, and maltose, but not sucrose, can be hydrolysed by maltase. Even a slight difference in the configuration of two isomeric substances is sufficient to affect their reactivity with a particular enzyme, *e.g.* the two methyl-glucosides (p. 659), which are represented by the spatial formulæ:



the only difference being the arrangement of the H and OCH_3 attached to the upper carbon atom. Of these two compounds the α can be hydrolysed by maltase but not by emulsin, and the β by emulsin but not by maltase, and hence the names α and β glucase are sometimes used for the two enzymes maltase and emulsin. Numerous other examples of the same type have been met with, especially in the case of polypeptides (*Fischer* and *Bergell*, B. **36**, 2592; **37**, 3103). As most of the natural glucosides are hydrolysed by emulsin but not by maltase, they are regarded as analogous to the β-methyl-glucoside, with complex radicals in place of the methyl group. Maltose on the other hand is an α glucoside resembling the α-methyl compound in configuration.

It has been proved in many cases that a particular enzyme can act not merely as a hydrolysing but also as a synthesizing agent. The process of hydrolysis is frequently a balanced reaction, although in the majority of cases the equilibrium is mainly in the direction of analysis and not synthesis. The synthesizing activity of an enzyme was first demonstrated by *Croft-Hill* (J. C. S. 1898, 634; 1903, 578) in the case of maltase. The greater portion of the maltose is hydrolysed to glucose, but a certain proportion of disaccharose is always present, and

in a solution of glucose maltase can produce a certain amount of a disaccharose, which at first was thought to be maltose, but has since been proved (*E. F. Armstrong*, 1905) to be a mixture of maltose and isomaltose. Invertase, lactase, emulsin, and lipases have all been shown to possess synthetical activity. The formation of starch in plant and glycogen in animal tissues is probably largely due to the activities of synthesizing enzymes; and *Potterin* has succeeded in synthesizing a triolein, one of the common constituents of natural fats, by means of a lipase.

The rate of hydrolysis by means of enzymes has been studied by different authorities. The investigations of *O'Sullivan* and *Thompson* (J. C. S. 1890, 834) and of *Hudson* (J. Am. C. S. 1908, 1160, 1564; 1909, 655) prove that the inversion of sucrose by invertase constant values for K can be obtained by using the ordinary equation for a unimolecular reaction, provided that the complications attending the mutarotation of the glucose and fructose (p. 658) are avoided by adding a small quantity of alkali before taking the polarimetric reading. The alkali stops the inversion, and at the same time rapidly brings about equilibrium between the α- and β-glucoses and the α- and β-fructoses, so that the normal rotatory power of invert sugar is given. *Hudson's* results clearly prove that the α-modifications of glucose and fructose are first formed.

A view generally held with regard to the mechanism of enzyme reaction is that combination (absorption compounds) occurs between the enzyme and the substrate (the substance decomposed), and that it is this compound which reacts with water. The fact that a specific enzyme can hydrolyse only particular substrates is in harmony with this view, as it is known that chemical constitution plays an important part in absorption. In living tissues a number of complex substances are present which are capable of interfering with the action of an enzyme. These are termed anti-enzymes. Some are normally present in tissue, others appear to be formed when an enzyme is injected into the tissue.

XLIX. CATALYTIC ACTION OF FINELY-DIVIDED METALS AND METALLIC OXIDES

Attention has already been drawn to the reduction of carbon compounds by hydrogen gas, using finely-divided metals or metallic oxides as catalysts (p. 610). Within recent years it has been shown that finely-divided solids can act as catalysts in various other reactions.

Oxidations.—One of the most interesting of these is the decomposition of primary alcohols into aldehydes and hydrogen when passed through a tube containing iron, zinc, brass, zinc oxide, ferric oxide, or stannic oxide At 660° in the presence of zinc, ethyl alcohol gives an 80-per-cent yield of acetaldehyde, other primary alcohols behave in a simular manner, and isopropyl alcohol gives an almost quantitative yield of acetone.

The reactions

$$\begin{array}{ll} \text{Primary alcohol} & \rightleftarrows \text{ aldehyde} + H_2 \\ \text{Secondary alcohol} & \rightleftarrows \text{ ketone} + H_2 \end{array}$$

are reversible in the presence of the catalyst, as an aldehyde and hydrogen when heated in contact with zinc or iron yield an alcohol. When alcohols are heated with hydrogen under pressure, and in contact with zinc or iron, the final products consist mainly of hydrocarbons if the temperature is fairly high, *e.g.* isoamyl alcohol yields considerable amounts of propane and methane. The formation of these latter is probably due to the following series of reactions:—

$$\begin{array}{ll} (CH_3)_2CH\cdot CH_2\cdot CH_2\cdot OH & \rightarrow (CH_3)_2CH\cdot CH_2\cdot CHO + H_2 \\ (CH_3)_2CH\cdot CH_2\cdot CHO & \rightarrow (CH_3)_2CH\cdot CH_3 + CO \\ (CH_3)_2CH\cdot CH_3 + H_2 & \rightarrow CH_3\cdot CH_2\cdot CH_3 + CH_4. \end{array}$$

Reduced benzene derivatives can be oxidized to benzene compounds, but pentamethylene derivatives are not oxidized. *Zelinsky* shows (B. **44**, 3121) that palladium black can also bring about oxidations at about 200°–300°—*e.g.* hexamethylene → benzene (ibid. p. 2302)—and gives an example, viz.: methyl-tetrahydro-terephthalate, which is both oxidized and reduced by hydrogen in the presence of palladium black.

Dehydration.—When alcohols are heated at 400°–500° in the presence of aluminic oxide (Al_2O_3) a decomposition into olefine and water occurs, no aldehyde being formed. This appears to be a simple method for obtaining an olefine from

the corresponding alcohol. It has been shown that the aluminic oxide loses its activity when strongly heated and rendered insoluble in acids or alkalis. Later experiments have shown that when the alcohols are heated under pressure with the oxide, the primary decomposition is into water and an ether, and that at higher temperatures the ether yields an olefine and water:

$$2CH_3\cdot CH_2\cdot OH \longrightarrow (CH_3\cdot CH_2)_2O + H_2O \quad (400°)$$
$$(CH_3\cdot CH_2)_2O \longrightarrow 2CH_2{:}CH_2 + H_2O \quad (530°).$$

This reaction is characteristic of primary and secondary alcohols, and does not occur in the absence of the catalyst, even when higher temperatures are used. The first reaction is reversible, as ether, under similar conditions, yields a certain amount of alcohol.

Unsaturated hydrocarbons can also be obtained by the action of aluminic oxide on cyclic alcohols; thus menthol (p. 578) yields menthene. The same catalyst at 200°–300° is able to transform ethylene oxide and its homologues into the isomeric aldehydes:

$$\begin{matrix} CH_2 \\ | \\ CH_2 \end{matrix}\!\!>\!O \longrightarrow CH_3\cdot CH{:}O.$$

A similar change occurs in the absence of the catalyst, but at a higher temperature, viz. 500°–600° *Bouveault* (Bull. Soc. Chim 1908 [4], **3**, 119) finds that good yields of aldehydes can be obtained by passing primary alcohols over copper coils heated by an electric current Secondary alcohols under similar conditions yield ketones and hydrogen, and ketonic alcohols, $R\cdot CH(OH)\cdot CO\cdot R$, yield diketones, $R\cdot CO\cdot CO\cdot R$, and hydrogen.

Unsaturated alcohols undergo molecular transformation and yield saturated aldehydes:

$$C_nH_{2n-1}\cdot CH_2\cdot OH \longrightarrow C_nH_{2n+1}\cdot CH{:}O.$$

Numerous other substances, *e.g.* pumice, animal charcoal, sand, red phosphorus, and aluminic phosphate, can decompose alcohols into olefines and water, but oxide of aluminium appears to be the best (*Senderens*, C. R. 1907, **144**, 381, 1109). *Bouveault* has designed a special apparatus for the preparation of olefines by this method.

The action of silica as a catalytic agent is extremely characteristic Pure precipitated silica, moderately calcined, decom-

poses ethyl alcohol at 280°, yielding pure ethylene. After it has been more strongly calcined, it induces decomposition only at a higher temperature, and then yields ethylene and water together with hydrogen and aldehyde. Pulverized quartz can yield as much as 50 per cent of the theoretical amount of hydrogen and 50 per cent of ethylene. Similarly, alumina which has been strongly calcined decomposes part of the alcohol into hydrogen and aldehyde. Experiments made with gypsum ($CaSO_4$, $2H_2O$) dehydrated below 400° and with anhydrite ($CaSO_4$) indicate that the catalytic dehydration of alcohols is effected by substances which are capable of forming temporary hydrates. Thoroughly calcined gypsum or natural anhydrite decomposes alcohol at high temperatures only, and then yields mainly hydrogen and acetaldehyde; on the other hand, gypsum which has been dehydrated at a moderate temperature is capable of combining with water, and decomposes alcohol at about 400°, yielding ethylene (*Senderens*, Bull. Soc. Chim. 1908 [4], **3**, 197, 633).

Sabatier and *Maihle* (Annales, 1910 [viii], **20**, 289) have studied the action of the following metallic oxides on primary alcohols, more especially ethanol: ThO_2, Al_2O_3, Cr_2O_3, SiO_2, TiO_2, BeO, ZrO_2, UO_2, Mo_2O_5, Fe_2O_3, V_2O_3, ZnO, MnO, CdO, Mn_3O_4, MgO. The first four act almost entirely as dehydrating agents, and at 340°–350° give 90–100 per cent yields of olefine and little or no hydrogen. On the other hand, the last five oxides bring about oxidations, and give practically 100 per cent of hydrogen and no olefine. BeO and ZrO_2 give approximately equal volumes of hydrogen and olefine, *i.e.* they are mixed catalysers, as are practically all the intermediate oxides. According to these chemists the activity of finely-divided metals or oxides is due to the formation of unstable additive compounds; *e.g.* in catalytic oxidations of unstable hydrides:

Alcohol + metal → metallic hydride + aldehyde
Metallic hydride → metal + hydrogen,

such hydrides are readily decomposed, and yield the metal which can react with a further quantity of alcohol. With the readily reducible metals, SnO, CdO, &c., a small amount of metal is formed, and this reacts as above. As the activity does not increase with time, as might be expected as more oxide becomes reduced, it is suggested that the metal gradually becomes less finely divided and hence less active. Oxides

which are not readily reduced may form unstable compounds with hydrogen or with the aldehyde. The mechanism of catalytic dehydration does not consist in the formation of unstable hydrates of the catalyst as at first supposed, but in the formation of alkyl salts, formed by the union of the alcohol with the acidic oxide used as catalyst:

$$ThO_2 + 2EtOH \longrightarrow ThO(OEt)_2 + H_2O$$
$$ThO(OEt)_2 \longrightarrow 2C_2H_4 + ThO(OH)_2$$
$$ThO(OH)_2 \longrightarrow ThO_2 + H_2O.$$

Esterification.—*Sabatier* and *Maihle* (C. R. 1911, **152**, 494) have shown that TiO_2 is a good catalyst for the conversion of acids and alcohols into esters The method is to allow a mixture of molecular proportions of the vapour of the two compounds to pass over a column of the dioxide kept at 290°–300°. The yield of ester is about 70 per cent, and the process is extremely rapid. A similar method may be used for hydrolysing esters, *e.g.* allowing a mixture of the ester vapour with an excess of steam to pass over the dioxide at 280°–300°. Similar results are obtained with thorium oxide, provided aromatic acids are used.

Formation of Amines, Thiols, Ketones.—Amines are formed when a mixture of an alcohol and ammonia is passed over thorium dioxide at 350°–370° (C. R. 1909, **148**, 898); thiols (mercaptans) are formed when a mixture of alcohol and hydrogen sulphide is passed over the dioxide at 300°–360° (C. R. 1910, **150**, 1217, 1569). The yields are especially good with primary alcohols, and even phenol gives a 17-per-cent yield of thiophenol at 430°–480°; and metallic sulphides, especially CdS, at 320°–330°, decompose thiols into alkyl sulphides and hydrogen sulphide. Ketones can be prepared by the action of acid anhydrides or acids on thorium dioxide at 400° (*Senderens*, C. R. 1909, **149**, 213, 995; 1910, **150**, 111, 702, 1136). Simple and mixed aliphatic ketones and mixed aromatic aliphatic ketones have been prepared, the mixed ketones by using mixtures of two acids. Aromatic acids containing the carboxylic group attached to the benzene nucleus do not react unless mixed with an aliphatic acid, but acids of the type of phenylacetic do. The reaction probably consists in the formation of a salt and its subsequent decomposition into ketone, carbon dioxide, and water.

Formic acid behaves somewhat differently from the other fatty acids (*Sabatier* and *Maihle*, C. R. 1911, **152**, 1212). Finely

divided Pd, Pt, Ni, Cu, Cd, and ZnO or SnO decompose it into carbon dioxide and hydrogen. TiO_2 and W_2O_5 yield water and carbon monoxide, and SiO_2, ZrO_2, Al_2O_3, &c., give both reactions.

L. UNSATURATION

A. Types of Unsaturation.—Unsaturated compounds are usually defined as those which are capable of uniting with another substance (element or compound) without disruption of their original structure. Two main types of such compounds have been dealt with in the previous chapters.

I. Cases in which the addenda unite with two different atoms of the original compound. Such are the compounds supposed to contain double or triple linkings between C and C, C and O, C and S, C and N, N and N, as seen in the groups of olefine and acetylene derivatives, carbonyl compounds, thiocarbonyl derivatives, nitriles and Schiff's bases, azo-compounds.

II. Cases in which the addenda unite with one and the same atom of the original compound, as in the conversion of amines into salts and quaternary ammonium compounds, the formation of oxonium salts from ethers, &c., and the formation of sulphonium salts from alkyl sulphides.

The presence of such unsaturated groups as amino and hydroxyl, and also the alkylated groups, $\cdot NHR$, $\cdot NR_2$, $\cdot OR$, produce marked effects on the properties of the compounds into which they are introduced. In the aromatic series they render the compounds much more reactive towards reducing, oxidizing, and substituting reagents (cf. p. 409). When further substituents are introduced, *e.g.* Cl, Br, SO_3H, NO_2, &c., these almost invariably take the ortho and para positions with respect to the unsaturated group. These groups also tend to make the compound luminesce under the influence of electric discharges under small pressures. They are also the most powerful *auxochromes* known; *i.e.* when introduced into a compound containing chromophores, such as, $\cdot N{:}N$, $C{:}O$, $C{:}C$, NO_2, &c., they produce a deepening of the colour of the compound.

In examples of the first type the question as to whether addition or not takes place depends upon a variety of factors.

(1) Whether the double linking is between C and C, C and O, C and N, or N and N. Thus although both olefines and carbonyl derivatives combine with hydrogen, the first group adds on bromine readily, whereas the second does not; and the second combines with hydrogen cyanide or sodium bisulphite more readily than the first group does. (2) The nature of the groups already attached to the two atoms which are united by the double linking Thus although most olefine derivatives combine with bromine, compounds in which there are several negative groups, such as Ph, Br, CN, CO_2H, already attached to the two carbon atoms, do not form additive compounds with bromine (*Hugo* and *Bauer*, B. **37**, 3317), although they contain an olefine linking (3) The nature of the addenda. It has been pointed out already (p. 44) that chlorine combines most readily and iodine least readily, but that hydrogen iodide combines more readily than hydrogen chloride or bromide. (4) Conditions of the experiment, *e.g.* nature of solvent, sunlight, temperature, presence of a catalyst, &c. Phenyl-propiolic acid does not combine with hydrogen chloride when in aqueous solution below 80°.

B **Properties of Unsaturated Acids as affected by the position of the Double Bond.**—Acids which contain a double bond in the $\alpha\beta$ position differ in many respects from isomeric acids in which this bond is further removed from the carboxylic group.

The $\alpha\beta$ unsaturated acids are reduced much more readily than their isomerides by sodium amalgam and water This is somewhat remarkable, since in the case of other additive reactions, for example, the addition of bromine, the $\alpha\beta$ unsaturated acids are less reactive, *i.e.* do not combine with bromine so readily as $\beta\gamma$ unsaturated acids or other acids in which the double bond is far removed from the carboxyl group (*Sudborough* and *Thomas*, J. C. S 1910, 715, 2450). The readiness with which $\alpha\beta$ unsaturated acids can be reduced may perhaps be accounted for by the presence of the conjugated double bonds (cf. p. 681)—

$$\mathrm{R\cdot\overset{4}{C}H{:}\overset{3}{C}.I\cdot\overset{2}{C}{:}\overset{1}{O}} + 2H \longrightarrow \underset{\mathrm{OH}}{\mathrm{R\cdot CH_2\cdot CH{:}C\cdot OH}} \longrightarrow \underset{\mathrm{OH}}{\mathrm{R\cdot CH_2\cdot CH_2\cdot C\cdot O}}$$

1 : 4 addition takes place, but the resulting unsaturated glycol is unstable and, by a wandering of an atom of hydrogen, yields the saturated acid.

J. Bougault (C. R. 1905, i. 9) shows that $\beta\gamma$ unsaturated acids combine with the elements of hypoiodous acid (HIO), yielding lactones, whereas the isomeric $\alpha\beta$ acids do not. This provides the basis of a method for separating a mixture of an $\alpha\beta$ and $\beta\gamma$ unsaturated acid.

One of the best methods of separating a mixture of $\alpha\beta$ and $\beta\gamma$ unsaturated acids is due to *Fittig* (B. 1894, **27**, 2667; A. 1894, **283**, 51), and consists in heating the acids for a few minutes at 140° with a mixture of equal volumes of concentrated sulphuric acid and water. The $\alpha\beta$ acid is unaffected by this treatment, whereas the $\beta\gamma$ acid is converted into a γ-lactone (p. 217) which is insoluble in sodium carbonate solution.

$$(CH_3)_2C{:}CH\cdot CH_2\cdot CO\cdot OH \longrightarrow (CH_3)_2C\begin{cases}CH_2\cdot CH_2\\ O--CO\end{cases}.$$

When this method is used only the $\alpha\beta$ acid can be recovered. A method by means of which both acids can be recovered is the separation by fractional esterification, as an $\alpha\beta$ acid is esterified much less readily than isomeric unsaturated acids (*Sudborough* and *Thomas*, J. C. S. 1911, 2307).

One of the best methods for determining the position of the double bond in the case of an olefine acid is by an examination of the oxidation products (p. 162). These consist, as a rule, of a mixture of a monobasic and a dibasic acid, as the carbon atoms between which the olefine bond functionated both yield carboxylic groups; *e.g.* $R\cdot CH{:}CH\cdot CH_2\cdot CO_2H$ gives $R\cdot CO_2H$ and $CO_2H\cdot CH_2\cdot CO_2H$. Cf. also Oleic acid, p. 165.

Dimethylacrylic acid, $(CH_3)_2C{:}CH\cdot CO_2H$, when oxidized yields acetone, $(CH_3)_2CO$, and oxalic acid or its oxidation product carbonic acid.

The conversion into ozonides and the decomposition of these (p. 624) is also used for the determination of the position of the double linking.

Another method adopted for determining the position of an olefine bond is by an examination of the hydrobromide. If the bond is in the $\alpha\beta$ position the bromo-derivative of the saturated acid loses hydrogen bromide when treated with alkali and yields the original olefine acid.

$$\underset{\text{Crotonic acid}}{CH_3\cdot CH{:}CH\cdot CO_2H} \longrightarrow \underset{\beta\text{-Bromobutyric acid}}{CH_3\cdot CHBr\cdot CH_2\cdot CO_2H} \longrightarrow \underset{\text{Crotonic acid.}}{CH_3\cdot CH{:}CH\cdot CO_2H.}$$

A $\beta\gamma$ or $\gamma\delta$ unsaturated acid also yields a hydrobromide, but when this is treated with alkalis hydrogen bromide is eliminated and a lactone formed.

$$CH_3\cdot CH{:}CH\cdot CH_2\cdot CO_2H \longrightarrow CH_3\cdot CHBr\cdot CH_2\cdot CH_2\cdot CO\cdot OH$$

$$CH_3\cdot CH\begin{cases} CH_2\cdot CH_2 \\ O\text{—}CO \end{cases}.$$

The presence of olefine linkings, as in maleic anhydride, increases to an appreciable extent the readiness with which the anhydride combines with water (*Rivett* and *Sidgwick*, J. C. S. 1910, 1677).

An extremely simple method of determining whether the double bond is in the $\alpha\beta$ position or not, is by an examination of the rate of esterification of the unsaturated acid and of its saturated analogue by the catalytic method. If the unsaturated acid has a much lower rate of esterification than its reduction product the conclusion may be safely drawn that the double bond is in the $\alpha\beta$ position, as $\beta\gamma$ unsaturated acids are esterified somewhat more quickly than their saturated analogues, and acids in which the double bond is still further removed from the carboxyl group have much the same esterification constants as the corresponding saturated acids (*Sudborough* and *Gittins*)

For the stereochemistry of compounds containing only one ethylene linking, cf. p. 243. When two or more olefine bonds are present in the molecule, the isomerism is more complex. Not merely can we have structural isomerides, which differ in the relative positions of the olefine linkings, but also the number of stereoisomerides increases.

For compounds of type, Cab:C:Cab, see p. 634.

C. **Compounds with Conjugate Double Bonds.**—One of the most interesting groups containing two double linkings are the compounds with conjugate double bonds. Within recent years numerous experiments have been made with compounds containing two double bonds in the relative positions indicated by the formula—

$$R\cdot \overset{4}{C}H{:}\overset{3}{C}H\cdot \overset{2}{C}H{:}\overset{1}{C}H\cdot R.$$

These have been termed conjugated double bonds by *Thiele*, and extremely interesting results have been obtained by the study of the additive reactions of such compounds. It is

found that the atoms or radicals added on do not, as a rule, become simply attached to the carbon atoms 1 and 2 or 3 and 4, but to numbers 1 and 4; so that a new ethylene linkage is created in position 2.3. Thus cinnamylideneacetic and cinnamylidenemalonic acids when reduced yield 1:4-dihydro-derivatives (*Ruber*, B. 1904, **37**, 3120)—

$$C_6H_5\cdot CH:CH\cdot CH:CH\cdot CO_2H + 2H \longrightarrow C_6H_5\cdot CH_2\cdot CH:CH\cdot CH_2\cdot CO_2H$$

and

$$C_6H_5\cdot CH:CH\cdot CH:C(CO_2H)_2 + 2H \longrightarrow C_6H_5\cdot CH_2\cdot CH:CH\cdot CH(CO_2H)_2$$

Sorbic acid (p. 166) yields $CH_3\cdot CH_2\cdot CH:CH\cdot CH_2\cdot CO_2H$; similarly butadiene, $CH_2:CH\cdot CH:CH_2$, reacts with bromine, yielding 1.4-dibromo-$\Delta^{2\ 3}$-butene, $CH_2Br\cdot CH:CH\cdot CH_2Br$. Similar results have been obtained when the double bonds are between carbon and oxygen; thus benzil,

$$\overset{1}{O}:\overset{2}{C}(C_6H_5)\cdot\overset{3}{C}(C_6H_5):\overset{4}{O},$$

when reduced under special conditions yields $OH\cdot C(C_6H_5):C(C_6H_5)\cdot OH$ $\alpha\beta$-dihydroxy-stilbene.

That additions do not always take place in the 1.4-positions is shown by the following examples. Methyl cinnamylidenemalonate adds on bromine in the 3.4-positions and yields $C_6H_5\cdot CHBr\cdot CHBr\cdot CH:C(CO_2Me)_2$ (*Heinichser* and *Thiepel*, A. 1904, **336**, 223). The addition of potassium hydrogen sulphite to cinnamylidenemalonic acid occurs in the 1:2-position, and the product is—

$$C_6H_5\cdot CH:CH\cdot CH(SO_3K)\cdot CH(CO_2H)_2$$

(*Kohler*, Am. 1904, **31**, 243); similarly with hydrogen cyanide Unsaturated aldoximes and ketoximes when reduced yield unsaturated amines, indicating that the addition of hydrogen—

$$R\cdot\overset{4}{C}H:\overset{3}{C}H\cdot\overset{2}{C}H:\overset{1}{N}\cdot OH + 4H \longrightarrow R\cdot CH:CH\cdot CH_2\cdot NH_2 + H_2O$$

occurs in the 1:2-position (*Harries*, A. 1903, **330**, 193); $\alpha\beta$ unsaturated ketones also add on sulphinic acids in the 1:2 (carbonyl) position (Am. 1904, **31**, 163). *s*-Diphenylbutadiene, $CHPh:CH\cdot CH:CHPh$, also adds on bromine in the 1:2-position.

Thiele (A. 1889, **306**, 87) has attempted to account for the

characteristic 1:4-addition of most of the compounds with conjugated double bonds by his theory of *partial valencies*.

It is supposed that when two atoms are united by a double bond the whole of the energy of the atoms is not used up, but that there is a slight residual affinity or *partial valency* which *Thiele* denotes by dotted lines, *e.g.*:

RCH:CHR.

He considers the power of forming additive compounds is due to the presence of such partial valencies.

Now in a system with two double bonds in positions 1:2 and 3:4 there are four partial valencies, and according to *Thiele* two of these, viz. 2 and 3, are supposed to have neutralized one another and only 1 and 4 are active. This is usually represented by the formula—

R·CH:CH·CH:CH·R,

and hence the usual 1·4-addition with compounds containing conjugated double bonds. *Thiele's* theory does not account for the numerous exceptions mentioned above.

Probably it is simpler to regard the compound as containing 4 residual valencies in the 1, 2, 3, 4 positions, and to conclude that the question as to which of these will be used up in the formation of an additive compound depends largely on the nature of the addenda and the nature of the groups already attached to the atoms numbered 1, 2, 3, and 4.

The reaction between compounds with conjugated double bonds and Grignard's reagents consists in many cases of 1:4-addition. See *Kohler* (Am. 1904, **31**, 642, 1905, **33**, 21, 35, 153, 333; **34**, 568; 1906, **35**, 386; **36**, 177, 529; 1907, **37**, 369; **38**, 511; 1910, **43**, 412, 475).

D. **Compounds of Di- and Trivalent Carbon.** — **Carbon monoxide** may be written either as C:O or C⋮O. In the first formula both carbon and oxygen atoms are represented as being divalent, and in the latter formula both are tetravalent. It has been argued that the formula, C:O, is probably the correct one, as when the monoxide forms additive compounds the two addenda become attached to carbon and not one to carbon and one to oxygen. Thus with chlorine we get carbonyl chloride, $O{:}C\langle^{Cl}_{Cl}$, the constitution of

which is determined by the fact that it reacts with alcohol, forming ethyl chloro-carbonate and finally ethyl carbonate, $O:C(OEt)_2$. With sodium hydroxide carbon monoxide gives rise to sodium formate:

$$O:C + NaOH = O:C\begin{matrix}H\\ONa,\end{matrix}$$

and with hydrogen chloride it yields the unstable formyl chloride, $O:C\begin{matrix}H\\Cl\end{matrix}$. Although vapour-density determinations indicate that in a mixture of the two gases very little combination has taken place, yet *Gattermann's* synthesis of acid chlorides, by the action of a mixture of carbon monoxide and hydrogen chloride on aromatic compounds in the presence of aluminium chloride, proves that a small amount of an additive compound exists, and that its structural formula is the one represented above.

Carbylamines.—On p. 104 the conclusion has been drawn that in the carbylamines (alkyl isocyanides) the alkyl group must be attached to nitrogen and not to carbon, and therefore they are to be represented as R·N:C or R·N:C. In the latter formula the carbon atom is represented as being divalent, and the arguments used in support of this formula are similar to those used in the case of carbon monoxide, viz. the two addenda invariably unite with the carbon atom and not one with carbon and one with nitrogen. The following examples can be given:—(*a*) with chlorine: $RN:CCl_2$; (*b*) with acyl chlorides: $R\cdot N:C\begin{matrix}COPh\\Cl\end{matrix}$; (*c*) with hydrogen sulphide: R·N:CH·SH = R·NH·CH:S (an alkylated thioformamide); (*d*) with oxygen: R·N:C:O, alkyl isocyanates; (*e*) with sulphur: R·N:C:S, mustard oils; (*f*) with *Grignard* reagents:

$$R\cdot N:C\begin{matrix}R\\MgI\end{matrix} \xrightarrow[H_2O]{} R\cdot N:C\begin{matrix}R\\H,\end{matrix}$$

an imino-derivative which is hydrolysed to an aldehyde, O:CH·R; (*g*) with ethyl hypochlorite. Cf. *Nef*, A. **287**, 273

Metallic Cyanides.—Both nitriles and carbylamines are alkyl derivatives of hydrogen cyanide, and can be obtained by the action of alkyl iodides or potassium alkyl sulphates on different metallic cyanides, *e.g.* potassium cyanide and ethyl iodide yield ethyl cyanide, whereas the same iodide with silver cyanide yields mainly ethyl carbylamine. Although two series of alkyl derivatives exist, only one hydrogen

cyanide is known. Certain of its reactions point to the nitrile structure $H \cdot C \vdots N$, and others to the carbylamine formula $H \cdot N : C$; it is a typical tautomeric substance. The view generally held with regard to the metallic cyanides is that they have a carbylamine structure. The arguments used are briefly as follows:—(1) The similarity between the additive reactions of metallic cyanides and those of carbylamines (*a*) with bromine potassium cyanide yields potassium bromide and cyanogen bromide; although an additive compound cannot be isolated, the reaction is in complete harmony with the view that an unstable compound,

$$K \cdot N : C \begin{matrix} Br \\ Br \end{matrix},$$

is formed which breaks up into KBr and $N \vdots C \cdot Br$; (*b*) potassium cyanide and benzoyl chloride yield benzoyl cyanide, $N \vdots C \cdot CO \cdot C_6H_5$, but here again an additive compound, $K \cdot N : CCl \cdot COC_6H_5$, is probably first formed; (*c*) potassium cyanide combines with oxygen and sulphur in much the same manner as the carbylamines; (*d*) with ethyl hypochlorite a compound, $HN : C(OEt) \cdot CN$, *ethyl cyano-imino-carbonate*, is formed. The reaction can be represented as follows:—

$$K \cdot N : C \longrightarrow K \cdot N : CCl \cdot OEt \xrightarrow{KCN} K \cdot N : C(OEt) \cdot CCl : NK \longrightarrow KCl + K \cdot N : C(OEt) \cdot CN.$$

(2) Both alkyl carbylamines and alkali cyanides dissolve silver cyanide yielding double salts, whereas alkyl cyanides do not. (3) Tetramethylammonium cyanide, which probably has a constitution similar to that of the metallic cyanides, yields trimethylamine and methylcarbylamine when heated. This last argument by itself is of but little value, as a comparatively high temperature is required and molecular rearrangements could occur.

Reactions of Metallic Cyanides. Formation of Nitriles and Carbylamines.—The following reactions occur:—

Potassium cyanide $\xrightarrow{RI}$ alkyl cyanides, $R \cdot C \vdots N$
Potassium cyanide $\xrightarrow{R \cdot COCl}$ acyl cyanides, $R \cdot CO \cdot C \vdots N$.

Silver cyanide $\xrightarrow{RI}$ alkyl carbylamines, $R \cdot N : C$
Silver cyanide $\xrightarrow{R \cdot COCl}$ acyl cyanides, $R \cdot CO \cdot C \vdots N$.

The reactions cannot be due to the tautomerism of silver cyanide, as no cases are known where a heavy atom like silver can wander. The view that carbylamines are first formed by simple exchange in all cases, and then in three of the four reactions the carbylamine becomes transformed into a nitrile, is untenable, as carbylamines cannot be transformed into nitriles. The reverse process is also improbable, as carbylamines are formed from nitriles at high temperatures only.

The views of *Nef* (A. **287**, 274) as modified by *Wade* (J. C. S. 1902, 1596) are that in all four cases additive compounds are first formed. When the metallic radical in the cyanide is feebly positive, then feebly positive alkyl compounds combine with N, but negative acyl derivatives combine with C. With a strongly positive metallic atom in the cyanide, *e.g.* KCN, both alkyl and acyl derivatives combine with N. Thus with AgNC and EtI we have addition to N. Similarly with EtNC and EtI; but with AgNC and AcCl, and EtNC and AcCl, we have addition to C. With KNC and EtI and also with KCN and AcCl the addition is to C.

$$K\cdot N{:}C + EtI \longrightarrow K\cdot N{:}C\!<\!{}^{Et}_{I} \longrightarrow KI + N{\vdots}CEt$$

$$Ag\cdot N{:}C + EtI \longrightarrow {}^{Ag}_{Et}\!>\!N\!<\!{}^{C}_{I} \longrightarrow AgI + Et\cdot N{:}C$$

$$Ag\cdot N{:}C + AcCl \longrightarrow Ag\cdot N{:}C\!<\!{}^{Ac}_{Cl} \longrightarrow AgCl + N{\vdots}C\cdot Ac.$$

It may appear remarkable that in reaction 2 the alkyl iodide adds on to the nitrogen atom and leaves the carbon divalent. *Nef* assumed that the conversion of the silver salt into carbylamine was an example of direct displacement, but *Wade* proves that dry silver cyanide is able to absorb methyl iodide at its boiling-point, yielding a viscid mass which evolves methylcarbylamine when more strongly heated. The constitution of this additive compound is based on a study of the products from alkyl iodides and alkylcarbylamines; when hydrolysed these compounds yield *small amounts* of secondary amines, and hence, according to *Wade*, must be represented as:

$$\begin{matrix} Me\cdot N{:}C \\ Me\diagup\diagdown I, \end{matrix}$$

and similar formulæ are given to the products from silver cyanide and alkyl iodides.

Sidgwick (P. 1905, 120) concludes that in all cases addition takes place at the carbon atom:

$$M\cdot N{:}C\!\!<^{R}_{I},$$

where M represents either K or Ag. Such a compound contains the grouping:

$$a\cdot N{:}C\!\!<^{b}_{a}$$

characteristic of the oximes of aldehydes and of unsymmetrical ketones (cf. pp. 137, 428), and can therefore exist in *syn*- and *anti*-configurations. Potassium cyanide is supposed to yield the *syn*-compound:

$$\begin{matrix} R\cdot C\cdot I \\ \vdots\!\!\ddot{N}\cdot K, \end{matrix}$$

which readily loses potassium iodide, as both metal and halogen are on the same side of the molecule, and thus yields a nitrile. Silver cyanide, on the other hand, yields the *anti*-compound:

$$\begin{matrix} R\cdot C\cdot I \\ Ag\cdot\ddot{N}. \end{matrix}$$

Silver iodide is not readily split off, as the metal and halogen are now on different sides of the molecule. It therefore undergoes the *Beckmann* transformation (p. 429), yielding

$$\begin{matrix} Ag\cdot C\cdot I \\ R\cdot\ddot{N} \end{matrix},$$

which loses silver iodide and forms C:N·R, an alkyl carbylamine.

Although the metallic cyanides are usually represented by a carbylamine structure, it does not follow that hydrogen cyanide is to be represented in a similar manner. Arguments based on a study of its physical and chemical properties have been brought forward; some point to the one, and others to the alternative formula, but probably, on the whole, the properties are more in harmony with the nitrile structure, H·C⋮N. It is possible that it may be, like the tautomeric substance, ethyl acetoacetate, a mixture of the two compounds but mainly nitrile. (For summary see *Sidgwick*, "The Organic Chemistry of Nitrogen", p. 209)

Fulminic acid, C:N·OH, is known chiefly in the form of its

silver and mercury salts. The latter was first prepared in 1800 by *Howard*, by the action of alcohol and nitric acid on mercuric nitrate. It crystallizes in lustrous prisms, explodes with great violence when heated or struck, and is largely used in the manufacture of percussion caps, dynamite cartridges, &c. In 1824 *Gay-Lussac* and *Liebig* showed that the silver salt had the same percentage composition as silver cyanate, and thus afforded one of the first examples of isomerism. They also showed that double salts, *e.g.* $KAg(CNO)_2$, could be obtained. Various formulæ have been proposed. *Kekulé* suggested the formula $NO_2 \cdot CH_2 \cdot CN$, nitroacetonitrile; *Hollemann* suggested a glyoxime peroxide formula,

$$\begin{matrix} CH\text{——}CH \\ \ddot{N}\cdot O\cdot O\cdot \ddot{N} \end{matrix};$$

and *Steiner* in 1883 the formula $OH \cdot N{:}C{:}C{:}N \cdot OH$, di-isonitroso ethylene. It will be noticed that all these formulæ represented the molecule as containing two carbon atoms. The reasons for this were: (1) It is obtained from ethyl alcohol. (2) With bromine or iodine it yields ethane derivatives. (3) As it forms double salts the acid was thought to be dibasic. Various arguments were brought forward in favour of and against the first two formulæ, but the question has been definitely decided by the preparation of nitroacetonitrile (*Steinkopf* and *Bohrmann*, B. **41**, 1044) and of glyoxime peroxide (*Jowitschitsch*, A. **347**, 233), and showing that they differ from fulminic acid. The main argument in favour of *Steiner's* formula is that fulminates yield hydroxylamine when treated with concentrated hydrochloric acid, just as *V. Meyer* had previously shown that oximes do. *Steiner* was able to prove that the whole of the nitrogen can be removed in this way in the form of hydroxylamine, and also that formic acid is the second product:

$$C_2H_2O_2N_2 + 4H_2O \rightarrow 2H_2CO_2 + 2NH_2OH.$$

Such a reaction proved that *Kekulé's* formula could not be correct.

In 1894 *Nef* (A. **280**, 303) suggested the simple formula $C{:}N \cdot OH$, now generally accepted, which represents the acid as the oxime of carbon monoxide. The following arguments were adduced: (1) By the action of one equivalent of hydrogen chloride on one of the silver salt, no trace of silver chloride is formed, but an additive product, which was shown to be the

chloride of formhydroxamic acid, or formyl-chloride oxime, Cl·CH:N·OH. This forms colourless crystals volatile at the ordinary temperature, and decomposes readily. With aniline it yields formanilide oxime, NHPh·CH:N·OH or NPh:CH·NH·OH. (2) It can be synthesized from a compound containing one carbon atom, namely nitromethane. The mercuric salt of nitromethane, when heated with water, yields water and mercury fulminate:

$$CH_2{:}NO{\cdot}OM \longrightarrow H_2O + C{:}N{\cdot}OM.$$

(3) With nitrous acid it yields methylnitrolic acid (p. 96).

$$C{:}N{\cdot}OH + H{\cdot}NO_2 \longrightarrow NO_2{\cdot}CH{:}N{\cdot}OH.$$

(4) According to *Scholl* (B. **32**, 3492; **36**, 10, 322, 648), when benzene is treated with mercury fulminate and a mixture of anhydrous and hydrated aluminium chloride, benzaldoxime is formed (70 per cent). The water of the hydrated chloride liberates hydrogen chloride, which combines with the fulminate, yielding the additive compound, OM·N:CHCl, which then condenses with the benzene in the manner of the *Friedel-Crafts* reaction, yielding $C_6H_5{\cdot}CH{:}N{\cdot}OM$, from which the free oxime is liberated by means of mineral acid.

The hydrolysis of a fulminate to formic acid and hydroxylamine by means of hydrochloric acid is almost undoubtedly preceded by the formation of an additive compound:

$$OH{\cdot}N{:}CH{\cdot}Cl + H_2O \longrightarrow OH{\cdot}N{:}CH{\cdot}OH$$
$$OH{\cdot}N{:}CH{\cdot}OH + H_2O \longrightarrow O{:}CH{\cdot}OH + NH_2OH.$$

Free fulminic acid can be obtained by the action of an excess of sulphuric acid on a solution of potassium fulminate and extraction with ether. It volatilizes with the ether when this is distilled, and readily polymerizes to meta-fulminic acid. *Nef* has pointed out the remarkable analogy between hydrogen cyanide and fulminic acid. No direct estimations of the molecular weight of fulminic acid have been made, but an indirect determination by *L. Wohler* (B. 1905, **38**, 1351) points to the simple formula HCNO. The method is based upon the determination of the value of *van't Hoff's* dissociation factor *i* for the sodium salt in 0·2 to 0·1 *N* solution. The value was found to be 1·85, the usual value for the salt of a monobasic acid. Also the increase in molecular conductivity in passing from *N*/32 to *N*/1024 solution was found to be 5 units, corresponding with *Ostwald's* value 4–8 for the salt of a monobasic acid.

The following has been suggested by *Wieland* as the probable course of the reaction in the preparation of a fulminate from ethyl alcohol: Oxidation to acetaldehyde, formation of isonitroso-acetaldehyde, oxidation to isonitroso-acetic acid, $HO \cdot N{:}CH \cdot CO_2H$, nitration to nitro-isonitroso-acetic acid, decomposition into carbon dioxide and methylnitrolic acid, conversion of methylnitrolic acid into nitrous and fulminic acids.

A polymer of fulminic acid, known as fulminuric acid, has been shown to be cyanonitroacetamide,

$$NO_2 \cdot CH(CN) \cdot CO \cdot NH_2.$$

Tervalent Carbon: Triphenyl-methyl.—In attempting to prepare hexaphenylethane by the action of finely divided silver or zinc on triphenylchloromethane in benzene solution, *Gomberg* (J. Am. 1900, **22**, 757) obtained a substance which contained oxygen, but in the absence of air the product was free from oxygen, and when the solution was carefully evaporated a compound with pronounced unsaturated properties was isolated. It combines vigorously with oxygen, yielding the **peroxide**, $CPh_3 \cdot O \cdot O \cdot CPh_3$, m.-pt 185°–186°, which is transformed by sulphuric acid into triphenylcarbinol; it also combines with iodine, yielding triphenyliodomethane, and forms additive compounds with ethers, ketones, esters, nitriles, &c. It was suggested that these properties pointed to the formula, CPh_3, for the hydrocarbon, a formula which contains a tervalent carbon atom. The corresponding ion, $\overset{+}{C}Ph_3$, appears to be formed when triphenylchloromethane is dissolved in liquid sulphur dioxide, as such solutions are good conductors of the electric current. Molecular weight determinations by the cryoscopic method point to the double formula, $(CPh_3)_2$, for the hydrocarbon. *Tschitschabin* (B. **37**, 4709) has suggested that the product is hexaphenylethane, and has supported this conclusion by a study of the properties of pentaphenylethane, which is somewhat unstable and readily attacked by oxygen, and is completely ruptured by hydrochloric acid at 150°. Quinonoid formulæ have also been suggested, the symmetrical formula I by *Heintschel* (B. **36**, 320, 579), and formula II by *Jacobson* (B. **37**, 196):

(I) $CPh_2{:}C\langle \begin{matrix} CH \cdot CH \\ CH{:}CH \end{matrix} \rangle CH \cdot CH \langle \begin{matrix} CH{:}CH \\ CH{:}CH \end{matrix} \rangle C{:}CPh_2$

(II) $CPh_2 \cdot CH \langle \begin{matrix} CH{:}CH \\ CH{:}CH \end{matrix} \rangle C{:}CPh_2$

According to *Schmidlin* (B **41**, 2471) two forms of triphenylmethyl exist, a colourless and a yellow. When freshly dissolved in benzene the solution is colourless but changes gradually to orange-yellow. The colour is destroyed by shaking the solution with air, but returns again on standing, and it is argued that the yellow form reacts with air more readily than the colourless compound. In solution there is an equilibrium between the colourless and coloured forms, and the equilibrium is displaced in favour of the colourless by lowering the temperature. The general view is that the equilibrium may be represented by the equation:

$$\underset{\text{Colourless}}{CPh_3 \cdot CPh_3} \rightleftharpoons \underset{\text{Yellow}}{2CPh_3};$$

and this view is supported by *Wieland* (B. **42**, 3020), who shows that in naphthalene solution, which contains more of the yellow form than the benzene solution does, the molecular weight is much less than that required by the formula $(CPh_3)_2$, indicating that the yellow compound presumably has the composition CPh_3. *Schlenk, Weickel,* and *Herzenstein* (A. **372**, 1) have prepared a **tri-diphenylmethyl**, $C(C_6H_4 \cdot C_6H_5)_3$, by the action of finely divided copper on tri-diphenylchloromethane, and have been able to show that in solution it is monomolecular. The corresponding bimolecular form is not known. Its solutions have a deep-violet colour, and it reacts readily with oxygen, giving a colourless peroxide. Corresponding diphenyl-diphenylmethyl, $CPh_2 \cdot C_6H_4 \cdot Ph$, and phenyl-di-diphenylmethyl, $CPh(C_6H_4 \cdot Ph)_2$, have been prepared; they exist in both coloured and colourless modifications.

Just as colourless hexaphenylethane tends to break up into coloured triphenylmethyl, so pentaphenylethane when heated in anisole solution in absence of air breaks up into CPh_3 (yellow) and $CHPh_2$, the formation of the latter is proved by the formation of tetraphenylethane due to the union of two $CHPh_2$ radicals.

E. **Ketens.**—*Wilsmore* (J. C. S. 1907, **91**, 1938; 1908, **93**, 946) has isolated the simplest possible ketone, $CH_2:CO$, which he terms **keten**, and which may be regarded as a new anhydride of acetic acid. It is obtained by the action of a hot platinum wire on acetic anhydride; numerous other substances are formed at the same time, but a 10-per-cent yield is obtained. It is a colourless gas at the ordinary temperature, has a characteristic odour, and reacts with hydrogen chloride, ammonia,

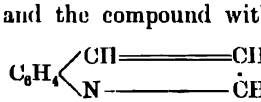
and aniline, yielding acetyl chloride, acetamide, and acetanilide respectively. When kept for some time it polymerizes, yielding **cyclobutane-1:3-dione**, $CH_2\langle\begin{matrix}CO\\CO\end{matrix}\rangle CH_2$, b.-pt. 126°–127°, which combines with water to acetoacetic acid (p. 226), and with aniline to acetoacetanilide (J. C. S. 1910, 1978).

Homologues of keten, *e.g.* **dimethyl-keten**, $(CH_3)_2C{:}CO$, and **diphenyl-keten**, $(C_6H_5)_2C{:}CO$ (*Staudinger*, B. 1905, **38**, 1735; 1906, **39**, 968; 1907, **40**, 1145, 1149), have also been prepared. The method consists in the action of zinc on α-bromoisobutyryl bromide and diphenyl-chloroacetyl chloride respectively. The compounds are unstable and readily polymerize. Dimethyl-keten forms stable compounds with tertiary amines, and with water, alcohol or amines give isobutyric acid, its ester or amide:

$$CMe_2C{:}CO + HX \longrightarrow CHMe_2{\cdot}C\langle\begin{matrix}O\\X\end{matrix}$$

The presence of a keten group, $\cdot CH_2\cdot CO\cdot$, is of great importance in the syntheses of numerous cyclic compounds (cf. *Collie*, J. C. S. 1907, **91**, 1806).

The homologues are frequently divided into (*a*) aldoketens, (*b*) ketoketens. The aldo group comprises keten, its monoalkyl substituted derivatives, and carbon suboxide. They are colourless, incapable of autoxidation, and are polymerized by pyridine. The keto group consists of the dialkylated derivatives. These are coloured, readily undergo autoxidation, and form additive compounds with tertiary amines, such as pyridine, quinoline, and acridine. These products from dialkyl ketens and tertiary amines are stable and have basic properties; they contain two molecules of keten combined with one of the base, and the compound with quinoline is represented as



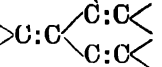
(A. 1910, **374**, 1). They also form additive compounds with substances containing the groupings C:N and C:O, for example *Schiff's* bases and quinones. Diphenyl keten and quinone yield the β-lactone, $O{:}C_6H_4\langle\begin{matrix}CPh_2\\O\end{matrix}\rangle CO$, which decomposes into CO_2 and $O{:}C_6H_4{:}CPh_2$, diphenyl-quinomethane, when heated (*Staudinger*, B. 1908, 906, 1355, 1493).

Ethyl ethylketene-carboxylate, $CO_2Et \cdot CEt:CO$, is colourless, and does not yield additive compounds, but readily polymerizes, yielding a cyclobutane derivative.

F. **Unsaturation and Physical Properties.**—Unsaturation, especially in the case of compounds with conjugate linkings, produces a marked effect on numerous physical properties. The phenomena which have been most closely studied are those on the refraction and dispersion of light. The effect of such a conjugate linking as in $CHMe:CH \cdot CH:CHMe$, is to produce a considerable increase or *exaltation* in the specific and molecular refraction and dispersions. In the case mentioned the molecular refraction is about one unit greater than the value calculated from the atomic refractions + two olefine linkings. The existence of such exaltation is frequently used as an argument in favour of the presence of conjugate linkings (either two olefine or an olefine and carbonyl) in the compound examined. In the case of hexatriene, $CH_2:CH \cdot CH:CH \cdot CH:CH_2$, the exaltation is 2·06 units. Exaltation is also observed when an acetylene linking is in conjugation with a carbonyl group. According to *Moureau* (Annales, 1906, [8], **7**, 536), and *Muller* and *Bauer* (J. Chim. Phys. 1903, **1**, 190), the exaltation in certain series of compounds increases with the negative character of the substituents. Little or no exaltation is met with in the case of benzene, furane, diacetyl, and similar compounds, although the formulæ usually written for these compounds contain conjugate bonds. This may be due to special symmetrical ring structure or to mutual neutralization of residual affinities. Unsaturated groups such as amino, vinyl and allyl, when present, in benzene compounds and directly attached to the nucleus, produce exaltation, probably owing to a readjustment of residual affinity. Exaltation is extremely well marked in compounds containing conjugate linkings, which, in their turn, are conjugate to the ethylene bonds in phenyl groups: *e.g.* diphenyl-butadiene, $CHPh:CH \cdot CH:CHPh$, has an exaltation of 15 units (*Klages*, B. **40**, 1768); cinnamylideneacetic acid, $CHPh:CH \cdot CH:CH \cdot C(OH):O$, of 10·5 units, and diphenyl-hexatriene, $CHPh:CH \cdot CH:CH \cdot CH:CHPh$, of 24 units (*Smedley*, J. C. S. 1908, 876).

Some of the most accurate work on unsaturated compounds has been carried out by *Auwers* and *Eisenlohr* (J. pr. **82**, 65; **84**, 1, 37). They compare the specific refractions × 100, and not molecular refractions, and make use of the following values for atomic refractions n_D as determined by *Eisenlohr* (Zeit.

phys. **75**, 585): CH_2 = 4·618, C = 2·418, H = 1, O (in carbonyl) = 2·211, O (in ethers) = 1·643, O (in hydroxyl) = 1·525, Cl = 5·967, Br = 8·865, I = 13·900, olefine linking = 1·733, and acetylene linking = 2·398. They find that a single conjugation in a hydrocarbon produces an exaltation of approximately 1·9 units, but that this value is reduced to an appreciable extent by the introduction of substituents. The amount of this interference depends upon the number and position of the substituents. In cinnamene and its β-substituted derivatives the exaltation is about 1·0, and when three substituents are present the exaltation is only 0·45. They conclude that for a given type of compound the exaltation is fairly constant, and within such limits the existence of the exaltation may be made use of in discussions bearing on constitution.

When several pairs of conjugate linkings are present, it is found that the exaltation is much greater when these all form a single chain (cf. hexatriene) than when they are "crossed" as in 

Semicyclic double bonds (p. 574) and rings formed of three atoms, *e.g.* trimethylene, also produce optical exaltation.

For effects of unsaturation on heats of combustion, see *Auwers* and *Roth* (A. **373**, 239, 267).

For effects of unsaturation on optical activity, see *Frankland* and others, J. C. S. 1906, 1854, 1861; 1911, 2325; *Hildich*, J. C. S. 1908, 1, 700, 1388, 1618; 1909, 331, 1570, 1578, 1910, 1091; 1911, 218, 224, Zeit. phys 1911, **77**, 482; *Rupe*, A. **373**, 121.

LI. ALIPHATIC DIAZO- AND TRIAZO-COMPOUNDS

A. Diazo-compounds.—By the action of nitrous acid on a solution of a salt of a primary aromatic amine, the important group of diazo or diazonium salts are formed. It is generally stated that aliphatic amino-compounds differ from the aromatic in this respect, and immediately yield the corresponding hydroxy-compounds. A few aliphatic amino-compounds do, however, yield diazo-derivatives with cold nitrous acid; one of the best known of these compounds is ethyl diazo-acetate, .

CO_2Et (p. 212), a yellow oil, b.-pt. 141°. It differs from the aromatic diazonium salts in having both nitrogen atoms attached to carbon, and may be regarded as the anhydride of a diazo hydroxide, $OH\cdot N{:}N\cdot CH_2\cdot CO_2Et$. It is extremely reactive, and the N_2 group is readily replaced by I_2, HCl, H_2O, &c. With concentrated alkalis it yields **bis-diazo-acetic acid**:

$$CO_2H\cdot C\begin{matrix}N\\ \\ NH\cdot NH\end{matrix}\!\!>\!\!\begin{matrix}N\\ \\ N\end{matrix}\!\!<\!\!C\cdot CO_2H$$

(*Curtius, Darapsky,* and *E. Muller*, B 1907).

The simplest aliphatic diazo-compound is **diazo-methane**, $CH_2\begin{matrix}N\\ \\ N\end{matrix}$, which may be regarded as the anhydride of $CH_3\cdot N{:}N\cdot OH$. Diazo-methane is most conveniently prepared by decomposing nitroso-methyl-urethane, $CH_3\cdot N(NO)\cdot CO_2Et$, with alkali, the compound, $CH_3\cdot N{:}N\cdot OK$, being formed as an intermediate product (*Hantzsch* and *Lehmann*, B. 1902, **35**, 897).

It is a yellow, odourless gas at atmospheric temperature, and is excessively poisonous. It is characterized by its reactivity, and will readily convert acids into methyl esters, alcohols and phenols into methyl ethers, aniline and its homologues into secondary amines, and aldehydes into ketones. It is also capable of uniting with unsaturated compounds, yielding heterocyclic derivatives, *e.g.*

$$\begin{matrix}CH\\ \\ CH\end{matrix}\!\!>\!\!\begin{matrix}N\\ \\ CH_2\end{matrix}\!\!>\!\!N + \begin{matrix}CH\\ \\ CH\end{matrix}\!\!>\!\!\begin{matrix}NH\\ \\ CH\cdot CH\end{matrix}\!\!>\!\!N \text{ pyrazole.}$$

$$\begin{matrix}CH_2\\ \\ CH_2\end{matrix}\!\!>\!\!\begin{matrix}N\\ \\ CH_2\end{matrix}\!\!>\!\!N + \begin{matrix}CH_2\cdot NH\\ \\ CH_2\cdot CH\end{matrix}\!\!>\!\!\text{pyrazolin.}$$

Cf. p 528.

B. **Triazo-compounds.**—*Forster* (J. C. S. 1908, **93**, 72, 669, 1070, 1174, 1859, 1865) has obtained a number of fairly simple aliphatic triazo-derivatives containing the univalent grouping, $\begin{matrix}N\\ \\ N\end{matrix}\!\!>\!\!N\cdot$. *Ethyl triazo-acetate*, $N_3\cdot CH_2\cdot CO_2C_2H_5$, obtained by the action of sodium azide, NaN_3, on an alcoholic solution of ethyl chloro-acetate, is a colourless liquid, b.-pt. 44°–46° under 2 mm. pressure, and has a sweet odour suggestive of chloroform. From this ester *triazo-acetic acid*, m.-pt. 16°, and almost as strong an acid as bromo-acetic, and *triazo-acetamide*, m.-pt. 58°, have been obtained by the ordinary

methods. *Triazo-acetone*, acetonyl-azoimide, $N_3 \cdot CH_2 \cdot CO \cdot CH_3$, obtained from chloro-acetone, is a colourless liquid, b.-pt. 54° under 2 mm. pressure. It has the properties of a ketone, *e.g.* yields a semicarbazone, m.-pt. 152°, and is instantly decomposed by alkalis. *Ethyl α-triazo-propionate* and the isomeric β-compound have been prepared, and also *α-triazo-propionic acid*, $CH_3 \cdot CHN_3 \cdot CO_2H$, the last of which has been resolved into optically active components. *Ethyl β-triazo-propionate* is so readily decomposed by alkalis that the corresponding acid and amide have not been prepared. *Allyl-azoimide*, $CH_2:CH \cdot CH_2 \cdot N_3$, b.-pt. 76·5°; *triazo-ethyl alcohol*, $N_3 \cdot CH_2 \cdot CH_2 \cdot OH$, b.-pt. 60°/8 mm.; *triazo-acetaldehyde*, an oil, together with numerous esters derived from triazo-ethyl alcohol, have been prepared. Bis-triazo-compounds can be obtained, *e.g. bis-triazo-ethane*, $N_3 \cdot CH_2 \cdot CH_2 \cdot N_3$, and *ethyl bis-triazo-acetate*, $CH(N_3)_2 \cdot CO_2Et$, but are extremely explosive. Triazo-malonic acid and ethyl triazo-acetoacetate appear to be incapable of existence, but substituted derivatives, *e.g.* $CH_3 \cdot CO \cdot CN_3Me \cdot CO_2Et$, and even a bis-triazo-compound, $CH_3 \cdot CO \cdot C(N_3)_2 \cdot CO_2Et$, are known. *Triazo-ethylene*, $N_3 \cdot CH:CH_2$, can be obtained by eliminating hydrogen iodide from triazo-ethyl iodide. It is a pale-yellow liquid, b.-pt. 26°, and yields an oily dibromide. Numerous aromatic triazo-compounds have also been prepared, mainly from diazonium salts. (Cf. J. C. S. 1907, 855, 1350; 1909, 183; 1910, 126, 254, 1056, 1360, 2570.)

Staudinger and *Kupfer* (B. 1911, **44**, 2197) and *J. Thiele* (ibid. 2522) suggest that aliphatic diazo-compounds have an open-chain structure, *e.g* diazo-methane, $CH_2:N:N$, and like the aromatic diazonium salts contain a quinquevalent nitrogen atom. The arguments brought forward are: (1) The fact that the diazo-compounds can be obtained by the oxidation of hydrazones of ketones:

$$RR_1C:N \cdot NH_2 + O \longrightarrow RR_1C:N:N + H_2O.$$

(2) The azo group is reactive, yet in the numerous reactions of the aliphatic diazo-compound such a group does not take part.

In a similar manner hydrazoic acid and its derivatives are represented by open-chain formulæ, *e.g.* HN:N:N. Such a structure accounts for the fact that by the action of *Grignard* reagents azides yield diazo-amino-compounds:

$$R \cdot N:N:N \longrightarrow R \cdot N:N \cdot NHR'.$$

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