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TO
ORGANIC CHEMISTRY

WORKS OF ALEXANDER LOWY

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AN INTRODUCTION TO ORGANIC CHEMISTRY

BY

ALEXANDER LOWY, PH.D.

Professor of Organic Chemistry, University of Pittsburgh

AND

BENJAMIN HARROW, PH.D.

Associate Professor of Chemistry, College of the City of New York

THIRD EDITION

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PREFACE TO THIRD EDITION

THE very cordial reception which the first two editions of this book have received at the hands of the teaching and student body has prompted us to take the opportunity offered by the publishers to prepare a new edition. Since the appearance of the second edition four years ago, several important advances have been made in organic chemistry. Perhaps the most striking, and in many ways an unexpected advance, has dealt with the aliphatic series of compounds. A new chart—the development of products derived from ethylene—as well as a number of additions in the first part of the book, are evidence of this striking advance. Newer conceptions of sugar structure, a synthesis of sucrose, and the artificial production of a rubber-like substance may also be mentioned. But it may be said, in general, that the more important recent advances in the field of organic chemistry have been included—at least, such of them as can be included in an elementary text; and the reading references have also been brought up to date.

Our thanks are due to many friends for advice and criticism.

ALEXANDER LOWY.
BENJAMIN HARROW.

January, 1932.

PREFACE TO FIRST EDITION

In the preparation of this work the authors have tried to keep a number of objects constantly in mind. In the first place, they desired to embody in the work material which could be satisfactorily treated in a course in which the theory of organic chemistry is covered in two semesters (two hours a week). They were also anxious that such material should include not only the well-recognized basic principles of organic chemistry, but also its more recent and more important applications; the entire story being woven together into a simple and readable narrative.

The authors have also kept in mind the many connecting links that bind organic chemistry to a number of other sciences,—to medicine, dentistry, pharmacy; to agriculture; to the biological sciences; hence, the inclusion of such chapters as those dealing with lipoids; nucleoproteins and their decomposition products; the chemical changes which foodstuffs undergo in the body; plant and animal pigments; enzymes, vitamins and hormones; organic compounds of arsenic and other metals; dyes and stains, etc.

The text can, therefore, be appropriately used in connection with a lecture course, not only by the student who is taking organic chemistry as part of a general academic course, or as preparation for a more extended course in chemistry, but by one who is preparing for the medical, dental, pharmaceutical or other biological sciences.

The book is not intended to act as a guide for laboratory manipulations; details for the preparation of compounds are, therefore, intentionally omitted. Neither, with a few exceptions, are boiling points, melting points or other physical constants included in the body of the work; some of these will be found in the form of a table in the appendix.

To aid the student in naming organic compounds, a brief chapter (XXXVII) is devoted to this topic.

The structure of benzene and its derivatives is shown in

heavy and light lines, the heavy lines representing double bonds. This is in accordance with a plan originally proposed by one of the authors.[1]

The two colored charts, taken in conjunction with Chapter XXXIV (a brief outline for the identification of organic substances), should serve, to some extent, the purposes of a review.

A number of charts throughout the text, illustrating the uses of a few important chemicals, have been incorporated if only to give the student some idea of the many and diverse uses to which organic substances may be put.

In the opinion of the authors, the student should at the very outset be given some opportunity for collateral reading; hence, the references at the end of chapters and the general references at the end of the book.

The glossary has been added to explain a number of medical terms used in the text.

Photographs of a few of the outstanding leaders in organic chemistry have been included.

The authors have freely consulted various text-books and journals and they wish to acknowledge their debt to the men responsible for the texts and articles.

For their kindness in giving permission to reproduce diagrams, the authors wish to thank the following: The Marland Oil Co. (Petroleum Refining); R. F. Remler of the Mellon Institute of Industrial Research, and the National Wood Chemical Association (Uses of Methanol, Uses of Acetic Acid, Uses of Acetone, Uses of Formaldehyde); The U. S. Industrial Alcohol Co. (Ethyl Alcohol); D. Van Nostrand Co. (two colored charts); and Cain and Thorpe: "Synthetic Dyestuffs and Intermediate Products" (Substituents in Naphthalene Ring).

The authors are indebted to Dr. Tesh for complete proof-reading and to other members of the Department of Chemistry of the University of Pittsburgh for criticism.

The authors will at all times welcome suggestions and criticism.

ALEXANDER LOWY.
BENJAMIN HARROW.

[1] *Journal of the American Chemical Society*, **41**, 1029 (1919).

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NOTE FOR STUDENT

REMEMBER that the laws in chemistry hold for organic as well as for inorganic chemistry. Correlate as many of the new facts with facts with which you are already familiar from your previous studies.

Classification in organic chemistry has been carried to an exceptional degree. One type reaction often gives the key to hundreds of individual reactions. Emphasize, therefore, type formulas and type reactions and make constant use of paper and pencil to practice the writing of formulas and equations.

To broaden your outlook, consult as frequently as possible the reading references given at the end of chapters.

Periodically refer to the "Replacement of Elements and Groups" on the next page.

How can resourcefulness be acquired? Do it by pumping into a man information? No, not at all. There is only one thing which will really train the human mind, and that is the voluntary use of the mind by the man himself. You may aid him, you may guide him, you may suggest to him, and, above all, you may inspire him; but the only thing that is worth having is that which he gets by his own exertions, and what he gets is proportionate to the effort he puts into it. It is the voluntary exercise of his own mind, and I care very little about what he exercises it upon.—A. LAWRENCE LOWELL.

AN INTRODUCTION

TO

ORGANIC CHEMISTRY

CHAPTER I

INTRODUCTION

LONG ago man conceived the idea that between the living and the lifeless there is a sharp dividing line. A careful study of the colors of the spectrum, or a consideration of evolutionary problems, might have made him reconsider this view. It would have been more logical to assume that we probably cannot tell just where the "lifeless" ends and the "living" begins. That, indeed, is the modern point of view.

Even as late as a century ago, chemists still had faith in the classification of chemical compounds into "organic" or "inorganic," the "organic" being distinguished from the "inorganic" on the supposition that the former had some kind of "vital" or "life force," which made it seem quite impossible that a chemist could ever hope to reproduce an "organic" substance in the laboratory. (Formerly substances of mineral origin were classed as "inorganic"; those of animal or vegetable origin were classed as "organic.")

These notions of "organic" and "inorganic" were rudely shaken by the work of Wöhler, a distinguished German chemist, who, in 1828, succeeded in preparing urea in his laboratory by heating ammonium cyanate (p. 119), $[KCNO + (NH_4)_2SO_4]$. Now if any one compound can be called "organic," such a distinction certainly belongs to urea, for it is the chief end product of the decomposition of proteins in the body and is the principal nitrogenous constituent of the urine.

This epoch-making work of Wöhler's was not, as is generally supposed, at once accepted unconditionally. Sometimes the scientist does not take to scientific changes any more quickly than

does the average citizen to social or political changes. But in time other examples of the production of "organic" substances in the chemist's laboratory were recorded, and the old idea became less and less important. Chemists prepared or synthesized acetic acid, fats, alcohol, oxalic acid, mustard oil, oil of bitter almonds, sugars, camphor, uric acid, indigo, adrenaline, protein-like substances and thousands of others, more or less complex—all, however, typically "organic" substances. And we are far from having reached the limit. It is conceivable that in the not distant future some of the food we use will be made in the chemist's laboratory. Many are of the opinion that a judicious combination of the work of the physical chemist and the organic chemist will result, eventually, in solving the riddle of life itself.

We still retain the words " organic " and " inorganic," though we no longer think of them in the time-honored sense. What we call **" organic " chemistry** may more aptly be called **the chemistry of the carbon compounds,** for that is just what " organic " chemistry deals with.

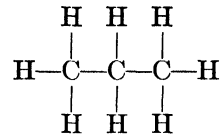
But in reality we do not draw the line too sharply. Such compounds as carbon dioxide, carbon monoxide, carbon disulfide, hydrogen cyanide and the carbonates are usually included in texts on inorganic chemistry, though, of course, they are carbon compounds, and according to the definition should be included under "organic" chemistry.

The fundamental laws of chemistry, which the student has taken up in his inorganic chemistry course, apply to organic chemistry with equal or perhaps greater force. If, then, the dividing line between "organic" and "inorganic" chemistry is not a sharp one, why the necessity for having these two subdivisions? We shall enumerate a number of reasons.

1. The number of compounds of carbon known to-day exceed 225,000, and the number of compounds which do not contain carbon are only about 26,000.

2. In general, organic and inorganic compounds show marked differences in solubility, the former being usually soluble in ether, alcohol, chloroform, benzene, etc., while the latter are not; whereas many of the inorganic compounds are soluble in water and the organic ones are not.

3. The atoms of carbon have the unique property of combining with one another to form chain-like structures—a property not frequently shown by other elements: for example,



4. Organic compounds are, as a rule, less stable than inorganic; they are much more easily susceptible to chemical and physical changes. (Organic compounds are decomposed at relatively low temperatures.)

5. " Type " reactions are quite frequent in organic chemistry. For example, there are hundreds of organic compounds which react with nitric acid to form " nitro " compounds (p. 231), hundreds of which react with reducing agents to yield " amino " compounds, etc.

6. There is often a marked difference in the velocity of reaction. The change of one organic compound to another is usually a relatively slow process, whereas the transformation of inorganic substances is often practically instantaneous.

7. Reactions in organic chemistry are, as a rule, mostly non-ionic, the solutions being non-conductors of electricity; whereas, reactions in inorganic chemistry are largely ionic. This explains, for example, why, when solutions of sodium chloride and silver nitrate are mixed, an immediate precipitate of silver chloride is obtained, whereas, we get no precipitate upon mixing solutions of pure carbon tetrachloride (CCl_4) and silver nitrate. Organic acids, bases and salts ionize.

8. Reactions in organic chemistry often tend to become quite complex, and there are possibilities of many " side " or " secondary " reactions (p. 227).

9. The complexity in structure exhibited by some organic compounds is quite unknown among inorganic compounds (p. 319).

10. Organic compounds often show a property called " isomerism " which we shall discuss later in some detail (p. 21), but this phenomenon is very little known in inorganic chemistry. For example, when we write HNO_3 we have reference to nitric acid, and to nitric acid alone, but when we write C_2H_6O this may stand for ethyl alcohol or for methyl ether, and the only way we can distinguish the one from the other is by writing graphic or structural formulas (p. 21), which give some idea of the arrangement of the atoms within the molecule. That is the reason why graphic and structural formulas are used so extensively in organic chemistry (pp. 14, 279).

Importance and Applications.—We have already mentioned the fact that more than 225,000 compounds are grouped under organic chemistry. Many of these find various applications in our daily life. Some of them are so common that merely mentioning their names will suggest to the student many of their applications. Picking a few of these substances more or less at random, we may refer to starch, sugar, fats, oils, proteins, paper, rayon, soap, explosives, photographic developers, bakelite, anesthetics, disinfectants, antiseptics, dyes, drugs, waxes, ether, natural gas, perfumes, glue, citric acid, alcohol, saccharin, artificial food colors, caffeine, cellulose, camphor, rubber, flavoring essences, gasoline, vaseline, coal tar, glycerine, aniline, indigo, salvarsan, lacquer industry (duco, etc.), etc. And it may be added that the various transformations which the foodstuffs and cellular tissue undergo in the plant and animal kingdom, involving complex syntheses and decompositions, are essentially those which can best be studied by the organic chemist.

Other Sciences Based on Organic Chemistry.—Physiological (or Bio-) chemistry (which deals with the chemical processes that take place in animals and plants), food chemistry, and organic analysis, all have their basis in organic chemistry. Various aspects of medicine, dentistry and pharmacy require training in organic chemistry. We shall illustrate this interdependence with a few examples.

A problem of general importance in bacteriology is to find some substance which has the property of destroying a certain type of bacteria without at the same time injuring the body tissues. Ehrlich, the German physician, who was also a trained chemist, found a cure for syphilis by the use of arsphenamine (p. 339) (also called salvarsan and " 606 "), which he synthesized in the laboratory. More recently the work of Jacobs and Heidelberger at the Rockefeller Institute, N. Y., on the application of various arsenical compounds to medicine, holds out hope that one of these will prove of distinct value in the treatment of sleeping sickness. Mention may also be made of the use of "chloramine-T" (p. 282) and other organic compounds containing chlorine, in the treatment of infected wounds. During the war, Dakin and Carrel found that " chloramine-T," given under certain conditions, is strong enough to destroy micro-organisms, without at the same time harming the tissues.

Another problem, this time of particular importance to physi-

ologists and general medical practitioners, is the isolation, in a chemically pure state, of the active principles of glands in the body. One of the active principles of the adrenal glands, adrenaline (or, as it is sometimes called, "epinephrine") has not only been isolated from the gland, but has actually been synthesized in the laboratory. In this work Abel of Johns Hopkins and the late Takamine, a Japanese chemist who had established himself in the United States, took leading parts. Lately, the active principle of the thyroid gland, thyroxin, has been isolated by Kendall of the Mayo Clinic in Rochester, Minn., and Harington has also succeeded in synthesizing it. And we may mention that insulin, ("iletin") an active principle of the pancreas, which has been shown by the Canadian, Banting, to play such an important rôle in diabetes, has lately been obtained in a crystalline form by Abel.

Cocaine, novocaine, butyn, benzyl alcohol, benzyl benzoate and ethylene as anesthetics; hexyl resorcinol, dibromin as antiseptics; mercurochrome-220 as a germicide; the essential constituents of chaulmoogra oil in the treatment of leprosy; caffeine and related substances as diuretics; barbital (veronal), allonal and luminal as hypnotics; thymol and carbon tetrachloride as a cure for hookworm; the relation of ergosterol and vitamin D and the relation of vitamin E to the problem of reproduction; the isolation and the ultimate synthesis of glutathione, a cell constituent related to body oxidation; and the extraction of the active principle of the parathyroid gland are only a few illustrations of the comparatively recent developments in the application of organic chemistry to medicine.

At so rapid a rate is progress in this field, that, in the last few years, several noteworthy discoveries have been made. For example, sucrose has been made in the chemist's laboratory (p. 179); a new form of synthetic rubber has been announced (p. 40); hematin, the important component of hemoglobin, has been synthesized; carotin, a hydrocarbon, is apparently the forerunner of vitamin A; a liver extract cures pernicious anemia; and active extracts of hormones from the reproductive glands, from the adrenals and from the pituitary have been obtained.

Sources of Organic Substances.—*A.* Organic compounds may be traced either to the plant or animal kingdom. Out of carbon dioxide, water, and various constituents from the soil, in the presence of light, the plant builds a veritable galaxy of substances: sugars, starches, cellulose, alkaloids (morphine in opium—

nicotine in tobacco), acids (citric and tartaric), salts ("tartar" in grapes), esters (flavoring substances of fruits), essential oils (peppermint, lemon), camphor, vegetable oils (linseed, cotton-seed, olive), herbs (from which drugs are made and which were so largely used in days gone by), gum arabic, flavoring substances (vanilla), dyes (indigo, logwood, fustic), perfumes, tannin (from nutgalls), etc.

B. Plants and animals furnish us with fats, proteins, carbohydrates, enzymes and vitamins, and we often go to the animal kingdom for a number of products, such as urea, uric acid, gelatin, toxins and antitoxins.

C. Destructive Distillation of Coal.—When soft coal is strongly heated in a retort, this complex substance breaks down into a number of (chemically) simpler substances. The conversion of a complex substance into a number of simpler substances by the aid of heat (in the absence of air) is known as "destructive distillation." The destructive distillation of coal yields coal gas (illuminating gas), ammonia, coke and coal tar. Coal tar, at one time discarded as a useless by-product, is now the starting-point for any number of organic products (some 225 compounds have been so far isolated). Out of coal tar we get benzene, toluene, naphthalene, anthracene, carbolic acid, the cresols, etc.; and these substances (the source of many aromatic compounds, see p. 211), in turn, yield thousands of other organic compounds, many of them of great value as dyes, perfumes, drugs, etc. (see chart, p. 211). Perkin, an Englishman, was the first (in 1856) to prepare a coal-tar dye, but the development of the dye industry is due largely to the Germans, who, prior to the late war, were responsible for much research work in this field. Post-war developments in this country and in England have already reached such a stage as to ensure the establishment of permanent dye and other related industries.

D. Destructive Distillation of Wood.—The important products obtained from wood are acetic acid, methanol (wood alcohol), acetone, (indirectly), wood tar, combustible gases and charcoal.

E. Destructive Distillation of Bones.—This yields animal charcoal (bone black) and bone oil, out of the latter of which a number of nitrogenous compounds, characterized by their disagreeable odor, are obtained (pyridine and quinoline are examples).

F. Fractional Distillation of Petroleum.—A mixture of two or more liquids having different boiling-points may usually be sepa-

rated from one another by a process of distillation, the liquid with the lower boiling-point distilling over first. A process which separates two or more liquids by making use of their different boiling-points is called "fractional distillation." The fractional distillation of petroleum yields a number of important commercial products, such as naphtha, gasoline, kerosene, gas oil, lubricating oil, cylinder oil, vaseline, etc.

G. Natural Gas.—Within the past few years there have been important new developments due to the production of compounds of practical importance from natural gas. Many of these new compounds have been synthesized from ethylene as the starting material. (See chart facing p. 142.)

H. Fermentation.—It was for a long time supposed that in the conversion of sugar into alcohol by means of yeast, the living cells of the latter were primarily responsible for the change. We now know that what brings about this change is not the cells themselves, but substances produced by the cells, known as "enzymes." Changes analogous to the conversion of sugar into alcohol are known as "fermentation." The sweet apple juice turns to cider (due to the formation of alcohol), and finally to cider vinegar (due to the oxidation of the alcohol into acetic acid). Milk on standing, or when "inoculated" with bacteria, becomes sour, due to the conversion of lactose (milk sugar) into lactic acid.

I. Putrefaction.—Putrefaction may be defined as the decomposition of animal or vegetable substances brought about largely by micro-organisms, resulting in diverse products, some of which have a foul odor. Among the products of putrefaction are amines, fatty acids, ammonia and its compounds, H_2S, methane, etc.

Purification of Organic Compounds.—Most of the organic compounds when first prepared are impure. Before the physical constants and chemical analyses (qualitative and quantitative) of a compound can be determined, it must be obtained in a pure state. For details of the methods used in the preparation of chemically pure substances, we must refer the student to appropriate laboratory texts (see p. 386), and only the barest outline will be given here.

The substance as first prepared is generally in an impure state. It may be purified by one or more of several processes, such as crystallization, distillation, sublimation, extraction, dialysis, precipitation, decolorization (for details refer to laboratory manuals quoted). Almost all pure organic compounds have a definite

melting-point (m.p.), or boiling-point (b.p.), or both. The melting- or boiling-point of the compound is, therefore, determined after the preliminary process of purification. A definite m.p. or b.p. is an important criterion of purity; in addition, the specific gravity, solubility, crystalline structure, refractive index, optical activity, etc., are also made use of. (The principles involved, as well as the details of manipulation, will become familiar to the student as a result of his laboratory work.) Having obtained the pure product, the next step is an analysis of the compound.

Elements Present in Organic Compounds.—Numerous as the compounds of carbon are, most of them contain but two to five different elements in the molecule. There are hundreds of compounds which contain merely the elements carbon and hydrogen. These are known as hydrocarbons. Methane (CH_4), benzene (C_6H_6), naphthalene ($C_{10}H_8$) and anthracene ($C_{14}H_{10}$), are examples. Many contain the element oxygen in addition to carbon and hydrogen; as for example, the sugars, fats, starches, alcohols, ethers, acetic acid and glycerol. Many are composed of carbon, hydrogen and nitrogen, as hydrocyanic acid and aniline. Examples of compounds containing carbon, hydrogen, oxygen and nitrogen are some of the alkaloids, proteins, indigo and urea; and those containing carbon, hydrogen and a halogen are chloroform and iodoform.

Often, in addition to the elements already mentioned, we find sulfur and phosphorus. Many of the proteins contain appreciable quantities of the former element, and the phosphatides, such as lecithin and cephalin, which are important cellular constituents, contain phosphorus. (Hopkins has isolated a substance from cells, to which he has given the name " glutathione," which contains sulfur and which is regarded as a substance that plays a very important rôle in all cellular oxidations. Quite recently he has synthesized this substance.)

Elements in addition to those already mentioned are often met with. Following the pioneer work of Ehrlich on salvarsan, very many organic compounds of arsenic, antimony, bismuth and mercury have been prepared. Quite recently an organic compound of lead, lead tetraethyl, has been used to prevent " knocking " in automobiles (p. 199). Many salts of organic acids, such as those of sodium, potassium, calcium, etc., are found in nature or may be prepared in the laboratory.

Analysis of Organic Compounds.—(Detailed directions are given in laboratory manuals.)[1] Before a quantitative analysis of a compound is made, a qualitative analysis, involving the detection of the elements present, is undertaken. In the course of the qualitative analysis, carbon in most organic compounds may be detected by heating the compound with copper oxide, the carbon thereby being oxidized to carbon dioxide, the presence of which may be shown with lime water. The same process oxidizes any hydrogen present to water, which is usually seen to collect in the upper (cooler) part of the tube. Nitrogen may be detected either by heating the substance with soda lime (NaOH+CaO), thereby converting the nitrogen into ammonia, or by fusion with sodium, whereby sodium cyanide is formed (Na+C of organic compound +N), which is then converted into ferrocyanide by heating with a ferrous salt, and ultimately to " prussian blue " by the addition of a ferric salt. Halogens may be recognized by heating the compound with copper oxide in a non-luminous flame, whereby a green coloration is obtained, due to the volatilization of the copper halide, or by making use of the sodium fusion test, whereby the halogen is converted into the corresponding sodium salt, which may then be tested with silver nitrate. (Remember that the halogen in organic combinations is mainly in a non-ionizable form, and therefore does not react with a solution of silver nitrate prior to its decomposition.)

If sulfur is present it may be recognized by fusion with sodium, whereby sodium sulfide is formed, and a solution of this compound when placed on a silver coin forms silver sulfide (brownish-black).

Phosphorus and any of the other elements (such as the metals) are detected just as in inorganic analysis. The test for phosphorus requires a preliminary fusion with an oxidizing mixture (such as potassium nitrate and sodium carbonate).

We have no satisfactory test for oxygen.

Many of the qualitative tests serve as the basis for the quantitative determinations. The carbon dioxide and water formed by the oxidation of a compound containing carbon and hydrogen

[1] Benedict, Elementary Organic Analysis; Cohen, Laboratory Manual of Organic Chemistry; Fisher, Laboratory Manual of Organic Chemistry; Gattermann, Practical Methods of Organic Chemistry; Kingscott and Knight, Methods of Quantitative Organic Analysis; Mulliken, Identification of Pure Organic Compounds; Price and Twiss, A Course of Practical Organic Chemistry; Pregl, Quantitative Organic Microanalysis; Sudborough and James, Practical Organic Chemistry.

are collected and weighed, and from the amounts of the products formed, the percentages of carbon and hydrogen in the original compound are calculated. The nitrogen in a compound may either be determined by the " Kjeldahl " method, whereby the element is converted into ammonia, or by the " Dumas " absolute method, whereby nitrogen gas is set free and its volume measured.

In the determination of the halogens, the compound is either oxidized with fuming nitric acid in presence of silver nitrate, the resulting silver halide weighed and the halogen calculated; or the compound is heated with pure calcium oxide, and the halogen in the resulting calcium halide determined either by precipitation or titration with silver nitrate.

Sulfur in an organic compound is determined by heating with fuming nitric acid, thereby converting it to sulfuric acid. This is then precipitated as barium sulfate with barium chloride. The percentage of sulfur is calculated from the weight of barium sulfate.

For estimating phosphorus and other elements, the methods outlined in inorganic quantitative analysis are followed.

Neither in its detection nor in its determination is there a good method available for oxygen when present in an organic compound. The general procedure is to determine the percentage of all the other elements present in the compound, subtract the total from 100, and " call " the difference the per cent of oxygen.

The principles underlying the analytical methods are quite simple, but the details for the quantitative determination of C, H, N and the other elements, are rather complex.

Experimental details have been worked out to determine percentages of elements even when as small a quantity as .002–.003 gram of a compound is available.[1]

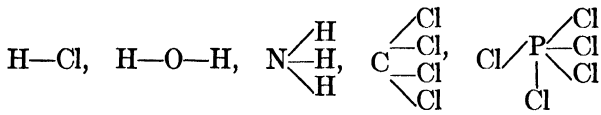
The analysis just discussed is what is known as " ultimate " or " elementary " analysis. It refers to the precentage of the elements present in the compound. There is still another type of analysis, known as " proximate," with which the clinical, pharmaceutical or food chemist has much to do. This " proximate " organic analysis deals with the determination of ingredients present in a mixture, such as the fat or protein in milk, or the various nitrogenous constituents and sugar in urine, or the percentage of alcohol in wine, etc.

The quantitative analysis enables us to arrive at what is known

[1] Pregl, Quantitative Organic Microanalysis.

as the "empirical" or "simplest" formula; but this may not necessarily prove to be the "true" or "molecular" formula. For example, a quantitative analysis of acetylene and benzene would yield the same "empirical" formulas for both, namely, CH; yet acetylene is written C_2H_2 and benzene C_6H_6. In order to arrive at the actual or "molecular" formula, whether C_2H_2 or C_6H_6, we must further proceed to a molecular weight determination, based on vapor density, or boiling-point, or freezing-point, etc. Here again the reader is referred to laboratory manuals or to books on physical chemistry for further details.[1]

Valence and Structure in Inorganic Chemistry.—Our studies in inorganic chemistry have led us to define valence as the number of atoms of hydrogen with which one atom of an element combines or replaces. To show such relationships graphically in any compound, we indicate valencies by lines or "bonds," each line representing one valency. Thus:



where not only are hydrogen, oxygen, nitrogen, carbon and phosphorus shown to be mono-, di-, tri-, tetra- and pentavalent elements, respectively, but these valencies are indicated by bonds, each bond representing one valency.

In organic chemistry, the use of graphic formulas is very extensive indeed, for only by some such method can the distinguishing features of a compound be brought out at a glance.

The difficulties that confront us may be seen from the following example, which has already been touched upon once before. HNO_3 is the formula for nitric acid and for this compound alone, but C_2H_6O stands for grain alcohol or methyl ether, and C_4H_{10} may represent two different compounds. Although the molecular formulas are the same, the physical and chemical properties are more or less different. We say that in these cases the different compounds are due to differences in the internal structure of the

[1] Findlay, Practical Physical Chemistry; Getman, Laboratory Exercises in Physical Chemistry; Gray, Manual of Practical Physical Chemistry.

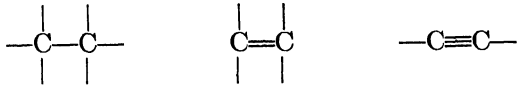
molecule, and our graphic formulas, which we shall use so much, attempt to give us a picture of such differences. Of course, these graphic formulas do not, and cannot represent the actual differences of any two compounds, or for that matter the actual structure of any one compound. Matter, to begin with, has three, not two, dimensions in space, and no structure drawn on paper can truly represent actual conditions. Nevertheless, these two-dimensional formulas have proved of inestimable value in clearing up many difficulties, as the student will appreciate when he proceeds to the various chapters.

The Fundamental Bases underlying the Structural Theory of Organic Chemistry:

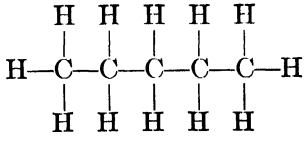
1. The valence of carbon, almost without exception, is four,[1] and is represented as

where any one bond bears exactly the same relationship to the carbon atom as any other bond. These valencies may be represented as directed toward the corners of a regular tetrahedron, constructed around the carbon atom as a center, and are, therefore, equidistant from each other in space.

2. Carbon atoms may be united either by single, double or triple bonds:



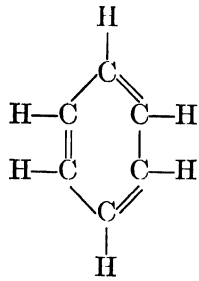
3. Carbon atoms may form a "straight" or "open" chain; for example,



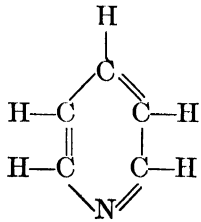
[1] There are several striking exceptions, however, such as CO (p. 163), C=NOH (p. 164), R—N=C (p. 162), and $(C_6H_5)_3C$ (p. 218).

[2] It is suggested that at this point the instructor illustrate by means of models the probable spatial arrangement (in the form of a regular tetrahedron) of the methane molecule.

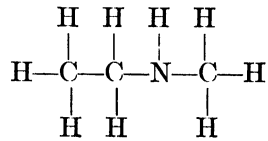
4. Carbon atoms may form a " closed " chain; for example,



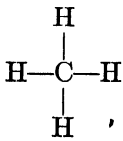
5. Other elements besides carbon may enter a carbon chain, or a ring: e.g.,

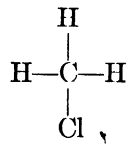


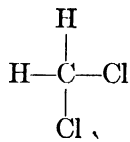
or

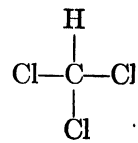


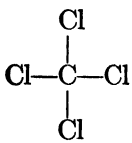
6. Elements may substitute one another in compounds; that is, one element in a compound may be removed, and another may take its place; for example,

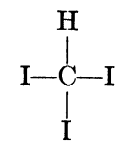


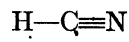


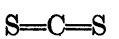


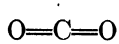


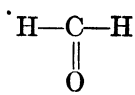




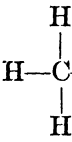




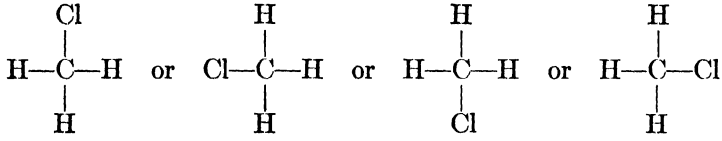




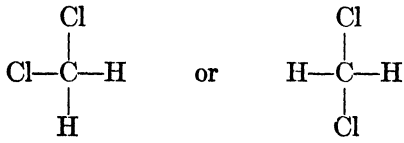
It must not be supposed that when we write methane,



we have any intention of fixing the atoms in space. In any case—and this has already been referred to—two-dimensional configurations cannot truly represent the structure of any form of matter. But we do wish to emphasize that in the formula for methane the four hydrogen atoms are to be regarded as of equal value, so that when a hydrogen atom is replaced by a chlorine atom, it does not matter whether we write



for they all represent one and the same compound, namely, monochloromethane; nor, if two hydrogen atoms are replaced by two chlorine atoms, does it matter whether we write



for both represent the same compound, dichloromethane.

The Electron Conception of Valence.—Based on modern work on the structure of the atom, many chemists have been busy recently developing ideas of valency in accord with the electronic conceptions of matter. As early as 1907 J. J. Thomson stated that for each valency bond established between two atoms, the transference of one—negatively charged—corpuscle (electron) from one atom to the other has taken place, the atom receiving the corpuscle (electron) acquiring a unit negative charge, while the atom losing the electron acquires a unit positive charge. Thus, a neutral H atom and a neutral Cl atom would become positively and

negatively charged, respectively, should the H atom lose an electron to the Cl atom:

$$H - \ominus \rightarrow H^+$$
$$Cl + \ominus \rightarrow Cl^-$$
$$H^+ + Cl^- \rightarrow HCl$$

An atom is capable of losing or gaining as many electrons as it has valencies and may function either as a positively or negatively charged atom. (Most elements have a greater tendency to behave one way than another.) If the Cl atom loses an electron, it becomes positively charged; e.g., hypochlorous acid, $\overset{+}{Cl}\ \overset{--}{O}\ \overset{+}{H}$; but if it gains an electron, it becomes negatively charged; e.g., $\overset{+}{H}\ \overset{-}{Cl}$.

A divalent atom may function in three ways: through the gain of two electrons; through the loss of two electrons; and through the simultaneous loss of one electron and gain of another; e.g.,

$$\overset{--}{O} \qquad \overset{++}{O} \qquad \overset{+-}{O}$$

With a trivalent element there are four possibilities:

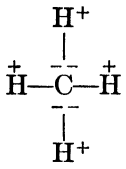
$$N\overset{-}{=} \qquad N\overset{-}{+} \qquad N\overset{-}{\ddagger} \qquad N\overset{+}{\ddagger}$$

An atom, then, whose valence is n may function electronically in $n+1$ different ways.

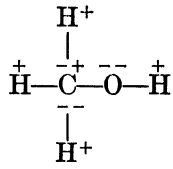
If this conception be applied to carbon, we might expect the carbon atom, with its tetravalency, to function in five different ways:

$$\overset{----}{C} \qquad \overset{---+}{C} \qquad \overset{--++}{C} \qquad \overset{-+++}{C} \qquad \overset{++++}{C}$$

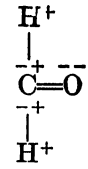
Applying the electronic conception of valence to a few simple carbon compounds—to methane, methanol (wood alcohol), formaldehyde, formic acid and carbon dioxide—we get the following:



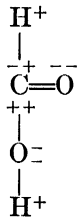
CH_4



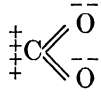
CH_4O



CH_2O



CH_2O_2



CO_2

(Consult the references at the end of the chapter—Falk and Nelson, Noyes and Langmuir.)

Classification of Organic Compounds.—There are two main divisions, the "**aliphatic**" and the "**aromatic.**"

The aliphatic compounds are related to methane, CH_4, and are "open chain." They get their name from the fact that animal and vegetable fats belong to this series.

The aromatic ("ring" or "cyclic") compounds are related to benzene, C_6H_6, and many are characterized by fragrant odors; hence the name.

The line of demarcation of aliphatic and aromatic compounds is not a sharp one, for not all aliphatic compounds can be directly traced to fatty substances, nor do all aromatic compounds have odors. On the other hand, many aliphatic compounds possess very characteristic odors. Nevertheless, there are, as a rule, some general differences which help to differentiate the two great divisions, perhaps the most important being differences in a number of chemical properties (p. 213).

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CHAPTER II

SATURATED HYDROCARBONS OR PARAFFINS AND PETROLEUM

As its name implies, a hydrocarbon is a compound containing hydrogen and carbon.

Methane, CH_4, is the simplest compound of the hydrocarbon group.

Occurrence.—The decomposition of vegetable and animal matter gives rise to this gas. One of the gases arising from marshes is methane, hence its name "marsh gas." It is also one of the gases produced in intestinal putrefaction. It forms a large percentage of the constituents found in natural gas (80 per cent and above) and coal gas (30–40 per cent). Fires and explosions in coal mines are mainly due to the ignition of mixtures of methane and air; hence methane is also known as " fire-damp."

Preparation.—Methane may be synthesized from its elements by passing hydrogen over carbon in presence of nickel (catalyst) at 475°.

$$C+2H_2 \rightarrow CH_4$$

It may also be obtained by the action of water on certain carbides, such as aluminum carbide:

$$Al_4C_3+12H_2O \rightarrow 3CH_4+4Al(OH)_3$$

This reaction is of interest since it led Moissan, the French chemist, to speculate on the origin of natural gas. He held this to be due to the action of water on various metallic carbides. (It must be remembered that methane is not always the product formed when water acts on a carbide. The student will recall that water acts on calcium carbide, for example, to give acetylene.)

The laboratory method depends upon heating a mixture of fused sodium acetate and soda lime (NaOH+CaO):

$$CH_3 \cdot \boxed{COONa+NaO} H \rightarrow CH_4+Na_2CO_3$$

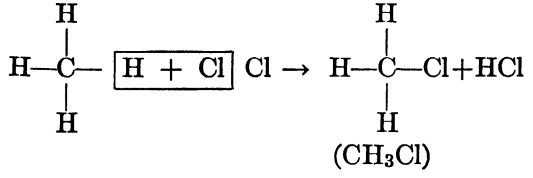
(The sodium acetate is the sodium salt of acetic acid, $CH_3 \cdot COOH$. The latter, in turn, may be regarded as methane, CH_4, having one of its hydrogens replaced by the COOH group, known as the "carboxyl" group. See p. 85.)

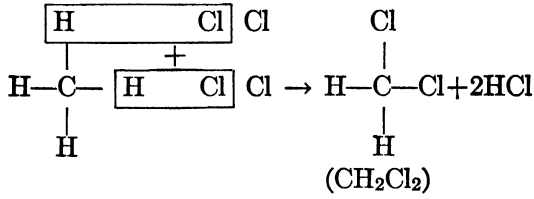
Properties.—It is a colorless gas with a slight odor, and burns with an almost non-luminous flame:

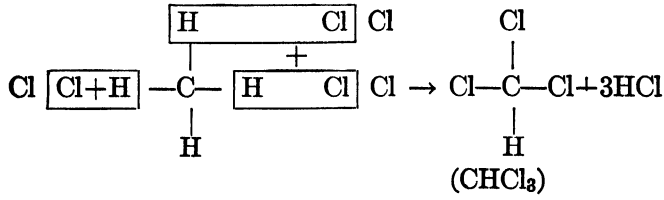
$$CH_4 + 2O_2 \rightarrow CO_2 + 2H_2O$$

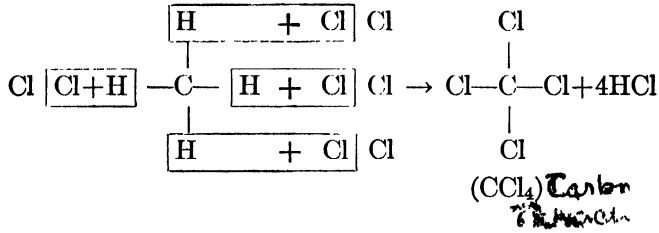
Methane has high fuel value. If mixed with air and ignited, it explodes; this explains many explosions in coal mines ("fire-damp").

The chemical properties of methane apply to the entire group of saturated hydrocarbons (p. 26) of which methane is the first member. Methane is an inactive and stable compound. (Methane and other hydrocarbons of this series are known as **paraffins**, which means "little affinity.") The common reagents, such as hydrochloric, nitric, sulfuric and chromic acids, and sodium and potassium hydroxides, do not react with it. On the other hand, the halogens, such as chlorine and bromine, react rather vigorously with methane, particularly in the presence of sunlight:









You will notice, in these examples, that the chlorine replaces the hydrogen in the molecule. Whenever an element or a group of elements replaces another element or group of elements in a compound, the process is known as "substitution." Such reactions are characteristic of saturated hydrocarbons. CH_3Cl, CH_2Cl_2, $CHCl_3$ and CCl_4 are chlorine substitution products of methane.

CH_3Cl = methyl chloride or monochloromethane;
(CH_3 = methyl group) (monovalent).

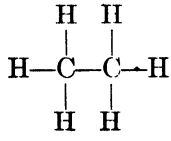
CH_2Cl_2 = methylene chloride or dichloromethane;
(CH_2 = methylene group) (divalent);

$CHCl_3$ = trichloromethane or chloroform.

CCl_4 = tetrachloromethane or carbon tetrachloride.

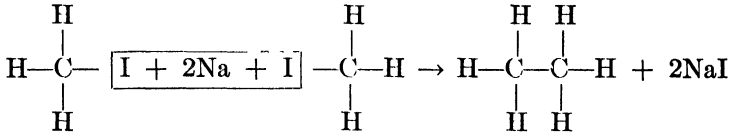
(Many of these names need not be memorized. If the student will but remember that these compounds are substitution products of methane, he will have little difficulty in naming them. In CH_3Cl, for example, the compound may logically be regarded as methane in which one of the hydrogen atoms has been replaced by chlorine; hence the name "monochloromethane." But it must also be remembered that the CH_3 group is known as a "methyl" group; hence also the name "methyl chloride.")

Ethane, C_2H_6. This is the second member of the paraffin series, and in its general physical and chemical properties shows resemblances to methane. It is found in natural gas and petroleum and is separated by fractional distillation from other hydrocarbons. Its formula is represented by



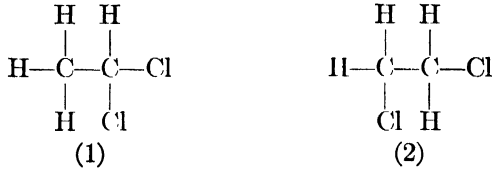
and it differs from methane by CH_2. It may be regarded as methane in which one of the hydrogens is replaced by a CH_3 group; that is, $CH_3 \cdot CH_3$, methyl methane, or dimethyl.

Further light on the structure of ethane is shed by the way in which it can be synthesized. Methyl iodide reacts with sodium in the following way (*Wurtz* synthesis):



In other words, the formation of ethane is here shown to be a coupling of two methyl groups.

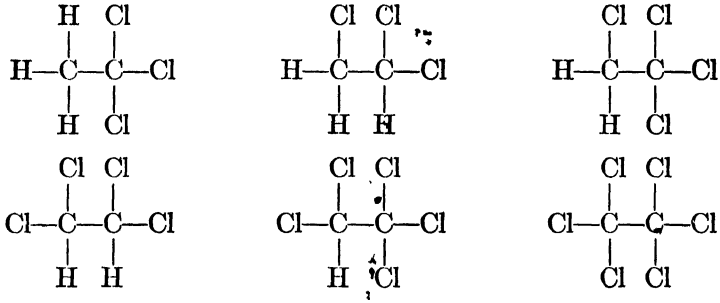
Isomerism.—Experience has shown that only one mono-substitution product of ethane can be obtained, but it is possible to obtain two di-substitution products, both having the same molecular formula, $C_2H_4Cl_2$, but differing from one another in physical and chemical properties. Here we clearly have a case of isomerism, and the graphic formulas bear this out:



(1) (2)

for in (1) we see two chlorine atoms attached to the same carbon atom, and in (2) the two chlorine atoms are attached to two different carbon atoms. Whenever we have two or more compounds having the same molecular formula, but differing in physical and chemical properties, we have an example of isomerism, and the individual compounds are known as isomers. (Let us illustrate this question of isomerism with an analogy. Suppose we take the figures 4, 7, 5. It obviously makes very much of a difference as to whether we write 475 or 754 or 547 or 745 or 574 or 457. Yet all we have done is to *rearrange* the figures; and by merely rearranging the numerals we have obtained *totally different* sums. So it may be with two compounds such as are illustrated above: they may have the same empirical formulas, yet be quite different substances because of the different *arrangement* of the atoms within the molecule.)

Experience has also shown that there are but two tri-, two tetra-, one penta-, and one hexa- substitution products of ethane; and the student can confirm this by studying the graphic formulas:



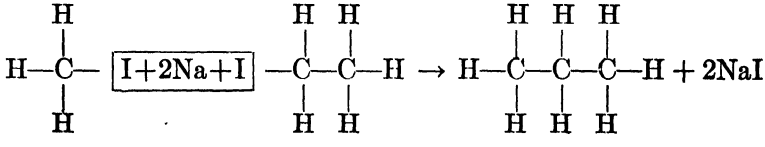
In naming substitution products of ethane, the system adopted for methane is used:

CH_4	CH_3
Methane	Methyl radical
C_2H_6	C_2H_5
Ethane	Ethyl radical

C_2H_5I, for example, is ethyl iodide, or iodoethane, and C_2H_5OH is ethyl hydroxide, or hydroxyethane.

(The name for the radical corresponding to the hydrocarbon is obtained by changing the suffix-*ane* into -*yl*.)

Propane, C_3H_8.—We have seen that ethane, C_2H_6, may be regarded as methane, CH_4, to which CH_2 has been added. Similarly, propane, C_3H_8, may be regarded as ethane, C_2H_6, to which CH_2 has been added; or as C_2H_6 in which one of the hydrogens has been replaced by a CH_3 group. Its structure becomes evident by examining its synthetic method of preparation. Ethyl iodide and methyl iodide react in the presence of sodium to form propane. The principle was made use of in the synthesis of ethane, and may be made use of in the synthesis of other hydrocarbons.

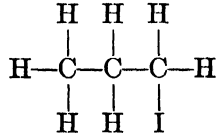


In this reaction ethane and butane, C_4H_{10}, are also produced. (Why?)

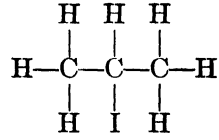
(Why may propane be called ethylmethane, or dimethylmethane, or methylethane, or methyl ethyl?)

(If C_3H_8 is propane, what would its radical, C_3H_7, be called?)

We pointed out that in ethane we have but one mono-substitution product and two di-substitution products, and we saw how the graphic formulas helped to explain these facts. When we come to propane, we find that two mono-substitution products are possible, one differing from the other in physical and chemical properties. Here again the graphic formulas are helpful in explaining experimental facts:



(1)



(2)

for it will be seen that in (1) the iodine atom is attached to a carbon atom, which in turn is attached to two hydrogen and one carbon atoms, whereas in (2) the iodine atom is attached to a carbon atom which in turn is attached to two carbon and one hydrogen atoms.

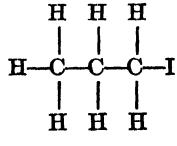
Butanes, C_4H_{10}.—Two butanes with this formula are known.

In the preceding paragraph we pointed out that there are two isomeric propyl iodides which, for convenience, we shall now write according to the "structural" or "constitutional" formulas.

$$\underset{(1)}{CH_3 \cdot CH_2 \cdot CH_2I} \quad \text{and} \quad \underset{(2)}{CH_3 \cdot CHI \cdot CH_3}\ ^1$$

Now, it may be asked, what will happen if first (1) and then (2) are treated with methyl iodide in the presence of sodium? Are

[1] Periods are often used in place of bonds when writing structural or constitutional formulas, so that $CH_3 \cdot CH_2 \cdot CH_2I$ really means $CH_3—CH_2—CH_2I$, which in turn indicates



As the student proceeds with his studies in organic chemistry, he will find it unnecessary to indicate either dots or dashes for at least some of the simpler types of compounds.

we going to get two identical compounds? This is hardly likely, since (1) and (2) are different. In reality, the two compounds obtained are different,—different in properties, but alike in having the same molecular formula, C_4H_{10}.

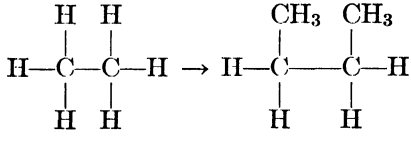
$$CH_3 \cdot CH_2 \cdot CH_2 \boxed{I + 2Na + I} CH_3 \rightarrow CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_3 + 2NaI$$
(3)

$$CH_3 \cdot CH \begin{matrix} \boxed{I} \\ + \boxed{2Na} \\ + \boxed{I} \end{matrix} \cdot CH_3 \rightarrow CH_3 \cdot \underset{\displaystyle CH_3}{CH} \cdot CH_3 + 2NaI$$
(4)

(3) and (4) are isomeric, (3) being known as normal (" straight-chain ") or *n*- butane, and (4) as *iso*- (" branched-chain ") butane.

(Why may normal butane be given any one of the following names: methylpropane, ethylethane, diethyl, propylmethane and symmetrical dimethylethane? Why may isobutane also be called trimethylmethane and unsymmetrical dimethylethane?)

(If two of the hydrogens in ethane which are attached to two different carbon atoms are replaced by methyl groups, we get butane or symmetrical dimethylethane:



If, however, the two hydrogen atoms replaced by two methyl groups are on the same carbon atom, then we get isobutane, or unsymmetrical dimethylethane.)

Propane and the butanes are used for refrigerating purposes.

Pentanes, C_5H_{12}.—Three pentanes are known:

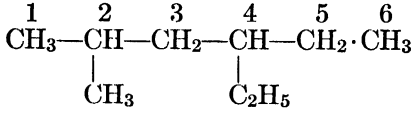
$CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_3$ *n*-pentane

$CH_3—\underset{\displaystyle CH_3}{CH}—CH_2 \cdot CH_3$ isopentane

$H_3C—\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{C}}—CH_3$ tetramethylmethane or neopentane

(Give as many names to these compounds as you can.)

Nomenclature of Saturated Hydrocarbons.—Select the longest chain of carbon atoms in the molecule and number the carbon atoms. Consider the side chains as substituents. For example,



2-methyl-4-ethyl hexane.

The table on page 26 includes a few normal hydrocarbons and the corresponding monovalent radicals.

From the table we conclude the following:

1. Every hydrocarbon in this series is saturated (single bonds).
2. The name of each hydrocarbon ends in *ane*.
3. The hydrocarbons from CH_4 to C_4H_{10} are gases, from C_5 to C_{16}, liquids at ordinary temperatures, and from C_{17}, solids.
4. The melting- and boiling-points increase with the increase in molecular weight.
5. The difference between any two consecutive members in this series is CH_2.

(Whenever we have a series of compounds where the difference between any two consecutive members is CH_2, we get what is known as a **homologous** series. The word "homologue" signifies "a member of the series." Homologous series are frequently met with in organic chemistry, and we shall refer to them repeatedly. The great value in the study of these homologous series lies in the fact that members of such a series are really members of the same family, and, therefore, show strong family resemblances; or, to speak in terms of chemistry, strong chemical resemblances. This does not mean that the members of an homologous series are exactly alike chemically; but it does mean that they have certain common characteristics which distinguish them from other classes of compounds.)

6. Their type formula may be represented algebraically by C_nH_{2n+2}.
7. The names of the radicals end in "yl," the suffix "ane" of the hydrocarbon being changed to "yl" (meth*ane* → meth*yl*).
8. The type formula for radicals is C_nH_{2n+1} (monovalent.)
9. The paraffins are known as "alkanes"; hence the group is

PARAFFIN SERIES *

Formula	Name	Boiling-Point	Melting-Point	Name of Monovalent Radical	Formula of Radical
CH_4	Methane	−164	−184	Methyl	CH_3
C_2H_6	Ethane	− 89 3	−172	Ethyl	C_2H_5
C_3H_8	Propane	− 44.1	....	Propyl	C_3H_7
C_4H_{10}	Butane	− 0.1	−135	Butyl	C_4H_9
C_5H_{12}	Pentane	+ 36.3	−130	Amyl or Pentyl	C_5H_{11}
C_6H_{14}	Hexane	+ 68.9	− 94	Hexyl	C_6H_{13}
C_7H_{16}	Heptane	+ 98.2	− 97	Heptyl	C_7H_{15}
C_8H_{18}	Octane	+125 8	− 56	Octyl	C_8H_{17}
C_9H_{20}	Nonane	+149.5	− 51	Nonyl	C_9H_{19}
$C_{10}H_{22}$	Decane	+173	− 32	Decyl	$C_{10}H_{21}$
$C_{11}H_{24}$	Undecane	+194.5	− 26.5	Undecyl	$C_{11}H_{23}$
$C_{12}H_{26}$	Dodecane	+214.5	− 12	Dodecyl	$C_{12}H_{25}$
$C_{13}H_{28}$	Tridecane	+234	− 6.2	Tridecyl	$C_{13}H_{27}$
$C_{14}H_{30}$	Tetradecane	+252.5	+ 5.5	Tetradecyl	$C_{14}H_{29}$
$C_{15}H_{32}$	Pentadecane	+270 5	+ 10	Pentadecyl	$C_{15}H_{31}$
$C_{16}H_{34}$	Hexadecane	+287.5	+ 19	Hexadecyl	$C_{16}H_{33}$
$C_{17}H_{36}$	Heptadecane	+303	+ 22.5	Heptadecyl	$C_{17}H_{35}$
.	.	.	.	.	.
.	.	.	.	.	.
.	.	.	.	.	.
.	.	.	.	.	.
$C_{60}H_{122}$	Hexacontane	....	+101	Hexacontyl	$C_{60}H_{121}$
.	.	.	.	.	.
.	.	.	.	.	.
.	.	.	.	.	.
.	.	.	.	.	.
C_nH_{2n+2}	Alkane	....	....	Alkyl	C_nH_{2n+1}

* A fairly complete table is given at this point to illustrate to what extent a series has been investigated. In the other portions of the book where tables will be given, only the first few members of a series will be included.

spoken of as an "alkyl group." The alkyl group is represented by the letter "R."

Lower members have anesthetic properties while the higher ones beginning with $C_{12}H_{26}$ have no physiological effects.

General Methods of Preparation.

1. $R\boxed{COONa + NaO}H \rightarrow RH + Na_2CO_3$

   $CH_3COONa + NaOH \rightarrow CH_4 + Na_2CO_3$

2. $R\boxed{X + 2Na + X}R \rightarrow R-R + 2NaX$ (Wurtz synthesis)

   $C_2H_5I + 2Na + IC_2H_5 \rightarrow C_4H_{10} + 2NaI$

3. $R\boxed{X + H}H \rightarrow RH + HX$

   $C_2H_5Br + H_2 \rightarrow C_2H_6 + HBr$

(X refers to halogens.)

General Properties.—The paraffins are insoluble in, and lighter than water, and soluble in alcohol, ether, chloroform, benzene, etc. As a rule, their odor is rather pleasant. They are flammable.

General Chemical Properties.—All the paraffins are very stable and inactive. At ordinary temperature they are not acted upon by nitric, sulfuric, hydrochloric or chromic acids, or sodium hydroxide. Chlorine reacts in sunlight to form substitution products. Bromine reacts less readily. Iodine does not react at all. (The student will be puzzled at this point to explain how the various iodide compounds used in the *Wurtz* synthesis for paraffins are prepared. We must refer him to the chapters on unsaturated hydrocarbons—p. 34—and alcohols—p. 57—for an answer.)

Petroleum or Crude Oil.—The history of the development of the petroleum industry in the United States is instructive. The Indians in Western Pennsylvania first discovered oil floating on surface waters. By them it was used as a remedy for all physical ills. In the middle of the last century, it occurred to a Colonel Drake that, since oil came to the surface of springs, it was probably present in much larger quantities beneath the earth's surface. He thereupon proceeded to drill a well near Oil Creek, Pa. and, before he had dug 100 feet, oil came to the surface in such quantities that all of it could not be collected.

The industrial importance of petroleum is recognized the world over. Coal alone takes precedence over it as a fuel. It is largely, though not entirely, made up of hydrocarbons, but not all the hydrocarbons belong to the paraffin series—the series we have studied in the present chapter. Some of them belong to a type of hydrocarbons with which we shall become acquainted in the next chapter.

Petroleum is found in many parts of the world, but more particularly in the United States (Pennsylvania, California and Texas), Mexico, Russia (the Baku region), Roumania and Persia. The natural product is usually dark in color, with a characteristic odor, and with a specific gravity that is usually, but not always, less than water. It may be regarded as a mixture of substances, mostly hydrocarbons.

The various products derived from petroleum are obtained by means of fractional distillation, the first fraction consisting of products which pass into the distillate below 200°, the second, those that pass over between 200°–275°, and the third, those which pass over above 275°. Each fraction is again redistilled and divided into more fractions, ultimately yielding substances of commercial value. In many refineries the division into fractions is based on specific gravity.

The light oils (up to 200°) include petroleum ether, benzine, gasoline and ligroin; the illuminating oils (from 200°–275°) include kerosene; and the lubricating oils (275° and up) include spindle, machine and cylinder oils, etc. In addition, many products of commercial value are obtained, such as vaseline, paraffin, etc.; and the tar residue in the still is used in road-making, artificial asphalt, roofing, etc. If the temperature is high enough, petroleum coke in the place of tar is formed. Due to its high purity, this coke finds extensive use in the manufacture of electrodes.

Commercially, the most important product obtained from petroleum is gasoline, a mixture of hydrocarbons of relatively low molecular weight, such as pentane, hexane, heptane, etc. The process of purification consists of treating the gasoline with sulfuric acid—incidentally one of the most important uses for this acid—whereby many objectionable impurities are removed; the sulfuric acid in turn being removed by washing with water and subsequently with sodium hydroxide solution.

By a careful study of the physico-chemical reactions involved (such as temperature and pressure), American chemists have developed methods of increasing the yield of gasoline. The "cracking" process, used so extensively to-day, consists in breaking up the more complex into the simpler hydrocarbons; for example,

$$C_{18}H_{38} \rightarrow \underset{\text{kerosene}}{C_{10}H_{22}} + \underset{\text{gasoline}}{C_7H_{16}} + \underset{\text{carbon}}{C}$$

In this way fuel oil (b.p. 275°–350°) is converted into the simpler hydrocarbons. At the present time approximately one-third of the gasoline being produced is derived from cracking heavy oils.

Albolene, nujol and petrolatum are petroleum products used extensively in medicine as intestinal lubricants, and, in pharmacy, as bases for ointments, salves, etc.

Recently, Bergius has perfected a process for the "liquefaction of coal" so that from 50–60 per cent of the latter can be transformed into oil by hydrogenation under high pressure; and Fischer has synthesized hydrocarbons from carbon monoxide and hydrogen at atmospheric pressure and at relatively low temperature.

(Times have changed, indeed. Less than thirty years ago, kerosene cost more than gasoline; the latter, in fact, was regarded little more than a nuisance. To-day it would be hard to conceive of many substances more valuable in commerce than gasoline. Wherever minute quantities of the fuel can be found, it is carefully extracted. Even the small amount found in natural gas is extracted and recovered. Gasoline recovered from the gas that comes from a producing oil well is known as "casinghead" gasoline.)

The chart facing p. 29 outlines the salient features of petroleum refining at a typical plant and names the important commercial products obtained.

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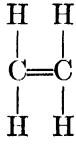
An eight-reel motion picture "The Story of Petroleum" can be secured, free of charge, from the Bureau of Mines, Pittsburgh, Pa.

CHAPTER III

UNSATURATED HYDROCARBONS OR OLEFINS AND ACETYLENES

So far we have been dealing with hydrocarbons that are saturated. When bromine comes in contact with a hydrocarbon of the methane series, C_nH_{2n+2}, it can enter the compound by substitution only, not by addition; that is, by eliminating one or more hydrogen atoms from the molecule and substituting other atoms, but not by adding an outside atom without any elimination. In this chapter we take up two series of unsaturated compounds, where, as we shall see, atoms can enter the molecule without others leaving it. One series is known as the **olefins**, C_nH_{2n}, characterized by



and the other, the **acetylenes**, C_nH_{2n-2}, characterized by

(The student must not draw the conclusion that because there is more than one bond between two atoms, the union between such atoms is correspondingly stronger. On the contrary, since bonds represent strains, the greater the number of bonds between any two carbon atoms, the greater the strain, and hence the greater the chemical reactivity of the compound; so that ethylene is more reactive than ethane and acetylene more than ethylene.) [1]

[1] The instructor may illustrate these "strains" by the use of *Kekulé* models.

Olefin Series, C_nH_{2n}—Alkenes

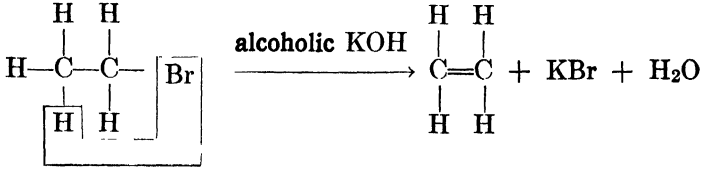
CH_2	(hypothetical)	Methylene
C_2H_4		Ethylene or ethene
C_3H_6		Propylene or propene
C_4H_8		Butylene or butene
C_5H_{10}		Amylene
etc.	(Compare with the paraffins, p. 26.)	

These compounds constitute an homologous series, just as the paraffins, for there is the same difference between any two consecutive members—CH_2; but it will be noticed that the corresponding olefins have two hydrogen atoms less than the paraffins. The simplest known member of the olefin series, ethylene, combines with chlorine to form an oil ($C_2H_4Cl_2$); hence the name **olefin** (" oil-forming ").

In naming these compounds, we change the ending *ane* of the paraffin containing the same number of carbon atoms into *ylene* or *ene*; *e.g.*, C_2H_6 (eth*ane*)—C_2H_4 (eth*ylene* or eth*ene*).

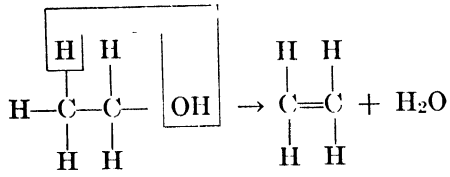
We shall describe one member of this series, ethylene, in some detail, and the general characteristics of the other members can be gleaned from a study of this one.

Preparation of Ethylene, C_2H_4.—One method is by the action of an alcoholic solution of sodium or potassium hydroxide on ethyl bromide, a method of preparation that gives us an insight into the structure of the compound:



If, instead of using an alcoholic solution of sodium or potassium hydroxide, we use an aqueous solution, ethyl alcohol, C_2H_5OH, is produced (p. 54).

Another is to treat ethyl alcohol with a strong dehydrating agent, such as P_2O_5 or H_2SO_4.

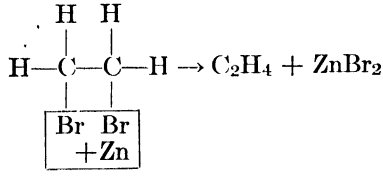


(An alcohol contains an OH group; see p. 49.)

Ethylene is now obtained commercially from ethane, which in turn is derived from natural gas (see chart facing p. 142):

$$C_2H_6 \xrightarrow[(\text{"cracking"})]{\text{heat to } 850^\circ} C_2H_4 + H_2, \text{ etc.}$$

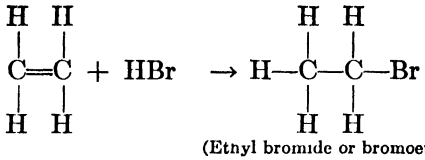
Also, by the action of sodium or zinc on ethylene bromide (dibromoethane):



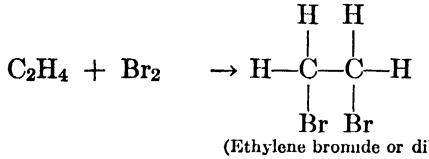
($C_2H_4Br_2$ may be regarded as ethylene, C_2H_4, to which two bromine atoms have been added; or ethane, in which two of the hydrogens attached to different carbon atoms are replaced by bromine.)

Properties.—Ethylene is a colorless gas with a sweetish odor. It burns with a smoky, luminous flame, and forms explosive mixtures with air. It is present in coal gas to the extent of 4–6 per cent, and is partially responsible for its luminosity. It is produced, therefore, in the destructive distillation of coal. Recently, Dr. Luckhardt, of the University of Chicago, has shown that ethylene is a powerful anesthetic and has even some advantages over nitrous oxide. Recently, ethylene has also been introduced in California for coloring mature citrus fruits (oranges, lemons, etc.). For industrial developments of ethylene chemistry see chart facing p. 142.

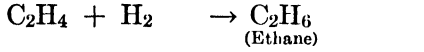
The characteristic properties of ethylene are dependent upon the presence of a double bond, and therefore upon its unsaturated character. It combines with halogen acids, with halogens, with hydrogen, with sulfuric acid, with hypochlorous acid, with ozone, etc., and is used as the starting material for the preparation of many organic compounds.



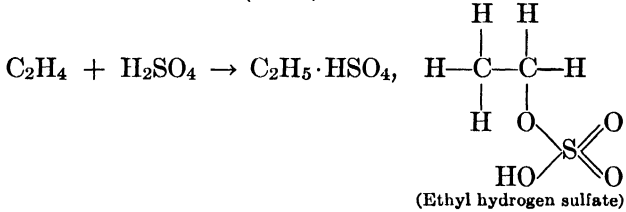
(Ethyl bromide or bromoethane)



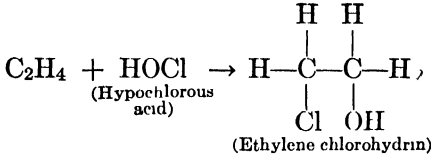
(Ethylene bromide or dibromoethane)



(Ethane)

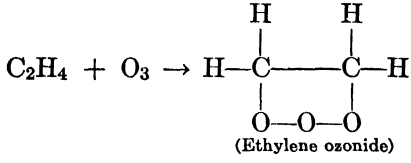


(Ethyl hydrogen sulfate)



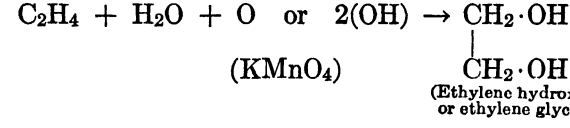
(Ethylene chlorohydrin)

(Whenever a compound has a halogen atom attached to a carbon atom, and an OH group to another carbon atom, we speak of it as a " halohydrin "; hence chlorohydrin, as in the above.)



(Ethylene ozonide)

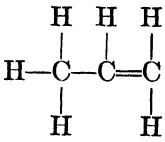
A test sometimes used for the detection of the double bond is based on the action of very dilute potassium permanganate; the violet color of the permanganate disappears, due to its decomposition. The reaction may be represented thus:



(Ethylene hydroxide or ethylene glycol)

(The student must clearly understand that C_2H_4 alone represents the gas ethylene, but C_2H_4 may be present as a divalent group in a compound; for example, ethylene bromide, $C_2H_4Br_2$.)

Higher homologues. C_3H_6,



(Propylene or propene)

C_4H_8=(*a*) $CH_3 \cdot CH_2 \cdot CH=CH_2$ (1-Butene or ethyl ethylene)

(*b*) $CH_3 \cdot CH=CH \cdot CH_3$ (2-Butene or sym-dimethyl ethylene)

(*c*) $CH_3-C(CH_3)=CH_2$ (2-Methyl-1-propene or unsym-dimethyl ethylene)

(In naming an olefin, a number is employed to indicate the position of the double bond; this number denotes the unsaturated carbon atom which lies nearest to the end of the chain.)

Sometimes the Greek letter Δ is used to denote the double bond, so that (*a*), (*b*) and (*c*) may also be written Δ^1-Butene; Δ^2-Butene; 2-Methyl-Δ^1-propene. (The methods of preparation and properties are analogous to those given for ethylene.)

Acetylene Series—C_nH_{2n-2}—Alkines

C_2H_2 Acetylene or ethine
C_3H_4 Propine or methyl acetylene
C_4H_6 Butine or dimethyl acetylene or ethyl acetylene
etc.

These also constitute a homologous series. The members contain two hydrogen atoms less than the corresponding members of the olefins, or four hydrogen atoms less than the corresponding paraffins. They are named by changing the *ane* ending of the paraffins into *ine*, so that eth*ane*, C_2H_6, for example, becomes

eth*ine*, C_2H_2. This series is known as the **acetylene** series, for acetylene is the most important member.

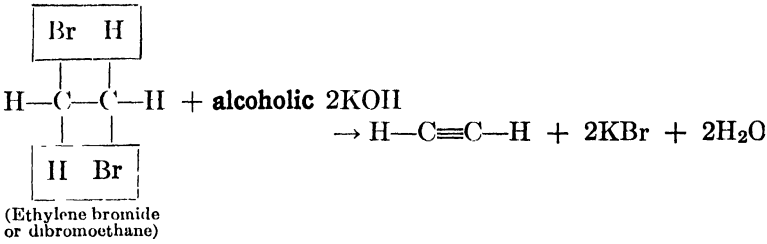
As before, we shall discuss a typical member in some detail.

Acetylene, C_2H_2, has the formula H—C≡C—H, which shows it to have a triple bond and therefore indicates that it is even more unsaturated than ethylene,[1] a view which is confirmed by a study of its reactions. Acetylene is an extremely reactive compound. Its formula may also be written as $=C=CH_2$ (p. 40).

Preparation.—One method is probably already familiar to the student. It is the action of water on calcium carbide:

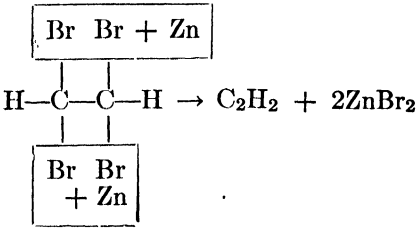
$$CaC_2 + 2H_2O \rightarrow C_2H_2 + Ca(OH)_2$$

Another is similar to a method used under the olefins:



(Ethylene bromide or dibromoethane)

So is the following:

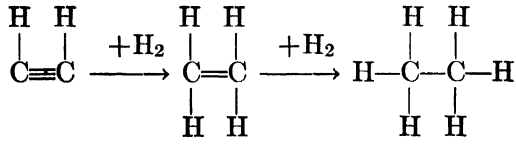


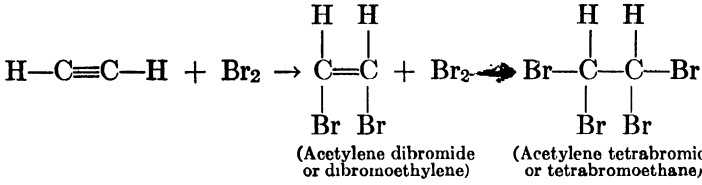
(Acetylene tetrabromide or tetrabromoethane)

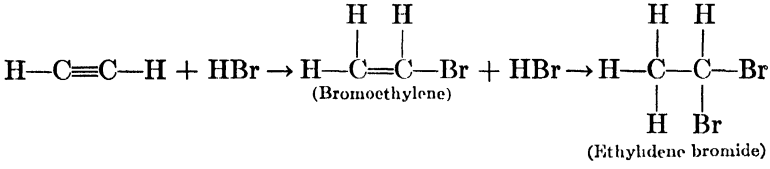
Acetylene is a colorless gas. When mixed with air in a special type of burner, it burns with a very brilliant white light and is used for illuminating purposes. When burned it gives out a large amount of heat. This is made use of in the oxy-acetylene torch (for cutting steel, etc.) wherein acetylene, supplied under pressure, is burned in the presence of oxygen. The gas is apt to explode if stored under pressure, but can be safely handled if it is first dissolved in acetone (as in " prestolite " tanks). Liquid acetylene is highly unstable and highly explosive.

[1] The instructor may illustrate this by the use of the *Kekulé* models.

Properties.—Since acetylene is an unsaturated compound, it will form addition products (like ethylene), but since it is more unsaturated than ethylene, it can add to itself more atoms than C_2H_4.







($CH_2Br \cdot CH_2Br$, ethylene bromide, or symmetrical dibromoethane, is isomeric with $CH_3 \cdot CHBr_2$, ethylidene bromide, or unsymmetrical dibromoethane.)

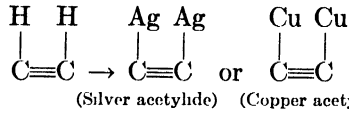
(The student must clearly understand that C_2H_2 alone represents the gas acetylene, but C_2H_2 may be present as a divalent group in a compound; for example, acetylene dibromide, $C_2H_2Br_2$. It may also be present as a tetravalent group; for example, acetylene tetrabromide, $C_2H_2Br_4$.)

When acetylene is passed over finely divided nickel, three molecules of it polymerize to form benzene:

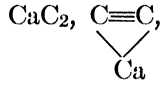
$$3C_2H_2 \rightarrow C_6H_6$$

(**Polymers** are substances having the same percentage composition, but different molecular weights. C_2H_2 and C_6H_6 have the same percentage of carbon and of hydrogen, but the molecular weight of acetylene is 26 and that of benzene is 78.)

Acetylene combines with ammoniacal silver chloride or copper chloride solution to form metallic derivatives (acetylides):



Many of them are highly unstable and explosive, particularly in the dry state. In fact, many of the explosions involving acetylene are due to the formation of these acetylides.



Higher homologues.

C_3H_4, $CH_3 \cdot C{\equiv}CH$ (Propine or methyl acetylene)

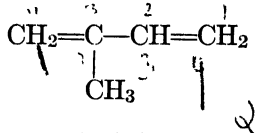
C_4H_6, (*a*) $CH_3 \cdot C{\equiv}C \cdot CH_3$ (2-Butine or dimethyl acetylene)

(*b*) $C_2H_5C{\equiv}CH$ (1-Butine or ethyl acetylene)

(The general properties correspond to those of acetylene, except that only the compounds with the structure —C≡C—H can form acetylides.)

(At this point review the nomenclature of hydrocarbons on the "Organic Type Formula" chart, p. 16.)

Compounds containing two double bonds are isomeric with those containing one triple bond; for example, $CH_3—C{\equiv}CH$ is isomeric with $CH_2{=}C{=}CH_2$. The name of a compound having one double bond ends in *ene*; a compound having two double bonds has the ending *diene*, e.g., $CH_2{=}C{=}CH_2$ is propadiene. The most important among the compounds containing two double bonds is **isoprene**

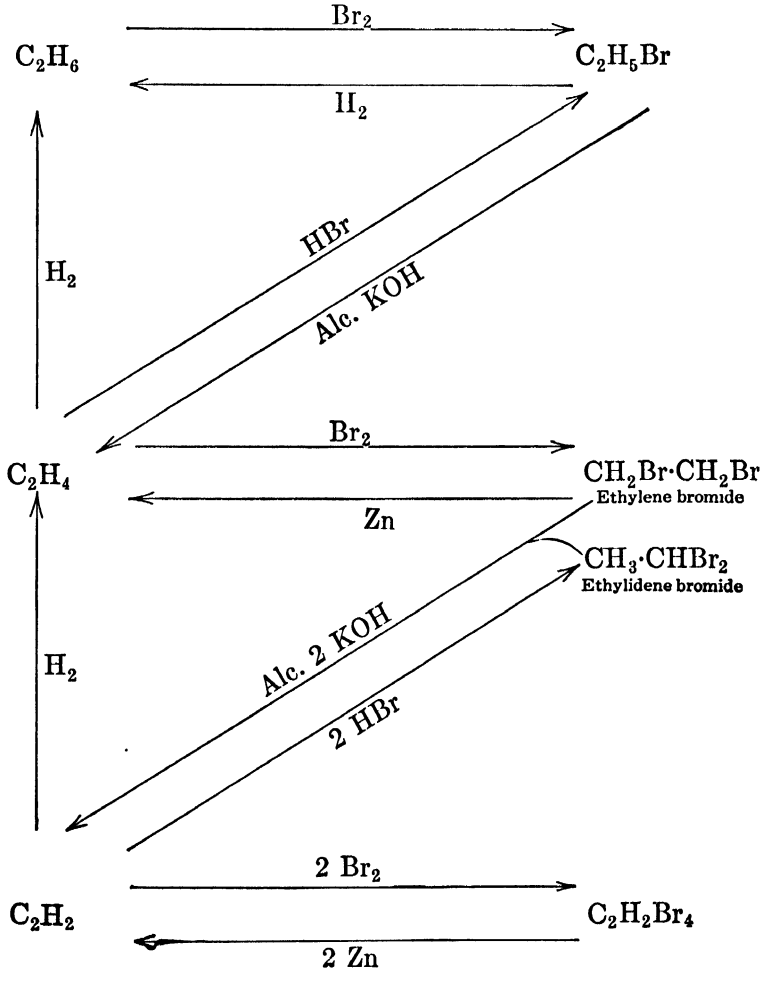


or 2-methyl-1,3-butadiene, which has been shown to be one of the decomposition products of caoutchouc (natural rubber), and which is obtained by the distillation of the latter. Isoprene itself (in presence of catalysts, as HCl, Na, etc.) has been polymerized back into a substance resembling caoutchouc, the resulting product showing some striking resemblances to natural rubber. The synthesis of rubber on an industrial scale, however, is a problem that still awaits solution. There seems to be little doubt in the minds of chemists that isoprene, or some substance closely analo-

gous to it in structure, will prove to be the starting-point of such a synthesis.

It has recently been shown that rubber when stretched shows an X-ray spectrogram similar to those of ordinary well-defined crystals. All X-ray interferences agree to a rectangular-rhombic crystal with a basic cell of $(C_5H_8)_8$. The number of combined molecules needed to produce the interferences are about 2000.

Very recently a very promising method of synthesizing rubber-like substances in the laboratory has been announced. In the



presence of complex cuprous salts, acetylene may be polymerized to vinylacetylene:

$$CH{\equiv}CH + {=}C{=}CH_2 \rightarrow CH{\equiv}C{-}CH{=}CH_2$$

(The $CH_2{=}CH$ monovalent group is known as the vinyl group.)

When vinylacetylene is treated with hydrogen chloride, **chloroprene** is obtained:

$$CH{\equiv}C{-}CH{=}CH_2 + HCl \rightarrow CH_2{=}\underset{\displaystyle Cl}{\overset{\displaystyle |}{C}}{-}CH{=}CH_2$$

2-Chloro-1,3-butadiene

By allowing the chloroprene to stand at room temperature and in the absence of direct light, it gradually polymerizes to a stiff, pale yellow, elastic mass, and resembles a " completely vulcanized soft rubber."

The diagram on page 39 makes clear some of the interconnections of compounds already discussed.

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CHAPTER IV

HALOGEN DERIVATIVES OF HYDROCARBONS

We have already observed that the action of chlorine on methane gives us the following substitution products: CH_3Cl, CH_2Cl_2, $CHCl_3$, CCl_4 (p. 19). It ought to be possible to prepare any one of these substances by employing the proper amount of chlorine. (Bromine is less reactive than chlorine. It produces analogous substitution products. Iodine does not react with methane.) It is found in practice, however, that a series of simultaneous reactions occur, yielding a mixture of chlorides. (Mention may be made at this point of the many attempts to produce chloroform, $CHCl_3$, on a commercial scale by the action of chlorine on methane; and also of methyl chloride, CH_3Cl, by a similar reaction. Methyl chloride can be easily hydrolyzed to methanol or wood alcohol, CH_3OH, and thus the synthetic methanol could then be prepared starting from natural gas, which contains methane. Research is being carried on at the present time along these lines.)

Monohalogen Derivatives of the Paraffins.—An alkyl halide (or monohalogen derivative of a hydrocarbon, p. 43), may be regarded as a saturated hydrocarbon in which one of the hydrogens is replaced by a halogen (F, Cl, Br, I). The following will make this clear:

C_nH_{2n+2}	C_nH_{2n+1} Group	$C_nH_{2n+1}X$ (alkyl halide)
Methane, CH_3H	Methyl Group, CH_3	Methyl chloride, CH_3Cl
Ethane, C_2H_5H	Ethyl Group, C_2H_5	Ethyl bromide, C_2H_5Br
etc.	etc.	etc.
Alkane, RH	**Alkyl Group, R**	**Alkyl halide, RX**

(RX is the type formula for an alkyl halide.)

ALKYL HALIDES

Chloride	Formula	B. P. ° C.	Bromide	Formula	B. P. ° C.	Iodide	Formula	B.P. ° C.
Methyl	CH_3Cl	−24	Methyl	CH_3Br	4.5	Methyl	CH_3I	43
Ethyl	C_2H_5Cl	12 5	Ethyl	C_2H_5Br	38 4	Ethyl	C_2H_5I	72
Propyl	C_3H_7Cl	46 5	Propyl	C_3H_7Br	71	Propyl	C_3H_7I	102
Isopropyl	C_3H_7Cl	36.5	Isopropyl	C_3H_7Br	59	Isopropyl	C_3H_7I	89
n-Butyl * etc.	C_4H_9Cl	77.5	n-Butyl etc.	C_4H_9Br	101	n-Butyl etc.	C_4H_9I	129

* n- is the abbreviation for " normal "

In each group the specific gravities decrease as the molecular weights increase. The specific gravity increases as we pass from a certain alkyl chloride to the bromide and in turn to the iodide having the same alkyl group.

These halides are insoluble in water but soluble in ether, benzene and alcohol. The halides are generally colorless liquids with a pleasant odor. On standing, they develop color (this is especially true of the iodides), due to decomposition, and are generally kept in amber-colored bottles.

General Methods of Preparation.—By the action of a halogen acid on an alcohol in presence of a dehydrating agent. (An alcohol contains the —OH group. Examples of alcohols are C_2H_5OH, ethyl alcohol, C_3H_7OH, propyl alcohol, and in general ROH.)

$$\underset{\text{Ethyl alcohol}}{C_2H_5\boxed{OH + H}}Br \rightarrow C_2H_5Br + H_2O$$

Or, more generally,

$$R\boxed{OH + H}X \rightleftarrows RX + H_2O$$

(Whenever throughout the text " R " is used in an equation, it implies that the reaction is a general one; or, in other words, is a " type " reaction. This does not necessarily imply that where specific examples are given, they cannot illustrate general type reactions. As a matter of fact, in most cases the specific examples do illustrate type reactions.)

This reaction is analogous to the "neutralization" reaction in inorganic chemistry, such as Na $\boxed{OH + H}$ $Cl \rightarrow NaCl + H_2O$. However, the production of NaCl is an instantaneous reaction, whereas the formation of RX is a comparatively slow process; and in the production of RX we must have a dehydrating agent present to remove the water as fast as it is formed, otherwise the reaction is reversible.

Another method is the action of a phosphorus halogen compound on an alcohol; e.g.,

$$\underset{\text{Propyl alcohol}}{C_3H_7OH} + PCl_5 \rightarrow \underset{\text{Propyl chloride}}{C_3H_7Cl} + POCl_3 + HCl$$

$$3C_3H_7OH + PBr_3 \rightarrow 3C_3H_7Br + \underset{\text{Phosphorous acid}}{H_3PO_3}$$

or

$$ROH + PCl_5 \rightarrow RCl + POCl_3 + HCl$$

$$3ROH + PX_3 \rightarrow 3RX + P(OH)_3$$

A third method consists in the addition of halogen acids to unsaturated compounds; e.g.,

$$\begin{array}{l} H\ H \\ |\ \ | \\ C{=}C \\ |\ \ | \\ H\ H \end{array} + HBr \rightarrow \begin{array}{l} H\ \ H \\ |\ \ \ | \\ H{-}C{-}C{-}Br \\ |\ \ \ | \\ H\ \ H \end{array}$$

or

$$C_nH_{2n} + HX \rightarrow C_nH_{2n+1}X \quad \text{or} \quad RX$$

Properties.—The halogen compounds react with many reagents to form diverse products. The following are examples of a number of type reactions:

$$2C_2H_5I + 2Na \rightarrow \underset{\text{Butane}}{C_2H_5{-}C_2H_5} + 2NaI$$

(The *Wurtz* Synthesis.)

$$C_2H_5I + Mg \rightarrow Mg\begin{array}{l}\diagup C_2H_5 \\ \diagdown I\end{array}$$

Magnesium ethyl iodide (I)

Compounds of type (I) are known as *Grignard's* reagent, the general type formula being R·Mg·X.

$$C_2H_5I + KCN \longrightarrow \underset{\text{Ethyl cyanide}}{C_2H_5CN} + KI$$

$$C_2H_5I + KOH\ (\text{aqueous}) \longrightarrow \underset{\text{Ethyl alcohol}}{C_2H_5OH} + KI$$

$$C_2H_5I + AgNO_2 \longrightarrow \underset{\text{Nitroethane}}{C_2H_5NO_2} + AgI$$

$$\underset{\text{Sodium ethylate}}{C_2H_5I + NaOC_2H_5} \longrightarrow \underset{\text{Ethyl ether}}{C_2H_5OC_2H_5} + NaI$$

$$C_2H_5I + NH_3 \longrightarrow \underset{\text{Ethyl ammonium iodide}}{C_2H_5N\begin{matrix}H\\H\\H\end{matrix}\,I}$$

$$C_2H_5I + HOH \longrightarrow C_2H_5OH + HI$$

$$C_2H_5I + \text{alc. } KOH \longrightarrow C_2H_4 + KI + H_2O$$

(At this stage the student is not expected to memorize these equations, but rather, by examining them, to understand why the halides find such extensive applications.)

(Many of the reactions illustrated are of the " double decomposition " type.)

Methyl chloride, CH_3Cl, and **Ethyl chloride,** C_2H_5Cl, are used as local anesthetics, for when sprayed upon the skin the liquids evaporate rapidly, thereby cooling the tissue. To some extent they are used for refrigerating purposes. Ethyl chloride is used in the preparation of lead tetraethyl (p. 199). **Ethyl bromide,** C_2H_5Br, has also been used as an anesthetic.

$\underset{\text{n-Propyl iodide}}{CH_3\cdot CH_2\cdot CH_2I}$ $\qquad$ $\underset{\text{Isopropyl iodide}}{CH_3\cdot CHI\cdot CH_3}$

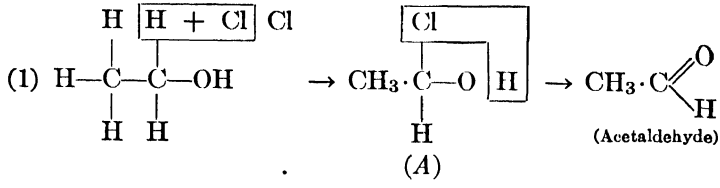
Dihalogen Derivatives of the Paraffins.—These have the general formula $C_nH_{2n}X_2$ ($C_2H_4Br_2$, dibromoethane, and $C_3H_6Cl_2$, dichloropropane, are examples). They are usually prepared by the addition of a halogen to an unsaturated hydrocarbon:

$$C_2H_4 + Br_2 \rightarrow \underset{\text{Ethylene bromide}}{C_2H_4Br_2}$$

(CH_2I_2 is of interest since it is the heaviest organic liquid, its specific gravity being 3.292 at 18°, ethylene dichloride, $CH_2Cl—CH_2Cl$, is used as a fumigant and also as a solvent for oils, fats, etc., and for the preparation of ethylene glycol (p. 63).

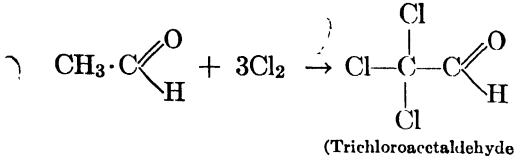
Trihalogen Derivatives of the Paraffins.—The important compounds of this type are chloroform, $CHCl_3$, bromoform, $CHBr_3$, and iodoform, CHI_3.

Chloroform, $CHCl_3$, is prepared by the action of chlorine (in the form of bleaching powder) on (1) ethyl alcohol or (2) acetone.

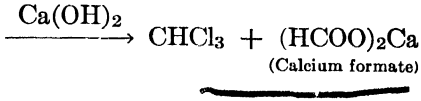


(Acetaldehyde)

(*A*)

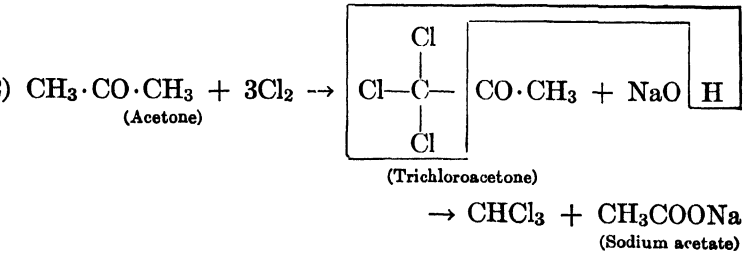


(Trichloroacetaldehyde or "chloral")



(Calcium formate)

(*A*) represents a hypothetical compound, or at least one which has not so far been isolated. Its instability, it would seem, is due to the Cl and OH groups being attached to the same carbon atom. The type formula for an aldehyde is $R—C\langle^{O}_{H}$. We shall discuss these aldehydes later, p. 73.



(Trichloroacetone)

(Sodium acetate)

Acetone is the simplest of the group of compounds known as "ketones." Their type formula is R·CO·R (p. 73).

In practice the necessary chlorine is obtained by the use of bleaching powder.

Chloroform is now made on a large scale by the reduction of CCl_4:

$$CCl_4 + H_2 \rightarrow CHCl_3 + HCl$$

Chloroform (trichloromethane) is a colorless liquid with a sweet taste and suffocating odor. Its b.p. is 61°. It is slightly soluble in water. It is non-flammable. Its anesthetic properties were discovered by Dr. Simpson of Edinburgh, in 1848.

Chloroform has a tendency to decompose when exposed to air and light:

$$CHCl_3 + O \rightarrow \underset{\text{(Phosgene)}}{COCl_2} + HCl$$

$$2CHCl_3 + 3O \rightarrow 2COCl_2 + Cl_2 + H_2O$$

To prevent this, ethyl alcohol (to the extent of about 1 per cent) is added to it. It is usually kept in dark (amber) colored bottles.

Pure $CHCl_3$ does not react with silver nitrate, but, if any decomposition has occurred, a precipitate of AgCl forms.

($CHCl_3$ alone is now rarely used as an anesthetic, for ether and ethylene have largely taken its place. Sometimes a mixture of ether and chloroform is used. The advantage of ether over chloroform is that it is less dangerous and the after-effects are not so pronounced.)

Acetone and chloroform combine to form **chloretone,** $(CH_3)_2 \cdot C(OH) \cdot CCl_3$, used extensively as a hypnotic, anodyne and preservative. Chloroform reacts with concentrated nitric acid to form **chloropicrin,** or nitrochloroform, a substance that was used in the late war as a lachrymator ("tear gas"):

$$CHCl_3 + HNO_3 \rightarrow CCl_3NO_2 + H_2O$$

When prepared on a large scale, the chloropicrin is made by the action of bleaching powder on picric acid (p. 279).

Chloroform is sometimes used as a "preservative" for the prevention of bacterial growth, though for most purposes toluene has largely taken its place. Chloroform is an excellent solvent for many organic compounds. It dissolves fats, rubber, etc.

Bromoform, $CHBr_3$, is prepared in a manner quite analogous to chloroform. Its anesthetic properties are less marked.

Iodoform (triiodomethane), CHI_3, is prepared by adding iodine to a warm solution of sodium carbonate containing alcohol or acetone—in principle analogous to the preparation of chloroform. The odor of iodoform is not only characteristic, but powerful, hence the reaction is used as a test for either alcohol or acetone. Iodoform is a powerful antiseptic and disinfectant. (The antiseptic properties are due to its gradual decomposition with the liberation of iodine.)

Tetrahalogen Derivatives of the Paraffins, CF_4, CCl_4, CBr_4 and CI_4. Of these, only the second, **carbon tetrachloride,** is important. It is made commercially by passing chlorine into carbon disulfide, using iron, iodine or antimony pentasulfide as a catalyst:

$$CS_2 + 3Cl_2 \rightarrow CCl_4 + S_2Cl_2$$

(We have already mentioned the production of CCl_4 from methane by the action of chlorine:

$$CH_4 + 4Cl_2 \rightarrow CCl_4 + 4HCl.)$$

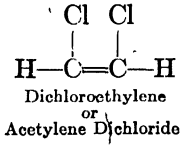
Carbon tetrachloride is a colorless liquid with an ethereal odor. It is a good solvent for gums and resins and is also a constituent of many cleaning solutions. It is an anesthetic, but is not used because of its bad effect on the heart. It is used in fire extinguishers ("Pyrene"). Its vapor produces severe headaches.

Dichlorodifluoromethane, CCl_2F_2, is now used as a refrigerant.

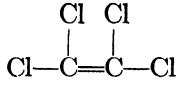
(During the past few years a number of chlorinated paraffins, used as solvents, have been prepared on a commercial scale. One such is tetrachloroethane, made by the action of chlorine on acetylene:

$$C_2H_2 + 2Cl_2 \rightarrow C_2H_2Cl_4.)$$

Halogen Derivatives of Unsaturated Hydrocarbons.—The names and structures of a few of these will be given:



Dichloroethylene
or
Acetylene Dichloride



Tetrachloroethylene

(These are used as solvents.)

$CH_2{=}CHBr$
Monobromoethylene

$CH_2{=}CHCl$
Monochloroethylene
(Vinyl chloride)

$\overset{1}{C}H\overset{2}{B}r{=}\overset{3}{C}HCH_3$
1-Bromopropylene

$CH_2{=}CBrCH_3$
2-Bromopropylene

$CH_2{=}CH\cdot CH_2Br$
3-Bromopropylene (allyl bromide)

($CH_2{=}CH\cdot CH_2$ is known as the allyl group.)

Bromoacetylene

Diiodoacetylene

READING REFERENCES

CLARK—Applied Pharmacology. (1923), chap. 9 (Anesthetics).

KILLEFFER—Cheap Ethylene Dichloride. *Industrial and Engineering Chemistry*, **19**, 636 (1927).

MIDGLEY AND HENNE—Organic Fluorides as Refrigerants. *Industrial and Engineering Chemistry*, **22**, 542 (1930).

EGLOFF, etc.—Halogenation of the Paraffin Hydrocarbons. *Chemical Reviews*, **8**, 1 (1931).

CHAI

ALCO

METHANOL, which is methyl (c
grain) alcohol, are the two most in
to this group.

The alcohols may be considered a
or more of the hydrogens are replaced b
also be regarded as derived from water i
gens is replaced by R; H—OH → R—O

The relationship of the hydrocarbons t
here:

CH_3H (methane) ——— CH_3OH (methanol o

C_2H_5H (ethane) ——— C_2H_5OH (ethyl alcohol)

C_3H_7H (propane) ——— C_3H_7OH (propyl alcohol)

etc. etc. etc.

RH (alkane) ——— ROH (alkyl alcohol)

Nomenclature of Alcohols.—There are a number of system
employed. (1) The ending *e* of the hydrocarbon containing the
same number of carbon atoms is changed to the ending *ol*:

C_2H_6, ethane ——— C_2H_5OH, ethan*ol*

C_3H_8, propene ——— C_3H_7OH, propenol

(2) The alcohol is named according to the alkyl group it contains: C_2H_5H, ethane ——— C_2H_5, ethyl group ——— C_2H_5OH, ethyl alcohol, or ethyl hydroxide.

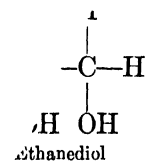
as " carbinol" derivatives:

ol "

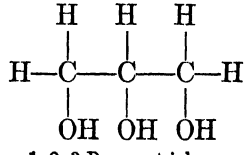
ethyl carbinol

, ethyl methyl carbinol

ol in which one of the hydrogen atoms
ethyl methyl carbinol is carbinol in which
placed by C_2H_5 and another by CH_3.)
in more than one OH group provided they
nt carbon atoms; *e.g.*



Ethanediol
or
2-dihydroxyethane
or
glycol

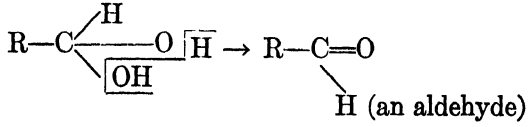


1, 2, 3-Propanetriol
or
1, 2, 3-trihydroxypropane
or
glycerol

etc.

We shall see in a later chapter that the sugars contain several OH groups.

(Two or more OH groups attached to the same carbon atom give rise, as a rule, to unstable compounds:



the unstable dihydroxy compound being converted into an aldehyde. We shall explain the oxidation of an alcohol to an aldehyde in this manner.)

An alcohol with one OH group is monatomic, with two OH groups, diatomic, with three, triatomic, etc.

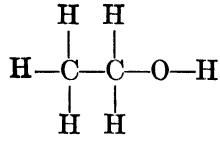
If we take an alcohol, such as ethyl alcohol, C_2H_6O, and treat it with sodium, only one atom of hydrogen (out of the six present) is liberated:

$$C_2H_6O + Na \rightarrow C_2H_5ONa + H$$

This particular atom of hydrogen obviously differs in some way from the other five atoms. The possibility that this difference is due to a difference in position within the molecule is borne out by the fact that when we treat the alcohol with, say, hydrogen iodide, one atom of iodine replaces one atom of hydrogen and one atom of oxygen,—one iodine, in other words, replaces one hydroxyl group:

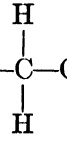
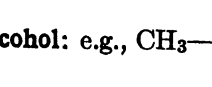
$$C_2H_5OH + HI \rightarrow C_2H_5I + HOH$$

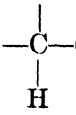
It would seem, therefore, as if one hydrogen in ethyl alcohol is attached, not to the carbon atoms (like the other five hydrogen atoms), but to the oxygen atom:

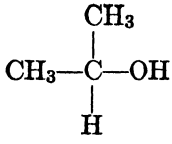


and all the reactions of the many alcohols known (some of which will be discussed presently) strengthen this view.

Types of Alcohols.

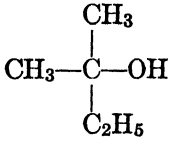
1. The presence of the group  indicates a **primary alcohol**: e.g.,  .

2. The group  indicates a **secondary alcohol**: e.g.,



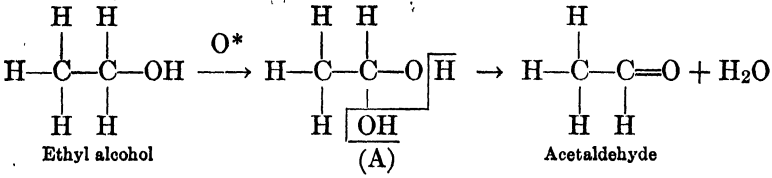
Isopropyl alcohol
or
dimethyl carbinol

3. The group indicates a **tertiary alcohol**: e.g.,



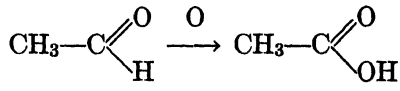
Dimethyl ethyl carbinol

These three types of alcohols yield various oxidation products. When a primary alcohol is oxidized, we first get an aldehyde; e.g.,



(It is believed that (A) is an intermediate compound, though it has not, as yet, been isolated. It has already been pointed out that a compound containing two OH groups attached to the same carbon atom is usually unstable, water splitting off in the manner shown.)

The aldehyde on further oxidation yields the corresponding acid:

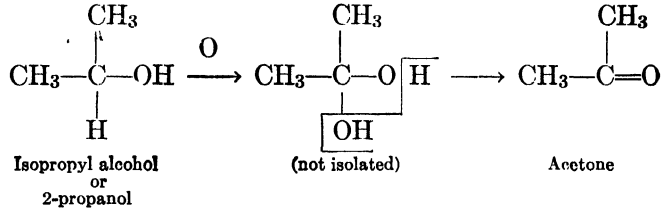


* O refers to oxidation

(Let us inform the student at this point that the group $-C\overset{O}{\diagdown\!\!\diagup}H$ is characteristic of aldehydes, and the group $-C\overset{O}{\diagdown\!\!\diagup}OH$ is commonly characteristic of organic acids.)

We see then that the oxidation of a primary alcohol yields first an aldehyde and then an acid containing the same number of carbon atoms as the original alcohol.

When a secondary alcohol is oxidized we get a ketone; e.g.,

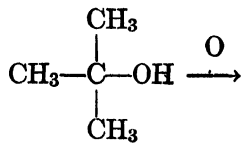


Isopropyl alcohol or 2-propanol — (not isolated) — Acetone

$\begin{matrix}R\\R\end{matrix}\!\!>\!C{=}O$ represents ketones, and acetone is the simplest member of the series. On further oxidation we get acids containing less carbon atoms than the original ketone or alcohol.

(There are two isomeric propyl alcohols, the normal, $CH_3 \cdot CH_2 \cdot CH_2OH$, and the iso, $CH_3—\underset{CH_3}{\overset{H}{C}}—OH$. The latter, being a secondary alcohol, yields a ketone—acetone—on oxidation; the normal, being a primary alcohol, yields first an aldehyde—propionaldehyde—and then an acid—propionic acid.)

When a tertiary alcohol is oxidized, a mixture of acids and ketones are obtained, each substance formed having less carbon atoms in its molecule than the original tertiary compound: e.g.,



Trimethyl carbinol or Tertiary butyl alcohol

$H \cdot COOH$ (Formic acid)
$CH_3 \cdot COOH$ (Acetic acid)
$CH_3 \cdot CO \cdot CH_3$ (Acetone)
$CO_2 + H_2O$

We therefore see that on oxidation

primary alcohol → aldehyde → acid
secondary alcohol → ketone → decomposition products
tertiary alcohol → decomposition products

Methods of Preparation.—Alcohols are produced in the course of destructive distillation (p. 58) and fermentation (p. 59). Other methods are the following:

The action of moist silver oxide or aqueous NaOH or KOH solution on an alkyl halogen compound, as

$$C_2H_5\boxed{I + Ag}OH \rightarrow C_2H_5OH + AgI$$

or

$$CH_3\boxed{Br + K}OH \rightarrow CH_3OH + KBr$$

The reduction of aldehydes (yielding primary alcohols); as

$$CH_3\cdot C\begin{matrix}=O\\ -H\end{matrix} + H_2 \rightarrow CH_3\cdot CH_2OH$$

Acetaldehyde

(The student will recall that the oxidation of a primary alcohol yields an aldehyde; we may therefore expect that the reduction of the aldehyde will yield the alcohol. The reducing agent may be sodium amalgam and water, or hydrogen in the presence of nickel, etc.)

The reduction of ketones (yielding secondary alcohols); as

$$\begin{matrix}CH_3\\ CH_3\end{matrix}\!\!>\!C=O \xrightarrow{+\,H_2} \begin{matrix}CH_3\\ CH_3\end{matrix}\!\!>\!CHOH$$

Acetone — Isopropyl alcohol

The action of nitrous acid on a primary amine (that is, a substance formed when one of the hydrogens in NH_3 is replaced by R, giving $R\cdot NH_2$; (see p. 138); as

$$C_2H_5NH_2 + HONO \rightarrow C_2H_5OH + N_2 + H_2O$$

Ethyl amine — Nitrous acid

The hydrolysis of esters; as

$$\underset{\text{Ethyl acetate}}{CH_3\cdot COOC_2H_5} + HOH \xrightarrow[\text{or bases}]{\text{In presence of acids}} \underset{\text{Acetic acid}}{CH_3COOH} + C_2H_5OH$$

(An ester is an acid in which the ionizable hydrogen is replaced by an alkyl group: $\underset{\text{(Acid)}}{R\cdot COOH} \rightarrow \underset{\text{(Ester)}}{R\cdot COOR}$.)

Various secondary and tertiary alcohols can be prepared by means of the *Grignard* reaction; e.g.,

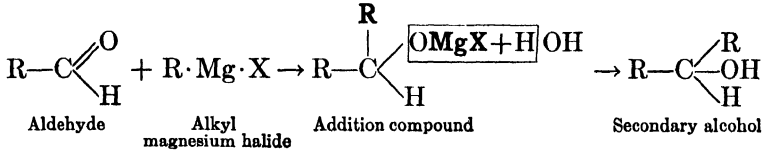
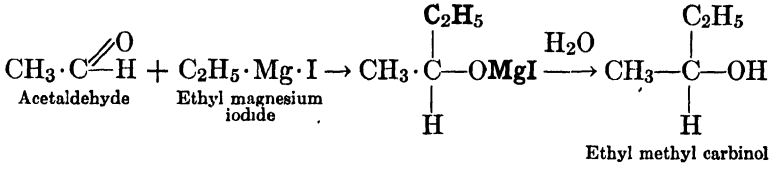


Illustration:



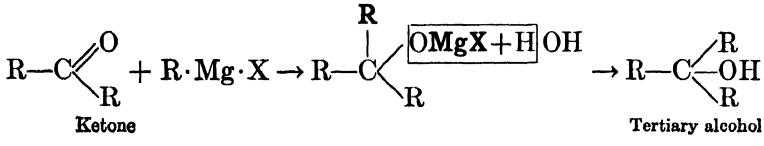
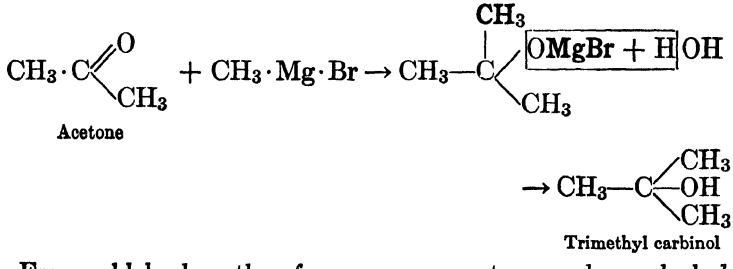
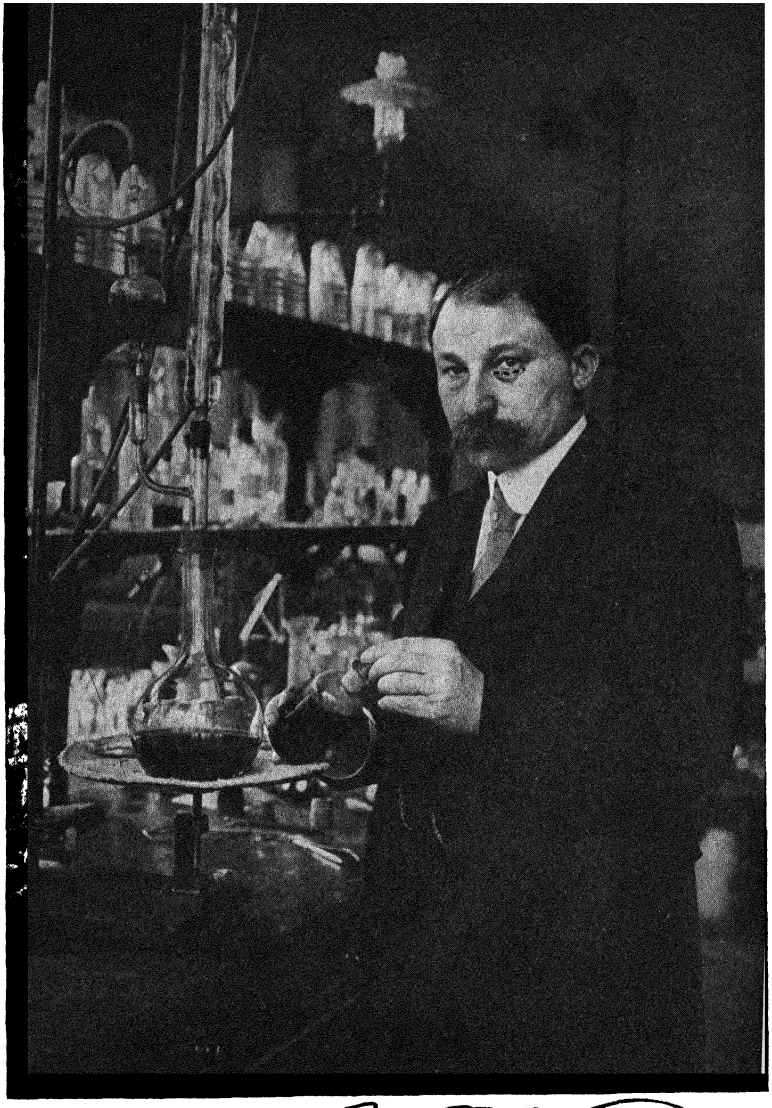
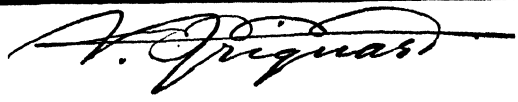


Illustration:



From aldehydes, therefore, we can get secondary alcohols, and from ketones, tertiary alcohols.





VICTOR GRIGNARD (1871–

PROFESSOR OF CHEMISTRY AT THE UNIVERSITY OF LYON (FRANCE). HIS DISCOVERY OF THE ORGANO-MAGNESIUM COMPOUNDS AND THEIR REACTIONS, FOR WHICH HE RECEIVED THE NOBEL PRIZE, HAS BEEN OF INESTIMABLE VALUE IN THE SYNTHESIS OF MANY ORGANIC COMPOUNDS.

Physical Properties.—The monatomic alcohols are colorless substances. The compounds from CH_3OH to C_4H_9OH are limpid liquids, those from C_5 to C_{11} are of oily consistency, and from C_{12} up are solids. The solubility in water decreases with increase in molecular weight. An increase in the number of OH groups in a compound tends to increase the sweetness; e.g., methanol CH_3OH, is not sweet; glycol, $C_2H_4(OH)_2$ is somewhat sweet; glycerol, $C_3H_5(OH)_3$, is sweet; and mannitol, $C_6H_8(OH)_6$, is still sweeter. The lower alcohols have characteristic odors; the C_8-C_{12} have rose- or lily-like odors and are used in perfumery, while the higher ones are practically odorless.

Chemical Properties.—The alcohols, like water (which they resemble in many ways), are neither acid nor alkaline in reaction. Like water again, the alcohols combine with compounds to form crystalline products; for example,

$$CaCl_2 \cdot 4CH_3OH, \quad PtCl_4 \cdot 2C_2H_5OH, \quad \text{and} \quad MgCl_2 \cdot 6CH_3OH$$

These compounds are said to contain "alcohol of crystallization." Sodium reacts with alcohol as it does with water, only less violently; e.g.,

$$2C_2H_5OH + 2Na \rightarrow \underset{\substack{\text{Sodium ethylate}\\ \text{or}\\ \text{sodium alcoholate}}}{2C_2H_5ONa} + H_2$$

As we have seen, the primary alcohols, on oxidation, yield aldehydes and acids; the secondary alcohols, ketones; and the tertiary alcohols, various decomposition products.

The OH group in the alcohol can be replaced by a halogen in a number of ways:

$$ROH + HX \rightarrow RX + H_2O \quad \text{(in presence of dehydrating agents)}$$

$$ROH + PCl_5 \rightarrow RCl + POCl_3 + HCl$$

$$3ROH + PCl_3 \rightarrow 3RCl + P(OH)_3$$

Alcohols combine with acids to form esters: e.g.,

MONATOMIC ALCOHOLS

Alcohol	Formula
Methyl	CH_3OH
Ethyl	$CH_3 \cdot CH_2OH$
n-Propyl	$CH_3 \cdot CH_2 \cdot CH_2OH$
Isopropyl	$CH_3 \cdot CH(OH) \cdot CH_3$
n-Primary butyl	$CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2OH$
n-Secondary butyl	$CH_3 \cdot CH_2 \cdot CH(OH) \cdot CH_3$
Primary isobutyl	$(CH_3)_2CH \cdot CH_2OH$
Trimethyl carbinol (tertiary butyl)	$(CH_3)_3C(OH)$
⋮	⋮
Cetyl	$C_{16}H_{33}OH$
Myricyl	$C_{30}H_{61}OH$

Methanol,[1] CH_3OH (also called methyl alcohol, wood alcohol, methyl hydroxide, carbinol, Columbian spirit and wood spirit). This alcohol does not occur free in nature. On a commercial scale it is obtained by the destructive distillation of hard wood (maple, beech, birch, oak, etc.). When wood is heated in retorts to about 400°, we obtain gases (used as fuel under the retorts), an aqueous distillate (known as "pyroligneous acid"), wood tar and charcoal (which remains in the retorts). The wood tar is a source for antiseptics (wood creosote), disinfectants, fuel, road-making, etc. The pyroligneous acid contains the acetic acid, as well as the methanol and acetone. The acetone of commerce is not obtained from this source (see p. 76).

Using a catalytic process, synthetic methanol is now manufactured from carbon monoxide and hydrogen,

$$CO + 2H_2 \rightarrow CH_3OH$$

The catalyst is zinc oxide; the temperature is about 400° and the pressure about 150 atmospheres.

A very recent process is from the by-products of the ethyl alcohol, butanol, acetone fermentation process (pp. 63, 84). In this fermentation pure hydrogen and carbon dioxide gases are

[1] The name "methanol" has now been officially adopted, largely with a view to preventing its use in the place of grain alcohol.

generated and the synthetic methanol process employed involves two steps. An adjustment is made in the relation of hydrogen to carbon dioxide by a simple scrubbing process under pressure, after which the mixture is further compressed and passed over the methanol catalyst at elevated temperature.

Properties and Uses.—Methanol is a colorless liquid with a somewhat disagreeable odor. b.p. 64.7°. It is a poison and gives rise to blindness when taken internally or applied externally. It burns with a blue flame, quite devoid of soot, to CO_2 and H_2O. On oxidation it first forms the corresponding aldehyde, formaldehyde ($H \cdot CHO$), and then formic acid ($H \cdot COOH$). The alcohol is used very largely as a solvent in the manufacture of varnishes and lacquers, especially those containing shellac; as a solvent for moving-picture films; in the preparation of denatured alcohol; in the manufacture of formaldehyde; and in the preparation of various dye intermediates.[1] Additional uses are given in the chart facing p. 58.

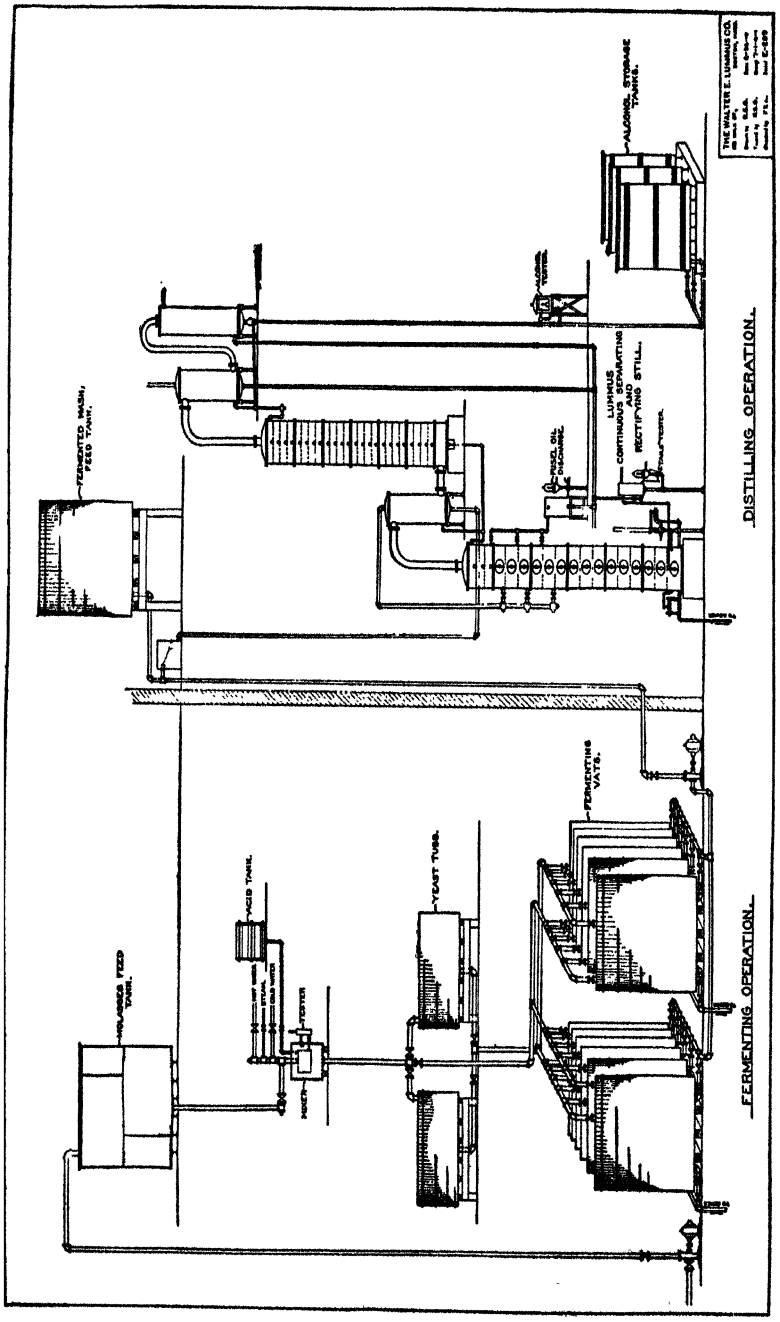
Ethyl Alcohol, C_2H_5OH (also called alcohol, ethanol, grain alcohol, ethyl hydroxide, Cologne spirit and wine spirit). The commercial method of making it is by a process called **fermentation** (fermentation is a process of decomposition brought about by substances secreted by various forms of vegetable and animal life), and in principle differs little from the methods that have been in use for centuries. Some starch-containing substance, such as a cereal (corn, rye, barley, etc.), or potatoes, is allowed to sprout. (The particular raw material used varies in different countries. Sugar and cane molasses from sugar mills are used in the United States; potatoes in Germany; and beet sugar in France.) This develops within the cell a substance known as diastase, a typical catalyst, and called an enzyme because it is produced as a result of cellular activity. The diastase converts the starch to maltose:

$$(C_6H_{10}O_5)_x + xH_2O \rightarrow xC_{12}H_{22}O_{11}$$

Another enzyme, maltase, which is also present, converts the maltose into glucose:

$$\underset{\text{Maltose}}{C_{12}H_{22}O_{11}} + H_2O \rightarrow 2\underset{\text{Glucose}}{C_6H_{12}O_6}$$

[1] A dye intermediate is an organic compound used in the manufacture of dyestuffs.


MOLASSES FEED TANK.
ACID TANK.
HEATER.
YEAST TUBS.
FERMENTING VATS.
FERMENTED WASH FEED TANK.
FUSEL OIL SEPARATOR.
LUNDIE CONTINUOUS SEPARATING AND RECTIFYING STILL.
ALCOHOL TESTER.
ALCOHOL STORAGE TANKS.
THE WALTER E. LUNDIE CO.
DISTILLING OPERATION.
FERMENTING OPERATION.

Yeast is now added, and the enzyme zymase, present in the yeast, converts the glucose into alcohol and carbon dioxide:

$$C_6H_{12}O_6 \rightarrow 2C_2H_5OH + 2CO_2$$

The best temperature for this fermentation ranges from 25–30°.

(Small quantities of impurities, such as glycerol, aldehydes, esters, succinic acid, butyl alcohol, isoamyl alcohol, etc., are also found.) The alcohol in the " wort " (which is the name given to the liquor formed in the course of the fermentation process and which contains from 6–10 per cent of alcohol), is purified by fractional distillation. Commercial ethyl alcohol contains about 95 per cent of alcohol. A still higher percentage of alcohol (" absolute," or nearly 100 per cent alcohol) may be obtained by the addition of calcium oxide (quicklime) or anhydrous copper sulfate (which are dehydrating agents) to the liquid and allowing it to stand a day or two; it is then distilled.

(Such substances as grape juice, corn syrup and molasses are already rich in glucose. Here the preliminary diastase treatment, consisting in the conversion of starch into glucose, is unnecessary.)

A recent process for the preparation of *synthetic ethyl alcohol* involves the following reactions:

$$C_2H_4 + H_2SO_4 \rightarrow C_2H_5 \cdot HSO_4$$

$$C_2H_5 \cdot HSO_4 \xrightarrow{H_2O} C_2H_5OH + H_2SO_4$$

Properties and Uses.—Ethyl alcohol is a colorless liquid, has a characteristic odor and a sharp burning taste (b.p. 78.4°). In the form of tinctures (alcoholic solutions or extracts of medicinal substances) it is extensively used in medicine. In certain diseases, such as pneumonia, it has proved a valuable therapeutic agent.

The use of alcohol in the industries is very extensive. As a preservative, as an antiseptic, in the preparation of denatured

alcohol and various drugs and medicinals, as a solvent in perfumery, " anti-freeze ", as an essential constituent necessary for the manufacture of iodoform, chloroform, vinegar and ether, alcohol is in constant demand. (Additional uses will be found in the chart facing p. 60.)

Denatured Alcohol.—This is alcohol which has been made unfit for drinking purposes and external applications, but which can still be used in the industries. Some of the substances used in " denaturing " are methanol, benzine, " aldehol," ether, acetone—substances with disagreeable odors and flavors, and possessing poisonous properties. No less than seventy different formulas have been granted in the United States for the preparation of denatured alcohol for various industrial uses. Denatured alcohol is tax-free.

Medicated Alcohol is alcohol unfit for drinking purposes, but suitable for external applications. Some of the substances used in the preparation of medicated alcohol are tartar emetic, formaldehyde, phenol, diethyl phthalate, benzene, acetone, zinc phenolsulfonate, etc.

Percentages of Alcohol in Beverages.—Beer = 2–5 per cent; wine = 7–11 per cent; fortified wine = 17–20 per cent; whiskey, brandy, gin, rum, etc. = 40–75 per cent.

The percentage of alcohol in a number of pharmaceutical preparations is relatively high. Aromatic spirits of ammonia = 68 per cent; spirits of camphor = 90 per cent; tincture of iodine = 83 per cent, etc. For further details consult U. S. Pharmacopeia X.

(Whenever fermented liquors are distilled, not only do we get ethyl alcohol, but also small quantities of esters and a number of the higher alcohols, the mixture of these higher alcohols being substances known as **fusel oil.** Some claim that the presence of fusel oil in liquors is far more harmful than the ethyl alcohol itself. In this connection the following information may be of interest. We know that the principal constituent of fusel oil is **isoamyl alcohol,** $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!CH\cdot CH_2\cdot CH_2OH$, and we know that the source of this is isoleucine, an amino acid obtained from the protein present in cereal or potato (see the chapter on proteins, p. 143. The bacteria present convert the isoleucine into isoamyl

alcohol. It has, however, been shown that this conversion—and hence the production of isoamyl alcohol—may be prevented by the addition of ammonium salts, which the bacteria prefer.) Amyl alcohol is at present manufactured on a commercial scale from the pentane fraction of natural gas by the following series of reactions.

$$C_5H_{12} \xrightarrow{\text{Chlorination}} C_5H_{11}Cl \xrightarrow{\text{Alkaline hydrolysis}} C_5H_{11}OH$$

Isopropyl alcohol, $\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!C\!<\!\begin{matrix} H \\ OH \end{matrix}$, is made by the reduction of acetone. It is now made by passing propylene gas into sulfuric acid and subsequent hydrolysis:

$$CH_3 \cdot CH{=}CH_2 + H_2SO_4 \longrightarrow CH_3 \cdot \underset{\displaystyle SO_4H}{\underset{|}{CH}} \cdot CH_2H$$

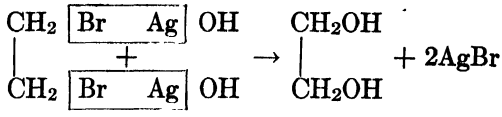
Isopropyl acid sulfate

$$\xrightarrow{HOH} CH_3 \cdot CHOH \cdot CH_3 + H_2SO_4$$

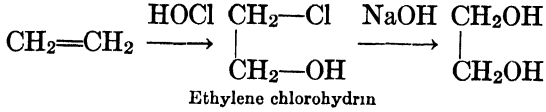
***n*-Butyl alcohol,** *n*-butanol, $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot OH$, is produced by the action of bacilli on materials containing starches and carbohydrates (corn) and is used on a large scale as a solvent in the nitrocellulose lacquer industry and for the preparation of esters. **Isoamyl alcohol,** $C_5H_{11}OH$, is converted to isoamyl acetate and thus used in the manufacture of varnishes and fruit essences. **Cetyl alcohol,** $C_{16}H_{33}OH$, forms (as palmitic ester) the chief constituent of spermaceti (a wax-like substance found in the head of the sperm whale), while **myricyl alcohol,** $C_{30}H_{61}OH$, is present as palmitic ester in beeswax and in Carnauba wax. The alcohols are prepared from all these esters by hydrolysis with boiling alcoholic KOH solution.

Diatomic Alcohols.—The simplest of these is dihydroxyethane, known as **ethylene glycol,** $\underset{\displaystyle CH_2OH}{\underset{|}{CH_2OH}}$. It is a compound intermediate in composition between ethyl alcohol and glycerol. Its properties are intermediate between these two compounds.

It may be prepared by the action of silver hydroxide on the corresponding dibromo-compound:

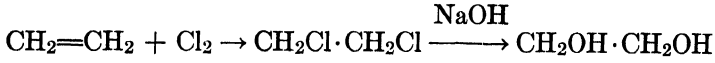


but commercially it is made from ethylene:



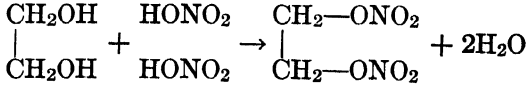
Ethylene chlorohydrin

or

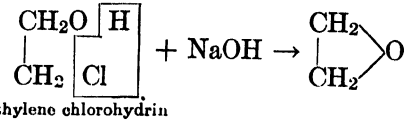


Ethylene glycol is used as a solvent, " anti-freeze " and preservative. The general chemical properties resemble the alcohols, except that we here deal with two OH groups instead of one OH group.

Ethylene glycol combines with HNO_3 (in the presence of H_2SO_4) to produce ethylene dinitrate (glycol dinitrate)

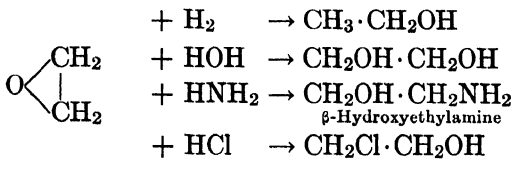


Ethylene oxide, , may be looked upon as an anhydride of glycol. It is produced by the following reaction.



Ethylene chlorohydrin

It is a very reactive compound and is used in synthetic organic chemistry.



Ethylene oxide is also used in fumigation and as an insecticide.

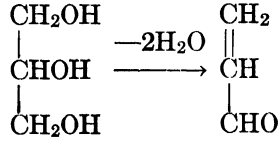
Triatomic Alcohols.—The best known of this group is **glycerol** (also called glycerine), $CH_2OH \cdot CHOH \cdot CH_2OH$ (or 1, 2, 3-propanetriol), which is produced as a by-product in the manufacture of soap (p. 99).

$$\underset{\text{(A typical compound in a fat)}}{C_3H_5(OOC \cdot C_{17}H_{35})_3} + 3NaOH \rightarrow \underset{\text{(A typical compound in a soap)}}{3C_{17}H_{35} \cdot COONa} + \underset{\text{(Glycerol)}}{C_3H_5(OH)_3}$$

(Details of this process will be given in the chapter on esters, p. 99.)

Properties and Uses.—Glycerol is a colorless, odorless, syrupy liquid, having a sweetish taste. It is miscible with water and alcohol and is a good solvent and a dehydrating agent. It is used in medicine; as a sweetening agent; as a preservative for tobacco; in perfumery; in cosmetics; in ink for rubber stamps, etc.

When glycerine is heated alone or in the presence of a dehydrating agent such as $KHSO_4$, **acrolein** is produced:



(The odor of burnt fat is due to the production of acrolein.)

As may be seen from its formula, glycerol is both a primary and a secondary alcohol, and may, therefore, be expected to show the properties of both types of alcohols. When oxidized, aldehydes, acids and ketones are formed. Treatment with acids gives esters. One of the compounds obtained when nitric acid and

glycerol react is of importance; and that is the glyceryl trinitrate or, as it is commonly called, **nitroglycerine.**

$$\begin{array}{l} CH_2OH \\ | \\ CHOH \\ | \\ CH_2OH \end{array} \quad \begin{array}{l} HONO_2 \\ + \\ HONO_2 \\ \\ HONO_2 \end{array} \rightarrow \begin{array}{l} CH_2{-}ONO_2 \\ | \\ CH{-}ONO_2 \\ | \\ CH_2{-}ONO_2 \end{array} + 3H_2O$$

(Conc. sulfuric acid is added to remove the water that is formed.) When nitroglycerine explodes the products formed are CO_2, H_2O, N_2 and N_2O.

The nitroglycerine is a dangerous explosive to handle, but when mixed with an inert substance, like infusorial earth, "kieselguhr," thereby becoming **dynamite,** it can be handled with much less risk, though none of its explosive properties are lost. (Starch and sawdust are now used in the place of "kieselguhr," and oxidizing agents such as ammonium or potassium nitrate are added to aid combustion.)

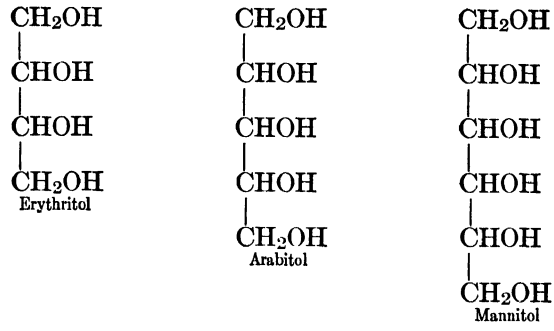
We owe the invention of dynamite to *Alfred Nobel,* a Swedish engineer, who accumulated a fortune as a result of his invention and who bequeathed it to the Swedish Academy for the purpose of founding the *Nobel Prizes.*

(Vapors of nitroglycerine produce severe headache. In medicine, a 1 per cent solution in alcohol is used. It has a powerful action on the arteries and is used as a heart stimulant.)

Since nitroglycerine freezes in winter and must be thawed before use, it is now being mixed with glycol dinitrate (ethylene dinitrate), which freezes at $-22.7°$. Glycol dinitrate is less sensitive to impact than nitroglycerine and is safer to use.

(Glycerol is formed in the digestive tract when the fat in food is hydrolyzed by the enzyme "lipase" of the pancreatic juice. It is also believed that glycerol plays an important part in the oxidation of fats and carbohydrates in the body, for it would seem that one of the intermediate substances formed in such oxidations is glycerol, or a substance very closely allied to it.)

Polyatomic Alcohols.—The careful oxidation of the penta- and particularly the hexa-hydroxy alcohols, leads to the compounds known as sugars; but these we shall discuss later. In the meantime, we shall merely mention the names of a few polyatomic alcohols, and write their formulas:



Erythritol occurs in nature, either in the free or combined state, in algae and certain lichens. A source of arabitol is gum arabic. The source of mannitol is the manna ash tree, which, however, is not believed to be related to the "manna" of the Bible. The hexanitrate of mannitol is a high explosive. Dulcitol and sorbitol are isomers of mannitol.

Unsaturated Alcohols

$CH_2{=}CHOH$, ethenol.

$CH_2{=}CH\cdot CH_2OH$, allyl alcohol, or Δ^2-1-propenol is present in pyroligneous acid.

(Remember that "Δ" indicates a "double bond," and that "Δ^2" indicates double bond in position 2. The ending "ol" in propenol indicates an alcohol, and the "1" before the name means that the OH group is in position 1.)

These compounds possess the general characteristics of alcohols, and being unsaturated compounds, they form additive products with hydrogen, with halogens, with halogen acids, etc.

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CHAPTER VI

ETHERS

ETHERS may be considered as derived from alcohols in which the H of the ROH is replaced by an R group; or they may be looked upon as derived from HOH in which both hydrogens are replaced by R groups. The ethers are really organic oxides. (HOH = H_2O = water = hydrogen oxide; and R—O—R = R_2O. For example, C_2H_5—O—C_2H_5 = $(C_2H_5)_2O$ = ethyl oxide, commonly known as "ether.")

Types of Ethers.—If the two R's represent the same groups, then we get a **simple ether.**

CH_3—O—CH_3, methyl ether
C_2H_5—O—C_2H_5, ethyl ether

If the two R's represent different groups, we get a **mixed ether.**

CH_3—O—C_2H_5, ethyl methyl ether
C_2H_5—O—C_3H_7, ethyl propyl ether

General Methods of Preparation.—The action of an alkyl halide on the sodium alcoholate; e.g.,

$$C_2H_5O\boxed{Na + I}C_3H_7 \rightarrow C_2H_5 \cdot O \cdot C_3H_7 + NaI$$

Sodium ethylate — propyl iodide — Ethyl propyl ether

(This method, the *Williamson's* synthesis, enables one to prepare either a simple or a mixed ether.)

Heating a mixture of silver oxide and alkyl halide; e.g.,

$$2C_2H_5I + Ag_2O \rightarrow (C_2H_5)_2O + 2AgI$$

Ethyl oxide or ethyl ether or **ether**

This reaction proves that ether is an oxide.)

General Properties —The ethers of low molecular weight are colorless, neutral liquids, more volatile than the corresponding alcohols and lighter than water. They are very stable and inactive, and are therefore used as solvents. The ethers, especially the lower members, are highly flammable.

Sodium, ammonia, alkalies and dilute acids have no action on them. Hydriodic acid acts in one of two ways:

$$ROR + HI \rightarrow ROH + RI$$

$$ROR + 2HI \xrightarrow[\text{(When heated)}]{} 2RI + H_2O$$

Phosphorus pentachloride has no action in the cold, but when heated,

$$ROR + PCl_5 \rightarrow 2RCl + POCl_3$$

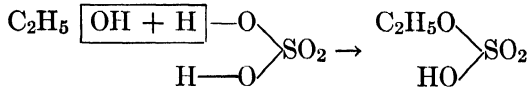
Steam at 150° decomposes them:

$$ROR + H_2O \rightarrow 2ROH$$

Chlorine replaces the hydrogens in the alkyl groups.

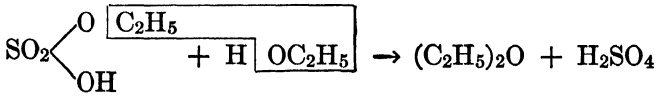
Ether, $C_2H_5—O—C_2H_5$ (also known as ethyl ether, sulfuric ether and ethyl oxide) is the most important substance of this group.

Ether is manufactured by the " continuous etherification process." Equimolecular proportions of alcohol and sulfuric acid are mixed:



Ethyl hydrogen sulfate or ethyl sulfuric acid

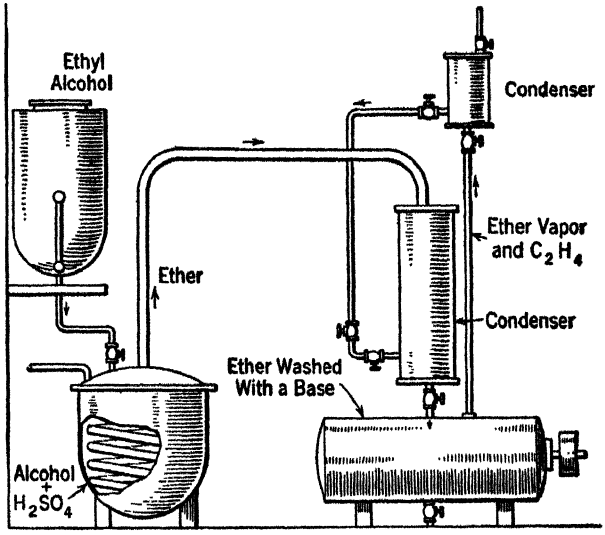
The mixture is now heated to 130–140° and more alcohol added:



(The sulfuric acid is regenerated and used over again until the acid becomes too weak to react with the alcohol.)

The equation may be expressed:

$$C_2H_5\boxed{OH + H}OC_2H_5 \xrightarrow{H_2SO_4} C_2H_5{-}O{-}C_2H_5 + H_2O$$



Manufacture of Ether.

Ether is now also made by the dehydration of two mols. of ethyl alcohol using Al_2O_3 as a catalyst (temperature, 240–260°). Still another method employs the following reactions:

$$2C_2H_4 + H_2SO_4 \longrightarrow (C_2H_5)_2SO_4$$

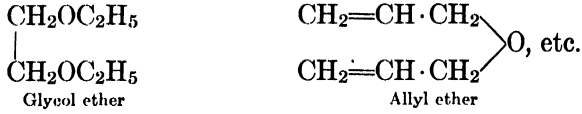
$$(C_2H_5)_2SO_4 \xrightarrow{\text{hydrolysis}} C_2H_5{-}O{-}C_2H_5 + H_2SO_4$$

Properties.—Ether is a colorless, volatile liquid, with a very characteristic odor. b.p. 34.6°. Specific Gravity = .736 at 0°. It is highly flammable, burning with a luminous flame, and is explosive when mixed with air and ignited. It is slightly soluble in water and is used for extracting certain substances from an aqueous solution. As a solvent for fats, oils, resins, alkaloids, etc., ether is unsurpassed. It can be used as a solvent for quite a number of organic substances. It also dissolves iodine, bromine, sulfur, phosphorus, ferric chloride, etc. It is used with alcohol in the manufacture of guncotton. Due to its rapid evaporation, it can be used for refrigerating purposes. As an anesthetic, it was

introduced in surgery by Dr. Morton, a Boston dentist, in 1846. As an anesthetic, ether is preferred to chloroform, for the physiological effects can be better controlled. Ether for this purpose must be highly purified.

(Ether, chloroform and other anesthetics are, chemically, more or less inert substances and are more soluble in lipoids—typical cell constituents—and lipoid solvents than in water.)

Other Ethers.



The mono ethyl ether of glycol, $\begin{matrix} CH_2OC_2H_5 \\ | \\ CH_2OH \end{matrix}$, is an excellent solvent for cellulose nitrate (p. 182).

For other ethers see chart facing p. 142.

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CHAPTER VII

ALDEHYDES AND KETONES

An aldehyde, R·CHO, may be regarded as a hydrocarbon wherein a hydrogen atom has been replaced by the ·CHO group. The type formula for an aldehyde is $R—C\begin{matrix}=O\\ \diagdown H\end{matrix}$, and for a ketone, $\begin{matrix}R\\ R\end{matrix}\!\!\diagup\!\!\diagdown C=O$; so that a ketone may be regarded as an aldehyde in which the H of the CHO group is replaced by R; and, on the other hand, an aldehyde may be regarded as a ketone in which one of the R groups is replaced by H. Both have the $\diagup\!\!\diagdown C=O$ or *carbonyl* grouping, have a number of common properties and they are, therefore, considered in the same chapter. The double bond both in the aldehydes and ketones indicates reactive substances.

(In the chapter on sugars, the student will discover that most of the sugars contain either aldehyde or ketone groupings, and that a number of their properties depend upon these groups; so that much that is gleaned from this chapter can be applied later.)

Nomenclature of Aldehydes.—(1) Change the *e* ending of the hydrocarbon having the same number of carbon atoms (or the *ol* ending of the alcohol) to *al.*

C_2H_6, ethane —— C_2H_5OH, ethanol —— $CH_3 \cdot CHO$, ethanal

(2) The aldehydes may also be named after the corresponding acids [1] formed when the aldehydes are oxidized.

$H \cdot COOH$, formic acid —— $H \cdot CHO$, formic aldehyde or formaldehyde

$CH_3 \cdot COOH$, acetic acid —— $CH_3 \cdot CHO$, acetic aldehyde or acetaldehyde

[1] Refer to p. 85.

$C_2H_5 \cdot COOH$, propionic acid —— $C_2H_5 \cdot CHO$, propionic aldehyde or propionaldehyde

$C_3H_7 \cdot COOH$, butyric acid —— $C_3H_7 \cdot CHO$, butyric aldehyde or butyraldehyde

etc.

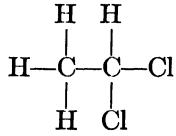
$$R \cdot COOH \text{ —— } R \cdot CHO$$

(Never write the group $\cdot C{-}OH$ to represent the aldehyde grouping, but always $\cdot CHO$. Remember that OH stands for alcohol and in alcohols the linking is R—O—H and in aldehydes, R—C(=O)—H.)

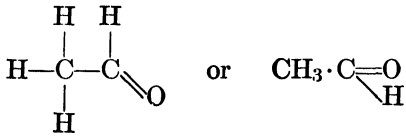
When an aldehyde is treated with phosphorus pentachloride, the reaction is quite different from that obtained when PCl_5 acts on an alcohol. Taking acetaldehyde as an example,

$$C_2H_4O + PCl_5 \rightarrow \underset{\text{Dichloroethane}}{C_2H_4Cl_2} + POCl_3$$

An examination of the dichloroethane reveals that it is the unsymmetrical variety, the two chlorine atoms being attached to the same carbon atom:



which suggests that the oxygen atom in aldehyde occupies a position in the chain corresponding to these two chlorine atoms; that is,



Nomenclature of Ketones, $R \cdot CO \cdot R$.—(1) Change the *e* ending of the hydrocarbon with the same number of carbon atoms to *one*:

C_3H_8, propane —— $CH_3 \cdot CO \cdot CH_3$, propanone

C_4H_{10}, butane —— $CH_3 \cdot CH_2 \cdot CO \cdot CH_3$, butanone

C_5H_{12}, pentane —— $CH_3 \cdot CO \cdot CH_2 \cdot CH_2 \cdot CH_3$, 2-pentanone

$CH_3CH_2COCH_2 \cdot CH_3$, 3-pentanone

etc.

(The type structure for ketone, R·CO·R, indicates that even the simplest ketone must contain at least three carbon atoms.) (2) Name the compound in accordance with the type of group represented by R, remembering that >C=O is the ketonic grouping:

CH_3—CO—CH_3, dimethyl ketone

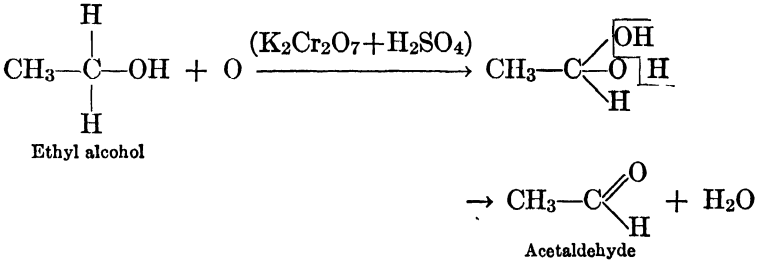
C_2H_5—CO—CH_3, ethyl methyl ketone

C_2H_5—CO—C_9H_{19}, ethyl nonyl ketone

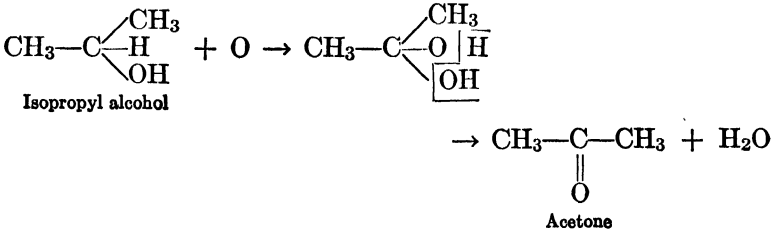
etc.

As with ethers, so with ketones: there are **simple and mixed ketones.** When R=R′ we have a simple ketone; when R is different from R′, we have a mixed ketone; so that $C_2H_5 \cdot CO \cdot C_2H_5$ is a simple ketone, and $C_2H_5 \cdot CO \cdot C_4H_9$ is a mixed ketone.

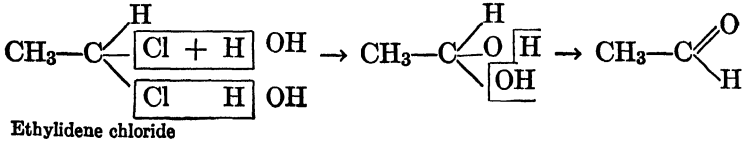
Preparation of Aldehydes and Ketones.—The oxidation of a primary alcohol yields an aldehyde; e.g.,



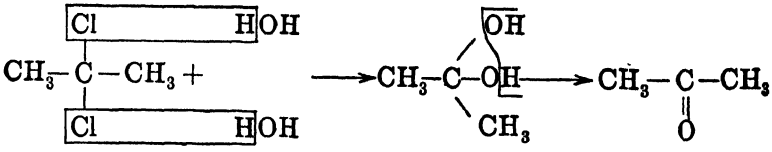
The oxidation of a secondary alcohol yields a ketone; e.g.,



Hydrolysis of dihalogenated hydrocarbons; e.g.,

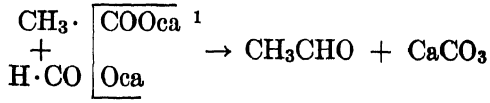


($CH_2Cl—CH_2Cl$ is ethylene chloride, but $CH_3 \cdot CHCl_2$ is ethylidene chloride.)

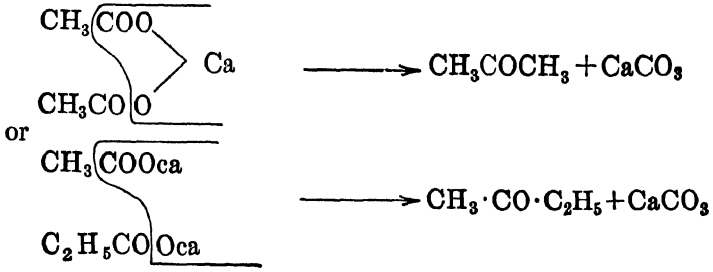


2, 2-Dichloropropane

Aldehydes may be obtained by heating the calcium salts of certain organic acids with calcium formate; e.g.,



When the calcium salts alone are heated we get ketones; e.g.,

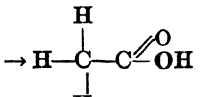
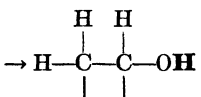
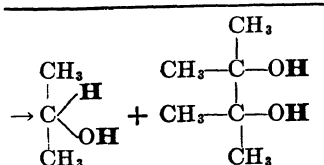
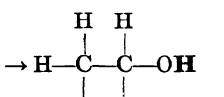
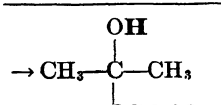
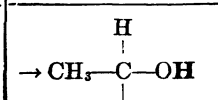


Chemical Properties of Aldehydes and Ketones.—We have already mentioned the fact that since both aldehydes and ketones contain the carbonyl, $>C=O$ group, they have many properties in common.

The $>C=O$ group may be looked upon as an unsaturated group, for it contains a double bond; which means that certain types of addition compounds are possible.

Acetaldehyde ($CH_3 \cdot CHO$) and **acetone** ($CH_3 \cdot CO \cdot CH_3$) are here taken as typical examples of aldehydes and ketones respectively.

[1] The true formula for calcium acetate is $\begin{matrix} CH_3 \cdot COO \\ CH_3 \cdot COO \end{matrix}\!\!>\!Ca$, but for the sake of convenience we have halved it, and write the symbol for calcium in small letters: ca = ½Ca.

Reagents Used	Aldehydes, e.g. $CH_3 \cdot CHO$	Ketones, e.g., $CH_3 \cdot CO \cdot CH_3$
Oxidation	 Acetic acid	→ Decomposition of molecule producing acids with lower carbon content as $H \cdot COOH$ and $CH_3 \cdot COOH$ and $CO_2 + H_2O$
Reduction	 A primary alcohol	 A secondary alcohol + A pinacol (tetramethyl glycol)
$NaHSO_3$ Sodium bisulfite	 Acetaldehyde sodium hydrogen sulfite	 Acetone sodium hydrogen sulfite
NH_2	 Acetaldehyde ammonia	Complex condensation products, in place of an addition compound, are formed

HCN	→ $CH_3-C(H)(CN)-OH$ Acetaldehyde hydrogen cyanide or ethylidene cyanohydrin	→ $CH_3-C(OH)(CN)-CH_3$ Acetone hydrogen cyanide
PCl_5	→ CH_3-CHCl_2 Ethylidene chloride	→ $CH_3-CCl_2-CH_3$ 2, 2-Dichloropropane
Halogens	→ substitute in CH_3 group: e.g., Cl_3C-CHO Trichloroacetaldehyde	→ substitute in CH_3 groups: e.g., $CCl_3 \cdot CO \cdot CH_3$ Trichloroacetone
$H_2N \cdot OH$ Hydroxylamine	$CH_3 \cdot CH=O+H_2N \cdot OH \rightarrow CH_3 \cdot CH=NOH$* Acetaldoxime	$(CH_3)_2C=O+H_2N \cdot OH \rightarrow (CH_3)_2C=NOH$ Acetketoxime
$H_2N \cdot NH_2$ Hydrazine or aminoamine	$CH_3 \cdot CH=O+H_2N \cdot NH_2 \rightarrow CH_3 \cdot CH=N \cdot NH_2$ Acetaldehyde hydrazone	$(CH_3)_2C=O+H_2N \cdot NH_2 \rightarrow (CH_3)_2C=N \cdot NH_2$ Acetone hydrazone

* The = NOH group is known as the "oxime" group.

Reagents Used	Aldehydes, e.g., $CH_3 \cdot CHO$	Ketones, e.g., $CH_3 \cdot CO \cdot CH_3$
$H_2N—NHC_6H_5$‡ Phenylhydrazine	$CH_3 \cdot C(H)=O+H_2 \cdot N \cdot NHC_6H_5 \rightarrow CH_3 \cdot C(H)=N \cdot NHC_6H_5$ Acetaldehyde phenylhydrazone	$(CH_3)_2C=O+H_2 \cdot N \cdot NHC_6H_5 \rightarrow (CH_3)_2C=N \cdot NHC_6H_5$ Acetone phenylhydrazone
C_2H_5OH (In presence of a dehydrating agent, such as HCl gas)	$CH_3—C(H)(H)OC_2H_5 \rightarrow CH_3—C(H)(OC_2H_5)_2$ Acetal	No similar reaction
	Aldehydes reduce ammoniacal silver nitrate solution to produce silver mirror	Ketones do not

‡ Phenylhydrazine is hydrazine wherein one hydrogen has been replaced by the monovalent C_6H_5 (phenyl) group (p 211) The phenyl group bears the same relationship to benzene, C_6H_6, that the methyl group does to methane.

Aldehydes

Formaldehyde, H·CHO (also known as methanal) is manufactured by passing methanol vapor and air over copper gauze:

$$CH_3OH + O \rightarrow HCHO + H_2O$$

The reaction is exothermic and the copper need not be heated except to start the reaction. It is a gas with irritating odor, soluble in water. The **formalin** of commerce is a 35–40 per cent aqueous solution of the gas. A small amount of methanol must be present in the formalin to prevent the polymerization of the formaldehyde. For disinfecting purposes, specially constructed lamps are used containing methanol, which when burnt (in the presence of copper or platinum) yields formaldehyde. It is used as a food preservative, disinfectant and germicide, both in the form of gas and in solution. In the manufacture of dyes, such as indigo, the hardening of photographic films, the preservation of tissues (hardening the albuminous material), the manufacture of synthetic resins, such as **Bakelite** (see the chapter on phenol, p. 252), formaldehyde finds uses. The chart facing page 80 shows in detail the uses of formaldehyde.

Ammonia and formaldehyde combine to form hexamethylenetetramine:

$$6HCHO + 4HNH_2 \rightarrow (CH_2)_6N_4 + 6H_2O$$

commonly known as **urotropine** or "aminoform," which finds a wide use as a diuretic, urinary antiseptic, liberating formaldehyde; and which is also used in the manufacture of synthetic resins.

It is believed that in the formation of sugars from carbon dioxide and moisture (in the plant kingdom), formaldehyde is an intermediate product. Emil Fischer, the eminent German chemist, has actually been able to obtain a sugar (acrose) from formaldehyde, by treating the latter with barium or calcium hydroxide, thereby forming "formose" (a mixture of sugars), and isolating the acrose from the formose. We shall take this up again in the chapter on sugars.

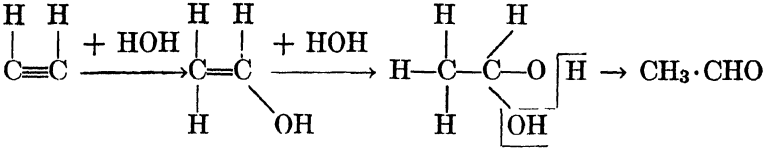
The conversion of formaldehyde into a sugar involves polymerization, and may be represented as

$$6HCHO \rightarrow C_6H_{12}O_6$$

Another polymer of formaldehyde may be obtained by treating the substance with sulfuric acid and evaporating the solution. The paraformaldehyde (also known as "paraform") so obtained

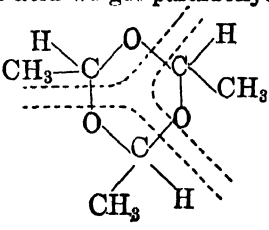
is a solid and is represented by the formula $(CH_2O)_x$, where x stands for a number not yet definitely fixed. The formaldehyde gas may again be obtained by simply heating this polymerized formaldehyde. There are lamps on the market which liberate formaldehyde in this way.

Acetaldehyde, $CH_3 \cdot CHO$ (also called ethanal), is manufactured by passing acetylene into dilute H_2SO_4 in presence of mercury salts (catalyst). It is probable that what happens may be represented thus:

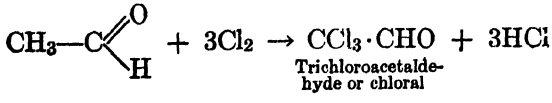


Acetaldehyde may be polymerized, just like formaldehyde. If acetaldehyde is treated with sulfuric acid we get **paraldehyde:**

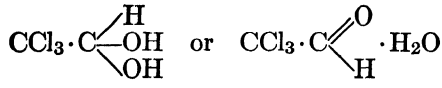
$$3CH_3 \cdot CHO \rightarrow (CH_3 \cdot CHO)_3 \text{ or}$$



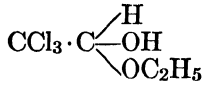
which, since it does not contain the carbonyl (>CO) group, no longer behaves like an aldehyde. If the temperature be lowered (say to 0°), instead of getting paraldehyde (a liquid), we get an isomeric compound, metaldehyde (a solid), with the same formula. Paraldehyde when heated with dilute acids is converted back to acetaldehyde. (Paraldehyde is used in medicine as a soporific It is not nearly so volatile and flammable as acetaldehyde, and for this reason acetaldehyde is often transported in the form of paraldehyde and reconverted into acetaldehyde by distillation with dilute acids.) Whereas PCl_5 reacts with aldehydes, replacing the O of the CHO group by two Cl atoms, chlorine gas displaces the hydrogen atoms in the alkyl part of the molecule; so that, if acetaldehyde be taken as a type, we may get the following:



Chloral is prepared on a large scale from ethyl alcohol (see page 45). Chloral is an oily liquid with a penetrating smell. It reacts with water, forming **chloral hydrate,**



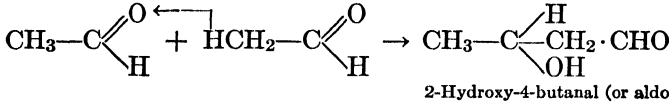
which is used as a soporific. In large doses, it acts as an anesthetic. Chloral also combines with alcohol to form a crystalline body



Chloral alcohol

Bromal, $CBr_3 \cdot CHO$, and iodal, $CI_3 \cdot CHO$ are also known.

By means of dilute alkali, or a zinc chloride solution, two molecules of acetaldehyde may be made to combine with one another to form aldol, a derivative of butyraldehyde.



2-Hydroxy-4-butanal (or aldol)

This is known as the **aldol condensation,** and, among other things, serves as a working hypothesis to explain the synthesis of fats in the plant kingdom and the conversion of sugars into fats in the animal body.

Higher aldehydes up to C_{22} are used in the preparation of synthetic perfumes and artificial fruit flavors.

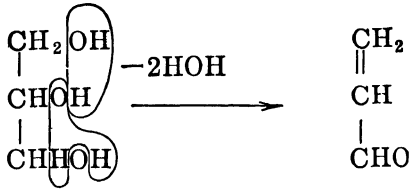
Aldehydes are detected (*a*) by their reduction of an ammoniacal silver nitrate solution to silver (silver mirror); (*b*) by the "resin" formation obtained with NaOH; (*c*) by the formation of a reddish violet color with magenta, which has been decolorized with SO_2 (the *Schiff* test); (*d*) by reduction of an alkaline copper sulfate solution (*Fehling's* test), giving the red cuprous oxide.

Glyoxal, $\begin{matrix} CHO \\ | \\ CHO \end{matrix}$, is a dialdehyde. Its dimethyl derivative is dimethyl glyoxal, $\begin{matrix} CH_3 \cdot C{=}O \\ | \\ CH_3 \cdot C{=}O \end{matrix}$, and the dioxime of the latter is

dimethyl glyoxime, $\begin{matrix} CH_3—C=NOH \\ | \\ CH_3—C=NOH \end{matrix}$, a substance used in the gravimetric determination of nickel.

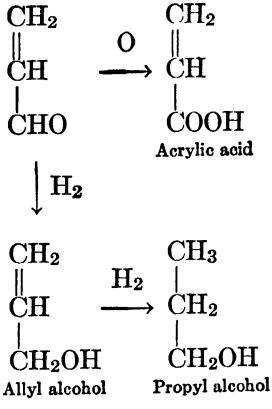
Unsaturated Aldehydes.—Acrylaldehyde, $CH_2=CH—CHO$, (commonly called **acrolein,** and sometimes called propenal), is prepared either (1) by the oxidation of allyl alcohol, or (2) by heating glycerol with a dehydrating agent, as $KHSO_4$, or (3) by heating fats and oils to a somewhat high temperature.

(1) $CH_2=CH—CH_2OH \xrightarrow{O} CH_2=CH\cdot CHO + H_2O$

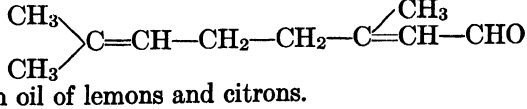
(2) 

(The odor of burning fat is mainly due to acrolein. Due to its toxic and lachrymatory properties, it was used as a "tear gas" during the late war.)

The properties of acrolein depend, first, upon the fact that it has a double bond (and is, therefore, an unsaturated compound), and second, that it is an aldehyde; so that we get reactions such as these:



Geranial or citral.



is found in oil of lemons and citrons.

Ketones

Acetone, $CH_3—CO—CH_3$ (also called propanone and dimethyl ketone) is prepared commercially by heating calcium acetate; by the catalytic dehydrogenation of isopropyl alcohol, and from the products obtained in the fermentation of corn, etc. (Weizmann process.)

This liquid has a characteristic odor, a peppermint-like taste, and is miscible with water. b.p. 56.1°. It is flammable.

Acetone is used in the manufacture of chloroform, iodoform, sulfonal, smokeless powder, celluloid, etc. The chart facing p. 84 shows in detail the uses of acetone.

Acetone is an excellent solvent for animal and vegetable oils and for fats, gums, resins, cellulose acetate, nitrocellulose, etc.

Its chemical reactions have already been given (pp. 77–79).

(Acetone is present in the urine and in the breath of persons suffering from severe diabetes.)

Higher ketones up to C_{22} are used in the preparation of synthetic perfumes and artificial fruit flavors.

Ketene is $CH_2=CO$. Aldoketenes have the formula $RCH=CO$ and ketoketenes $R_2C=CO$. They are very reactive substances. They react with water, alcohols, amines, ammonia, acids, etc.

$$R_2C=CO + HOH \rightarrow \underset{\text{Acid}}{R_2CH\cdot COOH}$$

$$RCH=CO + R'OH \rightarrow \underset{\text{Ester}}{RCH_2\cdot COOR'}$$

$$R_2C=CO + HNH_2 \rightarrow \underset{\text{Acid amide}}{R_2CH\cdot CONH_2}$$

Dimethyl ketene may be prepared by the following reaction:

$$\underset{\text{α-Chloroisobutyryl chloride}}{(CH_3)_2CCl\cdot COCl} + Zn \rightarrow \underset{\text{Dimethyl ketene}}{(CH_3)_2C=CO} + ZnCl_2$$

READING REFERENCES

Remler—Acetone, Its Properties and Uses (National Wood Chemical Association).

Walker—Formaldehyde and Its Polymers. *Industrial and Engineering Chemistry*, **23**, 1220 (1931).

Killeffer—Butanol and Acetone from Corn. *Industrial and Engineering Chemistry*, **19**, 46 (1927).

Howells—Aldol and Related Condensations. *Journal of Chemical Education*, **7**, 597 (1930).

Carothers—Polymerization. *Chemical Reviews*, **8**, 353 (1931).

CHAPTER VIII

ACIDS

An organic acid contains the "carboxyl" group,[1] —COOH $\left(-C\begin{matrix}=O\\ -OH\end{matrix}\right)$, and may be regarded as a hydrocarbon in which one or more of the hydrogens is replaced by COOH groups; e.g., CH_3H —— $CH_3 \cdot COOH$. If the compound contains one COOH group, it is known as a monobasic acid; if two such groups, dibasic; if three, tribasic; etc. We have analogous types in inorganic chemistry; e.g., HCl—H_2SO_4—H_3PO_4, etc.

Nomenclature.—Several acids have names that suggest their origin (formic from "formica," butyric from butter, valeric from "valeriana," palmitic from palm oil, etc.) The acids may also be named by changing the ending *e* of the hydrocarbons containing the same number of carbon atoms, to *oic*; so that

CH_4, methane becomes $H \cdot COOH$, methanoic acid
C_2H_6, ethane becomes $CH_3 \cdot COOH$, ethanoic acid
C_3H_8, propane becomes $CH_3 \cdot CH_2 \cdot COOH$, propanoic acid
C_4H_{10}, butane becomes (*a*) $CH_3—CH_2—CH_2—COOH$, butanoic acid

(*b*) $CH_3—\overset{(2)}{C}\begin{matrix}H\\ CH_3\end{matrix}—\overset{(1)}{COOH}$, 2-methyl-1-propanoic acid

This type of nomenclature is seldom used.

Or they may be named as derivatives of acetic acid, $CH_3 \cdot C\begin{matrix}=O\\ -OH\end{matrix}$; e.g.,

$C_2H_5—C\begin{matrix}H\\ CH_3\end{matrix}—COOH$, ethyl methyl acetic acid

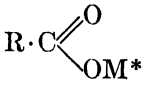
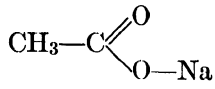
[1] Although other groups, like SO_3H, etc., are also acid groups.

or as the acids of the corresponding aldehydes:

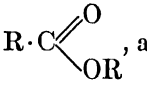
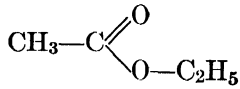
$H \cdot CHO$,	formaldehyde	—— $H \cdot COOH$,	formic acid
$CH_3 \cdot CHO$,	acetaldehyde	—— $CH_3 \cdot COOH$,	acetic acid
$C_2H_5 \cdot CHO$,	propionaldehyde	—— $C_2H_5 \cdot COOH$,	propionic acid

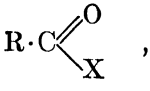
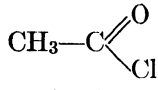
$$\mathbf{R \cdot CHO \text{ —— } R \cdot COOH}$$

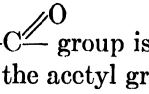
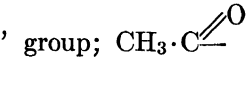
Types of Acid Derivatives.—Acids in which some element or group has been substituted in the $\cdot COOH$ group are called "acid derivatives" (they will be taken up in detail in a later chapter):

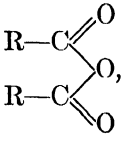
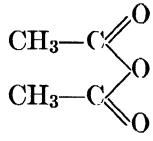

, a salt; as

Sodium acetate

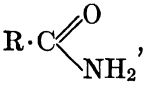
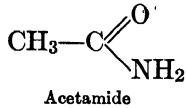
* M = metal.


, an ester; as

Ethyl acetate


, an acyl halide, as

Acetyl chloride

The  group is known as the "acyl" group;  group is the acetyl group.


an acid anhydride, as

Acetic anhydride


, an acid amide, as

Acetamide

An acid nitrile or an alkyl cyanide, as

Acetonitrile or methyl cyanide

Types of Substituted Acids.—Acids in which the $\cdot COOH$ groups remain, but substitution has taken place in the residual

groups (as CH_3), are known as "substituted acids." (They will be taken up in detail in later chapters.)

Illustration with acetic acid:

$CH_3 \cdot COOH$

$CH_2(Cl)$—COOH, chloroacetic acid

$CH_2(OH)$—COOH, hydroxyacetic acid

$CH_2(CN)$—COOH, cyanoacetic acid

$CH_2(NH_2)$—COOH, aminoacetic acid

$CH_2(COOH)$—COOH, carboxyacetic acid (known as malonic acid)

$CH_2(SO_3H)$—COOH, sulfoacetic acid

(The $-SO_3H$ group is known as the sulfonic acid group or sulfo group.)

The student should at this point thoroughly familiarize himself with these type compounds, as frequent allusion will be made to them.

MONOBASIC ACIDS (FATTY ACID SERIES[1]), R—COOH

General Methods of Preparation.—1. Oxidation of a primary alcohol, or of an aldehyde; e.g.,

$$CH_3 \cdot CH_2OH \xrightarrow{O} CH_3 \cdot CHO \xrightarrow{O} CH_3 \cdot COOH$$

2. Hydrolysis of esters (in presence of acids or alkalies); e.g.,

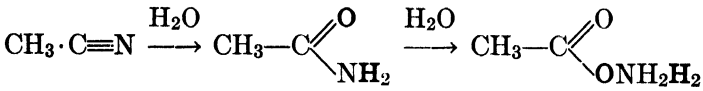
$$\underset{\text{Ethyl acetate}}{CH_3 \cdot COOC_2H_5} + HOH \rightarrow CH_3COOH + C_2H_5OH$$

[1] Named **Fatty acids** because many of them are contained in fats, or are formed from fats on hydrolysis.

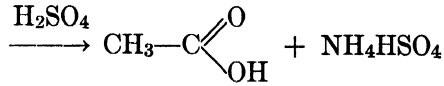
3. Hydrolysis of acyl halides with water; e.g.,

$$\underset{\text{Acetyl chloride}}{CH_3 \cdot COCl} + HOH \rightarrow CH_3COOH + HCl$$

4. Hydrolysis of alkyl cyanides or of acid amides; e.g.,



Methyl cyanide — Acetamide — Ammonium acetate



(—**CN group hydrolyzes to a —COOH group.**)

5. Decomposition of salts of organic acids with mineral acids; e.g.,

$$\underset{\text{Sodium acetate}}{CH_3 \cdot COONa} + H_2SO_4 \rightarrow CH_3 \cdot COOH + NaHSO_4$$

General Properties. The lower members up to $C_9H_{19} \cdot COOH$ are liquids with strong odors, and the higher ones, waxy solids. They ionize to a slight extent (e.g., $CH_3COO^-H^+$) but their salts ionize quite considerably. They are stable substances and difficult to oxidize.

The acids form:

(*a*) Salts with bases; e.g.,

$$CH_3 \cdot COO\boxed{H + HO}Na \rightarrow \underset{\text{Sodium acetate}}{CH_3 \cdot COONa} + H_2O$$

(*b*) Esters with alcohols; e.g.,

$$H—COO\boxed{H + HO}C_2H_5 \rightarrow \underset{\text{Ethyl formate}}{HCOOC_2H_5} + H_2O$$

(*c*) Acyl halides with PCl_5; e.g.,

$$\underset{\text{Propionic acid}}{C_2H_5COOH} + PCl_5 \rightarrow \underset{\text{Propionyl chloride}}{C_2H_5COCl} + POCl_3 + HCl$$

(*d*) Halogen substitution products (where halogen substitutes in the alkyl group); e.g.,

$$CH_3COOH + Cl_2 \rightarrow \underset{\text{Chloroacetic acid}}{\underset{\displaystyle Cl}{\underset{|}{CH_2 \cdot COOH}}} + HCl$$

NORMAL FATTY ACIDS *

Name	Formula
Formic acid	$H \cdot COOH$
Acetic acid	$CH_3 \cdot COOH$
Propionic acid	$C_2H_5 \cdot COOH$
Butyric acid	$C_3H_7 \cdot COOH$
Valeric acid	$C_4H_9 \cdot COOH$
Caproic acid	$C_5H_{11} \cdot COOH$
Heptoic acid	$C_6H_{13} \cdot COOH$
Caprylic acid	$C_7H_{15} \cdot COOH$
Nonylic acid	$C_8H_{17} \cdot COOH$
Capric acid	$C_9H_{19} \cdot COOH$
Undecylic acid	$C_{10}H_{21} \cdot COOH$
Lauric acid	$C_{11}H_{23} \cdot COOH$
.	.
.	.
.	.
[illegible]	$C_{15}H_{31} \cdot COOH$
[illegible]	$C_{16}H_{33} \cdot COOH$
[illegible]	$C_{17}H_{35} \cdot COOH$
[illegible]	$C_{19}H_{39} \cdot COOH$
.	.
.	.
.	.
Melissic acid	$C_{30}H_{59} \cdot COOH$

* For source of these acids, see chapter on fats. (p. 105)

Formic Acid, H—COOH (also known as methanoic acid) is a colorless liquid, with an odor resembling sulfur dioxide. It is the strongest acid of this series. It occurs in bees, ants, nettles and pine needles. (The "stinging" by bees is due to penetration of formic acid under the skin.)

Formic acid is manufactured by heating sodium hydroxide to 150°–170° with carbon monoxide under 6–7 atmospheres of pressure:

$$CO + NaOH \rightarrow HCOONa$$

Sodium formate

In the laboratory, it is prepared by heating oxalic acid with glycerol. The reactions involved are somewhat complex, but the essential feature may be represented thus:

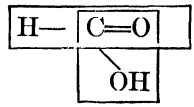
$$\begin{array}{|l} COOH \\ | \\ COO\,|H \end{array} \rightarrow HCOOH + CO_2$$

When formic acid is heated with sulfuric acid, we get carbon monoxide and water:

$$HCOOH \rightarrow CO + H_2O$$

(CO cannot be regarded as the anhydride of HCOOH since CO mixed with water does not give formic acid.)

Formic acid is a reducing agent. This may be explained on the theory that it contains an aldehyde (CHO) as well as an acid (COOH) group:



Formic acid is used in the manufacture of dyestuffs, in dyeing and finishing of textiles, in tanning, etc.

Acetic Acid.—$CH_3 \cdot COOH$ (ethanoic acid), occurs in fruits and oils in the form of esters. The common form, known as **vinegar,** is produced by the fermentation of fruit juices (such as the apple), which contain sugar. The sugar is first converted to alcohol (due to the presence of the enzyme, zymase), giving us cider, and the latter is oxidized to acetic acid by oxidizing bacteria present in the juice. For large scale production, dilute (6–9 per cent) alcoholic liquor (product of fermentation) is allowed to trickle over beechwood shavings, which are impregnated with "Bacterium aceti," or mother of vinegar. Air is admitted on the side of the vats to oxidize the C_2H_5OH into $CH_3 \cdot COOH$. The temperature is kept at about 35°. After the conversion of the alcohol to acetic acid, the product is sold as vinegar.

Vinegar contains from about 3–6 per cent of acetic acid, but also contains other acids (derived from fruit), esters, albuminous matter, etc. Stronger concentration of the acid is obtained from "pyroligneous acid," which contains acetic acid (4–10 per cent), this being separated from the other constituents of pyroligneous acid by conversion into calcium acetate, $(CH_3COO)_2Ca$ and the subsequent liberation of the acid by the addition of sulfuric acid.

Synthetic acetic acid is now made by the catalytic oxidation of acetaldehyde, which, in turn, is made from acetylene. (See p. 81.)

Glacial acetic acid is practically 100 per cent acetic acid, and, as its name implies, resembles ice when frozen.

Acetic acid is used as a solvent and to prepare acetates. It

is also employed in the manufacture of dyes, drugs (like acetanilide, p. 237) and white lead. The chart facing p. 90 shows the extensive uses of acetic acid.

Propionic Acid.—$C_2H_5 \cdot COOH$, is present in small amounts in pyroligneous acid.

Butyric Acid.—$CH_3 \cdot CH_2 \cdot CH_2 \cdot COOH$, occurs in two forms: as the normal (the formula for which has just been given), and the iso, $\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!\!CH \cdot COOH$. The normal variety is present in rancid butter, muscle, sweat, cheese, feces, etc. It has a disagreeable odor. (Calcium *n*-butyrate is one of the few substances more soluble in cold than in hot water.)

Isovaleric Acid, $\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!\!CH \cdot CH_2 \cdot COOH$, occurs in angelica and valerian roots.

Palmitic Acid, $C_{15}H_{31} \cdot COOH$, and **stearic acid,** $C_{17}H_{35} \cdot COOH$ are widely distributed, accompanied by oleic acid, $C_{17}H_{33} \cdot COOH$, in most animal and vegetable oils and fats, as the glyceryl esters. (See Chapter X.) From these esters the acids are obtained by hydrolysis; e.g.,

$$\underset{\text{Palmitin}}{C_3H_5(OOC \cdot C_{15}H_{31})_3} + 3HOH \xrightarrow[\text{steam} + H_2SO_4)]{\text{(Superheated}} \underset{\text{Palmitic acid}}{3C_{15}H_{31} \cdot COOH} + \underset{\text{Glycerol}}{C_3H_5(OH)_3}$$

The stearin candles of commerce consist of a mixture of palmitic with excess of stearic acid, and some paraffin added to prevent crystallization and brittleness.

Unsaturated Monobasic Acids

Acrylic Acid, $CH_2{=}CH \cdot COOH$ (also called propenoic acid) shows characteristic properties due to its double bond and to its carboxyl group.

Crotonic Acid, $CH_3{-}CH{=}CH \cdot COOH$, derives its name from croton oil.

Oleic Acid, $CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$, ($C_{17}H_{33} \cdot COOH$) is present as the glyceryl ester in fats and oils (p. 106), and is usually found associated with palmitic and stearic acids. Oleic acid is a liquid and on a large scale it is separated from the solid

palmitic and stearic acids by squeezing it out under hydraulic pressure. Commercial oleic acid is known as " Red oil " and is used for the manufacture of soap, greases, in the dry-cleaning industry, etc. It is an unsaturated acid, having its double bond between the ninth and tenth carbon atoms. With hydrogen, it is converted into the saturated stearic acid.

Linoleic Acid, $C_{17}H_{31}COOH$, contains two double bonds. It is present in the form of a glyceryl ester in linseed oil and other drying oils.

Dibasic Acids, $C_nH_{2n}(COOH)_2$

These compounds contain two carboxyl groups. (They are analogous to H_2SO_4, which contains two replaceable hydrogens.) They are capable of forming two series of salts, viz., acid and normal, and likewise two series of amides, esters, chlorides, etc. The general type reactions are analogous to those given for monobasic acids.

Oxalic Acid, $\begin{matrix}COOH\\|\\COOH\end{matrix}$, is present, in the form of salts (potassium, calcium, etc.) in some plants (oxalis variety). Rhubarb is rich in it. The urine often contains small quantities of calcium oxalate.

Preparation.—Sugars, cellulose and starch, when oxidized with nitric acid, yield oxalic acid. The commercial method is to heat sawdust with NaOH at 240°, which yields sodium oxalate. A still more recent method is to heat sodium formate (obtained from carbon monoxide and sodium hydroxide, p. 89) to 400°:

$$\begin{matrix}H\\H\end{matrix}\Big]\begin{matrix}COONa\\COONa\end{matrix} \rightarrow \begin{matrix}COONa\\|\\COONa\end{matrix} + H_2$$

Another method of preparation will be referred to because it is based on a reaction already discussed.

When cyanogen is hydrolyzed, we get oxalic acid:

$$\begin{matrix}CN\\|\\CN\end{matrix} + 4H_2O \rightarrow \begin{matrix}COONH_4\\|\\COONH_4\end{matrix} \rightarrow \begin{matrix}COOH\\|\\COOH\end{matrix} + 2NH_3$$

When oxalic acid is heated with sulfuric acid, we get carbon monoxide, carbon dioxide and H_2O:

$$\begin{matrix}\text{COOH}\\|\\\text{COOH}\end{matrix} \rightarrow CO_2 + CO + H_2O$$

(The student will remember the reaction as a laboratory method for the preparation of CO. The CO_2 is removed by passing the mixture of gases through alkali.)

Oxalic acid is a highly poisonous substance. It is used in analytical chemistry, in the manufacture of dyes, bleaching, metal polishes, tanning, etc. Oxalic acid is the strongest organic acid.

Malonic Acid, $CH_2\begin{matrix}\text{COOH}\\\text{COOH}\end{matrix}$, was first obtained by oxidizing malic acid (the acid present in apples, p. 131). Its synthesis is accomplished as follows:

$$CH_3\cdot COOH \xrightarrow{Cl_2} \underset{\displaystyle Cl}{CH_2\cdot COOH} \xrightarrow{KCN} \underset{\displaystyle CN}{CH_2\cdot COOH}$$

Cyanoacetic acid

$$\xrightarrow{\text{Hydrolysis}} CH_2\begin{matrix}\text{COOH}\\\text{COOH}\end{matrix}$$

When heated, malonic acid is first converted into acetic acid by the loss of CO_2:

$$CH_2\begin{matrix}\text{COOH}\\\text{COOH}\end{matrix} \rightarrow CH_3\cdot COOH + CO_2$$

and this proves malonic acid to be a dicarboxylic acid derivative of methane.

Succinic Acid, $\begin{matrix}CH_2\cdot COOH\\|\\CH_2\cdot COOH\end{matrix}$, occurs in amber, fossil wood and in the urine of animals. It is produced in processes involving

fermentation and may be obtained by distilling amber. Its synthesis may be accomplished thus:

$$\underset{\|}{CH_2}\ \xrightarrow{Cl_2}\ \underset{|}{CH_2Cl}\ \xrightarrow{2NaCN}\ \underset{|}{CH_2CN}\ \xrightarrow{\text{Hydrolysis}}\ \underset{|}{CH_2COOH}$$
$$\underset{CH_2}{\|}\qquad\qquad \underset{CH_2Cl}{|}\qquad\qquad \underset{CH_2CN}{|}\qquad\qquad \underset{CH_2COOH}{|}$$

Ethylene cyanide

When the acid is heated, it loses a molecule of water and is converted to its anhydride:

$$\begin{matrix} CH_2\cdot COOH \\ | \\ CH_2\cdot COOH \end{matrix} \rightarrow \begin{matrix} CH_2{-}C{=}O \\ | \qquad\quad O \\ CH_2{-}C{=}O \end{matrix} + H_2O$$

Succinic anhydride

Other examples of dibasic acids are methyl malonic acid (isosuccinic acid),

$$CH_3\cdot CH\begin{matrix} COOH \\ \diagup\!\diagdown \\ COOH \end{matrix};$$

glutaric acid,

$$CH_2\begin{matrix} CH_2\cdot COOH \\ \diagup\!\diagdown \\ CH_2\cdot COOH \end{matrix};\ \text{etc.}$$

Unsaturated Dibasic Acids

Two compounds with the formula $C_2H_2(COOH)_2$ are known, one being **maleic acid** and the other **fumaric acid.**

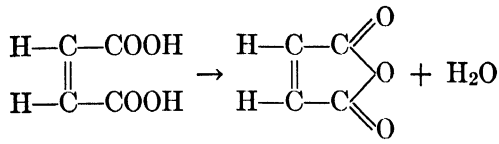
Fumaric acid occurs in various fungi, iceland moss, etc. Maleic acid is not a natural product. The formulas ascribed to the two isomers are:

$$\begin{matrix} H{-}C{-}COOH \\ \| \\ H{-}C{-}COOH \end{matrix} \qquad\qquad \begin{matrix} H{-}C{-}COOH \\ \| \\ HOOC{-}C{-}H \end{matrix}$$

Maleic acid (cis-form) — Fumaric acid (trans-form)

This type of isomerism is known as the "ethylene" or "geometric type," [1] When maleic acid is heated it produces an anhydride.

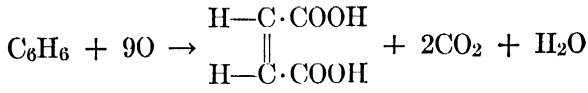
[1] It is suggested that the instructor show this type of isomerism with the Kekulé models.



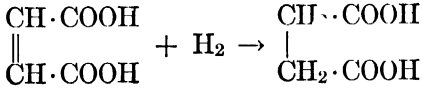
Fumaric acid does not yield an anhydride, which suggests that a compound represented by two ·COOH groups in juxtaposition has the maleic acid formula.

(The system of nomenclature adopted to distinguish between the two isomers is to term the compound with similar groups on the same side as the *cis*-form, and the compound with similar groups on opposite sides on the molecule as the *trans*-form.)

Maleic acid is prepared on a commercial scale by the catalytic (air) oxidation of benzene vapor:



Both fumaric and maleic acids on reduction yield succinic acid:



READING REFERENCES

WEISS AND DOWNS—Catalytic Oxidation of Benzene to Maleic Acid. *Journal of Chemical Education*, **2**, 1178 (1925).

CRANOR—Stearic Acid. *Industrial and Engineering Chemistry*, **21**, 719 (1929).

PARTRIDGE—Acetic Acid and Cellulose Acetate. *Industrial and Engineering Chemistry*, **23**, 482 (1931).

CHAPTER IX

SALTS AND ESTERS OF INORGANIC AND ORGANIC ACIDS

SALTS

SALTS of organic acids are important for a number of reasons. In the first place, they are used in the preparation of various organic compounds (see below); then again a number of them are the source of certain elements which the body needs; and finally a group of them belong to the household substances which go under the common name of "soap."

In inorganic chemistry, a salt may be looked upon as an acid in which the acid hydrogen is replaced by a metal; e.g.,

HCl	$NaCl$	H_2SO_4	$NaHSO_4$	Na_2SO_4
Acid	Salt	Acid	Acid salt	Neutral salt

In a similar way, when the acid hydrogen of an organic acid is replaced by a metal, we get a salt:

$R \cdot COOH$	$R \cdot COOM$*
Acid	Salt

For example: CH_3COONa (sodium acetate), $(H \cdot COO)_2Cu$ (copper formate), $C_{17}H_{33} \cdot COONa$ (sodium oleate), etc.

The naming of these salts is analogous to the naming of inorganic salts:

$H_2SO_4 \rightarrow Na_2SO_4$, sodium sulfate

$CH_3COOH \rightarrow CH_3 \cdot COOK$, potassium acetate

$\begin{matrix} COOH \\ | \\ COOH \end{matrix} \rightarrow \begin{matrix} COONa, \\ | \\ COONa \end{matrix}$ sodium oxalate

$\begin{matrix} CH_2 \cdot COOH \\ | \\ CH_2 \cdot COOH \end{matrix} \rightarrow \begin{matrix} CH_2COO \\ | \\ CH_2COO \end{matrix} \!\!>\!\! Cd$, cadmium succinate

* M = metal.

General Methods of Preparation.—1. The action of an acid on a base; e.g.,

$$CH_3 \cdot COOH + NaOH \rightarrow CH_3 \cdot COONa + H_2O$$

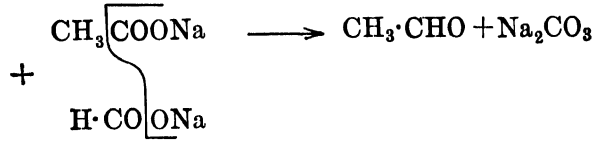
2. The action of an acid on an oxide, or a carbonate; e.g.,

$$2CH_3 \cdot COOH + CaCO_3 \rightarrow (CH_3 \cdot COO)_2Ca + CO_2 + H_2O$$

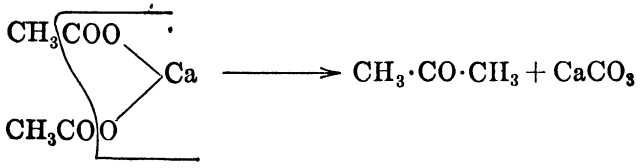
General Properties.—They are usually crystalline substances and often contain water of crystallization. Some, when heated with soda lime, yield hydrocarbons; e.g.,

$$\underset{\text{Sodium propionate}}{C_2H_5 \cdot \boxed{COONa + NaO}H} \rightarrow \underset{\text{Ethane}}{C_2H_5H} + Na_2CO_3$$

others yield aldehydes;



and still others, ketones;



The free acid may be liberated from these salts by the addition of a stronger acid; e.g.,

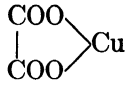
$$CH_3 \cdot COONa + H_2SO_4 \rightarrow CH_3COOH + NaHSO_4$$

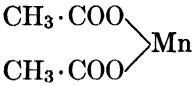
The ammonium salts, when heated, are first converted to the acid amides and then to the cyanides (the reverse process of converting a cyanide into the acid being one of hydrolysis); e.g.,

$$CH_3 \cdot COONH_4 \underset{+H_2O}{\overset{-H_2O}{\rightleftharpoons}} CH_3 \cdot CONH_2 \underset{+H_2O}{\overset{-H_2O}{\rightleftharpoons}} CH_3 \cdot CN$$

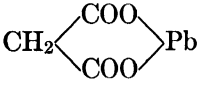
Very many salts are known. The names and composition of only a few of these will be given:

$H \cdot COONa$
Sodium formate


Copper oxalate


Manganese acetate

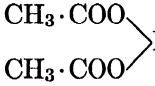
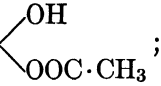
Lithium hydrogen (acid) oxalate


Lead malonate

$CH_3 \cdot CH_2 \cdot COONH_4$
Ammonium propionate

$CH_3 \cdot CH_2 \cdot CH_2 \cdot COOK$
Potassium butyrate

$C_{17}H_{35}COONa$
Sodium stearate

 is "sugar of lead"; the "basic lead acetate," used to purify sugar and many biological substances, is  ; "verdigris," or "green pigment," is a combination of copper hydroxide and copper acetate, $Cu(OH)_2 \cdot (CH_3COO)_2Cu$; "Paris green," the insecticide, is a combination of copper arsenite and copper acetate, $(CH_3COO)_2Cu \cdot Cu_3As_2O_6$; iron, aluminum and chromium acetates are used as mordants in dyeing and calico printing.

Soaps.—The sodium or potassium salts of some of the higher acids (obtained from fats and vegetable oils), such as palmitic, $C_{15}H_{31} \cdot COOH$; stearic, $C_{17}H_{35}COOH$; and oleic, $C_{17}H_{33}COOH$, are known as **soaps.** Without going into the details of manufacture of these soaps, it may be pointed out that the principle involved is the conversion of the fat into soap and glycerol by boiling with alkali, and the separation of the soap from the glycerol by a process known as "salting out," which means that salt (NaCl) is added to the mixture, whereby the soap comes to the surface and is then ladled off. The reaction may be represented thus:

$$\begin{array}{l} CH_2— \\ | \\ CH — \\ | \\ CH_2— \end{array} \begin{array}{|l} OOC\cdot C_{15}H_{31} \\ OOC\cdot C_{15}H_{31} \\ OOC\cdot C_{15}H_{31} \end{array} \begin{array}{l} Na \\ Na \\ Na \end{array} \begin{array}{l} OH \\ OH \\ OH \end{array} \rightarrow \begin{array}{l} CH_2OH \\ | \\ CHOH \\ | \\ CH_2OH \end{array} + 3C_{15}H_{31}COONa$$

Glyceryl palmitate or palmitin (a fat) — Glycerol — Sodium palmitate (a soap)

The solid soaps are sodium salts while the soft soaps are potassium salts. Soaps added to "hard" water (containing calcium or magnesium salts in solution) have their sodium atom replaced by either calcium or magnesium, thereby forming soaps insoluble in water:

$$2C_{17}H_{35}\cdot COONa + Ca(HCO_3)_2 \rightarrow (C_{17}H_{35}\cdot COO)_2Ca + 2NaHCO_3$$

Sodium stearate — Calcium stearate

This explains the "curds" formed when soap is used in hard water.

("Lead plaster" is a lead soap made from lead oxide or lead acetate, which has been boiled with fat and water. Lead, manganese or cobalt soaps are used as "dryers" in paints, to hasten the process of drying. Calcium soaps are used for lubricating greases. Zinc stearate finds extensive use in toilet powders. The "medicated" soaps contain one or more of such substances as carbolic acid, salicylic acid, sulfur, cresol, resorcinol, etc. Perfume and coloring materials are often added to soaps.)

The cleansing action of soaps depends upon the power to emulsify oils and fats which are then washed away in the form of small globules.

Esters

An **ester** is either an inorganic or organic acid in which the acid hydrogen has been replaced by an R group (or a salt in which the metal is replaced by an R group):

HCl,	acid	RCl,	ester
H_2SO_4,	acid	$RHSO_4$,	acid ester
		or R_2SO_4	ester
$HONO_2$,	acid	$RONO_2$,	ester
$HONO$,	acid	$RONO$,	ester
$CH_3\cdot COOH$,	acid	$CH_3\cdot COOR$,	ester
$\begin{array}{l} COOH, \\ \vert \\ COOH, \end{array}$	acid	$\begin{array}{l} COOR, \\ \vert \\ COOR, \end{array}$	ester
		or $\begin{array}{l} COOR, \\ \vert \\ COOH, \end{array}$	acid ester

Esters are widely distributed in nature, and are responsible for the characteristic odors of many fruits, flavors and flowers. They have very agreeable odors and are used as flavoring materials and in perfumes. Since they are volatile, the esters are also called "ethereal salts." They ionize to a very slight extent and are usually insoluble in water.

General Methods of Preparation.—1. By the interaction of an alcohol and an acid; e.g.,

$$C_2H_5\boxed{OH + H}I \rightarrow C_2H_5I + H_2O$$

$$C_2H_5\boxed{OH + H}OOC\cdot CH_3 \rightarrow \underset{\text{Ethyl acetate}}{CH_3\cdot COOC_2H_5} + H_2O$$

$$C_2H_5\boxed{OH + H}HSO_4 \rightarrow \underset{\text{Ethyl hydrogen sulfate}}{C_2H_5HSO_4} + H_2O$$

$$C_2H_5\boxed{OH + H}ONO \rightarrow \underset{\text{Ethyl nitrite}}{C_2H_5{-}O{-}N{=}O} + H_2O$$

2. By the interaction of a salt of an acid with an organic halide; e.g.,

$$CH_3COO\boxed{Ag + I}C_3H_7 \rightarrow \underset{\text{Propyl acetate}}{CH_3\cdot COOC_3H_7} + AgI$$

3. The action of an acyl halide on an alcohol or an alcoholate; e.g.,

$$C_2H_5O\boxed{Na + Cl}OC\cdot CH_3 \rightarrow CH_3\cdot COOC_2H_5 + NaCl$$

Acetyl chloride

General Properties.—The esters are neutral substances, insoluble in water. Though the salts ionize quite readily, the esters do not. Upon boiling with dilute acid or alkali, hydrolysis takes place, the process being known as **saponification** (a process employed in making soap); e.g.,

$$CH_3\cdot COOC_2H_5 + HOH \rightarrow CH_3COOH + C_2H_5OH$$

Ammonia converts them to the corresponding amide; e.g.,

$$CH_3\cdot CO\boxed{OC_3H_7 + H}NH_2 \rightarrow \underset{\text{Acetamide}}{CH_3\cdot CONH_2} + C_3H_7OH$$

Esters of Inorganic Acids.—(The alkyl halides discussed in Chap. IV (p. 44) are esters of hydriodic, hydrobromic and hydrochloric acids. They will not be discussed again in this section.)

Ethyl nitrite, $C_2H_5\cdot ONO$, has an apple-like odor. Its alcoholic solution is the "sweet spirit of nitre." **Isoamyl nitrite,**

$C_5H_{11}\cdot ONO$, is used in medicine as an antispasmodic and anodyne.

Ethyl nitrate, $C_2H_5ONO_2$, has a fruity odor. It is explosive.

Dimethyl sulfate, $(CH_3)_2SO_4$, may be prepared thus:

$$CH_3OH + HHSO_4 \rightarrow CH_3HSO_4 + H_2O$$

$$2CH_3HSO_4 \text{ heated} \rightarrow (CH_3)_2SO_4 + H_2SO_4$$

It finds use as a methylating agent (to introduce methyl groups into compounds). It is poisonous.

Ethyl sulfuric acid, $C_2H_5HSO_4$ (also called **ethyl hydrogen sulfate**), may be prepared by the action of conc. sulfuric acid on ethyl alcohol at 100°:

$$C_2H_5OH + H_2SO_4 \rightarrow C_2H_5HSO_4 + H_2O$$

It may be recalled at this point that when ethyl hydrogen sulfate is heated to about 170° we get ethylene (p. 32) and when treated with alcohol it yields ether (p. 70).

Diethyl sulfate, $(C_2H_5)_2SO_4$, is used as an ethylating agent. It has a peppermint-like odor. Unlike dimethyl sulfate, it is non-toxic.

Glyceryl trinitrate, commonly, but erroneously, called **nitroglycerine,** is prepared by the action of nitric acid on glycerine (H_2SO_4 is used as dehydrating agent):

$$\begin{array}{lcl} CH_2OH & HONO_2 & CH_2\text{-}ONO_2 \\ | & & | \\ CHOH & + HONO_2 \rightarrow & CH\text{—}ONO_2 + 3H_2O \\ | & & | \\ CH_2OH & HONO_2 & CH_2\text{—}ONO_2 \end{array}$$

It is used in medicine as a circulatory depressant and is the active constituent of dynamite (see p. 66).

Glyceryl phosphate (ortho) is prepared in a similar manner:

$$\begin{array}{l} CH_2OH \\ | \\ CHOH \\ | \\ CH_2OH \end{array} + \begin{array}{l} HO \\ HO \\ HO \end{array} \text{—} P = O \longrightarrow C_3H_5^{1}PO_4 + 3H_2O$$

Glyceryl orthophosphate

[1] The C_3H_5 group, if trivalent, is known as the glyceryl group; if C_3H_5 is monovalent, it is known as the allyl group.

(RCN may be regarded as an ester of HCN. This type of compound will be treated later—p. 161).

Esters of Organic Acids.—When an inorganic acid and an alkali react, a salt is immediately formed; when, however, an organic acid and an alcohol (in some respects the analogue of the alkali) react, the ester is formed, but slowly:

$$CH_3CO\boxed{OH + H}OC_2H_5 \rightleftarrows CH_3COOC_2H_5 + H_2O$$

When equimolecular quantities are used, only 66 per cent of the ester is produced. An increase of temperature increases the velocity of the reaction, but not the yield of ester. The latter may be increased by the addition of a catalyst, or a dehydrating agent, such as H_2SO_4 or HCl gas.

Saponification to which we have alluded (p. 100) is hydrolysis, and **esterification** is the reverse of this:

$$R\cdot COOH + HOR' \underset{\text{Saponification (weak acids or bases)}}{\overset{\text{Esterification (strong acids)}}{\rightleftharpoons}} R\cdot COOR' + H_2O$$

Many of these esters are known. They are used extensively in artificial fruit essences, flavors, perfumes, extracts, etc. Very many soft drinks on the market are artificially colored and flavored. Synthetic esters are used to flavor them and a number of coal-tar dyes to color them. Only a few can be mentioned here.

Ethyl acetate, $CH_3\cdot COOC_2H_5$, is used as a solvent for nitrocellulose, in the preparation of photographic films, and in resins and essences.

Isoamyl acetate, $CH_3\cdot COOC_5H_{11}$, is found in pear oil and is used as a solvent for gun-cotton and in the preparation of banana oil or " bronzing " liquid.

Ethyl butyrate, $C_3H_7\cdot COOC_2H_5$, is a constituent of pineapples.

Isoamyl isovalerate, $C_4H_9\cdot COOC_5H_{11}$, is found in apples.

Octyl acetate, $CH_3\cdot COOC_8H_{17}$, occurs in oranges.

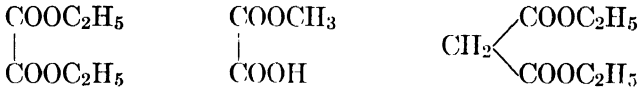
Ethyl formate, $H\cdot COOC_2H_5$, is a constituent of artificial rum.

Amyl butyrate, $C_3H_7\cdot COOC_5H_{11}$, has an apricot flavor.

Ethylene acetate, $CH_3 \cdot COOCH_2$ / $CH_3 \cdot COOCH_2$, is used as solvent for cellulose acetate and in cellulose nitrate lacquers.

As a result of the development of the lacquer industry during the last few years, many of these esters are now finding extensive use.

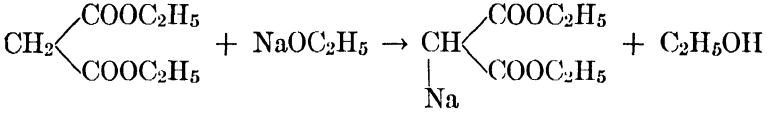
Myricyl palmitate, $C_{15}H_{31} \cdot COOC_{30}H_{61}$, is present in beeswax. The esters of dibasic acids are also well known; e.g.,



Ethyl oxalate — Methyl acid oxalate — Ethyl malonate (**malonic ester**)

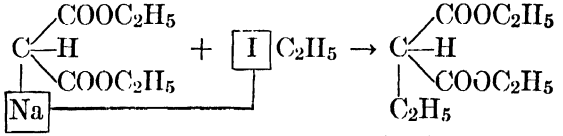
Uses of Malonic Ester.—Malonic ester can be used to synthesize homologues of malonic and acetic acids.

When malonic ester is treated with sodium or sodium alcoholate, the following reaction takes place:



Sodium malonic ester

If an alkyl halide is now added; e.g.,

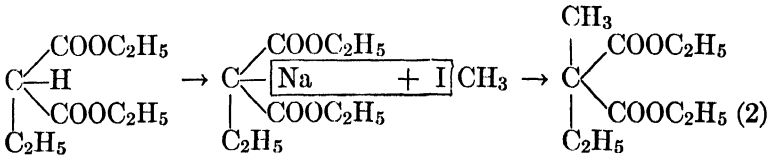


(1)

Ethyl malonic ester

a derivative of malonic ester is obtained.

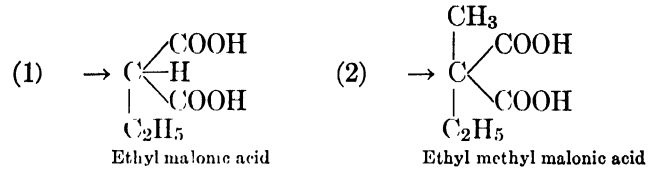
A second alkyl group (the same or a different one) may be introduced by repeating the above operation; e.g.,



(2)

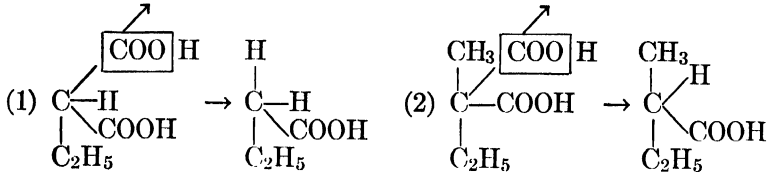
Sodium ethyl malonic ester — Ethyl methyl malonic ester

On hydrolysis with sodium hydroxide and subsequent acidification the following acids are formed:



Ethyl malonic acid — Ethyl methyl malonic acid

On heating, malonic acid and its derivatives lose carbon dioxide.



Butyric acid — Ethyl methyl acetic acid

(**Fats** and **vegetable oils** are glyceryl esters. They will be taken up in detail in the next chapter.)

READING REFERENCES

ROGERS—Manual of Industrial Chemistry. (1931), p. 1003 (Soaps and Soap Products).

PRESTON—The Modern Soap Industry. *Journal of Chemical Education*, **2**, 1035 (1925).

WHITMORE and LAURO—Metallic Soaps. *Industrial and Engineering Chemistry*, **22**, 646 (1930).

CHAPTER X

FATS AND OILS, WAXES AND LIPOIDS

Fats and Oils

These are glyceryl esters of fatty acids (usually of high molecular weight). An example of one of these substances is glyceryl palmitate (tripalmitin).

$$\begin{array}{l} CH_2\text{—}OOC\cdot C_{15}H_{31} \\ | \\ CH\ \text{—}OOC\cdot C_{15}H_{31} \\ | \\ CH_2\text{—}OOC\cdot C_{15}H_{31} \end{array}$$

The glyceryl esters of stearic ($C_{17}H_{35}COOH$), palmitic and oleic ($C_{17}H_{33}COOH$) acids constitute the main bulk of the fats and oils in food and of body fat.

If the three acid radicals in a fat or oil are the same, it is known as a simple glyceride, e.g., tripalmitin. A fat containing radicals of two or three different fatty acids is known as a mixed glyceride, e.g.,

$$\begin{array}{l} CH_2\text{—}OOC\cdot C_{17}H_{35} \\ | \\ CH\ \text{—}OOC\cdot C_{15}H_{31} \\ | \\ CH_2\text{—}OOC\cdot C_3H_7 \end{array}$$

Butyropalmitostearin

There is no essential chemical difference between fats and vegetable oils. **Stearin,** $C_3H_5(OOC\cdot C_{17}H_{35})_3$, and **palmitin,** $C_3H_5(OOC\cdot C_{15}H_{31})_3$ are solids, while **olein,** $C_3H_5(OOC\cdot C_{17}H_{33})_3$ is a liquid. The consistency of a fat or oil depends on the amount of solid or liquid esters present. The fats are solid at the ordinary temperatures, whereas the oils are liquid.

IMPORTANT FATS AND OILS

Fat or Oil	Contains the Glyceryl Ester of	Source of Fat or Oil
Almond oil	Oleic, palmitic, linoleic acids, etc.	Bitter or sweet almonds
Butterfat	Butyric, caproic, capric, palmitic, stearic, oleic acids, etc.	Cow's milk
Cacao butter	Palmitic, oleic, stearic, myristic acids, etc.	Seeds of cocoa nibs
Castor oil	Ricinoleic, stearic, oleic acids, etc.	Seeds of castor beans
Cocoanut oil	Caproic, caprylic, capric, lauric acids, etc.	Seeds of "cocos nucifers," kernel of nuts
Codliver oil	Oleic, myristic, palmitic, stearic acids and cholesterin, etc.	Livers of cod fish
Cottonseed oil	Oleic, stearic, palmitic, linoleic acids, etc.	Seeds of the cotton-plant
Hemp oil	Isolinolenic, oleic acids, etc.	Seeds of hemp
Human fat	Stearic, palmitic, oleic, butyric, caproic acids, etc.	Human beings
Lard	Stearic, palmitic, oleic, linoleic acids, etc.	Body fat of swine
Linseed oil	Linoleic, linolenic, oleic, palmitic, myristic acids, etc.	Seeds of flax
Maize oil	Arachidic, stearic, palmitic, oleic acids, etc.	Seed germs of corn oil
Menhaden oil	Palmitic, myristic, oleic, stearic, and other unsaturated acids, etc.	Bodies of menhaden fish
Mustard oil	Erucic, arachidic, stearic, oleic acids, etc.	Seeds of mustard
Neatsfoot oil	Palmitic, stearic, oleic acids, etc.	Hoofs of cattle
Olive oil	Linoleic, oleic, arachidic acids, etc.	Fruit of olive tree

IMPORTANT FATS AND OILS—*Continued*

Fat or Oil	Contains the Glyceryl Ester of	Source of Fat or Oil
Palm oil	Palmitic, lauric, oleic acids, etc.	Palm seed
Peanut oil	Arachidic, linoleic, hypogoeic, palmitic acids, etc.	Peanuts
Poppy oil	Linoleic, isolinolenic, palmitic, stearic acids, etc.	Poppy seeds
Rape oil	Erucic, arachidic, stearic acids, etc.	Rape seeds
Sperm oil	Oleic, palmitic acids, waxes, etc.	Head and blubber of sperm whale
Tallow	Stearic, palmitic, oleic acids, etc.	Fat of ox or sheep
Whale oil	Linoleic, isolinolenic acids, etc.	Blubber of whales

Oleomargarine consists mainly of refined lard, "oleo oil" (the soft part of beef fat) and cottonseed oil, often mixed with a small amount of butter and churned with milk or cream.

Hydrogenation of Oils.—Liquid fatty oils can be converted to fatty bodies of almost any desired degree of consistency by means of hydrogenation. The unsaturated liquid oils unite directly with hydrogen in presence of catalysts (nickel being used on commercial scale) to form saturated bodies.

$$\underset{\text{Olein (liquid)}}{C_3H_5(OOC\cdot C_{17}H_{33})_3} + 3H_2 \rightarrow \underset{\text{Stearin (solid)}}{C_3H_5(OOC\cdot C_{17}H_{35})_3}$$

Stearin has greater commercial value than olein. The "hardened fats" now find extensive use in the preparation of lard substitutes, in the manufacture of soap, etc. "Hardened" cottonseed oil, peanut oil and other edible oils have largely replaced lard compounds. "Crisco," "vegetol," are examples of "hardened" (or hydrogenated) vegetable oils.

Crude fats and oils range from yellow to red in color. The

refined products are generally yellow to colorless. Sometimes vegetable oils are green, due to the presence of chlorophyll (the green coloring matter of plants). Fats and oils are insoluble in water, but readily soluble in ether, benzene, chloroform, etc. The rancidity of a fat (as in butter-fat) is mainly due to hydrolysis (bacterial decomposition, or otherwise) and oxidation yielding the free fatty acids. Butter in this way produces butyric acid, which has a disagreeable odor.

Properties.—Fats can be hydrolyzed or saponified. When the glyceryl esters of stearic, palmitic or oleic acids are saponified with NaOH or KOH, soaps are formed:

$$\begin{array}{l} CH_2{-}OOC{-}C_{15}H_{31} \\ | \\ CH\ {-}OOC{-}C_{15}H_{31} \\ | \\ CH_2{-}OOC{-}C_{15}H_{31} \end{array} + 3NaOH \rightarrow \begin{array}{l} CH_2OH \\ | \\ CHOH \\ | \\ CH_2OH \end{array} + 3C_{15}H_{31}{-}COONa$$

Sodium palmitate (a soap)

This is the principle employed in the manufacture of soap. (The reaction also explains the hydrolysis of fats in the small intestine by the enzyme (lipase) which is formed in the pancreas.)

A number of methods used for identifying fats are:

1. Saponification value: the number of milligrams of KOH needed to saponify 1 gram of fat or oil.

2. The iodine number: the percentage of iodine absorbed by the sample. (The amount of " absorption," or extent of " addition " will depend upon the amount of unsaturated glycerides present—such as in olein, for example.)

3. Specific gravity.

4. Melting point.

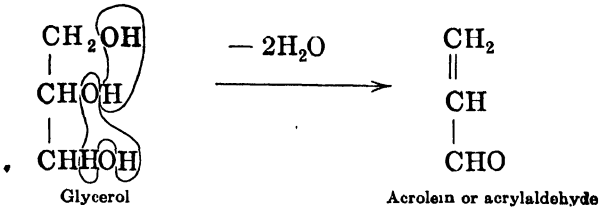
5. Index of refraction.

6. Viscosity and other physical constants.

(As has been stated, the fats in the body are first hydrolyzed into fatty acids and glycerol. A little soap is also formed, due to the alkalinity of the medium. The fatty acids and glycerol are absorbed as such through the lining of the small intestine, where they are re-synthesized again into fat, most of which passes into the lymphatic system, and finally finds its way into the blood stream. Some of the fat is oxidized in the cells to CO_2 and water—see the steps in this oxidation p. 189—but much of it

is often deposited in the adipose tissue, and acts as a reserve fuel.)

The fats and oils, when strongly heated, either alone, or with a dehydrating agent like $KHSO_4$, develop a penetrating odor, due to the formation of acrolein. This acrolein is really derived from the glycerol part of the molecule:



Glycerol — Acrolein or acrylaldehyde

Waxes

Waxes, like fats, are esters, but instead of containing the trihydroxy alcohol, glycerol, they contain high molecular weight monatomic alcohols, such as cetyl alcohol, $C_{16}H_{33}OH$, carnaubyl alcohol, $C_{24}H_{49}OH$, myricyl alcohol, $C_{30}H_{61}OH$, etc.

Among vegetable waxes, we have " carnauba wax," and among animal waxes, we have wool wax (or " lanolin "), beeswax, spermaceti, Chinese insect wax, etc.

Waxes (like fats) are soluble in ether, benzene, chloroform, carbon tetrachloride, etc. Since they do not contain glyceryl radical, they do not yield acrolein when heated. The waxes do not become rancid like fats and are less easily hydrolyzed.

Carnauba wax is derived from a species of palm; it is used in varnish, for candle making and for adulterating beeswax. Lanolin, obtained from wool grease, is used in pharmacy as a basis for salves, ointments and emulsions. Beeswax is derived from the honeycomb of bees and is used in candle making, in pharmacy, etc. Spermaceti, found in the head of the sperm whale, finds uses in candle making, in pharmacy and in confectionery. Chinese wax, secreted by an insect, is also used in candle making, in medicine and as a furniture polish, etc.

Lipoids

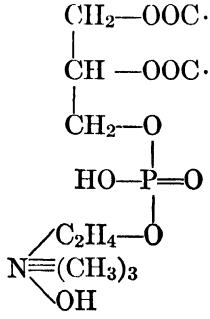
These are a group of substances, soluble in ether and the usual fat solvents, which are found in abundance in animal tissues, particularly in the brain. We know little at present about their physiological significance. They may be classified as follows:

1. Containing nitrogen and phosphorus (phosphatids); e.g., lecithin and cephalin (N : P as 1 : 1), and sphingomyelin (here N : P as 2 : 1).

2. Containing nitrogen: e.g., phrenosin and cerasin (the so-called " cerebrins " or " cerebrosides ").

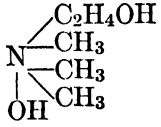
3. Nitrogen and phosphorus are absent; e.g., cholesterol.

Lecithin is a combination of glycerol, fatty acid, phosphoric acid and choline, and its structure may be represented as:

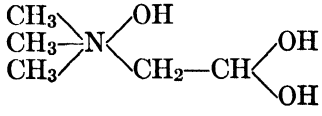


(R and R′ represent groups present in acids. As in fats, R and R′ may be the same or different.)

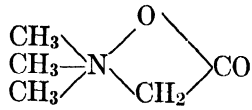
Choline,



or trimethyl-β-hydroxyethyl ammonium hydroxide, is closely related to **muscarine**—the aldehyde hydrate of choline—

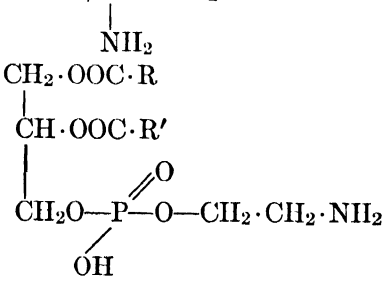


which is the poisonous constituent of the deadly toad-stool, and to **betaine**—the acid anhydride—



a non-toxic plant product. In a crude form, lecithin may be obtained by extracting egg yolk with ether and precipitating with acetone.

Cephalin is similar to lecithin in that it contains glycerol, fatty acids and phosphoric acid, but in the place of the base choline, it contains aminoethyl alcohol, $CH_2 \cdot CH_2OH$. Its constitution may be represented as



Unlike lecithin, cephalin is insoluble in alcohol. (Cephalin is sometimes written "kephalin.")

Sphingomyelin is a complex combination of phosphoric acid, choline, a base, sphingosine, $C_{17}H_{32}(OH)NH_2$, and an acid, lignoceric acid, $C_{25}H_{47} \cdot COOH$.

Phrenosin is a combination of cerebronic acid (the hydroxy acid of lignoceric), galactose and sphingosine.

Cerasin, like phrenosin, yields when hydrolyzed, galactose and sphingosine, but in the place of cerebronic acid gives lignoceric acid.

Cholesterol, $C_{27}H_{45}OH$, is an unsaturated secondary alcohol and a member of the terpene series, though its exact structure is not yet known. It is widely distributed in animal tissues, particularly in egg yolk and nervous tissue. (Isomers, **phytosterols,** are found in the vegetable kingdom.) "Lanolin," the fatty matter obtained from sheep's wool, is an ester of cholesterol. This alcohol is also present in bile and in blood. The determination of the amount of cholesterol in the blood is often of chemical

significance, since in gall stones, pregnancy, nephritis, diabetes, etc., the quantity may be in excess of the normal value.

Recently it has been shown by Hess and Steenbock that ultaviolet rays convert ergosterol into a substance showing antirachitic properties, a characteristic usually ascribed to vitamin D (p. 359). It is now believed that the precursor of vitamin D is probably this ergosterol, $C_{27}H_{41}OH$.

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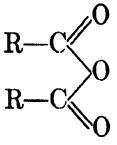
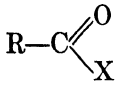
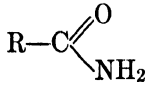
CHAPTER XI

ACID ANHYDRIDES, ACYL HALIDES AND ACID AMIDES

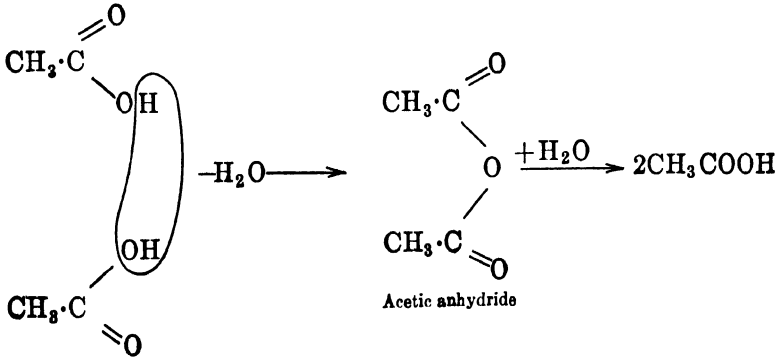
THE type formula for an acid anhydride is 

The type formula for an acyl halide is 

The type formula for an acid amide is 

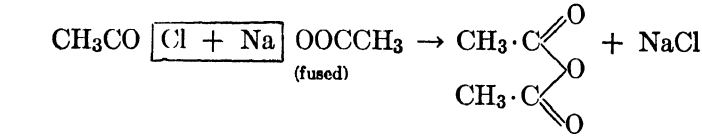
ACID ANHYDRIDES

Acid anhydrides are similar in many respects to inorganic acid anhydrides. Sulfur trioxide, for example, is the acid anhydride of sulfuric acid, for $SO_3 + H_2O \rightarrow H_2SO_4$. Similarly, acetic (acid) anhydride is the anhydride of acetic acid, for



(An anhydride may be looked upon as an acyl oxide.)

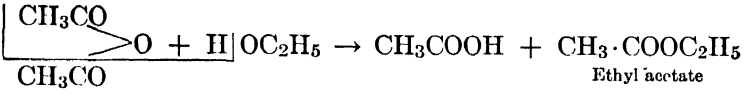
General Methods of Preparation.—1. By heating an acyl halide and the salt of an acid, e.g.,



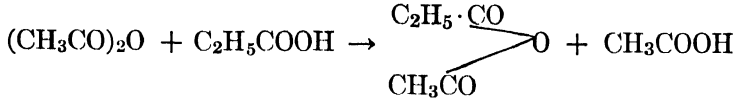
2. By the action of a dehydrating agent (such as P_2O_5) on the acid. Acetic anhydride may in this way be prepared from glacial acetic acid. However, the yield is poor.

Acetic anhydride is the most important member of the series and the general properties of these anhydrides can be illustrated by summarizing the properties of acetic anhydride. (Formic anhydride is not known.)

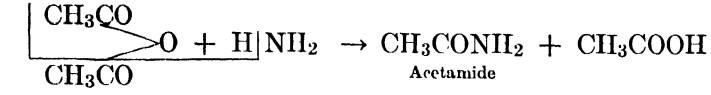
It has already been mentioned that acetic anhydride reacts with water to form acetic acid. With alcohol, a mixture of acid and ester is formed:



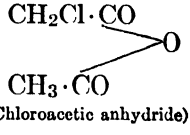
With propionic acid, a mixed anhydride is obtained:



With ammonia, the corresponding amide is formed:

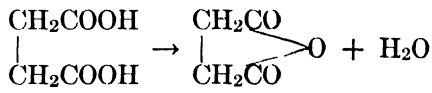


Chlorine and bromine yield substituted anhydrides; e.g.,

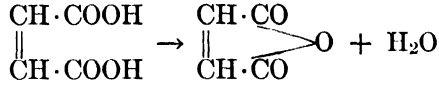


Acetic anhydride is a liquid with a pungent, suffocating odor. It finds extensive use as a means of introducing the CH_3CO (acetyl) group into compounds (for example, cellulose acetate.)

Succinic anhydride may be obtained by heating succinic acid:

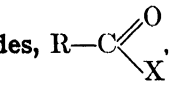


Similarly **maleic anhydride** may be obtained from maleic acid:



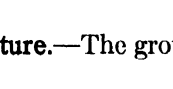
The properties of these compounds are analogous to acetic anhydride

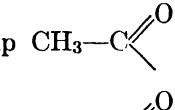
Acyl Halides

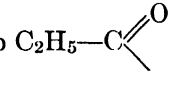
Acyl Halides,  , may be regarded as acids in which the OH of the COOH group is replaced by a halogen:

$$R \cdot COOH \rightarrow R \cdot COCl$$

(The acyl chloride compounds are common, but few of the corresponding iodide and bromide compounds are known, and they are used only infrequently.)

Nomenclature.—The group  is known as the "acyl" group.

The group  is known as the "acetyl" group.

The group  is known as the "propionyl" group.

Therefore, in naming the acyl halide, we need merely change the *ic* (last two letters) of the acid to *yl*.

(Formyl chloride is not known. When the attempt is made to prepare it, it breaks down into CO and HCl:

$$H \cdot COCl \rightarrow CO + HCl)$$

Acetyl chloride finds extensive use in organic syntheses and its preparation and properties will, therefore, be considered.

Preparation. 1. By the action of phosphorus pentachloride, phosphorus trichloride, or phosphorus oxychloride on acetic acid, or sodium acetate:

$$CH_3COOH + PCl_5 \rightarrow CH_3COCl + POCl_3 + HCl$$
$$CH_3COONa + PCl_5 \rightarrow CH_3COCl + POCl_3 + NaCl$$
$$3CH_3COOH + PCl_3 \rightarrow 3CH_3COCl + P(OH)_3$$

These reactions are analogous to those of $ROH \rightarrow RCl$. (See p. 43.)

2. The commercial method of obtaining the chloride is to heat sodium acetate and to pass sulfur dioxide and chlorine over it. The sulfur dioxide and chlorine combine to form sulfuryl chloride:

$$SO_2 + Cl_2 \longrightarrow SO_2Cl_2$$

which then reacts with the sodium acetate:

$$2CH_3COONa + SO_2Cl_2 \longrightarrow 2CH_3COCl + Na_2SO_4$$

3. $R\cdot COOH + \underset{\text{Thionyl chloride}}{SOCl_2} \longrightarrow R\cdot COCl + SO_2 + HCl.$

Properties.—Acetyl chloride is used extensively to introduce the $CH_3—C\langle^{O}$ (**acetyl**) group into organic compounds. It is a very reactive substance. The moisture of the atmosphere very readily converts it to acetic acid:

$$CH_3CO\boxed{Cl + H}OH \rightarrow CH_3COOH + HCl$$

Acetyl chloride reacts with sodium acetate to form acetic anhydride:

$$CH_3CO\boxed{Cl + Na}OOCCH_3 \rightarrow (CH_3CO)_2O + NaCl$$

and with ethyl alcohol to form an ester:

$$CH_3CO\boxed{Cl + H}OC_2H_5 \rightarrow \underset{\text{Ethyl acetate}}{CH_3\cdot COOC_2H_5} + HCl$$

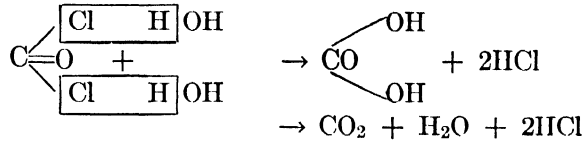
and with ammonia to form an amide:

$$CH_3CO\boxed{Cl + H}NH_2 \rightarrow \underset{\text{Acetamide}}{CH_3CONH_2} + HCl$$

If the OH groups in carbonic acid, $C\langle^{OH}_{OH}=O$ are replaced by Cl, we get $C\langle^{Cl}_{Cl}=O$ (chloro-formyl chloride), which is commonly known

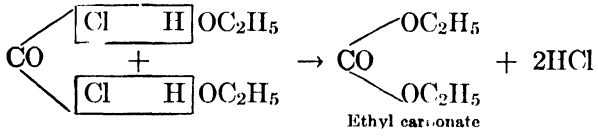
as **phosgene**. This substance is a colorless, suffocating gas. Owing to its poisonous character, the comparative ease with which it can be liquefied and prepared (by passing chlorine and carbon monoxide over charcoal), phosgene was used very extensively in the late war. It was loaded in shells and bombs and exploded when the shell struck ground. Phosgene is also used in the manufacture of dyes.

Water decomposes phosgene as follows:



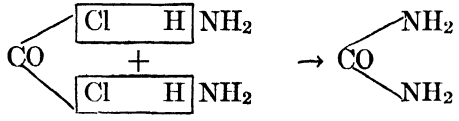
(The poisonous effects of phosgene are said to be due to the liberation of a high concentration of HCl gas.)

Ethyl alcohol forms an ester:

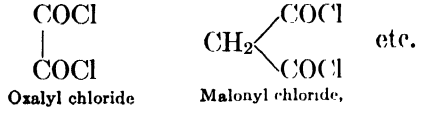


Ethyl carbonate

Ammonia transforms phosgene into urea (or carbamide):



Other acyl halides are:



Oxalyl chloride Malonyl chloride, etc.

Acid Amides

Acid Amides, R—C(=O)—NH_2, may be looked upon as acids in which the OH group is replaced by NH_2. Or, they may be regarded as derived from ammonia, NH_3, in which one of the hydrogen atoms is replaced by the RCO (acyl) group. The

—NH_2 group when attached to an acyl group is known as the "amido" group. If the —NH_2 group is attached to an alkyl group, it is known as the "amino" group.

The nomenclature is based on the names of the corresponding acids (amides of acids); e.g.,

$H \cdot CONH_2$, formamide

$CH_3 \cdot CONH_2$, acetamide

$C_2H_5 \cdot CONH_2$, propionamide

$C_3H_7 \cdot CONH_2$, butyramide, etc.

(With the exception of formamide, which is a liquid, all the others are solids.)

Preparation and Properties.—(**Acetamide** will be taken as a type.) 1. The action of ammonia on acetyl chloride:

$$CH_3CO\boxed{Cl + H}NH_2 \rightarrow CH_3CONH_2 + HCl$$

2. The partial hydrolysis of methyl cyanide:

$$CH_3CN + H_2O \rightarrow CH_3CONH_2$$

3. The action of ammonia on acetic anhydride:

$$\left|\begin{matrix} CH_3CO \\ \quad >O + H \\ CH_3CO \end{matrix}\right| NH_2 \rightarrow CH_3COOH + CH_3CONH_2$$

4. The dehydration of ammonium acetate (by heating):

$$CH_3CO\lfloor O \rfloor \overline{NH_2}\lfloor \underline{H_2} \rfloor \rightarrow CH_3CONH_2 + H_2O$$

Acetamide is transformed into ammonium acetate when boiled with acids or bases (compare with reaction 4 above):

$$CH_3CONH_2 + H_2O \rightarrow CH_3COONH_4$$

and when dehydrated forms methyl cyanide (compare with reaction 2 above);

$$CH_3CONH_2—H_2O \rightarrow CH_3CN$$

5. $CH_3CO\boxed{OC_2H_5 + H}NH_2 \rightarrow CH_3CONH_2 + C_2H_5OH$

Hofmann's reaction.—This is a method by which the CO group can be eliminated from an amide, so that $R \cdot CONH_2$ becomes RNH_2 (amine). When acetamide is treated with bromine in an alkaline solution the following reactions take place:

$$CH_3CONH_2 + Br_2 \rightarrow \underset{\text{Acetbromoamide}}{CH_3CONHBr} + HBr$$

$$CH_3CONHBr + 3KOH \rightarrow \underset{\text{Methylamine}}{CH_3NH_2} + KBr + K_2CO_3 + H_2O$$

Urea (carbamide or aminoformamide), $CO(NH_2)_2$, may be considered as the diamido derivative of carbonic acid, $CO(OH)_2$.

Its imide formula is

$$HN{=}C(NH_2)(OH)$$

This is a substance of great biological importance, since it is the chief end product resulting from the changes that proteins undergo in the body. (The amount of urea in the urine is directly proportional to the amount of protein present in the food which is eaten.)

Preparation.—1. By heating ammonium cyanate:

$$NH_4 \cdot CNO \rightleftarrows CO(NH_2)_2$$

This method was discovered by Wöhler in 1828. The student will recall that Wöhler's preparation is one of the earliest recorded instances of the laboratory preparation of an " organic " substance (p. 1).

2. By the action of ammonia on phosgene:

$$CO(Cl)(Cl) + 2NH_3 \rightarrow CO(NH_2)_2 + 2HCl$$

3. By the action of ammonia on ethyl carbonate:

$$CO(OC_2H_5)(OC_2H_5) + 2NH_3 \rightarrow CO(NH_2)_2 + 2C_2H_5OH$$

4. A very recent process depends upon the interaction of liquid NH_3 and liquid CO_2:

$$2NH_3 + CO_2 \rightarrow CO(NH_2)_2 + H_2O$$

This synthetic urea is now used extensively as a fertilizer.

Properties.—Urea is easily hydrolyzed, yielding carbon dioxide and ammonia. These same products are also obtained when the enzyme urease (found in the soya bean, etc.) is allowed to act on urea. (Incidentally, by far the best method for the determination of urea is based on its reaction with urease.) Nitrous acid liberates nitrogen, etc.:

$$CO(NH_2)_2 + 2HONO \rightarrow CO_2 + 2N_2 + 3H_2O$$

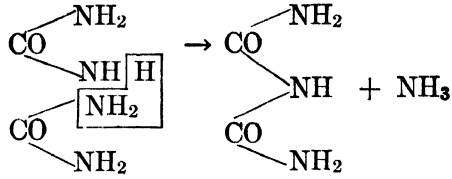
So does sodium hypobromite:

$$CO(NH_2)_2 + 3NaOBr \rightarrow CO_2 + N_2 + 3NaBr + 2H_2O$$

(This method was for a long time used to determine urea. The nitrogen evolved was measured, and from it the amount of urea in the sample was calculated. The determination at best is only approximate for the errors involved are high. The method has been entirely replaced by the urease method.)

Urea combines very readily with nitric and oxalic acids to form urea nitrate, $CO(NH_2)_2 \cdot HNO_3$, urea oxalate, $[CO(NH_2)_2]_2 \cdot (COOH)_2$, respectively. These salts crystallize very readily and are often used for identifying urea.

When urea is heated, two molecules combine to form a substance known as **biuret**:

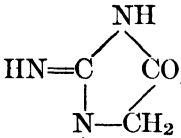


Biuret

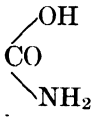
When a drop of copper sulfate and a few cc.'s of fairly concentrated alkali are added to biuret, a violet color is formed. This is known as the "biuret reaction." All proteins give the biuret reaction—a reason for assuming that the protein molecule has, among other things, a "biuret" configuration.

Urea combines with formaldehyde to form synthetic resins.

Guanidine, $HN{=}C(NH_2)(NH_2)$, is related to urea. **Creatine,** $HN{=}C(NH_2)(N(CH_3)-CH_2\cdot COOH)$, or methylguanidino-acetic acid is a constituent of muscle; and its anhydride, **creatinine,**

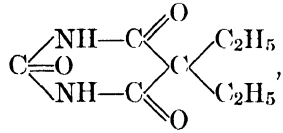


is a normal constituent of urine.

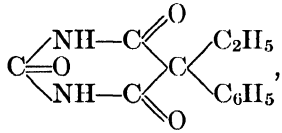


is carbamic acid.

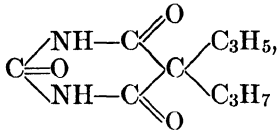
(A number of derivatives of urea, such as urethane, $CO(NH_2)(OC_2H_5)$, or ethyl carbamate, **barbital,**



or diethyl-malonyl urea, **luminal,**

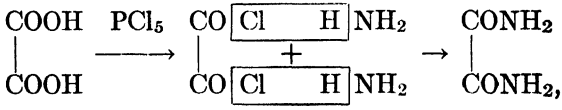


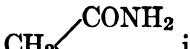
or phenyl ethyl malonyl urea, and **allonal,**

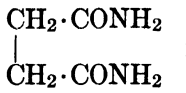


or allyl isopropyl malonyl urea (allyl isopropyl barbituric acid), are used extensively as hypnotics.)

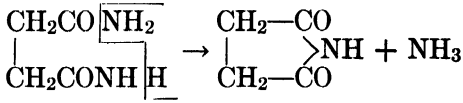
Oxamide, $CONH_2 \mid CONH_2$, is formed as follows:




is malonamide,


is succinamide

When succinamide is heated, we get succinimide, the $\rangle NH$ group being known as the imido group:



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SHONLE—Hypnotic Action and Chemical Structure. *Industrial and Engineering Chemistry*, **23**, 1104 (1931).

CHAPTER XII

HALOGEN SUBSTITUTED ACIDS AND HYDROXY ACIDS

THESE are acids in which one or more of the hydrogen atoms in the group, which is attached to the COOH group, is replaced by X, OH, CN, NH_2, etc. For example, $CH_2 \cdot COOH$ (with H), acetic acid, gives rise to

$CH_2 \cdot COOH$	$CH_2 \cdot COOH$	$CH_2 \cdot COOH$	$CH_2 \cdot COOH$
Cl	OH	NH_2	CN
Chloroacetic acid	Hydroxyacetic acid	Aminoacetic acid	Cyanoacetic acid

HALOGEN SUBSTITUTED ACIDS

Preparation.—The action of chlorine on acetic acid:

$$CH_3COOH + Cl_2 \rightarrow CH_2ClCOOH + HCl$$

$$CH_3COOH + 2Cl_2 \rightarrow \underset{\text{Dichloroacetic acid}}{CHCl_2COOH} + 2HCl$$

$$CH_3COOH + 3Cl_2 \rightarrow \underset{\text{Trichloroacetic acid}}{CCl_3COOH} + 3HCl$$

(The number of hydrogen atoms replaced by chlorine atoms depends upon the amount of chlorine used, the temperature and the time of the reaction. These reactions are carried out in the presence of sunlight and "carriers"—catalysts—such as iodine or sulfur.)

Analogous compounds may be formed by substituting bromine for chlorine, but here the reaction proceeds only under pressure and at higher temperatures. Iodine does not react. (In order to make such a substance as iodoacetic acid, we allow potassium iodide to react with chloroacetic acid: $CH_2Cl \cdot COOH + KI \rightarrow CH_2I \cdot COOH + KCl$.)

Better yields are obtained in the following way:

$$3CH_3\cdot COOH + PBr_3 \rightarrow 3CH_3\cdot COBr + P(OH)_3$$

$$CH_3\cdot COBr + Br_2 \rightarrow \underset{\text{Bromoacetyl bromide}}{CH_2Br\cdot COBr} + HBr$$

$$CH_2Br\cdot COBr + H_2O \rightarrow CH_2Br\cdot COOH + HBr$$

Direct halogenation always replaces the hydrogen attached to the α-carbon. The nomenclature may be gathered from this graphic illustration:—$\underset{\delta}{CH_2}—\underset{\gamma}{CH_2}—\underset{\beta}{CH_2}—\underset{\alpha}{CH_2}—COOH$.

The β-halogenated acids may be obtained in the following way:

$$\underset{\text{Acrylic acid}}{CH_2{=}CH\cdot COOH} + HBr \rightarrow \underset{\beta\text{-Bromopropionic acid}}{\begin{matrix}CH_2\cdot CH_2COOH\\ |\\ Br\end{matrix}}$$

(The halogen enters the position as far removed from the COOH group as possible.)

α- and β-halogenated acids may be prepared thus:

$$CH_2{=}CHCOOH + Br_2 \rightarrow \underset{\alpha,\,\beta\text{-Dibromopropionic acid}}{\begin{matrix}CH_2—CHCOOH\\ |\quad\ |\\ Br\quad Br\end{matrix}}$$

Halogenated acids may also be prepared from hydroxy-acids:

$$\underset{\beta\text{-Hydroxypropionic acid}}{\begin{matrix}CH_2\cdot CH_2COOH\\ |\\ OH\end{matrix}} + PCl_5 \rightarrow \underset{\beta\text{-Chloropropionyl chloride}}{\begin{matrix}CH_2—CH_2COCl\\ |\\ Cl\end{matrix}}$$

$$+ H_2O \rightarrow \underset{\beta\text{-Chloropropionic acid}}{\begin{matrix}CH_2—CH_2COOH\\ |\\ Cl\end{matrix}}$$

Properties.—Some of the properties (such as the formation of salts, esters, etc.) are due to the presence of a carboxyl group and some to the radical attached to the carboxyl group. For example, the greater the number of halogens attached to the carboxyl group, the stronger the acidity. Trichloroacetic acid,

CCl_3COOH, is a strong acid. The α-halogen acids in the presence of hot alkali yield the corresponding hydroxy-acids:

$$\begin{matrix} CH_2COOH \\ | \\ Cl \end{matrix} + HOH \rightarrow \begin{matrix} CH_2COOH \\ | \\ OH \end{matrix} + HCl$$

The β-halogen acids yield unsaturated acids when heated with water or alcoholic KOH; e.g.,

$$CH_3 \cdot \underset{\lceil Cl}{CH} - \underset{H \rfloor}{CH} \cdot COOH \rightarrow CH_3 \cdot CH{=}CH \cdot COOH$$

Butenoic acid (Crotonic acid)

(In certain cases—where, for example, sodium carbonate is used—CO_2 is also evolved, so that butenoic acid is converted to the corresponding unsaturated hydrocarbon, $CH_3 \cdot CH{=}CH_2$.)

The γ-halogen acids form with water inner anhydrides or lactones; e.g.,

$$\begin{matrix} CH_2 \cdot CH_2 \cdot CH_2 \cdot COOH \\ | \\ Cl \end{matrix} \xrightarrow{H_2O} \begin{matrix} CH_2 - CH_2 - CH_2 \cdot CO \lceil OH \\ | \qquad\qquad\qquad\quad | \\ O \lfloor H \end{matrix}$$

γ-Chlorobutyric acid

$$\rightleftarrows CH_2 \cdot CH_2 \cdot \underset{\lfloor\!\!\lfloor}{CH_2} - \underset{\rfloor\!\!\rfloor}{C}{=}O$$

Butyrolactone

With ammonia, the halogen-substituted acids form amino-acids:

$$CH_2Cl \cdot COOK + HNH_2 \rightarrow CH_2NH_2 \cdot COOK \rightarrow CH_2NH_2 \cdot COOH$$

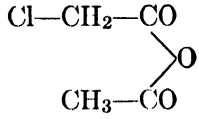
With potassium cyanide, we get the cyano-acids; e.g.,

$$CH_2Cl \cdot COOK + KCN \rightarrow CH_2CN \cdot COOK \rightarrow CH_2CN \cdot COOH$$

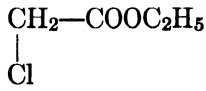
Very many of these halogen-substituted products are known. Chloroacetic acid, $CH_2Cl \cdot COOH$, is used in the manufacture of synthetic indigo. The vapors attack the eyes, and they also act corrosively on the skin. Trichloroacetic acid, $CCl_3 \cdot COOH$, also acts corrosively on the skin and is used to remove warts and other growths. It has recently come into use as a protein precipitant. When boiled with water we get chloroform:

$$CCl_3 \cdot COOH \rightarrow CHCl_3 + CO_2$$

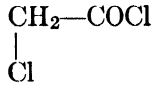
Many other halogenated acids of higher molecular weight are known. It is also possible to have halogenated acid derivatives. For example,



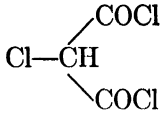
Chloroacetic anhydride



Ethyl chloroacetate



Chloroacetyl chloride



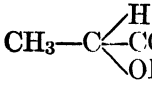
Chloromalonyl chloride

etc.

Hydroxy Acids

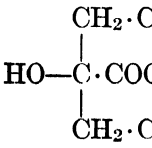
, carbonic acid or hydroxyformic acid

, hydroxyacetic acid or glycolic acid

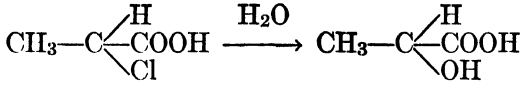
 , α-hydroxypropionic acid or lactic acid.

, hydroxysuccinic acid or malic acid.

, dihydroxysuccinic acid or tartaric acid.

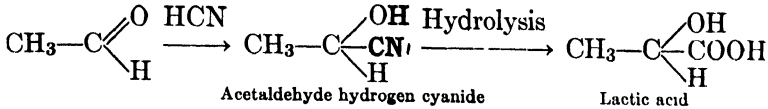
 , citric acid.

General Methods of Preparation.—1. Hydrolysis of halogen acids (base); e.g.,



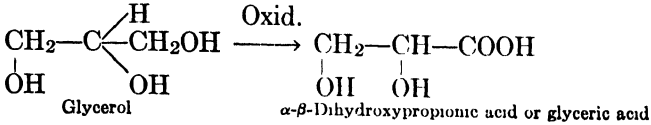
α-Chloropropionic acid — α-Hydroxypropionic acid or lactic acid

2. The hydrolysis of the addition product formed when hydrogen cyanide reacts with an aldehyde; e.g.,



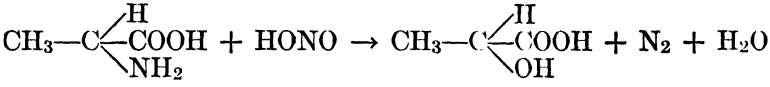
Acetaldehyde hydrogen cyanide — Lactic acid

3. The oxidation of a primary alcohol containing another hydroxyl group; e.g.,



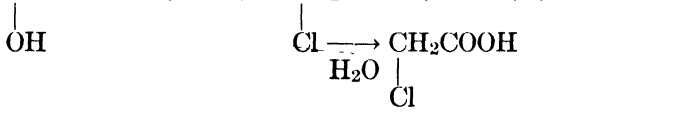
Glycerol — α-β-Dihydroxypropionic acid or glyceric acid

4. Action of nitrous acid on amino-acids; e.g.,

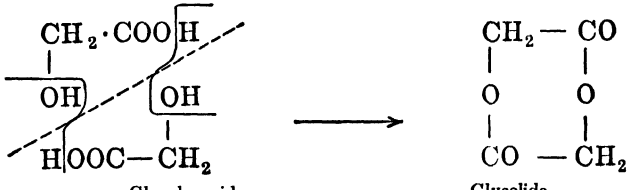


α-Aminopropionic acid

Properties.—As might be expected, these compounds show the properties both of hydroxy and carboxylic substances. The chloro-acids are formed with PCl_5; e.g.,



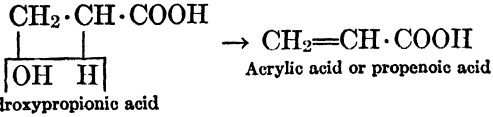
When the α-hydroxy-acids are heated, two molecules unite with the elimination of two molecules of water:



Glycolic acid — Glycolide

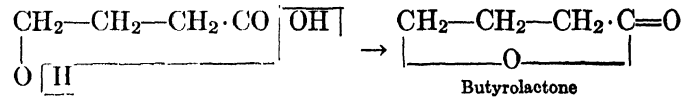
In a similar manner lactic acid is converted to lactide.

When β-hydroxy acids are heated, we get unsaturated acids; e.g.,



β-Hydroxypropionic acid — Acrylic acid or propenoic acid

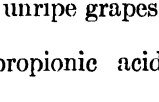
When γ-hydroxyacids are heated an inner anhydride (lactone) is formed; e.g.,



Butyrolactone

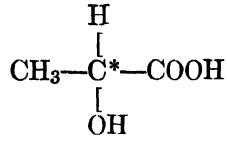
This is also true of δ-hydroxyacids.

Hydroxyacetic acid, $CH_2OH \cdot COOH$ (also known as **glycolic acid**) occurs in unripe grapes.

α-Hydroxypropionic acid,  (better known as **lactic acid**), is known in three forms, the dextro and levo optically active modifications, and the racemic, or inactive form (which can, however, be resolved into the two optically active forms).

Optical Activity.—Three forms of lactic acid are known. These three varieties have the same chemical and physical properties but behave quite differently towards polarized light. One turns the plane of polarized light to the right (and is, therefore, known as dextro, or *d*-lactic acid); the other turns it to the left (levo, or *l*-variety); and the third is inactive (*dl*). This last is made up of equal parts of the dextro and levo forms.[1]

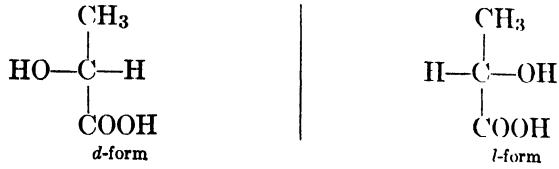
Le Bel and van't Hoff, quite independently of one another, discovered that all optically active substances have at least one carbon in the molecule attached to four different atoms or groups. For example, in lactic acid:



we have a carbon atom marked* which is attached to H, OH, CH_3 and COOH. Such a carbon atom is known as an **asymmetric carbon atom.**

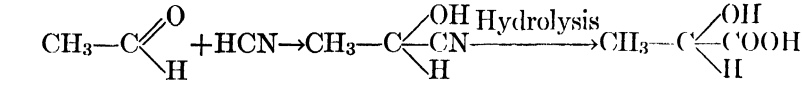
[1] By polarized light we mean light in which all the vibrations lie in one plane. An ordinary ray of light vibrates in every direction. Polarized light may be obtained by passing ordinary light through a Nicol prism or tourmaline plate—as illustrated in the instrument known as the "polarimeter." An optically active substance has the power of rotating this plane of polarized light, the extent depending, among other things, upon the nature of the substance. For further details, consult a practical physical chemistry; for example, Firth—Practical Physical Chemistry.

Structurally, the *d*-form of lactic acid is related to the *l*-form as an object is to its mirror image:



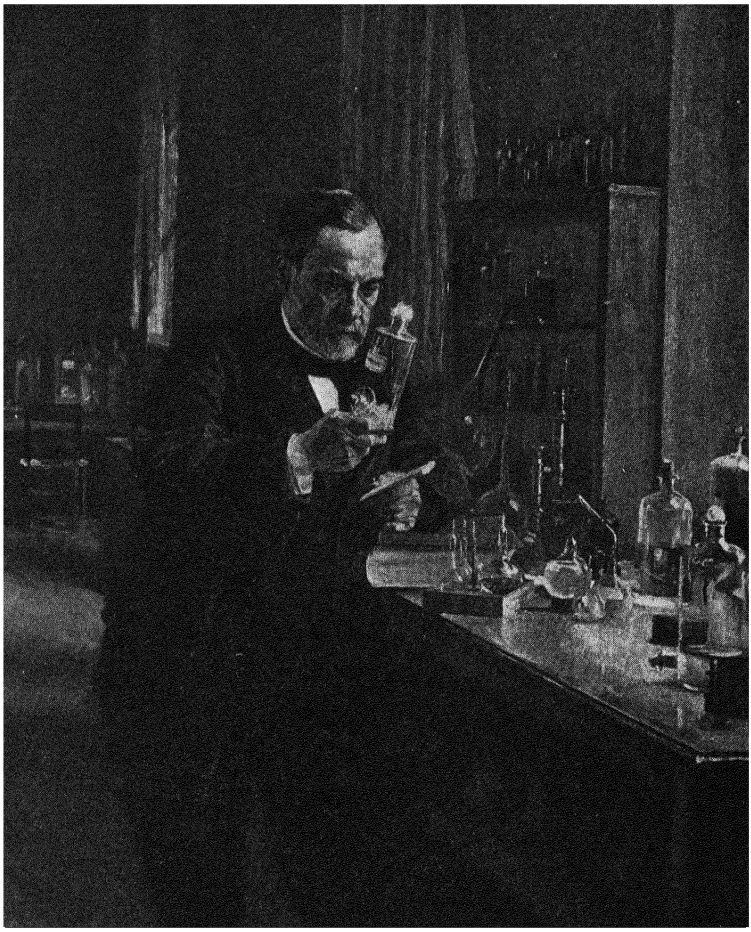
Usually, when a compound containing an asymmetric carbon atom is synthesized, we get equal parts of the dextro and levo varieties. Such a mixture is designated as *dl*-, or *i* (inactive), and is known as "racemic." This inactive mixture can, as a rule, be resolved into the active constituents in a number of different ways. One of these depends upon the property which certain organisms possess of destroying one component more rapidly than another. For example, bacteria destroy the *l*-lactic acid and penicillium the *d*-lactic acid.

The souring of milk is due to the formation of lactic acid (the inactive variety), and this is brought about by the action of certain bacteria (which are also present in the air) on the milk sugar or lactose present in the milk. The acid so formed precipitates the principal protein (caseinogen) in milk, giving rise to what is known as "curdling." The synthetic lactic acid of commerce is prepared from acetaldehyde, as follows:



Lactic acid is manufactured in the United States by the comparatively high temperature fermentation of cane or beet sugar, corn starch or corn sugar, by a pure culture of lactic acid bacteria. It is a colorless, viscous liquid and is used in medicine, dyeing and calico printing. The antimony, zinc and iron lactates are used as mordants. Silver lactate is a powerful antiseptic. Ethyl lactate is one of the best solvents for nitrocellulose and is therefore extensively used in the lacquer industry.

Dextro-lactic acid, or *d*-lactic acid (also called sarcolactic acid and paralactic acid) is found in muscle tissue, meat extract, blood and urine. Inactive muscle is alkaline and after activity it becomes acid, a change which has been ascribed to the formation



LOUIS PASTEUR (1822–1895)

CHEMIST, FOUNDER OF THE MODERN SCIENCE OF BACTERIOLOGY AND ONE OF THE GREATEST SCIENTISTS OF ALL TIMES. ONE OF HIS EARLIEST RESEARCHES DEALT WITH THE CRYSTALLINE FORMS OF TARTARIC ACID AND ITS SALTS (P. 132), AND THIS LED DIRECTLY TO LE BEL AND VAN'T HOFF'S CONCEPTION OF STEREOISOMERISM.

of lactic acid. When the *d*-acid is heated it loses its optical activity and is converted to the inactive or *dl*-variety.

Levo-lactic acid, or *l*-lactic acid, is obtained when sugar is fermented with *bacillus acidi levolactici.*

The *d*- and *l*- lactic acids and the *dl*- or *i*- variety show the same physical and chemical properties; they differ only as regards optical activity.

(The intermediate changes that proteins, fats and particularly sugars undergo in the body in their ultimate breakdown to carbon dioxide, water and simple nitrogenous bodies, are associated with the formation, it is believed, of lactic acid, among other substances. The evidence is accumulating to show that lactic acid is an important intermediate product in the decomposition within the body of the common foodstuffs.)

(An isomer of lactic acid is β-hydroxypropionic acid, or hydracrylic acid, $\begin{matrix}CH_2\text{—}CH_2\cdot COOH\\ |\\ OH\end{matrix}$, in which the hydroxyl group is in the β-position.)

Hydroxysuccinic acid, $\begin{matrix}CH_2\cdot COOH\\ |\\ CH(OH)\cdot COOH\end{matrix}$ (commonly known as **malic acid**) is present in unripe apples, cherries, grapes, etc. It may be prepared from bromosuccinic acid by the action of silver hydroxide:

$$\begin{matrix}CH_2\cdot COOH\\ |\\ CH\cdot COOH\\ |\\ Br\end{matrix} + AgOH \rightarrow \begin{matrix}CH_2\cdot COOH\\ |\\ CH\cdot COOH\\ |\\ OH\end{matrix} + AgBr$$

The commercial method of preparation is from maleic acid:

$$\begin{matrix}CH\cdot COOH\\ \|\\ CH\cdot COOH\end{matrix} + HOH \rightarrow \begin{matrix}CH_2\cdot COOH\\ |\\ CH\cdot COOH\\ |\\ OH\end{matrix}$$

Malic acid is optically active and has the general properties of hydroxy acids.

Dihydroxysuccinic acid, $\begin{matrix}CH(OH)\cdot COOH\\ |\\ CH(OH)\cdot COOH\end{matrix}$ (commonly known as **tartaric acid**), contains two hydroxyl groups and is a dibasic

acid. It can be prepared from dibromosuccinic acid by the action of silver hydroxide:

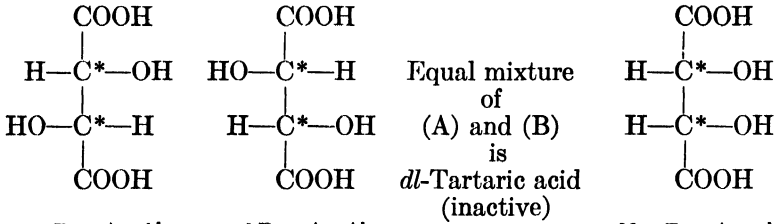
$$\begin{matrix}\mathrm{CHBr\cdot COOH}\\ |\\ \mathrm{CHBr\cdot COOH}\end{matrix} + 2\mathrm{AgOH} \rightarrow \begin{matrix}\mathrm{CH(OH)\cdot COOH}\\ |\\ \mathrm{CH(OH)\cdot COOH}\end{matrix} + 2\mathrm{AgBr}$$

The reduction of tartaric acid (with hydrogen iodide) first yields malic acid and then succinic acid. Interesting, also, is the fact that maleic acid, or fumaric acid, representing the unsaturated dibasic acids, may be converted to tartaric acid by oxidation with potassium permanganate:

$$\begin{matrix}\mathrm{CH\cdot COOH}\\ ||\\ \mathrm{CH\cdot COOH}\end{matrix} + \mathrm{H_2O} + \mathrm{O} \rightarrow \begin{matrix}\mathrm{CH(OH)\cdot COOH}\\ |\\ \mathrm{CH(OH)\cdot COOH}\end{matrix}$$

Maleic acid or fumaric acid

The following four forms of tartaric acid are known:



d-Tartaric acid (A) | *l*-Tartaric acid (B) | (C) | *Meso*-Tartaric acid (D)

Thus we have two forms of tartaric acid which are optically active [(*A*) and (*B*)]; and two which are optically inactive [(*C*) and (*D*)]. (*A*) is the mirror image of (*B*), while in (*D*) the upper part of the graphic formula is a mirror image of the lower part. (*C*) can be resolved into the *d*- and *l*-forms, while (*D*) cannot. (*C*) is said to be optically inactive by external compensation, while (*D*) is optically inactive by internal compensation.

d-Tartaric acid is the one found in grapes in the form of potassium acid tartrate. *l*-Tartaric acid may be obtained from the inactive form by " splitting " or resolution into the active isomers.

Racemic (inactive) or *dl*-acid, is found in grapes and is formed when the *d*-acid is boiled with NaOH solution. It may be resolved into the *d*- and *l*-forms.

A fourth variety, meso-tartaric acid (first prepared by Pasteur by heating the cinchonine salt of *d*-tartaric acid) is also inactive, but, unlike the racemic acid, cannot be resolved into the *d*- and *l*-forms.

(The history of tartaric acid is intimately associated with the development of our ideas of optical activity and of the asymmetric carbon atom; and with these ideas the names of Pasteur, van't Hoff and Le Bel will forever be linked. It was Pasteur who first showed that the racemic acid was really a mixture of two types of crystals, one the image of the other, and that when mechanically separated and dissolved in water, the one type turned polarized light to the right and the other turned it to the left, suggesting at once that the racemic acid was really a mixture of the *d*- and *l*-forms. The later researches of van't Hoff and Le Bel connected optical activity with the presence of one or more asymmetric carbon atoms within the molecule. There are two asymmetric carbon atoms in the molecule of tartaric acid; these have already been referred to.)

Salts of Tartaric Acid. — Potassium acid tartrate, $\begin{matrix}CH(OH)\cdot COOK\\ |\\ CH(OH)\cdot COOH\end{matrix}$ (also known as **cream of tartar**) is a constituent of baking powders, and is used in dyeing.

Sodium potassium tartrate, $\begin{matrix}CH(OH)\cdot COOK\cdot 4H_2O\\ |\\ CH(OH)\cdot COONa\end{matrix}$ (commonly known as **Rochelle salt**), is a constituent of Fehling's solution and is also used as a purgative (in " Seidlitz " powders).

Potassium antimonyl tartrate, $\begin{matrix}CH(OH)\cdot COOK\\ |\\ CH(OH)\cdot COO(SbO)\end{matrix}$ (also known as **tartar emetic**), is used in medicine as an emetic, and also in dyeing.

Citric acid, $\begin{matrix}CH_2\cdot COOH\\ |\\ HO—C—COOH\cdot H_2O\\ |\\ CH_2\cdot COOH\end{matrix}$, is a monohydroxy tribasic acid, and is found in lemons (from the juice of which it is commonly prepared), berries, limes and other acidulous fruits. It is also prepared on large scale by the fermentation of glucose or sucrose, by certain mould fungi as *citromycetes pfefferianus*. It is used in lemonade and other beverages, and in calico printing.

Magnesium citrate $(C_6H_5O_7)_2Mg_3$ is used as a laxative, and

ferric ammonium citrate, in blue-print paper manufacture and in calico printing. Sodium citrate is used extensively for the prevention of blood coagulation.

Acetoacetic acid, $CH_3 \cdot CO \cdot CH_2 \cdot COOH$, or acetyl acetic acid, and its ethyl ester, acetoacetic ester, $CH_3 \cdot CO \cdot CH_2 \cdot COOC_2H_5$ are here considered because the ester may be looked upon as a derivative of a β-hydroxy unsaturated acid:

$$CH_3 \cdot CO \cdot CH_2 \cdot COOC_2H_5 \quad \text{or} \quad CH_3 \cdot \underset{\displaystyle OH}{\overset{\displaystyle |}{C}} = CH \cdot COOC_2H_5$$

Acetoacetic acid is one of the "acetone bodies" present in the urine of persons suffering from diabetes, and it is commonly known as "diacetic acid." It is an unstable acid and decomposes into acetone:

$$CH_3 \cdot CO \cdot CH_2 \cdot \boxed{COO}H \rightarrow CH_3 \cdot CO \cdot CH_3 + CO_2$$

which explains the presence of acetone in the urine and breath of diabetics.

Acetoacetic ester, $CH_3 \cdot CO \cdot CH_2 \cdot COOC_2H_5$ (or, more correctly, ethyl acetoacetate) is a compound of considerable importance in synthetic organic chemistry. Claisen's explanation of its synthesis, which follows, is the one generally accepted to-day:

1. $2C_2H_5OH + 2Na \rightarrow 2C_2H_5ONa + H_2$

2. $CH_3-C(=O)-OC_2H_5 + NaOC_2H_5 \rightarrow CH_3-C(ONa)(OC_2H_5)(OC_2H_5)$

3. $CH_3-C(ONa)(OC_2H_5)(OC_2H_5) + H-CH \cdot COOC_2H_5 \rightarrow CH_3-C(ONa)=CHCOOC_2H_5 + 2C_2H_5OH$

Sodium acetoacetic ester

4. $CH_3-C(ONa)=CHCOOC_2H_5 + CH_3COOH \rightarrow CH_3-C(OH)=CHCOOC_2H_5 + CH_3COONa$

Acetoacetic ester

Tautomeric forms:

$$CH_3-C(OH)=CHCOOC_2H_5 \rightleftarrows CH_3-C(=O)-CH_2COOC_2H_5$$

Enolic Ketonic

Acetoacetic ester is prepared by the action of sodium on ethyl acetate. A small amount of alcohol is needed for reaction (1); additional quantities of alcohol are formed as shown in (3). The enolic form $\left(-C(OH)=CH-\right)$, first produced [see (4)], rearranges to the more stable keto form $\left(-C(=O)-CH_2-\right)$. An equilibrium mixture of the enolic and ketonic forms contains 7 per cent and 93 per cent respectively.

(The type of isomerism wherein, under certain conditions, a compound passes from one structural form into another, is known as **tautomerism.**)

This is characteristic of many compounds having the carbonyl group attached to a carbon or nitrogen atom to which also one or more hydrogens are attached.

$$\underset{\text{Ketonic form}}{-C(=O)-CH_2-} \rightleftarrows \underset{\text{Enolic form}}{-C(OH)=CH-}$$

$$\underset{\text{Lactam form}}{-C(=O)-NH-} \rightleftarrows \underset{\text{Lactim form}}{-C(OH)=N-}$$

Acetoacetic ester is a colorless liquid with a fruity odor.

Uses of Acetoacetic Ester.—Depending upon the reagents used, as well as the concentration of solutions, the following two types of decomposition take place:

(*a*) *Ketonic hydrolysis:*

$$CH_3\cdot CO\cdot \underset{H}{CH_2}\cdot \underset{O}{CO}\cdot \underset{H}{O\cdot C_2H_5} \xrightarrow[\text{acids or alkalies}]{\text{Dil. aqueous or alc.}} CH_3\cdot CO\cdot CH_3 + CO_2 + C_2H_5OH$$

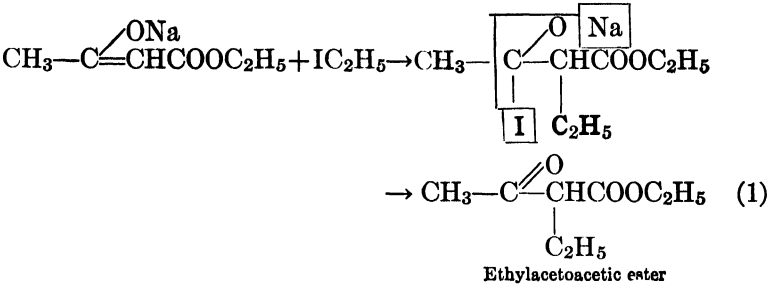
(*b*) *Acid hydrolysis:*

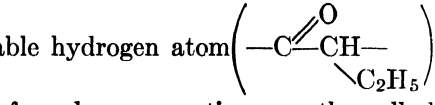
$$CH_3\cdot \underset{HO}{CO}\cdot \underset{H}{CH_2}\cdot \underset{HO}{CO}\cdot \underset{H}{O\cdot C_2H_5} \xrightarrow[\text{Conc. aqueous KOH}]{\text{Conc. alc. KOH or}} CH_3COOH + CH_3COOH + C_2H_5OH$$

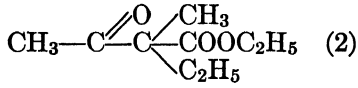
One or both hydrogens in the $-CO\cdot CH_2-$ part of the acetoacetic ester may be replaced by various groups, giving rise to substituted acetoacetic ester derivatives. (A somewhat analogous

case may be found in malonic ester, p. 103.) If one mole of sodium ethylate reacts with one mole of acetoacetic ester, the compound

is produced. This reacts with an alkyl halide, for example, as follows:



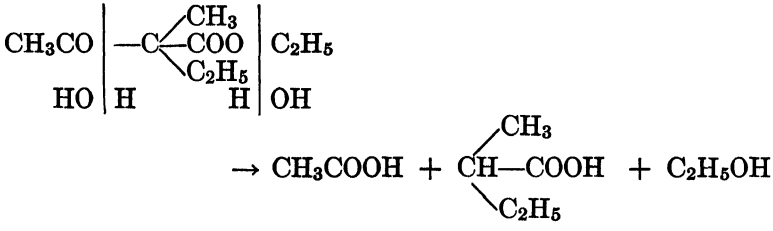
(1) still contains a replaceable hydrogen atom  and by means of a series of analogous reactions another alkyl group may be introduced, giving, for example:



Ethylmethylacetoacetic ester

On *acid hydrolysis*, (1) decomposes thus:

and (2):



which means that we are able to build up (synthesize) monobasic acids of the types R—CH_2COOH and $\begin{matrix}R\\R\end{matrix}\!\!>\!CHCOOH$.

On *ketonic hydrolysis*, (1) decomposes thus

$$\begin{matrix}CH_3COCH—\\ \quad\vert\\ \quad C_2H_5\\ \quad\quad H\end{matrix}\!\!\begin{vmatrix}CO\\ \\ O\end{vmatrix}\!\!\begin{matrix}OC_2H_5\\ \\ H\end{matrix} \rightarrow CH_3\cdot CO\cdot CH_2\cdot C_2H_5 + CO_2 + C_2H_5OH$$

and (2):

$$\begin{matrix}CH_3CO—C\begin{matrix}CH_3\\ \diagdown\\ C_2H_5\end{matrix}\\ \quad\quad\quad H\end{matrix}\!\!\begin{vmatrix}CO\\ \\ O\end{vmatrix}\!\!\begin{matrix}OC_2H_5\\ \\ H\end{matrix}$$

$$\rightarrow CH_3\cdot CO\cdot C\begin{matrix}CH_3\\ \diagdown\\ H\\ \diagdown\\ C_2H_5\end{matrix} + CO_2 + C_2H_5OH$$

which means that we are able to synthesize higher ketones of the types R—CO—$\begin{matrix}CH_2\\ \diagdown\\ R\end{matrix}$ and R·CO·$\begin{matrix}CH\\ \diagdown\\ R'\end{matrix}\!\!\begin{matrix}\diagup R\\ \\ \end{matrix}$.

(Acetoacetic ester is also used in the manufacture of antipyrine—p. 306—and a number of dyes.)

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CHAPTER XIII

AMINES OR ORGANIC BASES

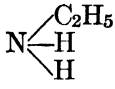
THESE compounds are derivatives of ammonia:

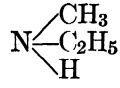
Ammonia

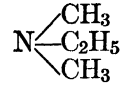
Primary amine

Secondary amine

Tertiary amine

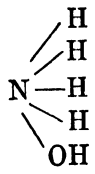

Ethylamine

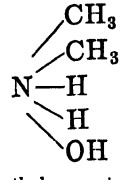

Ethyl methyl-amine

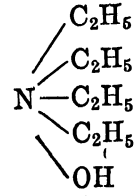

Dimethyl ethylamine

(In $R \cdot NH_2$ the $-NH_2$ is an amino group, in the $=NH$ is an imino group).

We have similar relationships in NH_4OH, where one or more hydrogens in the NH_4 group may be replaced by R groups.


Ammonium hydroxide


Dimethylammonium hydroxide

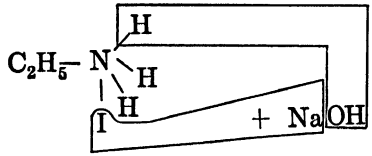

Tetraethylammonium hydroxide

Methods of Preparation of Primary Amines.—1. Theoretically the simplest method should involve the reaction between ammonia and an alkyl halide:

$$C_2H_5\boxed{I + H}NH_2 \rightarrow C_2H_5NH_2 + HI$$

but due to the basicity of $C_2H_5 \cdot NH_2$, an addition compound ($C_2H_5NH_3I$, ethylammonium iodide) is first formed, which may

be decomposed by means of alkali just as an ammonium salt may be decomposed by means of alkali:



$$\rightarrow C_2H_5NH_2 + H_2O + NaI$$

(This method is little used because of complicated secondary reactions which take place (p. 140)).

2. The action of bromine and a strong base on an amide, e.g.,

$$CH_3 \cdot CONH_2 + Br_2 + NaOH \rightarrow CH_3—CO—N\begin{matrix}H\\Br\end{matrix}$$

Acetamide — Acetbromoamide

$$CH_3CO \cdot NHBr + 3NaOH \rightarrow \underset{\text{Methylamine}}{CH_3NH_2} + Na_2CO_3 + NaBr + H_2O$$

In brief, $CH_3 \cdot CONH_2 \rightarrow CH_3 \cdot NH_2$

(This is known as the *Hofmann* reaction.)

Notice that the conversion of acetamide to methylamine involves the loss of a carbon atom. The *Hofmann* reaction is often used in the conversion of one member of a series to another containing one less carbon atom. (See indigo, p. 309.)

3. The reduction of alkyl cyanides; e.g.,

$$\underset{\text{Methyl cyanide}}{CH_3CN} + 2H_2 \rightarrow \underset{\text{Ethylamine}}{CH_3 \cdot CH_2 \cdot NH_2}$$

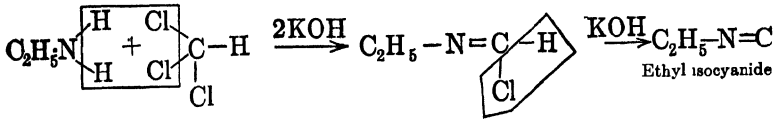
Properties of Primary Amines.—These compounds are more basic than ammonia and are readily soluble in water. They have a strong, fish-like odor, and their vapors are flammable. They combine with acids, giving such compounds as methylammonium bromide, $CH_3NH_2 \cdot HBr$; methylammonium nitrate, $CH_3NH_2 \cdot HNO_3$, and methylammonium sulfate $(CH_3NH_2)_2 \cdot H_2SO_4$.

The amines are acted upon by nitrous acid, yielding the corresponding hydroxy compounds:

$$CH_3 \cdot NH_2 + HONO \rightarrow CH_3OH + N_2 + H_2O$$

(The *Van Slyke* method for determining the rate of hydrolysis of a protein is based on this reaction. See under amino acids, p. 146.)

Chloroform and alcoholic potassium hydroxide react with primary amines with the formation of isocyanides (isonitriles).



(This is known as the **carbylamine reaction** and is used to distinguish primary from secondary and tertiary amines. The isocyanides have characteristic and highly disagreeable odors.)

Methylamine is a common constituent of many putrefactive mixtures.

Secondary and tertiary amines may be obtained by the following series of reactions:

$$CH_3NH_2 + ICH_3 \rightarrow CH_3{-}N(H)(H)(CH_3)\,I$$

Dimethylammonium iodide

$$(CH_3)_2NH\cdot HI + NaOH \rightarrow (CH_3)_2NH + NaI + H_2O$$

Dimethylamine (a secondary amine)

$$(CH_3)_2NH + ICH_3 \rightarrow (CH_3)_3N\cdot HI$$

Trimethylammonium iodide

$$(CH_3)_3N\cdot HI + NaOH \rightarrow (CH_3)_3N + NaI + H_2O$$

Trimethylamine (a tertiary amine)

(Trimethylamine can combine with methyl iodide to form tetramethylammonium iodide $(CH_3)_4\cdot N\cdot I$. Since the reactions given above proceed more or less simultaneously, it becomes somewhat difficult to separate the different amines.)

(For another method see p. 240.)

The physical properties of the secondary and tertiary amines are similar to those of the primary amines. Dimethylamine is used in the manufacture of rubber accelerators. Trimethylamine is produced by the destructive distillation of the residue obtained in the sugar beet industry. They, and the primary compound, are found in herring brine and in the products obtained from the distillation of nitrogenous substances.

By the action of ammonia on ethylene oxide we get the following:

$HO \cdot CH_2 \cdot CH_2 \cdot NH_2$, monoethanolamine
$(HO \cdot CH_2 \cdot CH_2)_2NH$, diethanolamine
$(HO \cdot CH_2 \cdot CH_2)_3N$, triethanolamine

These compounds are viscous, hydroscopic liquids. They are organic bases of mild alkalinity and react with fatty acids to produce soaps which are used in dry cleaning. These soaps are excellent emulsifying agents. Triethanolamine is a very good absorbent for acid gases.

The Action of Nitrous Acid on Primary, Secondary and Tertiary Amines.—It has already been stated that the action of nitrous acid on a primary amine forms the corresponding hydroxy compound: e.g.,

$$C_2H_5 \cdot NH_2 + HONO \rightarrow C_2H_5OH + N_2 + H_2O$$

With secondary amines, nitrous acid forms nitroso compounds e.g.,

$$(C_2H_5)_2N\boxed{H + HO}NO \rightarrow \underset{\text{Diethylnitrosoamine}}{(C_2H_5)_2N{-}NO} + H_2O$$

(The nitroso-compounds are usually yellow-colored, volatile liquids of aromatic odor.)

Tertiary compounds do not react with nitrous acid (though oxidation of an indefinite type may take place).

Nitrous acid is, therefore, used to distinguish the amines. (The "carbylamine reaction" given above, p. 140, is specific for primary amines.)

"Quaternary bases" are compounds related to ammonium hydroxide; e.g.,

$$NH_4OH \rightarrow \underset{\substack{\text{Tetramethylammonium}\\ \text{hydroxide}}}{N(CH_3)_4 \cdot OH}$$

(Choline, neurine and muscarine, compounds of physiological importance—See Chapter X—may be regarded as derivatives of quaternary bases.)

Tetramethylammonium hydroxide may be prepared thus:

$$N(CH_3)_4\boxed{I + Ag}OH \rightarrow N(CH_3)_4OH + AgI$$

It is a colorless, hygroscopic solid, the solution of which is strongly basic, resembling potassium hydroxide. When heated, it decomposes into trimethylamine:

$$N(CH_3)_4OH \rightarrow N(CH_3)_3 + CH_3OH$$

which is really a very good method for the preparation of tertiary amines.

Compounds containing two amino groups are known as diamines: Ethylenediamine may be made from ethylene bromide:

$$\begin{matrix}CH_2Br\\|\\CH_2Br\end{matrix} + \begin{matrix}HNH_2\\\\HNH_2\end{matrix} \rightarrow \begin{matrix}CH_2\cdot NH_2\\|\\CH_2\cdot NH_2\end{matrix} + 2HBr$$

Trimethylene diamine has the formula $CH_2\begin{matrix}\diagup CH_2\cdot NH_2\\\diagdown CH_2\cdot NH_2\end{matrix}$

Tetramethylene diamine, $\begin{matrix}CH_2\cdot CH_2\cdot NH_2\\|\\CH_2\cdot CH_2\cdot NH_2\end{matrix}$ or **putrescine,** and pentamethylenediamine, $(CH_2)_5(NH_2)_2$, or **cadaverine**, are putrefactive products of the corresponding amino acids, ornithine and lysine (p. 148), and are found among the putrefactive products in the intestine. It is the belief that the putrefactive products in the intestine are formed by the action of bacteria on various amino acids, which are converted into the corresponding amines by loss of CO_2; e.g.,

$$\begin{matrix}CH_2\cdot NH_2\\|\\(CH_2)_3\\|\\CH\cdot NH_2\\|\\COOH\end{matrix} \rightarrow \begin{matrix}CH_2\cdot NH_2\\|\\(CH_2)_3\\|\\CH_2\cdot NH_2\end{matrix} + CO_2$$

α, ε-Diaminocaproic acid or Lysine

Cadaverine

(The chemical properties of the diamines are similar to the monoamines, except that as we have to consider two primary NH_2 groups instead of one NH_2 group.)

(For a group of compounds related to the amines and of great physiological importance, such as choline, neurine, lecithin, betaine and muscarine, see Chapter X, p. 110.)

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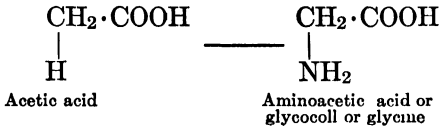
CHAPTER XIV

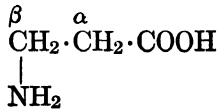
AMINO ACIDS AND PROTEINS

Amino Acids

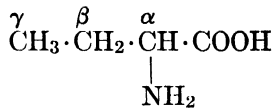
An amino acid is a compound in which a hydrogen in the group attached to the COOH is replaced by an NH_2 group; e.g.,



(The nomenclature is analogous to that used in the halogen and hydroxy substituted acids, so that



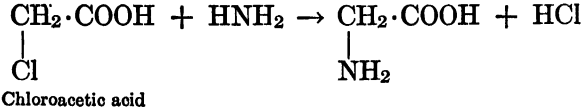
is β-aminopropionic acid; and



is α-aminobutyric acid.)

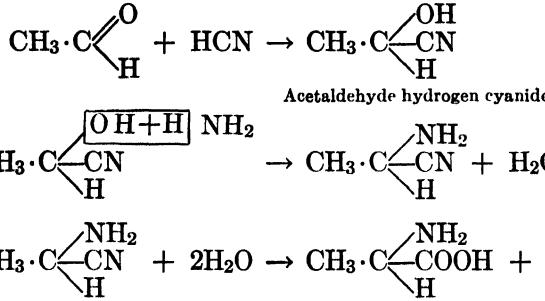
The α-amino acids are of great importance physiologically, since these are the main products obtained when proteins are hydrolyzed.

Methods of Preparation.—1. The action of ammonia on halogen acids; e.g.,



2. The action of hydrogen cyanide on aldehydes and ketones,

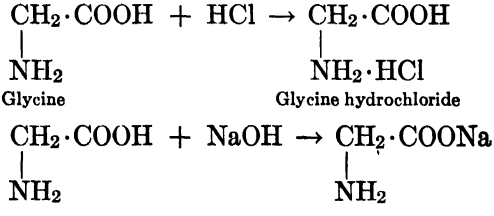
and the subsequent reaction with ammonia and ultimate hydrolysis; e.g.,



Acetaldehyde hydrogen cyanide

3. The hydrolysis of proteins (either by enzymes, acids or alkalies) yields a succession of products (metaproteins, proteoses, peptones, polypeptides), the final products being amino acids. (In the digestive tract, the enzymes pepsin, trypsin and erepsin hydrolyze the various proteins of the food into different amino acids.)

Properties.—Since the amino acids contain NH_2 and COOH groups, they may act as bases or acids; e.g.,



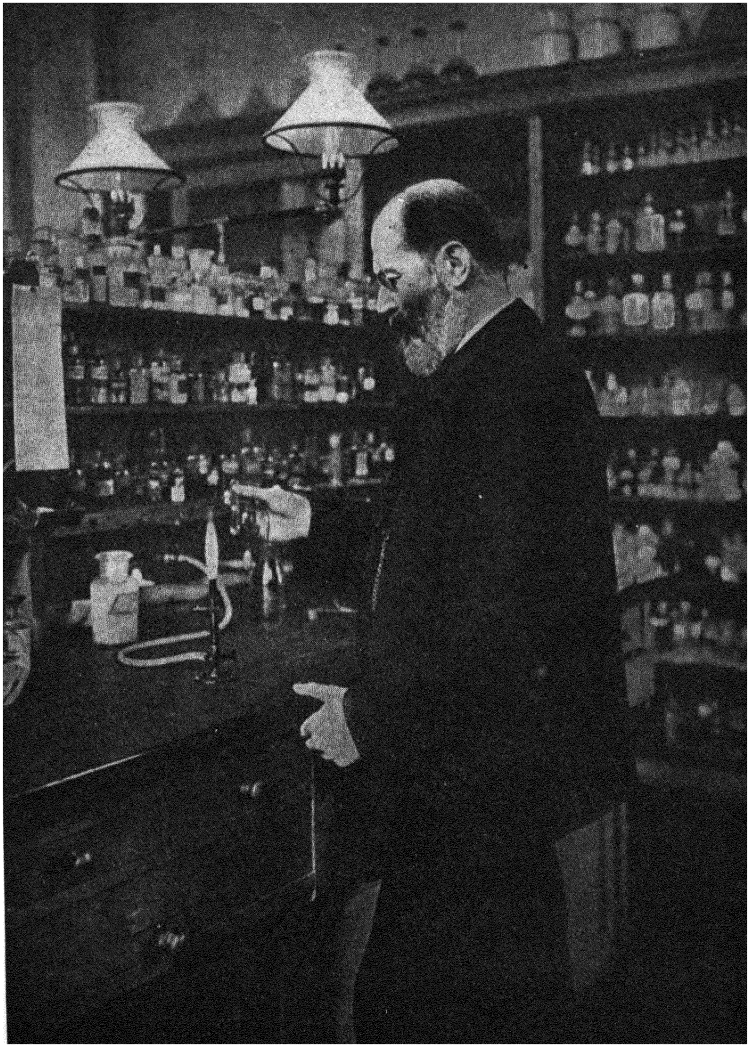
Glycine — Glycine hydrochloride

(They are, in reality, amphoteric substances, like aluminium hydroxide or zinc hydroxide. Glycine, for example, is a feeble electrolyte and is partially dissociated thus:

$$H_2N \cdot CH_2 \cdot COOH \rightleftarrows H_2N \cdot CH_2COO^- + H^+ \quad (A)$$

$$HO \cdot H_3N \cdot CH_2 \cdot COOH \rightleftarrows HO^- + H_3N \cdot CH_2 \cdot COOH^+ \quad (B)$$

At some particular hydrogen ion concentration, the dissociation represented by (A) will be equal to the dissociation represented by (B). This is the "isoelectric point," and at this point the solution is electrically neutral. The significance of the "isoelectric point" and its bearing on the behavior of such substances as proteins is only now beginning to be appreciated.)



EMIL FISCHER (1852–1919)

ONE OF THE FOREMOST ORGANIC CHEMISTS OF THE NINETEENTH CENTURY, DID MUCH TO ELUCIDATE THE CHEMISTRY OF CARBOHYDRATES (P. 169), PURINES (P. 155) AND PROTEINS (P. 149).

When dissolved in alcohol and saturated with hydrogen chloride (dehydrating agent), the amino acids form esters; e.g.,

$$\begin{matrix} CH_2\cdot COOH \\ | \\ NH_2 \end{matrix} + C_2H_5OH \rightarrow \begin{matrix} CH_2\cdot COOC_2H_5 \\ | \\ NH_2 \end{matrix} + H_2O$$

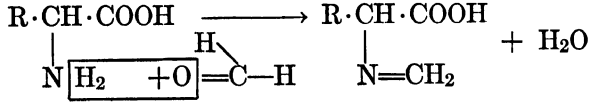
(Emil Fischer has used this " ester " method to separate the amino acids obtained by the hydrolysis of proteins.)

Nitrous acid converts amino acids into the corresponding hydroxy compounds with the liberation of nitrogen; e.g.,

$$\begin{matrix} CH_2\cdot COOH \\ | \\ NH_2 \end{matrix} + HONO \rightarrow \begin{matrix} CH_2\cdot COOH \\ | \\ OH \end{matrix} + N_2 + H_2O$$

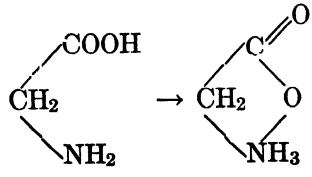
(This is the principle of the *Van Slyke* method for the determination of amino acids in blood and tissues, and for following the rate of protein hydrolysis.)

Aldehydes react with amino acids to form methylene derivatives; e.g.,

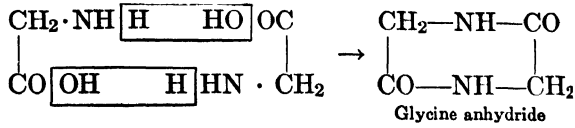


(This reaction converts an approximately neutral substance—because of the presence of the NH_2 and COOH groups—into an acid substance, by a substitution in the NH_2 group. Sörensen has used this principle for determining amino acids in blood, urine and tissues, and for estimating the extent of protein hydrolysis. The greater the hydrolysis, the more free NH_2 and COOH groups are formed and hence, when the NH_2 group is removed by formaldehyde, the greater the acidity of the hydrolytic products.)

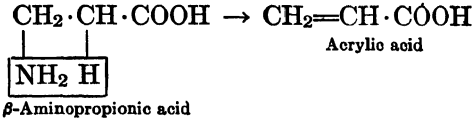
Since an amino acid contains a basic and an acidic group, internal neutralization is possible, with the resulting formation of " inner " salts:



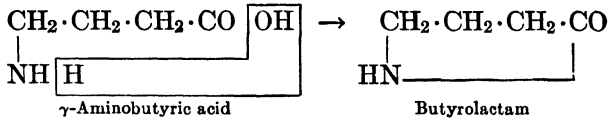
When an α-amino acid is heated, two of its molecules combine to form an anhydride:



β-Amino acids, when heated, lose ammonia and yield unsaturated acids:



γ-Amino acids give "lactams":



(These reactions are analogous to those given under hydroxy acids, p. 127.)

Several *amino acids obtained from the hydrolysis of proteins* are listed.

Glycocoll, $CH_2 \cdot COOH$ (with NH_2), also called glycine, is aminoacetic acid.

Alanine, $CH_3 \cdot CH(NH_2) \cdot COOH$, is α-aminopropionic acid.

Valine, $(CH_3)_2CH \cdot CH(NH_2) \cdot COOH$, is α-aminoisovaleric acid.

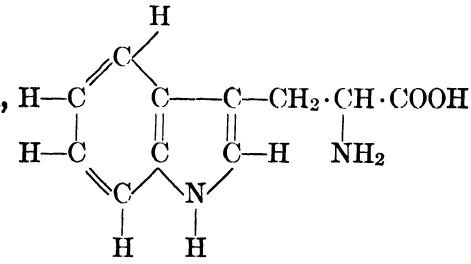
Leucine, $(CH_3)_2CH \cdot CH_2 \cdot CH(NH_2) \cdot COOH$, is α-aminoisocaproic acid.

Phenyl alanine, $C_6H_5CH_2 \cdot CH(NH_2) \cdot COOH$, is β-phenyl-α-aminopropionic acid.

Tyrosine, $\begin{matrix} CH_2\cdot CH\cdot COOH \\ \quad\quad | \\ \quad\quad NH_2 \\ C_6H_4\cdot OH \end{matrix}$ is α-amino-β-para-hydroxyphenyl-propionic acid.

(The student will appreciate the naming of some of these substances after he has studied the sections devoted to aromatic chemistry.)

Tryptophan,



is α-amino-β-indolepropionic acid.

Cystine, $\begin{matrix} CH_2—S—S—CH_2 \\ | \quad\quad\quad | \\ CH\cdot NH_2 \quad\quad CH\cdot NH_2 \\ | \quad\quad\quad | \\ COOH \quad\quad COOH \end{matrix}$

is di-(β-thio-α-aminopropionic acid.)

Aspartic acid, $\begin{matrix} CH_2\cdot COOH \\ | \\ CH\cdot COOH \\ | \\ NH_2 \end{matrix}$ is aminosuccinic acid.

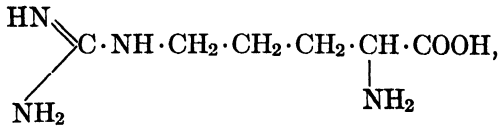
Glutamic acid, $\begin{matrix} CH_2\cdot COOH \\ | \\ CH_2 \\ | \\ CH\cdot COOH \\ | \\ NH_2 \end{matrix}$, is α-aminoglutaric acid.

On a commercial scale, glutamic acid is made by the hydrolysis of gluten or soy bean. The acid possesses decided meat-like taste, and because of this the monosodium salt has been introduced as a chemical condiment.

Lysine, $\begin{matrix} CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH\cdot COOH, \\ | \quad\quad\quad\quad\quad\quad\quad\quad | \\ NH_2 \quad\quad\quad\quad\quad\quad\quad NH_2 \end{matrix}$

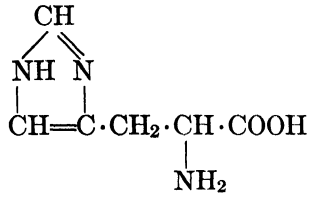
is α, ε-diaminocaproic acid.

Arginine,



is α-amino-δ-guanidino-valeric acid.

Histidine,



is α-amino-β-imidazolepropionic acid

Proteins

Proteins are essential, and in many ways, the most characteristic constituents of protoplasm. They may be regarded as combinations of α-amino acids. Their chemical properties are dependent upon the presence of these amino acids. Their physical properties, on the other hand, are largely due to the fact that they form colloidal solutions. Among the three classes of foodstuffs, fats, carbohydrates and proteins, the proteins alone contain the element nitrogen, and, as a rule, sulfur. The average percentage composition of proteins is (in per cent) $C=53$, $O=23$, $N=16$, $H=7$, and $S=1$.

They may be classified as follows:

Albumins.—Soluble in water and coagulated on boiling. (Examples: ovalbumin in egg white, lactalbumin in milk, serum albumin in blood, etc.)

Globulins.—Insoluble in water, but soluble in dilute solutions of a number of salts (such as sodium chloride) and coagulable on heating. (Examples: serum globulin in blood, edestin in hempseed, ovoglobulin in egg white, etc.)

Protamines.—Basic substances forming stable salts with mineral acids. In comparison with some of the other proteins, these yield relatively few amino acids on hydrolysis. They are soluble in water and not coagulated on heating. (Examples: salmine in salmon sperm, and in general, in the heads of ripe spermatozoa and in ova.)

Histones.—Somewhat similar to protamines. These are soluble in water and precipitated by ammonia. (Examples: globin in hemoglobin, scombrone in mackerel sperm, thymus histone, etc.)

Glutelins.—Proteins common in the vegetable kindgom. These are insoluble in neutral solvents, but soluble in dilute acids and alkalies. (Example: glutenin in wheat.)

Prolamines.—These are also common in the vegetable kingdom. They are soluble in 70–80 per cent alcohol (which distinguishes them from glutelins and other proteins), but, like other proteins, insoluble in absolute alcohol. They are also insoluble in water and neutral solvents. (Examples: zein in corn, gliadin in wheat and rye, hordein in barley, etc.)

Albuminoids.—These are found in the skeletal and connective tissue of animals, and are characterized by their far greater insolubility in reagents than other proteins. (Examples: keratin in hair, collagen in connective tissue, etc.)

The proteins which have so far been enumerated are known as "simple proteins," to distinguish them from the following "conjugated proteins":

Nucleoproteins.—These are combinations of protein and nucleic acid, and are characterized by yielding purine bases (p. 151) on hydrolysis. (Examples: nucleoprotein in thymus, pancreas, spleen, and in glandular tissue in general. They are found in nearly all cells, and particularly in the nuclei of cells.)

Glycoproteins.—Combinations of protein and a compound containing the carbohydrate group. They are characterized by yielding, on hydrolysis, a sugar which reduces *Fehling's-Benedict* solution. (Examples: mucin in saliva, osseomucoid in bone, tendomucoid in tendon, etc.)

Phosphoproteins.—These proteins, like the nucleoproteins, are rich in phosphorus, but, unlike the latter, do not yield purine bases on hydrolysis. (Examples: casein in milk, vitellin in egg yolk, etc.)

Hemoglobins.—Combinations of protein with a pigment-containing substance. (Example: hemoglobin in blood, which on hydrolysis yields the histone, globin, and the iron-containing substance, hematin.)

In addition to these, we have a number of "secondary" or "hydrolyzed" proteins, obtained in the course of hydrolysis

of proteins when acted upon by certain enzymes, acids or alkalies. They are:

Metaproteins.—These represent the first stage in protein hydrolysis. They are soluble in acids and alkalies, but insoluble in neutral solvents (from which they are coagulated on boiling).

Proteoses.—The primary proteoses are soluble in water, not coagulated on boiling, and precipitated by one-half saturated solution of ammonium sulfate. The secondary proteoses show similar properties, except that they require a completely saturated solution of ammonium sulfate for precipitation, a crude distinction, it must be confessed.

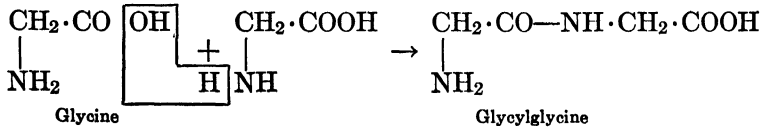
Peptones.—These are similar to the proteoses, but are not precipitated by ammonium sulfate.

As hydrolysis proceeds, we arrive at the **polypeptide** stage (compounds of a somewhat simpler type, chemically, than peptones), and finally obtain the individual **amino acids.**

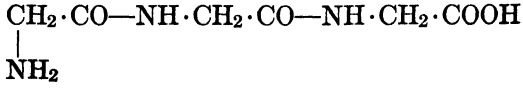
Composition of Proteins.—The various proteins, when completely hydrolyzed (by acid, alkali or enzyme) yield amino acids. The essential difference among proteins is in the number and in the amount of amino acids which they yield. Up to the present, about 20 of these amino acids have been isolated (see amino acids, p. 152), and the extent to which they occur in a number of proteins is given in the table on the following page.

The isolation of the various amino acids is a laborious task and cannot be discussed here.

Constitution of Proteins.—Emil Fischer has shown that the proteins may be regarded as combinations of amino acids, linked in the following way (to take the simplest case):



Glycylglycine (dipeptide) is the simplest example of a polypeptide. It, in turn, may combine with another molecule of glycine to form diglycylglycine (tripeptide).



PER CENT OF AMINO ACIDS ISOLATED FROM VARIOUS PROTEINS

	Gliadin—Wheat	Salmin—Salmon	Keratin—Sheeps' Horn	Ovalbumin—Cryst.	Muscle—Scallop	Japanese—Silk Cocoons	Globin—Horse Hemoglobin	Gelatin	Casein—Cow	Elastin
Glycocoll.....	0 02	0.00	0.45	0.00	0.00	35 00	0.00	16.5	0.45	25.75
Alanine.....	2.00	0 00	1.6	2.22	....	22.6	4.2	0.8	1.85	6.58
Valine.....	0 21	4 3	4.5	2.50	.....	.....	.....	1.0	7.95	1.4
Leucine.....	5.61	0.00	15.3	10.71	8.78	0.7	29.0	2.1	9.7	21.38
Proline.....	7.06	11.0	3.7	3.56	2.28	0 7	2 3	5.2	7.63	1.74
Phenylalanine.	2.35	0.0	1 9	5 07	4.90	1.3	4.2	0 4	3.88	3 89
Aspartic acid..	0.58	0.0	2.5	2 20	3.47	1 3	4.4	0.56	1.77	
Glutamic acid.	42.98	0.0	17.2	9.10	14.88	0.07	1.7	1 88	21.77	0.76
Serine..... ..	0.13	7.8	1.1	?	.....	.....	0.6	0.4	0 5	
Cystine.....	0.45	0.0	7.5	?	....	....	0 3	0 0	0 07	?
Tyrosine.....	1.20	0 0	3.6	1 77	1 95	9 7	1 3	0 00	4 5	
Arginine.....	3.16	87.4	2 7	4 91	7 38	...	5 4	7 62	3 81	0 3
Histidine.....	0 61	0 0	?	1 71	2 02	....	11 0	0 4	2 5	
Lysine.....	0 00	0.0	0 2	3 76	5 77	.....	4.3	2 75	7 62	
Ammonia.....	5.1	.....	?	1 34	1.08	.....	. .	..	1 61	
Tryptophan...	Pres.	0.0	. .	. ..	Pres.	....	Pres	0 0	1.5	

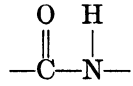
and so on. Of course, the combinations need not involve glycine only, but other amino acids may take a part in such reactions—in fact, any substance containing the NH_2 and COOH groups; so that the number of such possible polypeptides is very large.

Fischer has prepared an octadecapeptide, consisting of three leucine and fifteen glycine units, which is not easily distinguishable from a protein found in nature. Apart from being a colloid, this octadecapeptide is hydrolyzed by the enzyme trypsin (of the pancreas) into amino acids, just like any of the common proteins.

As further evidence of the polypeptide nature of proteins, it should be recalled that when proteins are hydrolyzed, polypeptides (such as glycyltyrosine) have actually been isolated from among the hydrolytic products.

General Reactions.—*Biuret.*—When the protein is mixed with a conc. solution of sodium hydroxide and a drop or two of dilute copper sulfate solution is added, a violet to pink color is obtained. (Generally the simpler the protein the more pinkish

the color, so that peptones show a distinct pink and albumins a distinct bluish-violet.) The reaction is given by nearly all substances containing two



groups attached to one another, to the same nitrogen atom, or to the same carbon atom. The name " biuret " is derived from the fact that biuret (which is obtained by heating urea, p. 120) gives this reaction.

Xanthoproteic.—Heating a protein solution with conc. nitric acid produces a yellow color. This is changed to orange on the addition of an excess of ammonium hydroxide. (The yellow color is dependent upon the formation of a nitro compound.)

Millon's.—Heating with Millon's reagent (essentially, mercury dissolved in nitric acid), a brick-red color or precipitate is obtained. (This reaction is given by phenol and phenolic derivatives.) The substance in the protein molecule responsible for this test is probably tyrosine.

Glyoxylic acid (Hopkins-Cole).—When the protein is mixed with glyoxylic acid and conc. sulfuric acid added, a violet ring is obtained. (This reaction is due to the presence of tryptophan in the protein molecule.)

Molisch.—With alpha-naphthol and conc. sulfuric, the protein solution forms a violet ring. (The reaction is due to the presence of the carbohydrate glucosamine in the protein molecule.)

(While no one of these color tests is evidence of the presence of a protein, any substance which gives two or more of these tests may be suspected of being a protein.) The following reactions are further confirmatory tests.

Proteins are precipitated by the salts of heavy metals, such as lead acetate, mercuric chloride, copper sulfate, etc.

The proteins are precipitated by the " alkaloidal reagents," such as phosphotungstic, phosphomolybdic, tannic, picric acids, etc.

Proteins are precipitated by strong alcohol.

Many of the proteins, like the albumins and the globulins, are coagulated on heating.

Recently proteins from beef blood have been introduced as food products. Serum albumin is mixed with dried egg yolks and used in preparing cakes, cookies, omelets, etc.

An even more important industrial development in the use of proteins is in the production of *karolith*, a product made from the casein of skim milk by hardening it with formaldehyde. The material is really a synthetic horn with advantages over horn itself. Karolith softens when moderate heat is applied and can therefore be bent and embossed. It can be dyed or stained and is now used quite extensively in the manufacture of a variety of buttons, pens, pencils, cigarette holders, etc.

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MITCHELL AND HAMILTON—Biochemistry of the Amino Acids.

HAN—Monosodium glutamate as a Chemical Condiment. *Industrial and Engineering Chemistry*, **21**, 984 (1929).

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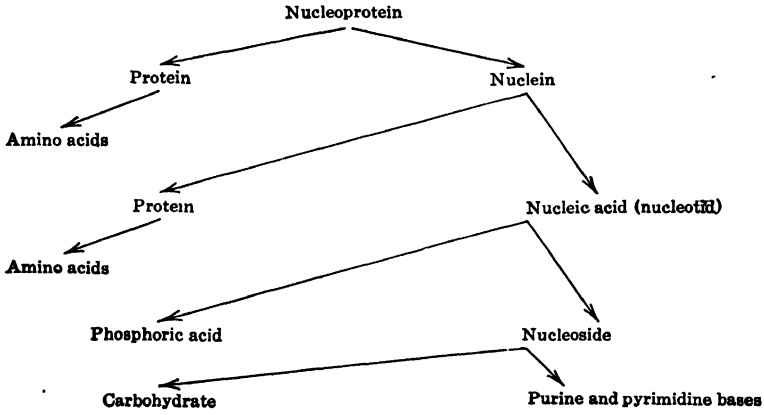
CHAPTER XV

NUCLEOPROTEINS, PURINES, URIC ACID AND PYRIMIDINES

Nucleoproteins are a group of combined proteins of especial interest to us, since, on the one hand, they are principally constituents of the nuclei of cells (animal and plant), and on the other, they yield, on decomposition, a group of important organic substances (purines and pyrimidines). They may be extracted from animal or vegetable sources by water or dilute alkali, and precipitated by acid (for example, the nucleoprotein in yeast may be extracted with dilute alkali and then precipitated by acid, or the lymphatic glands of the ox or sheep, or the thymus of a calf, may be extracted with water, and the nucleoprotein precipitated with acid.)

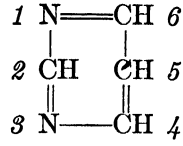
A careful study of the hydrolytic products of nucleoproteins shows that they, like the proteins and higher carbohydrates, "split up" in stages. The following is a schematic representation:



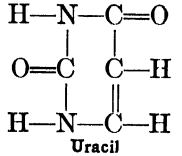
The nucleoprotein, in other words, may be regarded as a combination of protein and nucleic acid, the latter, in turn,

being a combination of phosphoric acid, carbohydrate (usually a pentose if the carbohydrate is of plant origin, and a hexose if of animal origin), and pyrimidine bases.

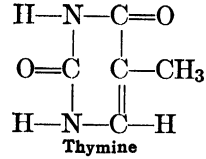
Among the common **pyrimidines** are uracil, thymine and cytosine. **Pyrimidine** itself has the formula:



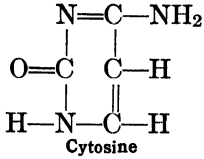
and uracil, thymine and cytosine have the following structures:



Uracil
or
2, 6-diketopyrimidine

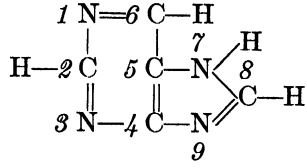


Thymine
or
2, 6-diketo-5-methylpyrimidine
or
5-methyl uracil

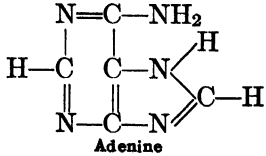


Cytosine
or
6-amino-2-ketopyrimidine

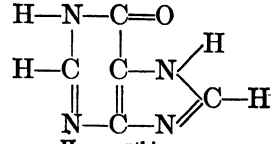
Among the **purine bases** are adenine, hypoxanthine and guanine. **Purine** itself has the formula:



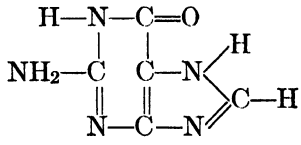
and the structures for adenine, hypoxanthine, guanine and xanthine are:



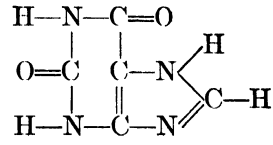
Adenine
or
6-aminopurine



Hypoxanthine
or
6-ketopurine

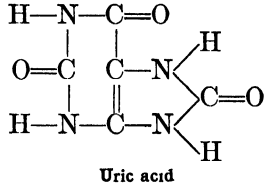


Guanine
or
2-amino-6-ketopurine



Xanthine
or
2, 6-diketopurine

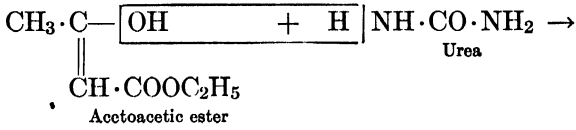
The purines are very largely oxidized to uric acid in the body:



Uric acid
or
2, 6, 8-triketopurine
(also called 2, 6, 8-trioxypurine)

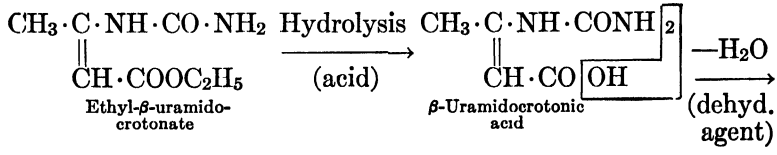
Uric acid is an important nitrogenous constituent of the urine. It is present in the joints, bladder, and in abnormally high amounts in the blood of persons suffering from gout and rheumatism.

We shall give one of several syntheses of uric acid. This will illustrate not only the synthetic preparation of an important purine derivative, but incidentally that of a pyrimidine derivative, namely, a methyluracil:



Acetoacetic ester

Urea

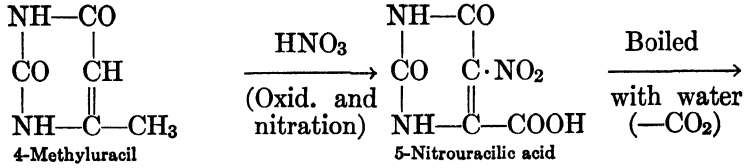


Ethyl-β-uramido-crotonate

(acid)

β-Uramidocrotonic acid

(dehyd. agent)

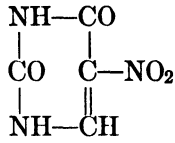


4-Methyluracil

(Oxid. and nitration)

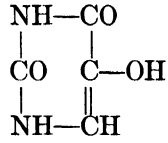
5-Nitrouracilic acid

with water (—CO_2)

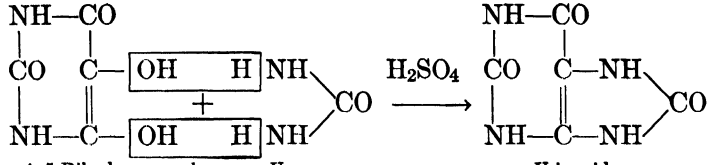


5-Nitrouracil

With tin and HCl, part of the 5-nitrouracil is reduced to the corresponding 5-amino-compound (5-aminouracil) and part of it to 5-hydroxyuracil:

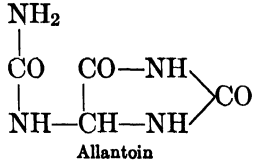


This compound is oxidized by bromine water to 4,5-dihydroxyuracil, which, when heated with urea and H_2SO_4, yields uric acid:

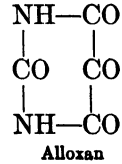


4, 5-Dihydroxyuracil Urea Uric acid

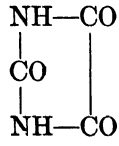
The oxidation of uric acid may yield any one of the following products (depending on the reaction and the reagent employed):



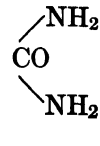
Allantoin



Alloxan



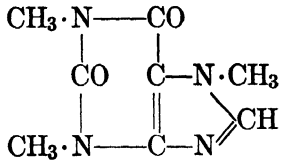
Parabanic acid



Urea

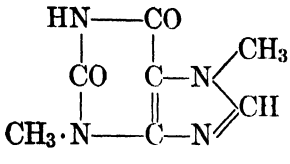
Allantoin occurs to a small extent in human urine, but in mammals, other than man and anthrapoid apes, it takes the place of uric acid, it being the principal end product of purine metabolism.

Other important purine derivatives are:



Caffeine or theine
or
1, 3, 7-trimethyl-2, 6-diketopurine
or
1, 3, 7-trimethylxanthine

and



Theobromine
or
3, 7-dimethyl-2, 6-diketopurine
or
3, 7-dimethylxanthine

Theobromine is present in cocoa beans (chocolate) and **theophylline** (isomeric with theobromine) occurs in tea leaves, while caffeine is a constituent of coffee (about 1 per cent) and tea (about 1–4 per cent).

Caffeine, theobromine and theophylline are strong diuretics, but caffeine is peculiar in having a strong excitant action upon the central nervous system.

READING REFERENCE

LEVENE AND BASS—Nucleic Acids.

CHAPTER XVI

CYANIDES, ISOCYANIDES AND OTHER NITROGEN COMPOUNDS

THE student having taken inorganic chemistry is already familiar, to some extent, with cyanide compounds. He has used potassium ferrocyanide and potassium ferricyanide in testing for iron salts; and he remembers potassium cyanide and hydrogen cyanide as examples of deadly poisons.

Cyanogen $(CN)_2$, is a colorless, poisonous gas, with a pungent odor, and burns with a blue flame, giving carbon dioxide and nitrogen. It may be prepared:

1. By heating ammonium oxalate with a dehydrating agent:

$$\begin{matrix} COONH_4 \\ | \\ COONH_4 \end{matrix} \underset{\text{Hydrolysis}}{\overset{P_2O_5}{\rightleftharpoons}} \begin{matrix} C{\equiv}N \\ | \\ C{\equiv}N \end{matrix} + 4H_2O$$

(The cyanogen can be hydrolyzed back to the ammonium oxalate.)

2. By heating mercuric cyanide:

$$Hg(CN)_2 \rightarrow Hg + (CN)_2$$

Hydrogen Cyanide, HCN (also called **hydrocyanic acid**), is a colorless, poisonous volatile liquid, burning with a violet flame. Its water solution is called "prussic acid." (Some attempt was made during the war to use it as a "poison gas.") It occurs in bitter almonds, wild cherry bark and other plant products. It is a very weak acid. Its formula may be represented as $H{-}C{\equiv}N \rightleftarrows H{-}N{=}C$. It may be prepared by heating sodium cyanide with sulfuric acid:

$$NaCN + H_2SO_4 \rightarrow HCN + NaHSO_4$$

a reaction quite analogous to the preparation of the halogen acids.

Hydrogen cyanide hydrolyzes to formic acid:

$$HCN + 2H_2O \rightarrow H{\cdot}COOH + NH_3$$

and reduces to methylamine:

$$HCN + 2H_2 \rightarrow CH_3 \cdot NH_2$$

It is used in medicine (a 2 per cent solution) in respiratory diseases and to quiet a cough. Recently, it has been recommended as a fungicide and insecticide (spraying trees). Ships are very often disinfected with HCN gas.

By the action of liquid hydrocyanic acid on calcium carbide (in the presence of a small quantity of water as a catalyst), calcium cyanide, $Ca(CN)_2$, a solid, is obtained. This substance liberates HCN on mere exposure to the air, and, being a solid, can be more easily handled than HCN.

Cyanogen Chloride, $CN \cdot Cl$, is a poisonous liquid of low boiling point, and was used as a " poison gas " in the late war. It may be prepared by the action of chlorine on hydrogen cyanide:

$$HCN + ClCl \rightarrow Cl—C{\equiv}N + HCl$$

Recently it has been recommended to replace HCN for disinfecting purposes.

Cyanamide, $CN \cdot NH_2$, is prepared by the action of ammonia on cyanogen chloride:

$$CN \cdot \boxed{Cl + H} NH_2 \rightarrow H_2N \cdot CN + HCl$$

(**Calcium cyanamide,** $CN \cdot NCa$, made by heating calcium carbide and nitrogen, $CaC_2 + N_2 \rightarrow CaCN_2 + C$, finds extensive use as a fertilizer, for in the presence of water it decomposes in the soil, liberating ammonia:

$$CN \cdot NCa + 3H_2O \rightarrow 2NH_3 + CaCO_3$$

The calcium cyanamide of commerce ($CaCN_2 + C$), goes under the name of " nitrolime.")

Alkyl Cyanides, R—C≡N

Nomenclature.—CH_3CN may be called either methyl cyanide, or cyanomethane, or acetonitrile. The —C≡N is the " nitrile " group, and the name of the substance depends upon the acid obtained when the substance is hydrolyzed. For example, CH_3CN is acetonitrile because it hydrolyzes to acetic acid. Similarly, $C_2H_5 \cdot CN$ is propionitrile.

Preparation.—1. The action of NaCN on an alkyl halide; e.g.,

$$CH_3 \boxed{I + Na} CN \rightarrow CH_3CN + NaI$$

2. Heating the corresponding amide in the presence of a dehydrating agent: e.g.,

$$CH_3CONH_2 - H_2O \xrightarrow{(P_2O_5)} CH_3CN$$

Properties.—The alkyl cyanides are reactive on account of their unsaturated character (a triple linkage):

$$CH_3{-}C{\equiv}N + H_2O \rightarrow \underset{\text{Acetamide}}{CH_3CONH_2} + H_2O \rightarrow \underset{\text{Ammonium acetate}}{CH_3COONH_4}$$

$$CH_3{\cdot}CN + 2H_2 \rightarrow \underset{\text{Ethylamine}}{CH_3{\cdot}CH_2{\cdot}NH_2}$$

ALKYL ISOCYANIDES, $R{-}N{=}C\!<$, (or $R{-}N{\equiv}C$)

Nomenclature. $CH_3{\cdot}N{=}C\!<$ may be called methyl isocyanide or methyl carbylamine. ($C_2H_5{-}N{=}C<$ is commonly spoken of as "carbylamine.")

In organic cyanides the R is connected to the carbon atom:

$$R{-}C{\equiv}N$$

whereas in the organic isocyanides the R is connected to nitrogen:

$$R{-}N{=}C\!< \quad (A)$$

[The formula (A) is selected because the isocyanides are highly reactive substances, forming, among other things, additive compounds.]

Preparation.—1. Action of silver cyanide on alkyl halide; e.g.,

$$RCl + AgNC \rightarrow RNC + AgCl$$

(which suggests that silver cyanide may exist in one of two forms, either as AgCN or AgNC).

2. The reaction of a primary amine with chloroform in an alkaline solution; e.g.,

$$CH_3NH_2 + CHCl_3 + 3KOH \rightarrow CH_3NC + 3KCl + 3H_2O$$

(This is a test for primary amines. See p. 140.)

Properties.—The isocyanides are colorless, poisonous liquids, with an extremely disagreeable and characteristic odor. They are very reactive; e.g.,

$$R\cdot N{=}C\!\!\begin{array}{l}\diagup\\\diagdown\end{array} + HCl \rightarrow R{-}N{=}C\!\!\begin{array}{l}\diagup H\\\diagdown Cl\end{array}$$

$$R\cdot N{=}C\!\!\begin{array}{l}\diagup\\\diagdown\end{array} + Cl_2 \rightarrow R{-}N{=}C\!\!\begin{array}{l}\diagup Cl\\\diagdown Cl\end{array}$$

$$R\cdot N{=}C\!\!\begin{array}{l}\diagup\\\diagdown\end{array} + S \rightarrow R{-}N{=}C{=}S$$

$$R\cdot N{=}C\!\!\begin{array}{l}\diagup\\\diagdown\end{array} + O \rightarrow R{-}N{=}C{=}O$$

(The C in $R\cdot N{=}C\!\!\begin{array}{l}\diagup\\\diagdown\end{array}$ seems to be very reactive and, therefore, unsaturated.)

(In this connection, it may be of interest to point out here that the reactivity of carbon monoxide is in reality due to the divalency of its carbon atom, e.g.,

$$C{=}O + Cl_2 \rightarrow C\!\!\begin{array}{l}\diagup Cl\\=O\\\diagdown Cl\end{array}$$

Phosgene

or

$$C{=}O + O \rightarrow CO_2$$

whereby the divalent carbon is transformed into the tetravalent form.)

To distinguish between the cyanide and the isocyanide, it is merely necessary to hydrolyze the compounds:

$$R\cdot C{\equiv}N + 2H_2O \rightarrow R\cdot COOH + NH_3$$

$$R{-}N{=}C\!\!\begin{array}{l}\diagup\\\diagdown\end{array} + 2H_2O \rightarrow R\cdot NH_2 + H\cdot COOH$$

We may also distinguish them by reduction:

$R\cdot C{\equiv}N + 4H \rightarrow R\cdot CH_2\cdot NH_2$, primary amine.

$R{-}N{=}C\!\!\begin{array}{l}\diagup\\\diagdown\end{array} + 4H \rightarrow R\cdot NH\cdot CH_3$, secondary amine.

Other Nitrogen Compounds

$R \cdot C{\equiv}N$	$R{-}O{-}C{\equiv}N$	$R{-}S{-}C{\equiv}N$
Alkyl cyanide	Alkyl cyanate	Alkyl thiocyanate
$R{-}N{=}C\langle$	$R{-}N{=}C{=}O$	$R{-}N{=}C{=}S$
Alkyl isocyanide	Alkyl isocyanate	Alkyl isothiocyanate

Isocyanic acid, HNCO, is an unstable liquid, but a polymer, cyanuric acid $(HNCO)_3$ is known.

RNCO compounds are prepared thus:

$$RI + \underset{\text{Silver cyanate}}{AgNCO} \rightarrow RNCO + AgI$$

Fulminic Acid, C=NOH, is a poisonous, very unstable liquid. Here again we have a divalent carbon represented.

Mercuric fulminate, $\begin{matrix} C{=}N{-}O \\ C{=}N{-}O \end{matrix}\rangle Hg$, and silver fulminate, C=N—OAg, are prepared when the respective metals are acted upon by nitric acid and alcohol. They are used as detonators in percussion caps to explode gunpowder, dynamite, T.N.T., and other explosives.

Allyl isothiocyanate, $CH_2{=}CH \cdot CH_2 \cdot N{=}C{=}S$, is present in black mustard seeds and is used in medicine as a powerful rubefacient and counterirritant. It is employed as a substitute for the mustard plaster.

Nitro Compounds, $R{-}N\langle^{O}_{O}$. The nitro group is $-N\langle^{O}_{O}$. These may be looked upon as nitric acid, $HO{-}N\langle^{O}_{O}$, in which the OH is replaced by R. The aliphatic nitro compounds are not important, but the aromatic ones are, as we shall see later (p. 230). The nitro compounds, $R{-}N\langle^{O}_{O}$, are isomeric with the alkyl nitrites, R—O—N=O, which have already been discussed on p. 100. For example, nitroethane, $C_2H_5{-}N\langle^{O}_{O}$ is

isomeric with ethyl nitrite, $C_2H_5—O—N=O$, though it differs from ethyl nitrate, $C_2H_5—O—N\begin{matrix}\diagup\!\!\diagup O\\ \diagdown\!\!\diagdown O\end{matrix}$.

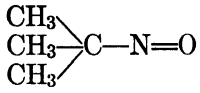
The nitro compounds may be prepared by the action of silver nitrite on halogen compounds; e.g.,

$$C_2H_5\boxed{I + Ag}NO_2 \rightarrow C_2H_5 \cdot NO_2 + AgI$$

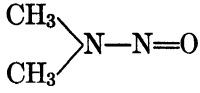
They are easily reduced to the corresponding amines; e.g.,

$$C_2H_5 \cdot NO_2 + 3H_2 \rightarrow \underset{\text{Ethylamine}}{C_2H_5NH_2} + 2H_2O$$

The nitroso group is represented by —N=O; e.g.,



Nitrosotrimethylmethane



Nitrosodimethylamine

READING REFERENCES

GROTTA—Development and Application of Initiating Explosives. *Industrial and Engineering Chemistry*, **17**, 134 (1925).

METZGER—Calcium Cyanide. *Industrial and Engineering Chemistry*, **18**, 161 (1926).

SIDGWICK—Structure of Divalent Carbon Compounds. *Chemical Reviews*, **9**, 77 (1931).

CHAPTER XVII

CARBOHYDRATES [1] AND RELATED COMPOUNDS

THE name **carbohydrate** (carbon hydrate) is derived from the fact that compounds belonging to this class contain C, H and O, the H and O being in the proportion of 2 : 1, respectively (as in water). There are, however, substances other than carbohydrates, such as acetic acid, ($CH_3 \cdot COOH$), and lactic acid ($CH_3 \cdot CHOH \cdot COOH$), which contain H and O in the proportions such as are found in water. On the other hand, a number of compounds belong to the carbohydrates although the proportion of H to O is not 2 : 1; e.g., rhamnose ($C_6H_{12}O_5$).

The more modern view is to regard carbohydrates as containing aldehyde-alcohol or ketone-alcohol groups; or compounds which upon hydrolysis are converted into substances containing such groups. (Organic Type Formulas, p. 16.)

Carbohydrates are mainly derived from the vegetable kingdom. Physiologically, the carbohydrates represent one of the three great classes of foodstuffs. Many of them are also of extreme importance in the industries.

In general, carbohydrates fall into two main classes; the sweet and crystalline compounds, called sugars; and the tasteless and non-crystalline compounds, termed starches, celluloses and allied products.

Carbohydrates are classified into:

A. Monosaccharides (no further hydrolysis with dilute acids):
- Diose, $C_2H_4O_2$, as glycolaldehyde, $CH_2OH \cdot CHO$.
- Trioses, $C_3H_6O_3$, as glyceraldehyde, $CH_2OH \cdot CHOH \cdot CHO$ or dihydroxyacetone, $CH_2OH \cdot CO \cdot CH_2OH$.
- Tetroses, $C_4H_8O_4$, as erythrose, etc.
- Pentoses, $C_5H_{10}O_5$, as arabinose, xylose, ribose, etc.
- Hexoses, $C_6H_{12}O_6$, as glucose, mannose, galactose, fructose, sorbose, etc.

B. Disaccharides, $C_{12}H_{22}O_{11}$ (yield two molecules of monosaccharides upon hydrolysis). Sucrose, maltose, lactose.

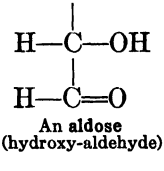
[1] Recently The International Union of Pure and Applied Chemistry proposed the term "**Glucides**" for carbohydrates and glucosides.

C. Trisaccharides, $C_{18}H_{32}O_{16}$ (yield upon hydrolysis three molecules of monosaccharides):
Raffinose.

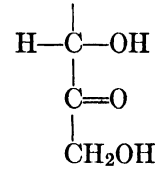
D. Polysaccharides, $(C_6H_{10}O_5)_x$, (yield upon hydrolysis more than three molecules of monosaccharides):
Starch, cellulose, dextrin, glycogen, inulin, gums, pectins, pentosans, etc.

(The ending " ose " generally refers to carbohydrates.)

The **monosaccharides,** or simple sugars, are aldehydes or ketones linked directly to carbon with OH group as



An aldose
(hydroxy-aldehyde)



A ketose
(hydroxy-ketone)

The trioses and tetroses are of theoretical rather than practical importance.

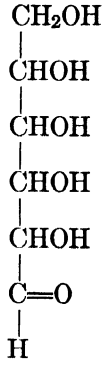
The **pentoses** in the form of more complex combinations, the *pentosans,* occur extensively in the plant kingdom and are found more particularly in the pectins and gummy substances of plants. The pentoses are obtained from the pentosans by hydrolysis with acids. Treated with concentrated hydrochloric acid and distilled, furfural is obtained (see p. 304), a process which forms the basis for the estimation of pentoses and pentosans. Among the more common pentose sugars are **arabinose,** obtained by hydrolyzing gum arabic; **xylose,** obtained by the hydrolysis of straw; and **ribose,** a constituent of nucleic acid (p. 155), found in yeast.

Extremely important, from our point of view, are the hexoses, the disaccharides and some of the polysaccharides.

Among the **hexoses,** $C_6H_{12}O_6$, ***d*-glucose** (also called dextrose) is the most important. It is present in the juice of many sweet fruits, such as grapes (hence grape-sugar). It is a normal, and very necessary constituent of blood, and, in pathological conditions (as in diabetes), accumulates to an abnormal degree in the blood and in the urine. Commercially, glucose is prepared by the hydrolysis of starch in presence of dilute acids.

$$(C_6H_{10}O_5)_x + x \cdot H_2O \rightarrow x(C_6H_{12}O_6)$$

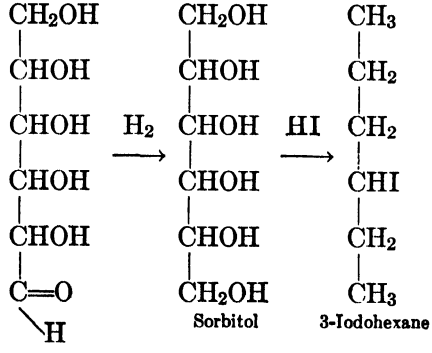
It may be obtained from many poly- and disaccharides. Since it rotates the plane of polarized light to the right, it is also called dextrose or *d*-glucose. Its formula may be written:



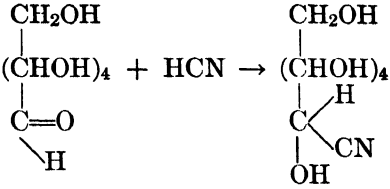
Some indication of how we arrive at such a structural formula may be given. In the first place, elementary analysis and molecular weight determinations give us the empirical formula $C_6H_{12}O_6$. The substance behaves like an alcohol, because it reacts with acetyl chloride or acetic anhydride to form acetyl derivatives:

$$R{-}O\boxed{H + Cl}OC{-}CH_3 \rightarrow R{-}OOC{-}CH_3$$

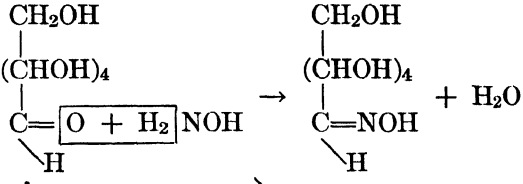
Since glucose forms a penta-acetyl derivative, it must contain five OH groups. On reduction, glucose first yields the corresponding alcohol, and ultimately (if HI is used) a normal six-carbon chain iodohydrocarbon, proving glucose to contain a normal chain of carbon atoms:



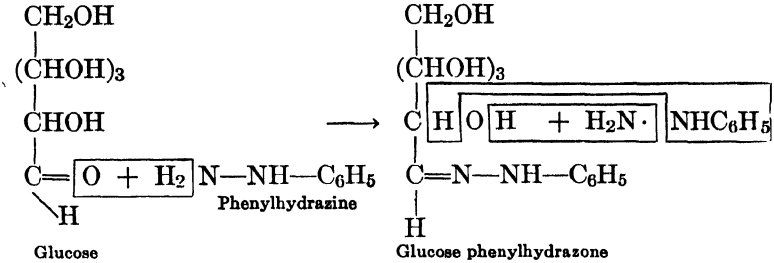
Glucose forms a cyanohydrin with HCN:

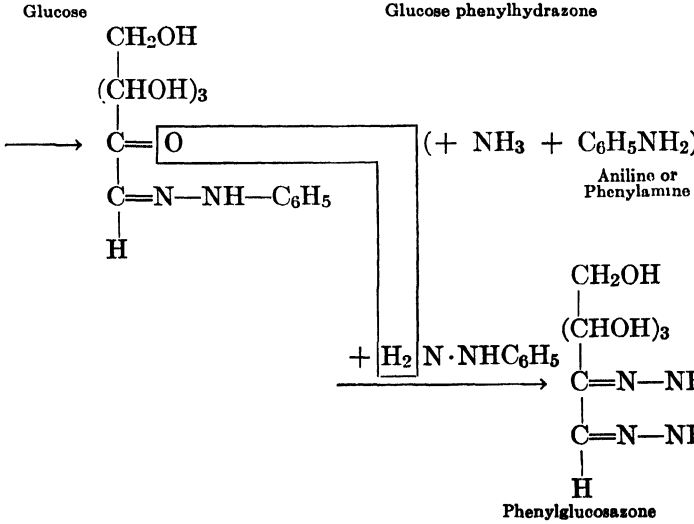


and an oxime with hydroxylamine, NH_2OH:

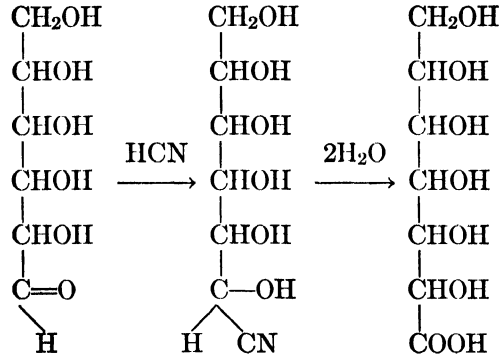


proving the presence of a carbonyl, $>CO$, group (see p. 73). The presence of this group may be further shown by the reaction of glucose with phenylhydrazine:





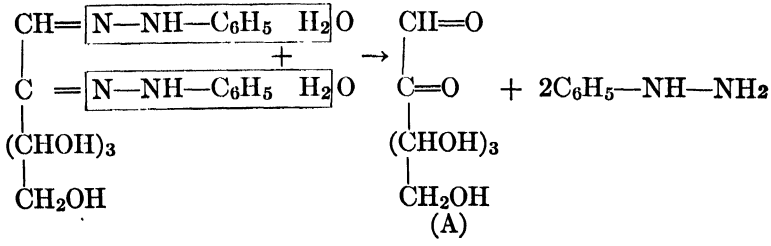
It now merely remains to determine the position of the CO group. This can be done in the following way: glucose is combined with HCN and the resulting product hydrolyzed (see p. 88).



The hydroxy acid is a normal, seven-carbon compound. The COOH group must be attached to the sixth carbon atom, and this, in turn, must have contained a CO group to have reacted with HCN. But the sixth carbon atom in glucose is the end carbon atom; therefore, the position of the CO group in glucose must be at the end carbon atom.

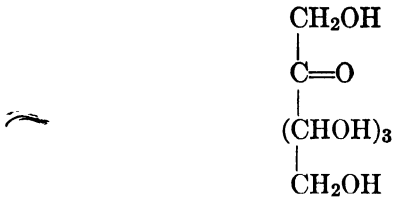
If we have gone into the constitution of glucose at some length, it is merely to illustrate the methods used in assigning formulas to the various carbohydrates.

The **osazone** formed when glucose and phenylhydrazine are brought together (p. 169), undergoes a very interesting transformation when warmed with concentrated hydrochloric acid:



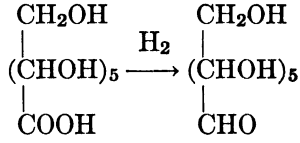
(A) is known as **glucosone** and is as an example of a class of compounds called **osones**.

By reducing glucosone we change the aldehydic into an alcoholic group and get



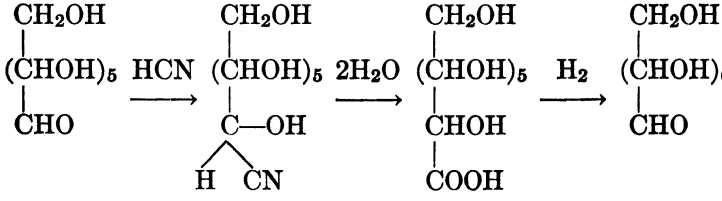
which, as may readily be seen, is a compound isomeric with glucose, but different from it in having a keto instead of an aldehyde group. This compound is none other than fructose (see p. 177). So that by means of the osone reaction we can pass from glucose to fructose. (Aldose → Ketose.)

We have seen how by the use of HCN we can pass from a six to a seven carbon compound (p. 170). Now it is possible to reduce such a compound:



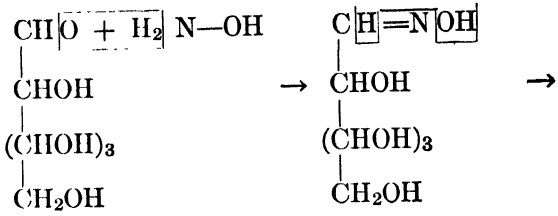
and obtain a product analogous in constitution to glucose except that it contains seven instead of six carbon atoms.

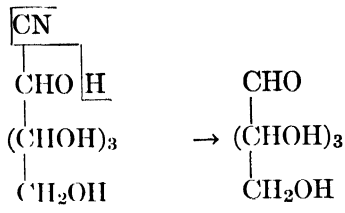
It is evident that this new compound may again be treated with HCN and the various steps repeated:

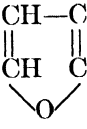


thereby obtaining an eight-carbon compound. Obviously, we have here a method by which the carbon content of a sugar may be *increased*—a very important process in synthetic chemistry.

An equally important and interesting procedure is to *decrease* the carbon content of a compound. This is done by first forming the oxime with hydroxylamine, then converting the product into the nitrile (by loss of water), and finally, by treatment with ammoniacal silver nitrate solution, splitting off HCN:





Properties of Glucose.—Like all carbohydrates, glucose reacts with the *Molisch* reagent (α-naphthol) and conc. H_2SO_4 to give a violet ring or color, a reaction said to be due to the formation of furfural,  (see p. 305), or its derivatives. Glucose forms an osazone with phenylhydrazine, a reaction already discussed. These osazones are of the utmost importance in the identification of a number of sugars, since they show definite crystalline forms and have definite melting points. Owing to the presence of the CHO group, glucose reduces ammoniacal silver solutions and the alkaline solutions of a number of metals, such as copper, bismuth and mercury. The best known of these reactions is the **Fehling's test,** which consists in heating glucose with a solution of copper sulfate, to which potassium hydroxide and Rochelle salt have been added; a yellowish red precipitate of cuprous oxide is obtained. (The theory of the reaction may be explained thus: in the absence of a reducing agent, such as glucose,

the cupric hydroxide that is first formed would be converted to black cupric oxide:

$$Cu(OH)_2 \rightarrow CuO + H_2O$$

but when glucose, or any other appropriate reducing agent is present, cuprous oxide, Cu_2O, which is yellow to red in color, is formed instead:

$$2Cu(OH)_2 \rightarrow Cu_2O + 2H_2O + O$$

Benedict has modified the Fehling reagent by mixing the copper sulfate with sodium citrate and sodium carbonate, producing a reagent which does not deteriorate even after long standing. The Benedict modification also has the advantage over Fehling's solution in that, when it is applied to test for glucose in the urine, neither uric acid nor creatinine—nitrogenous substances present in the urine—interfere with the test; nor does chloroform, which is often used as a preservative for the urine.)

Heated with picric acid, in the presence of KOH, glucose gives a red color—a reaction which forms the basis for a colorimetric determination of glucose in blood. (The reaction is said to be due to the reduction of picric (p. 280) to picramic acid;

$$C_6H_2\begin{cases}(NO_2)_3\\OH\end{cases} \rightarrow C_6H_2\begin{cases}(NO_2)_2\\NH_2\\OH\end{cases}$$

though the question has not been definitely settled.)

Yeast " ferments " glucose forming ethyl alcohol and CO_2:

$$C_6H_{12}O_6 \rightarrow 2C_2H_5OH + 2CO_2$$

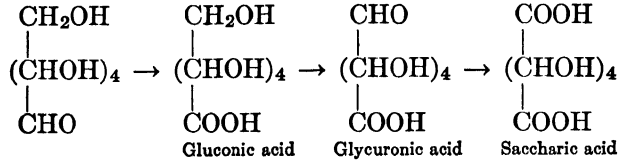
Glucose is optically active, turning the plane of polarized light to the right. If its formula be examined, it will be seen that glucose contains four asymmetric carbon atoms:

$$CH_2OH—\overset{*}{C}HOH—\overset{*}{C}HOH—\overset{*}{C}HOH—\overset{*}{C}HOH—CHO$$

From the number of asymmetric carbon atoms in a compound, we can, with the help of a simple equation supplied by van't Hoff, calculate the possible number of isomers. The equation is $A = 2^n$, where A represents the number of isomers and n the number of asymmetric carbon atoms. Applying this equation to glucose, $A = 2^4 = 16$; or there should be in all 16 possible stereoisomers. So far, no less than 14 of these have been isolated.

Glucose (both in the solid and in the form of syrup, as corn syrup) is used extensively in making confectionery, jellies, preserves, as table syrups, in the manufacture of alcoholic beverages, as a diluent (to increase bulk and weight) for dyes, in chewing gum, tobacco, etc.

On oxidation, glucose may give rise to the following products:

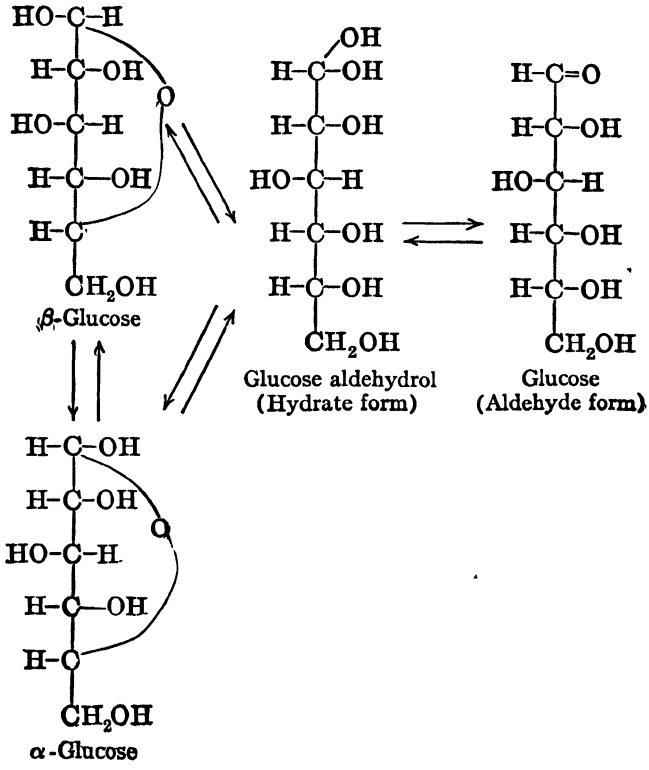


(Gluconic acid is now made by the electrolytic oxidation of glucose and also by the action of *Penicillium luteum purpurogenum* on glucose.)

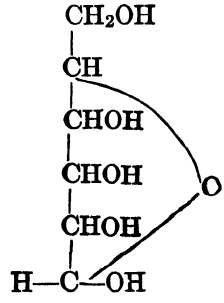
(Glycuronic acid is of importance physiologically, since it may combine with poisonous substances, such as phenol, chloral, etc., to make them inert.)

The optical activity of freshly prepared glucose solution diminishes on standing. This "mutarotation," as it is called, is due to the fact that there are, in reality, two forms of glucose, α- and β-glucose present, having different rotatory powers, and the optical activity of the resulting mixture will depend upon the amounts of each present. This view is further strengthened by the fact that two isomeric methyl glucosides are known (p. 176), one of them, α-methyl glucoside, yielding on hydrolysis one form of glucose (α-glucose), and the other, β-methyl glucoside, yielding on hydrolysis the other form of glucose (β-glucose). The optical rotation of the two forms of glucose varies widely, the *alpha* form being $+109°$ and the *beta* form $+22°$. If a solution of either form is allowed to stand, the rotation slowly changes and finally comes to an equilibrium at 52.5°.

These changes of glucose may be explained by the following changes:

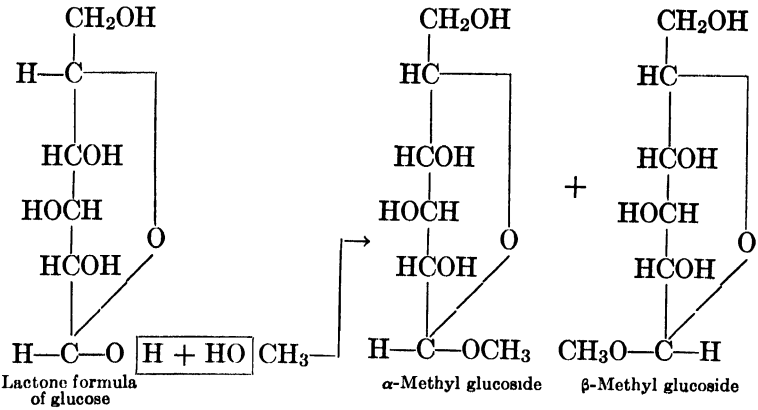


These facts, together with the additional fact that glucose is really not so reactive a compound as the usual structural formula indicates, has led to the conception of the *lactone structure* for the compound. This depends upon the possibility that a hydroxy compound of the glucose type may form an *amylene oxide ring.*



Besides the amylene oxide configuration, we may also have the ethylene, propylene or butylene oxide ring (1 : 2, 1 : 3, 1 : 4 ring). These types are collectively known as "gamma sugars," and they are more reactive than the 1 : 5 or amylene oxide sugar. One theory has it that a function of insulin (see p. 361) is to change the relatively stable 1 : 5 sugar into one of the more reactive gamma sugars.

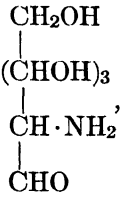
Glucosides.—When glucose reacts with methanol in presence of HCl, two compounds, α- and β-methyl glucosides, are obtained, the formulas of which may be represented thus:



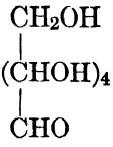
The two glucosides have different physical properties. They also behave differently towards enzymes. Maltase hydrolyzes the α- variety, but not the β-, and emulsin hydrolyzes the β-, but not the α-.

The naturally occurring glucosides belong to the β-form. On hydrolysis, glucose and other products are produced. The following glucosides occur in nature: phloridzin, found in the bark of fruit trees, which yields fructose and phloroglucinol when hydrolyzed. Phloridzin is often used to induce a form of diabetes in animals. Salicin, $C_6H_4\begin{cases}O\cdot C_6H_{11}O_5\\ CH_2OH\end{cases}$, on hydrolysis yields glucose and saligenin, or salicyl alcohol. Salicin occurs in willow bark. Amygdalin, $C_6H_5\cdot CH\begin{cases}CN\\ O\cdot C_{12}H_{21}O_{10}\end{cases}$, hydrolyzes to two molecules of glucose, HCN and benzaldehyde. It is found in bitter almonds. Arbutin, $C_6H_4\begin{cases}O\cdot C_6H_{11}O_5\\ OH\end{cases}$, hydrolyzes to glucose and hydroquinone. It is present in the leaves of the berry tree. Indican, present in the indigo plant, hydrolyzes into glucose and indoxyl, which rapidly oxidizes to indigo. Myronic acid is present in black mustard seed. On hydrolysis, it is con-

verted to dextrose, $KHSO_4$ and allyl isothiocyanate ($C_3H_5 \cdot NCS$). Ruberythric acid is present in madder root. On hydrolysis or fermentation, it is converted to the dye alizarin and glucose.

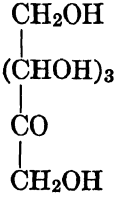
Glucosamine,  , a substance closely related to glucose, is an important constituent of glycoproteins, such as mucin and the various mucoids, and may be obtained from them by hydrolysis. It is also present in chitin, a constituent of the shells of the lobster. Glucosamine reduces Fehling's solution, and its general properties are much like those of glucose.

Galactose is an aldohexose, like glucose:



It is obtained by the hydrolysis of lactose or milk sugar. It is also an important constituent of the cerebrosides of the brain. Like glucose, it forms an osazone with phenylhydrazine (differing, however, in structure), and reduces Fehling's solution, but ferments slowly with yeast. On oxidation, it forms mucic acid (stereoisomer of saccharic acid), which also differentiates galactose from glucose.

Fructose, or levulose, or fruit-sugar, found in honey, has the formula:

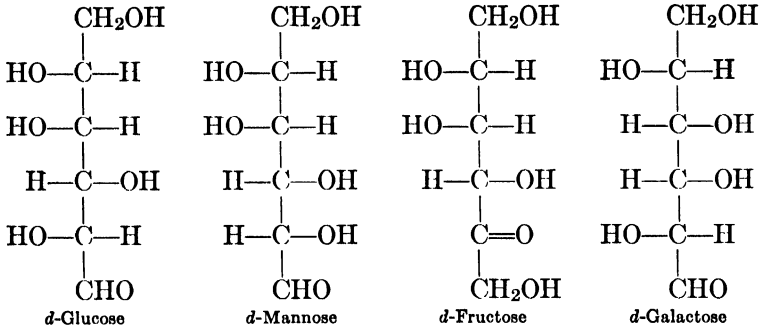


and is, therefore, a ketohexose, isomeric with glucose and galactose. Fructose, glucose and galactose are, physiologically, the three important hexoses. Fructose may be obtained by hydrolysis of

cane sugar or sucrose. Like the other two common hexoses, fructose reduces Fehling's solution and forms an osazone. The osazone with phenylhydrazine is the same as the one formed with glucose. It may be distinguished from glucose and galactose by the *Seliwanoff* test, which consists in heating fructose with resorcinol dissolved in dilute HCl, whereby a red color and a red precipitate are obtained. Fructose is 50 per cent sweeter than sucrose. A method has recently been proposed to prepare fructose in large quantities from the Jerusalem artichoke.

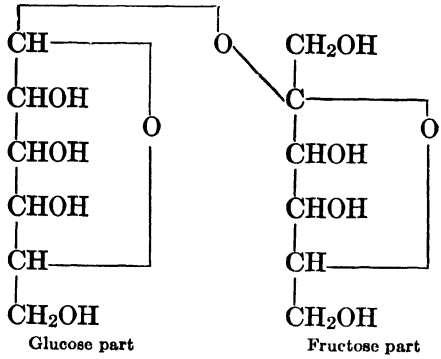
i-Fructose, $C_6H_{12}O_6$, is obtained by polymerization of six moles of formaldehyde with calcium hydroxide. A mixture of sugars is obtained known as " formose " from which *i*-fructose has been isolated. *i*-fructose is the racemic (*dl*) form.

The stereo-configuration of four of the hexoses can be shown by the following formulas:



What differences do you notice in these formulas?

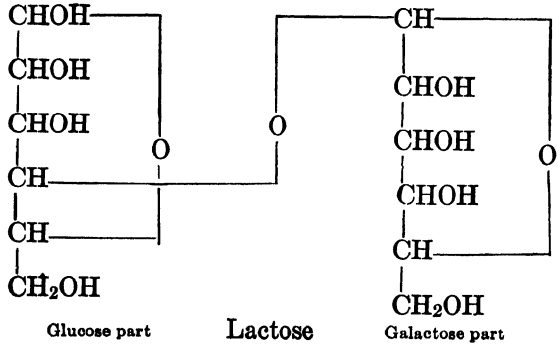
Sucrose, or cane sugar, $C_{12}H_{22}O_{11}$, is one of three physiologically important disaccharides, the other two being, lactose and maltose. On acid hydrolysis, sucrose yields a mixture of glucose and fructose (" invert sugar "). The same result is brought about by the enzyme *sucrase*, found in the small intestine. On a large scale, sucrose is obtained from sugar-cane, sugar-beet, etc. Unlike dextrose, fructose, galactose, maltose and lactose, five other important sugars, it does not reduce Fehling's solution, nor does it form an osazone—that is, it does not behave like an aldehyde or ketone sugar. To explain this, the suggested formula for sucrose does not contain a " free " CO group:



A recent noteworthy achievement has been the synthetic production of sucrose in the chemist's laboratory. Pictet has accomplished this by combining the tetraacetate of glucose with the tetraacetate of gamma-fructose. The octaacetate of sucrose so formed was hydrolyzed under pressure, giving sodium acetate and sucrose.

When sugar is heated above its melting-point, caramel is formed. This is a brown substance and is used extensively as a coloring material in food preparations.

(Whether the sugar is obtained from the sugar-cane or the sugar-beet, the principle involved in the extraction process consists in first separating the juice from the insoluble fiber, next in precipitating albuminous material and neutralizing the acids present, and finally in evaporating the filtrate and separating the crystals from the mother-liquor. The latter contains some 50 per cent of sucrose and is known as " molasses," a product used in the making of alcohol. If the " molasses " is derived from the sugar-cane, it may be used as table syrup and in the preparation of rum.)



Lactose, $C_{12}H_{22}O_{11}$, or milk sugar, occurs in milk to the extent of about 4 per cent. On hydrolysis, or by the action of the enzyme lactase in the small intestine, it yields glucose and galactose. Since it reduces Fehling's solution and forms an osazone, we assume that it contains a " free " CO group. (See formula on bottom of page 179.)

Maltose, $C_{12}H_{22}O_{11}$, or malt sugar, is found in malt, which is the sprouted grain of barley. This sprouted grain contains an enzyme, diastase, which converts the starch in the grain into maltose. A similar action occurs in the body when the enzyme ptyalin, found in saliva, acts on the starch in foods. When maltose is hydrolyzed by acids, or by maltase (an enzyme found in yeast and also in the small intestine) two molecules of glucose are obtained. (The maltase in yeast, acting on maltose, forms glucose, and then the zymase in yeast, acting on glucose, produces ethyl alcohol and CO_2.) Maltose behaves similarly to lactose, but the latter forms galactose as one of its products of hydrolysis, whereas maltose forms only glucose.

Raffinose, $C_{18}H_{32}O_{16}$, is a trisaccharide occurring in cotton seed, etc. It does not reduce Fehling's solution. On hydrolysis, it yields fructose, glucose and galactose. This hydrolysis may either be brought about by acids or by certain bacteria and yeasts.

Chitin, a tetrasaccharide, is probably composed of four glucosamine (p. **177**) units. It is prepared from the shells of lobsters or crabs.

Chondroitin, another tetrasaccharide, is contained in cartilage, often in combination with protein.

Starch, one of a number of polysaccharides having the general formula $(C_6H_{10}O_5)_x$, is widely distributed in the vegetable kingdom. It is synthesized in the plant by the combined action of carbon dioxide and water in the presence of chlorophyll. It is hydrolyzed in the body first to soluble starch, then to a number of dextrins, then to maltose and finally to glucose, and in the latter form is absorbed into the blood stream. Boiled with water, the granules swell and burst, and " starch paste " is obtained. Starch gives a blue color with iodine.

Dextrins of the general formula $(C_6H_{10}O_5)_x$, are considered somewhat less complex than starch itself, for the dextrins are obtained in the course of the hydrolysis of starch by enzymes.

Erythrodextrin gives a reddish-brown color with iodine and achrodextrin fails to give any color.

Glycogen, or "animal starch" $(C_6H_{10}O_5)_x$, is found almost exclusively in the animal kingdom, and particularly in the liver. It is the form in which carbohydrate is stored in the body. With iodine it gives a red color.

Inulin is a polysaccharide found in the tubers of the artichoke, dahlia, etc. Unlike starch, it is soluble in hot water and gives a negative reaction with iodine. On hydrolysis, it yields the monosaccharide levulose.

Cellulose, $(C_6H_{10}O_5)_x$, is the chief constituent of the cell wall of plants. Cotton fiber is almost pure cellulose, or "normal" cellulose. When hydrolyzed, cellulose yields glucose. Lignocellulose is probably a combination of cellulose with gums and resins, while pectocellulose is a combination of cellulose and a substance, pectin, the latter being responsible for the formation of jellies from fruit.

Cellulose is, chemically, highly inert. It may be dissolved (possibly with some changes) in *Schweitzer's* reagent (ammoniacal solution of copper oxide).

Acetyl derivatives may be obtained with glacial acetic acid, and acetic anhydride, showing cellulose to contain OH groups.

Industrially, cellulose is of immense importance. It is the chief ingredient of cotton, linen, hemp, etc., and of paper (which in turn, may be made from cotton and linen rags or from wood). Parchment paper is cellulose treated with conc. sulfuric acid. Mercerized cotton is cotton treated with sodium hydroxide solution, whereby the cotton is converted into a stronger fiber with a glossy appearance somewhat resembling silk. It takes dyes more readily than cotton.

Rayon, or as it was called for a time, *artificial silk,* is manufactured in one of four different ways. In the *nitrocellulose process,* the cotton linters are treated with a mixture of nitric and sulfuric acids, and the nitrocellulose so obtained is dissolved in alcohol and ether. The solution is then forced by pressure through capillary glass tubes and, by the application of blasts of hot air, the filaments which form, solidify. These filaments are still nitrocellulose in composition and highly flammable. The nitro group is therefore removed by treatment with sodium hydrosulfide. In the *cuprammonium process,* the linters or wood pulp are mixed with

copper hydroxide and the mixture dissolved in concentrated ammonia. The solution is forced through fine holes into a bath of caustic soda or sulfuric acid, thereby causing the filaments to coagulate. In the *acetate process* the linters are treated with acetic anhydride, glacial acetic acid and sulfuric acid also being present. The cellulose acetate so formed is precipitated with water and dissolved in acetone. The viscous solution is now forced under pressure through the capillary tubes to give rise to the fine filaments which, when spun in groups and twisted, gives rise to a yarn known in the trade as " Celanese " and " Lustron." Unlike the other varieties of rayon, which are really pure cellulose, this product is really cellulose acetate.

Cellulose acetate is more stable to heat and light than is cellulose nitrate. The former is now extensively used in the manufacture of non-inflammable photographic films, cellulose plastics, non-shatterable glass, phonograph records, lacquers, transparent wrappers, etc.

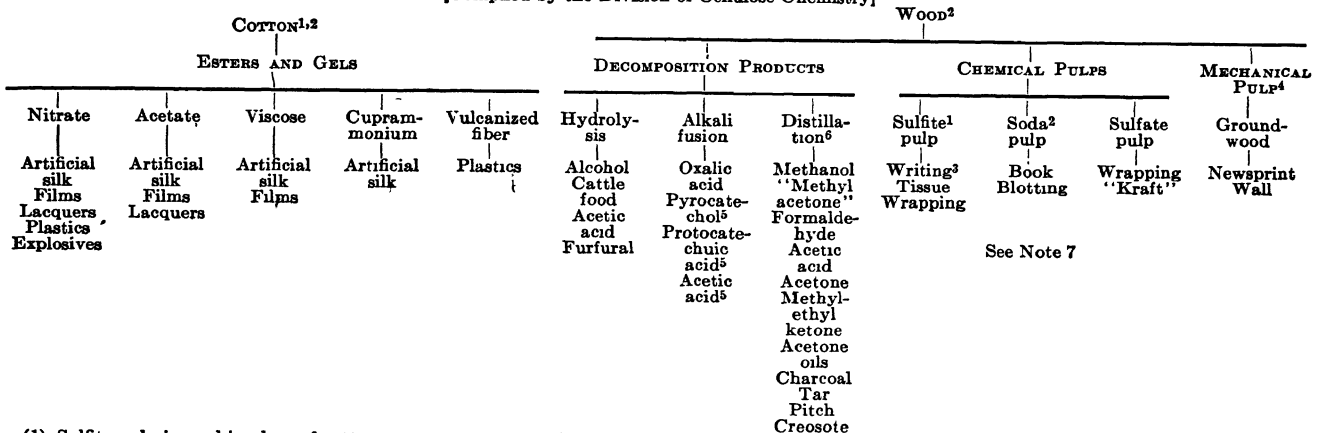
The method most commonly used in the preparation of rayon is the *viscose process*, a process by which 80 per cent of the total world's production of rayon is made. Spruce pulp or cotton linters are soaked in an 18 per cent caustic soda solution, thereby causing a swelling of the fibers and the production of a compound known as soda-cellulose. The soda-cellulose is next treated with carbon disulfide forming a product known as cellulose xanthate, which, unlike the cellulose, is a water-soluble compound, and which is known as " viscose." The solution is forced through fine holes and into sulfuric acid, the filaments so formed consisting of regenerated cellulose. In this process, as in the other three, the filaments are finally converted into skeins of twisted yarn. Here, as in the other processes, the skeins are bleached with chlorine. (In the viscose process, sulfur impurities arising from the use of carbon disulfide are removed by treatment with sodium sulfide prior to bleaching with chlorine.)

Within a generation rayon has taken a commanding place in the textile industry and is finding applications in all phases of the textile trade.

With nitric acid, cellulose forms various nitrate compounds. The higher nitrates (hexanitrate), such as gun-cotton (soluble in alcohol-ether-mixture), are explosives; and the lower nitrates are used in the manufacture of celluloid. Pyroxylin, a mixture

CHEMICAL PRODUCTS OF CELLULOSE

[Compiled by the Division of Cellulose Chemistry]



(1) Sulfite pulp is used in place of cotton to some extent especially in making the viscose products.

(2) Cotton linters are used for making certain paper pulps similar to the soda wood pulp.

(3) Rags are used a one or in mixture with sulfite pulp in high-grade writing papers.

(4) Mechanical pulp is, of course, not a chemical product, but its manufacture and use are so closely connected with the chemical pulp, especially sulfite pulp, that it is included here for completeness.

(5) Oxalic acid is the only product that has been made commercially by the alkali fusion of wood.

(6) Resinous wood distillation products are not included here because they are very largely products of the resin in the wood and not of the fiber.

(7) The papers mentioned here are only those that are made to a very large extent from the particular kind of pulp under which they are arranged. There are many different kinds of papers, but they cannot be readily arranged on this chart since they may be made up of so many different combinations of pulps

Following are some of these combinations:

	Sulfite (*A*)	Soda (*B*)	Sulfate (*C*)	Groundwood (*D*)
Newsprint				*A* and *D*
Book and magazine		*B*, *A*, and *B*;	*A*, *B*, and *D*	
Writing		*A*, *A* and rag paper		
Wrapping		*A*, *C*, *A* and *D*,	*C* and *D*	
Tissue		*A*, *A* and *D*		
Blotting		*B*		
Glassine		*A*		
Board		*D*, *A*, *C*, and old paper in various mixtures		
Wall		*D*, *D* and *A*,	*D* and *C*	
Bag		*A*, *C*, *A* and *D*,	*C* and *D*	

of lower cellulose nitrates, is used in preparing lacquers and making rayon and celluloid. It is soluble in amyl acetate and methanol.

An important product containing pyroxylin is known under the name of " Duco " and is used very extensively as a lacquer finish. The pyroxylin is dissolved in amyl acetate or other solvents, and small amounts of gums or resins are added, producing a lacquer. By the addition of finely ground pigments, pyroxylin enamels are produced. When a lacquer film is exposed to the air the solvents, which have acted as a vehicle for the pyroxylin, gums, pigments, immediately begin to evaporate, and in a short time a hard, tough film is produced. Linseed oil and other vegetable oil paints dry by air oxidation while the pyroxylin lacquers dry entirely by evaporation. Collodion, similar to pyroxylin in composition, is used for photographic films, as a protective covering for wounds, etc., and in the making of dialyzing bags. It is soluble in an alcohol-ether mixture. Celluloid is made by subjecting pyroxylin and camphor to heat and pressure. Cordite, a smokeless powder, is made by treating gun-cotton and nitroglycerine with acetone and some vaseline.

Mannans, Galactans, Hemicellulose, etc.—These substances, present in the seeds of numerous plants, resemble cellulose, but dissolve in dilute alkali and on hydrolysis yield not only glucose (as cellulose does) but other hexoses as well. Agar-agar is a galactan which yields galactose on hydrolysis. Mannans, as their name implies, yields mannose when hydrolyzed.

Gums, Pectins, Mucilages.—These are also polysaccharides containing pentose and hexose groups. The gums are probably carbohydrates combined with acids. Some are soluble, and others insoluble in water. Gum arabic, gum tragacanth, etc., are used as vehicles to suspend insoluble substances in aqueous emulsions. Mucilages form " viscous " liquids with water. The gelatinization of fruit extracts is due to the pectin present.

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CHAPTER XVIII

FOODSTUFFS AND THEIR CHANGES IN THE BODY

THE foodstuffs may be divided into carbohydrates, fats, proteins, mineral salts, water and vitamins. Some include oxygen in the list because of the very necessary part it plays in the oxidation of the foodstuffs in the body. We may dismiss the mineral salts, water and vitamins, because, so far as we know, they undergo no chemical changes preparatory to their absorption by the blood and tissues. We will confine ourselves to the carbohydrates, fats and proteins, because they do undergo profound chemical changes in the digestive tube and after they have left the digestive tube and enter the liver and various tissues of the body.

The fats and carbohydrates are ultimately oxidized to carbon dioxide and water, and eliminated as such. The proteins, aside from being oxidized to carbon dioxide and water, also form a number of nitrogenous products which appear chiefly in the urine, such as urea, uric acid, creatinine, etc. These nitrogenous products really represent incomplete stages in the oxidation of the protein, for the complete oxidation of protein would yield carbon dioxide, water and nitrogen.

Complex substances of the types of fats, proteins and carbohydrates are not immediately oxidized in the body to carbon dioxide, water, and relatively simple nitrogenous substances; there must be a number of intermediate steps in the process. During the past few years, organic and physiological chemists have been very busy tracing these steps. While there is still much to be elucidated, much has already been done, and a brief résumé of the work accomplished will be given here. For those desiring a more detailed account we must refer them to the references at the end of the chapter, particularly to Dakin's masterly monograph.

Carbohydrates.—The digestible carbohydrates are all broken down to monosaccharides before absorption. The enzyme

ptyalin (in saliva), amylopsin (in pancreatic juice), sucrase, maltase and lactase (in intestinal juice) hydrolyze the more complex carbohydrates to the hexoses,—glucose, levulose and galactose (p. 167). These are then absorbed through the walls of the small intestine, pass into the blood, thence to the liver, and there are synthesized to glycogen (p. 181) and stored as such. Whenever fuel is needed by the body, the glycogen reserve is called upon, and the glycogen is hydrolyzed to glucose, but this time to glucose only. Then this glucose is oxidized in the tissues to—ultimately—carbon dioxide and water.

It is believed that the first step in the oxidation of glucose is the splitting of the glucose molecule into two three-carbon molecules. It was believed at one time that the most probable three-carbon compound to be formed was lactic acid, since this substance is always produced by working muscle; but the view more generally held now is to regard either glyceraldehyde, $CH_2OH \cdot CHOH \cdot CHO$, or pyruvic aldehyde (methyl glyoxal) $CH_3 \cdot CO \cdot CHO$, as the first step in the decomposition of glucose, and lactic acid as a by-product obtained either from glyceraldehyde or pyruvic aldehyde. So that we may represent the first steps thus:

$$\underset{\text{Glucose}}{C_6H_{12}O_6} \rightarrow 2\underset{\text{Glyceraldehyde}}{CH_2OH \cdot CHOH \cdot CHO}$$

or

$$C_6H_{12}O_6 \rightarrow 2\underset{\text{Pyruvic aldehyde}}{CH_3 \cdot CO \cdot CHO} + 2H_2O$$

and lactic acid could then be formed in one of two ways:

$$\text{Glucose} \rightarrow \underset{\text{Glyceraldehyde}}{CH_2OH \cdot CHOH \cdot CHO}$$

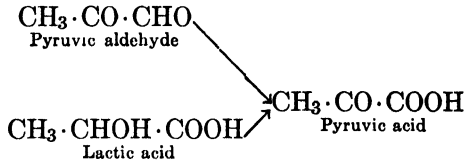
$$\rightarrow \underset{\text{Pyruvic aldehyde}}{CH_3 \cdot CO \cdot CHO} \rightarrow \underset{\text{Lactic acid}}{CH_3 \cdot CHOH \cdot COOH}$$

or, still better,

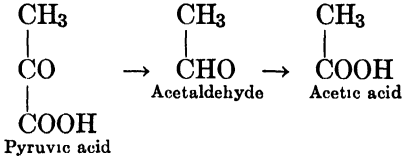
$$\text{Glucose} \rightarrow CH_3 \cdot CO \cdot CHO \rightarrow CH_3 \cdot CHOH \cdot COOH$$

(The action of alkali on glucose has been shown to yield the products mentioned in these reactions. Further, using surviving liver tissue, it has been possible to convert both pyruvic aldehyde and glyceraldehyde into lactic acid; and in diabetes, where the mechanism of the cell is disturbed, glyceraldehyde, pyruvic aldehyde and lactic acid have all been shown to produce glucose.)

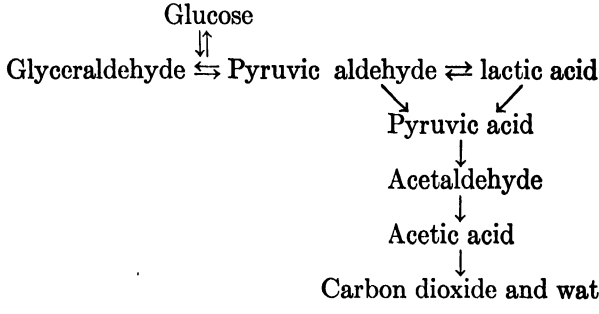
True oxidation probably comes into play at this point; that is to say, with the conversion of either pyruvic aldehyde, or lactic acid, into pyruvic acid;



Now it has been shown that in the organism, α-ketonic acids (of which pyruvic acid is an example) are changed into the fatty acid with one less carbon atom; in this case into acetic acid. It seems probable that the intermediate step here is acetaldehyde. (In this connection, it may be mentioned that yeast juice ferments pyruvic acid into acetaldehyde and carbon dioxide.) So that the steps are probably



The acetic acid is finally oxidized to carbon dioxide and water. Summarizing the various steps:



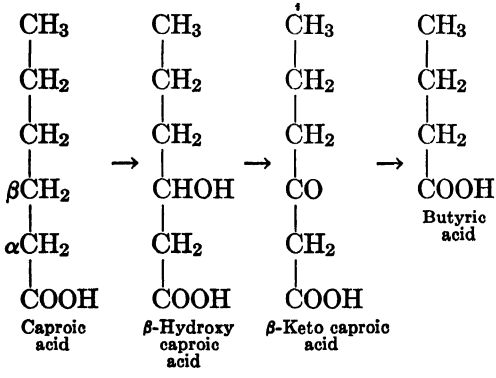
Fats.[1]—The straight fats, that is to say the glyceryl esters of stearic, palmitic and oleic acids (p. 105), are hydrolyzed in the digestive tract into glycerol and fatty acids. (Some fatty acid

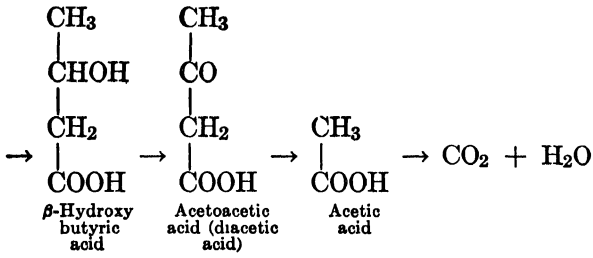
[1] The lipoids, such as lecithin and cholesterol (p. 110) often associated with fat in food, undergo changes in the body which are either too complex, or too little understood to be discussed here.

is also converted into soap, due to the alkalinity of the medium.) This is mainly brought about by the enzyme lipase (in the pancreatic juice), which, in turn, is very actively assisted by the "bile salts," the sodium glycocholate and sodium taurocholate (found in bile). The fatty acids and glycerol, immediately after absorption through the walls of the small intestine, are synthesized back again into fats, and as such pass from the lacteals into the lymph, into the thoracic duct, and thence into the general circulation. The fat not needed for immediate use is largely stored in the adipose tissues.

The preliminary step in the oxidation of fats is probably one of hydrolysis into glycerol and fatty acid. It may be assumed that the glycerol is first oxidized to glyceraldehyde, which would then, of course, follow the usual scheme of carbohydrate oxidation (p. 187). The oxidation of the fatty acid part of the molecule probably takes place in accordance with a theory first advanced by Knoop and known as Knoop's "β-oxidation theory." According to this view, the fatty acid is first attacked in the β-position, being changed to a hydroxy and then to an oxy (keto) acid. The α and β carbon atoms (with their hydrogen atoms) are probably next oxidized to carbon dioxide and water, leaving a fatty acid containing two less carbon atoms. Then the process is repeated until finally carbon dioxide and water are produced. At each stage of the process, two carbon atoms are removed, so that, if we start with stearic acid, containing C_{18} atoms, we pass to palmitic, C_{16}, then to C_{14}, etc.

To illustrate the process, let us assume, that we have reached the C_6 stage with caproic acid. The changes can be illustrated as





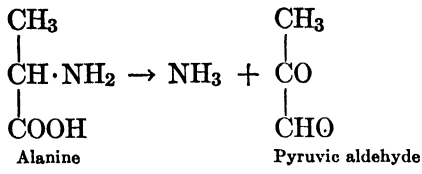
In diabetes, the poisonous "acetone bodies" or "acid bodies" which are so often produced, are derived from fats. These "acetone bodies" include butyric acid, β-hydroxybutyric acid, acetoacetic acid and acetone. The acetone is a by-product obtained probably from acetoacetic acid by the loss of CO_2. It would seem as if the diabetic has not only difficulty in oxidizing glucose, but also in completely oxidizing fats; the fats in his case are oxidized to the four-carbon stage and no further. Kahn, working with the knowledge that the naturally-occurring fats all contain an even number of carbon atoms, and stimulated by Knoop's theory that fatty acids are oxidized in such a way as to lose two carbon atoms at each stage, has synthesized an odd-carbon fat—from margaric acid, $C_{16}H_{33}\cdot COOH$, a C_{17} acid—, which, when given to the diabetic, is said not to produce "acetone bodies," because in the oxidation of this odd-carbon fat, the four-carbon acids are avoided; thus

$$C_{17} \rightarrow C_{15} \rightarrow C_{13} \rightarrow C_{11} \rightarrow C_9 \rightarrow C_7 \rightarrow C_5 \rightarrow C_3 \rightarrow C_1$$

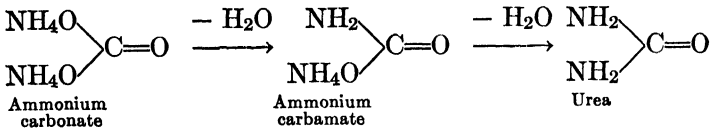
Proteins.—The proteins [1] are hydrolyzed in the digestive tract by the enzymes pepsin (in gastric juice), trypsin (in pancreatic juice) and erepsin (intestinal juice). The final hydrolytic products are amino acids (p. 152). The amino acids are absorbed as such, and either finally pass into the tissue to form tissue protein, probably in some such way as outlined in Fischer's synthesis of polypeptides from amino acids (p. 151), or are eliminated principally in the form of urea, by a process of "de-amination," which occurs very largely in the liver, but may also occur in other tissues. This process of "de-amination" is essentially the splitting off of the NH_2 group from the amino

[1] We refer here to the "simple" proteins (p. 149). The "conjugated" proteins (p. 150) present many difficulties.

acid. Dakin has shown that an α-amino acid, in water, undergoes spontaneous dissociation into the corresponding α-ketonic aldehyde and ammonia; so that if we take alanine as an example of an α-amino acid, we would get

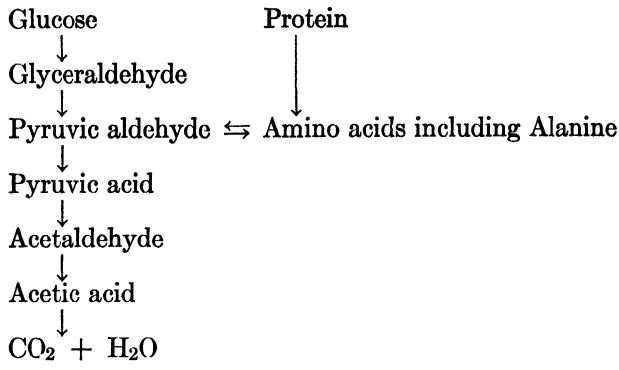


The pyruvic aldehyde would then most probably be further oxidized according to the scheme outlined under carbohydrates. (This, by the way, explains how proteins may also serve as a source of energy; and it also suggests how, in cases of diabetes, the carbohydrate is formed from protein.) The ammonia combines with carbonic acid, a constant product of metabolism, to give ammonium carbonate, which, by a process of dehydration, is finally converted into urea:



It has already been mentioned that in the urine we find nitrogenous products other than urea. Since protein is the only one of the three classes of foodstuffs which contains the element nitrogen, it is reasonable to assume that these nitrogenous products are of protein origin. Even under normal conditions a small quantity of ammonia (in the form of ammonium salts) is eliminated. We also find uric acid and purine bases, which are obviously derived from the nucleoproteins of the food (or body tissues) and the purine substances, such as are found in meat, for example (see p. 156). An appreciable amount of creatinine, and, to a less extent, creatine (see p. 121), is also found in the urine.

The probable interrelationships of protein, fat and carbohydrate in the body.—The connecting links between protein and carbohydrate have already been indicated. They will be shown schematically here:



What are the connecting links between fats and carbohydrates? How are we to explain that an excess of carbohydrate is so easily deposited in the form of fat? The glycerol part of the fat is obviously connected with the gylceraldehyde from glucose:

$$\text{Glycerol} \underset{\text{Reduc.}}{\overset{\text{Oxid.}}{\rightleftharpoons}} \text{Glyceraldehyde}$$

But how are we to suggest the possible formation of a complex fatty acid from the glucose molecule?

It has been suggested that the synthesis may be along the lines of an aldol condensation (p. 80). Starting with acetaldehyde, a product formed in the oxidation of glucose, two molecules of the aldehyde may condense to give:

$$CH_3CHO + CH_3CHO \rightarrow \underset{\beta\text{-Hydroxy butyraldehyde}}{CH_3 \cdot CH(OH) \cdot CH_2 \cdot CHO}$$

which may then combine with another molecule of acetaldehyde to give a 6-carbon compound, and so on, until the C_{16} or C_{18} is reached. By simultaneous reduction and oxidation, or the transfer of the oxygen attached to the β-carbon to the end carbon, the hydroxy aldehyde may be converted to the normal, saturated acid.

Another theory, largely due to Miss Smedley, and based on sound experimental evidence, may be summarized as follows: Pyruvic acid and acetaldehyde—both products formed in the oxidation of glucose—condense thus:

$$CH_3CHO + CH_3 \cdot CO \cdot COOH \rightarrow CH_3 \cdot CH{:}\,CH \cdot CO \cdot COOH + H_2O$$

The ketonic acid is next converted into its aldehyde and carbon dioxide in a manner similar to the conversion of pyruvic acid to acetaldehyde (p. 188).

(*A*) $CH_3 \cdot CH : CH \cdot CO \cdot COOH \rightarrow CH_3 \cdot CH : CH \cdot CHO + CO_2$

This aldehyde has two more carbon atoms than the acetaldehyde with which we started; it now condenses with another molecule of pyruvic acid, forming a ketonic acid with more carbon atoms; and so on.

The oxidation of the unsaturated ketonic acid (*A*) yields an unsaturated acid with one less carbon atom:

$CH_3 \cdot CH : CH \cdot CO \cdot COOH + O \rightarrow CH_3 \cdot CH : CH \cdot COOH + CO_2$

By reduction we obtain a fatty acid containing two more carbon atoms than the aldehyde from which we started.

READING REFERENCES

DAKIN—Oxidations and Reductions in the Animal Body.

LUSK—The Science of Nutrition. (1928), chaps. 10 (Protein) and 14 (Carbohydrate).

SHERMAN—Chemistry of Food and Nutrition. (1927), chap. 5 (Fate of Foodstuffs in Digestion).

CHAPTER XIX

SULFUR, PHOSPHORUS, ARSENIC AND ORGANO-METALLIC COMPOUNDS

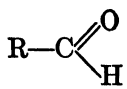
Sulfur Compounds

Sulfur is just below oxygen in the periodic table, and the two elements should, therefore, show close relationships. We find abundant evidence of such structural relationships in organic chemistry. An entire series of analogous compounds may be formed by substituting sulfur for oxygen in organic compounds.

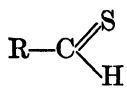
ROH	RSH	CH_3SH
Alcohol	Mercaptan or thioalcohol	Methyl mercaptan or methyl thioalcohol

They are called mercaptans for they combine with mercury compounds (*corpus mercurium captans.*).

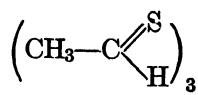
RO Metal	RS Metal	C_2H_5SNa
Alcoholate	Thioalcoholate or mercaptide	Sodium ethyl mercaptide
ROR	R—S—R	C_2H_5—S—C_2H_5
An ether or alkyl oxide	Alkyl sulfide or a thioether	Ethyl sulfide or ethyl thioether
HO—OH or H_2O_2	H—S—S—H or H_2S_2 as in Na_2S_2	R—S—S—R Organic disulfide



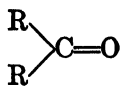
Aldehyde



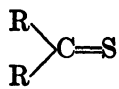
Thioaldehyde



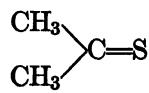
Trithioacetaldehyde



Ketone

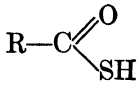


Thioketone

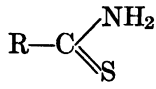


Thioacetone

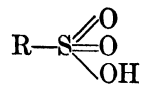
In addition to these types of compounds we have:



Thioacids



Thioacid amides



Alkanesulfonic acids, or alkyl sulfonic acids

Alkyl isothiocyanate

and others, showing in every case the close analogy of these sulfur compounds to the corresponding oxygen ones.

Many of these sulfur compounds may be prepared from their oxygen analogues by the use of phosphorus pentasulfide; e.g.,

$$5R{-}O{-}R + P_2S_5 \rightarrow 5R{-}S{-}R + P_2O_5$$

Most of the compounds having the structure R—S—H and R—S—R have exceedingly putrid disagreeable odors and are poisonous.

Mercaptans may be prepared:

1. By the action of potassium hydrogen sulfide on the halogen compound: e.g.,

$$C_2H_5\boxed{I + K}SH \rightarrow C_2H_5SH + KI$$

2. By the action of phosphorus pentasulfide on an alcohol; e.g.,

$$5C_2H_5OH + P_2S_5 \rightarrow 5C_2H_5SH + P_2O_5$$

Mercaptans are converted to mercaptides thus:

$$C_2H_5SH + KOH \rightarrow C_2H_5SK + H_2O$$

On oxidation, R—S—H (where the S is divalent) becomes R—S(=O)(=O)—OH, an alkanesulfonic acid (where the S is hexavalent).

Sulfides.—These may be prepared:

1. By the action of a thioalcoholate on the halogen compound:

$$R\boxed{X + Na}SR \rightarrow R{-}S{-}R + NaX$$

(Analogous to $R\boxed{X + Na}OR \rightarrow$ ROR— an ether— + NaX)

2. By the action of potassium sulfide on the halogen compound

$$2RCl + K_2S \rightarrow R{-}S{-}R + 2KCl$$

The thioethers on oxidation give, first, R—S(=O)—R, a sulfoxide and then R_2SO_2, a sulfone.

Mercaptans, sulfides, disulfides, etc., occur in petroleum.

Mustard gas (one of the most toxic gases used in the late war) is

$(ClCH_2 \cdot CH_2)_2S$ β, β′-dichloroethyl sulfide

It was manufactured by passing ethylene into sulfur monochloride,

$$2CH_2{=}CH_2 + S_2Cl_2 \rightarrow (ClCH_2{-}CH_2)_2S + S$$

Oil of garlic contains allyl sulfide:

$(CH_2{=}CH \cdot CH_2)_2S$

Sulfonal may be prepared from acetone by combining it with ethyl mercaptan in presence of a dehydrating agent and oxidizing the product with $KMnO_4$:

$$(CH_3)_2C{=}O + 2HSC_2H_5 \xrightarrow{HCl\ gas} (CH_3)_2C(SC_2H_5)_2 \xrightarrow{Oxid.} (CH_3)_2C(SO_2C_2H_5)_2$$

Acetone ethyl mercaptol — Diethyldisulfone dimethylmethane or sulfonal

Sulfonal has hypnotic properties and is used as a soporific. Trional is the ethyl derivative in place of one methyl group. The starting substance for its synthesis is $C_2H_5 \cdot CO \cdot CH_3$.

Thioacetic acid, CH_3COSH is prepared by the following reaction:

$$CH_3 \cdot COCl + KSH \rightarrow CH_3 \cdot COSH + KCl$$

Sulfoacetic acid is $CH_2(SO_3H)(COOH)$.

Trithioacetaldehyde, $\left(CH_3-C(=S)H\right)_3$ and thioacetone, $(CH_3)_2C=S$, are prepared by the action of H_2S on acetaldehyde and acetone, respectively.

The alkane sulfonic acids (or alkyl sulfonic acids) of the type $R-S(=O)_2OH$ are not of particular importance in the aliphatic series, but they are in the aromatic series.

Taurine, or β-amino ethanesulfonic acid, $CH_2(NH_2)-CH_2-S(=O)_2OH$, is a constituent of taurocholic acid, which in the form of its sodium salt is an important constituent of the bile.

Xanthic acid, $C(=S)(SH)(OC_2H_5)$, is the ethyl ester of dithiocarbonic acid. Cellulose xanthate $\left(C(=S)(SNa)(O\ \text{cellulose})\right)$ is produced when cellulose is heated with CS_2 and NaOH solution. This is the basis for the "viscose" artificial silk. Thiourea, $C(=S)(NH_2)_2$, is the sulfur analogue of urea, $C(=O)(NH_2)_2$, which in turn is the principal nitrogen end product in the metabolism of proteins in the body. Allyl isothiocyanate, $CH_2=CH-CH_2-N=C=S$, is present in mustard oil.

Phosphorus and Arsenic Compounds

According to the periodic table, nitrogen, phosphorus, arsenic and antimony belong to the same family of elements. This implies that compounds of P, As and Sb, analogous to N com-

pounds, should exist. These do exist. We have, for example, in inorganic chemistry:

NH_3	PH_3	AsH_3	SbH_3
Ammonia	Phosphine	Arsine	Stibine

and in organic chemistry:

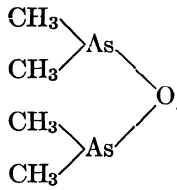
$(CH_3)_3N$	$(CH_3)_3P$	$(CH_3)_3As$	$(CH_3)_3Sb$
Trimethylamine	Trimethylphosphine	Trimethylarsine	Trimethylstibine

$(C_2H_5)_4N—OH$ $(C_2H_5)_4P—OH$ etc.

Tetraethylammonium hydroxide Tetraethylphosphonium hydroxide

(The phosphorus compounds are, as a rule, more reactive than the corresponding nitrogen compounds).

(A number of proteins, such as the nucleoprotein found in the nucleus of cells, the casein in milk, and the phosphatides—of which the lecithin of egg yolk and brain tissue is an example—contain the element phosphorus as an integral part of a complex molecule.) (See p. 110.)

Cacodyl oxide,  , is obtained when arsenic tri-

oxide and potassium acetate are distilled:

$$As_2O_3 + 4CH_3COOK \rightarrow (CH_3)_4As_2O + 2K_2CO_3 + 2CO_2$$

The name **cacodyl**—"stinking"—was given to the group $(CH_3)_2As$—by Bunsen, its discoverer. The cacodyl compounds are highly poisonous. The salts of cacodylic acid, $(CH_3)_2As\langle{}^{O}_{OH}$, as the sodium, calcium, iron and mercury cacodylates, are used in the treatment of syphilis, tuberculosis, malaria and pellagra.

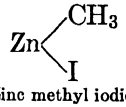
Ethyl dichloroarsine, $C_2H_5AsCl_2$, and $CH{=}CH \cdot AsCl_2$ (Cl), chlorovinyl dichloroarsine, known as "Lewisite"—were used as war gases.

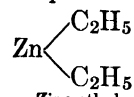
The antimony compounds are similar in structure to those of arsenic.

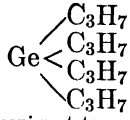
A number of very important arsenic compounds will be discussed under the aromatic series (p. 338).

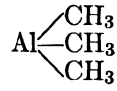
Organo-metallic Compounds

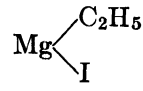
Various combinations of organic radicals with metallic elements are known. The following are examples:

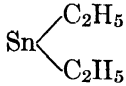

Zinc methyl iodide

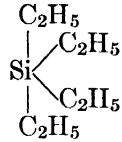

Zinc ethyl

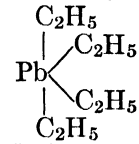

Germanium tetrapropyl


Aluminum trimethyl


Magnesium ethyl iodide


Tin diethyl


Silicon tetraethyl


Lead tetraethyl

Compounds of the type R—Mg—X, are highly important, since they are extensively used in organic chemistry. Only a few examples are given.

$$CH_3I + Mg \rightarrow CH_3 \cdot Mg \cdot I$$

$$CH_3 \cdot \boxed{Mg \cdot I + HO} H \rightarrow CH_4 + Mg(OH)I$$

For the preparation of secondary and tertiary alcohols see p. 55. Using the Grignard compounds, we can synthesize alcohols, ethers, aldehydes, ketones, acids, esters, nitriles, organometallic compounds, etc.

(Lead tetraethyl is used as the "anti-knock" compound in automobile engines. It may be prepared thus:

$$Na_4Pb + 4C_2H_5Cl \rightarrow Pb(C_2H_5)_4 + 4NaCl$$

The product sold as "ethyl gas" is gasoline containing a small quantity of lead tetraethyl and carbon tetrachloride or ethylene dibromide.)

READING REFERENCES

Wren—Organometallic Compounds of Zinc and Magnesium.

West and Gilman—Organomagnesium Compounds in Synthetic Chemistry. *National Research Council*, Washington, 1922.

Norris—The Opportunities for Research in Aliphatic Chemistry. *Industrial and Engineering Chemistry*, **18**, 262 (1926).

Kraus—The In-Organic Side of Organic Chemistry. *Journal of Chemical Education*, **6**, 1478 (1929).

From now on compare the following chapters with the corresponding ones in the aliphatic series.

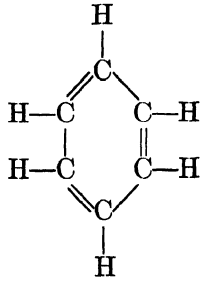
CHAPTER XX

INTRODUCTION TO CYCLIC COMPOUNDS

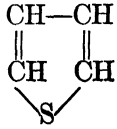
So far we have been studying the "open-chain," or "aliphatic" series of compounds. Now we are about to take up the "closed-chain" or "cyclic" compounds, which, in many respects possess properties differing from those of the aliphatic series.

The cyclic compounds may be subdivided into two main divisions:

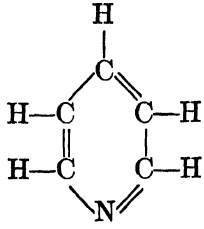
I. **Carbocyclic compounds,** containing a closed ring of carbon atoms such as benzene, for example,



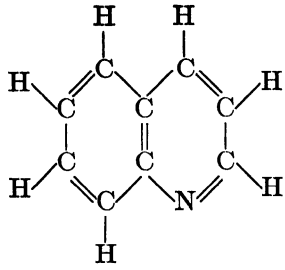
II. **Heterocyclic compounds,** containing a closed ring which, in addition to carbon atoms, may contain one or more atoms of other elements, such as thiophene,



or pyridine

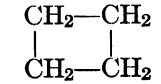


Combinations of carbocyclic and heterocyclic rings are also possible; for example, quinoline,

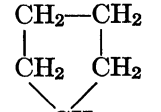


We have seen how the aliphatic series of compounds can be divided into typical groups, such as hydrocarbons, alkyl halides, alcohols, ethers, etc., and how the members of any one group show certain common characteristics which distinguish them from members of another group. Such typical divisions can also be made in the aromatic series, and here, to a certain extent, we find a series of compounds strictly analogous to those in the aliphatic series. Many of the type reactions which we shall consider in the following pages are those with which the student is already familiar.

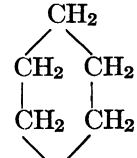
We have seen how the hydrocarbons of the aliphatic series can be classified into paraffins, C_nH_{2n+2}, olefins, C_nH_{2n}, and acetylenes, C_nH_{2n-2}. A series of compounds isomeric with the olefins are the following:



Cyclobutane
or tetramethylene



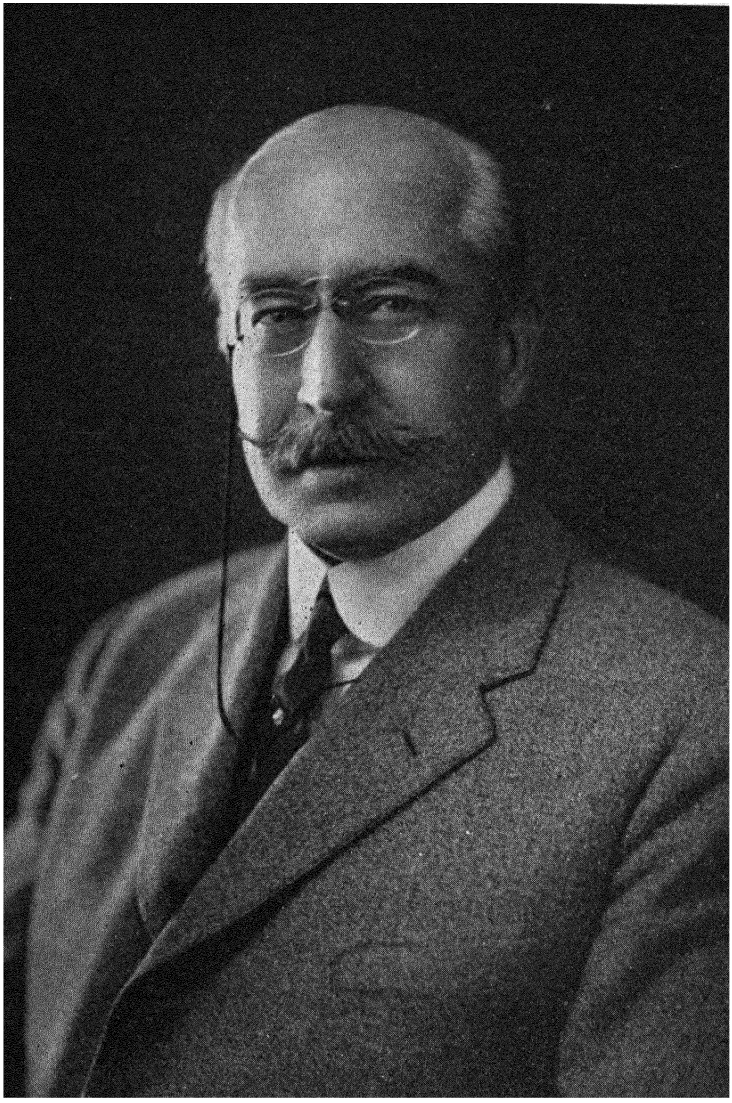
Cyclopentane
or pentamethylene



Cyclohexane
or hexamethylene

Unlike the olefins, these compounds are not readily oxidized with potassium permanganate, and they form substitution rather than addition products. They cannot, therefore, be represented as compounds having double bonds. In fact, to a certain extent, they rather resemble the paraffins, despite the fact that they are isomeric with the olefins; hence they are spoken of as the **cycloparaffins.**

The cycloparaffins, $(CH_2)_x$, are really the connecting link joining the aliphatic compounds on the one hand, and the aromatic, on the other.



MARSTON TAYLOR BOGERT (1868-)

PROFESSOR OF ORGANIC CHEMISTRY, COLUMBIA UNIVERSITY, HAS DONE EXTENSIVE WORK IN SYNTHETIC ORGANIC CHEMISTRY AND HAS HAD MUCH TO DO IN BUILDING UP A SCHOOL OF ORGANIC CHEMISTRY IN AMERICA

CHAPTER XXI

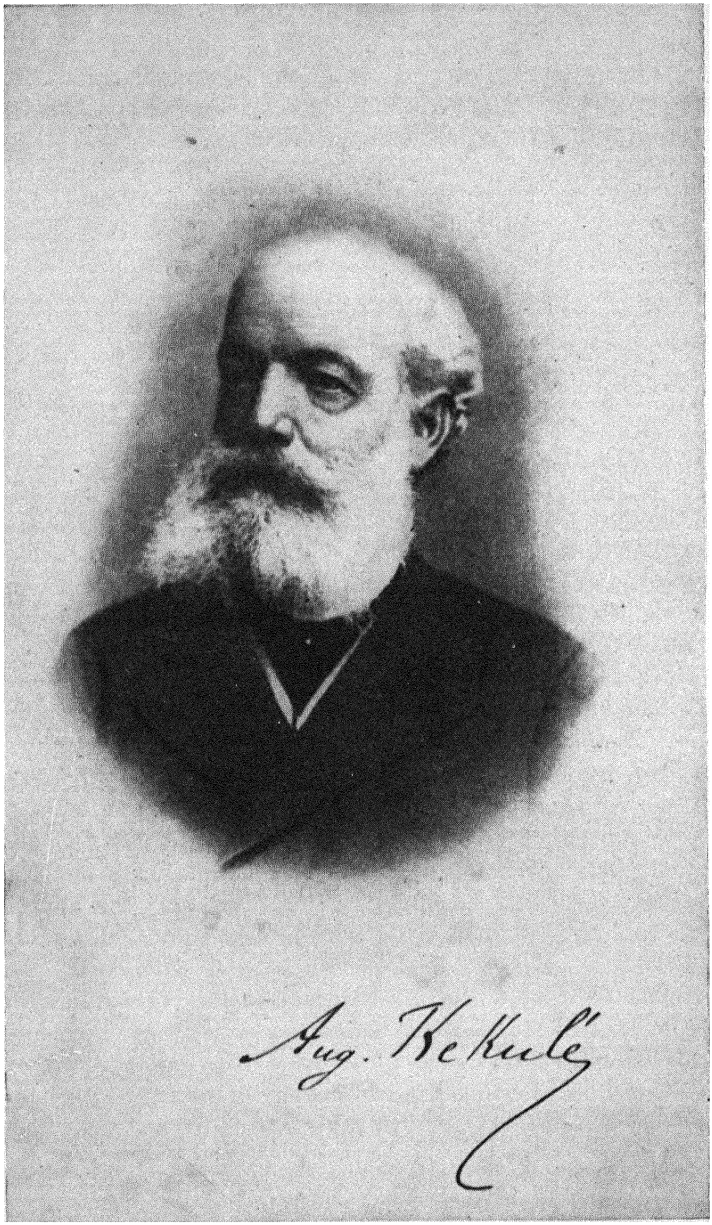
CONSTITUTION OF BENZENE AND THE AROMATIC HYDROCARBONS

THE division of our carbon compounds into "aliphatic" and "aromatic" is no less arbitrary than the division of chemistry into "organic" and "inorganic." The word "aromatic" came into use because many of the naturally occurring substances had an agreeable aroma (such as oil of bitter almonds, oil of wintergreen, vanillin, gum benzoin, turpentine oil, etc.), and these were put into a class by themselves. But a classification based on odor is of little value. Many of the aliphatic compounds (such as the esters) have an agreeable odor, and many belonging to the aromatic series possess little, or no odor.

Aliphatic compounds (the compounds so far considered) have been represented as straight chain compounds while the aromatic compounds will be represented by closed chain or ring formulas.

The aromatic compounds, as a whole, play a less important part in the chemical composition of living matter than do the aliphatic series. The proteins, fats, carbohydrates and phosphatides are largely of the aliphatic variety. On the other hand, many of the medicinals (drugs, antiseptics, etc.) come under the aromatic series. From the industrial standpoint, the vast group of synthetic dyes are largely recruited from the aromatic series.

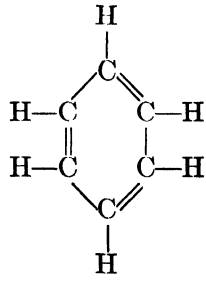
As we have seen, the mother substance of the aliphatic series is methane, CH_4. The mother substance of the aromatic series, on the other hand, is **benzene**, C_6H_6. It will at once be seen that compared with methane, benzene is low in hydrogen; its structure ought, therefore, to show double or triple bonds. But its properties, however, are more those of a saturated hydrocarbon, and any constitution assigned to it similar in type to



FRIEDRICH AUGUST KEKULÉ (1829–1896)

FIRST PROPOSED THE RING STRUCTURE FOR BENZENE AND ITS COMPOUNDS (P. 205).

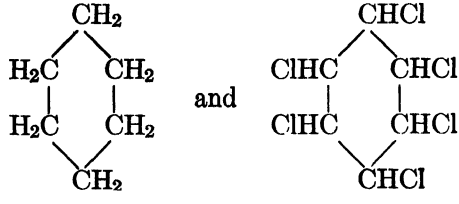
the one selected for ethylene or acetylene would grossly misrepresent the facts. This led Kekulé as far back as 1865 to propose a ring structure for benzene of the type:



and this formula is the one generally accepted to-day. It is no exaggeration to say that this benzene conception of Kekulé has proved of the utmost importance to the organic chemist, in giving him a tool with which to devise various possible chemical reactions.

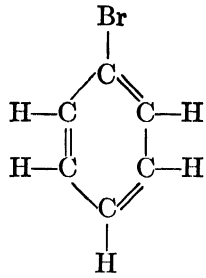
The structure of benzene, as suggested by Kekulé, is essentially that of a hexagon, containing six carbon and six hydrogen atoms. Any one hydrogen attached to a carbon atom is of equal importance to any other hydrogen attached to another carbon atom, and the carbon and hydrogen atoms all bear the same relationship to the molecule as a whole. There are, then, no preferences: any one atom in the molecule has exactly the same value as any other atom of the same element. The alternate double and single bonds satisfy the tetravalency of the carbon atom.

Kekulé's conception of the structure of the benzene molecule helps to explain many of the properties of benzene. According to this structure, the maximum number of hydrogen or chlorine atoms which can be added to benzene are 6, giving



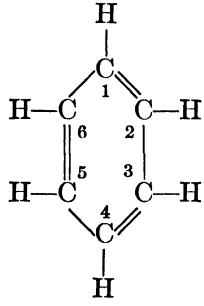
The addition of 6 hydrogen or 6 chlorine atoms implies the presence of three double bonds in the molecule.

If the benzene molecule is symmetrical and its carbon and hydrogen atoms are of equal value, then there can be but one, and no more than one, monosubstitution product, and the most extensive experimental work supports this view. For example, but one monobromobenzene,

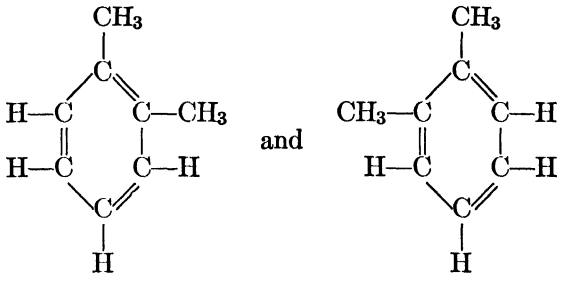


is known; it does not in the least matter to which carbon the bromine atom is attached.

On the other hand, Kekulé's benzene structure should allow for the possibility of three isomeric disubstitution products. If we number the carbon atoms as follows:

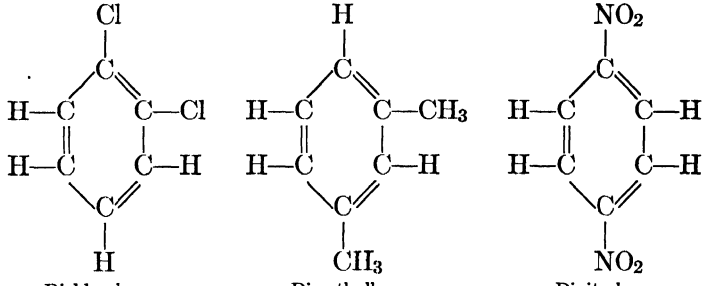


then we may have 1, 2, or 1, 6, or 2, 3 (or any adjacent pair) of hydrogen atoms replaced, giving an *ortho* (*o*-) compound; substitution in the 1, 3, or 2, 6, or 3, 5, or 1, 5 position will give a *meta*(*m*-) compound; and substitution in the 1, 4, or 2, 5, or 3, 6 position will yield a *para*(*p*-) compound.



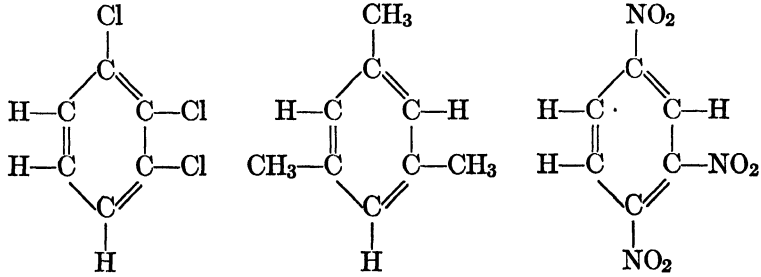
may be supposed at first sight to be different compounds, since in the one case the methyl groups are attached to two carbon atoms having a double bond in between, whereas in the other there is no double bond. But we must make the assumption that the double and single bonds are in continuous oscillation and not static.

Examples of disubstitution products are



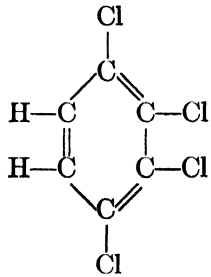
o-Dichlorobenzene | *m*-Dimethylbenzene | *p*-Dinitrobenzene

But three trisubstitution products are theoretically possible where the substituents are the same, and only three are actually known; e.g.,

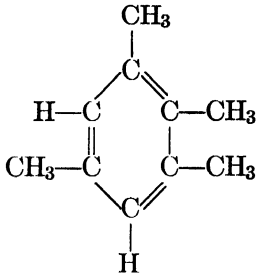


1, 2, 3-Trichlorobenzene (adjacent) | 1, 3, 5-Trimethylbenzene (symmetrical) | 1, 3, 4-Trinitrobenzene (unsymmetrical)

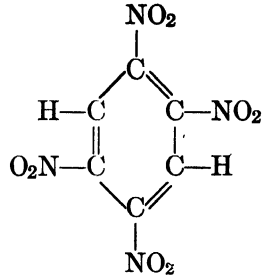
Where the tetrasubstitution products have like constituents, three isomers are possible: e.g.,



1, 2, 3, 4-Tetrachlorobenzene (adjacent)

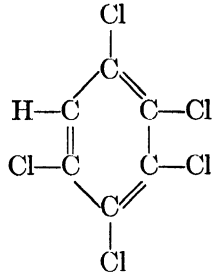


1, 2, 3, 5-Tetramethylbenzene (unsymmetrical)



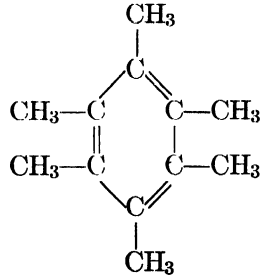
1, 2, 4, 5-Tetranitrobenzene (symmetrical)

With five substituents, but one compound is possible: e.g.,



Pentachlorobenzene

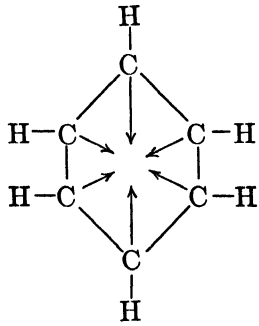
With six constituents but one compound is possible; e.g.,



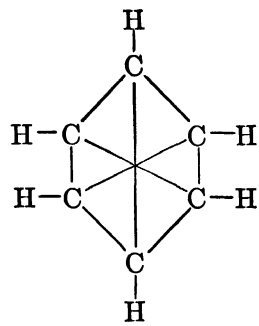
Hexamethylbenzene

There were many objections in the past in representing the benzene molecule as having double bonds. The objections

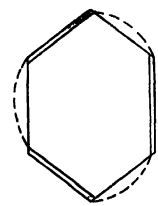
are still raised by every beginner in the subject. His studies of the unsaturated hydrocarbons (p. 34) lead him to believe that a compound whose formula has one or more double bonds is "unsaturated," and by virtue of that fact, shows some very specific properties; but, as has already been pointed out, the properties of benzene are not really those of an unsaturated compound at all. For example, benzene, unlike the olefins, or other unsaturated aliphatic compounds, does not react with dilute potassium permanganate; it does not react with hydrogen bromide; and with bromine it forms substitution rather than addition compounds. This has led a number of investigators to suggest formulas for benzene which do not contain the usual type of double bonds, such as:



Armstrong-Baeyer formula



Claus formula

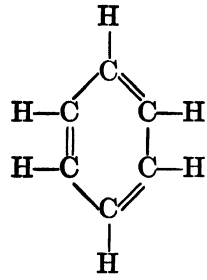


Thiele formula

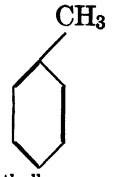
and others. (For those interested, we may refer them to Richter's Organic Chemistry, Vol. II, p. 41 (1922)). However, Kekulé's formula is still preferred by the majority of organic chemists, because it explains many of the chemical characteristics of benzene and its derivatives.

To simplify the writing of benzene and its derivatives we shall henceforth represent its structure as

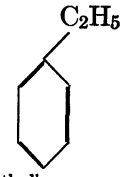
(Heavy lines indicate double bonds and light lines single bonds) bearing in mind that what is really meant is



In the compounds

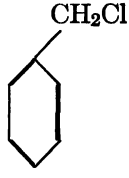


Methylbenzene

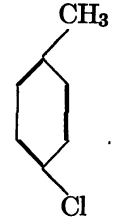


Ethylbenzene

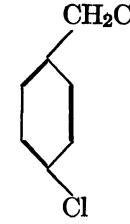
the CH_3 and C_2H_5 groups are spoken of as "side chains," the benzene residue being the "nucleus." Substitution may take place in the side chain, or in the residue, or in both, yielding various products; for example



Benzyl chloride [1]

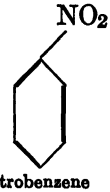


p-Chlorotoluene



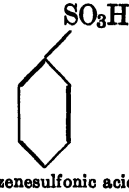
p-Chlorobenzyl chloride

Benzene differs from the paraffin hydrocarbons by the fact that whereas the latter are not acted upon by nitric or sulfuric acids, the former forms



Nitrobenzene

and



Benzenesulfonic acid

[1] The $C_6H_5.CH_2$ (monovalent) group is known as the "benzyl" group.

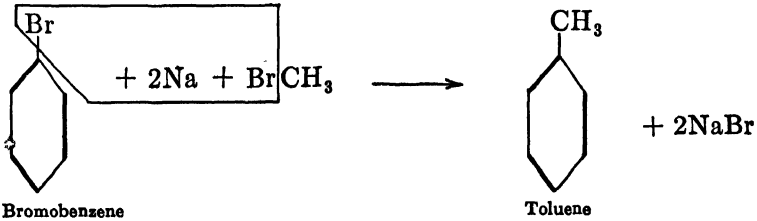
Sources of Aromatic Hydrocarbons.—The accompanying chart gives a list of the products obtained from the destructive distillation of coal and those of coal tar (among which we find the mother substances of the aromatic series of compounds, such as benzene, toluene, xylenes, naphthalene and anthracene).

(" Benzene " is to be sharply distinguished from " benzine." The latter represents a mixture of hydrocarbons obtained from petroleum, whereas the former, as we have seen, is a definite chemical compound, C_6H_6. Benzene is also sometimes called " benzol," a word we owe to German chemists. This name has little to recommend it, and is confusing, since the ending " ol " is usually reserved for substances containing the OH group. In the industries, the expression " 90 per cent benzol," signifies the fraction which distills below 100° C.; it contains about 70 per cent of benzene.)

Benzene and Some of its Homologues.—Like the hydrocarbons of the aliphatic series, and like the various classes of organic substances, benzene is the starting point of a homologous series:

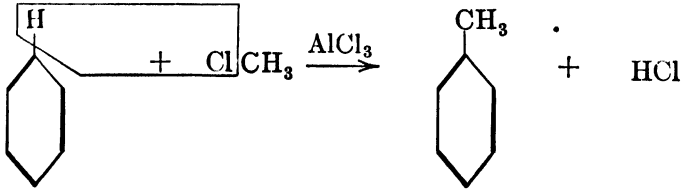
Benzene, C_6H_6	C_6H_5 group = phenyl (monovalent)
Toluene, C_7H_8	C_7H_7 group = tolyl (monovalent)
Xylenes, C_8H_{10}	C_8H_9 group = xylyl (monovalent)
Mesitylene, C_9H_{12} etc.	The monovalent radicals of the aromatic hydrocarbons are known as the aryl radicals. (Cf. alkyl groups.)

General Methods of Preparing Aromatic Hydrocarbons.—The hydrocarbons may be prepared by the *Fittig* synthesis, analogous to the *Wurtz* reaction already studied (p. 21), which consists of treating a mixture of the appropriate halides with sodium; e.g.,



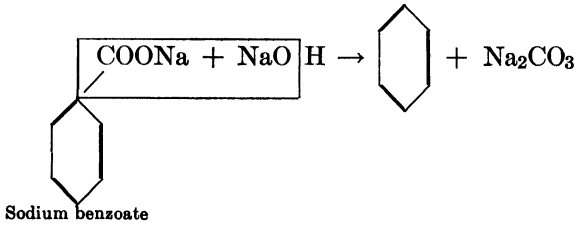
Bromobenzene Toluene

or by the *Friedel-Crafts* synthesis, in which the aromatic hydrocarbon and the appropriate halogen compound are made to react in the presence of aluminum chloride; e.g.,

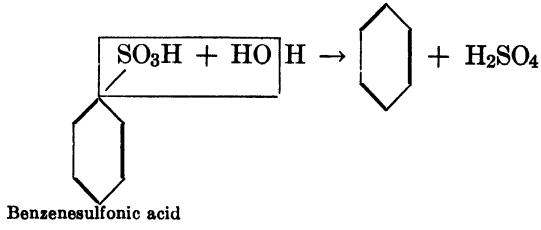


In this reaction HX is eliminated; the H atom must be linked to a carbon in a ring, while the X atom must be linked to a carbon not in a ring.

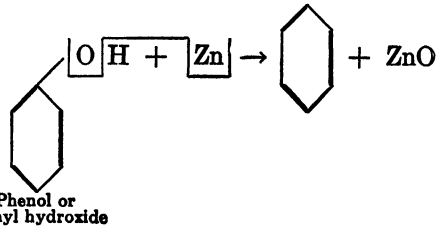
They may also be prepared by heating the salts of aromatic acids with soda lime—a reaction similar to one used in the preparation of the paraffins (p. 18); e.g.,



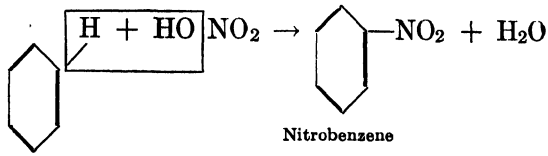
or, by the elimination of the SO_3H group from benzene compounds (by the use of steam, in the presence of acids); e.g.,



or, by distilling phenol with zinc dust; e.g.,



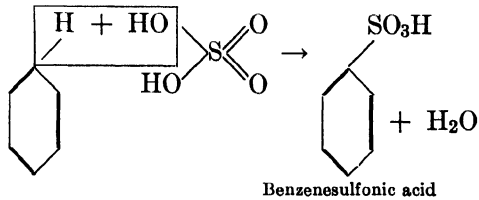
General Reactions of Aromatic Hydrocarbons.—Aromatic compounds react with nitric acid, forming nitro derivatives; e.g.,



Nitrobenzene

(This is known as **nitration.**)

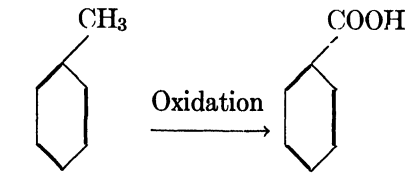
They also react with sulfuric acid forming sulfonic acids; e.g.,



Benzenesulfonic acid

(This is known as **sulfonation.**)

The "side chain," whether CH_3 or any other group, may be oxidized to the carboxyl group, COOH; e.g.,



Toluene or phenylmethane

Benzoic acid

(These reactions—nitration, sulfonation and oxidation—bring out the essential differences of aromatic and aliphatic hydrocarbons.)

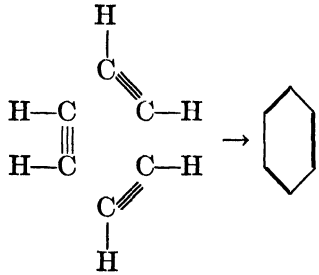
Benzene, C_6H_6, is the mother substance of the aromatic hydrocarbons. Commercially, it is obtained from coal tar. It is also present in California petroleum. It is a colorless liquid (b.p. 80.4°), burning with a smoky flame (due to the high percentage of carbon), and when its vapor is mixed with air and ignited it is explosive. It is used as a solvent for fats, resins, etc., and in the manufacture of a large number of aromatic compounds; e.g., nitrobenzene, chlorobenzene, etc. Crude benzene (benzol) is used extensively in motor fuel. Benzene is a narcotic which

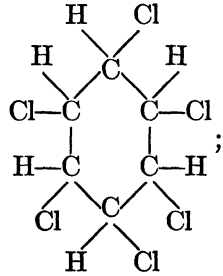
when swallowed or inhaled produces vertigo, delirium and convulsions.

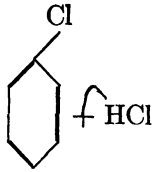
Preparation.—One method is to pass acetylene through a red hot tube:

$$3C_2H_2 \rightarrow C_6H_6$$

Here we have an example of how we can pass from an aliphatic to an aromatic compound—in this particular method, by "polymerization:"



With nitric and sulfuric acids, and with chlorine (long exposure to sunlight) we get, respectively, nitrobenzene, benzenesulfonic acid and benzene hexachloride,  ; chlorinated in the presence of iron, aluminum iodine, etc. (catalysts or "carriers"), we get



Chlorobenzene

Toluene, , or phenylmethane, or methylbenzene, is

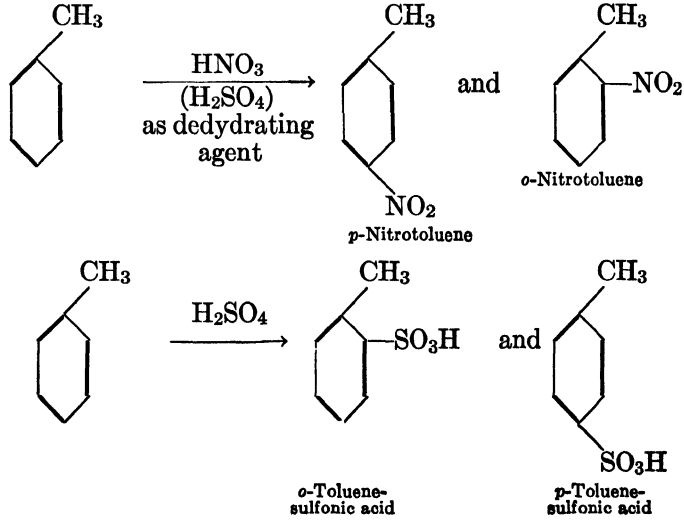
obtained from coal tar and also by the distillation of balsam of Peru and Tolu, b.p. 111°. (C_6H_5—monovalent is known as the " phenyl " group.) It may be prepared by the *Friedel-Craft* synthesis which has already been given (p. 212). Its properties are similar to those of benzene. When oxidized, it yields benzoic acid (p. 213).

Rules for Substitution in the Benzene Ring.—1. *If any one of the elements or groups, F, Cl, Br, I, R, OH, OR, CH_2X, NH_2, NHR or NR_2* (**these contain single bonds**) *is present in the ring, an element or group that may next be introduced will take the* **p-** *and* **o-** *positions with respect to the first group.*

2. *If any one of the groups, NO_2, SO_3H, CHO, COOH, CO·R or CN* (**these contain double or triple bonds**), *is in the ring, an element or group that may next be introduced will take (largely) the* **m-** *position with respect to the first group.* (The amounts of *m*-, *p*-, and *o*- products formed depend very largely upon such factors as temperature, concentration of reacting substances, the type of dehydrating agent, and other experimental factors.)

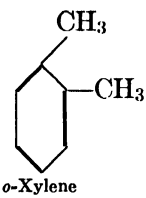
(It is essential before the student proceeds any further with the text that he thoroughly master these rules.)

An example of the application of these rules is immediately seen in the case of toluene. Toluene contains a methyl (R) group; hence, a second group will proceed simultaneously to the *p*- and *o*- positions; for example,

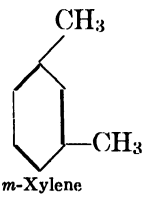


At low temperatures, the *o*- predominates, while at high temperatures the *p*-.

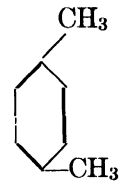
Xylenes, or dimethylbenzenes.—Since these are di-substitution products, three isomers are known:



o-Xylene

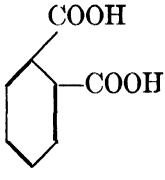


m-Xylene

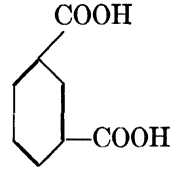


p-Xylene

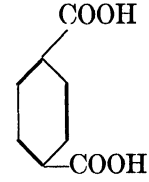
They are obtained from coal tar. On oxidation, the xylenes give the corresponding dibasic acids, indicating at the same time the position of the CH_3 groups:



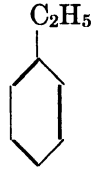
o-



m-

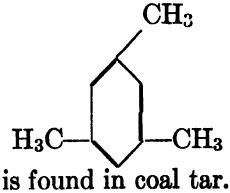


p-

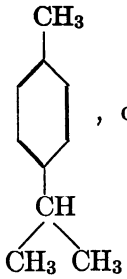
Ethyl benzene, 

, is an isomer of the xylenes, but is easily distinguished from them by the fact that on oxidation it yields benzoic acid,

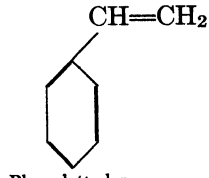
.

Mesitylene, 

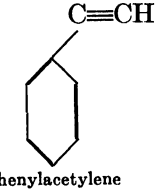
1, 3, 5 or symmetrical trimethylbenzene, is found in coal tar.

Cymene,  , or *p*-methylisopropylbenzene, is found in oil of thyme, oil of caraway, oil of eucalyptus, etc.

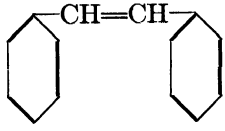
The number of hydrocarbons containing the benzene nucleus is large. Some are derived from coal tar, others are synthesized. A few of these compounds will be mentioned:



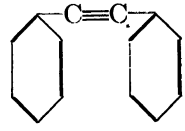
Phenylethylene or styrene



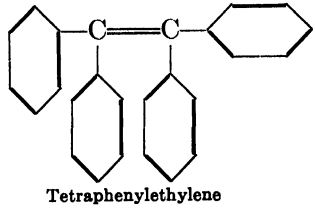
Phenylacetylene



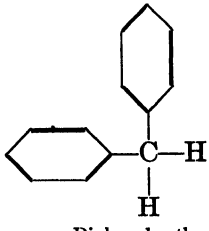
Symmetrical diphenylethylene or stilbene



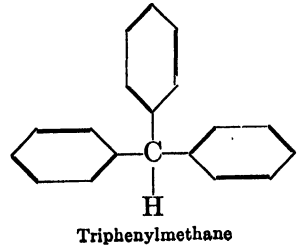
Diphenylacetylene or tolane



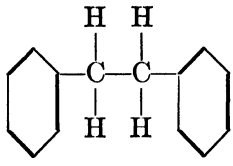
Tetraphenylethylene



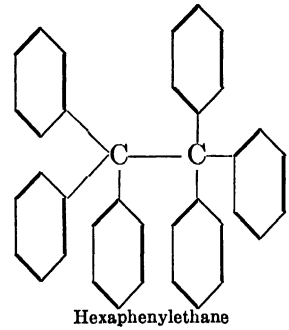
Diphenylmethane



Triphenylmethane

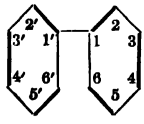


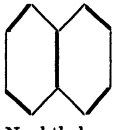
Symmetrical diphenylethane



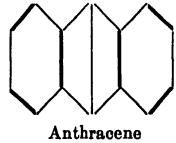
Hexaphenylethane

(Gomberg, of the University of Michigan, in studying the action of zinc upon triphenylchloromethane, has obtained a substance, **triphenylmethyl** $(C_6H_5)_3{\equiv}C$, in which one of the carbon atoms is apparently trivalent. $(C_6H_5)_3C{-}C(C_6H_5)_3 \leftrightarrows 2(C_6H_5)_3C$. Since the structure of organic compounds is so intimately bound up with the view that the carbon atom is tetravalent, Gomberg's triphenylmethyl, with its trivalent carbon atom, opens up many new lines of research.)

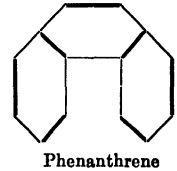
Diphenyl,  , or phenylbenzene, is made by the dehydrogenation of two mols. of benzene at an elevated temperature. Its high boiling point and its stability render this compound a very useful substitute for steam in boilers; it enables the apparatus to run at a higher temperature. Diphenyl, like benzene, may be chlorinated, nitrated, sulfonated, etc.



Naphthalene



Anthracene



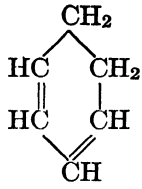
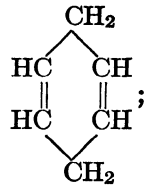
Phenanthrene

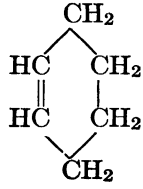
The last three compounds mentioned belong to the "conjugated" or condensed cyclic series, and will be taken up in detail in Chapter XXVIII.

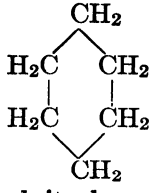
Hydroaromatic hydrocarbons are hydrogenated aromatic hydrocarbons; e.g., dihydrobenzenes:

MOSES GOMBERG (1866-)

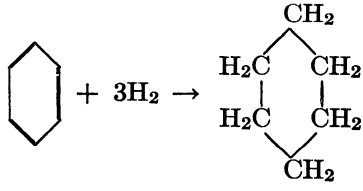
PROFESSOR OF CHEMISTRY AT THE UNIVERSITY OF MICHIGAN, IS ONE OF THE PIONEER WORKERS ON TRIVALENT CARBON AND FREE RADICALS (P. 218).


or

;

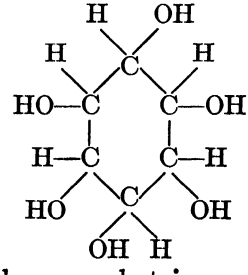
tetrahydrobenzene  and hexahydrobenzene or hexa

methylene,  . The last is found in Caucasian petro-

leum. It and its homologues are known as the naphthenes. The hexamethylene may be prepared by the *Sabatier* and *Senderen's* reaction (passing benzene vapor and hydrogen over finely divided nickel):



A derivative of hexahydrobenzene, known as hexahydroxy-

hexahydrobenzene, or inositol,  , is found in

heart muscle and other animal organs, but is present in larger amounts in unripe beans and peas. The empirical formula for this compound is $C_6H_{12}O_6$, and it has often been called a cyclic sugar, though in reality it possesses none of the common properties

READING REFERENCES

FINDLAY—The Treasures of Coal Tar.

WARNES—Coal Tar Distillation.

FINDLAY—Chemistry in the Service of Man. (1916), chap. 12 (Synthetic Chemistry).

SLOSSON—Creative Chemistry. (1920), chap. 4 (Coal Tar Colors).

JENKINS, MCCULLOUGH AND BOOTH—Syntheses in the Diphenyl Series. *Industrial and Engineering Chemistry*, **22,** 31 (1930).

CALDWELL AND SLOSSON—Science Remaking the World. (1923), pp. 48–79 (The Influence of Coal Tar on Civilization).

GOMBERG—Organic Radicals. *Chemical Reviews*, **1,** 91 (1924).

ROGERS—Manual of Industrial Chemistry. (1931), p. 827 (Coal Tar and Its Distillation).

HARROW—Eminent Chemists of Our Time. (1927), pp. 1–18, (Perkin and Coal Tar Dyes).

HOLLEMAN—Substitution in the Benzene Ring. *Chemical Reviews*, **1,** 187 (1924).

HOWE—Chemistry in Industry, Vol. I. (1924), chap. 4 (Coal, Coke and Their Products).

DARMSTAEDTER AND OESPER—August Kekulé. *Journal of Chemical Education*, **4,** 697 (1927).

NEWELL—Faraday's Discovery of Benzene. *Journal of Chemical Education*, **3,** 1248 (1926).

ASHDOWN—Earliest History of the Friedel-Crafts Reaction. *Industrial and Engineering Chemistry*, **19,** 1063 (1927).

SABATIER—How I Have Been Led to the Direct Hydrogenation Method by Metallic Catalysts. *Industrial and Engineering Chemistry*, **18,** 1005 (1926).

GOMBERG—Radicals in Chemistry, Past and Present. *Industrial and Engineering Chemistry*, **20,** 159 (1928).

GROGGINS—The Friedel-Crafts Reaction. *Industrial and Engineering Chemistry*, **22,** 620 (1930); **23,** 153, 893 (1931).

SCHNEIDER AND FROLICH.—Mechanism of Formation of Aromatics from Lower Paraffins. *Industrial and Engineering Chemistry*, **23,** 1405 (1931).

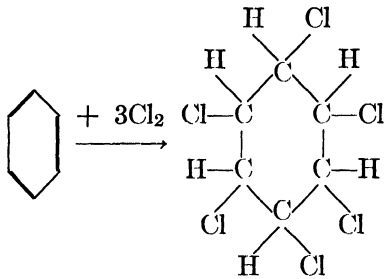
A two-reel motion-picture on "By-Product Coking" can be secured, free of charge, from The Koppers Company, Pittsburgh, Pa.

CHAPTER XXII

HALOGEN DERIVATIVES, SULFONIC ACIDS AND NITRO COMPOUNDS OF THE AROMATIC HYDROCARBONS

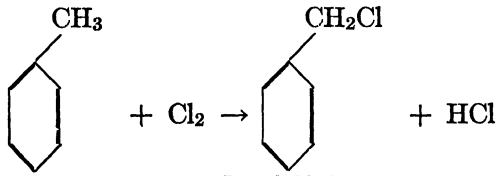
Halogen Compounds [1]

The halogens may react in one of three ways with aromatic hydrocarbons: (1) they may form addition products; e.g.,



Benzene hexachloride
or
hexachlorohexahydrobenzene

(This needs exposure to sunlight, but no carrier or catalyst.)
(2) Substitute in the side chain; e.g.,

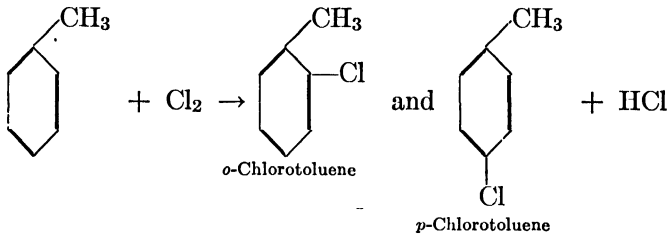


Benzyl chloride

[1] At this point the student is advised to review the chapter on aliphatic halogen compounds, p. 41.

(This is accomplished at the boiling temperature of toluene, in the presence of sunlight, or artificial light containing ultra-violet rays, but in the absence of a catalyst or halogen carrier.)

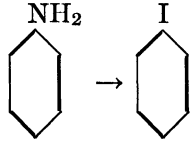
(3) The halogen may enter the ring; e.g.,



(This needs ordinary temperature, no sunlight and a carrier.)

The usual halogen " carriers " or catalysts, are $FeCl_3$, $FeBr_3$, $AlBr_3$, Fe, P, S, I, etc.

Preparation.—The halogen derivatives of the aromatic series may be prepared by direct halogenation with Cl_2 or Br_2, as just described (iodine does not react), or by the conversion of the corresponding amino compound into the halogen derivative, where the halogen takes the place of NH_2 : e.g.,



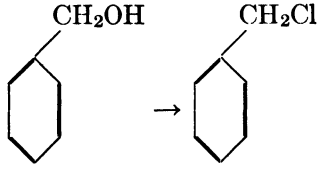
(See p. 243 for further details of the reaction.)

(Ethyl alcohol can be treated with hydrogen bromide, in the presence of sulfuric acid, to give C_2H_5Br, but when phenol,

, is treated with hydrogen bromide, no analogous reaction

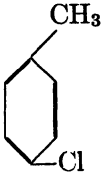
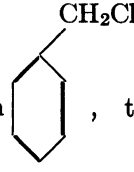
takes place. Again, when ethyl alcohol is acted upon by phosphorus pentachloride, PCl_5, we get C_2H_5Cl, but when phenol is similarly treated, only a small yield of chlorobenzene, is

obtained. On the other hand benzyl alcohol is readily transformed into benzyl chloride by PCl_5:

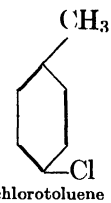


Notice that here the side-chain reacts. (The side-chain, in fact, behaves like an aliphatic, rather than like an aromatic group.)

In the place of chlorine the following substances are sometimes used to introduce the element: thionyl chloride, $SOCl_2$; chlorosulfonic acid, $ClSO_3H$; sulfuryl chloride, SO_2Cl_2; and sulfur mono- and sulfur dichloride, SCl and SCl_2.

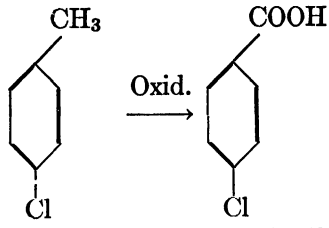
Properties.—Where the X is attached to the ring, as in  we get substances which may be colorless liquids or solids, with an agreeable odor, and which are stable; where the X is attached to the side-chain, as in  , the compounds have strong, disagreeable, pungent odors, are very reactive, and act as lachrymators. In general, they show the properties of the aliphatic halogen compounds of the type RX.

Some of the properties of the two types of halogen compounds may be summarized thus:

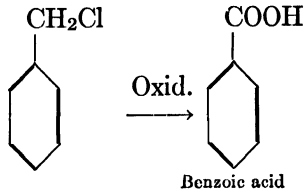
Reagents	Benzyl chloride	 *p*-chlorotoluene
KOH	Benzyl alcohol	No reaction
NH_3	Benzylamine	No reaction
KCN	Benzyl cyanide	No reaction

from which it may be seen that where the halogen is attached to the nucleus, we get a relatively inactive compound; but where it is attached to the side-chain a very active compound, similar in its properties to the aliphatic halogen derivatives, is obtained. (The *Fittig* reaction exemplifies a typical reaction for the type where the halogen is attached to the nucleus.) The above reactions hold good only when carried out under atmospheric pressure. It has been noticed that at higher pressures reactions may be obtained even when the halogen is connected to the nucleus.

Whether the X is attached to the ring or to the side-chain, may be determined in some such way as the following:

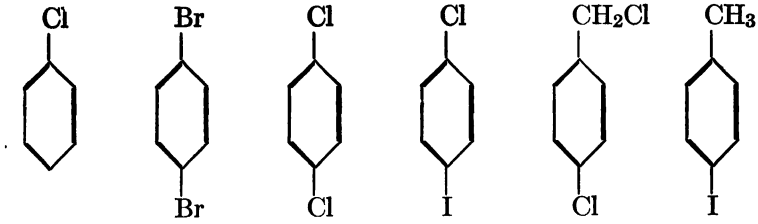


p-Chlorobenzoic acid



Benzoic acid

Hundreds of halogen compounds are known; only a few will be mentioned:

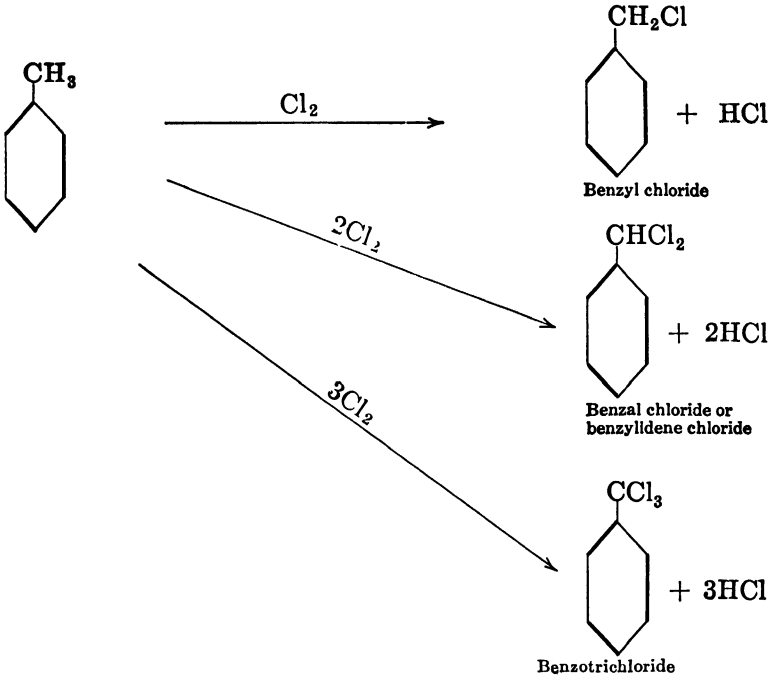


Chloro-benzene | *p*-Dibromo-benzene | *p*-Dichloro-benzene | *p*-Iodochloro-benzene | *p*-Chloro-benzyl chloride | *p*-Iodo-toluene or *p*-Tolyl iodide

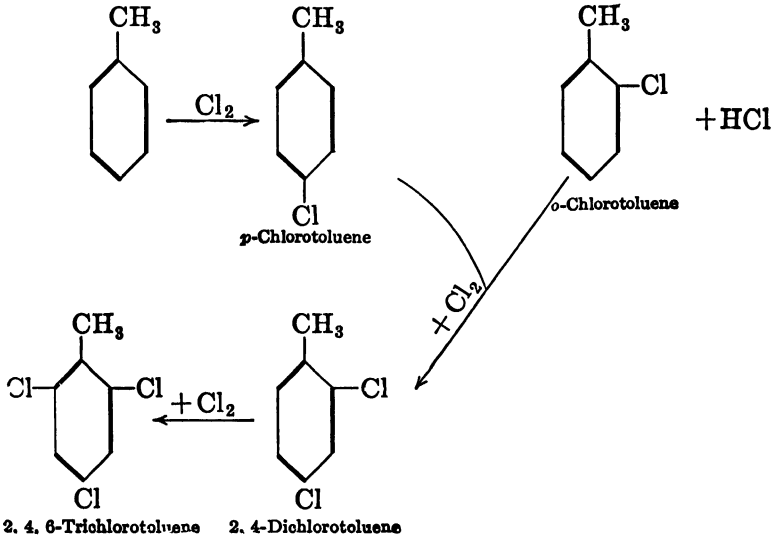
Chlorobenzene is manufactured by chlorinating benzene in presence of iron. It is used for the manufacture of dye intermediates.[1] *p*-Dichlorobenzene is used extensively to protect woolen goods from moths, and to protect the peach trees from the peach tree borer.

We may again refer to the preparation of these halogen compounds. Toluene, when acted upon by chlorine—in the presence of sunlight, in the absence of a "carrier," in the absence of moisture, and at boiling temperature—gives the following products:

[1] A dye intermediate is an organic substance used in the manufacture of dyes.



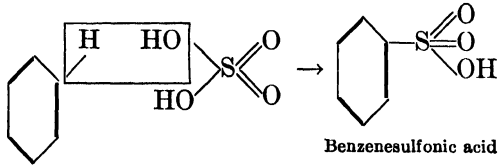
When, however, the chlorine and the toluene are made to react in the absence of sunlight and at room temperature, but in the presence of a carrier, we get:



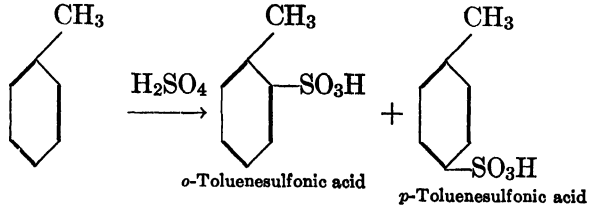
(A number of halogen derivatives of the aromatic series were used during the late war as **poison gases.** Some of these were benzyl bromide, $C_6H_5 \cdot CH_2Br$, diphenylchloroarsine $(C_6H_5)_2As \cdot Cl$, phenylcarbylamine chloride, $C_6H_5 \cdot N{=}C{=}Cl_2$ and xylyl bromide, $CH_3 \cdot C_6H_4 \cdot CH_2Br$, chloroacetophenone, $C_6H_5 \cdot CO \cdot CH_2Cl$. Since we are on the subject of war gases, we may include a few other compounds also used during the late war, although they really belong to the aliphatic series: bromoacetone, $CH_2Br \cdot CO \cdot CH_3$; bromoethyl methyl ketone, $CH_3 \cdot CO \cdot CHBr \cdot CH_3$; chloroacetone, $CH_2Cl \cdot CO \cdot CH_3$; nitrotrichloromethane — or chloropicrin — $CCl_3 \cdot NO_2$; β-dichlorodiethyl sulfide — mustard gas — $(C_2H_4Cl)_2S$; dimethyl sulfate, $(CH_3)_2SO_4$; dichloromethyl ether, $(CH_2Cl)_2O$; phosgene, $COCl_2$; trichloromethyl chloro-formate, $Cl \cdot COOCCl_3$, and hydrocyanic acid, HCN.)

Sulfonic Acids

Sulfonic acids are a very important class of organic compounds since from them phenolic compounds (p. 250), naphthols (p. 297), etc., are prepared. They are generally prepared by the direct sulfonation of the hydrocarbon; e.g.,



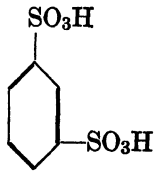
Benzenesulfonic acid



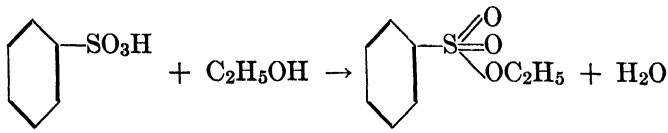
o-Toluenesulfonic acid

p-Toluenesulfonic acid

Benzenesulfonic acid when further sulfonated gives *m*-benzenedisulfonic acid:

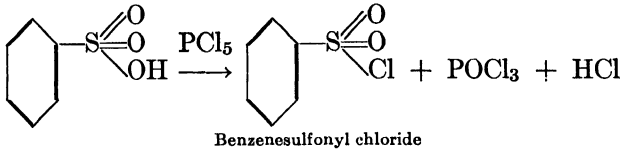


Properties. With alcohol, the sulfonic acids form esters; e.g.,



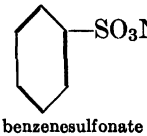
Ethyl benzenesulfonate (an ester)

The corresponding chloride is obtained with PCl_5; e.g.,



Benzenesulfonyl chloride

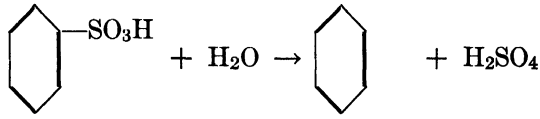
and with NaOH we form the sodium salt; e.g.,



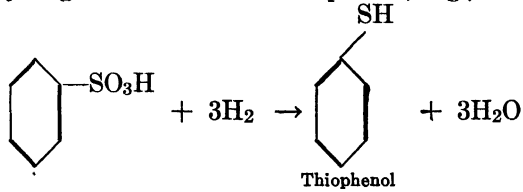
Sodium benzenesulfonate

(Notice the analogous reactions of the COOH group and the SO_3H group above.)

With steam under pressure, they are decomposed, yielding the hydrocarbon, e.g.,

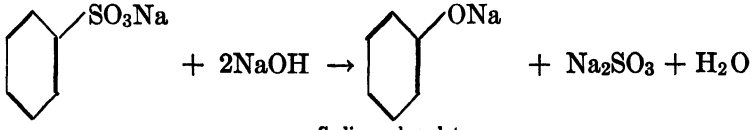


and with hydrogen are reduced to thiophenol; e.g.,

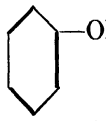


Thiophenol

When **fused** with NaOH, the sulfonic acids yield the sodium salts of the phenols; e.g.,

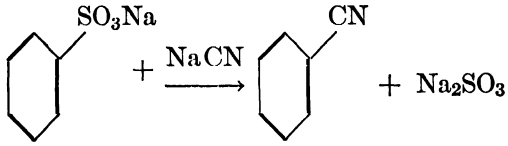


Sodium phenolate

from which the phenol,  , can be obtained by treating the solution with CO_2. (H_2CO_3).

(This is an extremely important commercial method used in the preparation of phenol and phenolic compounds. The sulfonic acid is first made from the hydrocarbon, then the former is fused with NaOH, and the resulting compound acidified.)

The sulfonic acids (salts) can be distilled with NaCN yielding the corresponding cyanides; e.g.,



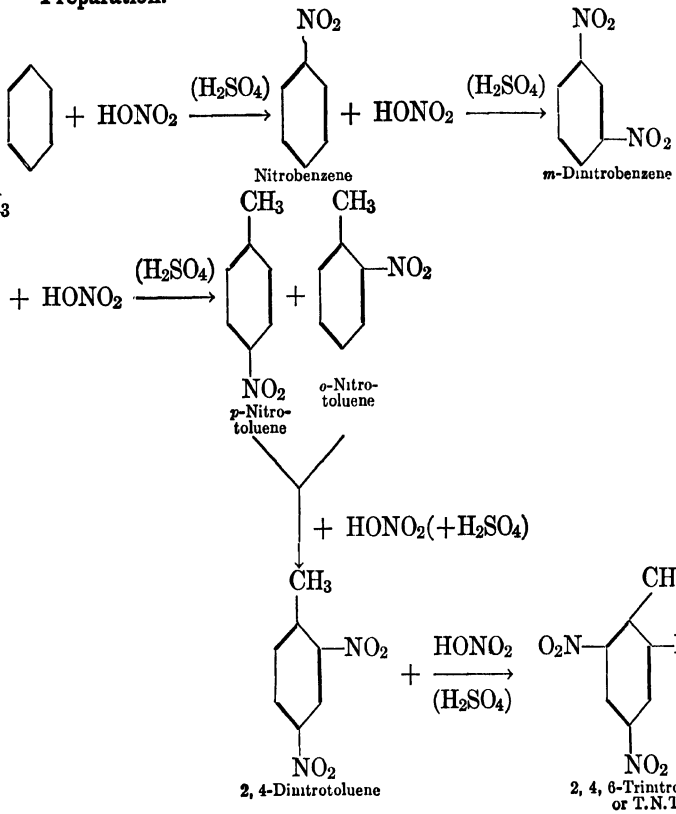
The free sulfonic acids are usually very soluble in water. In order to separate them from the excess of H_2SO_4, the Pb, Ca or Ba salts are usually prepared. The Pb, Ba and Ca sulfonates are soluble in water while the sulfates are insoluble. (For sulfonation, concentrated H_2SO_4 at elevated temperature must be used. Very often it is necessary to resort to fuming H_2SO_4.)

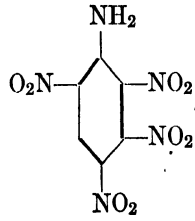
(Quite often organic compounds insoluble in water are sulfonated, converting them to water-soluble sulfonic acids. This is a procedure extensively used in the dye industry.)

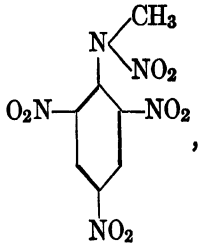
Nitro Compounds

These are a very important class of organic compounds. They are generally prepared by direct nitration with HNO_3. In some instances the nitration proceeds readily, in others it does not. In some cases dilute nitric acid can be used (provided no oxidation takes place); in others the nitration will proceed only with concentrated or fuming nitric acid. Sometimes NO_2 is used in place of nitric acid. In most cases the presence of sulfuric acid is necessary to absorb the water just as fast as it is formed in the reaction. Sometimes only fuming sulfuric acid will serve the purpose. In reality, a number of factors play their part in nitration—such as strength of nitrating acid (" mixed acid "—HNO_3 + H_2SO_4), amount of acid used, temperature of the reaction, length of time of nitration, agitation of the liquids, etc.

Preparation.

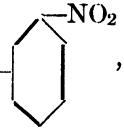


(T.N.A., tetranitroaniline,  , and tetryl,

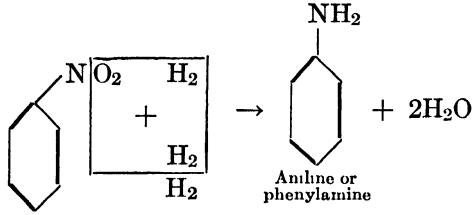
 , or, 2, 4, 6-Trinitrophenyl methyl nitroamine

are the most important high explosives.)

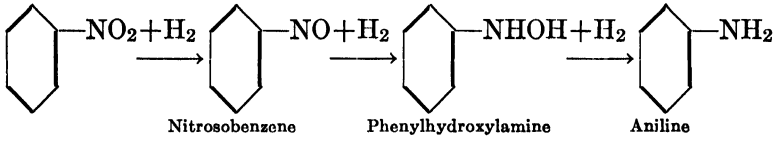
Properties.—The nitro compounds are usually pale yellowish liquids or solids, many of them being volatile with steam. Some of them—the higher nitro compounds, such as T.N.T.—are high explosives.

Nitrobenzene.—  , sometimes called "oil of mirbane,"

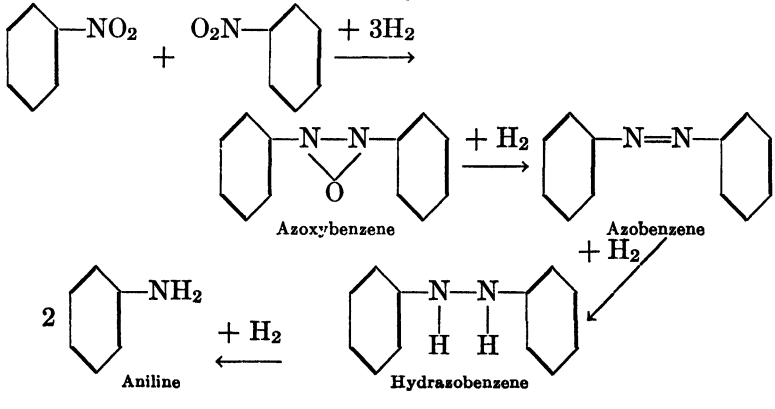
is a yellowish oil possessing the odor of bitter almonds, and is sometimes used in place of the latter in perfumes. It is also used in soaps, polishes and grease (due to its odor). It is manufactured from benzene on a very large scale for the purpose of preparing aniline, which is an important "dye intermediate,"

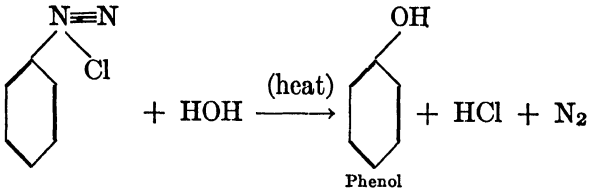


Reduction products of nitro compounds under varying conditions:

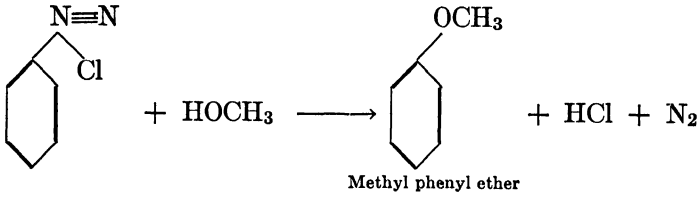


Dimolecular Reduction Products:

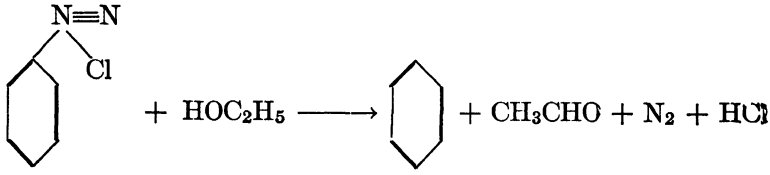


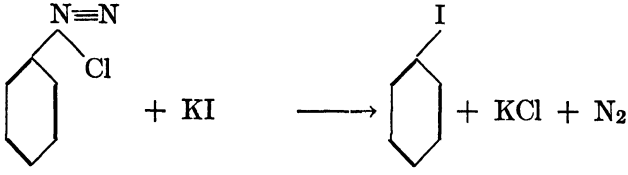


Phenol

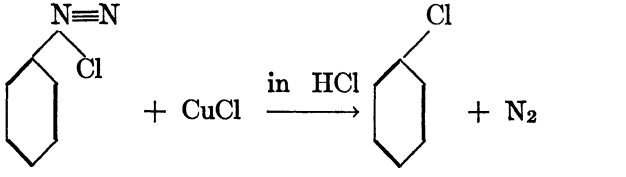


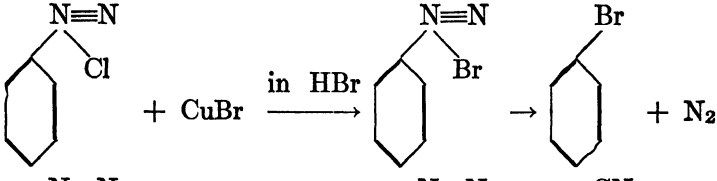
Methyl phenyl ether

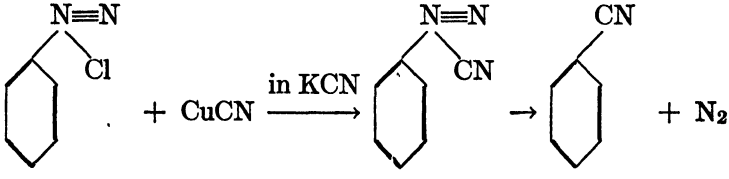




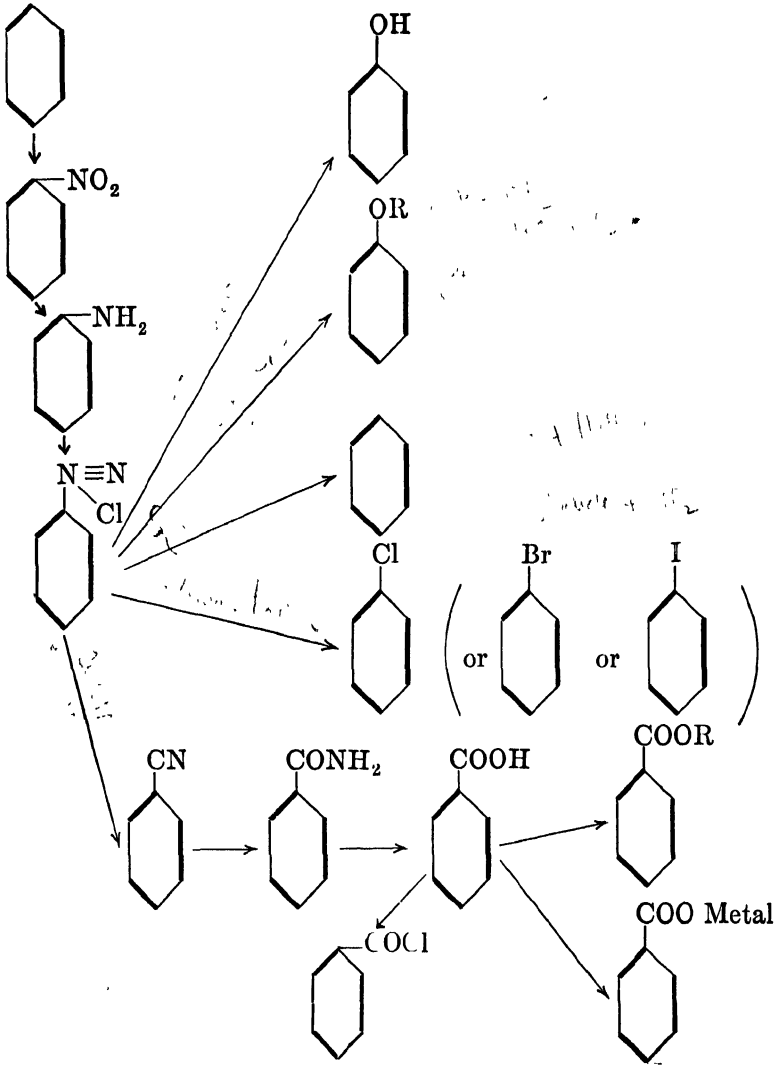
The following are known as the *Sandmeyer* reactions:





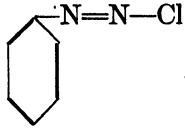


We may summarize these reactions to show the preparation of various types of aromatic compounds:

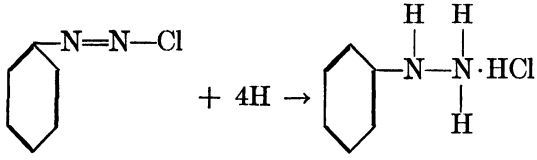


which gives an idea of the wide applicability which these diazonium compounds possess.

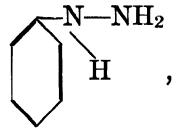
We must now proceed to reactions which are better explained

by the structure  . Upon partial reduction, the

following reaction takes place:



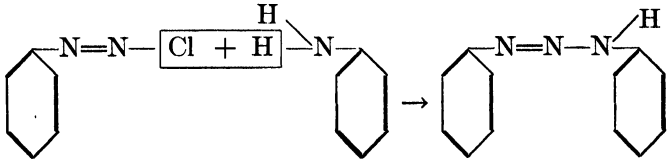
Phenylhydrazine hydrochloride

and the base, **phenylhydrazine**,  , may be obtained

by the addition of NaOH. (Hydrazine is $H_2N—NH_2$.)

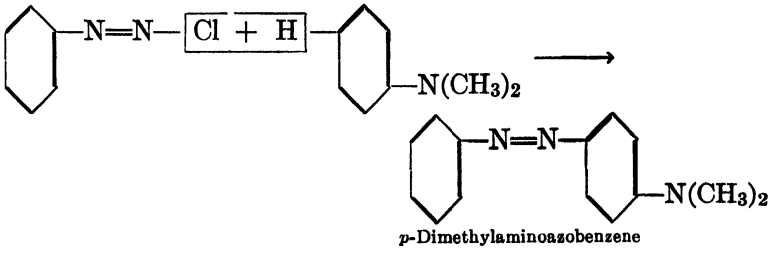
Phenylhydrazine, a poisonous liquid, has been used very extensively by Fischer and others in determining the structure of sugars. It is used in the identification of sugars (p. 169), in tests for aldehydes and ketones (p. 79), in the manufacture of antipyrine (p. 306) and various dyestuffs.

Diazobenzene chloride may be "coupled" with aniline (in neutral or weak acid solution) thus:



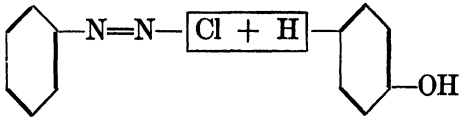
Diazoaminobenzene

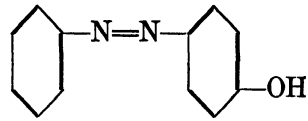
and with dimethylaniline:



p-Dimethylaminoazobenzene

and with phenol:



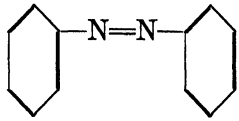


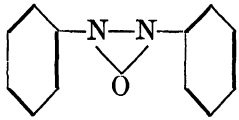
p-Hydroxyazobenzene

—reactions which are much better explained on the basis of a "diazo" rather than on a "diazonium" configuration.

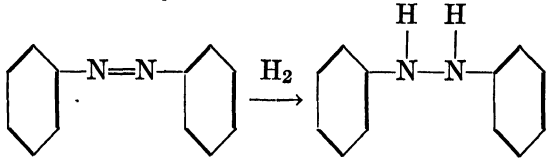
Reactions of the type just given are of great importance in the manufacture of azo dyes (p. 324).

The azo compounds are far more stable than the diazo compounds.

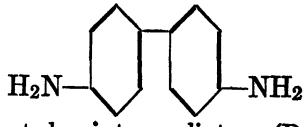
Azobenzene, 

, is prepared by distilling azoxybenzene, 

, with iron filings; or by the action of an alkaline solution of stannous chloride on nitrobenzene. It may be reduced to hydrazobenzene



which, when boiled with strong HCl undergoes an intramolecular rearrangement into *p,p'*-diaminobiphenyl, better known as **benzidine:**



which is an important dye intermediate. (Benzidine is also used in one of the tests to detect blood.)

READING REFERENCES

GROGGINS—Aniline and Its Derivatives. (1924), chap. 1 (Discovery of Aniline Oil); chap. 4 (Acetanilide).

GEER AND BEDFORD—The History of Organic Accelerators in the Rubber Industry. *Industrial and Engineering Chemistry*, **17**, 393 (1925).

CROSSLEY—The Contribution of Aniline to Economic and Social Progress. *Journal of Chemical Education*, **4**, 338 (1927).

CAIN—The Chemistry of Diazo Compounds.

BIGELOW—Azoxy Compounds. *Chemical Reviews*, **9**, 117 (1931).

CHAPTER XXIV

AROMATIC ALCOHOLS, PHENOLS AND ETHERS

We have already pointed out (p. 222) that in aromatic compounds substitution may occur either in the side-chain or in the nucleus, and that the products obtained when substitution takes place in the side-chain are quite different from those obtained when substitution takes place in the nucleus.

We have seen, in the case of the amines, for example, how the NH_2 group may be attached either to the nucleus or to the side-chain. This is equally true of the OH group. Where the OH is attached to the nucleus, it is known as a **phenolic** compound, and where it is attached to the side-chain it is an **aromatic alcohol**; e.g.,

Phenyl hydroxide
or
hydroxybenzene
or phenol
(A phenolic compound)

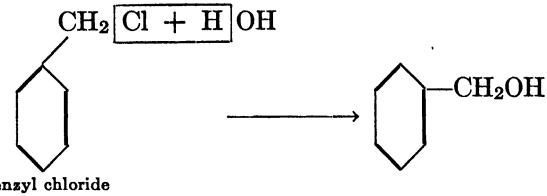
Phenylcarbinol
or
benzyl alcohol
(An aromatic alcohol)

(In the aromatic alcohols, the OH group is attached to an alkyl residue, or side-chain; the properties of these compounds, therefore, are closely analogous to those of the aliphatic alcohols. See Chapter V.)

Aromatic Alcohols

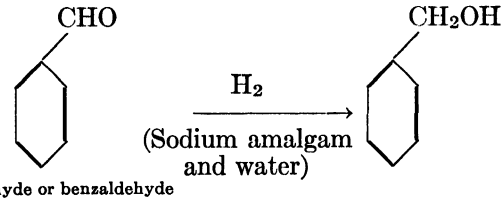
Benzyl alcohol,

, or phenylcarbinol occurs as esters in balsam of Peru and Tolu, storax resin, in oils of flowers, etc. It may be obtained as follows:



Benzyl chloride

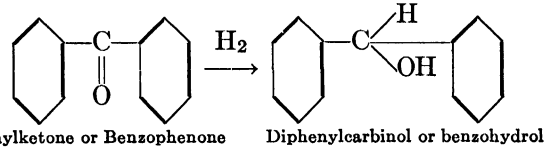
or



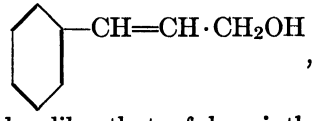
Benzoic aldehyde or benzaldehyde

It is used in perfumery, and in medicine as a local anesthetic.

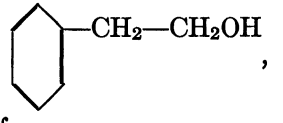
Diphenylcarbinol, or benzohydrol, is a secondary alcohol, and may be prepared by reducing the corresponding ketone.



Diphenylketone or Benzophenone Diphenylcarbinol or benzohydrol

Cinnamyl alcohol, 

, is present in storax, and has an odor like that of hyacinth. It is used in perfumery.

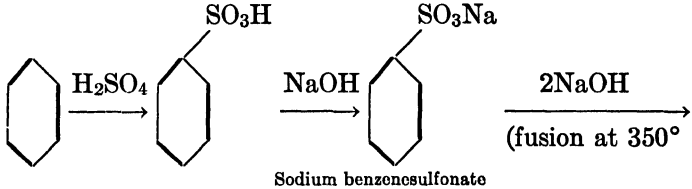
Phenylethyl alcohol, 

, is present in oil of rose and is used in perfumes.

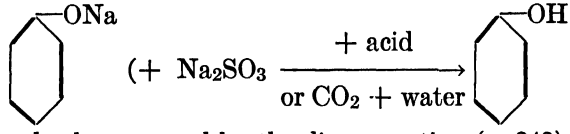
Phenols

The aromatic alcohols, like those of the aliphatic series, are neutral bodies, but when the OH enters the ring and we get a phenolic compound, then we obtain a very weak acid. The most important among these phenolic compounds is:

Phenol, , or phenyl hydroxide, or carbolic acid. It is present in wood tar and coal tar (see chart facing p. 211), from which much of it is obtained. It is also manufactured by making use of the following series of reactions:



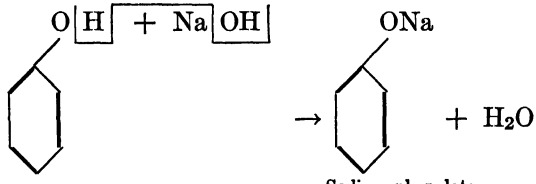
Sodium benzenesulfonate



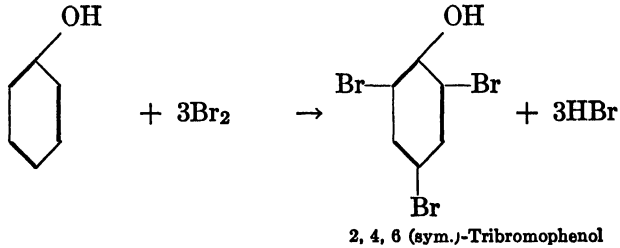
It may also be prepared by the diazo reaction (p. 243).

The most recent method for the preparation of phenol is by the hydrolysis of chlorobenzene with NaOH solution under high pressure.

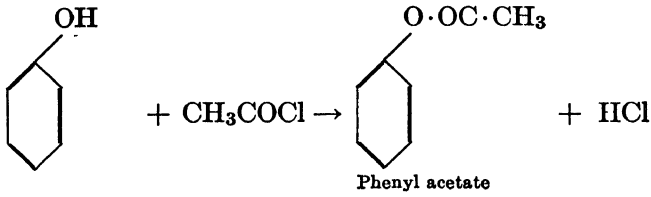
Properties.—Phenol is a very weak acid but slightly dissociated (less so than carbonic acid). It is very corrosive and poisonous. Some of its general reactions may be illustrated by the following:



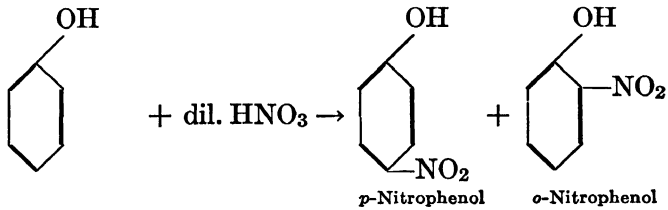
Sodium phenolate



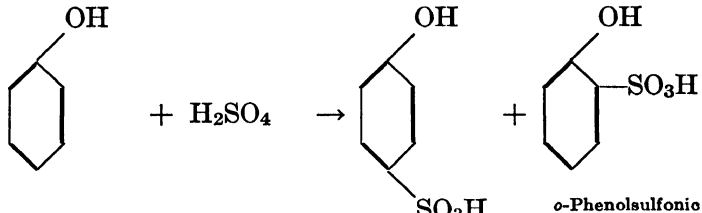
2, 4, 6 (sym.)-Tribromophenol



Phenyl acetate

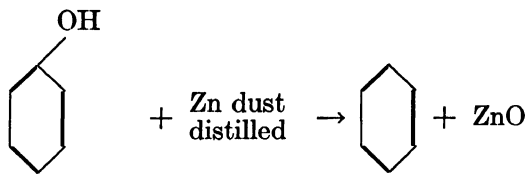


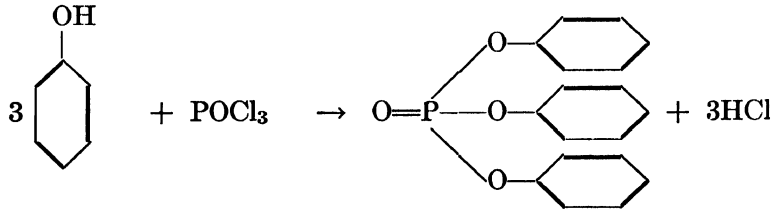
p-Nitrophenol *o*-Nitrophenol



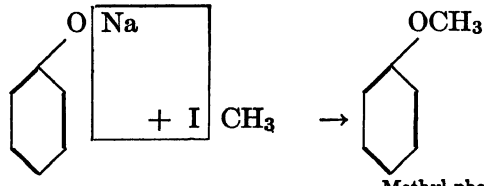
p-phenolsulfonic acid

o-Phenolsulfonic acid





Triphenyl phosphate (a camphor substitute)



Methyl phenyl ether or anisole or methoxybenzene

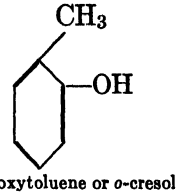
Phenol gives a violet coloration with ferric chloride. It is a colorless, crystalline substance which becomes liquid upon the addition of 15 per cent of water. It is a powerful antiseptic, disinfectant and germicide, and is used to a certain extent (in 3 per cent solutions) as a dressing for wounds, for disinfecting surgical instruments, rooms, etc.

Phenol is also used in the manufacture of explosives, dyes, developers, various medicinals, bakelite and other resins, etc.

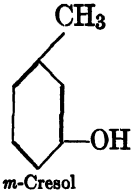
The resins, of which **bakelite** is an example, are sufficiently important to warrant a few words of description. Phenol combines with formaldehyde to produce a resinous material. These products—known as bakelite, etc.—vary in properties, for the particular type of resin obtained will depend upon the exact method employed in its preparation. Pure phenol and pure formaldehyde react very slowly, even when heated, but in the presence of catalytic agents, particularly bases—ammonia seems to be used in many cases—the action is accelerated. Where ammonia is used, it is believed that what first takes place is a reaction between the formaldehyde and the ammonia, forming hexamethylenetetramine (p. 80), and that the latter then combines with phenol, forming a resin, the chemical composition of which is not clear. This resin undergoes further changes when heated. It then becomes less fusible and less soluble. The raw bakelite, for example, is both soluble and fusible, but when heated becomes insoluble, infusible, very hard, strong and resistant. This bakelite is used in moulding materials, varnishes, enamels, lacquers, cements, pipe stems, cigar holders, handles, insulating substances, etc.

Recently glycerol and phenol have been made to combine to form a synthetic resin (called "acrolite") which has properties similar to the phenol-formaldehyde resin.

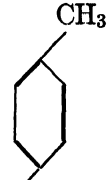
Cresols.



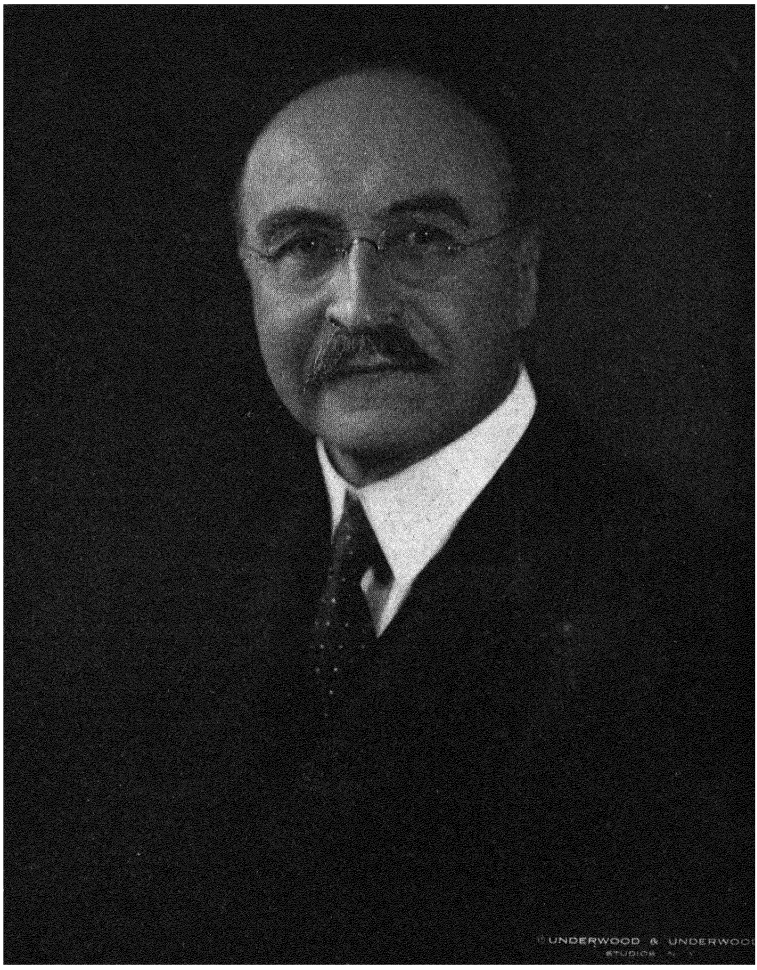
o-Hydroxytoluene or *o*-cresol



m-Cresol



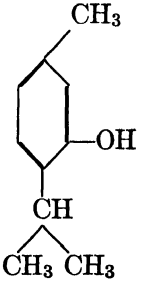
p-Cresol



LEO HENDRIK BAEKELAND (1863-)

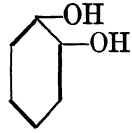
PRESIDENT OF THE AMERICAN CHEMICAL SOCIETY IN 1924 AND HONORARY PROFESSOR OF CHEMICAL ENGINEERING AT COLUMBIA UNIVERSITY, IS BEST KNOWN FOR HIS WORK ON "BAKELITE" (P. 252), SYNTHETIC PLASTICS IN GENERAL AND FOR "VELOX" (THE PHOTOGRAPHIC PAPER).

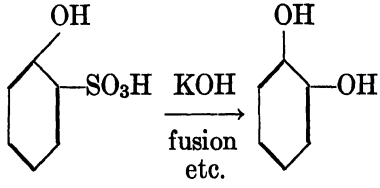
All three are present in coal tar and in wood tar, and all three act as antiseptics. They are known as "cresylic acid" or "tri-cresol." The properties of these cresols are, in general, similar to phenol. The cresols have greater germicidal power than phenol and are less poisonous. They are slightly soluble in water and are rendered more soluble by the addition of soap. Preparations such as lysol, creolin, phenoco, etc., contain cresols. Cresols are also used for the manufacture of synthetic resins, dyestuffs, explosives and organic chemicals.

Thymol,  , or 3-hydroxy-1-methyl-4-isopropyl-benzene,

occurs in oil of thyme, mint, and other essential oils, and is an important antiseptic. It is very often used in the treatment of hookworm and to preserve urine. Diiododithymol (prepared from thymol and iodine) is known as "aristol" and has largely displaced iodoform as an antiseptic.

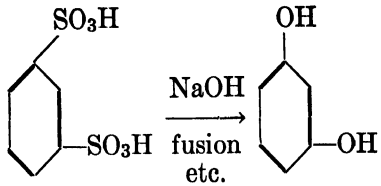
Polyhydroxy phenols.

o-Dihydroxybenzene,  , or **pyrocatechol,** occurs in "catechu" resin and is prepared from resins by fusing them with KOH, or from *o*-phenolsulfonic acid;



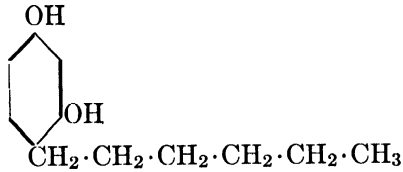
It is used in the manufacture of adrenaline and guaiacol.

Resorcinol, or *m*-dihydroxybenzene, or resorcin, is prepared thus:

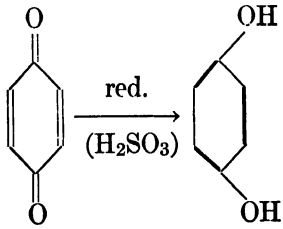


m-Benzenedisulfonic acid — Resorcinol

It is used as an antiseptic and an antipyretic, and in the preparation of dyestuffs.

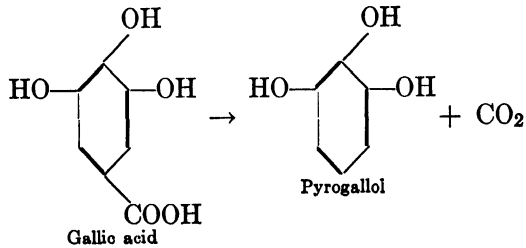
Hexylresorcinol,  , has recently been introduced as an internal urinary antiseptic. It is one of the most powerful among organic germicides.

Quinol, or *p*-dihydroxybenzene, or hydroquinone, is prepared from *p*-benzoquinone (p. 265) by reduction:



It is used as a photographic developer (that is, as a mild reducing agent, it being converted into benzoquinone).

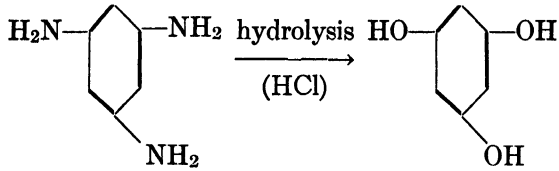
Of the three trihydroxybenzenes, **pyrogallol** (or pyrogallic acid) is obtained by heating gallic acid:



Gallic acid — Pyrogallol

It is a strong reducing agent and absorbs oxygen in alkaline solution—a property used in estimating oxygen in gas mixtures. Pyrogallol is also used as a photographic developer and in the manufacture of dyestuffs.

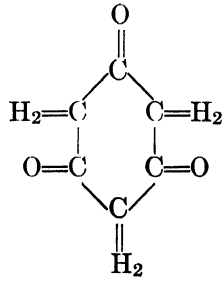
Phloroglucinol, or sym. (1, 3, 5)-trihydroxybenzene, may be prepared from the corresponding triamino compound:



sym-Triaminobenzene — Phloroglucinol

It occurs in the glucoside phloridzin and in different resins.

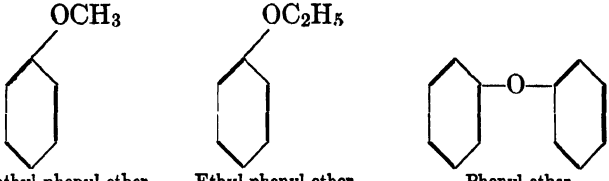
(The behavior of phloroglucinol towards reagents is worthy of discussion. That it is a trihydroxy compound is shown by the fact that it forms a triacetyl derivative with acetic anhydride. On the other hand, it forms a trioxime with hydroxylamine, indicating a ketonic structure—compare p. 135:



where, under certain conditions, the same compound may exist in two different forms, we have a case of **tautomerism.** This is to be distinguished from isomerism, where we have two different compounds having the same molecular formula.)

Phloroglucinol is used for the determination of furfural (p. 305)—a test based upon the production of a red color.

Ethers [1]

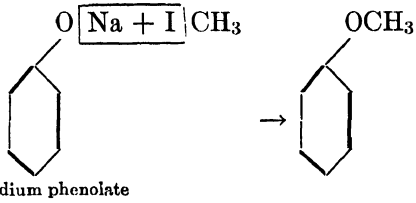


Methyl phenyl ether or anisole or methoxybenzene

Ethyl phenyl ether or phenetole or ethoxybenzene

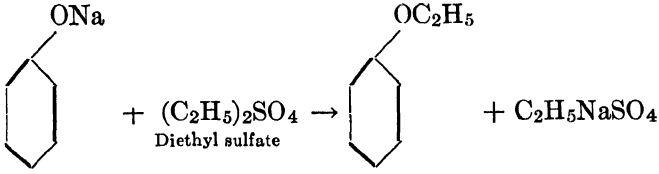
Phenyl ether or phenyl oxide

Ethers of the type of **anisole** and **phenetole** are produced thus:



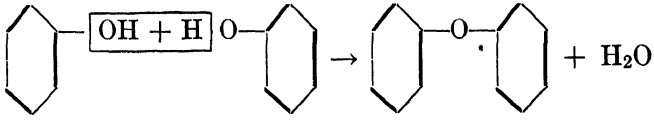
Sodium phenolate

or



Diethyl sulfate

The phenyl ether is prepared by heating phenol with zinc chloride:



It has a geranium-like odor.

These ethers are used in synthetic perfumes.

READING REFERENCES

SLOSSON—Creative Chemistry. (1920), chap. 7 (Synthetic Plastics).

ELLIS—Synthetic Resins.

BAEKELAND AND BENDER—Phenol Resins and Resinoids. *Journal of Industrial and Engineering Chemistry*, **17**, 225 (1925).

HOWE—Chemistry in Industry. (1924), chap. 19 (Synthetic Resins).

[1] The student is advised to review Chap. VI, p. 69.

LEONARD—The Significance of Hexylresorcinol and Its Homologues in Relation to the Problem of Internal Antisepsis. *Science*, **62**, 408 (1925).

MCINTOSH—"Acrolite"—A New Synthetic Resin. *Industrial and Engineering Chemistry*, **19**, 111 (1927).

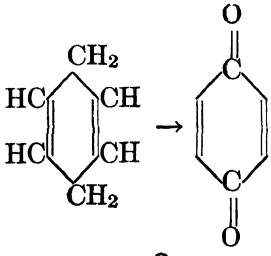
HALE AND BRITTON—Development of Synthetic Phenol from Benzene Halides. *Industrial and Engineering Chemistry*, **20**, 114 (1928).

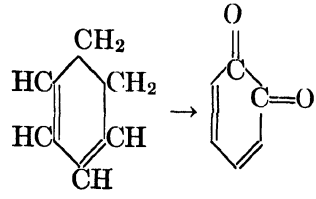
KIENLE—Synthetic Resins. *Industrial and Engineering Chemistry*, **22**, 590 (1930).

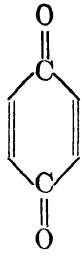
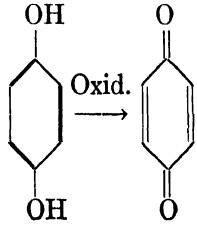
A motion picture on " The Story of Bakelite " can be secured from the Bakelite Corporation, 247 Park Ave., N. Y. City.

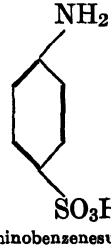
(When the 2CO groups are in the *p*-position with respect to one another, we get *p*-quinones, and when in the *o*-position, *o*-quinones. No *m*-quinones are known.)

The quinones may be regarded as derivatives of dihydrobenzenes in which $2(CH_2)$ groups are replaced by 2(CO) groups:

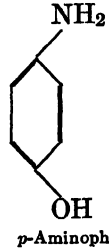




Quinone,  , or benzoquinone, may be prepared by the oxidation of hydroquinone:  or by the oxidation of aniline with $Na_2Cr_2O_7 + H_2SO_4$; or, by oxidizing amino and hydroxy compounds belonging to the *p*-series; such as



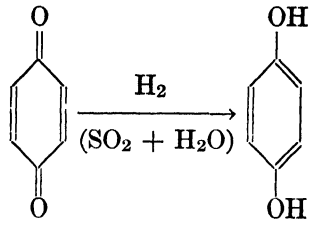
p-Aminobenzenesulfonic acid



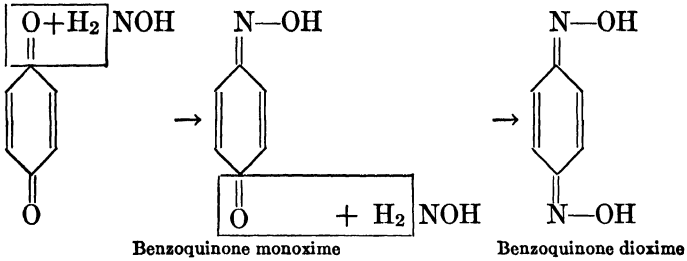
p-Aminophenol

, etc.

Benzoquinone is a yellow, crystalline solid, volatile with steam and possessing a pungent odor. It is reduced to hydroquinone;



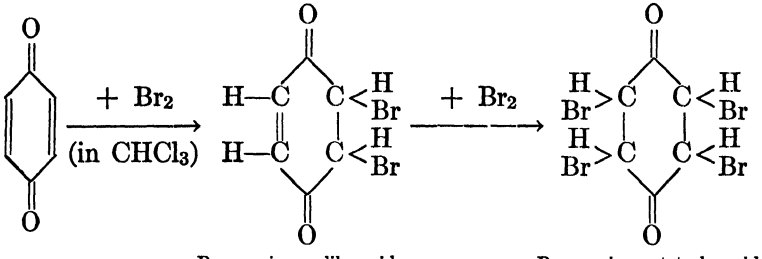
Quinone forms mono- and di- oximes:



Benzoquinone monoxime

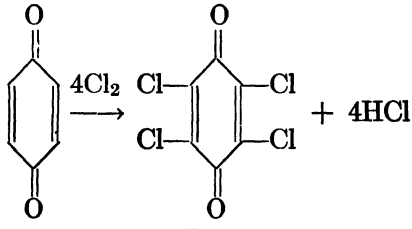
Benzoquinone dioxime

and halogen derivatives; e.g.,



Benzoquinone dibromide

Benzoquinone tetrabromide

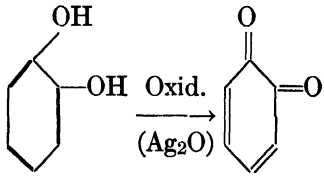


Tetrachlorobenzoquinone
or chloranil

(The halogen compounds as shown above illustrate either addition products within the ring—a fact which suggests that these quinones are quite unlike benzene derivatives—or substitution products.)

When hydroquinone is heated with ferric chloride, quinhydrone precipitates. This quinhydrone may be looked upon as a molecular complex of one mol. of quinone and one of hydroquinone, $C_6H_4(OH)_2 \cdot C_6H_4O_2$. This quinhydrone is used very extensively in *p*H determinations.

***o*-Benzoquinone** is prepared from catechol by oxidation:



(The structure of quinones has been used to explain the chemistry of dyestuffs and the relationship between color and chemical structure. See p. 317.)

READING REFERENCES

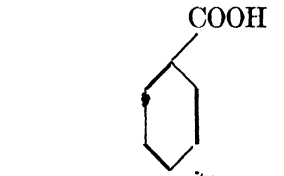
BOGERT—Recent Progress in Synthetic Perfumes. *Journal of Chemical Education*, **8**, 1311 (1931).

SAMPEY—Addition Reactions of Conjugated Double Bonds. *Journal of Chemical Education*, **4**, 872 (1927).

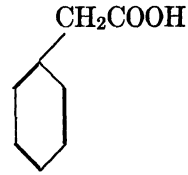
CHAPTER XXVI

AROMATIC ACIDS AND THEIR DERIVATIVES [1]

THE aromatic acids contain the COOH group attached directly to the ring or to the side-chain; e.g.,



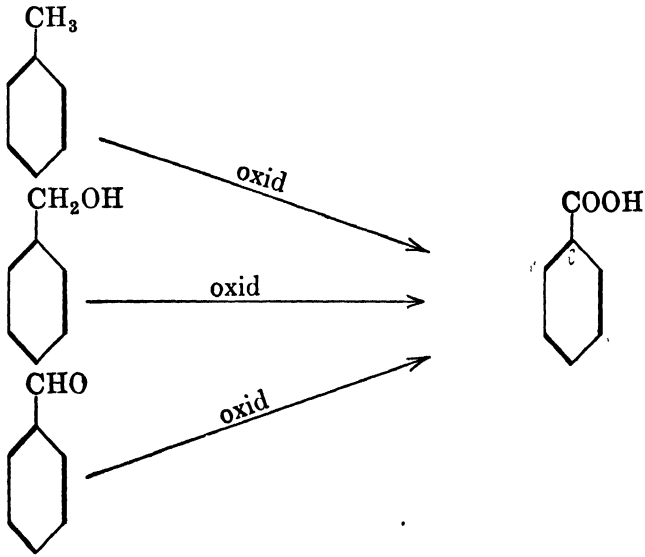
Benzoic acid or phenylformic acid



Phenylacetic acid

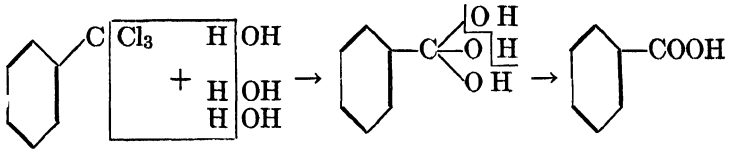
Many of the aromatic acids occur in nature (either in the free state or in the form of esters). We shall select benzoic acid as representative of the group.

Benzoic acid may be prepared by the oxidation of toluene, benzyl alcohol or benzaldehyde:

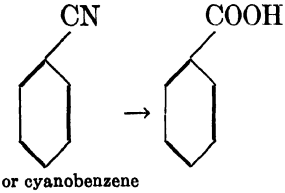


[1] The student should review Chaps. VIII, IX, XI, and XII.

or by the hydrolysis of benzotrichloride:

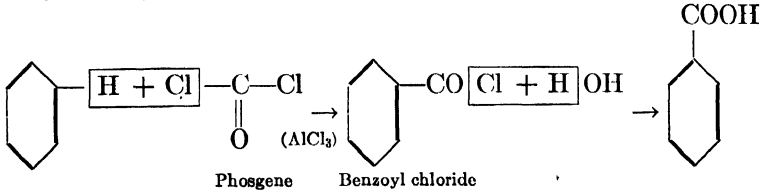


or by the hydrolysis of the corresponding cyanide:



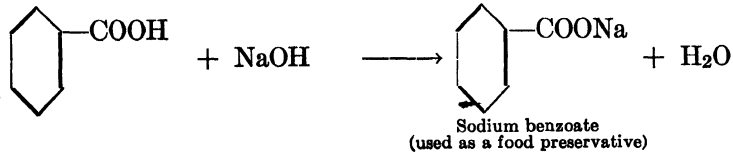
Benzonitrile or cyanobenzene

or by the application of the *Friedel-Crafts* reaction:

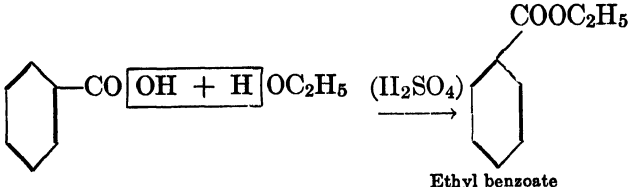


Phosgene Benzoyl chloride

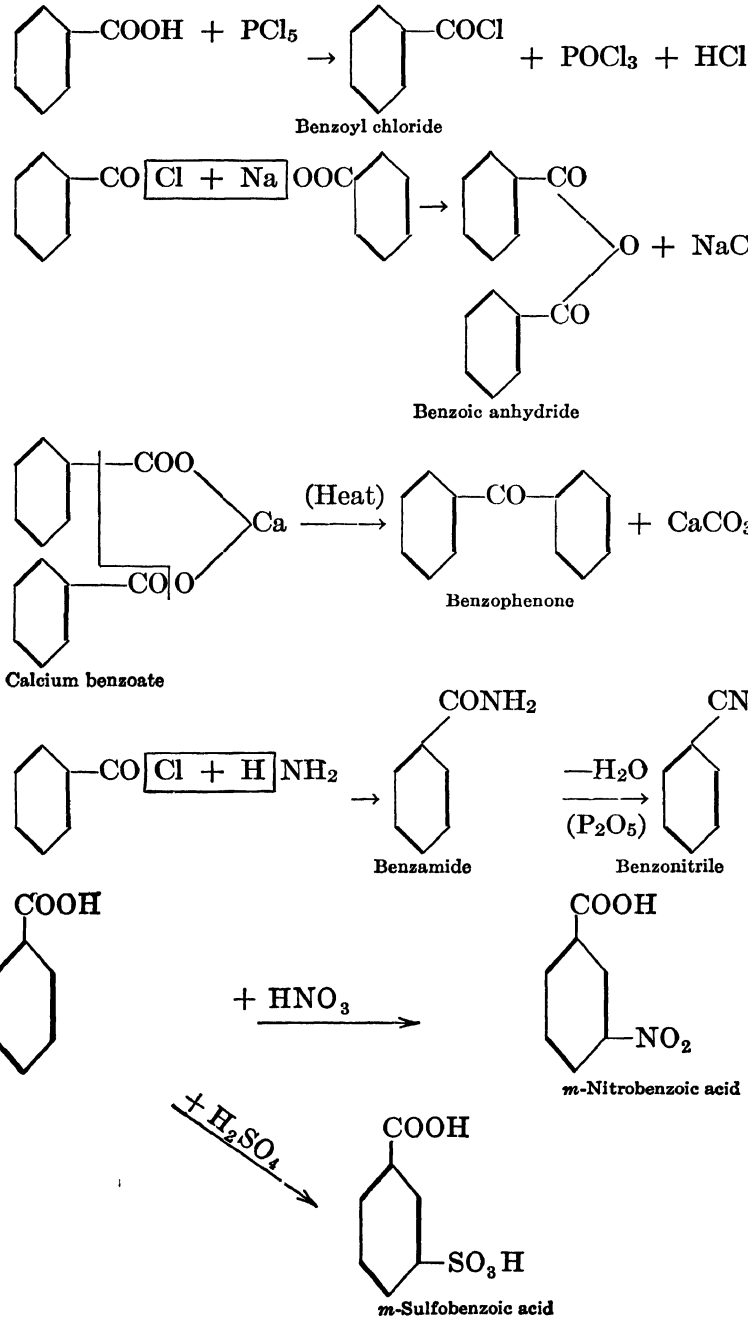
Benzoic acid occurs (as the free acid or as the ester) in gum benzoin, resins, balsams of Tolu and Peru, berries, etc. The free acid is generally purified by sublimation. Its properties are similar to those of compounds containing, on the one hand, a benzene nucleus, and on the other hand, a carboxyl group. Some of its reactions may be summarized as follows:

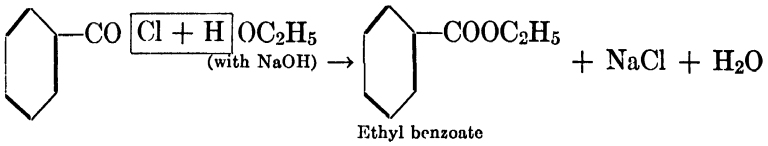


Sodium benzoate
(used as a food preservative)



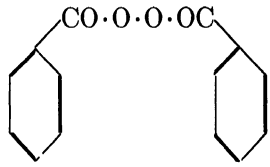
Ethyl benzoate
(used in artificial flavors and in perfumery)


—COOH + PCl5 → —COCl + POCl3 + HCl
Benzoyl chloride
—CO Cl + Na OOC— → —CO O + NaCl
—CO
Benzoic anhydride
—COO Ca
—CO O
Calcium benzoate
(Heat) →
—CO—
+ CaCO3
Benzophenone
—CO Cl + H NH2 →
CONH2
Benzamide
—H2O
(P2O5)
CN
Benzonitrile
COOH
+ HNO3 →
COOH
NO2
m-Nitrobenzoic acid
+ H2SO4 →
COOH
SO3H
m-Sulfobenzoic acid



Ethyl benzoate

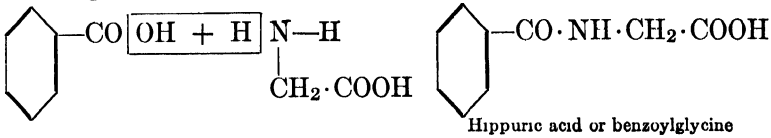
By the action of Na_2O_2 on benzoyl chloride, benzoyl peroxide,



is formed. The compound is highly explosive. It is used for bleaching, for oxidation, and as a polymerization reagent.

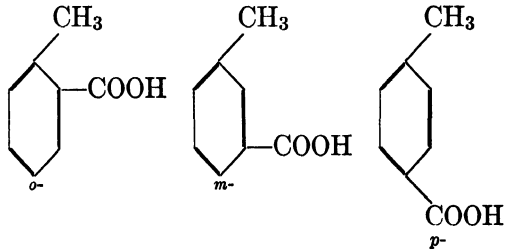
Benzoic acid itself finds use in medicine as an antiseptic and also in the manufacture of dyes. Sodium, lithium and ammonium benzoates are used as internal antiseptics. Sodium benzoate is used as a food preservative. Benzyl benzoate is used in perfumery, as an anesthetic, and it possesses much of the pain relieving qualities of opium without any of the latter's toxic or habit-forming dangers.

An interesting synthesis of hippuric acid in the body—by the kidneys—is brought about by the combination of benzoic acid (obtained from fruits, vegetables and, to some extent, proteins) and the amino acid, glycine, (obtained from the decomposition of proteins):

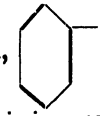


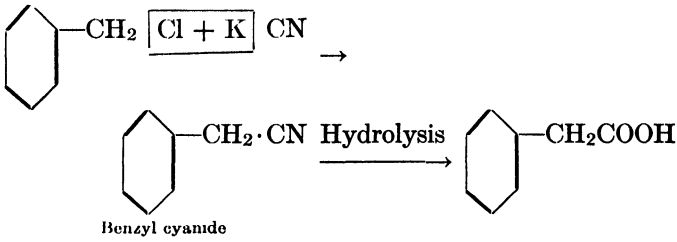
Hippuric acid or benzoylglycine

The toluic acids,

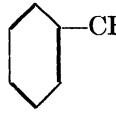


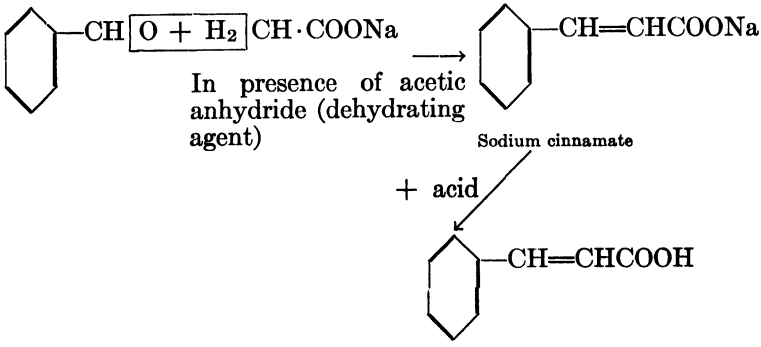
can be prepared by partial oxidation of the corresponding xylenes, or from the corresponding toluidines. (Diazo and *Sandmeyer* reactions.)

Phenylacetic acid,  , has its carboxyl group in the side-chain and is isomeric with the toluic acids. It may be prepared from benzyl chloride:



The acid and its esters are used in perfumery.

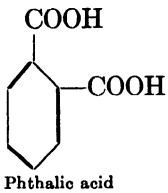
Cinnamic acid,  , or β-phenylacrylic acid, may be prepared by *Perkin's* reaction:



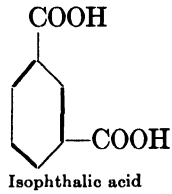
Esters of cinnamic acid and the acid itself are present in oil of cinnamon, resins, storax, balsams, gums, etc. The esters are used in flavoring materials and perfumery. The properties of cinnamic acid are those of a compound containing (*a*) a benzene nucleus, (*b*) a double bond structure, (*c*) a COOH group.

Hydrocinnamic acid, , or β-phenyl-propionic acid, is prepared from cinnamic acid by reduction (sodium amalgam and water).

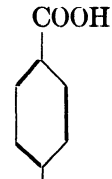
Of the **phthalic acids,**



Phthalic acid

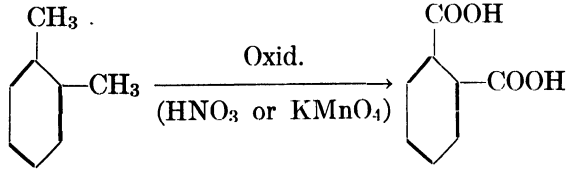


Isophthalic acid

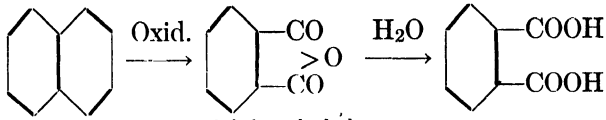


Terephthalic acid

the first, or phthalic acid, is the most important; it is used in the preparation of over 200 compounds. It may be prepared by oxidizing *o*-xylene:

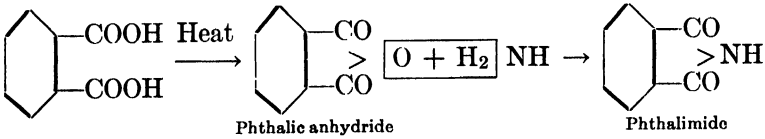


The commercial method is to pass the vapor of naphthalene and air over vanadium pentoxide (V_2O_5) (or other catalysts) at about 400°:



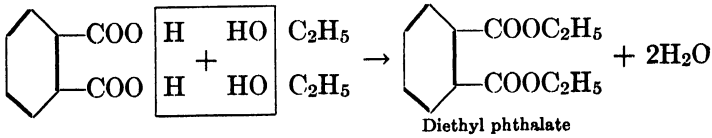
Phthalic anhydride

Some of the reactions of phthalic acid may be summarized:



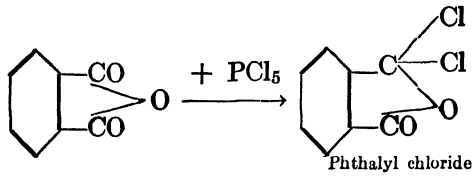
Phthalic anhydride

Phthalimide

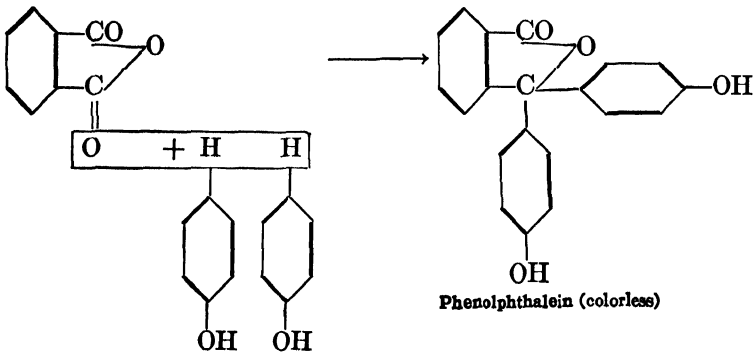


Diethyl phthalate

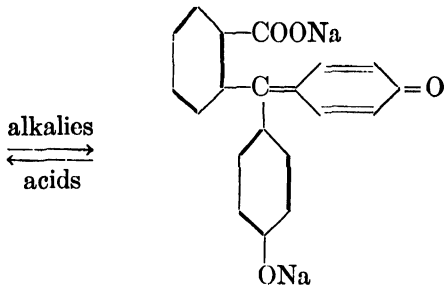
(The diethyl phthalate is a bitter substance and is used as a denaturant for ethyl alcohol.)



Phthalyl chloride



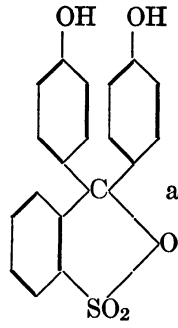
Phenolphthalein (colorless)

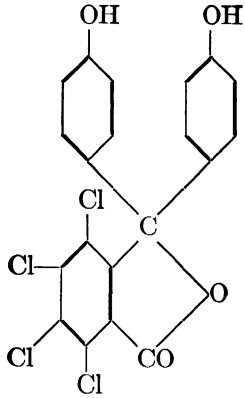


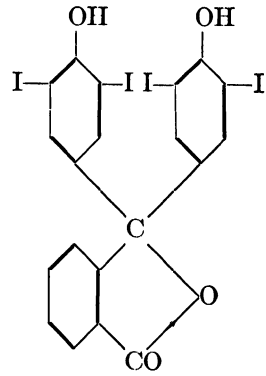
(Quinoid Structure) (pink)

Phenolphthalein is one of the best-known indicators. It is also used as a purgative. Phthalic anhydride is used in the manufacture of anthraquinone (p. 302), and in the manufacture of several important dyes.

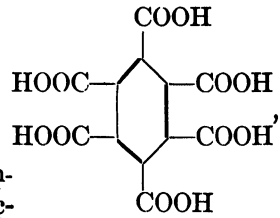
A considerable amount of phthalic anhydride is now being used in the manufacture of synthetic resins, such as glyptal, etc.

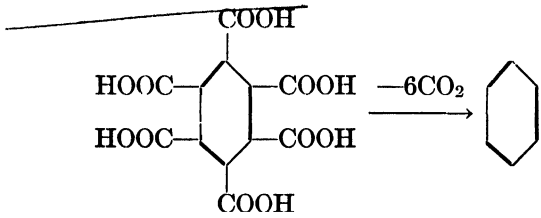
Phenolsulfonephthalein,  and phenoltetrachloro-





phthalein, and tetraiodophenolphthalein, are used to test the functional activities of the kidney and liver.

Mellitic acid,  , or benzene hexacarboxylic acid, may be prepared by the oxidation of graphite with HNO_3. Its aluminum salt occurs in nature as the mineral "honey stone." When heated with soda lime, the acid is converted into benzene:



READING REFERENCES

SHERWIN—The Fate of Foreign Organic Compounds—Benzoic acid, etc. —in the Body. *Physiological Reviews*, **2**, 238 (1922).

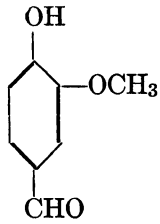
ANON.—Influence of Sodium Benzoate on Nutrition and Health of Man. (Agricultural Dept. Report 88.) Government Printing Office, Washington.

CHAPTER XXVII

ADDITIONAL AROMATIC COMPOUNDS CONTAINING MIXED GROUPS [1]

So far we have largely considered compounds containing single groups attached to the benzene ring, such as nitro compounds, sulfonic acids, phenols, aldehydes, etc.; and also, to some extent, a number of compounds containing dissimilar or mixed groups. In this chapter we shall consider additional compounds with unlike or mixed groups attached to the benzene ring. As thousands of such substances are known, only a few of the common and important ones can be mentioned.

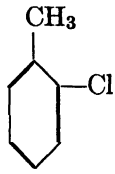
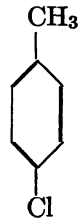
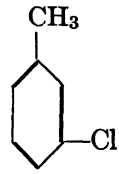
(Note to student: In studying the following compounds, the student should bear in mind that each group attached to the ring is responsible for certain characteristic reactions, and that the properties of the compound as a whole are, as a rule, the summation of properties exhibited by the individual groups present. For example, such a compound as

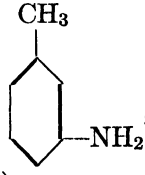


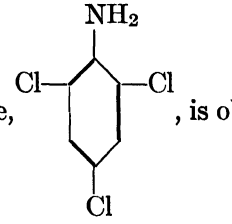
shows properties due (*a*) to the presence of the benzene ring, (*b*) to the OH group, (*c*) to the OCH_3 group and (*d*) to the CHO group.)

[1] The student is advised at this point to review the rules for substitution in the benzene ring (p. 215).

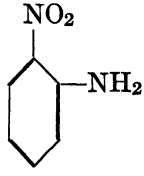
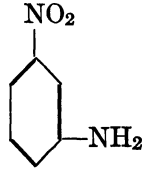
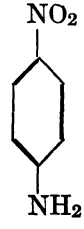
Chlorotoluenes, or tolyl chlorides.—Three isomers are known:

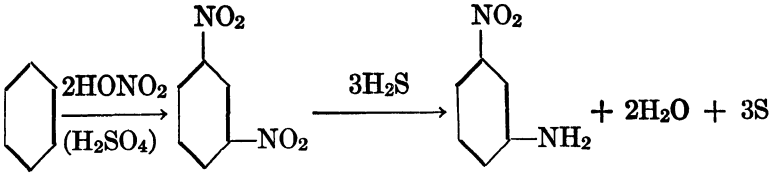
A mixture of the first two (*o*- and *p*-) is obtained when toluene is chlorinated (in presence of a halogen carrier). Direct chlorination of toluene does not yield the third, or *m*- variety; but we may start with *m*-toluidine,  , diazotize it, and apply the *Sandmeyer* reaction (p. 243).

Three isomeric **chloroanilines** are known. When aniline is treated with chlorine, sym.-trichloroaniline,  , is obtained.

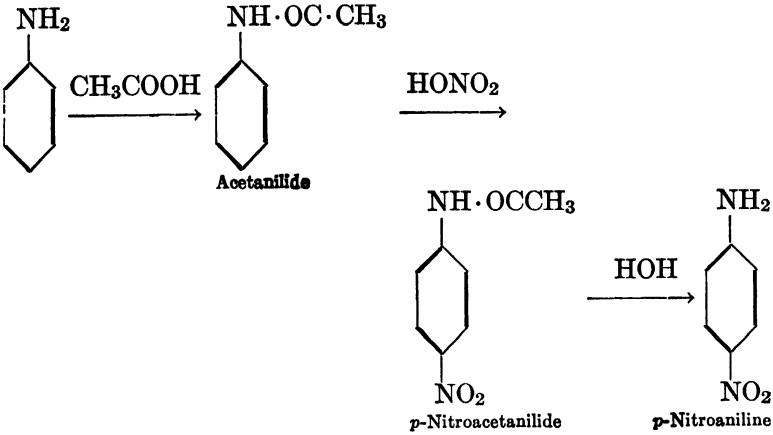
Of the three **nitroanilines**

the second (*m*-variety) is prepared by treating benzene with nitric and sulfuric acids to produce the *m*-dinitrobenzene, and then employing a sufficiently mild reducing agent to reduce but one of the NO_2 groups:

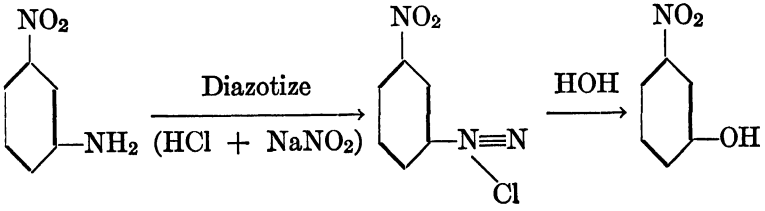


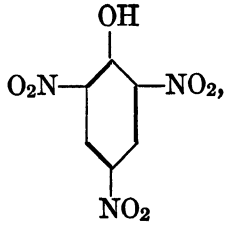
The *p*-nitroaniline is obtained as follows:



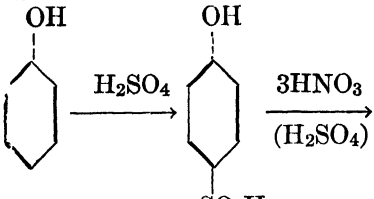
(The object of first acetylating is to "muzzle" the NH_2 group; or in other words, the NH_2 group must be protected against the oxidizing action of nitric acid.)

The *o*- and *p*-**nitrophenols** are prepared by direct nitration of phenol; the *m*- variety is prepared from *m*-nitroaniline:

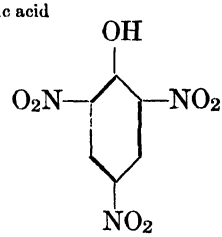


Picric acid,  or sym.-trinitrophenol, may

be prepared from phenol by nitration. Commercially, it is manufactured thus:

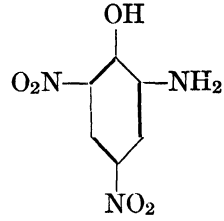


p-Phenolsulfonic acid



$+ H_2SO_4 + 2H_2O$

Picric acid is more strongly acidic than phenol, the increased acidity being due to the presence of the nitro groups. It is used in a colorimetric method for determining glucose in the blood, as a test for creatinine, as a precipitant for organic bases and proteins, as a "fixing" agent in histological work, in the treatment of the skin diseases and of burns, as an antiseptic, and in the manufacture of explosives. Picric acid is also used for the preparation of picramic acid,

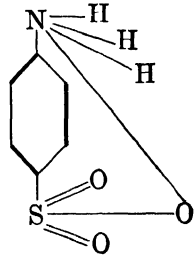


and sodium picramate, which in turn are converted into several green and brown dyes. (Many of the nitro compounds of the aromatic series, such as picric acid and T.N.T.—p. 231—are powerful explosives. They were used extensively during the late war.)

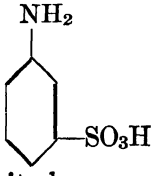
Sulfanilic acid,

, or *p*-aminobenzenesulfonic acid, is

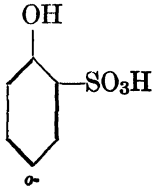
prepared from aniline by treatment with sulfuric acid, which first forms aniline acid sulfate, , and this on heating to 180° is converted to sulfanilic acid. The acid is used in the manufacture of several dyes. (Since this compound contains a basic—NH_2—and an acidic—SO_3H—group, an "inner salt," of the type

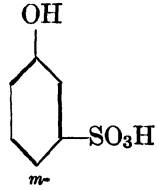


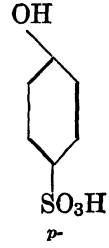
is possible. Compare with amino acids, p. 144.)

 is **metanilic acid.** It is prepared by reducing *m*-nitrobenzenesulfonic acid and is used in the preparation of azo dyes.

Of the **phenolsulfonic acids,**

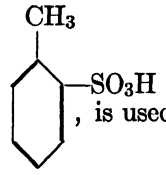


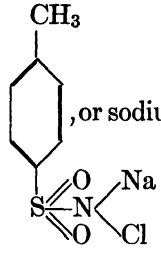


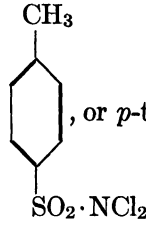


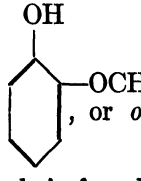
the *o*-variety is prepared by treating phenol with H_2SO_4 (in the cold), the *p*-, by heating phenol with H_2SO_4 to 96°, and the *m*-, by cautiously fusing (with NaOH) the *m*-benzenedisulfonic acid.

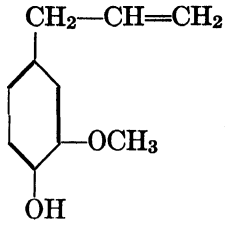
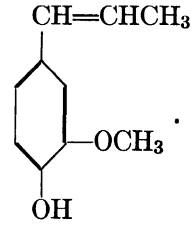
A mixture of the *o*- and *p*- is used as an antiseptic under the name "aseptol."

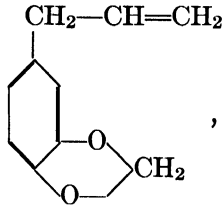
The *o*-Toluenesulfonic acid,  , is used in the preparation of saccharin (p. 291).

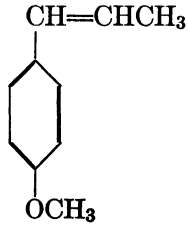
Chloramine-T,  , or sodium-*p*-toluenesulfon-*N*-chloramide or "chlorazene" (a derivative of *p*-toluenesulfonic acid), is used as an irrigating fluid in the treatment of wounds, as a mouth wash, and, in general, as an active germicide. (It has approximately four times the antiseptic value of phenol.) It was introduced by Carrel and Dakin during the late war.

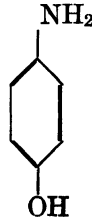
Dichloramine-T,  , or *p*-toluenesulfon-*N*-dichloramide, is also used in the treatment of infected wounds.

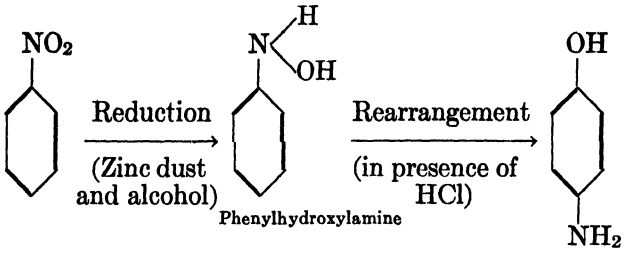
Guaiacol,  , or *o*-methoxyphenol, or the monomethyl ether of catechol, is found in gum guaiacum and in beechwood tar, and is obtained from guaiac resin by distillation. (The guaiac resin, dissolved in alcohol, is the "guaiac reagent" used in tests for oxidizing enzymes, blood, milk, etc.) Guaiacol, as well as some of its salts and esters, is used as internal antiseptic.

Eugenol,  , or 4-allyl-2-methoxyphenol, is present in oil of cloves. It is an antiseptic and local anesthetic used in dentistry. An isomer is isoeugenol,  .

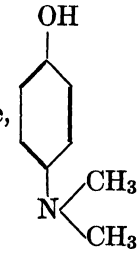
Safrole,  , or 1-allyl-3, 4-methylenedihydroxy benzene is the chief constituent of oil of sassafras. It is used as an anodyne.

Anethole,  , *p*-propenylanisole is found in anise seed oil and is used as an antiseptic.

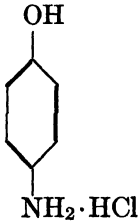
***p*-Aminophenol,**  , is prepared as follows:



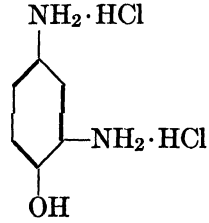
and is used as a photographic developer and in the manufacture of such dye intermediates as *p*-hydroxydimethylaniline,



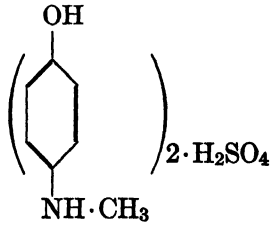
The 1, 4, or *p*-aminophenol type of compound and its derivatives make the best photographic developers. Some of the compounds used as photographic developers are:



Rhodinal or
p-aminophenol hydrochloride

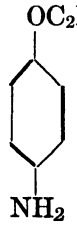


Amidol or
1, 3-diamino-4-hydroxybenzene
dihydrochloride

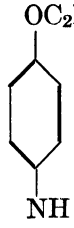


Metol

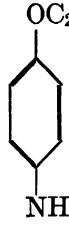
and there are number of others.

p-Phenetidine,  , or *p*-aminophenetole, is used in the

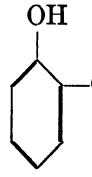
preparation of phenacetin, and often appears in the urine when phenacetin is administered.

Phenacetin,  , the acetyl derivative of *p*-phenetidine, is

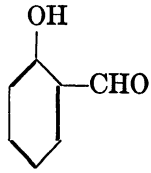
used as an antipyretic and analgesic.

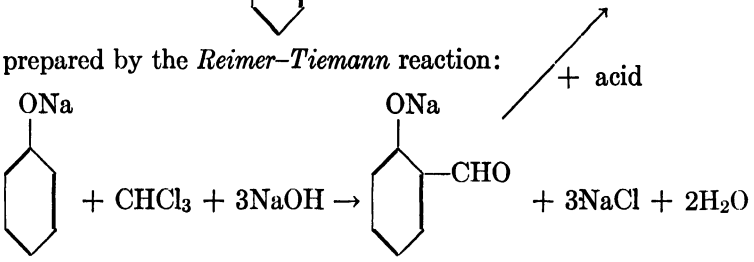
Dulcin,  , or *p*-phenetyl carbamide, is also

called "sucrol." It is two hundred times as sweet as cane sugar.

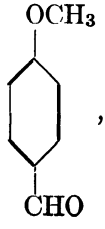
Salicyl alcohol,  , or *o*-hydroxybenzyl alcohol,

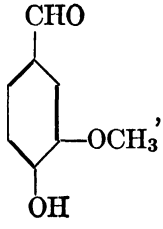
or saligenin occurs in combination with glucose in the glucoside salicin (present in willow bark). It has been recently recommended as a local anesthetic.

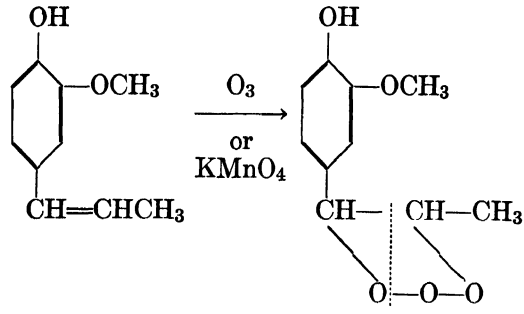
Salicylaldehyde,  , or *o*-hydroxybenzaldehyde, is prepared by the *Reimer–Tiemann* reaction:



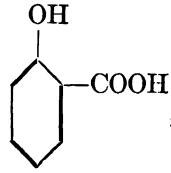
(The *p*-modification is also produced, but the *o*- and *p*- can be separated by steam distillation, the *o*- passing over with the steam.) This aldehyde occurs in oil of spiroea and oil of certain flowers and is used in perfumery and in the preparation of coumarin (p. 309).

Anisaldehyde,  , or *p*-methoxybenzaldehyde, is found in anise seed oil and is used in perfumery.

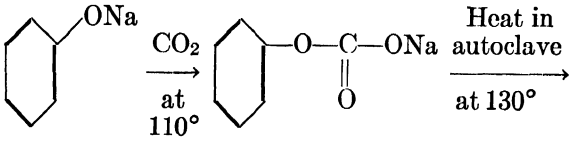
Vanillin,  , or *m*-methoxy-*p*-hydroxybenzaldehyde, is present in vanilla bean and is the chief constituent of extract of vanilla. It is manufactured by the oxidation of isoeugenol:



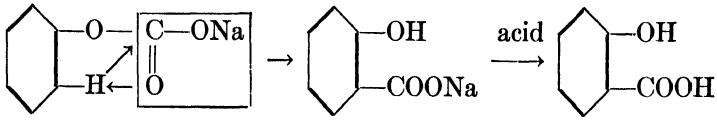
and also from guaiacol by the *Reimer–Tiemann* reaction (see above). It is used in perfumery, as a flavoring agent and as a gastric stimulant.

Salicylic Acid, 

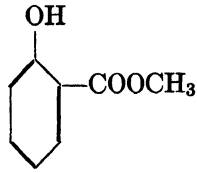
, or *o*-hydroxybenzoic acid, occurs in blossoms of meadow sweet, and, as its methyl ester in oil of wintergreen. It is prepared by the *Kolbe–Schmitt* reaction:

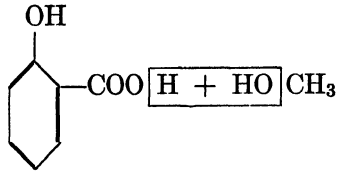


Sodium phenyl carbonate

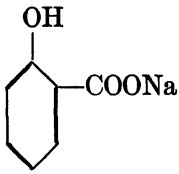


Salicylic acid is sometimes used in medicine for the treatment of rheumatic diseases, to check gastric fermentation and also as an antipyretic and intestinal antiseptic. It is most commonly administered in the form of some of its derivatives, such as salol, aspirin, sodium salicylate, strontium salicylate and methyl salicylate. It is employed to some extent in the preparation of corn cures and skin disease salves. Large quantities are used in the manufacture of dyestuffs.

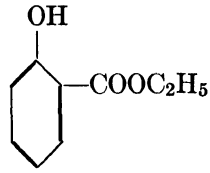
Methyl salicylate,  , is the chief constituent of "oil of wintergreen," and is the artificial oil of wintergreen. It is prepared by heating salicylic acid with methanol (esterification):



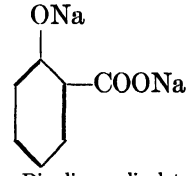
A number of the salicylates, and their derivatives, such as



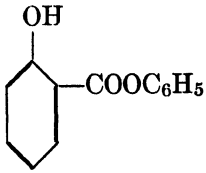
Sodium salicylate



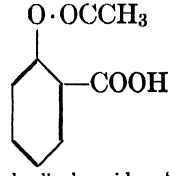
Ethyl salicylate



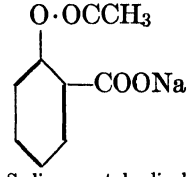
Disodium salicylate



Phenyl salicylate or "salol"



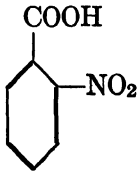
Acetyl salicylic acid, or "aspirin"

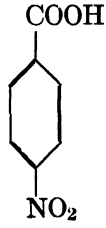


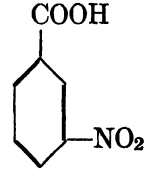
Sodium acetyl salicylate

are used as intestinal antiseptics and as antipyretics.

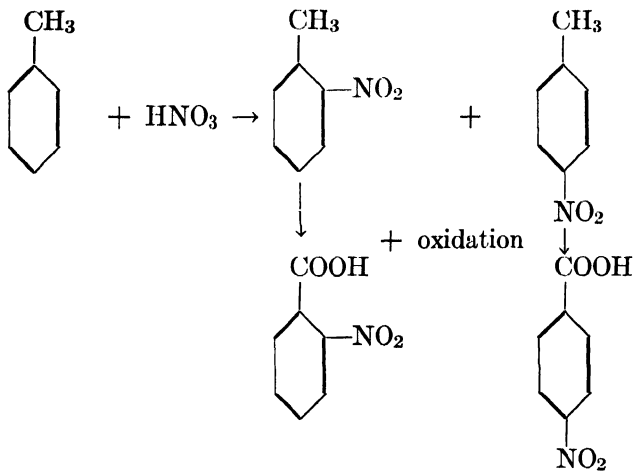
There are three isomers of **nitrobenzoic acid**:



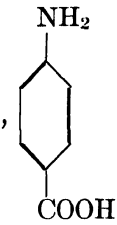
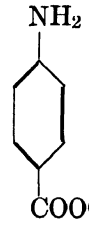
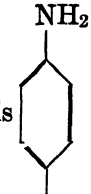




the first two being prepared from toluene; e.g.,

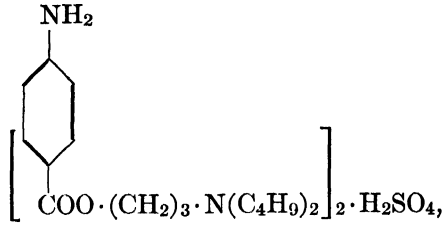


and the *m*-variety, by direct nitration of benzoic acid. On reduction they yield the corresponding amino acids.

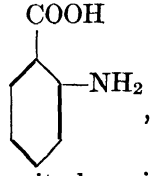
A number of derivatives of *p*-aminobenzoic acid,  are important local anesthetics. Anesthesine is  , ethyl *p*-aminobenzoate. Novocaine is 

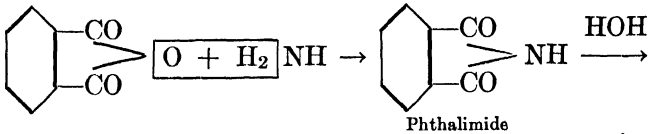
$COO \cdot CH_2 \cdot CH_2 \cdot N(C_2H_5)_2 \cdot HCl.$

It is only one-seventh as toxic as cocaine. Procaine is another name for novocain. Butyn is

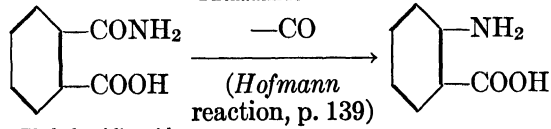


and is extensively used in dentistry and in ophthalmic surgery.

Anthranilic acid,  , or *o*-aminobenzoic acid, is prepared either from *o*-nitrobenzoic acid by reduction, or from phthalic anhydride:

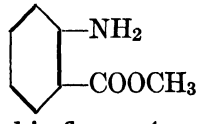


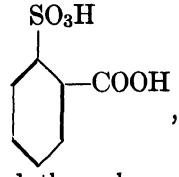
Phthalimide

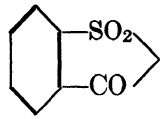


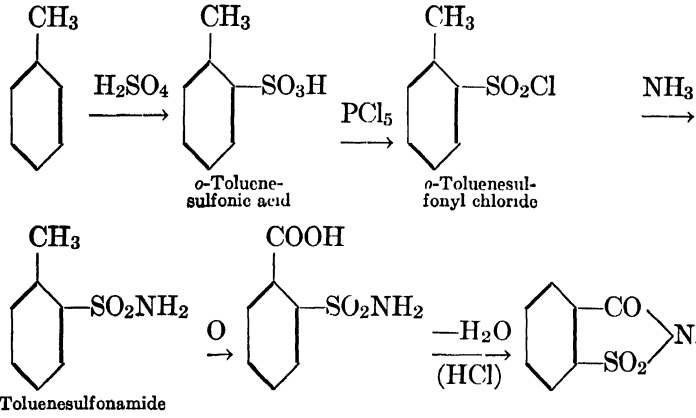
Phthalamidic acid

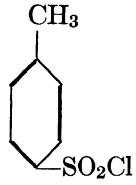
It is used as a dye intermediate and in the synthesis of indigo.

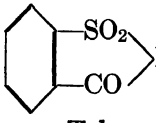
Methyl anthranilate,  , is a constituent of orange blossoms, and it is used in flavors (grape) and in perfumery.

***o*-Sulfobenzoic acid**  , is prepared by the sulfonation of toluene and the subsequent oxidation of the CH_3 group.

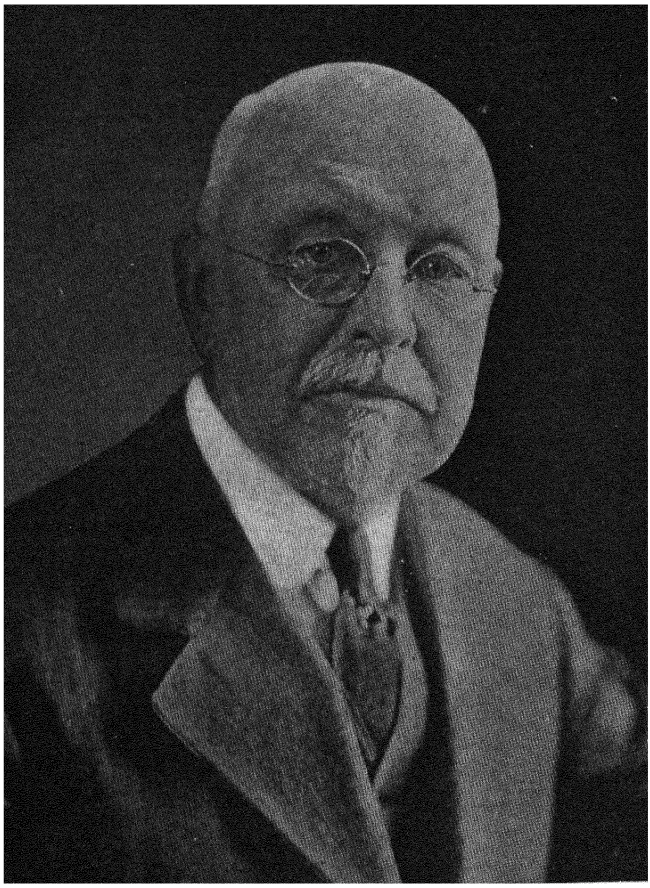
Saccharin,  , or *o*-benzoic sulfinide, may be prepared as follows:



(When toluene is sulfonated a mixture of *o*- and *p*-compounds is, of course, formed. These are separated at the sulfonyl-chloride stage  by filtering them with ice, the *p*-compound, being a solid at that temperature, remains on the filter, the *o*- going through in the form of a thick, oily liquid.)

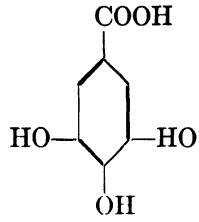
Saccharin was first prepared by Remsen. It is said to be about 550 times as sweet as sugar, and is used as a substitute for sugar in diabetes, and as sweetening agent in mouth-washes, tooth-pastes, etc. The substance has no nutritive value. (Since saccharin itself is not very soluble in water, the sodium salt  , which is very soluble, is manufactured.)

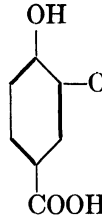
p-Toluenesulfonylchloride, is employed with *p*-toluenesulfonamide as a camphor substitute. *p*-Toluenesulfonic acid is also used in the manufacture of dyes. *p*-Toluenesulfonamide is employed in the preparation of chloramine-T.



IRA REMSEN (1846–1927)

FOR MANY YEARS PROFESSOR OF ORGANIC CHEMISTRY AT JOHNS HOPKINS UNIVERSITY (AND LATER ITS PRESIDENT), IS BEST KNOWN FOR HIS WORK ON SACCHARIN (P. 291) AND AS THE AUTHOR OF TEXT-BOOKS ON ORGANIC CHEMISTRY. HE HAS DONE MUCH TO FURTHER RESEARCH IN ORGANIC CHEMISTRY IN THIS COUNTRY.

Gallic acid,  3, 4, 5-trihydroxybenzoic acid, is found free, or as a glucoside in a number of plants (sumach, gall nuts, etc.), and may also be obtained by hydrolyzing tannins with acid. When heated, CO_2 is evolved and pyrogallic acid is formed (p. 255). Gallic acid is used in photography, ink and as an astringent.

Tannic acids.—These acids are found in gall nuts and other plants. Their exact constitution is not known, but since, on hydrolysis, they yield hydroxybenzoic acids, particularly gallic and protocatechuic,  , it is assumed that they are complex anhydrides of such acids.

The mother substances of these tannic acids are tannins, which are glucosides. (The names " tannic acid " and " tannins " are commonly used interchangeably.) These tannins are found in gall nuts, oak, chestnut, pine, hemlock, etc. They give characteristic blue-black or green-black colors with ferric chloride and are valuable astringents. They precipitate proteins and alkaloids. They are largely employed in the making of leather, as mordants in dyeing, and in the manufacture of inks.

READING REFERENCES

TILDEN—Chemical Discovery and Invention in the Twentieth Century. (1916), chap. 22 (Drugs).

FISCHER—Synthesis of Depsides, Lichin Substances and Tannins. *Journal of the American Chemical Society*, **36**, 1170 (1914).

HARROW—Eminent Chemists of Our Time. (1927), chapters dealing with Remsen.

BROWN—Forest Products. (1919), chap. 3 (Tanning).

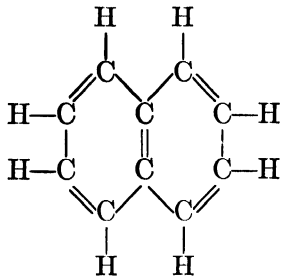
CLARK—Applied Pharmacology. (1923), pp. 80–84 (The Action of Salicylates).

GILMAN—Local Anesthetics. *Journal of Industrial and Engineering Chemistry*, **14**, 812 (1922).

CHAPTER XXVIII

NAPHTHALENE, ANTHRACENE AND THEIR DERIVATIVES

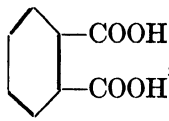
So far we have considered aromatic compounds containing the benzene nucleus; but now we begin to discuss compounds containing two or more condensed benzene rings, in which—to take an example—two carbon atoms are common to both rings:

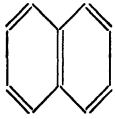


Naphthalene

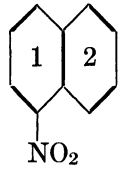
Naphthalene and anthracene are the most important of such compounds.

Naphthalene.—This hydrocarbon is obtained from coal tar in the fraction distilling over between 170–230° (middle or carbolic oil fraction. See chart facing p. 211); the crude product so obtained is purified by sublimation. Naphthalene crystallizes in lustrous plates, having a m.p. of 80° and a b.p. of 218°. It is very volatile and has a characteristic odor. It is used in the preparation of naphthalene compounds, in moth-balls, as an insecticide and germicide, in the manufacture of phthalic anhydride (p. 273), and dye intermediates (p. 311).

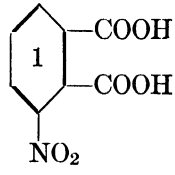
Naphthalene has the formula $C_{10}H_8$ and on oxidation yields phthalic acid,  , which proves the hydrocarbon to

contain a benzene ring, as well as some side-chains containing two carbon atoms in the *o*-position with respect to one another. That the actual constitution of naphthalene corresponding to $C_{10}H_8$ is  or two condensed benzene rings, is suggested by a number of reactions, of which two will be mentioned.

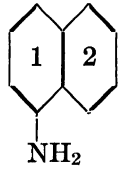
Naphthalene, like benzene, can be readily nitrated, yielding nitronaphthalene, and the latter reduced, giving aminonaphthalene. When nitronaphthalene is oxidized, we get nitrophthalic acid, but when aminonaphthalene is oxidized, we do not get aminophthalic acid, but just phthalic acid. If we write the structure for nitronaphthalene as



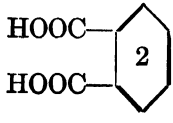
then it is plain that on oxidation, ring (2) must be oxidized to yield nitrophthalic acid



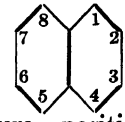
whereas if we write aminonaphthalene as



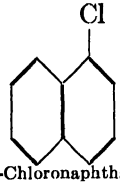
then it is equally evident that ring (1) must here be oxidized to yield phthalic acid



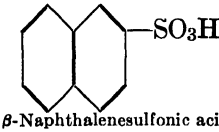
Obviously, then, there must be two benzene rings in naphthalene—two benzene rings having two carbon atoms in common.

Naphthalene has 8 replaceable hydrogen atoms: 

Since the molecule is symmetrical in structure, positions 1, 4, 5 and 8 are identical, and positions 2, 3, 6 and 7 are identical. We, therefore, have two possible monosubstitution products, a substituent at position 1 (or 4, 5, 8) being known as α- (*alpha*), and a substituent at position 2 (or 3, 6, 7) being known as β-(*beta*). For example,



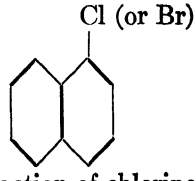
α-Chloronaphthalene

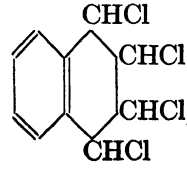


β-Naphthalenesulfonic acid

With disubstitution products, where the substituents are the same, 10 isomers are possible: 1 : 2, 1 : 3, 1 : 4, 1 : 5, 1 : 6, 1 : 7, 1 : 8, 2 : 3, 2 : 6, 2 : 7; but where they are dissimilar, 14 isomers become possible. Many substitution products and derivatives of naphthalene are manufactured, since they are used as dye intermediates, but only a few of these will be discussed here.

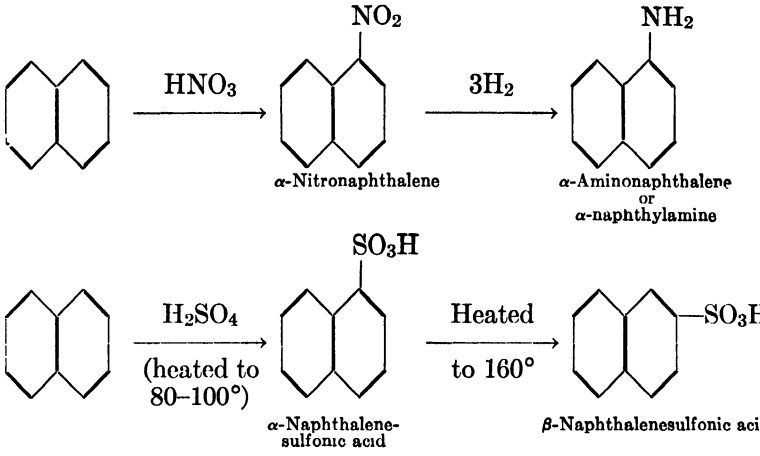
α-Chloro (or bromo) naphthalene



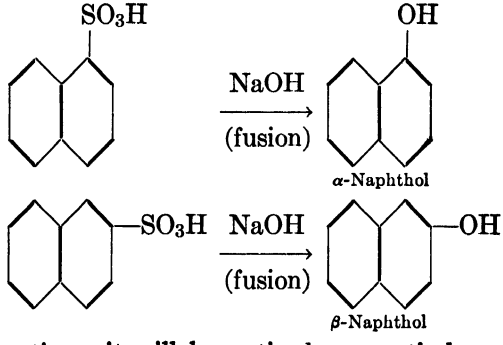
is prepared by the direct action of chlorine (or bromine) on boiling naphthalene. (The β-chloro—or bromonaphthalene—is prepared by indirect methods.) On the other hand, when chlorine (from potassium chlorate and HCl) is allowed to act on the hydrocarbon, naphthalene tetrachloride, 

an addition product is obtained.

Some other reactions are:

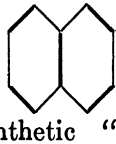


The sulfonic acids are used in the manufacture of naphthols:

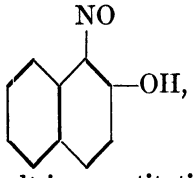


These reactions, it will be noticed, are entirely analogous to the preparation of phenol from benzenesulfonic acid (see p. 229). The naphthols are very important dye intermediates. α-naphthol is also used to test for the presence of carbohydrates (p. 172).

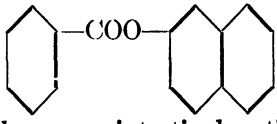
β-naphthol is employed internally as an intestinal antiseptic, and externally, in the form of ointment, for the treatment of skin diseases.



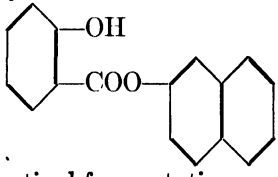
β-naphthyl methyl ether is known as synthetic "yara-yara" and is used in perfumery. The β-naphthyl ethyl ether is known as synthetic "nerolin" and is also used in perfumery.



α-nitroso-β-naphthol is used to determine cobalt in quantitative analysis.

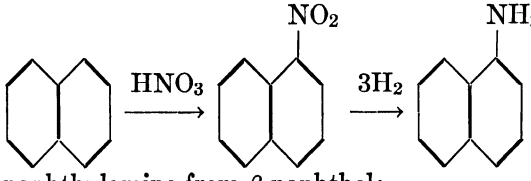


, β-naphthyl benzoate is used internally as an intestinal antiseptic in diarrhea and typhoid fever.

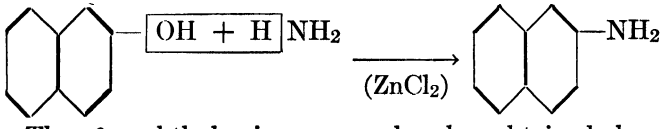


, β-naphthyl salicylate is useful in intestinal fermentations.

α-Naphthylamine is prepared from naphthalene:



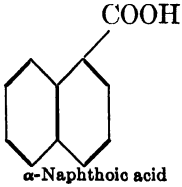
and β-naphthylamine from β-naphthol:



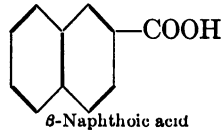
The β-naphthylamine may also be obtained by heating β-naphthol with ammonium chloride and NaOH in an autoclave at 160°. The naphthylamines are used extensively for the manufacture of dye intermediates and azo dyes (p. 325).

(Just as the NH_2 group in aniline, etc., can be diazotized—see p. 241—so can the NH_2 group in naphthalene compounds.)

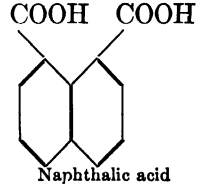
Examples of acids derived from naphthalene are:



α-Naphthoic acid

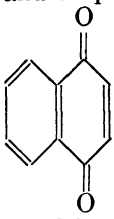


β-Naphthoic acid

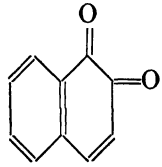


Naphthalic acid

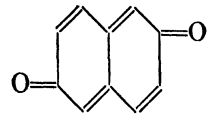
and of quinones:



α-Naphthoquinone

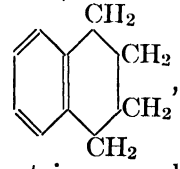
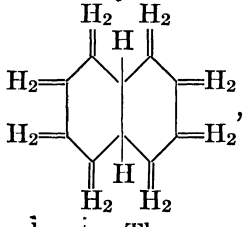


β-Naphthoquinone

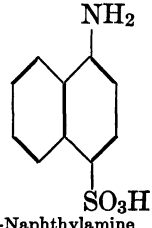


Amphi-Naphthoquinone

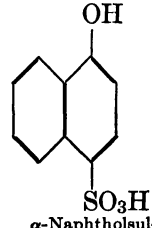
(The α-variety may be prepared by oxidizing naphthalene with chromic acid in the presence of glacial acetic acid.)

("Tetralin," or naphthalene tetrahydride,  , which has been suggested as a motor fuel and solvent, is prepared by reducing naphthalene with hydrogen in the presence of nickel as catalyst. A somewhat similar compound, "decalin,"  , has also been suggested as motor fuel and solvent. They are also used in textile soaps and in detergents.

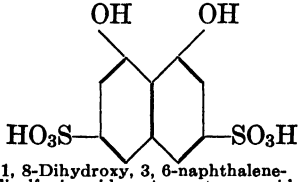
Many dye intermediates containing different substituents in the naphthalene ring are manufactured. A few of these are:



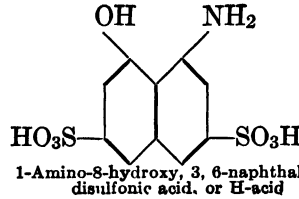
α-Naphthylamine sulfonic acid or naphthionic acid



α-Naphtholsulfonic acid



1, 8-Dihydroxy, 3, 6-naphthalenedisulfonic acid or chromotropic acid



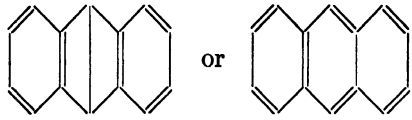
1-Amino-8-hydroxy, 3, 6-naphthalenedisulfonic acid, or H-acid

The following chart shows the position of entering substituents in the naphthalene ring.

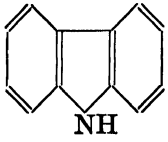
If a hydrogen atom in naphthalene is replaced

by	Cl		Br		OH		OR		NO_2		NH_2		NHR		SO_3H		CN		COOH	
in the position	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2
the new group	enters in the position																			
Cl	4		4		2?	1								1			5	5or8	5	
Br	4 5or8	? 5or8	4 5	8		1			5or8				4	1	5		5		5	
NO_2	4	8	4	8	2	1	2 4	1 6or7 8	5 8		5 8	5 8	2 4	1	4 5 8	4 5 8	5 ?		5 8	5 8 ?
SO_3H under 100°	4 5	6 8	4 ?	6 8	2 4	6 8			5 6 7		4	5 8			5 6	5	5 ?		α β β	α
SO_3H above 100°	5	6			2	6 7					5 6	6 7				5 6 7				
NO					2 4	1														
COOH					2	1 3														

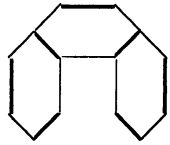
Anthracene, $C_{14}H_{10}$, or



is separated from coal tar in the fraction which boils over 270° (see chart facing p. 211). (From this fraction **carbazole**,



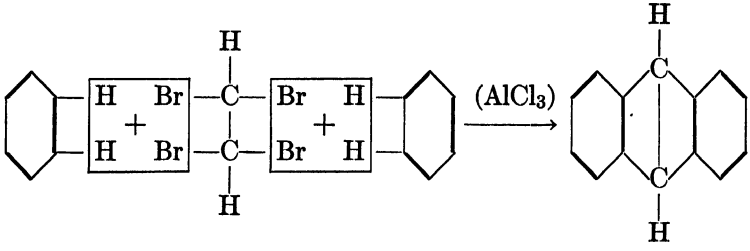
and **phenanthrene**,



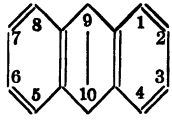
are also recovered).

The process by which this hydrocarbon is purified is a rather laborious one. The final purification is carried out by sublimation with superheated steam (m.p. 216°, b.p., 360°). Anthracene comes in the form of colorless, glistening leaflets, having a blue fluorescence. It is used in the manufacture of anthraquinone and its derivatives.

The structure of anthracene has been confirmed by a number of syntheses of the compound, one of which will be given: In the presence of $AlCl_3$, two molecules of benzene combine with one molecule of tetrabromoethane to form anthracene (*Friedel–Crafts* reaction.)

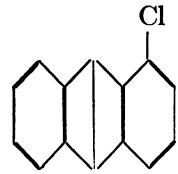


The positions of the replaceable hydrogen atoms are numbered thus:

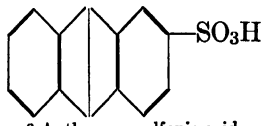


and from its structure it may be seen that positions 1, 4, 5 and 8 bear exactly the same relationship to the molecule. This is also

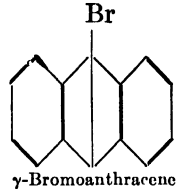
true of positions 2, 3, 6 and 7, and of 9 and 10. There are possible, therefore, three mono-substitution products; 1, 4, 5 or 8- being known as α-; 2, 3, 6 or 7, as β; and 9 or 10 as γ (gamma); e.g.,



α-Chloroanthracene

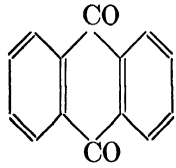


β-Anthracenesulfonic acid



γ-Bromoanthracene

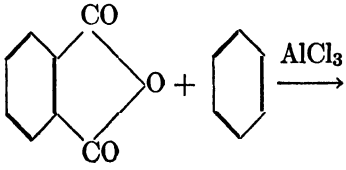
The most important derivative of anthracene is anthraquinone,

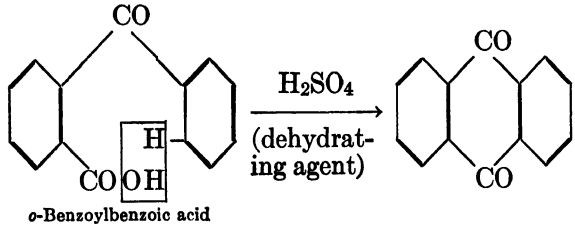


which is prepared from anthracene by oxidation with chromic acid ($Na_2Cr_2O_7$ and H_2SO_4).

(Nitric acid does not give rise to nitro-derivatives with anthracene, but converts it to anthraquinone—an indication that the central nucleus in anthracene is somewhat different from the two outer benzene nuclei.)

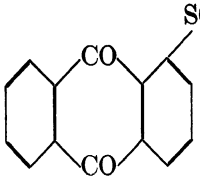
Anthraquinone is manufactured on a large scale, for it is used in the manufacture of dyes (such as alizarin) and dye intermediates. It is synthetically produced from phthalic anhydride by condensing the latter with benzene.



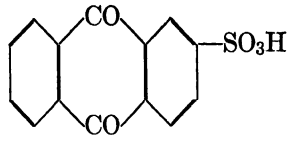


o-Benzoylbenzoic acid

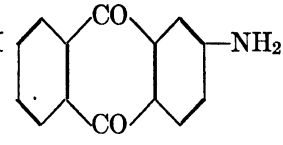
A number of other important anthraquinone derivatives used in the manufacture of dyes are:



α-Anthraquinone-sulfonic acid

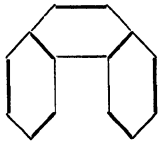


β-Anthraquinone-sulfonic acid

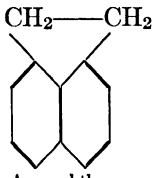


β-Aminoanthraquinone

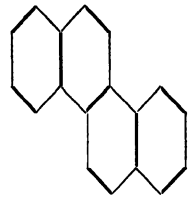
A few other condensed ring compounds obtained from coal tar are:



Phenanthrene $C_{14}H_{10}$



Acenaphthene $C_{12}H_{10}$



Chrysene $C_{18}H_{12}$

READING REFERENCES

BARNETT—Anthracene and Anthraquinone.

KLIPSTEIN—The Development of Synthetic Anthraquinone. *Industrial and Engineering Chemistry*, **18**, 1327 (1926).

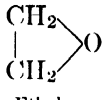
PHILLIPS—Chemistry of Anthraquinone. *Chemical Reviews*, **6**, 157 (1929).

A careful survey of the compounds so far studied will reveal that they have been prepared by making use of one or more of the following type reactions: halogenation, reduction, alkylation, oxidation, condensation, nitration, sulfonation, amidation, alkali fusion, nitrosation, hydrolysis, internal rearrangement, etc. Many of the substances prepared in this way are classed as dye "intermediates" and are used in the preparation of dyes, which are taken up in Chapter XXX.

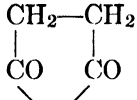
CHAPTER XXIX

HETEROCYCLIC COMPOUNDS

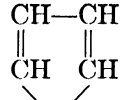
THE "cyclic" or "ring" compounds so far considered, with a few exceptions, such as succinic anhydride, lactones, etc., have contained the same elements within the ring (in this particular case, carbon atoms; hence **carbocyclic**). There are, however, very many compounds containing "cycles" in which elements other than carbon are also present; these are known as **heterocyclic,** for example,



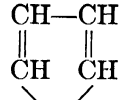
Ethylene oxide



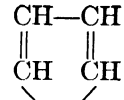
Succinic anhydride



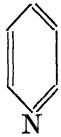
Thiophene



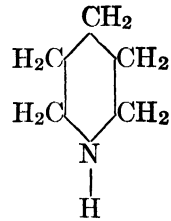
Furan



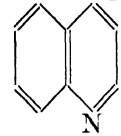
Pyrrole



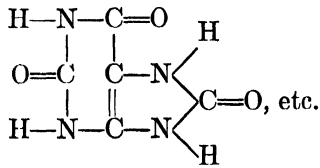
Pyridine



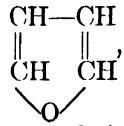
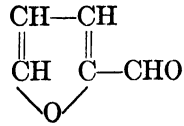
Piperidine or Hexahydropyridine

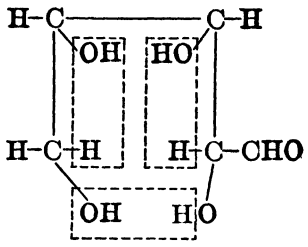


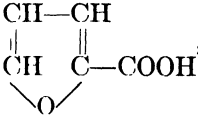
Quinoline

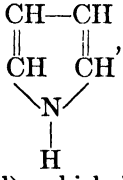
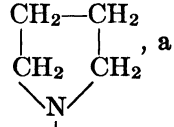
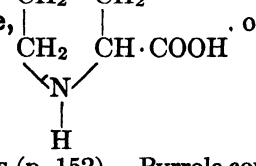


Uric acid or 2, 6, 8-triketopurine (trioxypurine)

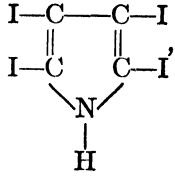
Furan,  , or furfuran, occurs in pinewood tar. Its most important derivative is **furfural,**  , or furfuraldehyde, which may be obtained from a pentose sugar, or pentosans, when boiled with hydrochloric or sulfuric acid (see p. 167):



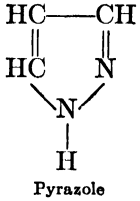
(This serves as the basis for the detection and estimation of pentoses and pentosans.) Commercially, furfural is prepared from corn and maize cobs, oat hulls, and other waste cereal products rich in pentoses or pentosans. It is used in the manufacture of synthetic resins, disinfectants, deodorizers, solvents, paint and varnish remover, etc. The general properties of furfural are similar to those of benzaldehyde. On oxidation, we get pyromucic acid,  , which, as its name implies, may also be prepared by heating mucic acid, $COOH \cdot (CHOH)_4 \cdot COOH$, an oxidation product of galactose (p. 177) or lactose. (The *Molisch test* for carbohydrates—p. 172, is said to be dependent upon the production of furfural or its derivatives.)

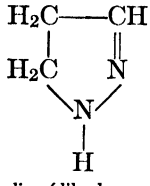
Pyrrole,  , is present in coal tar and in bone oil (Dippel's oil), which is a product of the destructive distillation of bones. (The pyrrole ring is present in a number of alkaloids.) It may be reduced to **pyrrolidine,**  , a carboxylic acid derivative of which is **proline,**  , one of the decomposition products of proteins (p. 152). Pyrrole compounds may be

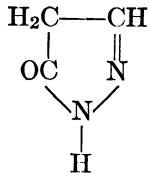
obtained from the destructive distillation of leather scrap and of gelatin.

Iodol,  , or tetraiodopyrrole, is an antiseptic, and is sometimes used in place of iodoform.

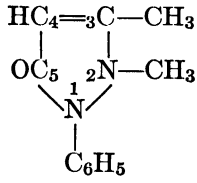
Other nitrogen-containing compounds are:


Pyrazole

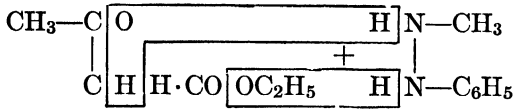

Pyrazoline (dihydropyrazole)


Pyrazolone

A derivative of the last compound is **antipyrine**:

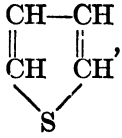


or 2, 3-dimethyl-1-phenyl-5-pyrazolone, which is made by condensing acetoacetic ester with methylphenylhydrazine:

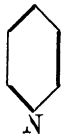


Antipyrine is used as an antipyretic and analgesic. (The 4-dimethylamino derivative of antipyrine is known as "pyramidon" and is used for similar purposes.)

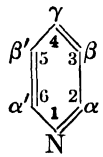
Phenyl methyl pyrazolone is used in photography and is known as "developer Z."

Thiophene,  , occurs in crude benzene and is the mother-substance of many sulfur-containing compounds, b.p. 84°. It is separated from benzene by repeated extraction with H_2SO_4

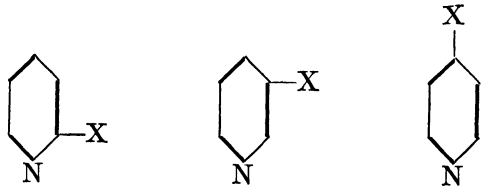
(thiophene is readily sulfonated, while benzene is not), and may be identified by the "indophenin" reaction (a mixture of isatin, thiophene and H_2SO_4 gives a blue color).

Pyridine,  (which may be looked upon as benzene in which one CH is replaced by N), is found in coal tar in the "light oil" fraction, in tobacco smoke, in *Dippel's* oil, and in crude ammonia. Pyridine is soluble in water, the solution being slightly alkaline in reaction. It has a characteristic, putrid odor and is an extremely stable substance, not being attacked by chromic acid (CrO_3) or nitric acid. It is used to denature alcohol. (The pyridine ring is present in a number of alkaloids.)

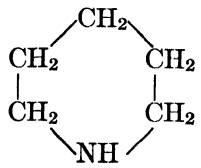
The positions in pyridine are numbered

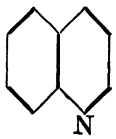


The compound has three mono-substitution products of the type

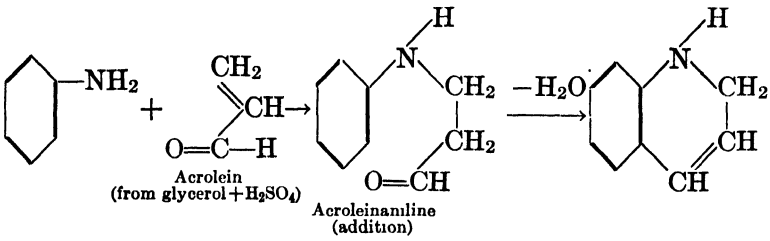


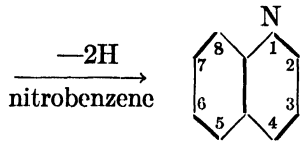
When reduced, pyridine yields **piperidine**, a substance which occurs in pepper and has a pepper-like odor.

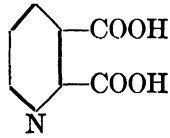


Quinoline,  , a condensation of one benzene and one

pyridine ring, is present in coal tar and bone oil, and may be prepared by the *Skraup's* reaction, in which a mixture of aniline, glycerol, H_2SO_4 (dehydrating agent) and nitrobenzene (oxidizing agent) are heated:





On oxidation, quinoline yields quinolinic acid, 

(What does naphthalene yield on oxidation?)

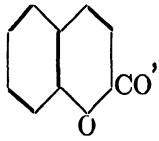
(The quinoline ring is present in certain alkaloids.)

A quinoline derivative known as "plasmochin" has been introduced as a new remedy for malaria.

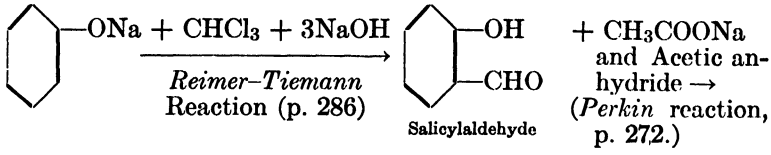
8-Hydroxyquinoline is used in the quantitative determination of metals, especially aluminum.

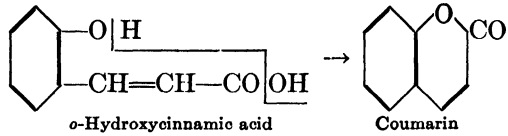
Isoquinoline,

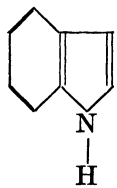
, is found in coal tar. (The isoquinoline grouping is present in a number of alkaloids.)

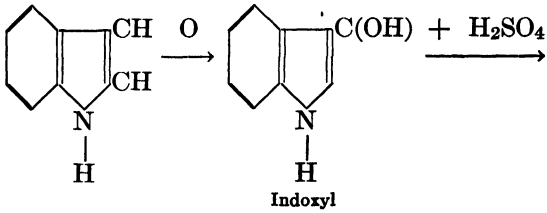
Coumarin, 

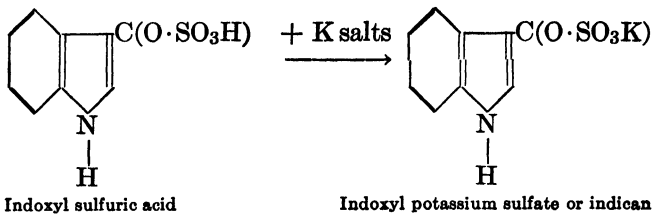
, is the sweet-smelling constituent of tonka bean, and freshly-mown hay. It is used extensively in flavoring extracts, flavoring tobacco, perfumery and as an adulterant for vanillin. It is made by the following series of reactions:





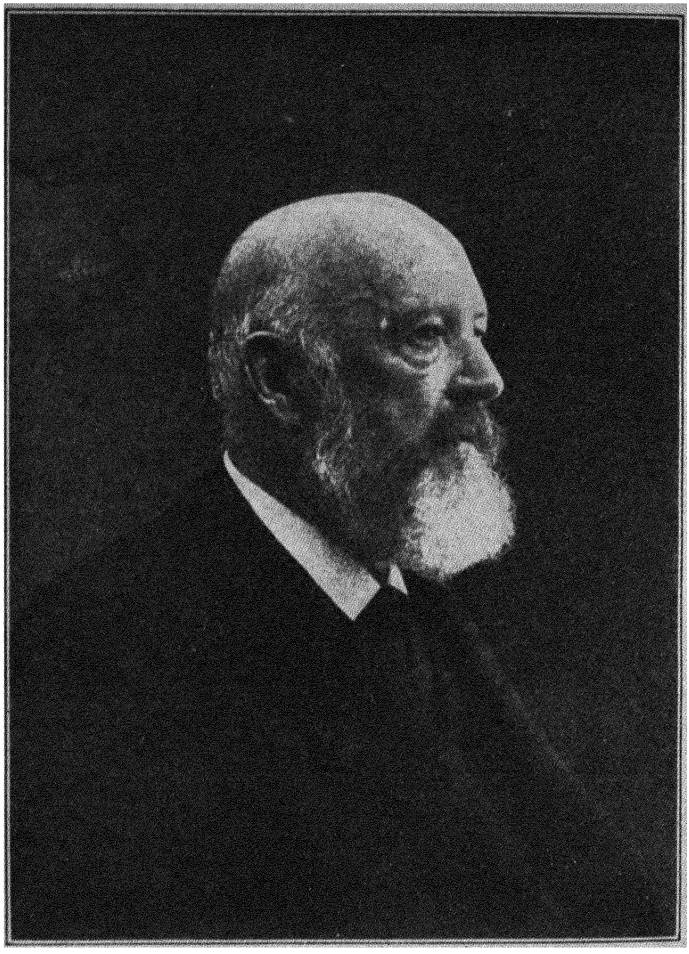
Indole,  , represents a condensation of the benzene and pyrrole rings, and is an intestinal product formed when proteins putrify. Indole is a highly toxic substance and is de-toxified by being converted into indican, in which form it is eliminated in the urine:





(The amount of indican in the urine is a rough indication of the extent of putrefaction within the intestine.)

Indigo is a natural product obtained from the indigo plant (in which it occurs as the glucoside "indican")—which grows in tropical countries—and is one of the oldest and best known vat dyes. Its synthesis in the chemist's laboratory (by Baeyer)

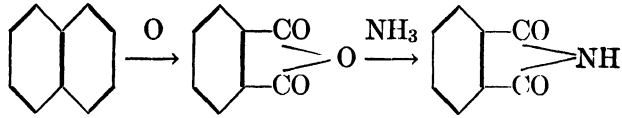


Adolf Baeyer

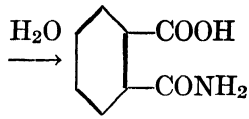
JOHANN FRIEDRICH WILHELM ADOLF BAEYER (1835–1917)

RESPONSIBLE FOR THE SYNTHESIS OF INDIGO (P. 309), WAS ONE OF THE MOST FRUITFUL WORKERS IN ORGANIC CHEMISTRY DURING THE NINETEENTH CENTURY.

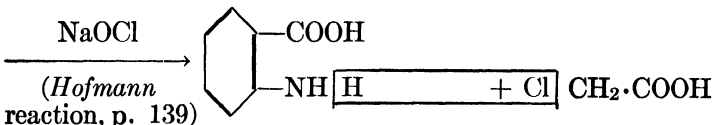
ranks as one of the great achievements in the history of organic chemistry. It may be produced artificially by the following series of reactions:



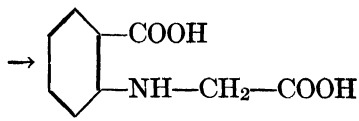
Naphthalene — Phthalic anhydride — Phthalimide



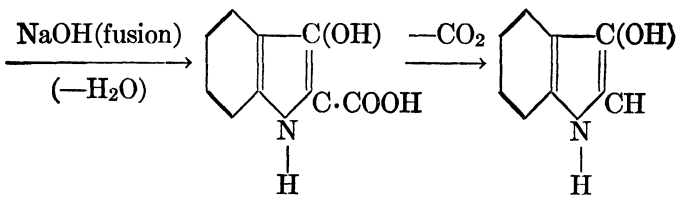
Phthalamidic acid



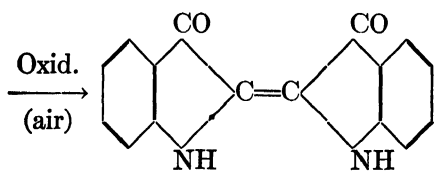
Anthranilic acid or *o*-aminobenzoic acid — Chloroacetic acid



Phenylglycine-*o*-carboxylic acid

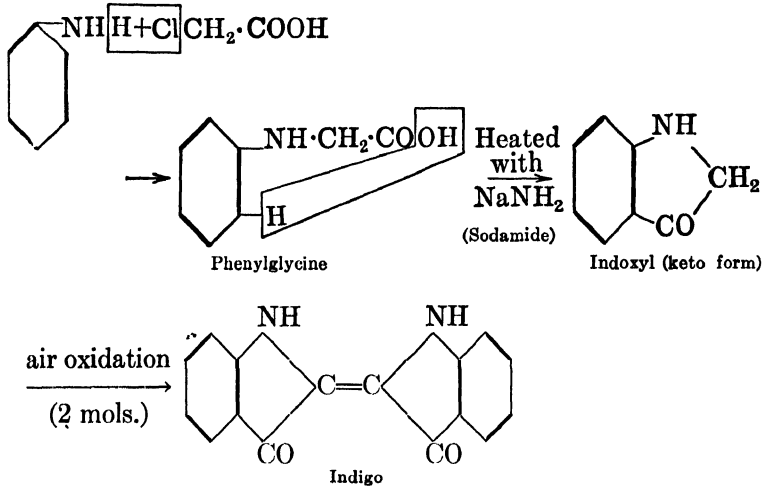


Indoxylic acid — Indoxyl (enol form)



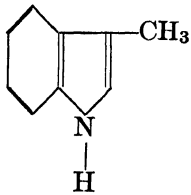
Indigo

On a commercial scale at the present time, indigo is prepared as follows:

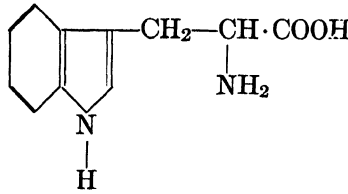


Prior to the World War the production of synthetic indigo accounted for 28 per cent of the total production of coal-tar dyes. Despite the fact that there are over one thousand chemically different dyes now in commercial production, indigo has maintained its position as the leader in quantity.

(The disodium salt of indigodisulfonic acid, known also as "indigo carmine," is used as a food color.)

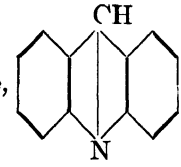
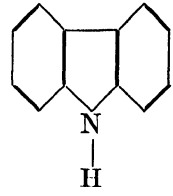
Skatole, 

, or β-methylindole, is also a putrefactive product formed in the intestine and its fate in the body is similar to that of indole. It is present in feces and has an extremely disagreeable odor.

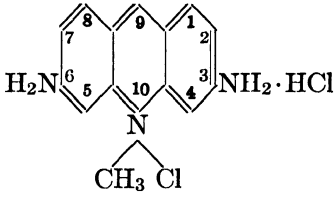
Tryptophan, 

, or α-amino-β-in-

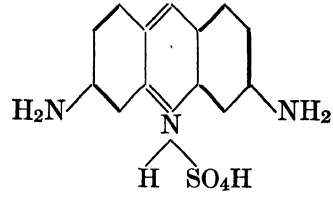
dolepropionic acid, has already been referred to under amino acids (p. 148).

Two other heterocyclic compounds are **acridine**,  , present in coal tar, and **carbazole**,  or dibenzopyrrole, present in anthracene oil. Carbazole is used in the manufacture of dyes.

Two important derivatives of acridine have recently been introduced in medicine:



Acriflavine or
3, 6-diamino-10-methylacridinium chloride hydrochloride



Proflavine
or
3, 6-diaminoacridinium hydrogen sulfate

They are strongly antiseptic and non-toxic.

READING REFERENCES

MICHELMAN—Pyrrole from New Sources. *Industrial and Engineering Chemistry*, **17**, 471 (1925).

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CHAPTER XXX

DYES AND STAINS

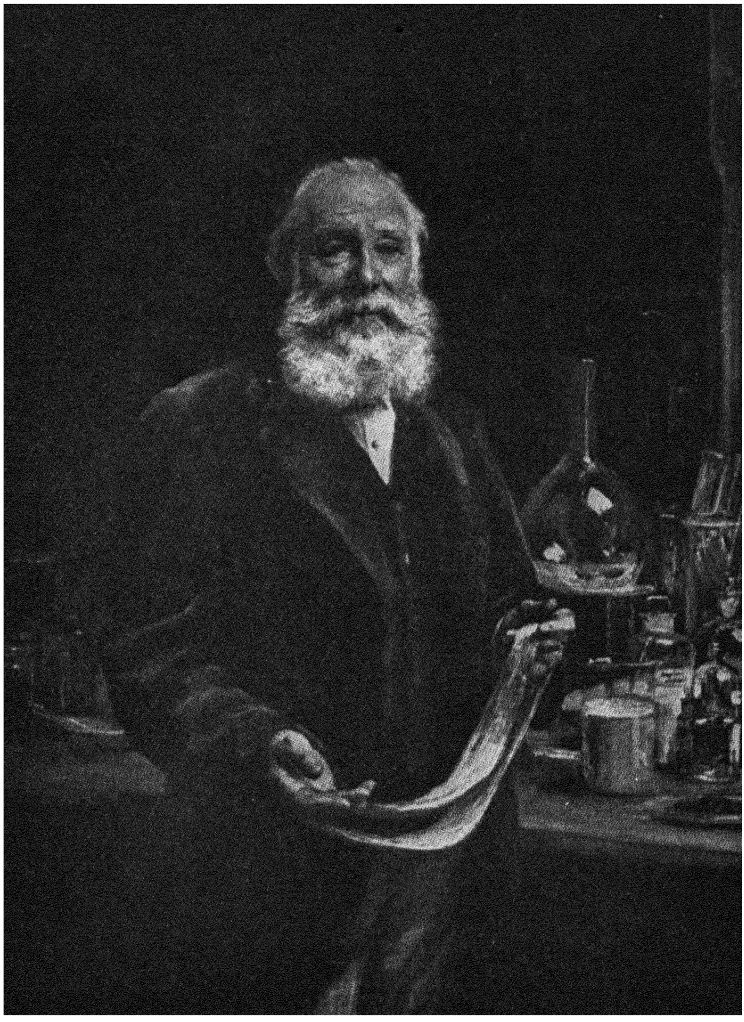
Dyes

Dyes have a wide application. They are applied to cotton, linen, silk, wool, paper, straw, wood, leather, feathers, hair, fats, waxes, soaps, inks, food, condiments (jams, macaroni, candy), varnishes, paints, etc. In analytical chemistry, dyes are used as indicators (e.g., phenolphthalein, congo red, methyl orange). In histology and bacteriology, they are used for staining microscopical preparations (e.g., methylene blue, acid fuchsin, safranine, eosin, gentian violet, neutral red, Bismarck brown). Dyes are also used as explosives (picric acid, picrates, trinitrocresols, etc.); in photography (eosin, erythrosin, etc.); as antiseptics (acriflavine, proflavine, malachite green, mercurochrome-220, etc.); in geographic and sanitary investigations, dyes (eosin, fluorescein) have been used to reveal whether any connection existed between flowing waters, sewage contamination, etc.

Dyes have been used from the very earliest times. Until the middle of the last century, those used for dyeing and printing were the vegetable dyes, coloring substances from certain insects (as cochineal) and molluscs, and a number of mineral colors. In 1856, Perkin, in attempts to prepare quinine artificially, found that aniline (a coal-tar product) could be oxidized with chromic acid to yield a violet dye, to which was given the name "mauve." This was the first coal tar dye to be prepared, but since then no less than 3000 dyes derived from coal tar products have appeared on the market.

The dyes, then, may be either "natural" or "artificial." Among the former are logwood, fustic, Brazil wood, turmeric, natural indigo, etc., and they still find uses. The artificial dyes, however, play a much more important part in the industries. The ones of particular value are "fast" to light, rubbing and washing.

Dyes are also classified in accordance with their behavior towards fabrics as "substantive" or "direct" and "adjective" or "mordant" dyes. The "direct" dye can be applied directly (without a mordant) to the fabric, usually silk or wool. The "adjective" or "mordant" dye needs a "go-between"—a third substance which attaches itself to the fabric on the one hand, and the dye on the other; this third substance is the



WILLIAM HENRY PERKIN (1838–1907)

PREPARED THE FIRST COAL-TAR DYE, "MAUVE" (P. 314), AND IS THEREFORE CALLED THE "FATHER" OF THE COAL TAR DYE INDUSTRY.

" mordant "—" bite into "—(e.g., various aluminium, chromium and iron salts, tannic acid, etc.). The combination of a mordant and a dye is known as a color " lake," the color of the " lake " varying with the type of mordant used. By using different mordants with the same dye, various colored lakes are produced. " Mordant " dyeing is mainly used for cotton goods. (In " direct " dyeing, the fabric is immersed directly in the prepared dye bath, heated to the required temperature, and agitated for a certain length of time.)

We cannot in this volume go into the various theories which have been suggested to explain the process of dyeing, beyond merely enumerating them: the chemical theory—a combination of the dye with the components of the fabric or certain constituents of the cell; the mechanical theory, based on adsorption; the solution theory, somewhat like the solution of one metal in another, as in an alloy; and the colloid theory, based on the colloidal properties of the reacting substances.

From the practical standpoint, the classification of dyes depends upon their behavior towards fibers.

The dyes are divided into:

(1) *Acid dyes*, which include nitro compounds and the sodium salts of sulfonic and carboxylic acids. These are direct dyes for wool and silk (in an acid bath), but are not adapted for the dyeing of cotton. The usual method employed here is to boil the material with the color solution in the presence of Glauber's salt and dilute sulfuric acid. (These dyes fade rapidly when the fabric is washed with soap or washing powders, but are resistant or " fast " to the effects of sunlight.)

(2) *Basic dyes*, substances which readily combine with acids to form salts. They are " direct " dyes for silk, artificial silk and wool, but not for cotton and linen. The last two have first to be " mordanted," the mordant used being acid in character (such as tannic acid, for example), since the dye itself is basic. Fabrics dyed with basic dyes fade when exposed to sunlight. The basic dyes owe their basic character to the presence of an amino group, and usually appear on the market as hydrochlorides, zinc double salts, compounds with oxalic acid, etc. The basic dyes were the first coal-tar colors, mauve itself (p. 314), being a basic dye.

(3) *Direct cotton dyes*, usually sodium salts of sulfonic and carboxylic acids and generally contain the azo (—N=N—) grouping. They are adsorbed by the fiber directly and are used

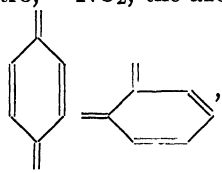
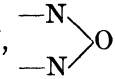
mainly for dyeing cotton material (in the presence of NaCl or Na_2SO_4).

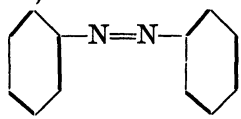
(4) *Sulfur dyes*—produced from various aromatic organic compounds by the action of sulfur and sodium sulfide. They are used for dyeing cotton and are fairly " fast " to washing.

(5) *Vat dyes.* These dyes are first reduced (generally with sodium hyposulfite, usually called sodium hydrosulfite, $Na_2S_2O_4$), the fabric being then agitated in the reduced dye bath and exposed to the air (whereby the dye is oxidized). Examples of such dyes are indigo and anthraquinone dyes. They are very stable, being the " fastest " colors known.

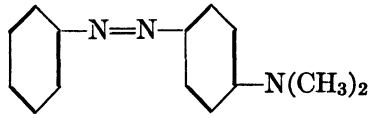
(6) *Mordant dyes,* which are generally of a phenolic or acidic character. Here mordants must be used to fix the dye to the fabric. Examples of mordant dyes are the coloring matters of dye woods (such as logwood and fustic) and alizarin.

(7) *Ingrain dyes.* These include substances (such as aniline black and para red) which are really only formed in the dye bath as a result of the chemical combination of two or more compounds. They are mainly cotton dyes.

The classification just described is a somewhat empirical one and arose in response to the practical needs of the dyer. There is still another classification, a more scientific one, based on the presence of certain groups in the molecule of the dyestuff. All dyes, in the first place, contain a **chromophore,** or color-producing group, such as the nitro, $-NO_2$, the azo, $-N=N-$, the nitroso, $-NO$, the quinoid  , CO, CS, CN,  (azoxy) groups, etc. But before the colored body can become a dye, it must also possess either acidic or basic characteristics, so that it can attach itself to the fiber, or to the tissue (within the cell). These acidic or basic properties are given to the dye when **auxochrome** groups are present, such as OH, SH, NH_2, NHR, NR_2, etc. For example, azobenzene,

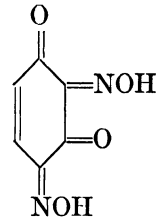
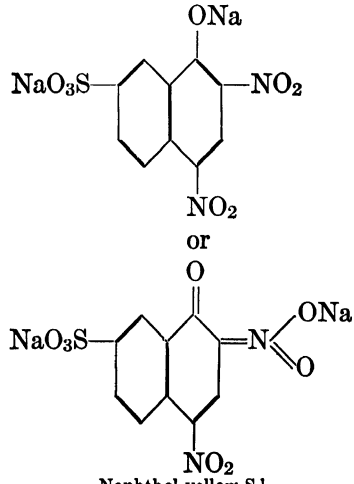


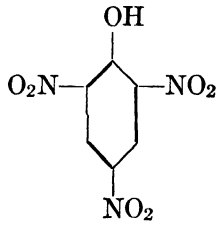
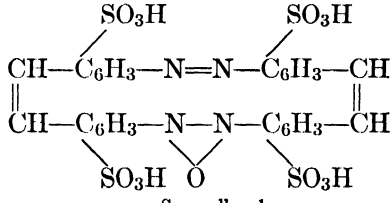
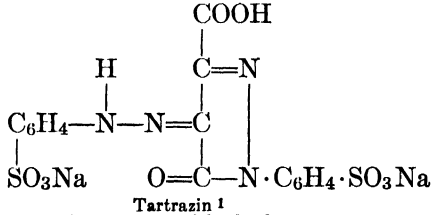
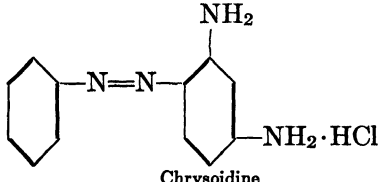
which is a colored compound, is not a dye, but *p*-dimethylamino-azobenzene,



is a dye.

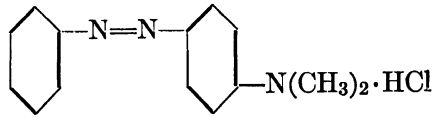
The entire subject of dyes is so extensive, that nothing more than a few members of the class can be mentioned here. However, the latest, and generally accepted classification of dyes will be given, and each type will be illustrated by one or more examples of dyes, stains or indicators in use. (The student should make a point here of noting the presence of chromophore and auxochrome groups in these compounds.)

Classes of Dyestuffs	Examples
Nitroso dyes	 Resorcin green (Dye)
Nitro dyes	 Naphthol yellow S [1] (Dye and food color)

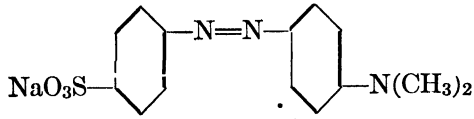
Classes of Dyestuffs	Examples
	 Picric acid (Dye and explosive)
Stilbene dye	 Sun yellow [1] (Dye)
Pyrazolone dyes	 Tartrazin [1] (Dye, stain and food color)
Azo dyes	 Chrysoidine (Dye)

[1] Notice the presence of the sulfonic acid grouping, or of its salt, as part of the structure of some of these dyes. The presence of this group increases the solubility of the dye in water.

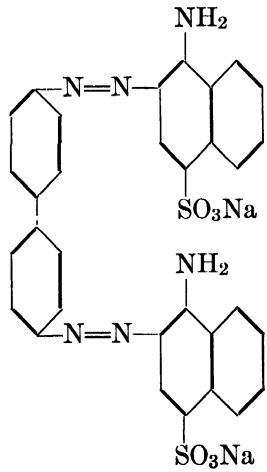
Classes of Dyestuffs	Examples



Butter yellow
(Dye and indicator)

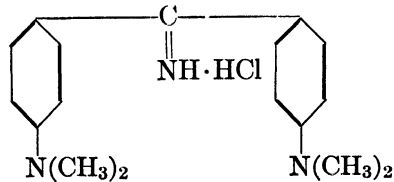


Methyl orange
(Dye and indicator)



Congo Red
(Dye and indicator)

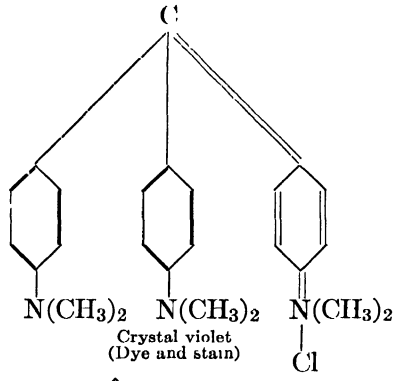
Diphenylmethane dyes



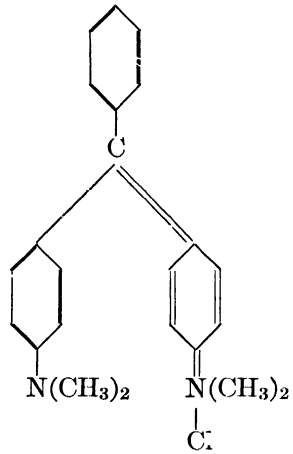
Auramine
(Dye)

Classes of Dyestuffs	Examples

Triphenylmethane dyes

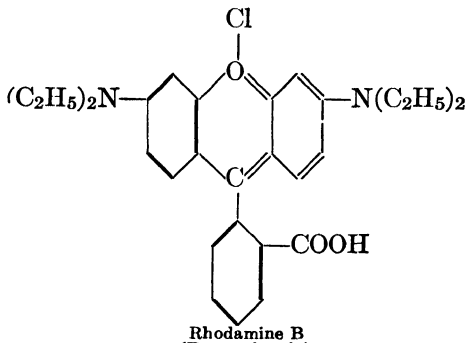


Crystal violet
(Dye and stain)

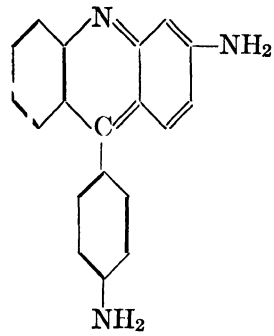
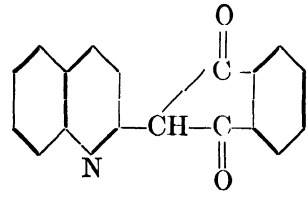
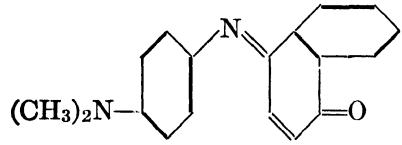
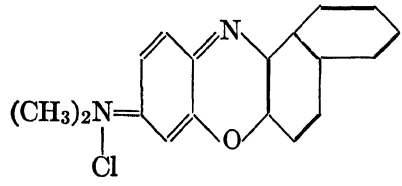


Malachite green
(Dye and stain)

Xanthene dyes

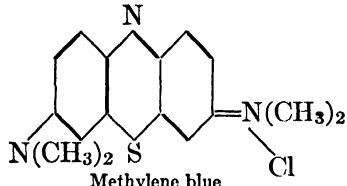


Rhodamine B
(Dye and stain)

Classes of Dyestuffs	Examples
Acridine dyes	 Chrysaniline (Dye)
Quinoline dyes	 Quinoline yellow (Dye)
Indophenol dyes	 Indophenol blue (Dye)
Oxazine dyes	 Meldola's blue (Dye)

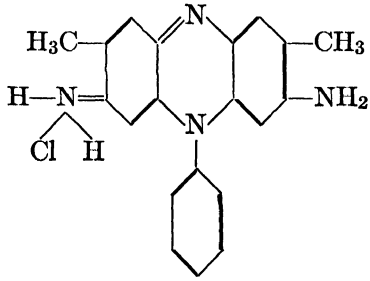
Classes of Dyestuffs	Examples

Thiazine dyes



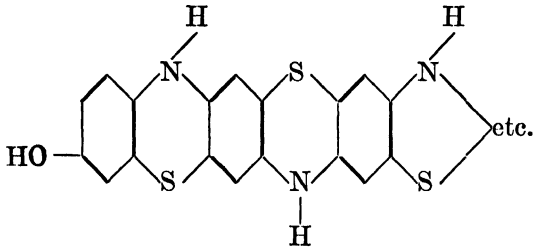
Methylene blue
(Dye and stain)

Azine dyes



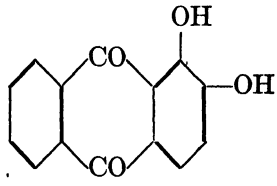
Safranine
(Dye and stain)

Sulfur dyes



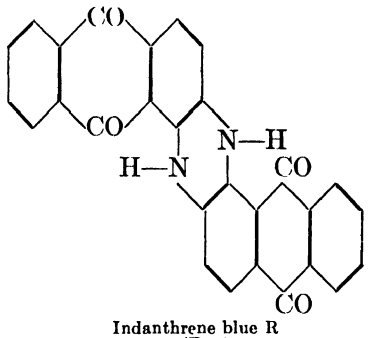
Sulfur black
(Dye)

Anthraquinone dyes



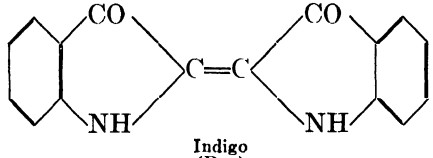
Alizarin
(Dye and indicator)

Classes of Dyestuffs	Examples



Indanthrene blue R
(Dye)

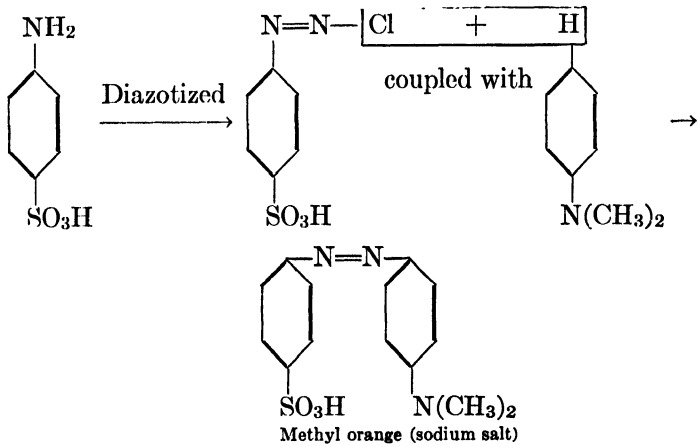
Indigo dyes



Indigo
(Dye)

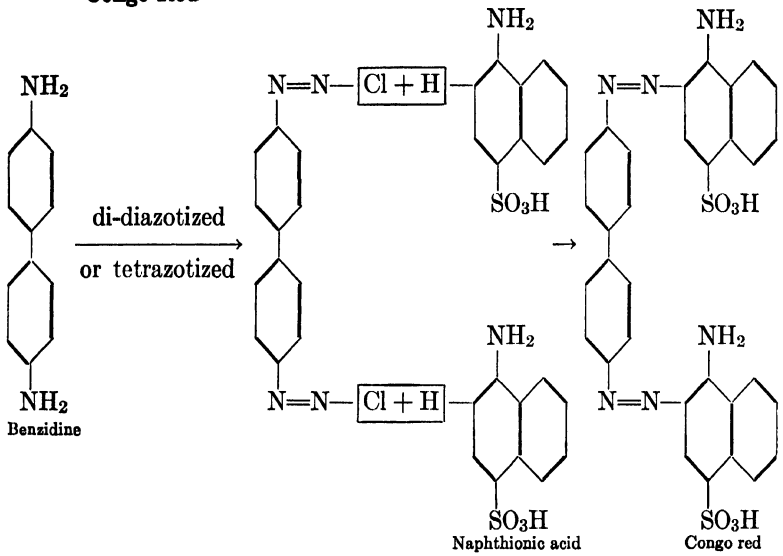
While the preparation of all of the above dyes cannot be given here, the principles employed in the synthesis of a few of them will be included.

Methyl Orange

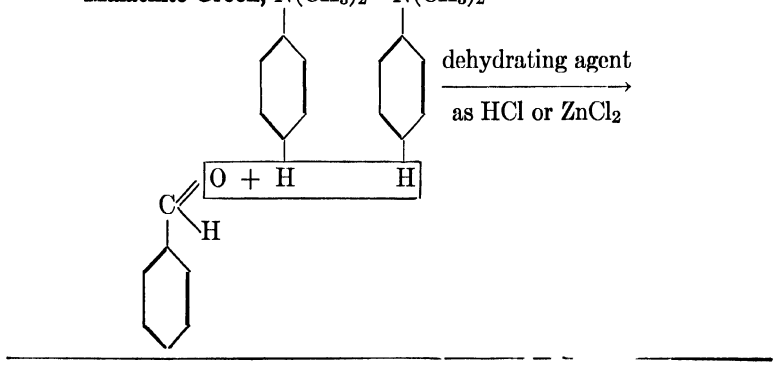


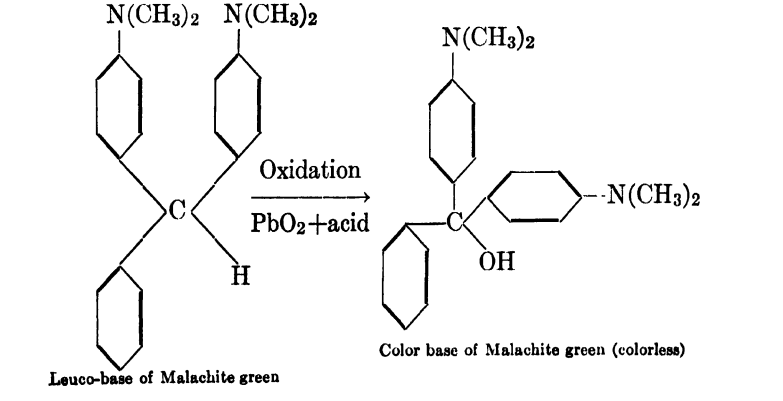
Methyl orange (sodium salt)

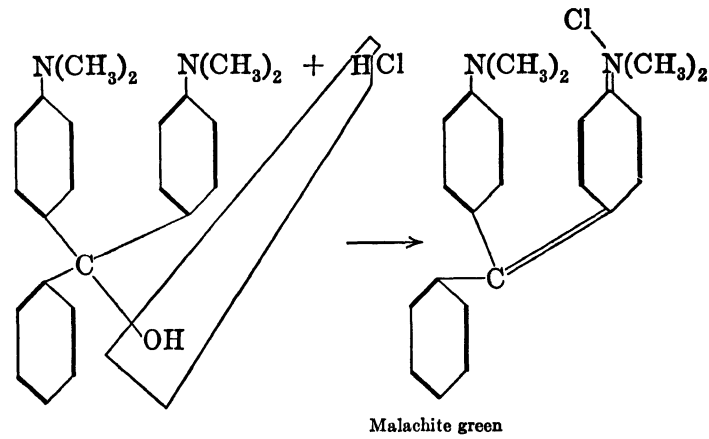
Congo Red



Malachite Green, $N(CH_3)_2$ $N(CH_3)_2$

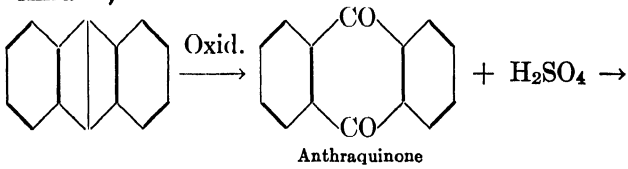




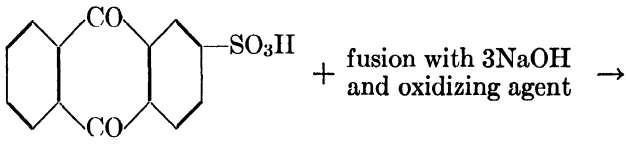


Malachite green

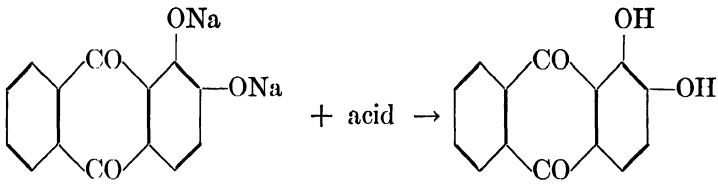
Alizarin,



Anthraquinone



β-anthraquinonesulfonic acid



Alizarin

(The preparation of phenolphthalein is given on p 274 and of indigo on p. 309).

Stains

Dyes have come into use in bacteriology, because very often various bacteria can be differentiated by " staining " them with dyes. A stain is a dye or any other substance which colors tissues so that they can be submitted to microscopic examination.

Basic aniline dyes are the type of stains commonly used; these show special affinity for the nuclei of cells. Acid dyes are also sometimes used; these usually have a selective affinity for the protoplasm. Some of the most commonly employed aniline dyes are methylene blue, gentian violet, fuchsin, crystal violet, safranine, etc.

The chemistry of the process involved in staining is probably not unlike that which occurs in dyeing; there may be a chemical combination between the dye and the protoplasm of the cell, or a process of adsorption may be involved, or possibly both processes are operative.

(Recent research has resulted in the production of a "tripan-red" type of dye, of unpublished composition, known as "Bayer 205," which appears to be the most active trypanocide yet discovered. It has been used with success in advanced cases of African sleeping sickness.)

READING REFERENCES

TILDEN—Chemical Discovery and Invention in the Twentieth Century (1916), chap. 21 (Production of Dyes); chap. 30 (Natural Colors).

WOOD—Chemistry of Dyeing.

RAMSEY AND WESTON—Artificial Dyestuffs.

PERKIN AND EVEREST—The Natural Organic Coloring Matters.

ROGERS—Manual of Industrial Chemistry. (1931), p. 1255 (Dyestuffs and Their Applications).

WATSON—Color in Relation to Chemical Constitution.

HARROW—Eminent Chemists of Our Times. (1927), (Perkin and Coal-tar Dyes).

HERTY—American Progress in Dye Manufacture. *Journal of Industrial and Engineering Chemistry*, **16**, 1021 (1924).

CONN—Biological Stains.

ROSE—Growth of the Dyestuffs Industry. *Journal of Chemical Education*, **3**, 973 (1926).

SHREVE—An Outline of the Dye Industry. *Journal of Chemical Education*, **3**, 1259 (1926).

ROWE—Colour Index.

FIESER—Discovery of Synthetic Alizarin. *Journal of Chemical Education*, **7**, 2609 (1930).

See p. 391 for list of books on Dyestuffs.

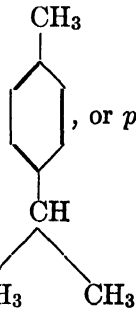
CHAPTER XXXI

TERPENES AND RELATED SUBSTANCES

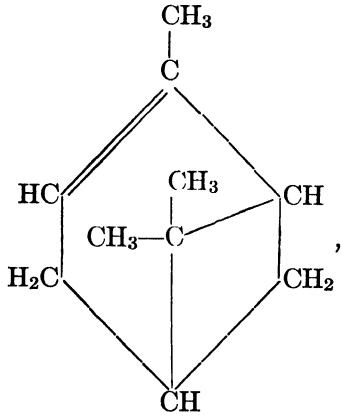
THE terpenes are complex hydrocarbons, usually with the formula $C_{10}H_{16}$, present in, or obtained from, such substances as camphor, oil of turpentine and particularly "essential oils." ("Essential oils" are the products obtained when certain plants—such as the conifer and citrus—barks, leaves or flowers are distilled with steam; or when the oil is pressed or extracted with organic solvents. They are usually sweet-smelling substances containing a number of related organic compounds and are extensively used as flavors, in perfumery and in medicine.)

The compounds classified as terpenes fall into several classes:

C_5H_8—hemiterpenes,
$C_{10}H_{16}$—terpenes (true terpenes),
$C_{15}H_{24}$—sesquiterpenes,
$(C_{10}H_{16})_x$—polyterpenes.

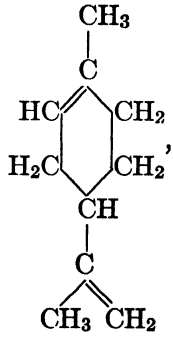
The terpenes are hydroaromatic hydrocarbons, closely related to **cymene,**  , or *p*-methylisopropylbenzene. Every terpene contains a hydrogenated benzene nucleus and either a methyl and isopropyl group, or radicals related to these groups.

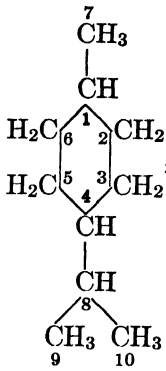
Some of the more important compounds belonging to the terpene group are as follows:

Pinene,  , is the chief constituent

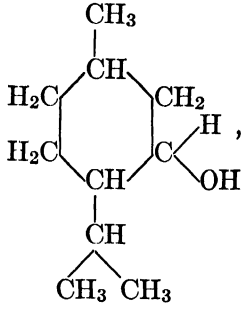
of oil of turpentine. Owing to the presence of a double bond, it forms addition products with halogens, halogen acids, nitrosyl chloride, nitrogen peroxide, etc. One such product, pinene hydrochloride (obtained by uniting pinene with hydrochloric acid), is "artificial camphor," which resembles camphor.

(When crude turpentine is distilled with steam, pure turpentine or "oil of turpentine" collects in the distillate and "rosin," or "colophony," a solid resin, remains in the still. The oil of turpentine is used in paints and varnishes and the rosin is used in soap making, varnishes, sealing wax, etc.)

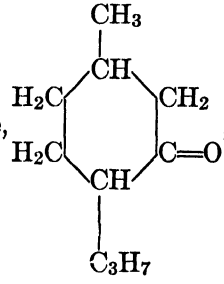
Limonene,  , is present in oil of lemon, lime, etc.

Menthane,  , or hexahydrocymene, is not a

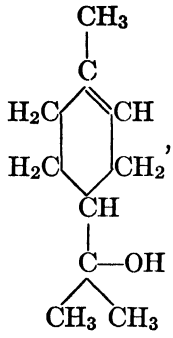
natural product, but we have a number of important substances related to it.

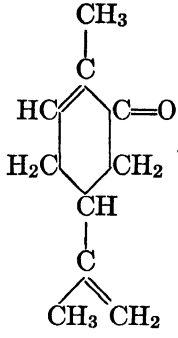
Menthol,  , or menthanol, occurs in oil of

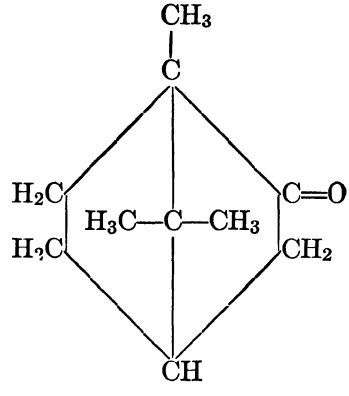
peppermint. It has a peppermint-like odor and finds extensive use as a flavoring agent.

Menthone,  , or menthanone, is the ketone cor-

responding to menthane, and is also found in oil of peppermint. Like other ketones, it may be reduced to a secondary alcohol (in this case to menthol).

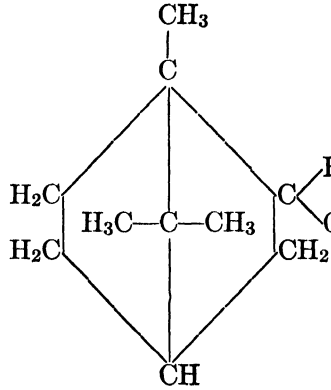
Terpineol,  , is found in essential oils and has an odor resembling that of lilacs.

Carvone,  , is the principal constituent of oil of caraway and possesses the characteristic odor of this oil.

Camphor,  is obtained from the camphor tree by steam distillation. It may also be obtained synthetically from pinene hydrochloride (p. 329). It is largely used in the manufacture of celluloid (p. 184) and in pharmaceutical preparations. (The artificial camphors on the market are either pinene hydrochloride or triphenyl phosphate, p. 251. Artificial

camphor does not have the same structure as natural or synthetic camphor.)

Borneol,



OH is the secondary alcohol obtained from camphor (a ketone) when the latter is reduced. It occurs in nature, being known as "Borneo-camphor," and has a camphor-like odor.

The following are the important olefin terpenes:

Isoprene, $CH_2{=}C(CH_3){-}CH{=}CH_2$, or 2-methyl-1, 3-butadiene (see p. 38), is obtained by the distillation of rubber or caoutchouc.

Citrene, $CH_3{-}C(CH_3){=}CH{-}CH_2{\cdot}CH_2{-}C(CH_3){=}CH{-}CH_3$, is a terpene obtained from lemon oil.

Geraniol (the alcohol),

$$CH_3{-}C(CH_3){=}CH{-}CH_2{-}CH_2{-}C(CH_3){=}CH{-}CH_2OH$$

is found in rose and geranium oils; and **citral** (the aldehyde),

$$CH_3{-}C(CH_3){=}CH{-}CH_2{-}CH_2{-}C(CH_3){=}CH{-}CHO,$$

in lemon and orange oils.

Citronellal, $(CH_3)(CH_2{=})C{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH(CH_3){\cdot}CH_2{\cdot}CHO$ occurs in oils of citrus fruits.

TABLE OF ESSENTIAL OILS

Oil	Chief Known Constituents
Allspice	Eugenol; sesquiterpene
Angelica Root	Phellandrene; valeric acid
Angelica Seed	Phellandrene; valeric acid
Anise	Anethole; anisaldehyde
Birch	Methyl salicylate
Bitter Almond	Benzaldehyde; hydrocyanic acid; phenyloxyacetonitrile
Camphor	Camphor; borneol; pinene
Caraway	Carvone; *d*-limonene
Cedar Wood	Cedrene; cedar camphor
Celery Seed	Limonene; phenols
Cinnamon Bark	Cinnamaldehyde; eugenol
Citronella	Geraniol; citronellal
Clove	Eugenol
Cognac	Esters of caprylic acid
Eucalyptus	Phellandrene; cineol
Fennel	Anethole; fenchone
Garlic	Allyl propyl disulfide; diallyl disulfide
Geranium	Geraniol; citronellol
Ginger	Phellandrene
Guaiac Wood	Guaiacol
Hops	Humulene; geraniol; terpenes
Jasmine	Benzyl acetate; linalol
Juniper Berries	Pinene; cadinene; juniper camphor
Lavender	Linalyl acetate; linalol
Lemon	Limonene; phellandrene; citral; citronellol; geranyl acetate; linalol
Lime	*d*-Limonene; citral; methyl anthranilate
Mustard	Allyl isothiocyanate
Neroli	Linalyl acetate; linalol; geraniol: limonene
Nutmeg	Myristicin; pinene
Onion	Allyl propyl disulfide
Orange	Limonene
Pepper	Phellandrene; dipentene
Peppermint	Menthol; menthyl esters; menthone
Rose	Geraniol; citronellol; geranyl acetate
Sassafras	Safrol; eugenol; camphor; pinene; phellandrene
Spearmint	Carvone; limonene; pinene
Thyme	Thymol; carvacrol; cymene; linalol; borneol
Tolu	Esters of benzoic and cinnamic acids
Turpentine	Pinene

Valerian	Borneol; bornyl formate, acetate and isovalerianate; pinene; camphene
Wintergreen	Methyl salicylate
Ylang-ylang	Linalol; geraniol; benzoic esters; methyl ester of *p*-cresol.

(Oil of Chenopodium, an old household remedy for worms, is a mixture of various terpenes.)

READING REFERENCES

TILDEN—Chemical Discovery and Invention in the Twentieth Century. (1916), chap. 23 (Perfumes and Essential Oils).

DUNCAN—Some Chemical Problems of Today. (1911), chap. 7 (Camphor).

DUNCAN—The Chemistry of Commerce. (1907), chap. 8 (Floral Perfumes).

SLOSSON—Creative Chemistry. (1920), chap. 5 (Synthetic Perfumes and Flavors).

GILDEMEISTER AND HOFFMANN—The Volatile Oils.

ROGERS—Manual of Industrial Chemistry. (1931), p. 1049 (Essential Oils, Synthetic Perfumes and Flavoring Materials); p. 1090 (Resins, Gums and Turpentine).

BOGERT—The Flower of the Organic Chemist: Perfumes Natural and Synthetic. *Journal of Industrial and Engineering Chemistry*, **14**, 359 (1922).

POWER—The Distribution and Characters of Some of the Odorous Principles of Plants. *Journal of Industrial and Engineering Chemistry*, **11**, 344 (1919).

ANON.—Turpentine. (Agricultural Bulletin 898.) Government Printing Office, Washington.

CLARK—Applied Pharmacology. (1923), chap. 7 (Anthelminthics—Oil of Chenopodium, etc.)

HOWE—Chemistry in Industry, Vol. I. (1924), chap. 16 (Perfumes and Flavors); chap. 20 (Chemistry in the Rubber Industry).

CHAPTER XXXII

VEGETABLE ALKALOIDS

VEGETABLE alkaloids are basic nitrogenous substances which occur in plants usually in combination with organic acids (citric, tartaric, oxalic, malic, etc.) and which are characterized by powerful physiological activity. They contain the elements C, H, N or C, H, O and N and are complex in constitution, generally containing pyrrole, pyrrolidine, pyridine, quinoline or isoquinoline groups in their structure. Only a very brief presentation of the subject can be given here.

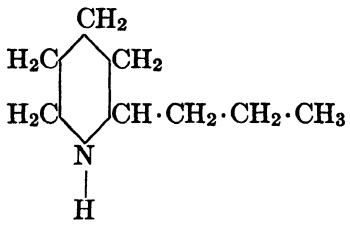
Alkaloids occur in dicotyledonous plants. Most of them are crystalline (coniine and nicotine are liquids) and most of them are levorotatory. They are insoluble in water, soluble in alcohol, ether, chloroform, etc., to a greater or less extent, form water-soluble salts with acids, have a bitter taste and some are excessively poisonous. Most of the alkaloids are used in the form of salts, such as hydrochloride, nitrate, bisulfate, sulfate, phosphate, etc.

The following substances, known as "alkaloidal reagents," precipitate alkaloids from their aqueous or acid solutions; tannic acid, potassium-mercuric iodide ($KI+HgI_2$), phosphomolybdic acid, picric acid and phosphotungstic acid. (The "alkaloidal reagents" are quite often used to precipitate proteins.)

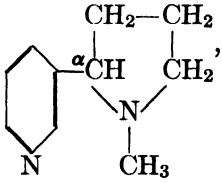
Color reactions are frequently used to identify certain alkaloids.

The method of extraction from plants often consists in extracting with acidified (HCl or H_2SO_4) water and reprecipitating with bases.

The number of alkaloids known is very large; only a few of the more important ones can be mentioned here.

Coniine,  , or α-propylpiperidine,

is obtained from the seeds of spotted hemlock and has been produced synthetically. It is very poisonous, has a disagreeable odor and an acrid taste. (Chemically, it is the simplest alkaloid.)

Nicotine,  , or α-pyridyl-N-methyltetrahydropyrrole, is present in tobacco leaves and is used as an insecticide.

Piperine, $C_{17}H_{19}NO_3$, occurs in pepper, from which it is extracted.

Atropine, $C_{17}H_{23}NO_3$, obtained from the *Deadly Nightshade* (belladonna), is used as a mydriatic (dilating the pupil) in ophthalmic surgery.

Homatropine, an artificial alkaloid derived from atropine, dilates the pupil more rapidly than atropine and the effect is not as lasting.

Cocaine, $C_{17}H_{21}NO_4$, is contained in coca-leaves. It is used as a local anesthetic in minor operations, though, owing to its extreme toxic properties, it has been largely replaced by novocaine, butyn, etc. (p. 290).

Quinine, $C_{20}H_{24}N_2O_2$, is obtained from cinchona bark, etc. It is used in the treatment of malaria, as a "bitter" (to increase appetite), to reduce fever, etc.

Cinchonine, $C_{19}H_{22}N_2O$, from cinchona bark, resembles quinine in its physiological properties, though its effects are not so pronounced.

Strychnine, $C_{21}H_{22}N_2O_2$, and **brucine,** $C_{23}H_{26}N_2O_4$, occur together in the seeds of nux vomica and in *St. Ignatius'* beans. Strychnine is an extremely poisonous substance, acting on the spinal cord and producing characteristic convulsions. In very

small doses, it is used as a tonic, to increase the appetite, as a heart stimulant and in various forms of paralysis. Brucine acts similarly.

Morphine, $C_{17}H_{19}NO_3$, is the chief alkaloid of opium (which is the dried juice of the seed capsules of a variety of poppy). It is used as an analgesic and as a soporific.

Heroine is a diacetyl derivative of morphine. Its effects are, in general, similar to those of morphine. It is used as a sedative and to lessen coughing.

Narcotine, $C_{22}H_{23}NO_7$, and **codeine**, $C_{18}H_{21}NO_3$, are also present in opium and are closely related to morphine.

Dionine is an artificial alkaloid made from morphine (ethyl morphine) and is used to produce sleep and relieve pain.

Pilocarpine is the active principle obtained from the leaves of *Pilocarpus jaborandi*, a Brazilian shrub. It is used principally to increase perspiration.

Emetine, the active alkaloid of ipecac, is used in the treatment of amoebic dysentery (because of its destructive action on amoebae) and also in the treatment of pyorrhoea alveolaris, an infected condition of the teeth sockets.

READING REFERENCES

PICTET AND BIDDLE—The Vegetable Alkaloids.

BARBOUR—Local Anesthetics. *Science*, **51**, 497 (1920).

CLARK—Applied Pharmacology. (1923), chap. 5 (The Action of Quinine in Malaria).

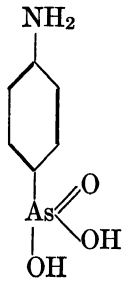
THORBURN—A Century of Alkaloids. *Journal of Chemical Education*, **2**, 886 (1925).

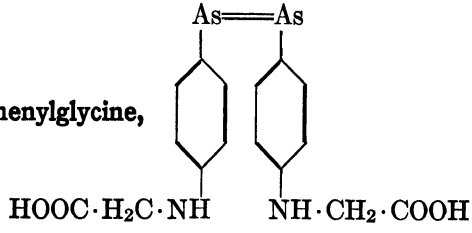
CHAPTER XXXIII

ARSENIC AND MERCURY COMPOUNDS OF THE AROMATIC SERIES

ARSENIC and mercury compounds, particularly the former, have found wide application in the treatment of diseases caused by protozoa (such as in syphilis). The organic combinations of these metals have an advantage over the inorganic compounds in that they are less toxic to mammals and more toxic to protozoan parasites.

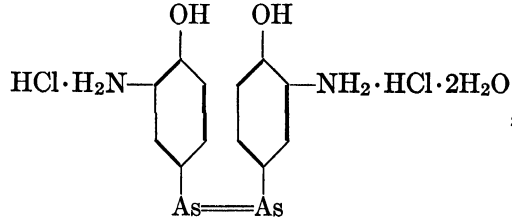
ARSENIC COMPOUNDS

Arsanilic acid,  , or *p*-aminophenylarsinic acid, may be regarded as being derived from arsenic acid, $AsO(OH)_3$, in which one OH group is replaced by aniline, and is prepared by combining aniline with arsenic acid. The monosodium salt is known as "atoxyl" and "soamin" and, though used at one time in the treatment of syphilis, relapsing fever, etc., it is now chiefly of interest as an intermediate in the preparation of salvarsan.

Arsenophenylglycine, 

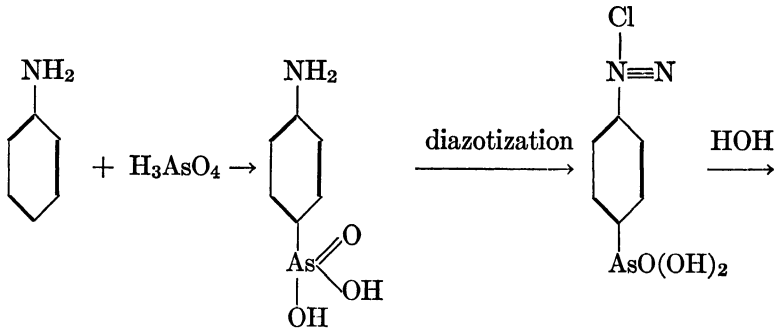
was introduced by Ehrlich as a substance even less toxic than atoxyl and of a higher trypanocidal power.

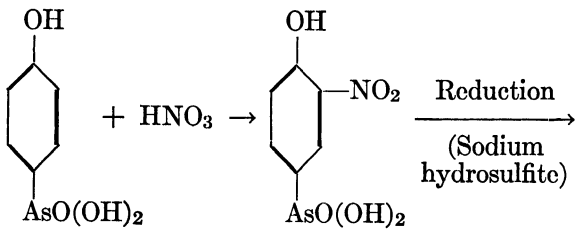
Salvarsan,



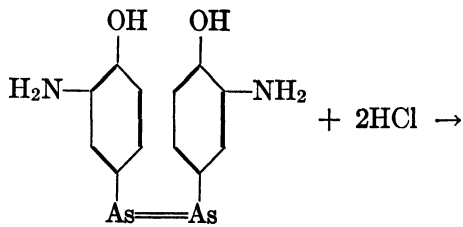
,

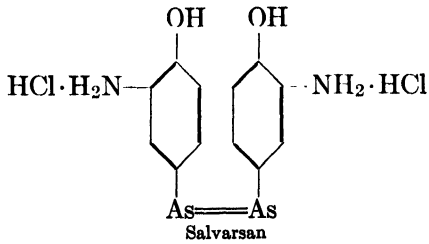
or 3,3′-diamino-4,4′-dihydroxyarsenobenzene dihydrochloride, known also as arsphenamine and "606," was first synthesized by Ehrlich and introduced by him for the treatment of syphilis. One method of preparing it is as follows:





p-Hydroxyphenylarsinic acid

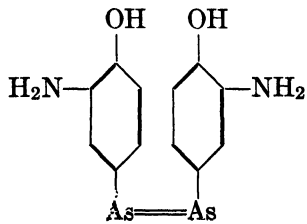




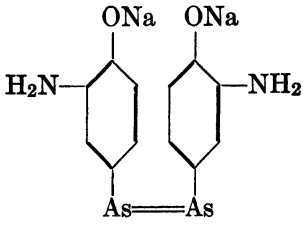
Salvarsan

While we cannot, in this book, enter into a prolonged discussion regarding the interesting question of the effect of chemical structure upon physiological action, Ehrlich's discovery of salvarsan deserves a few words of comment. When Ehrlich first began his celebrated research, he was aware of the fact that trypanosomes—a group of parasites—are killed by a number of dyes and a number of organic arsenic compounds, of which "atoxyl" was the most important. This compound contains pentavalent arsenic. The important discovery was made that although it would cure animals of trypanosomiasis, it had no toxic action upon trypanosomes *in vitro*. After many trials with many arsenical compounds, Ehrlich was in a position to formulate this general rule: that only compounds containing trivalent arsenic were effective in killing trypanosomes, and that the effectiveness of compounds containing pentavalent arsenic depended upon their reduction in the body to the trivalent form. The most efficient substances were found to be compounds containing trivalent arsenic joined to a benzene ring and containing also an amino group. This was later still further improved upon by the discovery that the most effective compounds were those containing an OH group in the *p*-position, an amino group, and arsenic—as in salvarsan itself.

Salvarsan, that is the dihydrochloride salt, is soluble, but it forms an acid solution, and is irritant and toxic. By the addition of two gram molecules of NaOH to one of salvarsan, the neutral base is obtained:

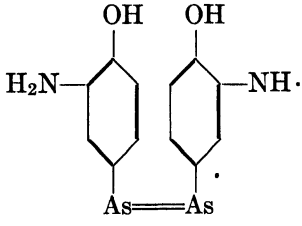


This is insoluble. Upon the further addition of two gram molecules of NaOH, the sodium salt is produced:



and this is soluble in water. It is the form of salvarsan generally used.

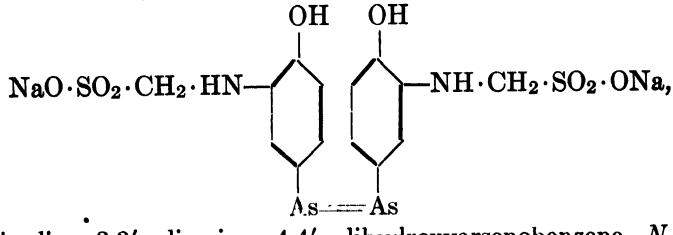
Neosalvarsan,



or sodium 3,3′-diamino-4,4′-dihydroxyarsenobenzene-*N*-methylenesulfinate, is also known as neoarsphenamine or "914" and was introduced by Ehrlich because of its greater solubility than salvarsan. It is prepared by combining salvarsan with sodium formaldehyde sulfoxylate ($HOCH_2 \cdot OSONa$).

Silver salvarsan and silver neosalvarsan have the same uses as salvarsan, but it is claimed that the presence of silver in the molecule raises the toxicity to parasites without increasing the toxicity to mammals. "Luargol," which contains antimony in addition to silver and arsenic, is another salvarsan derivative for which therapeutic claims have been made. "Galyl" is a salvarsan derivative containing phosphorus in addition to arsenic.

Sulfarsenol (Sulfarsphenamine),



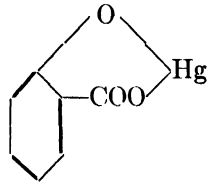
or disodium 3,3′-diamino-4,4′-dihydroxyarsenobenzene-*N*-di-

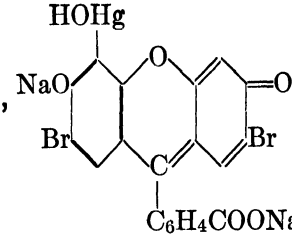
methylenesulfonate, is similar in its uses to neosalvarsan, but it is claimed that its solutions are more stable in the presence of air.

("Tryparsamide," , recently synthesized by Jacobs and Heidelberger, has been successfully applied in the treatment of human sleeping sickness.)

$(C_6H_5)_2As \cdot Cl$, diphenylchloroarsine, was used as a "sneeze" gas in the war.

Mercury Compounds

Mercuric salicylate,  is used as an antiseptic and antisyphilitic.

"Mercurochrome-220,"  , a mercurial derivative of fluorescein, has recently been introduced as a very active germicide and is gradually replacing tincture of iodine used for that purpose.

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CHAPTER XXXIV

A BRIEF OUTLINE FOR THE IDENTIFICATION OF ORGANIC COMPOUNDS

THE identification of an organic compound is not a simple matter. We have no methods quite as clearly defined as those of inorganic chemistry.

In the identification of an organic compound, the first step is to make certain that the compound is in a pure state—a fact which may very often be determined by ascertaining the boiling point or melting point, or by associating the compound with some other physical constant, such as specific gravity, etc.

In the next place, an elementary analysis should clearly indicate the elements present in that compound. Once this is determined, certain limits are immediately set as to the kind of compound it can be. For example, a compound which upon analysis shows the elements C, H and O only, cannot be an amine.

The classification of organic compounds and many of their most characteristic reactions are intimately bound up with the presence, within the molecules of these compounds, of various "groups," such as OH, NH_2, COOH, etc. In this chapter the attempt will be made to give a brief résumé of some of the reactions used for identifying such groups. Incidentally, this chapter ought to serve, to some extent, as a review.

Hydrocarbons.—Usually, these are colorless gases, liquids or solids, insoluble in water and soluble in alcohol and ether. (Where tests reveal that no elements other than carbon and hydrogen are present, the indications would immediately point to the presence of a hydrocarbon.) The paraffin hydrocarbons are very inert substances. The olefins add two bromine atoms to form saturated compounds, and the acetylenes generally respond to the

formation of metallic acetylides. The aromatic hydrocarbons may, as a rule, be nitrated, to form nitro derivatives:

$$\underset{\text{Benzene}}{C_6H_6} + HONO_2 \rightarrow \underset{\text{Nitrobenzene}}{C_6H_5 \cdot NO_2} + H_2O$$

Where the aromatic compounds contain a side-chain (as a CH_3 group, for example), this can be oxidized (by chromic acid or potassium permanganate or dilute nitric acid) to the carboxyl group. The hydrocarbons with condensed benzene nuclei (such as naphthalene, anthracene, etc.) are solids and may be identified by their oxidation products and, very often, by the fact that they form well-defined picrates (with picric acid) with definite melting points. The terpene hydrocarbons (such as pinene) present many difficulties when attempts are made to isolate them. Sometimes a number of physical properties (boiling point, density, specific rotation, etc.) prove helpful.

Halogen compounds.—The aliphatic compounds are almost non-ionizable and practically insoluble in water. The alkyl chlorides are lighter than water while the bromides and iodides are heavier. They are hydrolyzed to the corresponding alcohols; e.g.,

$$C_2H_5\boxed{Br + H}OH \xrightarrow{\text{alkali}} C_2H_5OH + HBr$$

With the aromatic halides, where the halogen is attached to the benzene nucleus, we get substances which are either liquids or solids, with a faint, agreeable odor, and insoluble in water. They are stable compounds and do not, for example, react with potassium hydroxide. They are utilized in the *Fittig* synthesis. The aromatic halogen compounds, with the halogen in the side-chain, behave similarly to the aliphatic halogen compounds and possess lachrymatory properties.

Alcohols.—As a rule, the monohydroxy alcohols are colorless liquids, neutral in reaction and some of them have a characteristic odor and taste. The solubility in water decreases with increasing molecular weight. The polyatomic alcohols are oily liquids or crystalline solids, soluble in water, and less soluble, or altogether insoluble in ether.

Primary alcohols when oxidized (with chromic acid, for example), give first an aldehyde and then an acid; secondary alcohols yield ketones; and tertiary alcohols break down into

carboxylic acids containing fewer carbon atoms than the original compound.

The OH group is very often identified by forming esters, either with acetyl chloride or acetic anhydride; e.g.,

$$R \cdot OH + (CH_3CO)_2O \rightarrow CH_3 \cdot COOR + CH_3COOH$$

Many of these esters have characteristic odors and by submitting them to a quantitative hydrolysis, it becomes possible to determine whether the original compound contains one or more OH groups. (For every OH group, one acetyl group is used.)

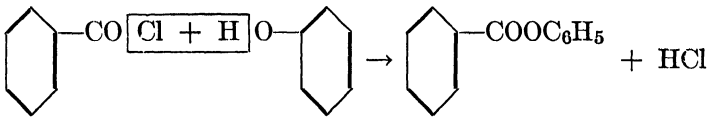
Phenols.—These are usually crystalline solids. (The solubility in water increasing with the number of OH groups present in the ring.) They are weak acids, being dissolved in alkalies forming salts.

Nearly all phenols give a precipitate of a polybromophenol when treated with bromine water; e.g.,

$$C_6H_5OH + 3Br_2 \rightarrow C_6H_2(OH)Br_3 + 3HBr$$

and yield deeply colored solutions with ferric chloride. Many give the *Liebermann* test (a deep blue or green color, when the phenol is dissolved in cold conc. H_2SO_4, and a little $NaNO_2$ added). (This test is also used for identifying the nitroso group.)

Phenols, like alcohols, combine with acetic anhydride to form esters; they also form esters with acyl chlorides and these can be identified by their melting or boiling points; e.g.,

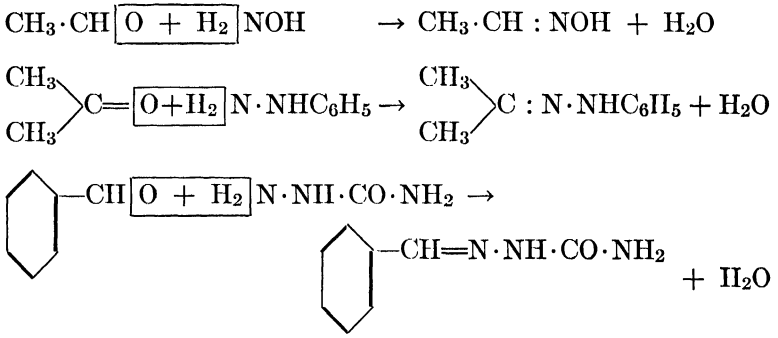


Ethers.—These are neutral, chemically inactive liquids. They are often identified by their boiling points, or by the following reaction:

$$R—O—R + 2HI \text{ heated} \rightarrow 2RI + H_2O$$

Aldehydes and Ketones.—The lower aldehydes are liquids possessing a characteristic odor, and, unlike ketones, reduce *Fehling's* or ammoniacal silver nitrate solution. For purposes of identification, aldehydes and ketones may be combined with hydroxylamine to form oximes, with phenylhydrazine to form phenyl-

hydrazones, and with semicarbazide (aminourea) to form semicarbazone; e.g.,



Benzaldehyde semicarbazone

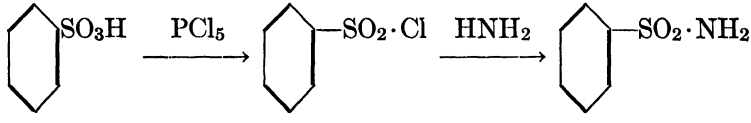
Most aldehydes give the *Schiff* test (restoring the pink color to a solution of magenta which has been decolorized with SO_2).

Carboxylic acids.—The lower aliphatic monobasic acids (as formic and acetic) are liquids, soluble in water, but the solubility decreases with increasing molecular weight. The higher members (like palmitic and stearic) are solids, insoluble in water. The aliphatic polybasic acids (like oxalic and succinic) are solids, soluble in water. Many of the aromatic acids (like benzoic and *o*-toluic) are not very soluble in cold, but more so in hot water.

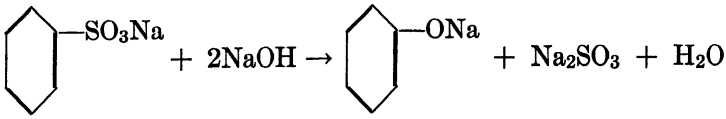
The acidity of the substance may be determined by titrating with standard alkali. The conversion of the acid to the corresponding ester (with alcohol and a dehydrating agent) and the elimination of the carboxyl group (in the form of CO_2) by heating with soda lime, are often of help in identifying the acid. Often the acid is converted to its acyl halide; e.g.,

$$C_2H_5 \cdot COOH + PCl_5 \rightarrow C_2H_5 \cdot COCl + POCl_3 + HCl$$

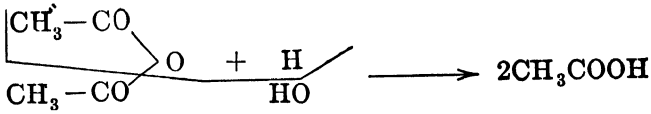
Aromatic sulfonic acids.—As a rule, these are soluble substances, difficult to crystallize. For purposes of identification, the corresponding amide is prepared by first forming the sulfonchloride with PCl_5 and then converting the latter to the amide—with definite m.p.—:



Fusion with alkali to form the corresponding phenol is also sometimes employed:



Acid anhydrides.—As a rule, the aliphatic compounds are colorless liquids, insoluble in water and soluble in alcohol and ether. The aromatic compounds are solid. They are usually identified by hydrolyzing them to the corresponding acids or salts; e.g.,



Acyl halides.—These are pungent-smelling liquids, easily convertible (hydrolysis) into the corresponding acids; e.g.,

$$CH_3CO\boxed{Cl + H}OH \rightarrow CH_3COOH + HCl$$

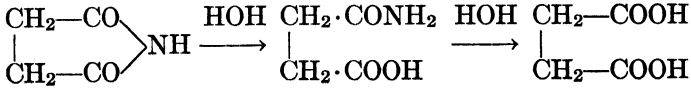
Acid amides.—These are, as a rule, well defined, crystalline substances. They can be hydrolyzed with boiling alkali to the corresponding acids (salts); e.g.,

$$CH_3 \cdot CO\boxed{NH_2 + H}OH \xrightarrow{\text{alkali}} CH_3COOH + NH_3$$

or

$$C_6H_5 \cdot CONH_2 + HONO \longrightarrow C_6H_5 \cdot COOH + N_2 + H_2O$$

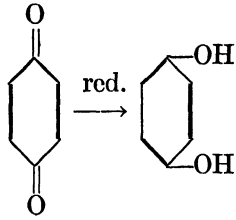
Acid imides, like the amides, are hydrolyzed by boiling with alkalies:



Esters.—These are volatile compounds, insoluble in water, with agreeable odors. The esters may be hydrolyzed with alkali; e.g.,

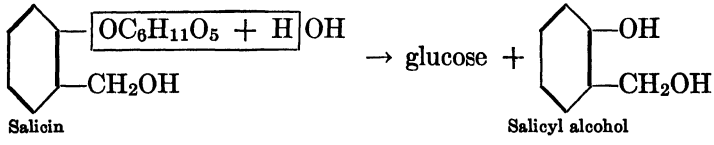
$$CH_3COO\boxed{C_2H_5 + HO}H \rightarrow CH_3COOH + C_2H_5OH$$

Quinones.—These are colored compounds (yellow or red). The *p*-benzoquinone is volatile with steam. As a rule, they can be reduced;



Carbohydrates. These are solids soluble in water (except the polysaccharides, such as starch, etc.). Among the polysaccharides, starch gives a blue color with iodine, and glycogen and the dextrins, a violet to a violet-red. The sugars (lactose, maltose, galactose, levulose, glucose) reduce *Fehling's* solution and form osazones with phenylhydrazine. Sucrose or cane sugar is a notable exception. They are optically active.

Glucosides.—On hydrolysis, these yield glucose, in addition to one or more substances; e.g.,



Salicin Salicyl alcohol

Amines.—The lower members of the aliphatic amines (like methylamine) are flammable gases, with an odor resembling ammonia; the higher members (like butylamine) are liquids. With acids they form salts, soluble in water and in alcohol. The aromatic amines are either liquids (like aniline) or solids (like diphenylamine).

With aliphatic amines, nitrous acid converts the primary amine into the corresponding alcohol:

$$R \cdot NH_2 + HONO \rightarrow R \cdot OH + N_2 + H_2O$$

the secondary amine is converted into the yellow nitrosoamine:

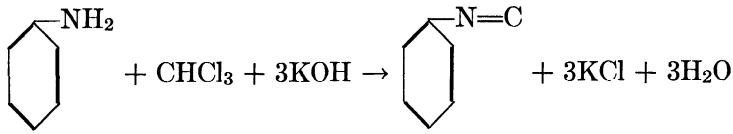
$$R_2NH + HONO \rightarrow R_2N \cdot NO + H_2O$$

and the tertiary amine is not acted upon.

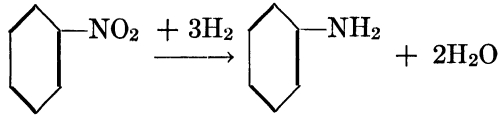
With the aromatic amines, the manner in which nitrous acid behaves will be dependent upon whether the NH_2 group is in the nucleus or in the side-chain. If the amino group is in the nucleus,

diazonium salts are formed (in the cold) which are converted to phenols on heating; if the NH_2 group is in the side-chain, then the compound behaves like an aliphatic amine. With secondary aromatic amines, nitrous acid yields nitroso derivatives similar to those obtained with aliphatic secondary amines. A tertiary amine such as dimethylaniline reacts with HONO to produce *p*-nitrosodimethylaniline.

The primary amines, whether aromatic or aliphatic, give the carbylamine reaction (the isocyanide is formed which has a disgusting odor); e.g.,



Nitro compounds.—Only the aromatic nitro compounds are of importance. Usually, these are oily liquids or solids, insoluble in water and dilute HCl. They are identified by being reduced to the corresponding amines; e.g.,



Cyanides and Isocyanides.—The cyanides are liquids or solids with an agreeable odor. They are hydrolyzed to the corresponding acids; e.g.,

$$CH_3CN + 2H_2O \rightarrow CH_3COOH + NH_3$$

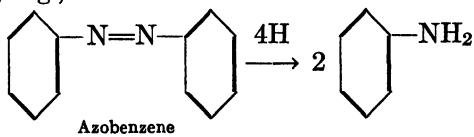
and are reduced to the primary amines; e.g.,

$$CH_3 \cdot CN + 4H \rightarrow CH_3 \cdot CH_2 \cdot NH_2$$

The isocyanides or carbylamines possess a disgusting odor. On hydrolysis, they yield formic acid and an amine; e.g.

$$CH_3 \cdot N{=}C + 2H_2O \rightarrow CH_3 \cdot NH_2 + H \cdot COOH$$

Azo compounds.—These are colored solids and include a large class of important dyes. They yield, on reduction, amino compounds; e.g.,



Azobenzene

Purines, of which uric acid and caffeine are examples, are not easily identified. Most of them give the *murexide* test (evaporate the substance on a water bath to dryness with conc. HNO_3, cool and make alkaline with ammonia or NaOH; a violet or red color is produced).

Alkaloids.—These are mostly solids (nicotine, and coniine are exceptions), soluble in alcohol, somewhat less soluble in ether, chloroform and benzene, and usually insoluble in water. Most of them are levorotatory. They dissolve in acids, forming salts, and are reprecipitated by alkalies. Alkaloids are not easily identified, but as a class they are precipitated by the "alkaloidal reagents," such as tungstic, phosphomolybdic, tannic and picric acids, potassium-mercuric iodide, etc. Many of them are identified by color reactions with H_2SO_4 and an oxidizing agent.

Sulfur compounds.—The sulfonic acids have already been treated. The only others that need be mentioned here are the mercaptans (e.g., C_2H_5SH) and the sulfides (e.g., $(C_2H_5)_2S$). Both types of compounds have very disagreeable odors.

Terpenes and allied compounds.—These substances are flammable, mostly volatile, possess characteristic odors and are insoluble in water, but soluble in many organic solvents. They do not belong to the aliphatic or to the aromatic series of compounds and are, as a rule, complex in structure. Certain derivatives are usually prepared in order to identify them.

Proteins.—These are complex substances consisting, in the main, of linkages of amino acids. They are identified by a number of color tests. With the *Millon's* reagent (mercuric nitrate containing nitrous acid) most of them give a red color or precipitate. When heated with HNO_3 a yellow color is developed and this is changed to an orange on the addition of ammonia (*xanthoproteic* reaction). When mixed with a strong solution of KOH and a drop or two of $CuSO_4$ is added, a violet color is obtained (biuret reaction).

General Solubilities of Classes of Organic Compounds

General Rule.—A solvent dissolves those compounds which are chemically closely allied to it.

Hydrocarbons and their halogen substitution products are either insoluble or only very slightly soluble in water. They dissolve in alcohol, ether, benzene, etc.

The solubility of a compound in water increases with the

increase of oxygen content; especially is this true when the oxygen atoms are combined with hydrogen as in —OH groups.

The homologues of low molecular weight of the aliphatic series, such as alcohols, aldehydes, ketones, amines, and acids, are soluble in water; but the solubilities decrease with increasing molecular weight.

Alkali salts of acids, salts of amines, sugars, polybasic acids, hydroxy acids, sulfonic acids, and polyhydroxy alcohols are soluble in water.

Esters are very slightly soluble in water, but soluble in alcohol and ether.

Ether dissolves very many organic compounds. (Not salts of acids.) It is slightly soluble in water and is used for extracting products from aqueous solutions.

Acid anhydrides are soluble in alcohol and ether.

Fats and oils are insoluble in water, but readily soluble in benzene, ether, chloroform, etc.

Nitro compounds are insoluble in water but soluble in alcohol and ether.

The presence of a sulfonic acid group increases the solubility of an organic compound in water.

The hydroxy derivatives of aromatic hydrocarbons are soluble in water, but more so in alcohol and ether.

The *p*-compounds are less soluble in the various solvents than the isomeric *o*- and *m*- compounds.

Alkaloids are usually insoluble in water, but soluble in alcohol, chloroform, benzene, etc.

Homologues are mutually soluble.

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KINGSCOTT AND KNIGHT—Methods of Quantitative Organic Analysis.

MULLIKEN—A Method for the Identification of Pure Organic Compounds.

KAMM—Qualitative Organic Analysis.

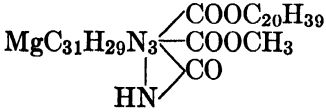
CHAPTER XXXV

PLANT AND ANIMAL PIGMENT

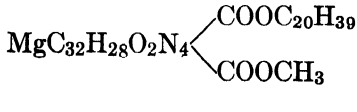
Chlorophyll, Carotin, Xanthophyll, Flavones, Anthocyanins, Hemoglobin and Bile Pigments

Chlorophyll.—The chemistry of chlorophyll, the green pigment in plants, has been worked out by Willstätter and his pupils. Without going into any details, some of the essential points as to its structure and general characteristics may be given.

Chlorophyll is really a mixture of two substances:



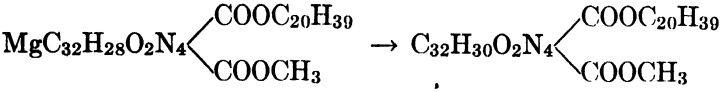
Chlorophyll *a*



Chlorophyll *b*

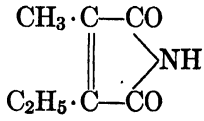
Both contain the element magnesium in organic combination, and both are esters of a tribasic acid, chlorophyllin, combined with phytol, $C_{20}H_{39}OH$ (an unsaturated alcohol) and methanol.

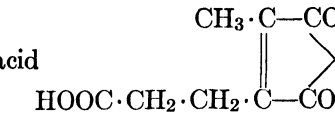
With alkali the ester groups in chlorophyll are hydrolyzed, giving the corresponding carboxylic acids (chlorophyllins). The COOH groups can next be removed by heating with alkali. Acids (oxalic or HCl) remove the magnesium from the molecule; e.g.,



Chlorophyll *b* → Pheophytin *b*

When chlorophyll *a* or chlorophyll *b* is oxidized, we get, among other products, methyl ethyl maleinimide

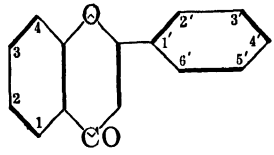


and hematinic acid  , products which are formed in the oxidation of hemoglobin.

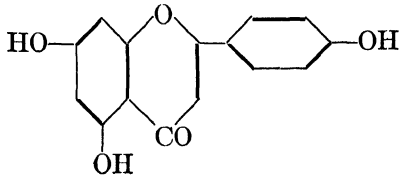
Carotin is associated with chlorophyll in the green leaf. It is a hydrocarbon with the formula $C_{40}H_{56}$.

Xanthophyll, also associated with chlorophyll (and carotin), has the formula $C_{40}H_{56}O_2$. By oxidation, xanthophyll may be obtained from carotin, and *vice versa* by reduction, xanthophyll yields carotin. It is assumed that both these pigments play an important rôle in plant respiration. (Pigments from the egg yolk and blood serum have been isolated which are identical with carotin and xanthophyll.)

Flavones.—A number of yellow substances derived from flavone occur in plants



Some of these are chrysin (1, 3-dihydroxyflavone) which occurs in several varieties of poplar; apigenin (1, 3, 4′-trihydroxyflavone)

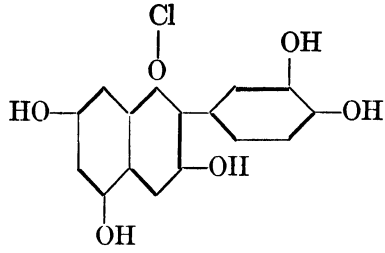


found in parsley and celery in the form of glucosides; etc.

Anthocyanins are red, violet and blue pigments present in flowers, fruits, leaves of plants, etc., in the form of glucosides. By hydrolysis, the anthocyanins are converted into glucose (or other monosaccharide) and anthocyanidins.

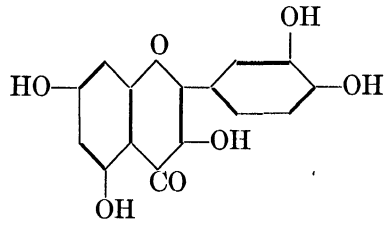
It is believed that these anthocyanins are reduction products of flavones (and *vice versa*, that flavones are oxidation products of anthocyanins), and that changes from one to the other are brought about in the plant by oxidizing and reducing enzymes.

The anthocyanin in the cornflower and the rose is known as "cyanin," and this, on hydrolysis, yields two molecules of glucose and cyanidin (an anthocyanidin):



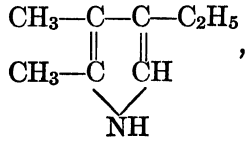
Cyanidin

This cyanidin, Willstätter has also obtained by reducing quercitin, a hydroxyflavone:



Quercitin or 1, 3, 3′, 4′-tetrahydroxyflavonol

Hemoglobin, the red pigment in blood, is a combination of hematin, an iron-containing substance, and globin, a protein belonging to the group of histones. It forms compounds with oxygen and carbon monoxide, forming oxyhemoglobin and carboxy-hemoglobin, the latter being the more stable. "Hemin" (or "hematin hydrochloride") is obtained from dried blood by boiling with glacial acetic acid. Very characteristic dark plates and prisms are obtained, which may be identified under the microscope. This method is made use of for the detection of blood. When hemoglobin is treated with H_2SO_4, the iron is set free as ferrous sulfate and hemotoporphyrin, an iron-free hematin, is obtained. From this substance, hemopyrrole,



may be obtained—a substance, which is also a decomposition product obtained from chlorophyll.

Bile pigments (bilirubin, biliverdin, bilicyanin, etc.) are the substances which are responsible for the characteristic color of bile. They are formed in the liver and originate from the hemoglobin of the blood. Bilirubin, $C_{32}H_{36}N_4O_6$, a reddish-brown pigment, found in abundance in carnivora, is oxidized (even by the oxygen of the air) to biliverdin, $C_{32}H_{36}N_4O_8$, a green pigment, found largely in the bile of herbivora. (Hydrobilirubin, a reduced product of bilirubin, is probably isomeric with stercobilin, the pigment of the feces, and with urobilin, a pigment in urine.) The *Gmelin's* test for bile pigments—the play of colors obtained when conc. HNO_3 is added to bile—is dependent upon the production of various colored oxidation products of the type of bilirubin, biliverdin, etc.

Melanins.—This group includes several different varieties of amorphous black or brown pigments which are insoluble in water, alcohol, ether, chloroform, dilute acids, and which occur in skin, hair, etc. They are said to be derived from the amino acids tyrosine (p. 148) and tryptophan (p. 312).

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WILLSTÄTTER—Chlorophyll. *Journal of the American Chemical Society*, **37**, 323 (1915).

CHAPTER XXXVI

ENZYMES, VITAMINS, HORMONES

Enzymes

These are catalytic substances produced as a result of cellular activity. They are responsible for many of the chemical changes which occur in the body.

So far enzymes have not been isolated in the pure condition,* but they can be classified because they are "specific" in their action; that is to say, ptyalin, the enzyme found in saliva, will act on starch and one or two other carbohydrates, but not on proteins, whereas pepsin, the enzyme found in the gastric juice of the stomach, will act on proteins but not on carbohydrates.

A few of the common enzymes, giving their distribution, the substances acted upon ("substrates") and the end products formed, are given on the following page.

The ending *ase* has been adopted to denote an enzyme; for example, sucr*ase* is an enzyme, its name also suggesting that it acts on the sugar sucrose. However, old names, such as pepsin, trypsin and rennin, still remain.

Enzymes are soluble in water, dilute salt solutions, dilute alcohol and glycerol. Like the proteins, they are precipitated by ammonium sulfate and concentrated alcohol. They are very easily adsorbed by various substances and show colloidal properties. They are, as a rule, destroyed at the temperature of boiling water, and their action is inhibited, but not destroyed at 0 °C. The enzymes act best (or show an optimum activity) around 37–45° C.

Enzymes are extremely susceptible to changes in hydrogen ion concentrations, and for each enzyme there is a particular p_H at which its reactivity is at a maximum ("optimum reaction").

*Recently Nothrop has isolated pepsin and trypsin in what appear to be in pure forms, and the same may be said of Sumner's urease.

For example, the p_H of trypsin is 8.0, that of pepsin 1.4, and of ptyalin 6.7. Since the neutral point is p_H 7, this means that trypsin acts best in an alkaline solution, whereas pepsin acts best in a decidedly acid solution, and ptyalin is most reactive in a slightly acid medium.

Name and Class	Distribution	Substrate	End-products
Ptyalin	Saliva	Starch, dextrin, etc.	Maltose
Lactase	Intestinal juice and mucosa	Lactose	Glucose and galactose
Maltase	Blood serum, liver, saliva, pancreatic and intestinal juices and lymph	Maltose	Glucose
Sucrase or invertase	Intestinal juice and mucosa	Sucrose	Glucose and fructose
Zymase	Yeast	Sugars	Alcohol, CO_2, etc.
Urease	Micrococcus ureae, soy bean, etc.	Urea	Carbon dioxide and ammonia
Steapsin or lipase	Pancreatic juice	Fats	Fatty acid and glycerol
Catalase	Plant and animal tissues	Hydrogen peroxide	Oxygen or oxidation products
Peroxidase	Plant and animal tissues	Organic peroxides	Active oxygen or oxidation products
Erepsin	Intestinal mucosa and juice, other tissues	Peptids, also peptones and casein	Simpler peptids and amino acids
Rennin	Gastric juice	Casein	Paracasein
Thrombin	Blood	Fibrinogen	Fibrin
Trypsin	Pancreatic juice	Proteins	Proteoses, peptones, peptids, amino acids
Pepsin	Gastric juice	Proteins	Proteoses, peptones, and peptids

VITAMINS

It has recently been found that besides proteins, fats, carbohydrates and mineral salts, there are other, as yet, ill-defined substances which, though needed in but minute quantities, are essential to life. These substances are known as *vitamins*. At least five vitamins have been detected. For purposes of identification, the vitamins are often called A, B, C, D and E. The presence of all five of these vitamins is essential to well-being. As a matter of fact, very few foods contain all five. Milk is one of the rare exceptions, but even then the quantity of vitamin C which it contains is dangerously small. It is only by eating a variety of foods that we assure ourselves a liberal allowance of all five types of vitamins.

Vitamin A.—This is present in abundance in milk, butter, egg-yolk, cod-liver oil, and to a lesser extent, in beef fat and in many vegetable foods (lettuce, spinach, cabbage, carrots, potatoes, etc.). Lard and vegetable oils, such as olive oil are practically devoid of it. Cereals in general (wheat, rye, barley, etc.) contain little. In a general way, the statement may be made that this vitamin is present in green leaves and in the embryos of many seeds. Recently carotin, $C_{40}H_{56}$, has been shown to be transformed into vitamin A in the liver.

Vitamin B.—This is more abundant than either of the other two. In fact, nearly all natural foods contain some of it. Yeast is particularly rich in this vitamin; so are milk and orange juice. The cereals contain it but only the outer layers, so that in patent flour there is much less of this vitamin than in whole wheat flour. Vitamin B really consists of two vitamins—vitamin B_1(F), the anti-neuritic vitamin; and vitamin B_2(G) the anti-pellagra vitamin.

Vitamin C.—Most fresh fruits and fresh vegetables contain this vitamin. The emphasis is advisedly put on fresh material. The orange and the tomato are particularly good examples.

Vitamin D is present in greatest abundance in cod-liver oil and in much smaller quantity in milk. It is apparently produced when some foods are irradiated with ultra-violet light. Vitamin D is apparently synthesized when ergosterol is irradiated.

Vitamin E is particularly present in the wheat germ.

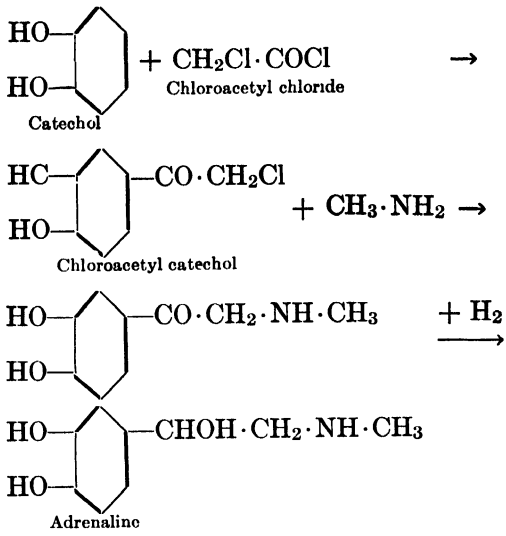
Effect of heat and oxidation.—All five vitamins are more or less susceptible to heat, so that any process involving this operation—cooking or canning—is apt to destroy, or greatly lessen, the efficacy of the vitamins. The general experience has been that heating for a long time at a comparatively low temperature is even more harmful than heating for a short time at a comparatively high temperature. Of the five, the vitamin C seems the most susceptible to heat. The activity of a number of the vitamins is lessened by exposure to air or oxidation. This is particularly true of vitamins A and C.

Diseases due to lack of vitamins.—Four diseases have been identified as being due to vitamin deficiency. One of them is beri-beri, involving a general paralysis of the system and is due to a lack of vitamin B_1(F); a second is the vitamin the absence of which gives rise to pellagra—B_2(G); another is scurvy, involving choppy gums and loose teeth and is due to lack of vitamin C; the fourth is xerophthalmia, and eye disease, involving a lack of vitamin A; and the fifth is rickets, a disease involving faulty bone construction, due to lack of vitamin D. Vitamin E is concerned with the process of reproduction.

Hormones

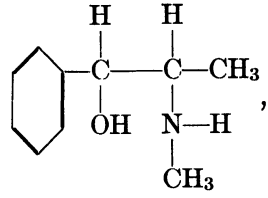
In the body there are various ductless glands (glands without tubes), such as the thyroid, the pituitary, the adrenals, etc., which manufacture specific substances that find their way into the blood stream and influence other organs of the body. The substances so manufactured are called "hormones" (from the Greek "to excite") or "chemical messengers." These hormones profoundly influence various activities of the body. In at least two instances hormones have been isolated in the pure condition.

Adrenaline.—One of the hormones of the adrenal glands may be isolated from the latter by first treating concentrated adrenal extracts with alcohol, lead acetate, etc.; then precipitating the active substance by the addition of concentrated ammonia. The precipitate is purified by repeatedly dissolving in acid and reprecipitating with ammonia. The adrenaline may be synthesized by the following reactions:



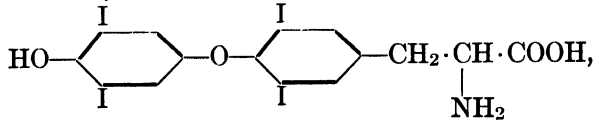
Adrenaline is most frequently used to constrict the blood vessels and thereby increase the blood pressure. It is by far the most powerful known hemostatic (checks bleeding).

Recently an extract from the cortex of the adrenal gland has been obtained which cures a rare ailment known as "Addison's disease."

Ephedrine.— 

, α-hydroxy—β-methyl-aminopropylbenzene, or its hydrochloride, has uses similar to adrenaline.

Thyroxine is the hormone in the thyroid gland. Kendall has isolated it from the gland. Harington has determined its formula to be



β-[3, 5-diiodo-4-(3′, 5′-diiodo-4′-hydroxyphenoxy) phenyl-α-amino-propionic acid, and he has also succeeded in synthesizing the substance.

It is administered in diseases involving a deficient secretion of the thyroid gland.

Insulin.—This is the hormone present in the pancreas, and its absence, as Banting and Macleod have shown, gives rise to diabetes. Abel has recently obtained insulin in crystalline form, and while he has not yet determined its formula, he and Funk find that it contains a high percentage of sulfur. An extract containing insulin is now universally used in the treatment of diabetes. The extract has to be injected.

Pituitrin, an impure extract of the pituitary body, which contains the hormone, is used to promote uterine contractions and to stimulate peristalsis.

The anterior part of the pituitary has recently been shown to consist of at least two hormones, one dealing with the growth process and the other having an accelerating effect on the sex process.

Secretin represents a hormone present in the intestinal mucosa which plays an important part in controlling the flow of pancreatic juice into the small intestine, and thereby aids in digestion.

A **parathyroid hormone** has recently been obtained by Collip which seems to play an important part in regulating the calcium metabolism of the body.

Doisy has obtained an active extract (hormone) from the ovaries; and active extracts have also been obtained from the male glands.

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Harington and Barger—Thyroxin III.—Constitution and Synthesis of Thyroxin. *Biochemical Journal*, **21**, 169 (1927).
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CHAPTER XXXVII

NOMENCLATURE OF ORGANIC COMPOUNDS

THE number of organic compounds is in excess of 225,000, and the naming of such compounds presents no little difficulty. Some of the methods adopted for naming organic compounds have been referred to in the various chapters of the book. In the present chapter, the methods adopted will be briefly summarized. In addition, the naming of various groups, and the principles involved in the naming of a number of somewhat complex compounds, will be given. **It is hoped that such an outline will prove of value to the student of chemistry who is about to begin more advanced work in organic chemistry, or in one of its many applications, and who will have occasion to consult the standard reference books and the current literature.**

It would be well, at the outset, for the student to review the chart at the beginning of the book, which gives type formulas. From this chart, as well as from various chapters in the book, we may deduce the following rules:

A word ending in	*Indicates*
-ane	paraffin
-ene or *-ylene*	olefin
-ine	acetylene
-diene	diolefin
-diine	diacetylene
-ene	aromatic hydrocarbon (as a rule)
-ol	hydroxyl group
-diol	two hydroxyl groups
-al	aldehyde
-one	ketone (or quinone)
-ic (sometimes *-oic*)	acid
-ase	enzyme
-ose	sugars
-ate, -ite	salts, esters

In naming[1] a compound so as to indicate that oxygen is replaced

[1] These suggestions are taken from the publications of the *American Chemical Society.*

by sulfur, the prefix *thio* is used; e.g., HCNS, *thio*cyanic acid; $CS(NH_2)_2$, *thio*urea.

Hydroxyl derivatives of hydrocarbons end in *-ol*, as glycer*ol*, resorcin*ol*, pyrocatech*ol*.

The names of the groups NH_2, NHR, NR_2, NH or NR end in *-ido* only when they are substituents in an acid group, otherwise in *-ino*; e.g., $CH_3 \cdot C(=NH)(OC_2H_5)$, ethyl im*ido*acetate; $CH_2(NH_2) \cdot CH_2 \cdot COOH$, β-am*ino*propionic acid.

Hydroxy is used to designate the hydroxyl group; e.g., $CH_2(OH) \cdot COOH$, *hydroxy*acetic acid.

Salts of organic bases with hydrochloric acid are called *hydrochlorides;* e.g., $C_6H_5NH_2 \cdot HCl$, aniline *hydrochloride.*

Compounds which are not alcohols, but have received names ending in *-ol* are spelled *-ole*, as anis*ole*, ind*ole*. C_6H_6 is called *benzene* (not benzol), C_7H_8 *toluene*, etc.

The endings *-ine* are used for basic substances, and *-in* for glycerides, glucosides, bitter principles, proteins, etc.; e.g., anil*ine*, pur*ine*, morph*ine*; but gelat*in*, palmit*in*, amygdal*in*, album*in*, prot*ein*.

In naming organic compounds the connective *o* is used in such names of substituent radicals as *amino-*, *bromo-*, *cyano-*, and *iodo-*; e.g., bromobenzene, chloroacetic acid, nitroaniline.

Acid radicals, such as C_6H_5CO, end in *-yl*, and their compounds with halogens, as C_6H_5COCl, are called *chlorides*, *bromides*, etc.; e.g., benzoyl *chloride.*

The names butane, pentane, etc., are used only for the normal hydrocarbons, with the prefix *cyclo-*, for saturated cyclic hydrocarbons.

To designate ortho-, meta-, para-, dextro-, levo-, racemic, symmetrical, secondary, tertiary and meso, we use *o-*, *m-*, *p-*, *d-*, *l-*, *dl-*, *sym-*, *sec-*, *tert-* and *meso-*, respectively.

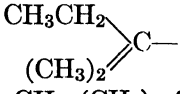
me, *et*, etc., are abbreviations for methyl, ethyl, etc., groups.

Numerals precede the part of the name to which they refer; e.g., 2-bromo-3-methylbenzenesulfonic acid.

For complex cyclic compounds requiring fixed numberings, the student is referred to Richter's Lexikon der Kohlenstoff-Verbindungen, Vol. 1.

The following list gives the names of a number of important organic radicals: [1]

acenaphthenyl $C_{12}H_9$—
acetamido CH_3CONH—
acetenyl = ethinyl
acetimido $CH_3C(:NH)$—
acetonyl CH_3COCH_2—
acetoxy $CH_3CO \cdot O$—
acetyl CH_3CO—
acetylene = $CH \cdot CH$=
acridyl $C_{13}H_8N$—
acrylyl $CH_2 : CHCO$—
adipyl —$OC \cdot (CH_2)_4 \cdot CO$—
alanyl $CH_3 \cdot CHNH_2 \cdot CO$—
alkoxy RO—(*any alkyl radical attached by oxygen*)
allyl $CH_2 : CH \cdot CH_2$—
β-allyl = isopropenyl
amidoxalyl $H_2N \cdot CO \cdot CO$—
amino (amido) H_2N—
amoxy $CH_3 \cdot (CH_2)_4 \cdot O$—
amyl $CH_3 \cdot (CH_2)_4$— or C_5H_{11}

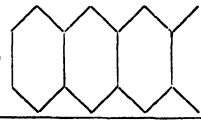
tert-amyl 

amylidene $CH_3 \cdot (CH_2)_3 \cdot CH$=
anilino C_6H_5NH—
anisal *p*-$CH_3O \cdot C_6H_4 \cdot CH$=
anisoyl *p*-$CH_3O \cdot C_6H_4 \cdot CO$—
anisyl (*o*, *m* or *p*) $CH_3O \cdot C_6H_4$—
anisylidene = anisal

anthranilo *o*-C_6H_4

anthranoyl *o*-$H_2N \cdot C_6H_4 \cdot CO$—
anthraquinonyl (*from anthraquinone, 2 isomers*)
anthryl (*from anthracene, 5 isomers*)

[1] The list is taken from one prepared by the editors of *Chemical Abstracts* or the "Decennial Index" and brought up to date in subsequent editions.

anthrylene (*from anthracene, 11 isomers*) 

antipyryl (*from antipyrine*) $OC^{5}\cdot N^{1}(C_6H_5)\cdot N^{2}(CH_3)\cdot C^{3}(CH_3):C^{4}—$

arseno —As=As—

arsino (*from arsinic acid*) (OH)OAs=

arsinoso O : As—

arsono (*from arsonic acid*) $(HO)_2OAs—$

arsyl $H_2As—$

arsylene HAs:

asaryl 2,4,5-$(CH_3O)_3\cdot C_6H_2—$

asparagyl $H_2N\cdot CO\cdot CH_2\cdot CHNH_2\cdot CO—$

aspartyl $—CO\cdot CH_2\cdot CHNH_2\cdot CO—$

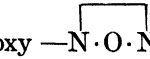
auro Au—

azido = triazo

azimino (azimido) —N : N·NH—

azino =N·N=

azo —N : N—

azoxy 

benzal $C_6H_5\cdot CH=$

benzamido $C_6H_5\cdot CONH—$

benzenyl $C_6H_5\cdot C\equiv$

benzilyl $Ph_2C(OH)CO—$

benzidino (*from benzidine*) $H_2N\cdot C_6H_4\cdot C_6H_4\cdot NH—$

benzimido $C_6H_5\cdot C(:NH)—$

benzohydryl $(C_6H_5)_2CH—$

benzohydrylidene = diphenylmethylene

benzoxy $C_6H_5\cdot COO—$

benzoyl $C_6H_5\cdot CO—$

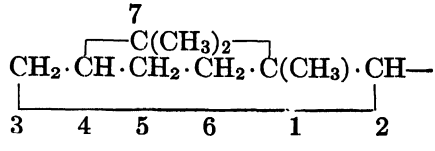
benzoylene $—C_6H_4\cdot CO—$

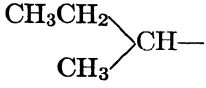
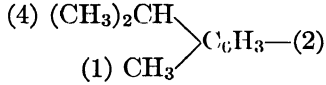
benzyl $C_6H_5\cdot CH_2—$

benzylidene = benzal

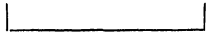
biphenylene $—C_6H_4\cdot C_6H_4—$

biphenylenedisazo $—N:N\cdot C_6H_4\cdot C_6H_4\cdot N:N—$

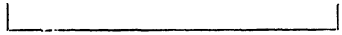
bornyl (*from borneol*) 

boryl O : B—
bromo Br—
Δ^1-butenyl $CH_3CH_2CH : CH$—
Δ^2-butenyl $CH_3 \cdot CH : CH \cdot CH_2$—
Δ^3-butenyl $CH_2 : CH \cdot (CH_2)_2$—
butoxy $CH_3 \cdot (CH_2)_3 \cdot O$—
butyl $CH_3(CH_2)_3$—
sec-butyl 
tert-butyl $(CH_3)_3C$—
butylene $—CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2—$ [1,4-form]
butylidene $CH_3 \cdot (CH_2)_2 \cdot CH=$
butyryl $CH_3 \cdot (CH_2)_2 \cdot CO$—
camphanyl (*from camphane*) $C_{10}H_{17}$
camphoroyl (*from camphoric acid*) $C_8H_{14}(CO)_2$:
camphoryl (*from camphor*) $C_{10}H_{15}O$—
camphorylidene (*from camphor*) $C_{10}H_{14}O$:
carbamido $H_2N \cdot CO \cdot NH$—
carbamyl $H_2N \cdot CO$—
carbanilino = phenylcarbamyl
carbazyl (*from carbazole, 5 isomers*) $C_{12}H_8N$—
carbethoxy $C_2H_5O \cdot OC$—
carbomethoxy $CH_3O \cdot OC$—
carbonyl OC=
carbonyldioxy $—O \cdot CO \cdot O—$
carboxy $HO \cdot OC$—
carvacryl 
cetyl $CH_3(CH_2)_{14}CH_2$—
chloro Cl—
chloromercuri ClHg—
cinnamal $C_6H_5 \cdot CH : CH \cdot CH=$
cinnamenyl = styryl
cinnamyl $C_6H_5CH : CHCO$—
cinnamylidene = cinnamal
cresotyl (*from cresotic acid*) 2, 3-$(OH)(CH_3)C_6H_3CO$—
cresoxy = toloxy
cresyl (10 *isomers*) (*o*, *m* or *p*) $(HO)(CH_3) \cdot C_6H_3$—
cresylene = tolylene
crotonyl $CH_3CH : CHCO$—

cumal p-$(CH_3)_2CH \cdot C_6H_4 \cdot CH=$
cumenyl $(CH_3)_2 \cdot CH \cdot C_6H_4-$
cuminal = cumal
cyano NC—
cyclobutyl $CH_2 \cdot CH_2 \cdot CH_2 \cdot CH-$

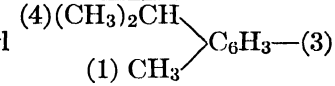


cyclohexenyl (*from cyclohexene*, 3 *isomers*) C_6H_9-
cyclohexyl (*from cyclohexane*) $C_6H_{11}-$
cyclohexylidene $CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot C=$

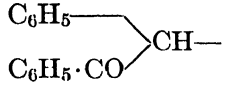


cyclopentenyl (*from cyclopentene*) C_5H_7-
cyclopentyl (*from cyclopentane*) C_5H_9-
cyclopropyl $CH_2 \cdot CH_2 \cdot CH-$

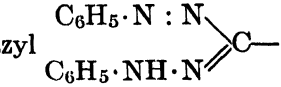
cymyl



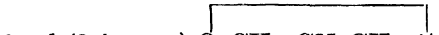
desyl



diazo —N : N—
diazoamino = azimino
diazoöxy —N(: O) : N—
epoxy —O— (*to different atoms already united in some other way*)
ethene = ethylene
ethenyl $CH_3C\equiv$
ethinyl CH ⋮ C—
ethoxalyl $C_2H_5O \cdot OC \cdot CO-$
ethoxy C_2H_5O-
ethyl CH_3CH_2-
ethylene $-CH_2 \cdot CH_2-$
ethylenedioxy $-O \cdot (CH_2)_2 \cdot O-$
ethylidene $CH_3CH=$
fenchyl (*from fenchyl alcohol*) $C_{10}H_{17}-$
fluoro F—
fluorylidene (*from fluorene*) $C_{13}H_8$:
fluoryl (*from fluorene*, 5 *isomers*) $C_{13}H_9-$
formamido HCONH—
formazyl



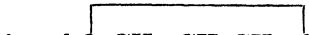
formyl OCH—


fural (2 *isomers*)

furfural = fural

furfuryl = furyl

furfurylidene = fural


furoyl

furyl (2 *isomers*)

furylidene = fural

geranyl (*from geraniol*) $C_{10}H_{17}$—

glutamyl —OC·CHNH$_2$·(CH$_2$)$_2$·CO—

glutaryl —OC·(CH$_2$)$_3$·CO—

glyceryl

glycolyl HOCH$_2$·CO—

glycyl H$_2$NCH$_2$·CO—

glyoxyl OCH·CO—

guaiacyl = *o*-anisyl

guanido H$_2$N·C(:NH)·NH—

guanyl H$_2$N·C(:NH)—

hendecyl CH$_3$·(CH$_2$)$_{10}$—

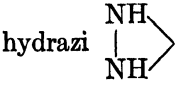
heptyl CH$_3$·(CH$_2$)$_6$—

hexadecyl = cetyl

hexyl CH$_3$·(CH$_2$)$_5$—

hippuryl PhCONHCH$_2$CO—

homopiperonyl (3,4)(CH$_2$O$_2$)·C$_6$H$_3$·CH$_2$·CH$_2$—


hydrazi (*to same atom*)

hydrazino H$_2$N·NH—

hydrazo —HN·NH— (*to different atoms*)

hydrazono H$_2$N·N=

hydroxamino HONH—

hydroximino = isonitroso

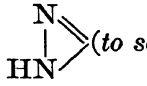
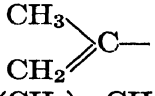
hydroxy (hydroxyl) HO—

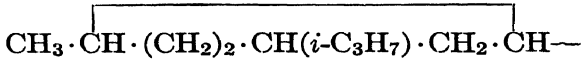
-idene *added to any radical usually means a double bond at point of attachment*

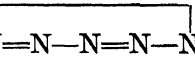
imidazolyl (*from imidazole*, 4 *isomers*) C$_3$H$_3$N$_2$—

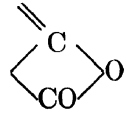
imino (imido) NH=

indenyl (*from indene*, 7 *isomers*) C$_9$H$_8$—

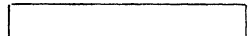
indyl (*from indole, 7 isomers*) C_8H_6N—
indylidene (*from indole*) C_8H_7N :
iodo I—
iodoso OI—
iodoxy O_2I—
isoallyl = propenyl
isoamoxy $(CH_3)_2 \cdot CH \cdot CH_2 \cdot CH_2O$—
isoamyl $(CH_3)_2 \cdot CH \cdot CH_2 \cdot CH_2$—
isoamylidene $(CH_3)_2 \cdot CH \cdot CH_2 \cdot CH$=
isobutenyl $(CH_3)_2 \cdot C$=CH—
isobutoxy $(CH_3)_2 \cdot CH \cdot CH_2O$—
isobutyl $(CH_3)_2CH \cdot CH_2$—
isobutyryl $(CH_3)_2 \cdot CH \cdot CO$—
isocyano C : N—
isodiazo  (*to some atom*)
isohexyl $(CH_3)_2 \cdot CH \cdot (CH_2)_3$—
isoindyl (*from isoindole, 4 isomers*) C_8H_6N—
isoleucyl $CH_3 \cdot CH_2 \cdot CH(CH_3) \cdot CHNH_2 \cdot CO$—
isonitro HOON=
isonitroso HON=
Δ_2-isopentenyl $(CH_3)_2 \cdot CH \cdot CH$: CH—
isophthalal (*m*) = $HC \cdot C_6H_4 \cdot CH$=
isophthalylidene = isophthalal
isopropenyl 
isopropoxy $(CH_3)_2 \cdot CHO$—
isopropyl $(CH_3)_2 \cdot CH$—
isopropylidene $(CH_3)_2 \cdot C$=
isoquinolyl (*from isoquinoline, 9 isomers*) C_9H_6N—
isothiocyano S : C : N—
isovaleryl $(CH_3)_2 \cdot CH \cdot CH_2 \cdot CO$—
isoxazolyl (*from isoxazole, 5 isomers*) C_3H_2ON—
keto O= (*to same atom*)
leucyl $(CH_3)_2 \cdot CH \cdot CH_2 \cdot CHNH_2 \cdot CO$—
malonyl —OC·CH_2·CO—
menthyl (*from menthane*)



mercapto HS—
mercuri HHg— or —Hg—
mesityl (*from mesitylene*) 3,5-$(CH_3)_2C_6H_3CH_2$—
methene = methylene
methenyl CH≡
methionyl —$SO_2CH_2SO_2$—
methoxy CH_3O—
methyl CH_3—
methylene CH_2=
methylenedioxy —O·CH_2·O—
methylol = (hydroxymethyl)
naphthal $C_{10}H_7CH$=
naphthalimido (*from naphthalic acid*) $C_{10}H_6(CO)_2N$—
naphthenyl $C_{10}H_7C$≡
naphthobenzyl $C_{10}H_7CH_2$—
naphthoxy $C_{10}H_7O$—
naphthoyl $C_{10}H_7CO$—
naphthyl (1- *or* 2-) $C_{10}H_7$—
naphthylene $C_{10}H_6$=
naphthylidene $C_{10}H_7$
nitramino O_2N·NH—
nitrilo N≡
nitro O_2N—
aci-nitro = isonitro
nitroso ON—
octyl CH_3·$(CH_2)_7$—
oxalyl —OC·CO—
oxamido H_2N·CO·CONH—
oximido = isonitroso
oxy —O— (used as a connective; cf. epoxy and keto)
pentamethylene —$CH_2(CH_2)_3CH_2$—
pentazido 
pentenyl (*like butenyl*)
pentyl = amyl
perimidyl (*from perimidine, 8 isomers*) $C_{11}H_7N_2$—
perthio (*replacing O only*) S : S—
phenacyl C_6H_5·CO·CH_2—
phenacylidene PhCOCH :
phenanthryl (*from phenanthrene, 9 isomers*) $C_{14}H_9$—

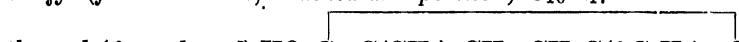
phenanthrylene (*from phenanthrene*) $C_{14}H_8$:
phenethyl $C_6H_5 \cdot CH_2CH_2$—
phenetido $C_2H_5O \cdot C_6H_4 \cdot NH$—
phenetyl (*o*, *m* or *p*) $C_2H_5O \cdot C_6H_4$—
phenoxy C_6H_5O—
phenyl C_6H_5—
phenylazo $C_6H_5 \cdot N : N$—
phenylcarbamido $C_6H_5 \cdot NHCONH$—
phenylene (*o*, or *p*) C_6H_4=
phenylenedisazo —N : NC_6H_4N : N—
phenylidene (*o* or *p*) $\overset{\Big\lceil\!\!\Big\lceil}{CH} : CH \cdot CH_2 \cdot CH : CH \cdot C$=
phenylureido = phenylcarbamido
phosphazo —N : P—
phthalal =$CH \cdot C_6H_4 \cdot CH$= (*o*)
phthalamido (*o*) $HO_2C \cdot C_6H_4 \cdot CONH$—
phthalidene (*from phthalide*) C_6H_4 
phthalidyl (*from phthalide*) $C_6H_4CO \cdot O \cdot \overset{\Big\lceil\!\!\Big\lceil}{CH}$—
phthalimido (*o*) $C_6H_4(CO)_2N$—
phthalyl —$OC \cdot C_6H_4 \cdot CO$— (*o*)
picryl (2,4,6)$(NO_2)_3 \cdot C_6H_2$—
piperidyl (*from piperidine*, 4 *isomers*) $C_5H_{10}N$—
piperonyl (3,4)$(CH_2O_2)C_6H_3 \cdot CH_2$—
piperonylidene (3, 4)$(CH_2O_2)C_6H_3 \cdot CH$=
pivalyl (*from pivalic acid*) $(CH_3)_3CCO$—
prolyl (*from proline*) $\overset{\Big\lceil\!\!\Big\lceil}{NH} \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH \cdot CO$—
propargyl HC ⋮ $C \cdot CH_2$—
propenyl $CH_3 \cdot CH : CH$—
propenylidene $CH_3CH : C$:
propiolyl HC ⋮ $C \cdot CO$—
propionyl $CH_3 \cdot CH_2 \cdot CO$—
propoxy $CH_3 \cdot CH_2 \cdot CH_2O$—
propyl (*n*) $CH_3 \cdot CH_2 \cdot CH_2$—
propylene —$CH(CH_3) \cdot CH_2$—

propylidene $CH_3 \cdot CH_2 \cdot CH=$
pseudoallyl = isopropenyl
s-pseudocumyl (1,3,4) $(CH_3)_3 \cdot C_6H_2-$
pseudoindyl (*from pseudoindole, 7 isomers*) C_8H_6N-
pyranyl C_5H_5O-
pyrazolyl (*from pyrazole, 4 isomers*) $C_3H_3N_2-$
pyridyl (*from pyridine, 3 isomers*) C_5H_4N-
pyridylidene C_5H_5N :
pyrimidyl (*from pyrimidine*) $C_4H_3N_2-$



pyrroyl $CH : CH \cdot CH : CH \cdot N \cdot CO-$
pyrryl (*from pyrrole, 3 isomers*) C_4H_4N-
quinolyl (*from quinoline, 7 isomers*) C_9H_6N-
quinonyl = quinoyl
quinoxalyl (*from quinoxaline*) $C_8H_5N_2-$
salicyl (*o*) $HO \cdot C_6H_4-$
salicylal (*o*) $HO \cdot C_6H_4 \cdot CH=$
salicylyl (*o*) $HO \cdot C_6H_4 \cdot CO-$
selenino $(HO)O \cdot Se-$
seleno $Se=$
selenocyano $NCSe-$
selenono $(OH)_2OSe-$
selenonyl $-SeO_2-$
selenyl $HSe-$
silicono $(OH)O \cdot Si-$
silicyl H_3Si-
silicylene $H_2Si=$
stannyl H_3Sn-
stearyl $CH_3 \cdot (CH_2)_{16} \cdot CO-$
styrene $-CH(C_6H_5) \cdot CH_2-$
styrolene = styrene
styryl $C_6H_5 \cdot CH : CH-$
succinamyl $H_2N \cdot CO \cdot CH_2CH_2 \cdot CO-$
succinyl $-OC \cdot CH_2CH_2 \cdot CO-$
sulfamino $HO_3S \cdot NH-$
sulfamyl $H_2NO \cdot OS-$
sulfhydryl = mercapto
sulfino HO_2S-
sulfinyl $OS=$
sulfo HO_3S-

sulfonamido $R \cdot SO_2 \cdot NH$—
sulfonyl $R \cdot SO_2$—
sulfuryl = sulfonyl
tauryl $H_2N \cdot CH_2CH_2SO_2$—
telluro Te=
terephthalal (*from terephthalaldehyde*) : HCC_6H_4CH :
tetramethylene = 1,4-butylene
tetrazyl (*from tetrazine, 2 isomers*) CHN_4—
thiazyl (*from thiazole, 3 isomers*) C_8H_2NS—
thienyl (*from thiophene, 2 isomers*) C_4H_3S—
thio —S—
thiocarbonyl SC=
thiocyano NCS—
thiohydroxy = mercapto
thiol (*S replacing O in OH*) } Used in place of "thio" only
thiono (*S replacing O in* CO) } when required for distinction
thionyl = sulfinyl
thujyl (*from sabinane, attached at 2 position*) $C_{10}H_{17}$—

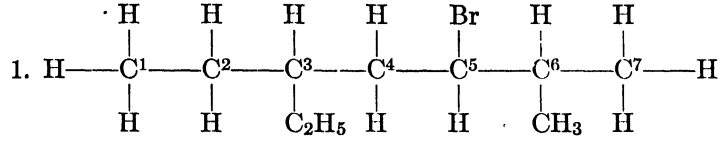


thymyl (*from thymol*) $HO \cdot C : C(CH_3) \cdot CH : CH \cdot C(i\text{-}C_3H_7) : C$—
toloxy (*o, m* or *p*) $CH_3 \cdot C_6H_4O$—
toluino (*o, m* or *p*) $CH_3 \cdot C_6H_4 \cdot NH$—
toluyl (*o, m* or *p*) $CH_3 \cdot C_6H_4 \cdot CO$—
α-toluyl $C_6H_5 \cdot CH_2 \cdot CO$—
tolyl (*o, m* and *p*) $CH_3 \cdot C_6H_4$—
α-tolyl = benzyl
tolylene (6 *isomers*) $CH_3 \cdot C_6H_3$=
α-tolylene = benzal
triazeno $NH_2 \cdot N : N$—

triazo $N : N \cdot N$—
triazolyl (*from triazole*) $C_2H_2N_3$—
trimethylene $—CH_2CH_2CH_2—$
tryptophyl (*from tryptophan*) $C_{11}H_{11}O_2N_2$—
tyrosyl (*from tyrosine*) $p\text{-}HO \cdot C_6H_4 \cdot CH_2CHNH_2 \cdot CO$—
undecyl = hendecyl (in sense $C_{11}H_{23}$—)
uramino = carbamido
ureido (*by some used synonymously with carbamido*)
$—NH \cdot CO \cdot NH—$
valeryl $CH_3 \cdot (CH_2)_3 \cdot CO$—

valyl (*from valine*) $(CH_3)_2 \cdot CH \cdot CHNH_2 \cdot CO—$
vanillal $(3,4)(CH_3O)(HO) \cdot C_6H_3 \cdot CH=$
vanilloyl $(3,4)(CH_3O)(HO) \cdot C_6H_3 \cdot CO—$
vanillyl $(3,4)(CH_3O)(HO) \cdot C_6H_3 \cdot CH_2—$
veratral $(3,4)(CH_3O)_2 \cdot C_6H_3 \cdot CH=$
veratroyl $(3,4)(CH_3O)_2 \cdot C_6H_3 \cdot CO—$
veratryl $(3,4)(CH_3O)_2 \cdot C_6H_3 \cdot CH_2—$
veratrylidene = veratral
vinyl $H_2C : CH—$
vinylene $—CH : CH—$
vinylidene $H_2C : C :$
xanthyl (*from xanthene, 6 isomers*), $C_{13}H_9O—$
xyloyl (*from xylic acid, 7 isomers*) $(CH_3)_2 \cdot C_6H_3 \cdot CO—$
xylyl (9 *isomers*) $(CH_3)_2 \cdot C_6H_3—$
xylylene $—H_2C \cdot C_6H_4 \cdot CH_2—$

We shall now illustrate with a number of examples some of the methods employed in naming compounds:

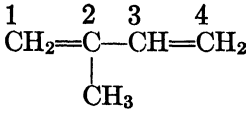
1.


(*a*) In naming this compound, first select the longest straight chain. In this case, it would be a seven-carbon chain. Therefore, the naming will center around the saturated hydrocarbon heptane.

(*b*) Consider the elements and groups other than hydrogen as substituents.

(*c*) Therefore the name of this compound becomes:

3-ethyl-6-methyl-5-bromoheptane

2.


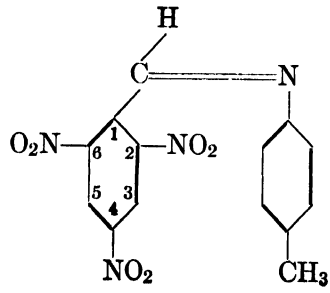
(*a*) Selecting the longest chain, we have four carbon atoms.

(*b*) Since there are two double bonds in this chain, the name of the compound must end in *-diene* and center around the unsaturated hydrocarbon butadiene.

(*c*) The name of this compound becomes 2-methyl butadiene.

(*d*) But to indicate the positions of the double bonds, the final name becomes 2-methyl-1. 3-butadiene (isoprene).

3.

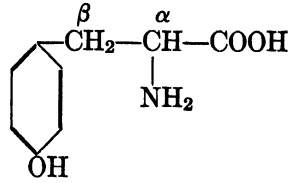


(*a*) This compound contains the benzal (divalent) group wherein the three hydrogens in positions 2, 4, 6, are replaced by three nitro groups.

(*b*) In addition, we have *p*-toluidine, where in place of the two hydrogens in the amino group, there is a double bond.

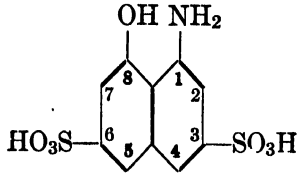
(*c*) Therefore, the name of this compound becomes 2, 4, 6-trinitrobenzal-*p*-toluidine.

4.



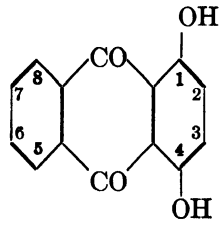
This compound is named α-amino-β-*p*-hydroxyphenylpropionic acid (tyrosine), because it has an amino group attached to the α-carbon atom and the *p*-hydroxyphenyl group attached to the β-carbon atom.

5.



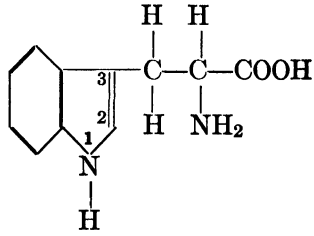
This compound is named 1-amino-8-hydroxy-3,6-naphthalenedisulfonic acid. ("H-acid")

6.



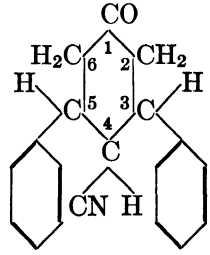
This compound is named 1, 4-dihydroxyanthraquinone (quinizarin.)

7.



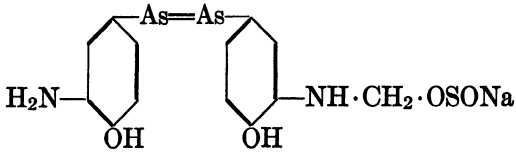
This compound is named α-amino-β-3-indolepropionic acid (Tryptophan).

8.



This compound is named 3,5-diphenyl-4-cyanocyclohexanone-1.

9.



This compound is named sodium 3, 3'-diamino-4, 4'-dihydroxyarsenobenzene-N-methylenesulfinate.

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APPENDIX

GLOSSARY

Active principles include carbohydrates, alkaloids, glucosides organic acids, resins, oils and fats, volatile oils, protein bodies and ferments.

Analgesics are drugs which relieve pain when absorbed into the blood.

Anesthetics are drugs which produce insensibility to pain. (Local anesthetics are drugs which produce insensibility to pain at the site of application.)

Anodynes are drugs which relieve pain when applied locally. They are usually milder in action than the analgesics.

Antacids are drugs which neutralize acids.

Antidote is an agent which affects a poison either physically or chemically or both so as to remove it from the body or alter its character by forming with it an insoluble or inert compound.

Antifebrin is another name for acetanilide (used to decrease fever).

Antipyretics are drugs which reduce fever.

Antiscorbutic is an agent effective against scurvy.

Antiseptics are substances which check the growth of bacteria.

Antispasmodics are drugs which lessen contractions of muscles, and also lessen convulsions.

Aperients are substances which produce mild movements of the bowels.

Aromatics are spicy substances which increase the secretion of the stomach and the intestines.

Astringents are drugs which contract or harden the tissues.

Bactericide is an agent which destroys bacteria.

Balsams are semi-fluid, resinous and fragrant vegetable juices of many varieties.

Bitters are drugs which increase the appetite because of their bitter taste.

Cardiac stimulants are drugs which increase the activity of the heart.

Cardiac depressants are drugs which lessen the heart action.

Carminatives are drugs which produce a feeling of comfort in the stomach and relieve the formation of gas in the stomach and the intestines.

Catabolism is the breaking down of tissue material in the body.

Cathartics are drugs which cause movements of the bowels.

Caustics are substances which burn or destroy tissues.

Counterirritants are drugs which act on the skin.

Cyanosis signifies "blueing" of the skin.

Deodorants are remedies which destroy unpleasant odors.

Disinfectants are drugs which check the growth of bacteria.

Diuretics are drugs which increase the flow of urine.

Emetics are drugs which produce vomiting.

Expectorants are drugs which increase coughing and bronchial secretions.

Febrifuges are drugs which reduce fever.

Gums are amorphous, transparent substances which are widely disseminated in plants.

Hemostatics are substances which check bleeding.

Hypnotics are drugs which produce sleep.

Lachrymator is a substance which produces the secretion and discharge of tears.

Lacteal is any one of the intestinal lymphatics which absorbs fats.

Laxatives are drugs which produce mild movements of the bowels.

Myotics are drugs which narrow (contract) the pupil of the eye.

Mydriatics are drugs which widen (dilate) the pupil of the eye.

Narcosis is the state of profound unconsciousness produced by a drug.

Narcotic is a drug which produces stupor or complete insensibility.

Parasiticide is an agent which destroys the animal and vegetable parasites found upon the human body.

Peristalsis is the worm-like movement by which the alimentary canal propels its contents.

Purgatives are drugs which produce moderately active and frequent movements of the bowels.

Putrefaction is the decomposition of animal or vegetable substances effected largely through micro-organisms, and resulting in the production of various solids, liquids and gases, some of which have a foul odor.

Refrigerants are substances which relieve thirst and cool the patient, in fever.

Resins are complex bodies of resinous character. They are generally considered to be oxidation products of hydrocarbons such as terpenes.

Respiratory stimulants are drugs which increase the depth and frequency of breathing.

Respiratory depressants are drugs which lessen the frequency and depth of breathing.

Rubefacients are drugs which redden the skin by widening (dilating) the capillaries.

Sedatives are drugs which lessen the activity of an organ or part of the body.

Somnifacients or **Soporifics** are drugs which produce sleep.

Styptics are substances which stop bleeding.

Trypanocidal power is the power possessed by certain bodies of destroying certain parasites found in the blood of man and of animals.

Vaso-constrictor is a drug which increases arterial pressure.

Vaso-dilator is a drug which lowers arterial tension.

Vermicides are drugs which destroy worms.

Vertigo means dizziness.

Vesicatories or **Vesicants** are drugs which produce blisters.

BOILING AND MELTING POINTS OF A NUMBER OF ORGANIC COMPOUNDS

Since very few physical constants are given in the body of the work, we shall here give the boiling and melting points of a number of compounds which the student is apt to encounter.[1]

NAME	m. p., ° C.	b. p., ° C.
Acetaldehyde	−120	21
Acetamide	82	222
Acetanilide	114	305
Acetic acid	16.7	119
Acetic anhydride	.....	139
Acetone	− 94	55.6
Acetonitrile	− 45	81
Acetyl chloride	.....	55
Allyl alcohol	−129	96
Amyl acetate	− 75	148
Aniline	− 6.5	184.4
Aniline hydrochloride	198	245
Anthracene	216	360
Anthraquinone	285	380
Benzaldehyde	− 13.5	179
Benzene	5.4	80.4
Benzenesulfonic acid	52	
Benzidine	127	400
Benzoic acid	121	249
Butyl alcohol	− 79	116
Camphor	176	209
Carbon disulfide	−111	46
Carbon tetrachloride	− 23	78
Chloroform	− 63	61
Cinnamic acid	133	300
Citric acid	153	decomposes
o-Cresol	30	191
m-Cresol	11	202
p-Cresol	35	202
p-Cymene	− 73	175
Dimethylaniline	2	194
Diphenyl	70.5	254
Ethyl acetate	− 82	77
Ethyl alcohol	−114	78.4
Ethyl bromide	−115	45
Ethyl butyrate	− 93	120

[1] For others, consult Olsen—Chemical Annual (Van Nostrand).

NAME	m. p., ° C.	b. p., ° C.
Ethyl chloride	−140	12.5
Ethyl ether	−116	35
Ethyl iodide	−118	72
Ethylene glycol	− 17	199
Formaldehyde		− 21
Formic acid	7.5	100
Furfural	− 36	55 (17 mm.)
Glucose	146	
Glycerol	17	291
Hydrocyanic acid	− 10	26
Iodoform	119	sublimes
Isoamyl alcohol	−117	131
Isopropyl alcohol	− 85	83
Lactic acid	18	119 (12 mm.)
Methanol	− 95	65
Methyl iodide	− 66	45
Methyl salicylate	− 8	222
Naphthalene	80	218
α-Naphthol	96	279
β-Naphthol	122	285
α-Naphthylamine	50	300
β-Naphthylamine	111	306
Nitrobenzene	5	210.8
Oxalic acid	189	150 + sub.
Phenol	45	182.6
Phthalic acid	213	
Phthalic anhydride	131	284.5
Pyridine	− 42	116
Pyrogallol	132.5	293
Resorcinol	118	280
Saccharin	228 dec.	sub.
Salicylic acid	157	sub.
Sulfanilic acid	288	
Thymol	50	231.8
Toluene	− 93	111
o-Toluidine	− 21	199.7
m-Toluidine	− 13	203
p-Toluidine	45	200
Urea	132	dec.
Vanillin	81	285 dec.
o-Xylene	− 27	144
m-Xylene	− 53	139
p-Xylene	15	138

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