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ORGANIC CHEMISTRY

FOR

ADVANCED STUDENTS

PART II

STRUCTURE

BY

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PREFACE TO THE FOURTH EDITION

THE developments both on the theoretical and practical side of organic chemistry which have taken place since the University laboratories resumed their normal activities after the war rendered a careful revision of the previous edition necessary. The new volumes will be found to contain a considerable amount of additional matter.

Among the subjects which find a place in the present edition are the theories of Lewis and Langmuir and Sir J. J. Thomson on the structure of the atom, with its application to organic reactions by Robinson and Kermack, Lapworth, Lowry, Kenner and others, the work of Irvine, Haworth, and Hudson on the constitution of the carbohydrates; the developments of Baeyer's strain theory by Thorpe and Ingold; the use of Sir W. Bragg's X-ray spectrograph for determining the crystal structure of organic compounds; the photochemical studies of Baly and Heilbron; the biochemical work of Neuberg; whilst a brief reference is made to the newer theories of catalysis by Armstrong and Hilditch, Langmuir, Rideal, Taylor and others. In the section on stereochemistry will be found some account of the recent experiments by Senter and Drew on the Walden inversion, by McKenzie and Wren on racemisation, by Kenner and by Mills on the resolution of new forms of asymmetric molecules, and by Brady and Dunn on the inversion of the aldoximes. In Part III an account is given of the synthetic researches of Ruzicka on the terpenes and allied substances, of Fischer and Freudenberg on the tannins, of Willstätter, Hess, and W. H. Perkin on the alkaloids, of T. B. Johnson and his collaborators

on the pyrimidine bases, of Biltz on the xanthine bases, of Pyman on the glyoxaline group, and of Levene and Jones on nucleic acids. A few new reactions, as, for example, those of Hoesch and von Braun, will be found in their appropriate section in Part I. The important branch of organic chemistry which deals with the colouring matters of flowers and their constitution has been exhaustively treated by A. G. Perkin and Everest in their monograph on the natural dyestuffs, and is purposely omitted; the no less important branch relating to synthetic drugs and their physiological action is as yet too incomplete and unsystematised to be usefully included.

J. B. COHEN.

September, 1923.

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ORGANIC CHEMISTRY

PART II

CHAPTER I

PHYSICAL PROPERTIES AND STRUCTURE

A COMPLETE knowledge of the structure of the different kinds of atoms and the forces inherent in them would enable us to picture not only the chemical attributes of different substances, but also the atomic and molecular forces which determine their cohesion (capillarity, viscosity, and density) in the liquid state, their crystalline form in the solid condition, their heat of fusion, of vaporisation, and of formation, and their action on light (refraction, rotatory polarisation, absorption, &c.). But so limited is our knowledge of the nature of the atom that not only are we unable to predict with any degree of confidence any one of the above attributes of the compounds into which the atoms enter, but there are few cases in which these properties have been brought into direct relation in one and the same substance. The reverse process, namely, by observations of the various physical attributes of compounds to connect them with those chemical properties upon which our knowledge of structure mainly rests, has afforded an attractive field for investigation. The application of the process to the study of organic compounds offers unusual advantages from the fact that it is in this domain of chemistry that the determination of structure by chemical methods has been pushed to its farthest extent.

Let us consider for a moment how a series of purely empirical observations of physical properties, resting upon no theory of atomic relations, may be made to subserve the study of structure. Suppose a particular physical property of a homologous series of paraffins to be determined, the results must be so formulated that a comparison can be instituted between the molecular effect of the different members of the series. Experiment will probably reveal a numerical difference (increase or decrease) between the successive members, and thus the value for CH_2 is given. Other series, such as those of the aldehydes and acids, may be taken, and the difference between parallel members of the two series will give the value for hydroxyl oxygen; the difference between aldehydes and multiples of CH_2 will determine the value for carbonyl oxygen, and so forth. Thus, a number

of constants will be obtained for certain atoms or groups from which the values for compounds of unknown structure may be calculated and compared with those derived from direct observation.

It may happen, however, that the property is merely additive, that is to say, there is a constant value for each element independently of the nature of its attachment. Such a purely additive property is mass and also the resistance of a gas or vapour to penetration by α rays. It is clear that it will tell us no more than the molecular formula. The question of structure will not be touched. We have therefore to distinguish between a purely additive property and one which is partly additive and partly constitutive, such as refractivity or rotatory polarisation. Again, we find physical properties very differently influenced by constitutive relations. The cause of rotatory polarisation is, on its qualitative side, a purely constitutive one, that is to say, it is determined entirely by atomic arrangement and not by mass. On its quantitative side it is partly additive and partly constitutive, depending both on the mass and structure of the molecule. The connection between the two is at present so ill-defined that constitutively the property has little value.[1]

Consequently, in selecting a physical property which is capable of throwing light on molecular structure, we must be guided by the numerical amount as well as by the constancy of the constitutive effect. For if the numerical value—say between singly and doubly linked oxygen or carbon or between an open and closed chain of carbon atoms—is very small, it may be masked by errors of observation, or, again, if it varies from member to member in the same or different series, it will fail to give that constant value, which should serve as a basis for calculation. For example, the refractive constant for hydroxyl oxygen (O′) has been found to vary between 1·38 and 1·62 in one series, that of ester oxygen (O<) between 1·45 and 1·99 in another, the mean of the first being 1·49, that of the second 1·65. It is clear that the line of division between the effects of the two kinds of oxygen union is not sufficiently sharp to enable the nature of the union in a given individual to be foretold from its refractivity. Again, the refractive value of one double bond is fairly constant, but a second double bond in its vicinity has usually more than double the value. Thus, *constancy* of constitutive effect becomes an important factor in ascertaining structure.

The power of selective absorption of organic liquids and substances in solution stands in a somewhat different category from other physical properties, inasmuch as the relations here are largely

[1] P. F. Frankland, *Trans. Chem. Soc.*, 1912, 101, 654.

qualitative and cannot be represented numerically. Like rotatory polarization on its qualitative side, the property can only be usefully applied for constitutive purposes on the basis of a satisfactory theory. At the same time the position and character of the absorption bands of similarly constituted substances will often reveal the structural correspondence of certain groups.

I. MOLECULAR VOLUME

It is natural to suppose that the volume occupied by different kinds of atoms and molecules under similar conditions will be different, and it would not appear remarkable if the same atoms, differently combined, occupied different spaces. Should this be the case the molecular volume of a compound would afford valuable information as to its structure. How can we measure the size of a molecule? The volumes occupied by equivalent molecular weights of gases and vapours under the same conditions are the same, and they clearly cannot be employed for the purpose. Liquids possess certain advantages over solids, in that the former are homogeneous in every direction and do not exist in allotropic forms. If, then, we determine the volume in cubic centimetres occupied by 1 gram (that is, the reciprocal of the specific gravity) we shall obtain the relative volumes of equal masses in the liquid state, or, when multiplied by the molecular weight, the relative volume of molecular masses, or *molecular volume*. This is given by the expression,

$$V_m = \frac{\text{Molecular weight}}{\text{Density}}$$

We must remember that this expression includes the space between the molecules as well as that occupied by the molecules themselves. It also includes the space between individual atoms. Both these will be affected by change of temperature, and it is important therefore at the outset to fix upon a suitable temperature for comparison.

The difficulty in the choice of temperature has to some extent been met by the application of van der Waals' well-known gas equation to liquids :

$$\left(p + \frac{a}{v^2}\right)(v - b) = RT.$$

It can be shown that at the critical temperature and pressure $v = 3b$. It is not, however, necessary to determine the critical volume by direct observation, which would present many difficulties, for van der Waals has shown that *corresponding temperatures*, that is, temperatures which are equal fractions of the respective critical temperatures, may serve the purpose equally well. Kopp, who was the

first to make an exhaustive study of the subject, took as the standard temperature the boiling-point at atmospheric pressure, and, although he was not at the time aware of the fact, it has since been shown that this temperature is approximately the same fraction, that is, about two-thirds of the critical temperature measured on the absolute scale. Other observers have preferred to fix on one definite temperature and have examined substances at 0°, others again at the melting-point. All three methods possess certain advantages, and all, it may be added, have their defects, but there is little doubt that the boiling-point temperatures give on the whole the most regular series of results.

Kopp's measurements were made by taking the density at the ordinary temperature and calculating that at the boiling-point from the thermal expansion, but methods for direct observation have since been devised. From these earlier determinations Kopp [1] laid down the following general rules:

1. Among analogous compounds, the same difference of molecular volume corresponds to the same difference of composition.

2. Isomeric liquids have the same molecular volume.

3. By replacing two atoms of hydrogen by one atom of oxygen the molecular volume is unchanged.

4. An atom of carbon can replace two atoms of hydrogen without change of volume.

On the assumption that the molecular volumes were the sum of the atomic volumes of the elements, Kopp ascertained the value of the latter as follows: from a series of homologous compounds he found $CH_2 = 22$, and, according to rule 4, C = 11, H = 5·5, and from 3, O = 11. When these values were calculated for compounds of the formula $C_aH_bO_c$ it was seen that the molecular volumes did not invariably conform to the calculated values, and the property was therefore not strictly additive.

Kopp showed subsequently that the calculated value would correspond with the observed result if account were taken of the nature of the oxygen atom; whether, according to the theory of types then in vogue (Part I, p. 44), it was extra- or intra-radical oxygen, or, as we should now say, singly or doubly linked. The value for doubly linked oxygen was found a little higher than that for one atom of carbon, namely, 12·2, whilst hydroxyl oxygen was derived from the value of water, 18·8 less 2H = 11·0, which gives 7·8. On this new basis the calculated values for forty-five different compounds did not vary by more than 4 per cent. Acetic acid, for example, gave the following calculated and observed values:

[1] *Annalen*, 1855, **96**, 153, 303; see also Ostwald's *Lehrbuch*, 1884, vol. i, p. 810.

2C	= 22
4H	= 22
O″	= 12·2
O′	= 7·8
	64 (calc.)
	63·7 (obs.)

From the molecular volumes of compounds containing the halogens, sulphur, and nitrogen in place of hydrogen the following values were obtained:

Cl = 22·8	I = 37·5
Br = 27 8	S′ = 22·6

The values for nitrogen, like those for oxygen and sulphur, were found to vary in different compounds; in ammonia N = 2·3, the cyanogen group, CN = 28, and the nitro group, NO_2 = 33, which give enormous variations for nitrogen, supposing that the whole difference is concentrated on the one kind of atom, an assumption which is by no means certain. Kopp, at the close of his research, suggested that the volumes of elementary atoms might be multiples of a common constant, whose value lay between 5·1 and 5·9; but this view can hardly be sustained in face of those derived from H_2O and CS_2.

A similar view was entertained by Schroeder, who suggested that the atomic volumes of different atoms were the same or a multiple of the same number, which might vary slightly in different compounds, and he called this unit a *stere*, the value varying from 6 7 to 7·4.

C, H, O′ and $\frac{O''}{2}$ = 1 stere. The value for CH_2 would be about 21; O″O′ would also be 21 Formic acid, CH_2O_2, would be 2 × 21 = 42; acetic acid, $C_2H_4O''O' = 2 \times 21 + 21 = 63$, and so forth.

Many years later (1865) Buff took up the subject again and showed that unsaturated carbon and sulphur have, like oxygen, a higher value than the singly linked atoms. To doubly linked sulphur the number S″ = 28·3 was assigned.

Fresh light has been thrown on the effect of constitutive influences on molecular volumes by the work of Ramsay, Thorpe, and Lossen. The first described a method for estimating density at the boiling-point. Thorpe, from the results of very careful observations, was able to prove that structural isomers differ slightly in molecular volume, that liquid elements have the same atomic volume in the free state as when combined, and, using Kopp's numbers for C, H, and O, that chlorine, bromine, and iodine possess the constants 22·7, 28·1, and 36 0 respectively.

Lossen re-calculated on a uniform basis the material already collected. He found that the fatty acids and ethers closely follow Kopp's law and that the alcohols exhibit certain variations, methyl alcohol, for example, having a larger molecular volume than the calculated one and the higher alcohols a lower value. The aldehydes show a similar divergence. The molecular volumes of unsaturated compounds were generally higher than the calculated numbers. Among the aromatic compounds no general rule could be laid down so as to bring the observed and calculated results into harmony. Lossen concluded that whilst the elements in each class of compounds had a determinate value, it varied from one class to another.

Schiff was able to throw new light on the subject with the aid of a large amount of fresh material. He found, in the first place, that substances with a higher boiling-point possess a higher molecular volume. He found further that, among the esters, the molecular volume increases with an increase in the number of carbon atoms in the alcohol radical and with a decrease in that of the acid radical; but his most interesting achievement was the confirmation of Buff's view as to the increased value of the ethenoid linkage. This increase he estimated at four units; but he assumed that benzene was saturated, an assumption which is not always supported by its chemical or physical properties. A comparison of diisobutyl, $C_8H_{18} = 184{\cdot}5$, with ethyl benzene, $C_8H_{10} = 138{\cdot}95$, shows a difference of 45·45 for eight hydrogen atoms; but caprylene is $C_8H_{16} = 177{\cdot}2$, whereas it should be $138{\cdot}95 + \frac{3}{4} \times 45{\cdot}45 = 173{\cdot}14$, a difference of four units.

Later determinations have modified this result by a direct comparison of a saturated with an unsaturated compound containing the same number of carbon atoms.

More recently the study of molecular volumes has been taken up by Le Bas, who has published an interesting monograph on the subject.[1] He has reverted to the principle of the stere, taking as his unit the unit of valency. Thus, he finds from Krafft's values[2] for the molecular volumes of the higher paraffins at the melting-point, that $V_m/W = 2{\cdot}97$, in which V_m = molecular volume and W the sum of the valencies. The value for carbon is $4 \times 2{\cdot}97 = 11{\cdot}88$, and for hydrogen 2·97. This value for the valency unit increases with temperature and reaches 3·7 at the boiling-point.

With this brief historical introduction we will proceed to examine some of the experimental data.

[1] *The Molecular Volumes of Liquid Chemical Compounds*, by G. Le Bas. Longmans, Green & Co., 1915.

[2] *Ber.*. 1884. 17. 1371.

With a delicate balance it is possible to estimate specific gravities with accuracy to 1 part in 100,000, and, as this is the principal factor involved in the determination of molecular volumes, the method experimentally leaves little to be desired.

But on comparing results of different observers they are frequently found to vary by about one per cent. This is a significant fact, and is probably to be ascribed to the impurity of the substances employed, which would affect both boiling-point and thermal expansion as well as the specific gravity.

Isomeric Compounds. From his earlier observations, Kopp assumed that the atomic volumes were constant. If this were the case isomeric compounds should possess the same molecular volume. The following series represent different types of isomeric compounds and their molecular volumes:[1]

Substance.	B. P.	V_m	Δ per cent	Substance.	B P.	V_m	Δ. per cent.
n-Hexane	69°	140 0	2·5	Propyl aldehyde	49°	75 4	2·4
Diisopropyl	58	136·5		Acetone	56	77·2	
n Heptane	98·4	162·6	0·7	Ethylene chloride	84	85·3	4 0
Isoheptane	90·3	162 0		Ethylidene chloride	59	88 9	
n-Propyl alcohol	97·4	81·2	1 9	Diethylamine	55	109·0	2·6
Isopropyl alcohol	82·8	82 8		Butylamine	65	106·2	
n Butyl alcohol	108	102 1	—	*o*-Xylene	141	138·5	—
Trimethylcarbinol	83	102·4		*m*-Xylene	138	139 8	—
				p-Xylene	138	140 2	
Dipropyl ether	91	150 9	0 5				
Diisopropyl ether	69	151 6		Mesitylene	164	162 4	—
				Ethyl toluene	162	161 9	—
Methyl propyl ether	38·9	105·1	1·0	Propyl benzene	158	161·8	
Diethyl ether	34 9	106·1					
				Chlorotoluene	160	134·9	—
Methyl propyl ether	38·9	105·1	3·2	Benzyl chloride	175	133 5	
Butyl alcohol	117 0	101·9					
				Anisole	154	125·2	1·3
n-Butyric acid	162·5	108·2	—	*m*-Cresol	206	123·2	—
Isobutyric acid	154 1	108·9		Benzyl alcohol	203	122 8	
Methyl propionate	79 5	104·6	1·5	Aniline	184	106·4	4·6
Ethyl acetate	77·5	106·1	—	Picoline	133	111·5	
Propyl formate	81·0	106·2	1·8				
Butyric acid	162 5	108·2		Ethyl benzoate	209	174·6	2·4
				Phenyl propionic acid	280	170·4	

B.P. = boiling-point; V_m = molecular volume; Δ = difference

[1] Horstmann, Graham-Otto's *Lehrbuch der Chemie*, vol. i, 3, 875.

It will be seen from the above table that constitutive differences assert themselves in a very striking manner. The largest differences are found among compounds belonging to distinct classes, the smallest among position isomers; but this is not invariably the case, as, for example, the isomeric dichlorethanes and the isomeric butylamines, which show large differences, whereas cresol and benzyl alcohol are nearly identical.

Homologous Series. The value of CH_2 can be determined by a comparison of different homologous series. The following table gives the constants for different classes of compounds at the boiling-point and also the maximum and minimum values observed:

Series.	No of intervals.	Max and Min.	Mean.
Alcohols	8	19·7-22·4	21·1
Fatty Acids	8	21 6-23 4	22 4
Aldehydes (aliph.)	4	19 0-22·0	20 7
Amines (aliph.)	5	20 4-20 6	20 5
Alkyl iodides	10	21·1-24·3	22 6
Paraffins	13	—	22·7
Esters	15	21·2-27·7	24·4
Ethers	13	21·6-28 5	24 3
Hydrocarbons (arom.)	5	21·0-22·9	22·1
Olefines	5	20·3-23·1	21 8

It will be seen that there is not only a considerable variation in the constants in the different series, but a wide divergence in the minima and maxima for the same series. It should, however, be pointed out that as a rule the value for CH_2 increases in ascending the series, and the longer the series and the wider the range of boiling-points the larger the variation. For example, the normal paraffins show differences for CH_2 varying from 18 to 23·7.

Paraffin.	V_m.	Δ
CH_4	38·5	
C_2H_6	56·7	18·2
C_3H_8	74·6	17·9
C_4H_{10}	96·0	21·4
C_5H_{12}	117 8	21·8
C_6H_{14}	139·9	22 1
C_7H_{16}	162·5	22·6
C_8H_{18}	186·2	23·7

Lossen[1] assumed that the increase in the CH_2 value for successive members is 0·5 units: but it is clear that the amount is not constant. On the other hand Krafft's values for the higher paraffins at the melting-point show little or no variation. There is clearly

[1] *Annalen*, 1889, 254, 42.

some missing factor which should be introduced to bring the various constants into uniformity.

The Constants for Carbon, Hydrogen, and Oxygen. With so large a variation in the value for CH_2 it seems hopeless to find a constant for carbon and hydrogen which will satisfy the different series. The following methods have been adopted for estimating the value of carbon and hydrogen. By comparing benzene, C_6H_6, with butane C_4H_{10}, which have the same atomic volume ($V_m = 96$), Kopp concluded that $C_2 = H_4$. It follows, therefore, that if $CH_2 = 22$, H_2 will be 11. Another method is to compare the paraffins C_nH_{2n+2} with the aromatic hydrocarbons of the same carbon content C_nH_{2n-6}, which gives the difference for eight atoms of hydrogen. The values for the series are fairly constant and give a mean of 45·9 or $4 \times 11{\cdot}5$ for H_2. But, as Le Bas points out, such a comparison between aliphatic and aromatic hydrocarbons cannot be justified, seeing that the molecular volumes of the latter show a very marked contraction. If, in place of comparing paraffins with aromatic hydrocarbons, other compounds are taken, very different results are obtained. For example, the value for the olefine deducted from that of the corresponding paraffin gives the constant for H_2. Although the olefine contains a double bond which might affect the molecular volume, this appears not to be the case, since the value for the olefine is almost an exact multiple of the difference for CH_2 in the series.

	V_m.		Δ
C_3H_6	66·6	$3 \times 22{\cdot}2$	
C_4H_8	88·8	$4 \times 22{\cdot}2$	22·2
C_5H_{10}	110·0	$5 \times 22{\cdot}0$	21·2
C_6H_{12}	132·5	$6 \times 22{\cdot}1$	22·5
C_7H_{14}	154·8	$7 \times 22{\cdot}1$	22·3
C_8H_{16}	177·6	$8 \times 22{\cdot}1$	22·8
			22·2 Mean.

Calculated in this way the value for carbon becomes 14·8 and that of hydrogen (H_2) is 7·4.

Practically the same figure has been obtained by Le Bas by deducting from the paraffin C_nH_{2n+2} the value for $n \times CH_2$ thus:

$$(H) = C_5H_{12} - 5(CH_2) = 117{\cdot}8 - 5 \times 22{\cdot}1 = 7\,3 \text{ or } 2 \times 3\,65$$
$$(C) = 22{\cdot}1 - 7{\cdot}3 = 14{\cdot}8$$

Another method for estimating carbon is by deducting the value of the paraffin C_nH_{2n+2} from the olefine containing an additional carbon atom $C_{n+1}H_{2n+2}$. This gives a mean value for carbon of 14·6.

A very similar result is obtained by taking the differences between two homologous alcohols and an unsaturated alcohol of the carbon content of the lower member.

$$\left.\begin{matrix} C_nH_{2n+2}O \\ C_nH_{2n}O \end{matrix}\right\} = H_2$$

$$\left.\begin{matrix} C_nH_{2n}O \\ C_{n-1}H_{2n}O \end{matrix}\right\} = C$$

The values in this case work out to C = 14·3, H_2 = 7·0.

It must be remembered that neither value is constant, but increases, as already pointed out, in ascending the series. Moreover, the branched-chain when compared with the normal chain paraffins exhibit a slight contraction which Le Bas estimates at 0 5 units.

Hydroxyl oxygen (O′) may be determined by a comparison between the paraffin and alcohol, mono- and poly-hydric alcohols or phenols, or again aldehyde and acid. None of these methods yield very concordant results; by the first, the value for O′ fluctuates between 5·9 and 7·4.

Alcohol.	V_m	Δ	V_m	Paraffin.
C_3H_7OH	81 4	7·4	74·0	C_3H_8
C_4H_9OH	102·1	6·1	96 0	C_4H_{10}
$C_5H_{11}OH$	123·7	5·9	117·8	C_5H_{12}
$C_6H_{13}OH$	146 4	6 5	139·9	C_6H_{14}
$C_7H_{15}OH$	168 7	6 1	162 6	C_7H_{16}

The lower members show even larger variations.

By the second method Δ varies between 2·8 and 5 9.

Alcohol.	V_m	Δ	V_m	Glycol.
C_2H_5OH	62 1	2 8	64 9	$C_2H_4(OH)_2$
C_3H_7OH	81·4	4 0	85 4	$CH_3.CH\ OH.CH_2\ OH$
		2 8	81 2	$CH_2OH.CH_2\ CH_2OH$

	Phenol.	V_m	Δ	V_m	Aromatic hydrocarbon.
	C_6H_5OH	101·9	5 9	96	C_6H_6
o	$C_6H_4(CH_3)OH$	121 8	3 6	118 2	$C_6H_5(CH_3)$
m.	,,	123 5	5 3		
p	,,	123·8	5 6		

By the third method Δ varies between 7 and 12.

Aldehyde.	V_m	Δ	V_m	Fatty acid.
C_2H_4O	56 7	7·3	64	$C_2H_4O_2$
C_3H_6O	74·8	10 5	85 3	$C_3H_6O_2$
C_4H_8O	90 0	11 8	107·8	$C_4H_8O_2$
$C_5H_{10}O$	118·2	11·8	130·0	$C_5H_{10}O_2$

The value for O((ether series),[1] as determined by Le Bas by a comparison between the ethers and the paraffins with an equal number of carbon atoms, varies between 9·9 for the methyl ether series and 11·0 for the symmetrical series (i. e. containing the same radicals attached to oxygen). A similar comparison in the phenolic ether series gives values between 7 and 12.

Carbonyl oxygen (O″) shows the same unexplained variations. By comparing the olefine, C_nH_{2n}, with the aldehyde, $C_nH_{2n}:O$, the values derived from two sets of observations gave 6 6 in the one and 8·3 in the other. The value of O″ in terms of H_2 is given by a comparison of alcohols with acids, or aldehydes, ketones, with paraffins. In the latter case the differences are so small as to lie within the limits of experimental error, in other words, $H_2 = O'' = 7·4$.

Aldehyde.	V_m	Ketone.	V_m	Paraffin.	V_m
C_3H_7CHO	96	$C_2H_5 \cdot CO \cdot CH_3$	96 7	C_4H_{10}	96
C_4H_9CHO	118 2	$C_3H_7 \cdot CO \cdot CH_3$	118·3	C_5H_{12}	117 8
$C_5H_{11}CHO$	—	$C_4H_9 \cdot CO \cdot CH_3$	140 1	C_6H_1	139 9

On deducting from the values of the fatty acids, $C_nH_{2n}O_2$, that calculated for nCH_2, the value of $O'' + O' = 19·5$ and is approximately constant. The division of 19 5 between O″ and O′ is a matter of choice; but assuming $O' = H_2 = 7·4$, that of O″ will be 12, values not very different from those proposed by Kopp. From this it would appear that if $O' = H_2$, $O'' = H_3$. Between fatty acid and alcohol in which O″ replaces H_2 there is also an excess of 2 to 7 units, except in the case of the first member, where there is a decrease of 1 6 units.

Alcohol.	V_m	Δ	V_m	Acid.
CH_3OH	42 8	−1·6	41 2	CH_2O_2
C_2H_5OH	62 1	+1 9	64 0	$C_2H_4O_2$
C_3H_7OH	81·4	4·1	85 3	$C_3H_6O_2$
C_4H_9OH	102·1	5·7	107·8	$C_4H_8O_2$
$C_5H_{11}OH$	123 7	6·3	130 0	$C_5H_{10}O_2$
$C_6H_{13}OH$	146 4	6 1	152 5	$C_6H_{12}O_2$
$C_7H_{15}OH$	168 7	5 9	174 6	$C_7H_{14}O_2$

As no constant values can be attached to carbon, hydrogen, and oxygen, it seems useless to attempt to derive a molecular volume by the summation of atomic volumes. The only profitable way of pursuing the subject seems to be to confine it to the examination of

[1] O′ = oxygen in hydroxyl; O(= oxygen in ethers; O″ = oxygen in ketones and aldehydes.

the values in similarly constituted compounds in which the elements possess similar functions.

The Ethenoid Linkage and Ring Structure. The value of doubly linked carbon has been estimated by comparing the sum of the values of an olefine and saturated compound with the saturated compound corresponding to the sum of the elements of the other two, as, for example, $C_4H_{10} + C_4H_8$ and C_8H_{18}. The differences here seem to be largely dependent on temperature. At 0° the change from double to single linkage shows a shrinkage; at the boiling-point, a comparatively small increment or decrement in different cases. A similar result is obtained by examining the molecular volume in the olefine series. At 0° the mean difference for CH_2 is 15·9, but the molecular volume for C_nH_{2n} is much larger than n times the mean, whereas at the boiling-point, as already stated (p. 6), they are approximately the same.

Another way of estimating the value of the double bond is to compare the paraffin with the corresponding olefine.

Paraffin.	M. V. at b. p.	Olefine.	M. V. at b. p.	Δ
Butane	96·5	Butylene	89·9	6·6
Pentane	117·8	Amylene	110·2	7·6
Hexane	140·0	Hexylene	132·4	7·6
Heptane	162·6	Heptylene	154·8	7·8
Octane	186·3	Octylene	177·6	8·7

The decrement of 7·6 to 9 would account for the difference of H_2, and hence the value of the double bond is nil.

At the melting-point, on the other hand, a definite contraction for unsaturation is shown among a few of the higher olefines and acetylenes prepared by Krafft,[1] amounting to −2·56 for the olefine linkage and −3·2 for the acetylene linkage.

Ring structure may in the same way be estimated by comparing the values for the paraffins with those of the cycloparaffins at 0°.[2]

Paraffin.	M. V. at 0°.	Cycloparaffin.	M V. at 0°.	Δ
Butane	96·0	Cyclobutane	79·0	17·5
Pentane	112·4	Cyclopentane	91·1	21·3
Hexane	127·2	Cyclohexane	105·2	22·0
Heptane	142·5	Cycloheptane	118·0	24·5
Octane	158·3	Cyclo-octane	130·9	27·4
Nonane	174·3	Cyclononane	159·5	14·8

[1] *Ber.*, 1884, 17, 1371.
[2] Willstätter, *Ber.*, 1907, 40, 3981.

Deducting the value for H_2 (7–9 units) from the differences, it is clear that ring formation is attended by a considerable contraction.

A similar result is obtained by comparing the olefines and cycloparaffins at the boiling-point.

Olefine.	V_m	Δ for Ring.	V_m	Cycloparaffin.
Propylene	66·6	− 6·4	60·2	Cyclopropane
Butylene	88·8	− 8·8	80 0	Cyclobutane
Amylene	110·0	−12·0	98 0	Cyclopentane
Hexylene	132·5	−16·0	116·5	Cyclohexane
Heptylene	154·8	−20·8	134 0	Cycloheptane
Octylene	177·6	−26·4	151·2	Cyclo-octane

The amount of contraction varies with the size of the ring.

In the case of the benzene hydrocarbons the contraction is approximately 15 for each benzene nucleus.

Hydrocarbon.	V_m	$n \times 3{\cdot}7$	Δ
Benzene	96	110	−15
Toluene	118·3	133 2	−15·1
p-Xylene	140 5	155·4	−14·9
Mesitylene	162 8	177·6	−14 8
Naphthalene	147·2	177 6	2×-15 2
Anthracene	195·5	244·2	$3 \times -16{\cdot}2$

From these values Le Bas estimates the value in benzene rings for C = 12·8, H = 3 2, whilst in hydroaromatic compounds the value is increased to H = 4.

Hydrocarbon.	V_m	Δ	V_m	Cycloparaffin.
Benzene	96	20	116	Cyclohexane
Toluene	118·3	23·5	141 8	Methyl Cyclohexane
1.3-Xylene	140	25 1	165·1	1.3-Dimethyl Cyclohexane
1.4- ,,	140	24·6	164·6	1.4- ,, ,,
Pseudocumene	160 9	26 1	187·0	1.2.4-Trimethyl Cyclohexane
Mesitylene	162 8	25·2	187 0	1 3.5- ,, ,,

In calculating the theoretical value of the hydroaromatic hydrocarbons Le Bas ascribes the whole difference between it and the parent hydrocarbon to the additional hydrogen, which is represented by three different values. Thus, in the case of hexahydrotoluene, the calculated value is made up as follows:

C_6H_5-H	96 − 3·2	92·8
H_6	6 × 4	24·0
CH_3	7 × 3·7	25 0[1]
		141·8

[1] The value given by Le Bas for a methyl group in the side-chain is obtained by deducting the V_m for toluene from that of phenyl, viz. 25 5.

Constants for Oxygen. The various constants for oxygen in the hydroxyl, aldehydes and ketones, acids, ethers, and esters, are tabulated by Le Bas as follows:

		Alkyl.	Aryl.
O′	in OH (alcohols and phenols)	6·4	5·6
	in ,, (acids)	7·4	
	in $-OCH_3$	9·1	7 6
	in $-OR$	9·5-11 0	10-11
	in esters	7 4	
O″	in aldehydes and ketones	7·4	
	in acids	12·0	
O⟨		7·4-11	

Constants for other Elements. The values calculated by Le Bas for the halogens are F = 8·7; Cl = 22·1; Br = 27·0; I = 37·0, which do not differ greatly from those previously assigned by Kopp and Thorpe; but they vary with the position of the halogen atom as seen in the table of isomeric compounds. Sulphur is given as ⟩S″ = 25·6; and S″ = 21·6. In the case of the nitrogen compounds Le Bas's values are CN = 30 2; nitrogen 10-11 in the primary amines and 12-15 in the secondary and tertiary amines; but all are subject to variation with environment. Where sulphur and nitrogen form part of a ring there is contraction to the same extent as that in the aromatic hydrocarbons, as seen in the following examples:

Benzene.		Pyridine.	
(6CH) 3·7 × 30	111·0	(5CH) 3·7 × 25	92·5
Benzene V_m	96·0	N	12
Contraction	−15·0		104·5
		Pyridine V_m	89 5
			−15 0

Naphthalene.		Quinoline.	
$C_{10}H_8$ 3·7 × 48	177 6	C_9H_7 3 7 × 43	159·1
Naphthalene V_m	147 2	N	12
	−30·4		171 1
		Quinoline V_m	140 0
			31·1

To attempt, in the present state of our knowledge of molecular volumes, to elucidate structural formulae with any hope of success seems out of the question; but the very fact that the molecular volume is so sensitive to constitutive influences holds out the promise of future utility not possessed to the same degree by any other physical property.

II. MOLECULAR SOLUTION VOLUME[1]

In order to remove the disturbing effects of association or the formation of molecular aggregates, to which the irregularities in molecular volumes have been ascribed, Traube introduced the method of estimating molecular volumes in dilute solution, in which it may be supposed the molecules are present in the unassociated state. If we consider a quantity of solution containing one gram-molecule of dissolved substance, it is evident that the volume occupied by the substance is equal to the volume of the solution less the volume of the solvent, provided (and this is by no means probable) the whole change in volume is due to the solute. This is expressed by the following equation:

$$V_m = \frac{m+l}{d} - \frac{l}{\delta},$$

in which m is the molecular weight in grams of the solute, l the amount of solvent corresponding to the gram-molecule of solute, and d and δ the densities of the solution and solute respectively. It is called the *molecular solution volume*.

If the density of the solvent in the solution is the same as that of the pure solvent, it is clear that the result will give the molecular volume of the substance, and in certain solvents this appears to be the case. As a rule, especially in water, methyl alcohol, &c., there is a considerable contraction on solution.

Traube, in the course of a long investigation in which he determined the molecular solution volumes of a large number of organic compounds (non-electrolytes) in dilute aqueous solution, found that the effect was additive. By the differential method, already described in the foregoing section, for ascertaining atomic volumes, he was able to assign mean values to the atomic solution volumes of the individual elements. These values vary in different compounds according to their manner of combination and the nature of the compound, but the variations, in the case of carbon, hydrogen, oxygen, and the halogens, fall within narrow limits. The following table embodies Traube's results:

	At 15°		At 15°
CH_2	16·1	N‴	1·5
C	9·9	N(CN)	3·3
H	3·1	$N(NO_2)$	8·5–10·7
O′(CO . OH)	0·4	Cyclic formation	−8·1
O′(OH)	2·3	Double bond	−1·7
O″ and O⟨	5·5	Treble bond	−3·4
S (SH)	15·5	Benzene ring	−13·2
Cl, Br, I, CN	13·2	= [−8·1 + (3 × −1·7)]	

[1] I. Traube, Ahrens' *Vorträge*, 1899, 4, 255.

If the value calculated from the atomic volumes for a non-electrolyte in dilute aqueous solution is compared with the observed result, the former is found to be less by a nearly constant amount, namely, 12·4 c.c. For example, the calculated value for methyl alcohol in water is $9{\cdot}9 + (4 \times 3{\cdot}1) + 2{\cdot}3 = 24{\cdot}6$, the observed value is 37, or a difference of 12·4 c.c. This difference is termed by Traube the *molecular co-volume*. The following co-volumes were obtained for a series of alcohols:

	Co-vol.		Co-vol.
Methyl alcohol	12 4	Isoamyl alcohol	12·2
Ethyl ,,	12 1	Allyl ,,	12 7
Propyl ,,	12 4	Ethylene glycol	13 1
Isopropyl ,,	11 9	Glycerol	12 3
Isobutyl ,,	11 9	Erythritol	12 6

If, instead of water, the substance is dissolved in an organic solvent, the observed value for the molecular solution volume approaches more or less closely to that of the molecular volume of the pure substance. As the value is higher, there is consequently less contraction than when dissolved in water. The following examples will make this point clear:

	M S. V.		M. V.
	in water.	in benzene.	
Ethyl alcohol	52 8	58-58·2	58 1
Acetone	65 8	72 7-72·8	72 9
Acetoacetic ester	117 6	124 9-127 3	127 0

As the constants for the elements are calculated with water as solvent, it follows that the co-volume for substances dissolved in organic solvents, or in the pure state, must be greater than 12 4, provided they are not associated in solution. In such cases the co-volume varies between 23 and 27·5 in different classes of compounds.

	at 0°
Paraffins	23 9-25 3
Olefines	25 0-27 6
Aromatic hydrocarbons	23 1-24·4
Esters	22 6-26 8
Alkyl ethers	24·1-27 5

Excluding the lower values, usually given by the initial members of a homologous series, the mean co-volume for the normal hydrocarbons is 24·5 c.c. at 0° and 25 9 c.c. at 15°. In other series where association occurs, especially among hydroxy compounds, lower values are obtained.

The larger total contraction in aqueous solution is ascribed by Traube to two causes. The contraction of 12·4 c.c., which may be taken to be common to all solvents as well as to the pure substances, is supposed to correspond to the factor $v - b$ in van der Waals'

equation, that is, the space in which the molecules move. The additional amount, 13·5, is ascribed by Traube to osmotic pressure in aqueous solution or the attraction of the solute for the solvent.

The value was obtained by comparing the aqueous solution of a very slightly ionised acid with its completely ionised sodium salt. The contraction due to ionisation, i.e. the formation of two ions from one molecule, was 15 c.c., or allowing for the replacement of hydrogen by sodium (1·5) = 13·5 c.c.

This value must therefore be added to the molecular solution co-volume in aqueous solution in order to obtain the molecular co-volume of the pure substance or of its solution in an organic solvent.

The method, although giving fairly concordant results in aqueous solution, shares some of the disadvantages of the molecular volume method, namely, the wide variation in the values of certain elements, according to their environment. In solvents other than water (in which, it may be added, the bulk of organic substances are practically insoluble) the fluctuations are still larger and less trustworthy. Nevertheless, Traube[1] has applied the method with some success to following the dynamic isomerism in tautomeric compounds. The molecular volume of acetoacetic ester was ascertained, as well as its solution volume in various solvents. After an interval of several hours the substance and its solutions were again examined and the changes observed. The calculated molecular solution volume in water for the enol form is 116·1, for the keto form 117·56. The aqueous solution gave 117·16 and, after standing twenty hours, 117 56. The substance is therefore present in the keto form. In most of the other solvents used, excepting chloroform, there was a slight fall in value. In the case of formylphenylacetic ester, the solution in water, methyl alcohol, and acetone showed a diminution in molecular solution volume, that is, a change in the direction of the enol form ($O' = 2\,3$), the solution in ethyl acetate and benzene an increase, or change to the keto form ($O'' = 5{\cdot}5$) (see p. 364).

III. REFRACTIVITY

When a beam of light passes from air into a denser medium it is refracted, and the index of refraction is that number which gives the ratio of the sine of the angle of incidence to that of the angle of

[1] *Ber.*, 1896, 29, 1715.

refraction. If i and r (Fig. 1) are the angles of incidence and refraction, the index of refraction n is given by the expression,

$$n = \frac{\sin i}{\sin r}$$

or if ab and cd are perpendiculars drawn from the ends of the radii ob and oc to the line ad, the above ratio is given by the ratio of the lengths of the lines ab/cd.

This ratio is, in other words, the relative rate at which light travels through the two media. The value for light passing from a vacuum is slightly higher than from air, and the ratio is then called the 'absolute' index of refraction ; but the correction is rarely made.

The index of refraction further depends on the temperature of the

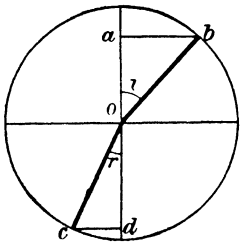


Fig 1.

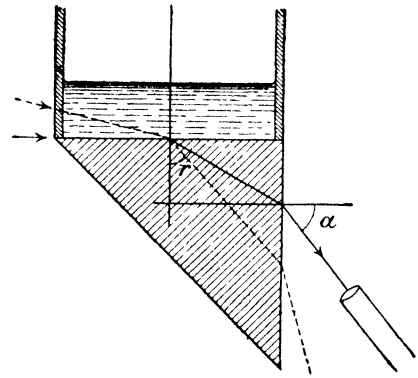


Fig 2.

liquid and on the kind of light, being smallest for the red and largest for the violet of the visible spectrum.

In the Pulfrich refractometer, which is the one commonly employed for delicate measurements, the light is focussed on to the liquid contained in a small glass cylinder cemented on to a carefully ground glass prism, as shown in the diagram, Fig. 2.

The glass, which is a denser medium than the liquid, causes refraction and, if the index of refraction of the glass is known, that of the liquid can be ascertained.

If a beam of light is allowed to enter the liquid at any angle it will be refracted on passing through the prism, as indicated by the dotted lines, and will be refracted a second time on passing into air. The angle which the refracted beam makes with the vertical will increase as the incident beam approaches the horizontal and will reach a maximum when it enters parallel to the interface of liquid

and prism. Beyond that it will undergo total reflection from the under surface of the prism. In the Pulfrich refractometer the source of light is so adjusted as to pass horizontally between liquid and prism and as it emerges is received into a telescope attached to a movable disc furnished with a scale graduated in degrees and minutes and a vernier by which the angle of refraction can be measured.

The index of refraction N of the glass being known, that of the liquid n may be determined as follows: at maximum refraction $\angle a = \angle r$.

$$\frac{N}{n} = \frac{\sin 90^\circ}{\sin r} \quad \text{and} \quad \frac{N}{1} = \frac{\sin a}{\sin (90^\circ - r)}$$

In order to eliminate r, we have

$$\frac{\sin a}{\cos r} = N \quad \text{or} \quad \cos r = \frac{\sin a}{N}$$

$$\cos^2 r + \sin^2 r = 1 \quad \text{and} \quad \sin r = \sqrt{1 - \cos^2 r}$$

$$\sin r = \sqrt{1 - \frac{\sin^2 a}{N^2}}$$

so that

$$n = N \sqrt{1 - \frac{\sin^2 a}{N^2}} = \sqrt{N^2 - \sin^2 a}$$

The value of N is usually furnished with the instrument, and tables are also supplied from which the index of refraction may be directly read off from the observed angle.

As light of different wave length is differently refracted, it is usual to employ monochromatic light of the sodium (Na_D), lithium (Li), or thallium (Tl) spectrum, or the red (H_α), blue (H_β), and violet (H_γ) lines of the hydrogen spectrum of a Geissler tube. The instrument is shown in Fig. 3. It consists of a glass prism, I, which, except on the face nearest the telescope, is enclosed by a metal jacket Above it is, cemented the glass cell containing the liquid under examination.

The light which emerges from the prism enters through a slit in the side of the telescope, where it falls on a reflecting prism, which transmits it parallel to the axis of the telescope to the eyepiece. The telescope E is clamped to a movable and graduated disc D by which the angle of refraction is measured. Other important parts of the instrument are the cooling-jacket S, the arrangement of which is shown in greater detail in Fig. 4, the condenser P for focussing the light, and the fine adjustment G connected with the graduated circle.

Although among organic substances the differences in refractive index fall within comparatively narrow limits (1·3–1·7), it is possible by means of the above instrument to read with accuracy to the fourth decimal. Moreover, estimations may be carried out rapidly with quantities of not more than three grams of material, so that

as far as precision and rapidity of manipulation are concerned, the method leaves little to be desired.

As the refractive index is largely influenced by density, it is necessary to find an expression which will eliminate this variable factor. By dividing by the density (water being taken at 4°) the masses of different substances in unit volume will become equal, and by further deducting the constant, unity, for the refractive index of air, the following expression is obtained: $r = \frac{n-1}{d}$.

The expression actually represents how much the refractive index of different materials of unit concentration is greater than unity. It was deduced empirically by Gladstone and Dale[1] from observations begun in 1858, and is termed *specific refractive index* or *specific refractivity*. It is indicated by the letter *r*.

A second formula, based on Maxwell's electromagnetic theory of light, was proposed simultaneously by H. A. Lorentz of Leyden and L. Lorenz of Copenhagen in 1880[2]: $r = \frac{n^2-1}{n^2+2} \cdot \frac{1}{d}$.

What is known as the molecular refractivity is obtained by multiplying the specific refractivity by the molecular weight (m) of the substance. The above two formulae will then become

$$M = \frac{n-1}{d} \cdot m, \text{ and } M = \frac{n^2-1}{n^2+2} \cdot \frac{m}{d}.$$

No definite conclusion has been reached as to which of the two expressions is the more trustworthy. Although English chemists as a rule employ the Gladstone-Dale or n formula, modern investigators on the Continent, where the bulk of the work in recent years has been carried out, adopt the Lorentz-Lorenz or n^2 formula.[3] On account of the preponderating amount of data which are calculated from the n^2 formula and to avoid the confusion which might arise by introducing two sets of figures, we have used this formula throughout. Moreover, it is claimed that the n^2 formula is independent of temperature, pressure, and state of aggregation. Whichever formula is used the temperature correction is so small as to be

[1] *Phil. Trans.*, 1858, 148, 887; 1863, 153, 323.

[2] See Nernst, *Theoretical Chemistry*, 6th edition, p. 311. Macmillan.

[3] Eisenlohr (*Spektrochemie organischer Verbindungen*, 1912, p. 12) has introduced a different system of estimating molecular refractivities, namely by multiplying the refractive index by the molecular weight or $M \times n_D^{20}$ which he terms the 'molecular refractive coefficient'. The method of estimating the numerical values of the different elements is the same as that adopted by previous observers, and in several papers he has recalculated the values according to the new formula (*Ber.*, 1920, 53, 1746, 2053; 1921, 54, 299). He claims for the new formula a more delicate means of determining molecular structure (*Ber*, 1921, 54, 319). The differences between the observed and calculated (or E) values, according to Eisenlohr, 'afford a sharp instrument for piercing the structure of the molecule and offer an invaluable criterion of the purity of the substances under observation'. These views have been criticised by K. v. Auwers (*Ber.*, 1922, 55, 21).

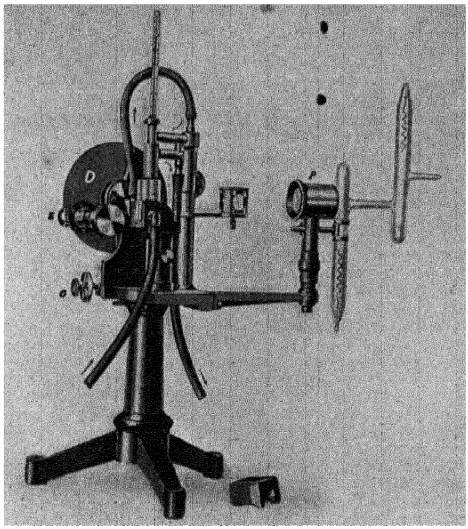


FIG 3

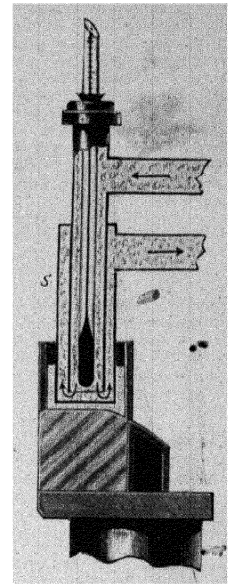


FIG 4.

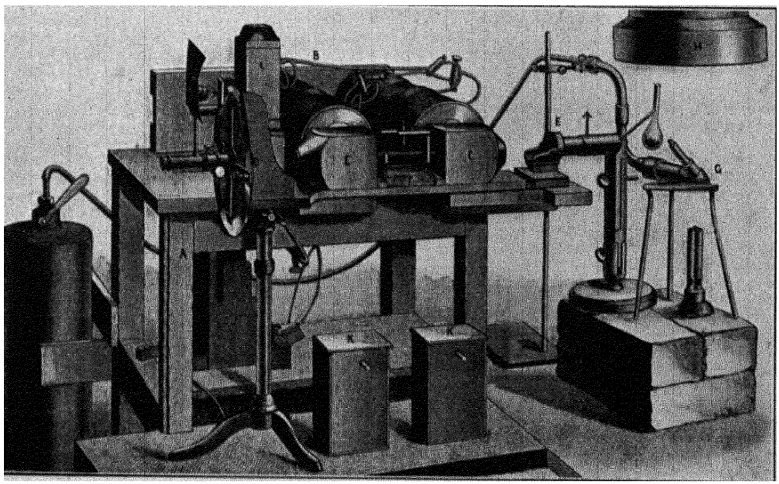


FIG 5

negligible, provided of course that the density of the substance under observation is accurately known.[1] The specific and molecular refractivities for different wave lengths are indicated by writing the symbol for the spectrum line below that of the element or M; thus H_α, Na_D, M_α, M_D, &c., represent the specific and molecular refractivities of the hydrogen α line and sodium D line. With a refractivity reading to the fourth decimal, the error in the molecular refraction of substance of molecular weight about 100 will lie within $\pm$ 0·2.

Although a few early observations on the refractivity of organic compounds have been recorded at different times, the first systematic study of the subject was begun by Gladstone and Dale, who published their first paper in 1858 and supplemented it by a more elaborate contribution in 1863.[2]

They determined the refractivity of a certain number of homologous and isomeric substances and showed that, if in a series of isomeric substances the mode of combination is the same, the refractivities are identical. 'Every liquid has a specific refractive energy composed of the specific refractive energies of its component elements modified by the manner of combination and which is unaffected by change of temperature.' They thus discovered the effect of constitutive differences. In the following year, Landolt[3] published a series of very accurate determinations in which the views of Gladstone and Dale on the refractive identity of isomeric fatty acids and esters were confirmed, and from his results the refractive values for carbon, hydrogen, and oxygen were estimated. Gladstone[4] in a later paper showed that elements having a 'lower atomicity' or, in other words, unsaturated atoms, possess a higher refractivity than when saturated. Since 1880 the subject, more especially on its constitutive side, has been actively developed by J. W. Brühl, who has added largely to the material collected by the first observers and has applied it to the study of many structural problems, which will be presently discussed.

In the following pages we have reproduced only such experimental data as serve the purpose of useful illustration. The values for the atomic refractivities have been collected and tabulated by Brühl[5] from observations of Landolt, Kannonikoff, and himself.

Isomeric Compounds. It has already been stated that among

[1] *Phil Trans.*, 1863, 153, 323.
[2] *Phil. Trans.*, 1858, 148, 8; 1863, 153, 323.
[3] Pogg., *Annalen*, 1864, 123, 595.
[4] *Trans. Chem. Soc.*, 1870, 23, 147.
[5] *Zeit. physik. Chem.*, 1891, 7, 140.

similarly constituted isomers, the refractivities were found to be identical.[1] The following table will illustrate this point and will at the same time indicate the kind of magnitudes which are obtained. The second column gives the specific refractivities for H_α. The figures in the third column are obtained by multiplying these numbers by the molecular weights, and therefore any error in the specific refractivity will vary in proportion to the molecular weight. The figures in the fourth column are differences in the molecular refractivities of the red H_α and violet H_γ lines in the hydrogen spectrum and give the amount of molecular dispersion, to which reference will be made later (p. 41).

	H_α	M_α	$M_\gamma - M_\alpha$
Propyl alcohol	0 2903	17·42	0 41
Isopropyl alcohol	0 2907	17 44	0·42
Propyl aldehyde	0 2747	15·93	0·41
Acetone	0 2767	16 05	0 43
Propionic acid	0 2354	17 42	0 42
Methyl acetate	0 2437	18·03	0 44
Ethyl formate	0 2423	17 93	0 44
Butyl alcohol	0 2974	22 01	0 52
Isobutyl alcohol	0 2967	21·96	0 51
Trimethyl carbinol	0 2985	22·09	0 53
Ethyl ether	0·3015	22 31	0 55
Butyl iodide	0·1807	33·25	1 26
Isobutyl iodide	0 1807	33 25	1·26
Isocaproic acid	0 2691	31·22	0·77
Isoamyl formate	0 2729	31 66	0 77
Ethyl butyrate	0 2690	31·20	0 75
Methyl isovalerate	0·2712	31·46	0 78
o-Xylene	0 3350	35 51	1·52
m-Xylene	0 3370	35·73	1 54
p Xylene	0 3368	35 70	1·56
Ethyl benzene	0 3343	35·44	1·50
Pseudocumene	0 3363	40 35	1 69
Mesitylene	0·3361	40 33	1·63

Stereoisomers. From the identity in the refractivities of isomeric compounds of such different characters as esters and acids, or alcohols and ethers, it seems improbable that spatial differences would assert themselves in a more conspicuous fashion. Nevertheless small differences have been observed among geometrical isomers though not among optical isomers. Maleic and fumaric acids according to Brühl show a difference of 0 67 units, and allocinnamic and cinnamic acid of 1·1 units in the molecular refractivity. In both cases it is the trans form which has the higher refractivity.

Another example is that of the isomeric dibenzoylethylenes, the cis form giving $M_\alpha = 74$ and the trans $M_\alpha = 71{\cdot}8$, a fact which has

[1] Brühl, *J. prakt. Chem.*, 1894. 50. 152.

been explained by a tendency for the cis modification to pass into the peroxide form.[1]

Homologous Series (constant for CH_2). The value of CH_2 has been determined from the molecular refractivities of a number of homologous series comprising 130 compounds. In each case the value for each series was obtained by Brühl by subtracting the first term from the last of the series, the first but one from the last but one, and so on, and then multiplying each of these differences by the number of CH_2 groups included between the selected members. The sum of the resulting numbers was then divided by the total number of CH_2 groups present. The same method was applied to other series. In this way it was assumed that the proper weight was given to the experimental values in the different series.[2]

	Number in series.	H_α	Na_D	H_β	H_γ	$H_\beta - H_\alpha$	$H_\gamma - H_\alpha$	
Hydrocarbons	66	4·60	4 62	4·67	4·72	0·072	0·118	
Aldehydes and ketones	92	4·60	4 62	4·67	4·71	0·069	0·112	
Acids	74	4 59	4·61	4 66	4·71	0 071	0 115	
Alcohols	81	4 61	4·63	4·68	4·72	0 070	0 112	
Esters	190	4 58	4·60	4 65	4 69	0 069	0·111	
	503	4·59	4 62	4 66	4·71	0 071	0·113	Mean

The mean value obtained for CH_2 (H_α) by Brühl was 4·57, that previously found by Landolt[3] from a smaller number of observations was 4·56, whilst the recalculated value obtained by Eisenlohr is 4·59. Although these numbers are in substantial agreement, and the values in the different series only fluctuate between 4·58 and 4 61, individual observations from which the above are taken show differences which lie much wider apart, namely, between 4·11 and 4·86. These fluctuations are not due to errors of observation in the specific refractivities, which can be determined with accuracy to the fourth decimal and would, therefore, not affect the first decimal in the molecular refractivity with a molecular weight up to 200. The differences must, then, be due either to impurities in some of the compounds examined, which might have a marked effect on the refractivities, or to the structural environment of the groups in

[1] Smedley, *Trans. Chem Soc.*, 1909, 95, 266.

[2] The values given by Brühl (*J prakt Chem.*, 1894, 50, 154) were recalculated by Eisenlohr (*Zeit. phys. Chem.*, 1910, 75, 585) and are given in the above table. The refractivities for the complete set of wave lengths have been estimated by interpolation where any have been omitted.

[3] *Annalen*, 1882, 213, 75.

question. Brühl and Wallach have indeed suggested that there are small structural differences peculiar to each compound which affect each atom in the molecule. It has also been pointed out by Landolt[1] and Eykman[2] that there exist certain irregularities among the initial members of a homologous series, but, seeing that these values are lower than the mean, it would not account for the higher abnormal values in certain series.

The Constants for Carbon, Hydrogen, and Oxygen. The value for doubly linked oxygen (O″) was obtained by deducting the calculated value for $(CH_2)n$ from a series of aldehydes and ketones which gave a mean of 2·32. The value for hydroxyl oxygen (O′) was determined by the difference between aldehydes and acids, mono- and poly-hydric alcohols, and also between acids and hydroxy acids. The mean in this case was 1·50. It will be noticed that the increment for the doubly linked oxygen is placed to the account of the oxygen atom exclusively, and not to the double bond, as in the case of the ethenoid linkage to be presently referred to. The constant for ester oxygen (O〈) was derived from the observed value for the aliphatic esters by deducting the calculated value for $n(CH_2)O''$ and gives a mean of 1 65. The constant for hydrogen was obtained by deducting the calculated values for $n(CH_2)O'$ from alcohols, $n(CH_2)O〈$ from esters, or $n(CH_2)$ from paraffins. The mean for H_2 is 2 2, and by deducting this number from the value for the CH_2 group (4·57) that of carbon, 2·37, is obtained.

Constant for the Double Bond (C=C). Unsaturation, as Gladstone first pointed out, raises the refractivity. By deducting the constant for saturated carbon from the observed value, Brühl and Conrady were able to assign a value to the double bond (|=|) which varied in different compounds from 1·63 to 2·17, the mean being 1·83. The variation is larger than that observed in the case of carbon, hydrogen, and oxygen, and, according to Eykman,[3] increases with the number of radicals attached to the doubly linked carbon atoms, which he determined as follows:

No radicals (ethylene)	1·51
One radical ($R\ CH\ CH_2$)	1 60
Two radicals ($RCH\ CHR$)	1·75
Three radicals ($R_2C\ CHR$)	1 88
Four radicals ($R_2C.CR_2$)	2·00 (*circa*)

[1] Pogg., *Annalen*, 1864, 123, 595

[2] *Rec. Trav. Chim. Pays-Bas*, 1893, 12, 160, 248; 1894, 13, 13; 1895, 14, 185; 1896, 15, 32.

[3] *Weekblad*, 1906, 3, 706.

The data available for the treble linkage are few, and the results show a wide divergence, the mean being fixed by Moureu[1] at about 2·49.

Constant for the Halogens. The refractivities of other elements have been determined in the same manner as those already discussed, namely, by estimating differences between the observed refractivity and that calculated or observed for the unsubstituted compound.

Generally speaking, the univalent elements (the halogens) show the most constant, whilst among multivalent elements (nitrogen, sulphur) the amount of variation admits of no definite constant being assigned, the value changing considerably in different classes of compounds. Even in the case of chlorine there is a certain amount of fluctuation, which appears to depend not only on the presence of the halogen atom but also on its environment.

The following table gives a list of the refractivity constants of the commoner elements for the H_α and Na_D lines, and also the maximum and minimum deviations determined for the H_α line. The second table gives Eisenlohr's recalculations along with the interpolated values for the H_β and H_γ lines and the dispersivities for $H_\beta - H_\alpha$ and $H_\gamma - H_\alpha$.[2]

Element	H_α (Brühl)	Na_D (Conrady)	Maxima and Minima H_α
Carbon C	2·37	2·50	2·31 — 2·47
Hydrogen H	1·10	1·05	1·03 — 1·15
Oxygen O′	1·70	1·52	1·38 — 1·62
,, O<	1·65	1·68	1·50 — 1·99
,, O″	2·32	2·28	2·21 — 2·51
Chlorine Cl	6·01	5·99	5·62 — 6·37
Bromine Br	8·86	8·92	8·64 — 9·06
Iodine I	13·80	14·12	13·58 — 13·91
Double bond |=	1·83	1·70	1·63 — 2·17
Treble bond |≡	2·49	2·10	2·00 — 2·60 (*circa*)

Element.	H_α	Na_D	H_β	H_γ	$H_\beta - H_\alpha$	$H_\gamma - H_\alpha$
Carbon C	2·41	2·42	2·44	2·46	0·025	0·056
Hydrogen H	1·09	1·00	1·11	1·12	0·023	0·029
Oxygen O′	1·52	1·52	1·53	1·54	0·006	0·015
,, O<	1·64	1·64	1·65	1·66	0·012	0·019
,, O″	2·18	2·21	2·24	2·26	0·057	0·078
Chlorine Cl	5·93	5·96	6·04	6·10	0·107	0·168
Bromine Br	8·80	8·86	9·00	9·15	0·211	0·340
Iodine I	13·75	13·90	14·22	14·52	0·482	0·775
Double bond |=	1·68	1·73	1·82	1·89	0·138	0·200
Treble bond |≡	2·33	2·40	2·50	2·53	0·139	0·171

It will be seen that the differences between the recalculated values and those given by Brühl and Conrady are in most cases inconsiderable.

[1] *Ann. Chim. Phys.*, 1906 (8), 7, 536.
[2] *Zeit. physik. Chem.*, 1910, 75, 585.

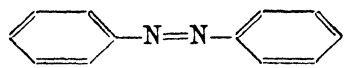
Constants for Nitrogen and Sulphur. The values for nitrogen have been determined by Brühl,[1] who, from an enormous mass of material, has compiled the following constants for nitrogen in different classes of compounds:

Group.	H_α	Na_D	Max. and Min. H_α
Hydroxylamines	2·33	2·48	3 examples
Hydrazines	2 32	2·47	2 17—2 45
Primary amines	2 31	2 45	2·19—2 45
Secondary ,,	2 60	2 65	2 40—2 83
Tertiary ,,	2 92	3 00	2 71—2 88
Prim. arom. amines	3 01	3 21	2 98—3·12
Second. ,, ,,	3 40	3 59	2 25—3·47
Tert ,, ,,	4 10	4 36	3·19—4 41
Aliph. nitriles	3 17	3 05	3 01—3 38
Arom. ,,	3 82	3·79	3 79—3 91
Aliph. oximes	3 92	3 93	3·79—4 10
Arom. ,,	—	—	4·68—5·86
Formamide	2 54	2 65 ?	—
Second. amides	2 23	2 27	2·10 2 38
Tert. ,,	2 63	2 71	2 38—2 87

For the groups containing nitrogen in different forms of combination the following values were obtained:[2]

Nitro group. NO_2	H_α	Na_D	Max. and Min. H_α
Alkyl nitrates	7 55	7 59	7 46—7 58
,, nitrites	7 37	7 44	7 28—7 48
Nitroparaffins	6 65	6 72	6 48—6 77
Arom. nitro-compounds	7 16	7 30	7 09—7 25
Nitramines, 1ary and 2ary	7 16	7 51	7·10—7 60
Nitroso group NO			
Nitrosamines	5 37	5·37	5 21—5 55
Nitrites	5 91	5 91	3 examples
Diazo group.			
	8·41	8 43	
	7 52	7 47	

The molecular refractivity of the azo group, according to Duval,[3] shows a constant increment above the calculated value of about 12 units for the lithium line, which he ascribes to the recurrent series of double bonds, producing, as they are known to do, an increase or exaltation in the value (see p. 29).



The values for sulphur depend, like those of nitrogen, on its mode

[1] *Zeit. physik. Chem.*, 1895, 16, 479; 1912, 79, 1.
[2] *Zeit. physik. Chem.*, 1898, 25, 647. [3] *Bull. Soc. Chim.*, 1912 (4), 17

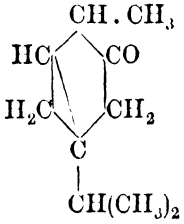
of combination, and show wide divergence. Nasini [1] has accumulated a certain amount of data by examining aliphatic mercaptans and sulphides, from which he derived the constant for S′, $H_\alpha = 7{\cdot}87$, and carbon bisulphide, which gave for S″ the value $H_\alpha = 9\ 02$. More recently Price and Twiss [2] have made some fresh observations and recalculated the values obtained by Nasini and others. They give the following values to sulphur :

Group.	H_α	N_{a_D}	H_β	H_γ	$H_\beta - H$	$H_\gamma - H_\alpha$
In mercaptans	7 63	7 69	7 83	7 98	0 20	0 35
,, sulphides	7·85	7 97	8·13	8 28	0 28	0·43
,, thiocyanates	7·85	7 91	8 08	—	0 23	—
,, disulphides	8·05	8 11	8·28	—	0 23	—

In xanthates, thiol carbamates, and other groups in which doubly linked sulphur occurs, the constant is much higher.

Ring Formation. The influence of simple ring formation in saturated hydroaromatic compounds is so small as to lie within errors of observation, at least among the members containing more than five carbon atoms in the ring. This view, which was advanced by Brühl, has since been confirmed by Auwers,[3] who, from a comparison of a large number of open-chain with corresponding closed-chain structures, concludes that the closing of a chain does not affect the refractivity or dispersivity of hydroaromatic compounds. Cyclopropane, cyclobutane, and their derivatives exhibit a slight increase above the calculated value, varying from 0·48 to 1·24 units, as shown by Tschugaeff,[4] who has utilised this fact in order to establish the bicyclic structure of thujone and its derivatives, which show a steady difference of about $M_D = 0\ 67$.

Thujone.



M_D obs.	44·78
calc.	44 11
	+ 0·67

Oestling [5] from a larger number of data has found nearly the same increase in value for the cyclopropane compounds, namely,

[1] *Ber.*, 1882, 15, 2888. [2] *Trans. Chem. Soc*, 1912, 101, 1259.
[3] *Annalen*, 1915, 410, 287; 1918, 415, 98; 1920, 420, 84
[4] *Ber.*, 1900, 33, 3125. [5] *Trans. Chem. Soc.*, 1912, 101, 467.

$M_D = 0{\cdot}71$, and for cyclobutane derivatives, $M_D = 0{\cdot}48$. An increase of the same order has also been observed by Semmler[1] in the case of sabinene and other bicyclic structures.

Aromatic Compounds. Benzene and its simpler derivatives give normal values when calculated on the basis of three ethenoid linkages.

Substance.	M_α obs.	M_α calc.	$M_\gamma - M_\alpha$
Benzene	25 93	26 25	1·18
Toluene	30 79	30 89	1 36
Ethyl benzene	35 44	35 37	1·50
Phenol	27·75	27·82	1 30
Benzyl alcohol	32 23	32 31	1 37
Chlorobenzene	30·90	31·22	—

Auwers[2] has studied the effect of alkyl groups on aromatic aldehydes, ketones, and esters, and has shown that a methyl or methoxy group produces marked exaltation in the para as compared with the ortho and meta positions, and that in consequence para derivatives may be readily distinguished in this manner.

Some of the more complex hydrocarbons give values much in excess of the theoretical.[3]

	M_α obs.	M_α calc.	Δ
Naphthalene	44 29	41 65	2 64
Anthracene	59 7	56·98	2 72
Phenanthrene	62 7	56·99	5·70

[1] *Ber.*, 1907, 40, 1120.

[2] *Annalen*, 1915, 408, 212.

[3] v Steiger (*Ber.*, 1921, 54, 1381; 1922, 55, 1968) has attempted to account for certain discrepancies between the observed and calculated values for molecular refractivities among aromatic compounds by a process which he has applied to the determination of heats of formation of C—C and C—H linkages in aromatic hydrocarbons (see p. 72) and which is based on Thiele's view of the structure of benzene, Debye and Scherrer's theory of the relation of graphite to benzene, and the different values of the C—C and C—H linkages in the aliphatic and aromatic series. By a process of deducting the molecular refractivity of one aromatic carbon compound from another, it is possible to arrive at a refractive value for the C—C and C—H linkages which are estimated at C—C = 2·96 and C—H = 1 39 for the D line, values which differ, as do the thermal values, from the refractivity of the corresponding aliphatic linkages and agree better with the observed values. The following are some of the observed and calculated values according to v. Steiger and Brühl.

	Found.	v. Steiger	Brühl.
Benzene	26 13	26·10	26 31
Diphenyl	52·38	52·38	50·41
Naphthalene	44·29	43·68	41·65
Phenanthrene	62·7	61·26	56·98
Anthracene	59·7		

Optical Anomaly. Brühl's value for the ethenoid linkage was based upon the refractivity of compounds containing one or two pairs of double bonds; but he has since made it abundantly evident that the relative position of the double bonds, where more than one pair is present, greatly influences the result.[1] This applies not only to pairs of ethenoid linkages, but to combinations of ethenoid and carboxyl linkages. Where they occur in juxtaposition or are *conjugated* (Part I, p. 145) they reinforce or exalt one another, raising the refractivity and producing what has been termed *optical anomaly* or *exaltation*. Where they possess a carbon atom in common, C : C : C, or are *cumulated*, or when separated or *isolated*, they give normal or nearly normal results, and the same is true of compounds with three isolated double bonds.[2] The following examples will illustrate the points referred to:

	M_α		EM_α
	obs.	calc.	
Diallyl $CH_2:CH.CH_2.CH_2.CH:CH_2$ (isolated)	28 77	28 89	−0·12
Valerylene $(CH_3)_2C:C:CH_2$ (cumulated)	24 34	24 39	−0 05
Isodiallyl $CH_3.CH:CH.CH:CH_2$ (conjugated)	29 87	28 89	+0 98
Hexatriene $CH_2:CH.CH:CH.CH:CH_2$ (twice conjugated)	30 58	28·52	+2 06

The difference between diallyl and isodiallyl is very striking, and still more that between diallyl and hexatriene.

A combination of isolated and conjugated ethenoid linkages and carbonyl groups produces a similar effect.

	M_α		EM_α
	obs.	calc.	
Crotonaldehyde $CH_3.CH:CH.CH:O$	21 29	20 24	+1 05
Mesityl oxide $(CH_3)_2C:CH.C(CH_3):O$	30 13	29 39	+0 74

That such anomalies occur is not altogether surprising in view of the chemical peculiarities of conjugated systems, to which attention has already been drawn. A similar effect of conjugation has been observed in the magnetic rotation, which also exhibits exaltation (p. 54).

No anomaly has been noticed where carbonyl groups are asso-

[1] *Ber*, 1907, 40, 878; 1908, 41, 3712.

[2] Auwers and Moosbrugger, *Annalen*, 1912, 387, 167.

[3] As exaltation is a differential effect and has no fixed value, Auwers calculates the difference on the specific refractivity × 100 in place of the difference in molecular refractivity, which changes with the molecular weight. The former is called the *specific exaltation* to distinguish it from the latter or *molecular exaltation*, and the two are denoted by the symbols $E\Sigma$ (specific) and EM (molecular) respectively. We have, as a rule, given the molecular exaltation.

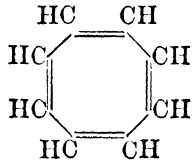
ciated,[1] but pairs of trebly linked or doubly and trebly linked atoms show exaltation as in the preceding examples.[2]

	M_a obs	M_a calc.	EM_a
Amylpropionitrile $C_5H_{11}C.C:N$	38·40	36 71	+1 69
Cyanogen C N C N	12 26	11·08	+1·18
Ethyl propiolate $CH{\cdot}C.C.O.OC_2H_5$	25·12	24 62	+0 50

If, on the other hand, the multiple bonds are isolated, the value is normal.

	M_a obs	M_a calc.	EM_a
Ethyl acetylene propionate $CH:CH.CH_2.CH_2.C\ O.OC_2H_5$	33 82	33·79	+0·03

Turning now to the aromatic compounds, optical anomaly has not been observed in benzene nor among its simpler derivatives (p. 28). It is certainly remarkable that the exaltation exhibited by hexatriene and still more by methyl heptatriene and methyloctatriene[3] should not have been reproduced in benzene, and although the normal value for the three double bonds in benzene was originally cited in favour of Kekulé's formula for that substance, the discovery of the phenomenon of exaltation tended at one time to throw the weight of evidence into the opposite scale, that is, in support of the centric formula.[4] But Willstätter's later discovery[5] that cyclo-octatetrene, in spite of normal refractivity, contains four true ethenoid linkages must neutralise to some extent the effect of the previous observations. Auwers[6] concludes from a large mass of data in which unsaturated open-chain compounds are compared with similarly constituted closed-chain structures that, 'as far as spectrochemistry can give an answer to the question (favouring the centric formula), it must be in the negative. It has been shown that benzene is optically no exceptional phenomenon, but is a special case of a general law, and is connected in many ways with other ring structures which assuredly contain no centric bonds.'



Cyclo-octatetrene.

[1] This may be due to the fact that the simplest compounds of this type, such as glyoxal and dimethylglyoxal, are too unstable to be investigated, and the refractivities of bodies like oxalic acid are modified by the influence of adjoining groups.

[2] Brühl, *Ber.*, 1907, 40, 1153.

[3] *Annalen*, 1918, 415, 129.

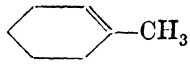
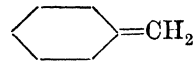
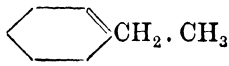
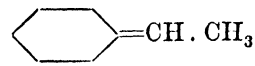
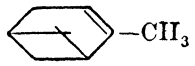
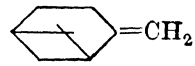
[4] Smedley, *Trans. Chem. Soc.*, 1908, 93, 383.

[5] Willstätter, *Ber.*, 1911, 44, 3428; 1913, 46, 523

[6] *Annalen*, 1918, 415, 139; Eisenlohr, *Spektrochemie*, 1912, p. 107.

Exaltation, however, asserts itself where conjugation of the aliphatic type exists either in relation to nucleus or side-chain, and then with increased effect the greater the number of double bonds and the closer their proximity to the nucleus.

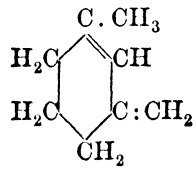
In the first place a double bond has a greater value outside than within the nucleus.[1]

			M_D calc.	EM_D
				
M_D	31.8	32.26	31.83	+0.43
				
M_D	36.52	36 82	36.43	+0.39
				
M_D	43 86	44 01	43 63	+0.38

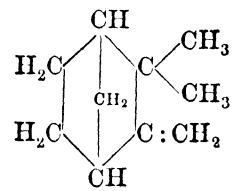
The value is also greater the nearer the double bond lies to the nucleus.

	M_D obs.	M_D calc.	EM_D
Eugenole $CH_3O.C_6H_4.CH_2\ CH\cdot CH_2$	48 2	47·7	+0 5
Isoeugenole $CH_3O\ C_6H_4.CH:CH\ CH_3$	49 2	47 7	+1 5
Safrole $CH_2O_2\ C_6H_3\ CH_2\ CH\ CH_2$	45 9	45·8	+0 1
Isosafrole $CH_2O_2\ C_6H_3\ CH:CH.CH_3$	47 6	45 8	+1 8

The formula originally assigned by Klages to dihydro-*m*-xylene, in which both double bonds were placed in the nucleus, has been modified in consequence of its abnormally high refractivity, one ethenoid linkage being transferred to the side-chain. The view has since proved to be correct on chemical grounds.



Dihydro-*m*-xylene.

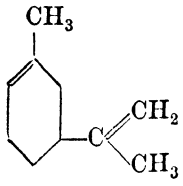


Camphene.

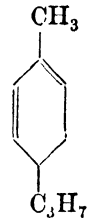
For similar reasons Auwers has suggested the above formula for camphene.

[1] Wallach, *Annalen*, 1908, 360, 34; Auwers and Ellinger, *Annalen*, 1912, 387, 200; Nasini, *Gazz. chem.*, 1884, 14, 150; 1885, 15, 59; 1890, 20, 356.

Among the hydraromatic compounds of established purity, sylvestrene and phellandrene (Part III, pp. 217, 215) afford an interesting comparison, for the former with its isolated double bonds shows a normal result, whereas the latter exhibits exaltation.[1]



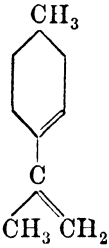
Sylvestrene.
$M_\alpha = 45{\cdot}07$



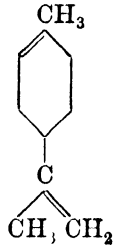
α-Phellandrene.
$M_\alpha = 45{\cdot}35$

Calc. M_α
$C_{10}H_{16}|=_2 = 44\ 97$

One more example must suffice. Perkin[2] has determined the refractivities of $\Delta^{3\,8(9)}$ menthadiene and of dipentene as follows:

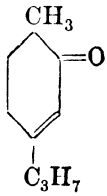


Menthadiene.
$M_\alpha = 46\ 02$

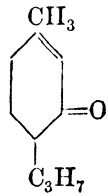


Dipentene.
$M_\alpha = 45{\cdot}23$

Hydraromatic ketones also show exaltation, as seen in the following examples, both of which contain a conjugated system.



Carvenone.
$M_\alpha = 46{\cdot}52$



Menthenone.
$M_\alpha = 46{\cdot}78$

Calc. $M_\alpha = 45{\cdot}82$

Finally, both the value of the single ethenoid linkage as well as systems conjugated in the side-chain seem to be enhanced by the proximity of the benzene nucleus, in illustration of which the following examples must suffice.[3]

[1] Auwers and Eisenlohr, *J. prakt. Chem*, 1910, 82, 105.
[2] *Trans. Chem. Soc*, 1906, 89, 814.
[3] It should be observed that the fact of exaltation being produced by the

	M_α obs.	M_α calc.	EM_α
Styrene $C_6H_5 \cdot CH \cdot CH_2$	35 98	35 08	+ 0 90
Phenylbutadiene $C_6H_5 . CH \cdot CH . CH : CH_2$	48 00	42 86	+ 5 16
Stilbene $C_6H_5 \cdot CH : CH . C_6H_5$	65 65	59 20	+ 6·45
Diphenylbutadiene $C_6H_5 . CH : CH . CH : CH . C_6H_5$	82·90	68 00	+ 14 90
Diphenylhexatriene $C_6H_5 . CH \cdot CH . CH : CH \cdot CH \cdot CH \cdot C_6H_5$	100·90	76·74	+ 24 16
Diphenyldiacetylene $C_6H_5 . C \cdot C \cdot C : C . C_6H_5$	74·86	64·86	+ 10 00

	M_α obs.	M_α calc.	EM_D
Benzaldehyde $C_6H_5CH : O$	31 77	31 01	+ 0·76
Cinnamic aldehyde $C_6H_5CH \cdot CH \cdot CH . O$	43 51	39·78	+ 3·73
Phenylpropiolic aldehyde $C_6H_5C \cdot C . CH : O$	41 50	38 22	+ 3 28
Cinnamylidene acetic acid $C_6H_5CH : CH . CH : CH \cdot C \cdot O . OH$	60 42	50 06	+ 10 36

From an examination of a series of unsaturated amino compounds and amides containing the group $\rangle N . C : O$, and a few unsaturated sulphur and chlorine derivatives, Eisenlohr[1] has expressed the view that elements possessing residual valency such as the halogens, nitrogen, sulphur, and phosphorus may produce exaltation when conjugated with a double bond. In a recent paper on the refractivities of aliphatic sulphur compounds, Price and Twiss[2] have arrived at the same conclusion.

Modified Optical Anomaly. It has been shown in the foregoing paragraphs that conjugation is consistently accompanied by an increase in refractivity. Brühl, indeed, went so far as to estimate the approximate value for conjugated double bonds. Semmler has adopted the same view. In *Die ätherischen Oele*, p. 67, he has laid down the rule that 'if we find the calculated molecular refractivity to agree with that observed, a terpene is present in which carbon and carbon are singly linked. This can only occur in the case of a terpene, $C_{10}H_{16}$, which is tricyclic, i.e. contains two bridged rings. If there is an increment of 1·7, a cyclic terpene with one bridge and one ethylene bond is present, as for example in pinene. If there is an increment of $2 \times 1{\cdot}7$ it indicates a monocyclic terpene without a bridged ring, but with two ethenoid linkages, as in limonene, phellandrene, &c. If again the increment is $3 \times 1{\cdot}7$ a terpene must be present with three ethenoid linkages, i.e. an olefinic terpene such as myrcene. If oxygen is present and the nature of the oxygen determined chemically, the presence or not of one or more double bonds can be ascertained in

proximity of a double link in the side chain of a benzene derivative may be taken as affording evidence in favour of Kekulé's formula for benzene, since it presupposes double bonds in the nucleus

[1] *Ber*, 1911, 44, 3188 [2] *Trans*, 1912, 101, 1259.

the same way. Borneol, terpineol, and geraniol can thus be distinguished.' We shall see presently that although optical anomaly may indicate roughly the structure of a terpene, such as Semmler suggests, no such definite rules, as he applies, can be laid down, and the above statement in the light of more recent research must undergo considerable modification.

Auwers and Eisenlohr[1] have shown by many examples that 'every disturbance (*Störung*) of the conjugation by substituents diminishes the exaltation'. The phenomenon is, in short, an extension of Eykman's observations on the change in value of a single ethenoid bond produced by the presence of certain radicals (p. 24). But the effect on a conjugated system is not restricted to alkyl groups. It is also produced by hydroxyl, methoxyl, and ethoxyl groups. These authors conclude that 'a sharp line cannot be drawn between normal and abnormal compounds, but that there is a gradual transition from one to the other. For in the application of chemistry to the determination of structure this point must be observed if errors are to be avoided.' The following examples, drawn from open-chain and cyclic compounds, have been selected to show the influence of the methyl group in producing what Auwers and Eisenlohr term *Störung*, or diminution of the exaltation. The radicals which are attached to the carbon atoms indicated by thick type produce the largest effect.

Substance.	Formula.	EM_α
Hexadiene	$CH_3 . CH : \mathbf{CH} . \mathbf{CH} . CH . CH_3$	+1·49
Diisopropenyl	$CH_2 : \mathbf{C}(CH_3) . \mathbf{C}(CH_3) : CH_2$	+0 60
Styrene		+0 84
β-Methylstyrene		+1 01
α-Methylstyrene		+0 45
Benzaldehyde		+0·73
Acetophenone		+0·41

In later papers Auwers[2] has shown that by replacing the alkyl group in methylstyrene in the β position by alkoxyl, the exaltation in refractivity is raised 60–70 per cent, whereas if the α position is substituted the refractivity is scarcely affected. Of the oxy-radicals,

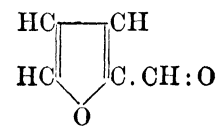
[1] *Ber.*, 1910, **43**, 806; *J. prakt Chem*, 1910, **82**, 65; see also Eisenlohr, *Jahrb. der Radioaktivität*, 1912, **9**, 333; Auwers and Westermann, *Ber.*, 1921, **54**, 2999.
[2] *Ber.*, 1911, **44**, 3514; 1912, **45**, 2764; *Annalen*, 1917, **415**, 169.

hydroxyl has the greatest effect, then alkoxyl, and finally acyloxyl, if the acyl radical belongs to a fatty acid. The depression (*Störung*) caused in $\alpha\beta$-dimethyl crotonic ester,

$$CH_3 . C=C-C=O$$
$$\quad\quad |\quad\quad |\quad\quad |$$
$$\quad\quad CH_3\ CH_3\ OC_2H_5$$

by the attachment of the methyl groups to the ethenoid carbon atoms has been found to eliminate the whole exaltation, and the value in this case is normal.

Optical Depression. The refractivity of certain carbo- and hetero-cyclic compounds, such as cyclo-penta-diene, thiophene, pyrrole, and furfurane compounds, is lower than the calculated value, and the phenomenon has been termed optical depression.[1] This effect is, however, more than neutralised by the introduction of substituents.[2] Furfuraldehyde, for example, shows exaltation, due no doubt to conjugation between the cyclic and aldehyde double bonds.



Action of Solvents. It has long been recognized that a solvent may affect refractivity in some cases and not in others. In determining refractivity it is therefore necessary to take this fact into consideration. Duval has examined the effect of different solvents on the refractivity of azobenzene and Brühl on that of acetoacetic ester.

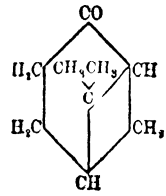
	M_{Li}		M_{Li}
Azobenzene	62 20	In Benzene	62 88
In Ethylene bromide	62 17	,, Cyclohexane	63 92
,, Nitrobenzene	62·23	,, Acetic acid	64 20

	M_α	M_D
Acetoacetic ester	31·80	31 96
In Water	31 64	31 79
,, Methyl alcohol	31 85	32 02
,, Chloroform	31·95	32 08
Calculated	31·42	31 57

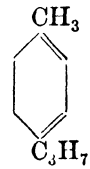
Application of Refractivity to Structural Problems. Although from what has been stated in the foregoing pages the refractivity method cannot claim great delicacy or definiteness in elucidating the complete structure of a compound, it may, if applied with discrimination, be used in solving doubtful points in the case of compounds and, especially, of isomeric compounds whose structure is mainly known.

[1] Brühl, *Ber.*, 1907, 40, 1157; Auwers, *Ber.*, 1912, 45, 3077.
[2] Auwers, *Annalen*, 1918, 415, 110.

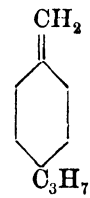
It has already been pointed out (p. 27) that Tschugaeff and Semmler were able to establish with great probability the structure of thujone and sabinene by noting the increment in refractivity which accompanies a 3-carbon ring. Wallach[1] applied the same principle to the case of isopinone, which gave the value $M_D = 39{\cdot}87$ instead of the calculated 39·51, and was thus able to establish the presence of a bridged ring of four carbon atoms.



The constitution of α- and β-terpinene has also been cleared up by the observed exaltation which determines the relative disposition of the double bonds.[2] The first gave an exaltation of +1 to +1 4 in different preparations, pointing therefore to a conjugated system, and the second +0·54, which, being too high for isolated double bonds, indicates an extra nuclear (or hemicyclic) double linkage.



α-Terpinene.

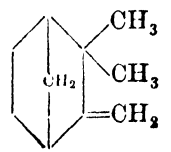


β-Terpinene.

The vexed question as to the formula for camphene has received a possible solution from its molecular refractivity.

Obs.		Calc.		
M_α	M_D	M_α	M_D	EM_D
43·78	44 02	43·29	43·51	0·51

The amount of exaltation coincides with that of a hemicyclic compound, the average of which is 0·51 for EM_D, but is too low for a saturated 3 or 4-carbon ring. It will therefore have the formula



[1] *Annalen*, 1907, 356, 227.
[2] Auwers and Eisenlohr, *J. prakt. Chem.*, 1910, 82, 107.

In the light of our present knowledge any attempt to solve the benzene problem by setting up an analogy between unsaturated open and closed-chain compounds (see p. 431) must for the present be relinquished for the following reasons: the hydroaromatic derivatives of benzene (di- and tetra-hydrobenzenes) are not known in a state of purity, and, if they were, would certainly exhibit the varying effects of conjugation. Moreover, the normal value for the double bonds in benzene places it, as do its chemical properties, in a separate category from the ethenoid compounds.

Refractivity and Dynamic Isomerism. A more fruitful line of investigation, briefly referred to on p. 364, has been the study of the keto-enol type of dynamic isomerism. The change from keto to enol form is accompanied by the formation of a double bond, which, if only one is present, means an increase of about 1·83 units, whilst the change from O″ to O′ produces a decrease of 0·82 units, giving therefore a net increase of 1·01 on the molecular refractivity. Thus, if the molecular refractivity is about a unit above the calculated value for the keto form, it points with great probability to the presence of a preponderating amount of the enol form. The process cannot, however, be extended to the determination of two enol groups, such as might occur with the 1 . 3 diketones, owing to the effects of conjugation in increasing the value abnormally.

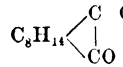
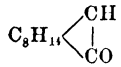
$$\underset{\text{I}}{-CH_2 . CO . CH_2 . CO . CH_2-} \qquad \underset{\text{II}}{-CH_2 . C(OH) : CH . CO . CH_2-}$$

$$\underset{\text{III}}{-CH_2 . C(OH) : CH . C(OH) : CH-}$$

An increase above the calculated value for II would not necessarily imply a dienol form having structure III.

From the following figures[1] it will be seen that, although it is possible to differentiate with some degree of confidence between a ketonic and enolic form, the method cannot at present be used for estimating with any degree of accuracy the relative quantities of the two isomers, nor in deciding on the presence of a multiple enolic grouping. Consequently, when numbers in the first column of the table exceed those in the third, some of the dienolic form may or may not be present, depending on the relative positions of the double linkages.

[1] Brühl, *J. prakt. Chem.*, 1894, **50**, 119 ; *Zeit. physik. Chem.*, 1899, **30**, 1 ; 1900, **34**, 81 ; *Annalen*, 1900, **312**, 34.

	M_α obs.	M_α calc. keto	M_α calc. enol	Principal constituent.
Acetone $CH_3 . CO\ CH_3$	16·05	16·08	17·04	keto
Pyruvic acid $CH_3 . CO . COOH$	17·86	17·67	18 68	,,
Ethyl acetoacetate $CH_3\ CO . CH_2\ COOC_2H_5$	31 89	31 53	32·55	,,
Ethyl oxaloacetate $C_2H_5OOC . CO . CH_2 . COOC_2H_5$	43 38	42·45	43 46	enol
Ethyl acetomalonate $CH_3 . CO\ CH(COOC_2H_5)_2$	48·60	47·02	48·04	,,
Acetylacetone $CH_3 . CO . CH_2 . CO\ CH_3$	27·45	25 31	26 32	,,
Methylacetylacetone $CH_3 . CO\ CH(CH_3)\ CO . CH_3$	30 75	29 88	30 89	,,
Diacetylacetone $CH_3 . CO . CH_2 . CO . CH_2\ CO . CH_3$	38 20	34 58	35 59	,,
Mesityloxide $(CH_3)_2C . CH\ CO\ CH_3$	30 13	29 47	30 40	,,
Ethyl acetoneoxalate $CH_3\ CO\ CH_2 . CO . COOC_2H_5$	39 07	36 22	37·24	,,
Methoxymethylene camphor 	55 97	52 89	54 05	,,
Camphocarboxylic ester 	59·46	59 12	60·13	keto
α-Formylphenylacetic ester $C_6H_5 . C(:CHOH) . COOC_2H_5$	53·06	51·07	52 08	enol

In addition to attempting to ascertain the nature of tautomeric substances by the refractivity method described above, Bruhl sought to follow the course of isomeric change in solution and to discover in this way the influence of the solvent.

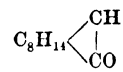
Notwithstanding the amount of carefully collected data,[1] the results, in the light of subsequent research, cannot be regarded as conclusive nor the conclusions entirely trustworthy. The method of experimenting consisted in ascertaining the molecular refractivity of the pure substance and then examining its refractivity in different solvents and at different temperatures and intervals of time. Most of the substances examined were such as would be obtained readily in both isomeric forms, and included mesityloxide oxalic ester, hydroxymethylene camphor, formyl camphor, formylphenylacetic ester, and camphocarboxylic ester (see p. 349).

[1] *Ber.*, 1891, 24, 3391, 3709. *J. prakt. Chem.*, 1894, 50, 209, 1895, 51, 1; *Zeit. physik. Chem*, 1900, 34, 1.

Thus, α-ethyl mesityloxide oxalate (enol) gives $M_\alpha = 57{\cdot}2$ and the β-ester (keto) $M_\alpha = 51{\cdot}10$. When the fresh enol form was dissolved in chloroform, methyl alcohol, and ethyl alcohol respectively, and allowed to stand, the following results were obtained :[1]

			M_α
$(CH_3)_2C\ CH.CO\ CH_2\ CO\ COOC_2H_5$	Chloroform solution	75 days	57·74
Mesityloxide oxalic ester	Ethyl alcohol	82 ,,	50·59
	Methyl alcohol	5 ,,	51·94

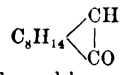
Hydroxymethylene camphor, on the other hand, gave much the same result in chloroform and methyl alcohol, after heating for seven hours or on standing for two days,



		M_α
Hydroxymethylene camphor	Chloroform solution 2 days	50 46
	Methyl alcohol ,,	50·92

whereas the calculated value for the enolic form is 46·33. The high number is no doubt due to exaltation from the proximity of ethenoid bond and ketone group.

Formyl bromocamphor is clearly ketonic in both solvents.



		M_α	M_α calc. (keto)
Formyl bromocamphor	Chloroform solution 2 days	56·94	56·08
	Methyl alcohol 5 ,,	56 32	

A very unaccountable result was observed by Bruhl with the two forms of formylphenylacetic ester. Whereas the α or liquid enol form falls in refractivity in alcohol solution in two hours from M_α 53 42 to 51 77 (calculated for keto form $M_\alpha = 51\ 07$), the solid or β compound, which is usually regarded as the keto form, gives in methylal solution nearly the same value as the enol isomer, namely, M_α 53·53, without undergoing isomeric change, for the original substance can be regained on evaporating the solvent. Brühl therefore concludes that there must be two enol forms and one ketonic substance, a result which is unsupported by any chemical evidence.

Another application of the refractivity method has been used in the case of camphocarboxylic ester in order to determine the structure of the sodium derivative,[2] which may be supposed to assume the enol form. The method is based upon the rule of Biot and Arago for mixtures, namely, that the refractivity of a solution is that of its collective constituents. Thus, the combined

[1] *Zeit. physik Chem.*, 1899, 30, 1

[2] J. W. Bruhl, *Zeit. physik. Chem.*, 1905, 50, 1.

refractivities of a solution of camphocarboxylic ester and sodium ethoxide in alcohol should agree with that of the constituents determined separately. If this is not the case isomeric change must have occurred. The differences (Δ) between the observed value for the pure ethyl ester and that calculated from its alcoholic solution in presence of sodium ethoxide are as follows:

Camphocarboxylic ester.	Per cent. in solution.	M_a Pure substance.	M_a Calc. from sol^n. of Na compound.	Δ
C_8H_{14} CH . $COOC_2H_5$ | CO	12·74	59 46	63 58	4 12
Keto form	14·20	,,	63 89	4 43
C_8H_{11} C . $COOC_2H_5$ ‖ C . OH	23 00	,,	63 94	4 48
Enol form	28 71	,,	63 83	1 37

Brühl's attempt to correlate the 'medial energy' of the solvent, as exhibited by its ionising and dielectric properties on the one hand and in promoting isomeric change on the other, is not supported by Dimroth's later observations.[1] The uncertainty which surrounds the whole method for determining keto-enol tautomerism has recently been illustrated in a very instructive way by Auwers.[2]

Knorr succeeded in separating by freezing the two forms of aceto-acetic ester and, having determined their refractive indices, which exhibit considerable divergence, proceeded to estimate in ordinary specimens the amount of enol present, which he found to be 2 per cent.[3] Now the amount of exaltation produced by the conjugated system of the enol form of acetoacetic ester may be deduced from the value of β-ethoxycrotonic ester, which gives an exaltation of $EM_D = 1{\cdot}8$ for acetoacetic ester (enol form). This value agrees exactly with the difference between the observed and calculated values of Knorr.

	Obs.	Calc.	Δ
Enol M_D =	34 42	32 62	1 8
Keto ,, =	32 00	31 57	0 43

The percentage of enol will therefore be obtained by taking the ratio of the differences between the observed and calculated values

[1] *Annalen*, 1904, 335, 1; 1904, 338, 143.
[2] *Ber.*, 1911, 44, 3525
[3] This was estimated from the refractive indices of different mixtures of the two pure substances, namely, enol $n_D^{19} = 1{\cdot}4480$ and keto $n_D^{19} = 1\,4225$, the ordinary specimen yielding $n_D^{19} = 1{\cdot}4230$, or 2 per cent.

for the keto form (0·43) and that between the calculated for the keto form and observed for the enol form (2·85) and multiplying by 100.

$$\frac{0{\cdot}43}{2{\cdot}85} \times 100 = 15 \text{ per cent.}$$

According to Auwers the calculated value $M_D = 31{\cdot}57$ for the keto form is probably different from the true value, which from Brühl's observations is a little higher, namely, 31·79. When this difference is introduced into the above expression, the percentage of enol will fall to 9 per cent.

$$\frac{(0{\cdot}43 - 0{\cdot}22)}{2{\cdot}85} \times 100 = 9 \text{ per cent.}$$

which approximates to the amount obtained by K. H. Meyer[1] from estimations of the bromine absorption.

Hantzsch[2] has recently applied the property of refractivity to determine the formation of salts from a pseudo acid (p. 365). The process is found to be accompanied by exaltation even when the original substance is enolic, thus indicating that subsidiary valencies are possibly involved in the production of aci salts (see p. 109). The change does not run parallel with the appearance of colour, for it is greater on passing from *p*-nitrophenol, which is colourless, to its coloured salts, than from the ortho compound, which is bright yellow, to its orange salts.

DISPERSIVITY

It has been stated that the refractive index of a substance varies with the kind of light employed, being greater the shorter the wave length. The difference in specific refractivity is, however, not the same for all substances, say for red and violet light. It does not follow, for example, that the refractivities of two substances which are the same for the H_α line should show an identical refractivity for the H_γ line. The difference between the specific refractivities for light of widely different wave length is called the specific dispersive power or *dispersivity*. The wave lengths usually chosen are the α and γ hydrogen lines or the sodium (D) and lithium (Li) lines. The value is obtained by deducting the specific refractivity for light of shorter wave length from that of longer wave length, using either the n or n^2 formula.

$$r_\gamma - r_\alpha = \frac{n_\gamma - 1}{d} - \frac{n_\alpha - 1}{d} = \frac{n_\gamma - n_\alpha}{d}$$

[1] *Annalen*, 1910, 380, 1212. [2] *Ber.*, 1910, 43, 95.

The *molecular dispersivity* is obtained by multiplying by the molecular weight (m) of the substance under examination.

$$M_\gamma - M_\alpha = \frac{(n_\gamma - n_\alpha)m}{d}$$

The expressions for the specific and molecular dispersivity derived from the n^2 formula are:

$$r_\gamma - r_\alpha = \frac{n^2{}_\gamma - 1}{(n^2{}_\gamma + 2)d} - \frac{n^2{}_\alpha - 1}{(n^2{}_\alpha + 2)d}$$

$$M_\gamma - M_\alpha = \left(\frac{n^2{}_\gamma - 1}{n^2{}_\gamma + 2} - \frac{n^2{}_\alpha - 1}{n^2{}_\alpha + 2}\right)\frac{m}{d}$$

The specific dispersivity is consequently a differential value depending on certain factors which, for purposes of comparison, need not necessarily be multiplied by the molecular weight, for in comparing molecular values an artificial disparity is in a sense introduced, as the difference is then a function of the molecular weight. On this account Auwers and Eisenlohr[1] multiply the specific refractivity by 100, or, in other words, convert the first two decimals in the specific refractivities into whole numbers, which they indicate by the symbol Σ, and the specific dispersivity is then $\Sigma_\gamma - \Sigma_\alpha$. The values obtained in either case are small, seldom exceeding one or two units (see p. 22), but, on the other hand, the effect of impurities, which may enormously modify the refractivity, is largely eliminated in what is essentially a differential method where the impurity affects the two quantities to a nearly equal extent. The dispersive constants for the different elements and for double and treble linkages have been determined by Brühl,[2] and also by Eisenlohr,[3] in the same way as the atomic refractivities (p. 25), but the numbers can only be regarded as approximate, and the observed and calculated values do not show the same agreement as the molecular refractivities. It is therefore customary to compare the observed and calculated molecular dispersivities, the latter being derived from the difference in the calculated molecular refractivities for different wave lengths, as already explained. According to Brühl, dispersivity is pre-eminently a constitutive property, and much more sensitive to structural differences than refractivity. For example, multiple linkages seem to affect the dispersivity in the same direction, but to a much more marked extent than the refractivity, and, among isomeric compounds, constitutional differences may be perceived more readily than by a comparison of refractivities only. The following examples will illustrate this point, in which conjugation is clearly indicated:

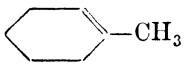
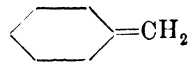
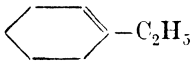
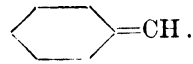
[1] *J. prakt. Chem.*, 1910, 82, 70. [2] *Zeit. physik. Chem.*, 1891, 7, 191.
[3] *Zeit. physik. Chem.*, 1910, 75, 585; 1912, 79, 129.

	$M_\gamma - M_\alpha$ obs.	calc.
Diallyl $CH_2 . CH\ CH_2\ CH_2\ CH : CH_2$	1 00	1·05
Isodiallyl $CH_3\ CH : CH\ CH : CH . CH_3$	1 57	1 05
Valerylene $(CH_3)_2C : C : CH_2$	0 94	0 94
Diisopropenyl $CH_2 : C(CH_3) . C(CH_3) : CH_2$	1·42	1·05

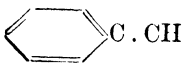
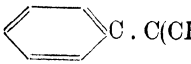
By a comparison of isomeric compounds of the formula $C_{10}H_{16}O$, Wallach has shown that those which are equally saturated have the same dispersivity, whilst Eykman[1] has pointed out that dispersivity affords a valuable indication of the position of the double bond. Between eugenole and isoeugenole or safrole and isosafrole the dispersivity produced by the allyl and propenyl side-chain above the calculated value is:

Allyl $—CH_2\ CH : CH_2$ from 0·024 to 0 029
Propenyl $—C . CH . CH_3$,, 0 035 ,, 0 043

that is, the nearer the side-chain double bond is to the nucleus the higher the dispersivity. Auwers and Ellinger[2] have more recently shown that dispersivity, like refractivity (p. 34), is increased by the double bond in the side-chain (exocyclic) as compared with that in the nucleus (endocyclic).

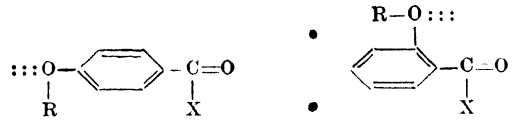
	$E\Sigma_\gamma - \Sigma_\alpha$ per cent. exaltation.		$E\Sigma_\gamma - \Sigma_\alpha$ per cent. exaltation
	0		6
	0		7

Also the presence of radicals attached to the ethenoid carbon atoms of a conjugated system decreases the dispersivity as it does the refractivity.

	$M_\gamma - M_\alpha$	$E\Sigma_\gamma - \Sigma_\alpha$	
	+ 0 74	0 62	45 per cent.
	+ 0·48	0 41	29

Auwers[3] has also studied the effect of substituents in the benzene nucleus and finds that, whilst alkyl groups produce little or no effect, an aldehyde, ketone, or ester side-chain causes exaltation of both refractivity and dispersivity which is increased in the case of the para substituted derivative (as compared with the ortho and meta) by alkyl groups; but more especially by groups with residual valencies, such, for example, as contain oxygen (hydroxyl, methoxyl, and ester groups). This is explained by the lengthening of the conjugated chain, which is greater in the para than in the ortho or meta positions.

[1] *Ber.*, 1889, **22**, 2786; 1890, **23**, 855 [2] *Annalen*, 1912, **387**, 200.
[3] *Annalen*, 1915, **408**, 212.



MAGNETIC ROTATION

In 1846 Faraday observed that if a beam of polarised light be passed through a transparent substance placed between the poles of an electro-magnet so that the light travelled along the lines of the field, it undergoes rotatory polarisation. As the rotation is dependent on the direction of the lines of the magnetic field, and not on the direction of the beam, the light may be reflected along its course and the amount of rotation multiplied. This behaviour distinguishes magnetic rotation from the rotation of optically active substances in which the direction of rotation is reversed by reflection. In other words, the direction of rotation will be in the inverse direction when viewed from the opposite end of the instrument in the case of magnetic rotation, but in the same direction in that of optically active substances. Faraday also showed that the amount of rotation of the polarised beam is proportional to the length of the layer traversed and the strength of the magnetic field. In this way an important relation was established between light and magnetic and electrical forces. Faraday was, however, unable to account for the phenomenon, and it is only since the introduction of the electronic theory that a satisfactory explanation has been forthcoming[1]

As our object in dealing with the subject is to explain its application to the structure of organic compounds, we do not propose to enter into a discussion of the phenomenon on its purely physical side. The following facts are, however, of importance. Wiedemann found that the rotation increases with decreasing wave length of light, and, according to Becquerel, the effect on optically active substances is identical whichever the direction of the field. The experiments of Verdet have shown that substances must be divided into two classes: those, including the larger number, which are rotated in the direction of the current producing the magnetic field, and a few, such as iron salts, which are deviated in the reverse direction.

The influence of temperature on magnetic rotation is small. The effect of rise of temperature is generally to diminish the rotation; but it depends on the structure of the substance, and, in a homologous series, it increases with the molecular weight. By comparing substances at the same temperature these influences are removed.

[1] *Modern Electrical Theory*, N. R. Campbell. Camb. Univ. Press, 1913

The application of *magnetic rotation* to the study of structure was first investigated by W. H. Perkin in 1882, and in his hands has become one of the most delicate and trustworthy of physical methods. His results are embodied in a series of memoirs which appeared at intervals down to the year 1907.[1]

The original apparatus used by Perkin is shown in Fig. 5, p. 20.[2] The apparatus subsequently underwent some slight modifications[3] which rendered its manipulation more convenient; but in its essential parts it remained unchanged.

It consists of an electro-magnet *B*, with hollow pole pieces *C*, *C*. *E* is the polariser and *D* the analyser, both firmly clamped (subsequently fixed to the same metal frame). *G* is the apparatus for producing a strong sodium flame, and consists of an iron tube containing metallic sodium, which is volatilised in a current of hydrogen. The light is filtered through a solution of potassium dichromate contained in the bulb of the distilling flask. *K*, *K* are copper vessels placed on the pole pieces, and cooled by a current of cold water to prevent the substance under examination rising in temperature. Two tubes, one holding the substance and the other water, are fixed to a movable carriage at *F* between the pole pieces. In the later form of construction water was caused to circulate through the pole pieces as well as round the substance contained in a copper cell.

A current was maintained from a battery of Groves cells, kept constant by a resistance and measured by means of a galvanometer.

As the method of determining magnetic rotation values is a comparative one, like that adopted in other physical measurements, it is necessary to fix on some standard substance for comparison, and for this purpose Perkin used water. If the same tube is used in all the determinations no correction for the length of the column of liquid is required. In order to compare the effect of equal masses of different liquids it is requisite to divide the observed result by the density. The rotation in unit length of tube α, divided by the density d, is called the specific rotation (r).

$$r = \frac{\alpha}{d}$$

When this expression is multiplied by the molecular weight m, the product is the molecular magnetic rotation (M) or the rotation

[1] *Trans. Chem. Soc.*, 1884, 45, 421; 1886, 47, 261; 1888, 53, 601; 1892, 61, 307; 1894, 65, 407; 1895, 67, 261; 1896, 69, 1058; 1902, 81, 315, 1906, 89, 849; 1907, 91, 835, 851.

[2] *Trans. Chem. Soc*, 1884, 45, 421.

[3] *Trans. Chem. Soc*, 1896, 69, 1027.

produced by equal numbers of molecules of the different substances examined.

$$M = \frac{r \times m}{r_1 \times m_1}$$

in which $r_1 \times m_1$ is the molecular rotation for water.

The following example will illustrate the method of calculation:

Observed rotation of water 32·595
" " " liquid 33·450

$$t = 22°,\ d\frac{22}{22} = 0{\cdot}8633$$

Molecular weight of water 18
" " " liquid 284

$$M = \frac{33{\cdot}45 \times 284}{32{\cdot}595 \times 18 \times 0{\cdot}8633}$$

When solutions are used the rotation of the solvent must be deducted from that of the solution.

The error of observation will depend mainly on the purity of the substance. With the same substance the experimental error does not as a rule exceed 1 per cent., so that with a specific rotation of 1 to 2 whole numbers the second decimal may vary by 1 unit.

Isomeric Compounds. The following groups of isomers, chosen from among different classes of compounds, exhibit larger or smaller, but in all cases consistent differences which exceed experimental error, and clearly point to differences of structure. The property is therefore not merely additive, but also constitutive.

Substance.	*M*	Δ	Substance.	*M*	Δ
Hexane	6·670	0 099	Nitro isobutane	4·99	0·38
Isohexane	6 769		Isobutyl nitrite	5·37	
Propyl alcohol	3 768	0 251	Benzyl alcohol	12 400	0 982
Isopropyl alcohol	4 019		*o*-Cresol	13 382	0·606
			m- "	12·776	0 008
Propyl aldehyde	3·332	0 182	*p*- "	12·768	
Acetone	3 514				
			o-Xylene	13·345	0 486
Propionic acid	3 462	0 100	*m*- "	12·859	0 049
Methyl acetate	3 362	0 202	*p*- "	12·810	0·604
Ethyl formate	3·564		Ethyl benzene	13 414	
Butyl alcohol	4·791	0·145	Benzyl chloride	14·014	0·295
Isobutyl alcohol	4 936	0 186	*o*-Chlorotoluene	13 719	0·473
Trimethyl carbinol	5 122	0·345	*p*- "	13 246	
Ethyl ether	4·777				
			Phenyl acetic ester	14·982	0 082
Propyl iodide	11·080	0·102	*o*-Toluic ester	15·064	0·320
Isopropyl iodide	11·182		*p*-Toluic ester	14·744	

Stereoisomers. Geometrical isomers have also a different magnetic rotation, the 'trans' modification being, as a rule, higher than the 'cis'.[1]

	M		M
Ethyl maleate	9 625	Ethyl citraconate	10 517
,, fumarate	10·112	Ethyl mesaconate	11 233

Optical isomers also differ in rotation:

	M		M
Ethyl tartrate	8 766	Dipentene	11·315
Ethyl racemate	8·759	*d*-Limonene	11·246
Glucose	6·723	*r* 3 8 (9) Menthadiene	12 939
Galactose	6 887	*d* ,, ,,	13·061
Lactose	12·714		
Maltose	12 690		

Homologous Series, Constant for CH_2. The following mean value for CH_2 has been derived from a large number of homologous series:

Series.	CH_2	Max and Min.	Series.	CH_2	Max. and Min.
Paraffins	1 051	0 999—1 113	Alkyl chlorides	1 015	1·014—1·017
Alcohols[2]	1 057	1 030—1 098	,, bromides	1 031	1·028—1·034
Aldehydes	1·022	—	,, iodides	1 031	1·005—1·066
Fatty acids	1 021	1 010—1 041	Phenyl ethers	1 053	1 052—1 058
Esters	1 023	1 015—1 032			

From the above figures Perkin has computed the mean value to be

$$CH_2 = 1{\cdot}023.$$

Series Constant. If there are n carbon atoms in a molecule belonging to a particular group of compounds, then by deducting the value for $n\,CH_2$ ($n \times 1{\cdot}023$) from the total magnetic rotation, a number is obtained which is nearly constant for the whole series of compounds belonging to that group. This number is called the *series constant* (S).

For example, in the series of fatty acids (omitting the first two members, which are abnormal) the series constant is 0 393.

	M	$n \times 1\ 023$	S
Propionic acid	3 462	$3 \times 1\ 023$	0 393
Butyric acid	4·472	$4 \times 1\ 023$	0 380
Valeric acid	5 513	$5 \times 1\ 023$	0 398
Oenanthylic acid	7 552	$7 \times 1\ 023$	0 391
Caprylic acid	8 565	$8 \times 1\ 023$	0 381
Pelargonic acid	9·590	$9 \times 1\ 023$	0 383
		Mean	0·393

[1] Perkin, *Trans. Chem. Soc.*, 1888, **53**, 591.

[2] In calculating the mean, the initial members which show an anomalous behaviour (the value is higher probably through association) are omitted. As Perkin (*Trans. Chem. Soc.*, 1884, **45**, 552) has pointed out, the two initial members of several homologous groups contain no simple CH_2 group

The molecular magnetic rotation is calculated from the equation,

$$M = S + n\,(1{\cdot}023).$$

The following table gives the series constants for different classes of compounds:

Series.	Formula.	S
Paraffins, norm.	C_nH_{2n+2}	0 508
,, iso	,,	0 631
Alcohols, prim.	$C_nH_{2n+2}O$	0 699
,, iso	,,	0·844
Aldehydes	$C_nH_{2n}O$	0 261
Ketones	,,	0 375
Fatty acids	$C_nH_{2n}O_2$	0·393
Unsaturated acids	$C_nH_{2n-2}O_2$	1 451
Dibasic acids	$C_nH_{2n-2}O_4$	0 196
Formic esters	$C_nH_{2n}O_2$	0 495
Acetic esters	,,	0·370
Esters of higher acids	,,	0 337
Methyl esters	,,	0 273
Ethyl esters	,,	0 337
Alkyl chlorides	$C_nH_{2n+1}Cl$	1 988
,, ,, iso and second.	,,	2 068
,, bromides	$C_nH_{2n+1}Br$	3 816
,, ,, iso and second.	,,	3 924
,, iodides	$C_nH_{2n+1}I$	8 011
,, ,, iso and second.	,,	8·099

Generally the increase for iso compounds is 0·112 (rather higher for alcohols and ethers); also, initial members containing no CH_2 group, such as isopropyl alcohol, are higher by 0 251.

The following examples will serve to illustrate the use of the above series constants:[1]

Levulinic acid $CH_3 . CO . CH_2 . CH_2 . COOH$

Ketone, series constant	0 375
Acid ,, ,,	0·393
2)	0·768
	0 384[2]
1 023 × 5	5·115
Calculated	5 499
Observed	5·518
Diff.	0 019

Ethyl lactate $CH_3 . CHOH . COOC_2H_5$

Sec. alcohol, series constant	0 844
Ethyl ester ,, ,,	0 337
2)	1·181
	0·590
1·023 × 5	5 115
Calculated	5 705
Observed	5·720
Diff.	0 015

[1] *Trans Chem. Soc.*, 1892, 61, 800

[2] The series constant in a case of this kind is the mean of the sum of the types.

Another method of calculating values is to determine the effect of replacement of hydrogen by other elements or groups. The numbers obtained in this way are not always concordant. For example, the successive replacement of hydrogen by halogen varies for each atom replaced.

CCl_4	6·582	
		1·023
$CHCl_3$	5·559	
		1 246
CH_2Cl_2	4·313	

The effect of a single substitution in the same homologous series is approximately the same and equal to the values derived from the series constants. The value of alcohol-hydroxyl, when it replaces hydrogen, can be obtained by comparing the series constant of the paraffins with that of the alcohols,

Paraffins—alcohols, H by OH $\quad 0\,699 - 0\,508 = 0{\cdot}191$

but, when applied to other series, little reliance can be placed on this value. Thus, when hydrogen is replaced by hydroxyl in aldehydes to form acids, the value is 0·132. Again, the replacement of hydrogen by hydroxyl in propionic ester to form lactic ester is 0 276, and not 0 213, the difference between the series constant for isoparaffins and isoalcohols. When ethyl replaces hydrogen in the fatty acids to form esters, the value for ethyl is $(2 \times 1{\cdot}023 + 0\,337) - 0{\cdot}393 = 1{\cdot}990$; but in the case of dibasic acids the value for each ethyl group is 1 95. When aldehydes are converted into acid chlorides, the substitution of hydrogen by chlorine increases the rotation by 1·669 units, but in other types it may vary from 1 459 to 1 724.

Constants for the Elements. From the different series constants it is possible to ascertain the values of the elements. The series constant for the paraffins is the equivalent of $H_2 = 0{\cdot}508$, or $H = 0\,254$. From $CH_2 = 1\,023$, the value for the carbon is $1{\cdot}023 - 0{\cdot}508 = 0{\cdot}515$. The series constant for the alkyl chlorides is 1·988. Deducting the value for hydrogen, Cl = 1·734. Oxygen in hydroxyl can be derived from the alcohols, ketonic oxygen from the aldehydes and ketones, and so forth. The following values have been calculated in this way:

Element.	Constant.	Element.	Constant.
H	0·254	Cl	1·734
C	0 515	Br	8·56
O′ (OH)	0·191	I	7·757
O″ (aldehydes)	0 261	N‴ (amines)	0·717
O″ (ketones)	0·375		

Constant for the Double Bond. The effect of an ethenoid linkage is to raise the rotation. A comparison of saturated with unsaturated fatty esters and of allyl with propyl alcohol gives an increase of 0·914—1·170, that is, without adding the value for the H atoms removed. Perkin takes 1·112 as the mean value; but it varies from that of the hydrocarbons, which give the lowest number, to that of the esters, in which it reaches a maximum.

	M	Δ
Trimethylethylene $(CH_3)_2C:CHCH_3$	6·208	0 578
Pentane C_5H_{12}	5·630	
Diallyl C_6H_{10}	8·420	0·947
Hexylene C_6H_{12}	7 473	0 827
Hexane C_6H_{14}	6·646	
Octylene C_8H_{16}	9·432	0·740
Octane C_8H_{18}	8 692	
Diamylene $C_{10}H_{20}$	11·472	0·734
Decane (calc.) $C_{10}H_{22}$	10 738	
Allylacetic acid $CH_2:CH.CH_2.CH_2.COOH$	6·426	0 913
Valeric acid $C_5H_{10}O_2$	5 513	
Allyl alcohol $CH_2:CH\ CH_2OH$	4·682	0 914
Propyl alcohol $CH_3.CH_2\ CH_2OH$	3·768	
Ethyl crotonate $CH_3.CH:CH.CO_2C_2H_5$	7 589	1 112
Ethyl butyrate $C_3H_7COOC_2H_5$	6·477	

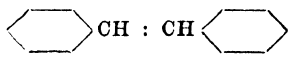
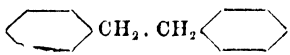
The same result is obtained in the aromatic series, if the double bond forms part of the ring.

	M	Δ
Cyclohexane	5·664	0·728
Tetrahydrobenzene	6 392	

The value is largely increased if the double bond is in the side-chain instead of in the nucleus:

	M	Δ
Styrene $C_6H_5CH:CH_2$	16·041	2 627
Ethyl benzene $C_6H_5.C_2H_5$	13 414	
Propenyl benzene $C_6H_5CH:CH.CH_3$	17 599	3·046
Propyl benzene $C_6H_5C_3H_7$	14·553	
β-Butenyl benzene $C_6H_5CH:C(CH_3)_2$	18·362	2·732
Butyl benzene $C_6H_5.C_4H_9$	15 630	
	Mean	2·834

With two benzene nuclei the value is still further enhanced:

	M	Δ
Stilbene 	33·143	
		8·146
Dibenzyl 	24·997	

If, on the other hand, the double bond in the side-chain is further removed from the nucleus the value falls, and may become normal.

	M	Δ
Isoeugenole $CH_3O.C_6H_3(OH)CH:CH.CH_3$	21 469	2 742
Eugenole $CH_3O.C_6H_3(OH)CH_2.CH\ CH_2$	18·727	

Another example is that of the allyl ether of phenol and the allyl ester of benzoic acid :

	M	Δ
Allyl benzoate $C_6H_5CO\ OCH_2\ CH\cdot CH_2$	15 722	0·849
Propyl benzoate $C_6H_5CO\ OC_3H_7$	14 873	
Allyl phenyl ether $C_6H_5O.CH_2\ CH:CH_2$	17·134	0·947
Propyl phenyl ether $C_6H_5O\ C_3H_7$	16 187	

In the last examples the differences approach that between allyl and propyl alcohol Δ = 0 914.

The effect of a treble bond compared with the saturated compound, in the few examples that have been studied, shows a rather smaller increase, fluctuating between 0 629 and 0·859.

Determination of Structure.[1] The application of magnetic rotation to determining structure includes cases of keto-enol tautomerism and the structure of cyclic compounds of the terpene series. We will indicate briefly how the first problem has been attacked. The question resolves itself into comparing the calculated values for the enol and keto forms with that observed for the pure substance.

The value for ethyl hydroxycrotonate $CH_3.C(OH):CH.COOC_2H_5$ may be calculated in various ways, as follows :

		M
	Ethyl crotonate	7 589
	OH in place of H in alcohols	0 194
		7 783
or,	Ethyl lactate $+CH_2$ (Ethyl hydroxybutyrate)	6 737
	Unsaturation $(+H_2)$	1 112
		7 849

The value for the ketonic form of acetoacetic ester may be computed as follows :

Series constant for acetic ester	0·370
,, ,, ketone	0 375
	2)0·745
Mean series constant	0 372
1 023 × 6	6 138
	6·510
The observed value for acetoacetic ester	6·501

[1] *Trans. Chem. Soc.*, 1892, **61**, 803.

The structure of acetoacetic ester, as determined in this way, is therefore entirely ketonic.

We will take one more example, that of acetyl acetone

$$CH_3 . CO . CH_2 . \overset{\epsilon}{CO} . CH_3,$$

which may exist as di-ketone, mono- or di-enol.

Calculated values for the ketone are:

M for acetone	3·514
M for acetyl in place of H	2·039
	5·553

or,

Series constant of acetone [1]	0·445
1 023 × 5	5·115
	5 560

Calculated value for the di-enol is.

M for glycol	2 943
1 023 × 3	3 069
	6 012
For unsaturation 1 112 × 2	2 224
	8 236

Calculated value for the mono enol is:

Series constant for isopropyl alcohol	0 950
,, ,, ketone	0 375
2)	1 325
	0 662
1·023 × 5	5 115
Acetopropyl alcohol	5 777
For unsaturation	1·112
	6 889

A similar method has been applied to the methyl derivative of acetyl acetone with the following result:

	Keto calc	Mono-enol calc	Di-enol calc.	Obs 16°	Calc per cent. mono-enol	di-enol
Acetyl acetone	5 553	6·889	8 236	7·166	80	20
					keto	mono-enol
Methyl acetyl acetone	6 519	8 882	9 295	7 237	46·4	53 6

At a temperature of 93° acetyl acetone gave 6·599, showing thereby an increase of keto form with rise of temperature.

[1] The series constant for a mono-ketone is taken, as that for a di-ketone is unknown; and by comparing the effect on introducing a second carboxyl or hydroxyl, Perkin considers that the second ketone group will not alter the constant (*Trans. Chem. Soc.*, 1892, 61, 814)

Ring Formation.[1] The effect of forming a closed from an open chain will be seen from the following examples:

	M	Δ	Calculated for—	*M*	Δ
Butyric acid $C_4H_8O_2$	4·472	−0·331	Formic acid + $3CH_2$	4·740	−0·599
Cyclopropane carboxylic acid $C_4H_6O_2$	4·141			4·140	
Valeric acid $C_5H_{10}O_2$	5·513	−1·465	Acetic acid + $3CH_2$	5·594	−0·546
Cyclobutane carboxylic acid $C_5H_8O_2$	5·048			5·048	
Caproic acid $C_6H_{12}O_2$	6·530	−0·639	Propionic acid + $3CH_2$	6·531	−0·640
Cyclopentane carboxylic acid $C_6H_{10}O_2$	5·891			5·891	
Capric acid $C_8H_{16}O_2$	8·580	−0·605	Valeric acid + $3CH_2$	8·582	−0·607
Methyl cyclohexane carboxylic acid $C_8H_{14}O_2$	7·975			7·975	

In the second half of the table, the calculated values for the saturated acids are compared with the corresponding ring compounds. Cyclopropane carboxylic acid, the first member of the series, is abnormal; but the abnormality vanishes when it is compared with the first member of the aliphatic series, namely, formic acid.

Perkin reckons ring formation with loss of H_2 at 0·6 in acids, esters, and ketones, but in hydrocarbons it is larger, and in dichlorocycloparaffins it is smaller.

	M	Δ
Hexane	6·646	−0·982
Cyclohexane	5·664	

Structure in the Terpene and Camphor Group. The rotation of camphor may be calculated as follows:

	M
Methyl hexyl ketone	8·509
$CH_2 \times 2$	2·046
Double ring 0·6 × 2	−1·200
Camphor, calc.	9·355
,, obs.	9·265

Limonene gives the following result:

	M
Paraffin $C_{10}H_{22}$, calc	10·738
Less ring formation (hydrocarbon)	0·982
	9·756
Unsaturation $\overline{=}_2$	1·440
$C_{10}H_{16}$, calc.	11·196
,, obs.	11·204

The difference in structure between bornyl chloride and pinene hydrochloride is very clearly brought out by this method. If the

[1] *Trans. Chem. Soc.*, 1902, **81**, 292.

two were identical, the calculated value should agree with that of pinene with the addition of HCl, 0·254 + 1·734 = 1·988, less the value of an ethenoid linkage (0·720). The value of bornyl chloride can then be calculated as follows:

		M
Pinene, obs.		10 294
HCl		1·988
		12 282
	Less	0·720
Bornyl chloride, calc.		11·562
,,	obs.	11 058
	Diff.	0 504

Consequently bornyl chloride must be differently constituted from pinene hydrochloride, as we know it to be on other evidence. If, on the other hand, it has a similar structure to borneol, its value will be that of borneol in which hydroxyl is replaced by chlorine. In passing from secondary octyl alcohol to octyl chloride there is a rise of 1·244 units. If the value is the same when borneol becomes bornyl choride we have:

	M
Borneol, obs.	9 806
Substituting OH by Cl	1·244
Calc.	11 050
Obs.	11 058

Magneto-rotatory Exaltation. A very interesting observation was made by Perkin in ascertaining the magnetic rotation of the synthetic members of the terpene series.[1] A comparison of two active menthadienes which are structurally closely related reveals a difference in rotation which can only be due to reinforcement produced by the conjugated linkages similar to that observed in the case of refractive exaltation (p. 29).

		M
$d\ \Delta^{3,8(9)}$	*p* Menthadiene	13 061
$d\ \Delta^{1,8(9)}$	,, (Limonene)	11 246
	Diff.	1 815

The discovery has thrown a new light on certain anomalous results connected with benzene and its derivatives.

Aromatic Compounds. Perkin found[2] that hexylene and diallyl give normal values (p 50); but there is a jump of 3·776 units with the introduction of the third double bond in hexatriene.

			M	Δ
Hexane	C_6H_{14}	$CH_3(CH_2)_4CH_3$	6 670	0 803
Hexylene	C_6H_{12}	$CH_3(CH_2)_3CH.CH.CH_3$	7 473	0·947
Diallyl	C_6H_{10}	$CH_2.CH(CH_2)_2CH:CH_2$	8 420	3·776
Hexatriene	C_6H_8	$CH_2.CH.CH:CH.CH.CH_2$	12·196	

[1] *Trans. Chem. Soc.*, 1906, **89**, 849 [2] *Trans. Chem. Soc.*, 1907, **91**, 806.

The difference between diallyl and hexatriene is of the same order as that observed in menthadiene, or $2 \times 1\,815 = 3{\cdot}630$, and at once explains the high rotation of benzene. On deducting 0 982 units from hexatriene for ring formation, the result is nearly identical with the observed value:

	M
Hexatriene	12 196
Ring formation	−0 982
Calc. for C_6H_6	11·214
Obs. ,,	11·284

A similar difference produced by conjugation has been noticed in the case of $\Delta^{1,3}$ dihydrobenzene:

	M
Cyclohexane	5 664
$\Delta^{1,3}$ Dihydrobenzene	8 093
Diff.	2 429

Several facts now become clear which were previously unexplained. For instance, the high value of the double bond next to the nucleus, which has been referred to under refractivity (p. 34), must be regarded as forming part of a conjugated system (p. 29).

		Value for [=]
Styrene		2·627
Propenyl benzene		3 046
Butenyl benzene		2 734

The same applies to eugenole, whilst in stilbene with its seven conjugated double linkages the increase as compared with dibenzyl amounts to 8·146, or adding the value for two benzene rings, 19·386, or 2·77 for each double bond. The same reasoning explains the high rotation of naphthalene, namely, 25 125. The value of the double bond may be calculated as follows:

	M
Cyclohexane −2H	5·156
$+(CH_2)_4$	3 776
	8 932

Deducting from 25·125 the above calculated value and dividing by 5 gives 3·24 for each double bond. But there are many other facts to the explanation of which these views will apply. Comparing diphenyl with diphenylmethane and allowing for the extra CH_2 group, the screening effect of the latter lying between the two sets of conjugated bonds is at once apparent:

	M
Diphenyl	25 304
Diphenylmethane $-CH_2$	23·337
	1 967

Reference has been made on p. 32 to a theory of Eisenlohr[1] in which he points out that when elements possessing residual valencies are in a conjugated position to a double bond, the effect is shown by a certain amount of optical exaltation. This idea had been previously foreshadowed by Perkin[2] in explaining the abnormally high values of certain groups attached to the benzene ring, especially NH_2 and $N(CH_3)_2$, and also the reverse effect of others, such as NO_2.

	M		*M*
Nitrobenzene	9 361	Aniline	16 076
Benzene	11 284	Benzene	11 284
	−1 923		+4·792

Generally the result of replacing H by NH_2 in the aromatic series is an increase in the rotation by 4–5 units, whereas in the aliphatic series it is about 1 unit This is seen by comparing a substance where the amino group is in a side-chain with one subtituted in the nucleus,

	M		*M*
p-Toluidine	16 188	*o*-Toluidine	17 200
Benzylamine	13 646	Benzylamine	13 646
	2 542		3 554

If the residual valency of the nitrogen is removed by forming the hydrochloride of the base, this exaltation disappears to some extent, the hydrochloride having only a slightly higher or lower value than the free base.

	M		*M*
Aniline hydrochloride	16 394	Dimethylaniline hydrochloride	18 326
Less HCl	2 245	Less HCl	2 245
	14·149		16 081
Aniline	16 076	Dimethylaniline	22 888

The same principle may account for the high value of hydroxyl when it replaces hydrogen in the nucleus. The difference in the rotations is about 0 85 units,

Benzene—Phenol	+0 856
Anethole—Isoeugenole	+0 848

whereas, when the hydroxyl is screened from the nucleus, the value falls nearly to the normal for aliphatic compounds (0·191).

Toluene—Benzyl alcohol	+0 243

In the same way the replacement of hydrogen by cyanogen in the nucleus and side-chain produces different results.

Benzene—Benzonitrile	+0 573
Toluene—Benzyl cyanide	+0 315

The nitro and carboxyl groups depress the rotation, the former lowering the value 1·35–1 94 units and the latter 0·817–0 918 units.

References.

The Relations between Chemical Constitution and some Physical Properties, by S. Smiles. Text-books of Physical Chemistry, Longmans, 1910

Graham-Otto, *Lehrbuch der Chemie*, vol iii. Vieweg, Brunswick, 1898.

[1] *Ber.*, 1911, **44**, 3188. [2] *Trans. Chem. Soc.*, 1896, **69**, 1161; 1907, **91**, 811.

THERMOCHEMISTRY AND STRUCTURE

Among the physical methods available for determining the structure of organic compounds, that of the heat given out on combustion naturally suggests itself; for the various ways in which the same atoms can group themselves in the molecule must represent a certain difference in internal energy which might be expected to manifest itself on combustion by corresponding differences in the amount of heat evolved. Thus, one might be led to expect that an ethenoid linkage of an unsaturated compound, by being more readily broken down than the single bond of a saturated compound, would absorb less energy by its rupture, and therefore give out more heat.

It might further be supposed that, as in refractivity, where constants were assigned to the atoms, the atoms would also possess definite heats of combustion according to their mode of combination. If this were the case, theoretical values might be deduced for the heat of combustion on the basis of a particular structure, which an experimental observation would confirm or disprove.

There is not the least doubt that the mass of experimental data which has been steadily accumulating for many years past points definitely in the direction indicated, yet as Wrede[1] has recently stated, 'when it is attempted to calculate the heat of combustion of any substance from its constitution by means of a formula and by using empirical constants, such attempts must be regarded as premature'

But if the anticipations of the utility of thermochemical measurements as a constitutive method have not so far been fully realised, it has not been due to any want of patience, skill, or scrupulous care on the part of the pioneers, Thomsen, Stohmann, Berthelot, and Louguinine, in this field of research, but rather to the peculiar experimental difficulties which the measurements entail. To write an account of the thermochemistry of organic compounds is in reality to describe the various stages in the development of the calorimeter.

Calorimetry. The principle of the method adopted by all observers has been the same, namely, to burn a given weight of the substance in a glass or metal vessel (combustion chamber) surrounded by a known weight of water contained in an outer vessel (calorimeter), and to note the rise of temperature of the water. The amount of heat

[1] *Zeit. physik Chem.*, 1910, 75, 81.

required to raise the temperature of 1 gram of water 1° C. is called a gram-calorie, and this has served as the general unit of measurement. A molecular-gram-calorie is the number of calories given out by the molecular weight of a substance in grams and divided by 1000.[1]

In order to calculate the heat of combustion it is necessary to know not only the rise of temperature of the water in the calorimeter, but also the amount of heat in calories absorbed by the combustion chamber and its accessories in raising it through the same temperature as the water, i. e. 'the water equivalent' of the chamber. It may be found either by calculation from the specific heat and weight of the various parts, or by ascertaining the specific heat of the vessel as a whole by heating it to a definite temperature and determining the rise on plunging it into water, or by burning in the chamber a given weight of a substance whose heat of combustion has been carefully ascertained. Such standard substances have been furnished by Fischer and Wrede,[2] who have determined with great precision the values of benzoic acid, cane-sugar, and naphthalene, all of which can be readily obtained with the requisite degree of purity.

The thermochemical studies of Julius Thomsen date from 1851 to 1885.[3] In his apparatus (Fig. 6) the combustion chamber consists of a cylindrical metal vessel of about 200 c.c. capacity, connected below with a spiral metal tube for conveying the products of combustion to the drying apparatus, and potash absorption tubes. The whole is enclosed in the calorimeter, which holds 2 to 3 litres of water and is closed at the top by an ebonite lid pierced with two holes for the thermometer and the shaft of the mechanical stirrer.

The other parts of the apparatus are the gas holders A and B for delivering oxygen to the burner, C and D containing combustible gases for examination, E the motor for actuating the mechanical stirrer, F the burner, and G the aspirator for drawing off the products of combustion. As the water in the calorimeter did not exceed by more than 1° the temperature of the room (being in the basement it could be kept nearly constant throughout the year) no external non-conductor was placed round the calorimeter. The substances

[1] It is generally assumed in these calculations that the specific heat of water is constant through the few degrees of temperature measured. Recently Fischer and Wrede (*Zeit. physik. Chem.*, 1909, 69, 218), using a platinum resistance thermometer, have made use of electrical units (kilowatt-second) which are easily transposed into C.G S units or into gram-calories (1 kilowatt-second = 0·2390 cals. at 15°) as occasion may demand.

[2] *Zeit. physik. Chem*, 1909, 69, 218.

[3] *Thermochemistry*, by Julius Thomsen, trans. by K A Burke. Text books of Physical Chemistry, Longmans

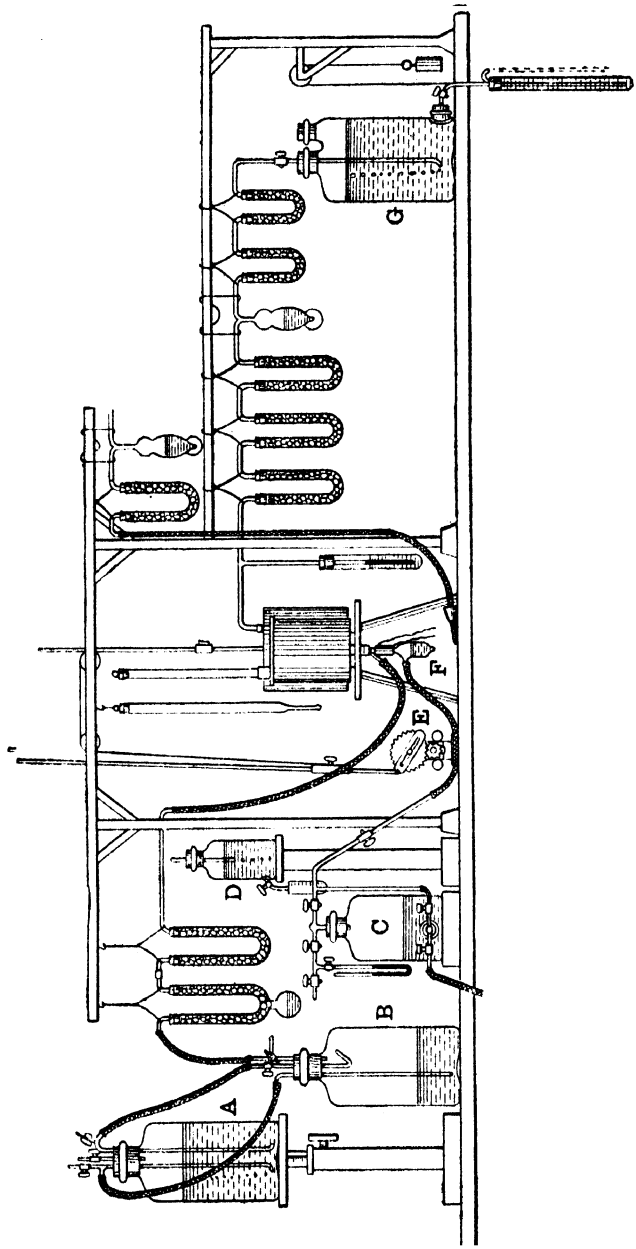


FIG. 6

which were either gases or volatile substances were burnt in a current of oxygen in a special form of apparatus called a 'universal burner',[1] shown in Fig. 7.

It consists of a glass bulb *a* drawn out into a long neck and surmounted by a platinum nozzle. The substance is introduced into the bulb containing a wick of cotton wool or asbestos which rises into the constricted part of the neck *b*. The neck is surrounded by a spiral of platinum wire which can be heated by a current of any required strength necessary to volatilise the substance, which is ignited at the nozzle, where it meets with a current of oxygen admitted through *c*. The burner is inserted below the combustion

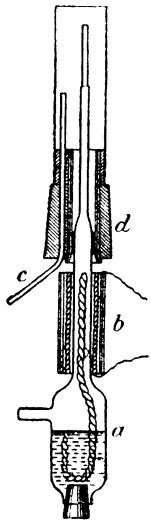


Fig. 7.

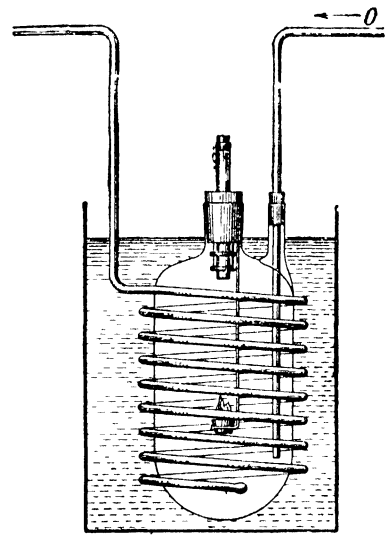


Fig 8

chamber and fixed by means of the rubber cork *d*. The electric current required to heat the wick and the flow of oxygen are so regulated as to ensure a perfectly steady flame, and the burner is then quickly inserted.

The composition of the substance being known, the quantity burnt was ascertained by the increase in the weight of the potash vessel due to the carbon dioxide drawn from the combustion chamber. In this way the heats of combustion of some 120 compounds were ascertained, including hydrocarbons, their chlorine, bromine, and iodine derivatives, alcohols, ethers, ketones, acids, amines and nitro

[1] *Ber.*, 1882, 15, 2999.

compounds. Although the use of the universal burner is open to criticism, owing to the fact that the amount of heat transferred to the combustion chamber cannot be accurately ascertained,[1] the results nevertheless are significant of the potentialities of thermochemical data and will be referred to presently.

Berthelot's original apparatus[2] (Fig. 8) consists of a vessel similar to Thomsen's but made of thin glass, which is not only a lighter material, but it also enables the process to be watched. Like Thomsen's vessel, it is furnished with a spiral glass tube for conveying the products to absorption vessels. The oxygen is introduced by means of a glass tube passing through the tubulus fused to the top of the combustion chamber, and the substance is burnt in a small lamp with asbestos wick.

The products of combustion are drawn through drying tubes, a potash apparatus, and then over heated copper oxide to convert any carbonic oxide into dioxide, which is absorbed and weighed, and any necessary correction introduced in case of incomplete combustion. The method is naturally restricted in its application to a few gases and to the more volatile liquids.

In 1885 Stohmann published his first experiments, in which he employed a modification of the Lewis Thomson calorimeter. The substance was mixed with powdered potassium chlorate containing a little manganese dioxide and ignited by a wire heated by an electric current. The combustion chamber being closed at the top and perforated at the bottom, the escaping gases were driven through the water of the calorimeter, to which they imparted their heat. The method only admitted of the combustion of the less volatile organic compounds, and the numerous corrections incidental to the process of combustion rendered it not altogether suitable or trustworthy. It was soon replaced by Louguinine's modification of Berthelot's apparatus, in which the various parts were made of metal instead of glass.[3]

The introduction of Berthelot's bomb calorimeter in 1885[4] effected a revolution in thermochemical measurement. The substance is burnt in a vessel filled with compressed oxygen. The combustion chamber (Fig. 9) is made of stout steel coated inside with platinum or enamel, and capable of withstanding a pressure of 25 to 50 atmospheres.

[1] Stohmann, *J. prakt. Chem*, 1886, **33**, 568.
[2] *Mécanique Chimique*, 1879, vol. i, p. 241 ; *Ann. Chim Phys.*, 1882 (5), 27, 347.
[3] *J prakt. Chem.*, 1886, **33**, 241, 572.
[4] *Ann. Chim. Phys.*, 1885 (6), **6**, 546 ; 1887 (6), 10, 433.

It has a capacity of 250 to 300 c.c. and weighs about 3 kilos. It stands in a calorimeter holding about 2 litres of water, which covers it to the neck. To restrict the amount of radiation, the calorimeter is surrounded by a larger vessel holding about 40 litres of water, which renders the apparatus independent of the external temperature of the room. The weighed substance, if solid, is compressed into pellets; if liquid it is enclosed in gelatine or celluloid capsules or in some inert absorbent material. It is placed on a platinum tray, where it is ignited by means of a fine iron wire, heated to redness by an electric current.[1] By this means the combustion is almost instantaneous and, as the bomb rapidly cools, equalisation of temperature is complete within a few minutes after ignition. Thus, instead of lasting an hour or more, as was the case with the older methods, the operation is over in about fifteen minutes from start to finish. The correction due to radiation is therefore greatly reduced and, as the combustion is usually complete, no correction is required for unburnt or partially burnt material. Moreover, as the products are all retained within the calorimeter, which is closed before ignition, the troublesome weighing of absorption vessels is eliminated and the single weight of the substance is all that is required. Apart from the small correction for radiation, account must be taken of (i) a small quantity of nitric acid, which is produced either from the nitrogen in the compound or from a trace of it in the oxygen used, and is estimated by washing out the bomb and titrating with alkali; (ii) the

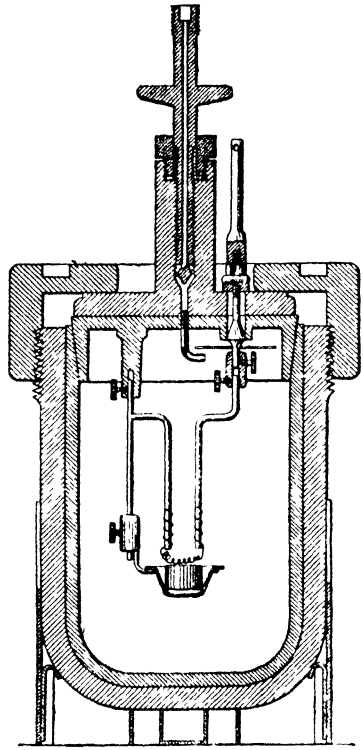


FIG 9.

[1] Details of manipulation, correction, and calibration of the calorimeter may be found in laboratory exercises in *Physical Chemistry* by Getman (Wiley & Sons, 1904), or in the following papers: Stohmann, *J prakt. Chem.*, 1894, **49**, 99; Fischer and Wrede, *Zeit. physik. Chem.*, 1909, **69**, 218; 1910, **75**, 81; and Roth, *Annalen*, 1910, 373, 249

heat given out by the ignition and burning of the iron wire, the two corrections together not exceeding as a rule 1 per cent. of the total heat of combustion. A further slight correction is sometimes required for the specific heat of substances when compared in different physical states, and also for the weight of substance reduced to a vacuum.

The following example is taken by way of illustration from a recent paper by Auwers, Roth, and Eisenlohr[1] of the heat of combustion of sylvestrene $C_{10}H_{16}$.

	Grm. cals.
5·5 mgrms. iron wire oxidised (1 mgrm. = 3·9 cals.)	21·4
4·34 c.c. NaOH to neutralise HNO_3 (1 c c = 1·3 cals.)	5·65
Heat given out by iron wire (1·9 secs, 1·35 volts 11 5 amp.)	7 05
	34·10
Less 0·2 mgrm. soot (1 mgrm. = 8·1 cals.)	−1·6
To be deducted	32·5
Rise of temperature in calorimeter	1·5905°
Less correction for radiation during experiment	0·0065
	1·5840°
Water equivalent 2623 × 1·5840	4154 8
Less above correction	−32 5
0·3837 grm. substance gave gram-calories	4122 3

$$\frac{4122\ 3 \times 136}{0\ 3837 \times 1000} = 1461\ 2 \text{ mol.-grm.-cals.}$$

The maximum and minimum value in four experiments showed a variation of 0 5 per cent., and, with carefully conducted bomb experiments, it is rarely that the variation reaches 1 per cent. The trustworthiness of the method may be further illustrated by the results of three independent observers using different bomb calorimeters and working at different places. The substances taken were cane-sugar, benzoic acid, and naphthalene. The numbers are given in grm.-cals. at constant pressure.[2]

	Stohmann.	Berthelot and Louguinine.	Fischer and Wrede.	Variation per cent.
Cane-sugar	3955·2	3961 7	3952·0	0·24
Benzoic acid	6322 3	6322 1	6325·4	0 05
Naphthalene	9628·3	9696·1	9667·8	0 70

It is interesting to compare these figures with those obtained by Stohmann for phenol in the three forms of apparatus employed by him at different times. The numbers are in mol.-grm.-cals.

[1] *Annalen*, 1910, 373, 269.

[2] As the heat of combustion in the bomb is determined at constant volume, it is customary to give in addition the value at constant pressure.

	Mol. grm. cals.	Variation per cent.
L. Thomson calorimeter	722	
Berthelot's original calorimeter with oxygen at the ordinary pressure	725·3	1·4
Berthelot's bomb calorimeter with compressed oxygen	732·5	

The differences in the results previously obtained by different observers show even greater discrepancies.

It is clear, therefore, that the thermochemical data obtained before the introduction of the bomb must be accepted with caution. Those of Stohmann since 1889, of Berthelot and his collaborators, and of Louguinine since 1885 may be brought into harmony with more modern results by comparison with standard substances, the values for which have been established by Fischer and Wrede.[1] Thomsen's results cannot, however, be corrected in this way, and will require complete and careful revision.

Heat of Formation. It is customary for some observers to give in addition to the heat of combustion a number termed *heat of formation*. This is derived from the number calculated for the heat evolved when the elementary carbon and hydrogen of the compound in question are completely burnt, by deducting from it the heat of combustion in mol.-grm.-cals. The value for carbon at one time presented a difficulty, because it is clear that solid carbon in the form of diamond, graphite, or charcoal does not correspond to its condition in the organic substance, nor was the heat of dissociation of molecular hydrogen known.

The heat of sublimation of diamond on the one hand and of graphitic carbon on the other has, however, been estimated approximately at 275 and 287 at.-grm.-cals. by Gruneisen and by Lummer,[2] each using a different method, whilst the dissociation of molecular hydrogen according to different observers requires between 90 and 100 grm.-cals.[3] It is therefore possible to arrive at an approximate value for the heat of formation of organic compounds. An attempt to do so has been made by Fajans[4] (based on some previous observations by Weinberg) in the following way: the heat of combustion of a simple hydrocarbon such as a paraffin consists of two factors, a plus quantity represented by the heat given out by the combustion of atomic carbon and hydrogen, and a minus quantity in the heat energy required to sever the carbon atoms from one another and the hydrogen atoms from the carbon atoms. That the last two quantities are approximately equal follows from a variety of observations, for example the equal values for CH_2 (see below) in ethane with 1 carbon and 6 hydrogen bonds and octane with 7 carbon and 18 hydrogen bonds; further, the equivalent heats of combustion of the isomeric octanes as determined by Richards and

[1] *loc. cit*
[2] Fajans, *Ber.*, 1920, 53, 655.
[3] Weinberg, *Ber.*, 1919, 52, 1501.
[4] *Ber*, 1920, 53, 643.

Jesse,[1] in which carbon is united in some cases with two other carbon atoms, in others with three. Again, tetramethyl methane, in which carbon is linked to four other carbon atoms, has the same heat of combustion (884·8 grm.-cals.) as that of methane (211 mol.-grm.-cals.), $+4\,CH_2$ (CH_2 is taken as 158 grm.-cals.).

Now the heat of combustion of the various forms of carbon lies between 94·3 and 94·7 at.-grm.-cals. Taking 287 as the heat of sublimation of solid carbon in the diamond, Fajans estimates the heat of combustion of atomic carbon as $94 + 287 = 381$ cals. In the same way, from the thermal value for the dissociation of molecular hydrogen, 81·3 grm.-cals, and its heat of combustion, 67·5 mol.-grm.-cals., the heat of combustion of the grm. atom of hydrogen is

$$\frac{81{\cdot}3 + 67{\cdot}5}{2} = 74{\cdot}4 \text{ grm.-cals.}$$

Fajans takes the heat of combustion of ordinary carbon as 106, and therefore the heat energy required for breaking of the two links of the carbon chain in a hydrocarbon will be represented by $381 - 106 = 275$ grm.-cals., or the value for one bond will be 137·5 grm.-cals. From these figures the value of the link C=H_2 may be estimated as follows :

$$H_2 \rightarrow H_2O \qquad C \rightarrow CO_2 \qquad -C\begin{matrix}H\\ \diagup\\ \diagdown\\ H\end{matrix} \qquad C{-}C$$

$$2 \times 74{\cdot}4 \; + \; 381 \; - \; 2x \; - \; 137{\cdot}5 \; = \; 158$$

$$2x = 234, \qquad x = 117.$$

The heat of formation for any hydrocarbon may then be calculated. Ethane, for example, will give :

$$2 \times 381 + 6 \times 74{\cdot}4 - 370 = 838 \text{ mol.-grm.-cals.}$$

or taking the heat energy of the 1 carbon and 6 hydrogen linkages the equation will be :

$$137{\cdot}5 + 6 \times 117 = 839{\cdot}5 \text{ mol.-grm.-cals.}$$

The heat of formation of single, double, and treble linkages may be calculated as follows :

$C_2H_6 = 838 - 6 \times 117$	C—C	136 grm.-cals.
$C_2H_4 = 720 - 4 \times 117$	C=C	252 „
$C_2H_2 = 599 - 2 \times 117$	C≡C	365 „

It therefore would appear that in the formation of unsaturated as well as saturated carbon chains from the atoms there is an evolution of heat.

Taking into consideration the doubtful value of some of the data derived from the earlier experimental methods, we may nevertheless learn a good deal from the character and significance even of these results. They have been conveniently tabulated by Stohmann.[2] The

[1] *J. Amer. Chem. Soc*, 1910, **32**, 292.

[2] *Zeit. physik. Chem*, 1890, **6**, 334, and 1892, **10**, 410.

heats of combustion are given in mol.-grm.-cals. both at constant pressure and volume with a reference to the observer and the original paper. The few data which we reproduce represent mol.-grm.-cals. at constant pressure, and the name of the observer is indicated by initials thus : T. = Thomsen ; St. = Stohmann ; St.* = Stohmann (bomb values) ; L. = Louguinine ; A. R. = Auwers and Roth ; F. W. = Fischer and Wrede.

Isomers. Isomeric compounds belonging to the same class have nearly the same heats of combustion. Small variations have however been observed, as, for example, between isomeric primary, secondary, and tertiary alcohols, and especially among unsaturated compounds, according to the position of the double bond, which will be presently considered. It seems to be well established that the more labile of two isomers gives the higher heat of combustion, and it is not unlikely that a careful revision of some of the values will bring this phenomenon into greater prominence.[1]

	Obs.	Mol. grm. cals.		Obs.	Mol grm. cals.
Propyl alcohol	L.	480 3	Thymol	St.	1353·7
Isopropyl alcohol	L.	478 3	Carvacrol	,,	1354 8
Caproic acid	St.	831·2	Glucose	St*	673·7
Isobutylacetic acid	St*	837 5	Fructose	,,	675 9
Diethylacetic acid	,,	837 6	Galactose	,,	669 9
			Sorbinose	,,	668·6
Ethylmalonic acid	,,	517 9			
Dimethylmalonic acid	,,	515 3	Cane-sugar	,,	1352·7
Glutaric acid	,,	515·0	Milk-sugar	,,	1351·4
Methylsuccinic acid	,,	515 2	Maltose	,,	1350 7
Propyl formate (vapour)	T.	546·6	*o*-Toluic acid	A R	921 4
Ethyl acetate ,,	,,	553 9	*m*-Toluic acid	,,	922 5
Methyl propionate ,,	,,	558 8	Phenylacetic acid	,,	930 9
			,, ,,	F.W.	933 4
Ethylene chloride	,,	272			
Ethylidene chloride	,,	272	Anthracene	St*	1694·3
			Phenanthrene	,,	1693 5
Phenyl ethyl ether	St.	1057 2			
m-Cresyl methyl ether	,,	1057·3			

Position- and Stereo-Isomers have also nearly identical heats of combustion :

		Mol. grm. cals.		
Position-Isomers.	Obs.	ortho.	meta.	para.
Dihydroxybenzenes	St*	685 2	683·4	683 3
Hydroxybenzoic acids	,,	729 5	729·0	725 9
Toluic acids	,,	929·4	929·1	927·4
Phthalic acids	,,	771·6	768 8	770 9
Xylenes	,,	1084·3	1084·2	1084·3

[1] Brühl, *J. prakt. Chem.*, 1894, **49**, 264.

The following geometrical isomers have, within experimental error, the same heats of combustion:

	Obs.	Mol. grm. cals.		Obs.	Mol grm. cals.
Citraconic acid	L.	477·6	cis Hexahydroterephthalic acid	St*	928 6
Mesaconic acid	,,	478 8	Trans- ,, ,,	,,	929·5

There are other cases in which the more labile form gives a distinctly higher value:

	Obs.	Mol grm. cals.		Obs.	Mol. grm. cals.
Maleic acid	L.	331 3	Oleic acid	St*	2669 2
Fumaric acid	,,	317 6	Elaidic acid	,,	2664 3
Angelic acid	St*	635 1	Allocinnamic acid	,,	1047·6
Tiglic acid	,,	626 6	Cinnamic acid	,,	1042·3

There is an unaccountable discrepancy in the values of tartaric and racemic acids, which give 261·7 and 278·7 mol.-grm.-cals respectively.

Homologous Series. A large number of homologous series have been examined by different observers, and in most cases a nearly constant difference has been noted. The following table gives the mean value for CH_2 and the minima and maxima for each series as determined by Stohmann:[1]

Series.	Mean.	Value for CH_2 Min. and Max.	
Aromatic Hydrocarbons	155 6	155·4—155 8	
Alcohols	156·1	154 6—156 9	
Phenols	156 3	153 9—157 2	
Phenol ethers	155·9	155 7—156 1	Mean = 156 3
Fatty acids, solid	156 6	155 0—157 6	
,, liquid	157·2	155 6—158 2	
Alkylmalonic acids	156 4	154 0—156 5	

Thomsen[2] from a similar series of eight different groups found the constant to be 158·5, and for another series of seven groups to be 157·1, or a mean of 157·8, whilst Berthelot[3] from a short series of hydrocarbons obtained a mean of 157·5. Seeing that many of the values have been determined by the older and less exact methods, it is not improbable that a revision would show a closer correspondence. Recent determinations by Fischer and Wrede[4] point to 156 as being a close approximation to the true value, whilst the same observers assign to H_2, from observations

[1] *J. prakt. Chem.*, 1886, 34, 326; 1887, 35, 28.
[2] *Thermochemistry*, by J. Thomsen, trans. by K. A. Burke, p. 391 et seq.
[3] *Ann Chim. Phys.*, 1893 (6), 30, 553.
[4] *Sitzungsber. Berl. Akad.*, 1904, 687; 1908, 129.

derived from a variety of different groups of compounds, a value varying from 41·4 to 51·9 cals.

Value for Hydroxyl Oxygen $(O')_b$ The value for hydroxyl oxygen has been determined by Stohmann[1] from the differences between the thermal values of the aromatic hydrocarbons and acids, on the one hand, and their hydroxy derivatives on the other:

	Mol. grm. cals.	Δ		Mol. grm. cals.	Δ
Benzene (solid)	777·3	45·0	Benzoic acid	771·7	43·6
Phenol	732 3	48 9	Hydroxybenzoic acid	728·1	51·2
Dihydroxybenzene	683·4	44 4	Dihydroxybenzoic acid	676·9	43·0
Trihydroxybenzene	639 0		Trihydroxybenzoic acid	633·9	

This would give a mean of 46; but the value is not constant, and is different for alcohols, ethers, and phenols, as the following series of isomeric substances shows:

Phenylmethyl ether	901·2 mol. grm. cals.
Benzyl alcohol	895 0 ,,
Cresols (mean)	882 0 ,,

There is a difference between the first and last of 19 cals., or more than 2 per cent., which cannot be ascribed to experimental error. The heats of combustion of the organic acids have brought out the interesting fact that the replacement of hydrogen by carboxyl, or, in other words, the addition of CO_2 to a compound, has a very small effect on the value, generally causing a small decrease of energy.[2]

	Mol. grm. cals.	Δ		Mol. grm. cals.	Δ
Formic acid	59 0	+1·2	Butane (calc.)	679 6	−2·4
Oxalic acid	60 2		Valeric acid	677·2	−2 0
			Propylmalonic acid	675·2	
Acetic acid	206·7	+0·6			
Malonic acid	207·3		Hexane	991·2	−2·4
			Ethyl propylacetic acid	988·8	+1 1
Propionic acid	364·0	−7 2	Ethylpropylmalonic acid	989·9	
Succinic acid	356·8				
Butyric acid	520·4	−5·4	Benzene (solid)	777·3	−5 6
Glutaric acid	515 0		Benzoic acid	771·7	

Another interesting fact, brought out by the work of Berthelot and of Stohmann and Langbein,[3] is that, in the formation of ethers and esters, the elimination of water by the union of alcohol with alcohol, phenol, or acid is unaccompanied by any large thermal effect, but is usually endothermic.

[1] *J. prakt. Chem.*, 1886, **33**, 467.
[2] *J. prakt. Chem.*, 1889, **40**, 223; 1890, **42**, 253.
[3] *J. prakt. Chem.*, 1889, **40**, 341; Berthelot, *Mécanique chimique*, vol. i, p. 407.

	Mol. grm. cals.		Mol. grm. cals.
Oxalic acid $+2CH_3OH$	401·4	Ethyl alcohol, 2 mols	651·4
Methyl oxalate	402·1	Ethyl ether	651·6

	Mol. grm. cals.
Phenol $+CH_3OH$	903·1
Phenylmethyl ether	905·5

The loss of water in anhydride formation of certain amino acids is estimated by Fischer and Wrede at 4·3 to 9·3 cals. By comparing certain acids with their amino derivatives the same observers assign the value 24·4—29·3 to the NH_2 group.

Although Thomsen[1] has calculated the thermochemical constants for carbon and hydrogen and for different kinds of organic groups and linkages and obtained values which agree well among themselves, they cannot be accepted without revision for reasons already given. At the same time they furnish striking evidence of the existence of such constants and the value which may be ultimately derived from them.

The Double Bond (|=). By comparing a series of saturated and corresponding unsaturated compounds of different types Brühl[2] found values which were anything but constant, varying from 30 to 50 cals. decrease in the unsaturated compound. Swientoslawski[3] found that the thermal effect of the double and treble bond varies with the molecular weight of the compound and the nature of adjacent radicals and has no definite value.

Conjugated Double Bonds. Stohmann and Langbein,[4] in comparing the heats of combustion of isomeric phenyl allyl and phenyl propenyl derivatives, showed that the more labile propenyl compounds gave 0·5—0·8 per cent. higher thermal values.

	Mol grm. cals.	Δ
Eugenole $(HO)(CH_3O)C_6H_3.CH_2.CH:CH_2$	1286·9	
Isoeugenole $(HO)(CH_3O)C_6H_3.CH:CH.CH_3$	1278·1	8·8
Safrole $H_2C\langle O \rangle C_6H_3.CH_2.CH:CH_2$	1244·7	
		10 2
Isosafrole $H_2C\langle O \rangle C_6H_3.CH:CH.CH_3$	1234 5	
Apiole $H_2C\langle O \rangle C_6H(OCH_3)_2CH_2.CH:CH_2$	1499 6	
		10·6
Isoapiole $H_2C\langle O \rangle C_6H(OCH_3)_2CH:CH.CH_3$	1489·6	

[1] loc. cit., p. 391.
[2] *J. prakt. Chem.*, 1894, **49**, 263.
[3] *J. prakt. Chem.*, 1892, **46**, 530.
[4] *J. russ. phys. chem. Ges.*, 1909, **40**, 1257, 1692, *Zeit. physik. Chem.*, 1909, **65**, 513.

The results seem to point to the effect of conjugation in the iso-compounds, which may be regarded as being in the more saturated or stable state, and therefore give out less heat on combustion.

Recently Auwers, Roth, and Eisenlohr[1] have very carefully ascertained the heats of combustion produced by conjugation in a series of terpenes containing both conjugated and unconjugated linkages. Taking the mean of the following three compounds as the normal value for $C_{10}H_{16}$ with two unconjugated linkages,

Limonene	1467	mean = 1464
Dipentene	1462	
Sylvestrene	1434	

the following differences from the normal value were observed :

Unconjugated $\|=_2$	Δ	Conjugated $\|=_2$	Δ	Bridged $\|=$	Δ
Limonene	+3	α-Phellandrene	−29	*d*-α-Pinene	+5
Dipentene	−2	Carvenene	−40	Camphene	+7
Sylvestrene	0	α-Terpinene	−36	Sabinene	+11

The presence of the bridged ring produces a distinct though small thermal effect ; but conjugation asserts itself very prominently.

Cyclic Compounds. The formation of a closed ring from an open-chain compound is attended by a gain of energy, if the loss of $H_2 = 69$ cals be taken into account. The following list of saturated open-chain and closed-chain dibasic acids will make this evident :

	Obs.	Mol. grm. cals.		Obs	Mol grm. cals.	Δ
Propane (vapour)	T	529 4	Cyclopropane	T	499 4	30 0
Glutaric acid	St.	515 0	Cyclopropane dicarboxylic acid	St.	483 6	31 4
Adipic acid	,,	668 9	Cyclobutane dicarboxylic acid	,,	642 5	26 4
Pimelic acid	,,	828 9	Cyclopentane dicarboxylic acid	,,	776 0	52 9
Suberic acid	,,	983 7	Hexahydrotere-phthalic acid	,,	929 0	54·7

The gain in energy diminishes in the 5- and 6 carbon rings, a circumstance which is readily explained by the strain theory (Part I, p. 199), according to which the 5- and 6-carbon rings produce least distortion of the bonds and therefore present the most stable arrangement.

Structure of Benzene. An attempt has been made to solve the 'benzene problem' by the aid of thermochemistry, and the subject is briefly referred to on page 434. On the assumption that the rupture of each double linkage produced the same

[1] *Annalen*, 1910, 373, 278 ; 1911, 385.

thermal effect, Stohmann instituted a comparison between benzene and its derivatives and their reduction products, from which it will be seen that between parallel pairs the thermal differences are the same, but not the same for each double bond in the same series. There is a 'jump' between benzene and the dihydro compound, the next two intervals are nearly equal, whilst there is again a slight increase between the tetrahydro and the saturated compound. Stohmann therefore drew the conclusion that benzene presents a structure which does not accord with the Kekulé formula.[1]

	Mol grm. cals.	Δ
Terephthalic acid	770 9	
$\Delta^{1,4}$ Dihydro ,,	836 1	65·2
$\Delta^{1,5}$ Dihydro ,,	842·7	71·8
$\Delta^{2,5}$ Dihydro ,,	845 8	74·5
Δ^{1} Tetrahydro ,,	882 8	46 7
cis-Hexahydro ,,	928 6	
trans-Hexahydro ,,	929 5	46 2
Suberic acid ,,	983·7	54 7

	Mol. grm. cals.	Δ
Terephthalic methyl ester	1112·7	68·6
$\Delta^{1,4}$ Dihydro ,,	1181·3	
—		
—		
Δ^{1} Tetrahydro ,,	1226·8	45 5
—		47·1
trans-Hexahydro ,,	1273·9	51·0
Suberic methyl ester (calc.)	1324·9	

	Mol grm. cals.	Δ
Phthalic acid	771 6	
$\Delta^{2,6}$ Dihydro ,,	843 1	71·5
Δ^{2} Tetrahydro ,,	881·6	38 5
—		
—		

	Mol. grm. cals.	Δ
Benzene	779 8	68·2
Dihydrobenzene	848 0	44·0
Tetrahydrobenzene	892·0	41 2
Hexahydrobenzene	933·2	58 0
Hexane	991·2	

Although the agreement between the different series is fairly concordant and at first sight appears to confirm Stohmann's conclusion, there are a number of other facts which must be considered before the Kekulé formula can be abandoned on this ground.[2]

In the first place, we have seen that the value for the double bond varies enormously in different compounds and even in compounds which are so closely related as geometrical isomers (p. 252), or the three dihydroterephthalic acids in the above table.

This variation is still more manifest in the relation between conjugated and unconjugated double linkages. Conjugation, as we have

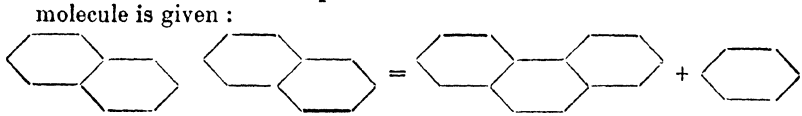
[1] A careful redetermination of the values for the saturated and unsaturated aromatic hydrocarbons by Roth and Auwers (*Annalen*, 1915, 407, 148) shows that the above differences are not quite correct, but that there is a gradual falling off from 64 cals between the aromatic hydrocarbon and the conjugated cyclohexadrene, to 50 cals between the latter and cyclohexene and 45 cals between cyclohexene and cyclohexane. In the case of the two dihydronaphthalenes, one being conjugated and the other not, there was a difference of 5 cals. less in the conjugated or more stable compound They consider that the nature of the conjugation and the symmetry of benzene would tend to produce greater stability and less free energy than in the other compounds, which would be indicated by a successive diminution in the thermal difference for each double bond.

[2] The subject has been very fully and fairly discussed by Brühl (*J. prakt. Chem.*, 1894 49. 260).

already pointed out, means increased stability and consequently a relatively smaller heat of combustion. The most recent and accurate determinations [1] of the values of sorbic, hydrosorbic, and caproic acid show a difference between the first two of 48·6 cals., and the last two of 42·6 cals. The conclusion is obvious that if there exists a difference between the highest and lowest value among isomeric dihydroterephthalic acids of 9·7 cals., it is impossible to foretell the effect of the additional double bond in terephthalic acid except that it is almost certain to have a value very different from the mean of that which divides the di- and tetra-hydro acids.

A very interesting contribution to the thermochemistry of aromatic compounds has been made by von Steiger.[2] Adopting the view of W. L. Bragg and Debye and Scherrer on the constitution of graphite (see p. 412), in which the benzene rings are arranged in loosely attached layers (cleavage planes) so that the fourth valency is so weak as to be almost negligible, and assuming further the equal distribution of valency between the carbon atoms, now acting as tervalent atoms, he has made the following observations.

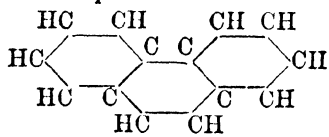
Taking a series of aromatic hydrocarbons, benzene, diphenyl naphthalene, phenanthrene, and triphenyl benzene, von Steiger has shown that the heats of combustion of the more complex ring systems, using Stohmann's values, will give those of less complexity by a simple process of subtraction. To take one example, by deducting from the heat of combustion of two naphthalene molecules that of one molecule of phenanthrene the value for one benzene molecule is given :



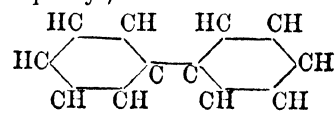
Naphthalene Phenanthrene. Benzene.

$2 \times 1217{\cdot}3 - 1709\,9 = 784\,7$, observed value = 785·4,

and although a great variety of combinations of this kind are given, there is a remarkably small divergence between the observed and calculated values. Another point of interest referred to in the paper is the method for ascertaining the heat of combustion of each carbon atom of the ring and from it to deduce its heat of formation. The first is effected by a process of subtraction similar to that described. Thus, if the heat of combustion of diphenyl is deducted from that of phenanthrene and the result divided by 2, there being two carbon atoms in phenanthrene more than in diphenyl,



$C_{14}H_{10}$



$C_{12}H_{10}$

or if the heat of combustion of four molecules of benzene be deducted from three of naphthalene and the result divided by 6 and so forth, the same number on the average, 100·4, is obtained, which therefore

[1] Fischer and Wrede, *Sitzungsber. Berl. Akad.*, 1904.
[2] *Ber.*, 1920, 53, 666 ; 1922, 55, 1968.

represents the heat of combustion of each carbon atom in the ring less the heat absorbed by the rupture of the adjoining carbon atoms. The lower value for graphite, 94·3, is accounted for by the loosening of the residual valency of the carbon atom which binds the cleavage planes.

As the number of bonds binding each carbon atom to its neighbours according to the Thiele theory is three, and as these are shared, each carbon atom absorbs $\frac{3}{2}$ of the valency. Taking the thermal values of Fajans, 381 and 74·4, as those of the gram atom of carbon and hydrogen respectively (p. 64), then the heat absorbed, x, in the breaking away of each carbon atom, or its heat of formation, will be given by the expression: $381 - \frac{3}{2}x = 100{\cdot}4 \qquad x = 187$

The heat of formation of the C—H linkage is obtained by deducting, for example, the value for diphenyl (1509 mol.-grm.-cals.) from that of two benzene molecules (2×785 mol.-grm.-cals.) whereby two C—H linkages are removed. The mean of a number of such determinations is 60·7 and is given by the expression:

$$y = \frac{187 + (2 \times 74{\cdot}4 - 60{\cdot}7)}{2} = 137{\cdot}7.$$

The different values for the C—C and C—H linkages in aromatic hydrocarbons and those of the aliphatic series (p. 67) is explained by the different distribution of the valency in the two series of hydrocarbons.

ABSORPTION SPECTRA AND STRUCTURE

Absorption of Light. The phenomenon of colour is associated with selective absorption, that is, with the absorption of certain light rays and the transmission or reflection of others. This is best observed in solution by allowing a beam of ordinary light to enter a liquid in which the coloured substance is dissolved, and then examining the spectrum after the light has passed through a prism. Certain dark bands in the spectrum, where absorption has occurred, will make their appearance. But absorption is not confined to the visible spectrum. There is an infra-red region, of long wave length, which is characterised by its heating effect, and an ultra-violet region, of short wave length, productive of chemical activity, where absorption may occur. Glass and water are transparent to visible light, but the former absorbs ultra-violet light and the latter infra-red light. In addition to the region of the ultra-violet, infra-red, and visible spectrum, absorption of both shorter (Röntgen) waves and longer (heat and electrical) waves has been observed. The following scheme gives the nature of the rays and range of wave lengths (λ) in different parts of the spectrum:

	Röntgen.	Ultra-violet.	Visible region.	Infra-red.	Heat rays.
λ	·01–1 $\mu\mu$	100–400 $\mu\mu$	400–800 $\mu\mu$	800 $\mu\mu$–1 μ	1 μ–10 μ

Electrical waves. Short. Long.

λ 1 mm.–10 mm. 1 cm.–1000 km.

1 $\mu\mu$ = ·000001 mm. 1 μ = ·001 mm.

The portion of the spectra which at the present time has a special significance in relation to chemical constitution is the region which includes the ultra-violet, visible, and infra-red. Absorption in the first two may be detected by photography, and in the last by the heating of an electrical resistance in an instrument known as

Langley's bolometer. According to Drude and others, it is probable that selective absorption in the visible and ultra-violet region is determined by the period of free vibration of the electron, caused by the electro-magnetic energy of the incident beam—in other words, by a process similar to that of 'resonance' in sound. As the number of these electrons was found to correspond roughly with the number of valency electrons present in the molecule, it follows that the latter must be concerned in the process of selective absorption (Part I, p. 99). It is important to bear this in mind in view of the constant association of colour with unsaturation. Seeing that the period of vibration of the electron can be determined by spectroscopic investigation, it seems natural to conclude that observations of this character should eventually throw some light on the structure of the atom as well as on the whole structure of the system emitting these vibrations, that is, on the constitution of the molecule.

Drude has further shown that the particles which absorb in the infra-red must have a change of opposite sign to the valency electrons, and possess a much larger mass; they are probably identical with the atoms.

Little is known as yet of the relation of the infra-red absorption to structure. The effect is apparently additive, and so far as it has been studied, the lines or bands, which are developed, can be traced to certain atoms or atomic groups. We shall therefore confine our attention to the results of observation on the absorption in the visible and ultra-violet region.

From what has been stated it will be inferred that absorption in the ultra-violet is not intrinsically different in its origin from that in the visible region, and the name 'invisible colour' has not inappropriately been assigned to selective absorption of these rays.

Experimental Method. Before discussing the structural causes and effects of visible and ultra-violet absorption, a brief outline will be given of the experimental method of investigation. The method in its essential features has been developed by Sir N. Hartley,[1] who, in conjunction with his collaborators, has carried out a series of investigations extending over many years. It consists in causing a beam of ordinary light, or one rich in ultra-violet rays (obtained with an arc from metallic electrodes), to pass through a solution of the substance and then through a spectrograph, provided in the case of ultra-violet absorption with quartz lenses and prism and a camera

[1] Hartley and Huntington, *Phil. Trans.*, 1879, 170, 257.

containing a photographic plate. The spectrum when photographed reveals the position of the absorption bands. The arrangement of the apparatus will be readily understood from Figs 10 and 11.

Fig. 10 is a diagrammatic illustration, in which *a* represents the metallic electrodes, *b* the absorption-cell containing the liquid,

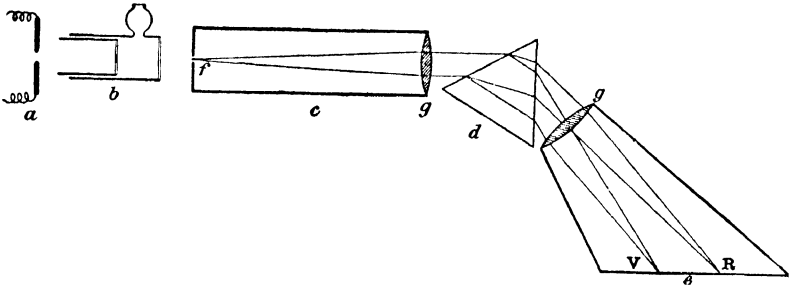


FIG 10

c the collimator tube, *d* the quartz prism, *e* the back of the camera with photographic plate, *f* the slit, and *g*, *g* quartz lenses.

Fig. 11 is a photograph of a general view of the apparatus.

The spectrum of ultra-violet light from metallic electrodes consists of innumerable lines distributed over the ultra-violet region, and the

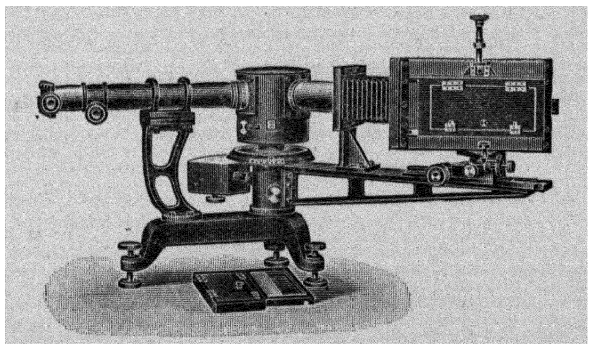


FIG. 11.

absence of these lines, produced by the absorbing medium, may be readily detected. The photographs, Figs 15 and 16, facing p. 78, show, at the top, the spectrum of the metallic lines, and below, the absorption bands produced by various strengths of solutions of cotarnine and its derivatives in different solvents.

A solvent is selected which is, as far as possible, diactinic, and

usually water, methyl and ethyl alcohol are employed for the purpose. A series of photographs are then taken on the same plate of different dilutions or of different thicknesses of liquid layer. We may suppose, for example, that the absorption of a normal solution of a layer 10 mm. thick is first determined, and the thickness reduced to 9, 8, ... 1 mm. A tenth-normal solution is then taken of 10 mm. thickness, which is equal to a normal solution of 1 mm.,[1] and

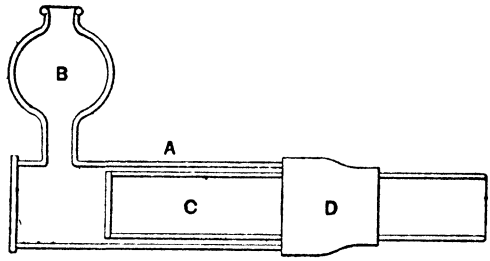


FIG. 12.

in the same way thicknesses of 9, 8 ... 1 mm. recorded. The latter may be again diluted and examined in different thicknesses and so a continuous series of spectra obtained, until a dilution is reached where no absorption occurs. This mode of recording results was introduced by Hartley, the oscillation frequencies (i. e. the reciprocals of the wave lengths) being plotted as abscissae against the concentrations as ordinates. The oscillation frequencies ($1/\lambda$) for the infra-red, visible, and ultra-violet regions are usually given in four figures, and are roughly represented as follows:

	Infra-red.	Visible.	Ultra-violet.
$\frac{1}{\lambda}$	1000-1390	1390-2540	2540-5000

Instead of preparing different strengths of solution, Baly and Desch[2] use an adjustable tube, furnished with quartz plates, for ultra-violet absorption, Fig. 12.

The liquid is introduced through the bulb B surmounting the

[1] According to *Beer's law* the intensity of colour in a solution is proportional to its concentration, that is, a layer of a certain concentration is equal to one of double the thickness and one-half the concentration. The law, it should be added, is not without its exceptions, which have been accounted for by ionisation, hydrolysis, association, union with the solvent, or some change of structure of the solute. The solvent also has its specific action, and according to *Kundt's rule*, the greater its index of refraction, the more the absorption bands are shifted towards the red. This rule is also not free from exceptions.

[2] *Trans. Chem. Soc.*, 1904, 85, 1029.

tube A, and the thickness of the liquid layer may be increased or diminished by pushing in or withdrawing the inner movable tube C, which is attached by the rubber band D. Also, instead of recording differences produced by cutting off equal layers of solution, it is now customary to calculate and plot the logarithms of the thicknesses, or, more frequently, to etch on the outer tube divisions corresponding to the logarithms of the thicknesses.[1] Thus, each thickness is the same multiple of the previous one, and successive exposures represent exactly equal proportionate increments or decrements of concentration.

The curve, Fig. 17, is plotted from the photographs, Figs. 15, 16 (p. 82) on the above principle. The curve follows the contour of the series of absorption bands. It will be seen that the thickest layer produces the broadest band. As the layer becomes thinner, the band may become narrower or break up into two or more bands, which finally disappear when the column of liquid is reduced below a certain thickness. The lowest point of the curve is called the *head*, and the length through which it extends, its *persistence*. The latter feature is of considerable importance in relation to the structure of the molecule.[2]

Absorption spectra among organic compounds may be divided broadly into two types, namely, those in which there is general absorption, that is, uniform absorption over a certain region of the spectrum, and those in which it is selective or banded. In the visible spectrum selective absorption is accompanied by the appearance of colour. The substances producing ultra-violet absorption are colourless, and

[1] Lowry and Desch, *Trans. Chem. Soc.*, 1909, 95, 822.

[2] As the edge of an absorption band is frequently ill-defined the difficulty is to some extent met by the use of the *spectrophotometer*. For ultra-violet rays the source of light is divided into two beams, one of which passes through the cell containing the solution, and then through a rotating sector of fixed aperture and the other through a rotating sector the aperture of which may be varied to any known extent. The two beams are reflected so as to enter the slit one above the other and appear on the photograph in juxtaposition. With diminishing length of the absorbent solution the aperture of the revolving sector is increased. In this way it is possible to determine when the two spectra are of equal intensity, and to ascertain at the same time the percentage of light absorbed by the solution. It is customary now to plot wave lengths against the logarithms of molecular extinction coefficients according to the formula $\log \frac{I_0}{I} \div dc$, where I_0 and I are the intensities of the incident and emergent light respectively, d the thickness of the absorbing layer, and c the molecular concentration.

have been divided by Hartley into three classes : those which produce general absorption, but which on dilution with inert solvents become readily transparent to the rays (aliphatic hydrocarbons)—in this class, substitution of hydrogen by OH, CO_2H, OCH_3, and NH_2 groups has little effect on the character of the absorption, and only affects its intensity ; secondly, those which absorb more strongly than the above and which are less influenced by dilution (cyclic compounds, furfurane, thiophene, pyrrole, piperidine, hydroaromatic

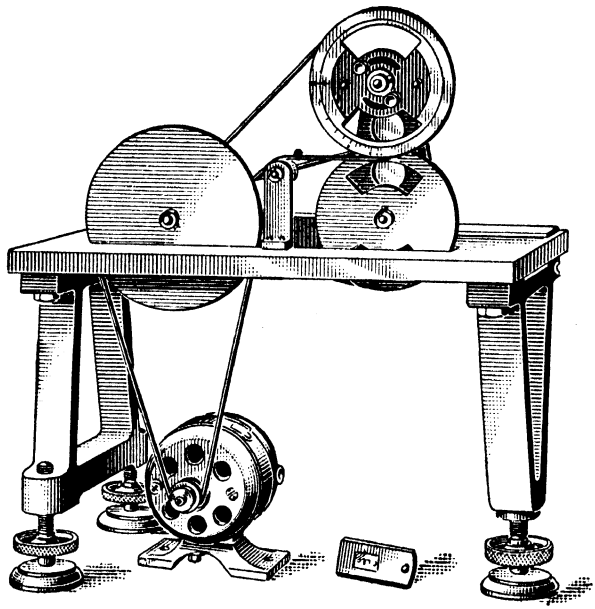


Fig. 12 a. Spectrophotometer.

compounds, &c.) ; and finally, those which exhibit a banded spectrum (benzene, naphthalene, pyridine, and their derivatives, and certain aliphatic ketones).

It is only by a banded spectrum and by the number, position, and persistence of the bands that a substance can be characterised. As yet no direct connection has been established between the structure of a compound and its absorption spectrum. It is impossible

to state *a priori* the kind of absorption which a particular type of compound will produce. All that can be definitely stated is that among the lower members of a homologous series increase in molecular weight is frequently accompanied by a shifting towards the red end of the spectrum; but the effect dies out among substances of high molecular weight.

Application of Absorption to Structure. The only method which is available for determining structure is one of comparison or analogy, based on the assumption that compounds of similar structure exhibit absorption curves of similar shape and showing similar frequencies.

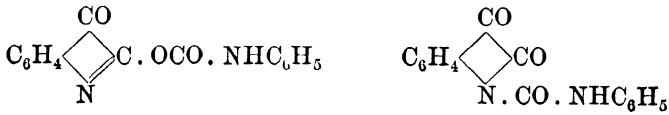
It is in this direction that the work of Hartley, Dobbie, Lauder, Baly, and others has proved so valuable, and for this purpose it is immaterial whether the effect is confined to the visible or ultra-violet region of the spectrum. The method has been applied with great success in deciding between alternative formulae, especially among tautomeric compounds, to which a brief reference is made on p. 369.

The Structure of Isatin. We will consider a few examples by way of illustration.[1] One of the most interesting is that of isatin, which forms two isomeric ethyl derivatives, one derived from the lactam, the other from the lactim structure. Baeyer regarded the free compound as representing the lactim formula (p. 330),

Isatin (Lactim). Pseudoisatin (Lactam).

Formulae for Isatin.

which agreed with the observation of Schunck and Marchlewski, that the substance yielded only one monoxime and one phenylhydrazone. Goldschmidt, on the other hand, found that isatin gave, with phenylcarbimide, a carbanilido derivative and not a carbamate, thereby indicating the lactam structure:



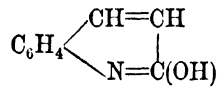
Isatin carbamate (Lactim). Carbanilido isatin (Lactam).

On comparing the absorption curves of the two isomeric methyl

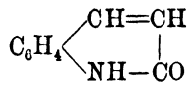
[1] See Hartley and Dobbie, *Trans.*, 1900, 77, 498.

derivatives with that of free isatin (Fig. 13), the close resemblance of the latter with the *N*-methyl ether established the structure definitely in favour of the pseudoisatin or lactam formula.[1]

The same method was employed in the case of carbostyril, by comparing it with the two methyl ethers, and the result was also in favour of the lactam formula:



Carbostyril (Lactim).



Pseudocarbostyril (Lactam).

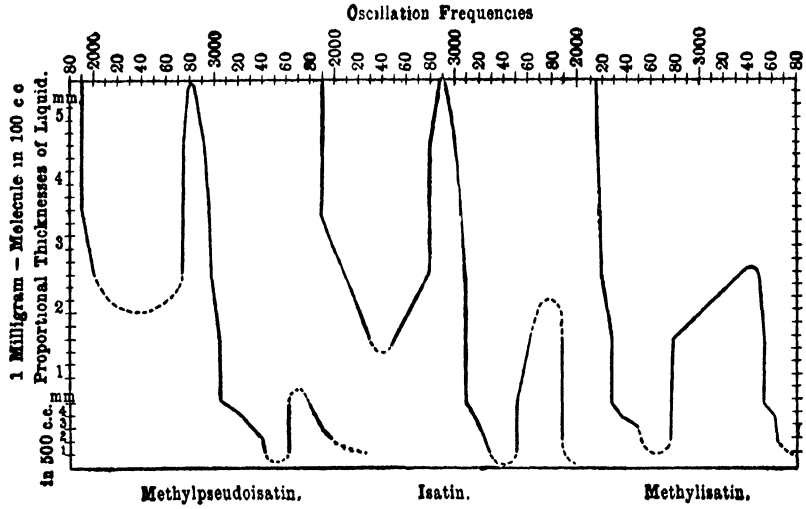
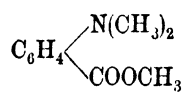


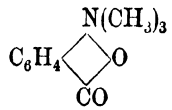
FIG. 13.

The curves of the two ethers and that of carbostyril are given in Fig. 14.

Ley and Ulrich[2] have also shown that it is possible to distinguish between an ortho-amino acid with an open or closed chain (betaïne) structure by means of the absorption curves. For example, the methyl ester of dimethylanthranilic acid has a different absorption curve from that of the isomeric betaïne.



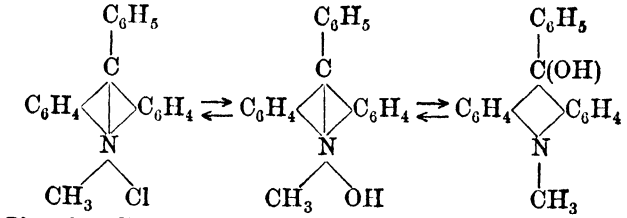
Dimethylanthranilic ester.



α-Benzbetaïne.

[1] Hartley and Dobbie, *Trans. Chem. Soc.*, 1899, 75, 640. [2] *Ber.*, 1909, 42, 3440.

Structure of the Alkaloids.[1] A reversible isomeric change similar to that of isatin and pseudoisatin is seen in the ammonium and pseudo-ammonium bases, which are discussed on p. 366, where reference is made to the case of phenylacridinium methyl chloride and its conversion into phenylmethylacridol.



Phenylacridinium methyl chloride.

Phenylmethylacridol (true ammonium base).

Phenylmethylacridol (pseudo-ammonium base).

Dobbie, Lauder, and Tinkler[2] have found that cotarnine (Part III, p. 358)

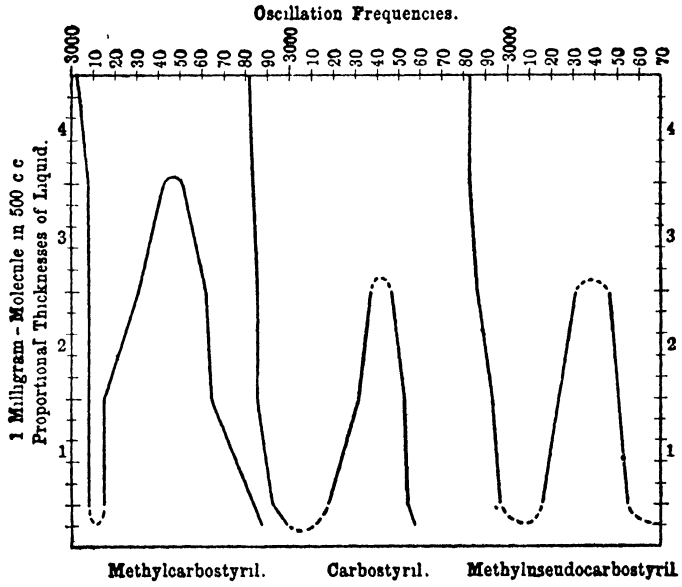


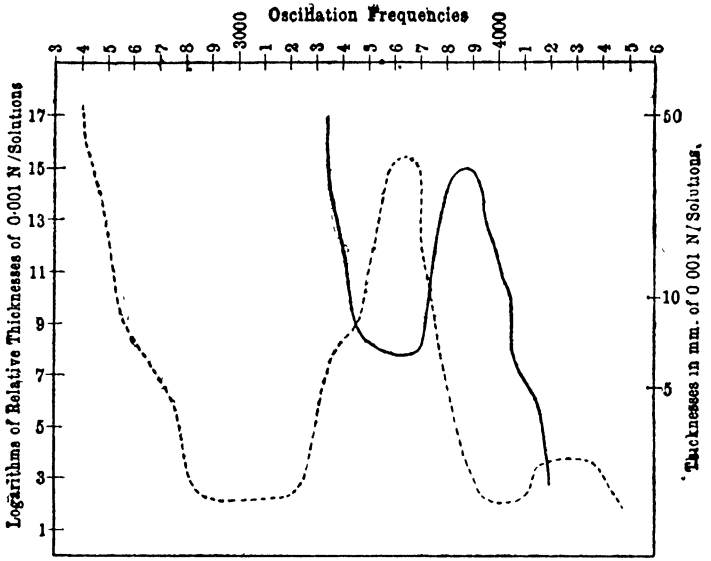
FIG. 14.

undergoes a precisely similar change, which may be followed in the same way by plotting its absorption curves. Whereas solutions of cotarnine in ether and chloroform are, like the solid base, colourless,

[1] *British Assoc. Report*, 1903, p. 126.
[2] *Trans. Chem. Soc.*, 1903, 83, 598; 1904, 85, 121.

its solutions in water or alcohol are yellow. The spectra of the colourless solutions agree with those of hydrocotarnine and cotarnine cyanide. The yellow solutions, however, give an absorption spectrum identical with that of the hydrochloride, but quite different from that given by the colourless solutions in ether and chloroform. Photographs of the spectra of cotarnine and its hydrochloride in water are shown in Fig. 15 (*a* and *b*), and of cotarnine and hydrocotarnine in ether in Fig. 16 (*a* and *b*)

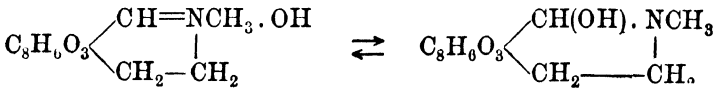
The curves are traced out in Fig. 17.



Full Line Curve = Cotarnine in Ether and Hydrocotarnine in Water
Dotted Line Curve = Cotarnine in Water and Cotarnine Hydrochloride.

FIG. 17.

In order to explain the existence of the two kinds of spectra, to one or other of which all the cotarnine compounds conform, the following formulae of Decker have been adopted:



Yellow ammonium base. Colourless pseudo-ammonium base.

In other words, the change is a reversible one, corresponding with that of phenylmethylacridinium hydroxide to phenylmethylacridol. Hydrocotarnine, the cyanide, and the solutions in ether and chloroform will be saturated and colourless,

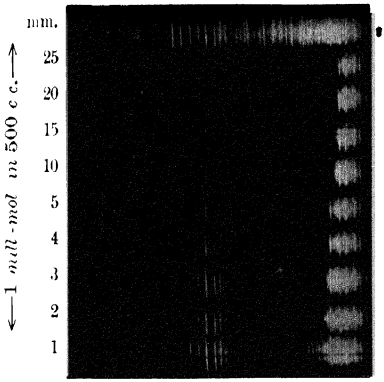


FIG 15 (*a*) Cotarnine (in water).

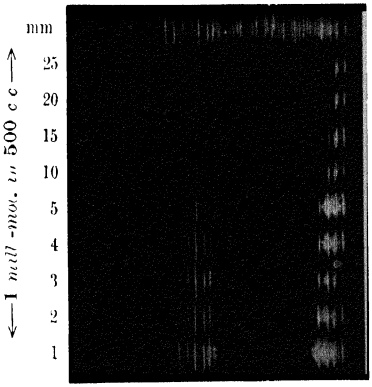


FIG. 15 (*b*) Cotarnine hydrochloride.

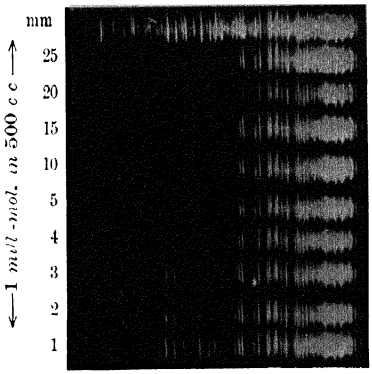


FIG 16 (*a*) Cotarnine (in ether).

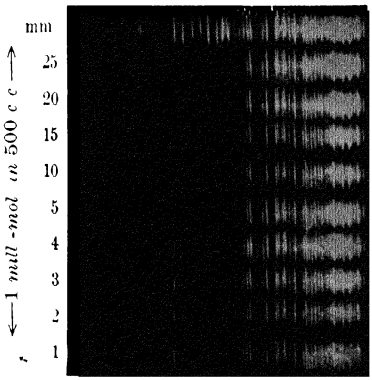
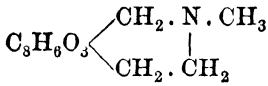
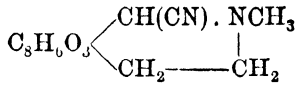


FIG. 16 (*b*). Hydrocotarnine

To face II p. 82

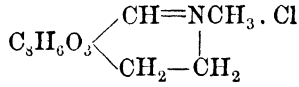


Hydrocotarnine.



Cyanocotarnine.

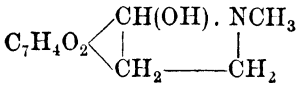
whereas the aqueous solutions and the salts will be unsaturated and coloured.



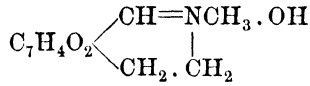
Cotarnine chloride.

It follows naturally that alkalis convert the yellow salt into the colourless base and that acids produce the reverse reaction, and these changes can be observed by the accompanying modification of the absorption spectra.

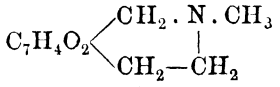
Hydrastine (Part III, p. 364) has been investigated in the same way. Like cotarnine it is colourless, giving colourless solutions in anhydrous alcohol, ether, and chloroform, but changing to yellow in water. The absorption spectra of the colourless and coloured solutions are different, the former resembling hydrohydrastinine and the latter the salts of hydrastinine and its solutions in water. The formulae are consequently represented as follows :



Colourless carbinol in ether and chloroform.



Yellow ammonium base and salts in water.



Hydrohydrastinine.

A knowledge of the complete structure of some of these alkaloids has demonstrated the utility and trustworthiness of the method.[1]

Stereoisomeric alkaloids have been shown to give the same spectra. Illustrations of this are afforded by *d*- and *dl*-corydaline, narcotine, and gnoscopine.[2] The spectra of quinidine and cinchonidine are identical with those of quinine and cinchonine, and are probably stereoisomeric. Active canadine and inactive tetrahydroberberine were found to have the same spectra. Subsequently Gadamer[3] resolved the latter into its components, one of which was identical with canadine.

Homologous alkaloids also give identical spectra, and the same is true when hydrogen is replaced by a methoxyl group. The fact that

[1] Tinkler, *Trans Chem Soc*, 1911, 99, 1340; Dobbie & Fox, *ibid.*, 1914, 105, 1689.
[2] *Trans. Chem. Soc*, 1900, 77, 498, 509. [3] *Arch. Pharm.*, 1901, 239, 648.

laudanine and laudanosine have the same spectrum, which is also similar to that of tetrahydropapaverine, shows that they are homologues and allied to the latter substance. Since these observations were made, laudanosine has been obtained synthetically and proved to be *N*-methyltetrahydropapaverine or the methyl ether of laudanine.[1] The presence or absence of small groups seems to have little effect on the absorption spectrum. The oxidation of an unsaturated side-chain to carboxyl also produces little modification, but the reduction of a ring causes fundamental changes.[2] Though papaverine and tetra-

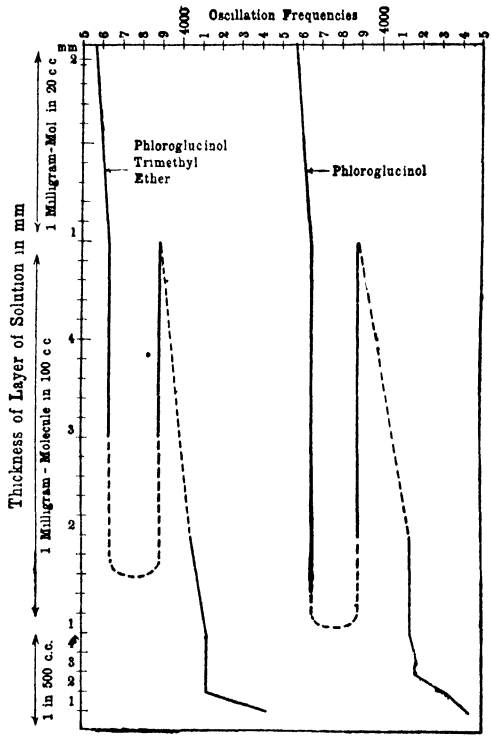


FIG. 18.

hydroberberine are isomeric, the difference in spectra is a proof of a difference of structure.[3] It may be laid down as a general rule that those alkaloids which agree closely in structure give similar absorption curves, while those which differ in essential features give dissimilar curves.

[1] *Ber*, 1909, 42, 1979.
[2] *Trans. Chem. Soc.*, 1885, 47, 691; 1900, 77, 846.
[3] Dobbie and Lauder, *Trans. Chem. Soc.*, 1903, 83, 626.

Keto-Enol Tautomerism. Hartley, Dobbie, and Lauder[1] were able to prove that phloroglucinol (which sometimes functions as a ketone and at other times as a phenol) had a true phenolic structure in the free state, by comparing its absorption curve with that of its methyl ether. It will be seen from these curves (Fig. 18) that the two bear a close resemblance, and seeing that the methyl ether can only represent the phenolic structure, that of the free compound must have the same.

In the same way, Hartley and Dobbie found that the two dynamic

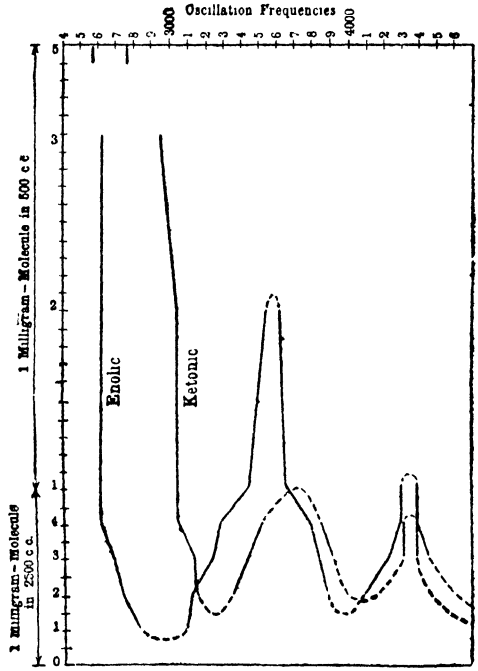


FIG. 19. Dibenzoylmethane.

isomers, dibenzoylmethane and α-hydroxybenzalacetophenone, could be readily differentiated.

$C_6H_5 . CO . CH_2 . CO . C_6H_5$
Dibenzoylmethane.

$C_6H_5C(OH) : CH . CO . C_6H_5$
α-Hydroxybenzalacetophenone.

They both exhibit two well-defined absorption bands, which, however, differ in position and persistence (Fig. 19).

In examining the ultra-violet absorption spectra of acetylacetone and certain metallic derivatives in alcoholic solution, Baly and Desch[2] found that all the substances show absorption bands (Fig. 21).

[1] *Trans. Chem. Soc.*, 1902, 81, 929. [2] *Trans. Chem. Soc.*, 1904, 85, 1029.

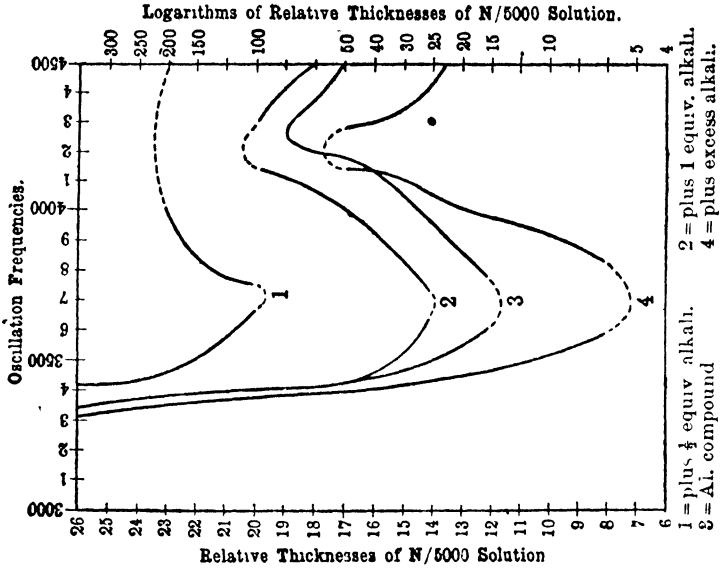


Fig. 20. Acetoacetic ester.

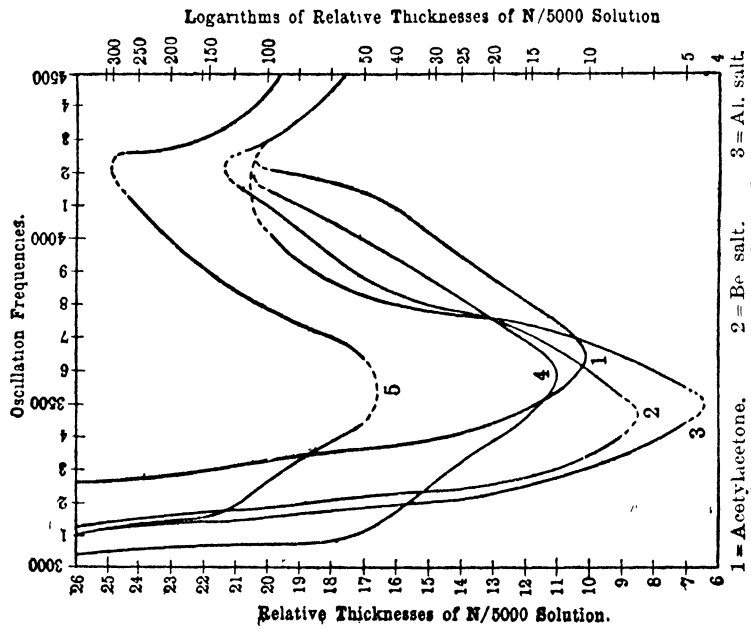
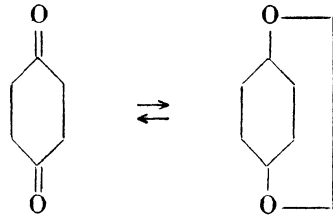


Fig. 21. Acetylacetone.

They are therefore closely allied in structure, and are probably enolic. In the case of ethyl acetoacetate, which is mainly ketonic (see p. 333), there is no band, whereas its metallic derivatives show a strongly banded absorption, almost identical with that of acetylacetone. Moreover, the addition of caustic soda develops a banded spectrum, the persistence of which increases with the addition of the alkali until it reaches a maximum (Fig. 20).

The authors originally suggested that the appearance of a banded spectrum was determined by a vibrational disturbance in the valency electrons produced by the process of dynamic change. A similar view was applied to the 1.2 diketones, the quinones, and certain other aromatic compounds which likewise show a banded spectrum. As tautomeric change is precluded in certain of these compounds, the vibrational disturbance was attributed to the recurrent making and breaking of linkages, termed *isorropesis* (ἰσορροπία = equipoise). Thus, in the quinones the following changes were assumed to recur:



There are many facts which render this theory improbable. Willstätter[1] found that *o*-benzoquinone exists in both a colourless and a red modification. Supposing the two isomers to represent the pure quinone and peroxide forms, neither compound should exhibit absorption bands. Moreover, dynamic isomerism is not necessarily accompanied by the presence of absorption bands.

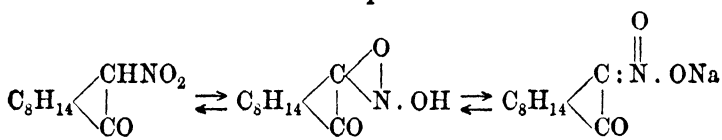
Dynamic Isomerism and Absorption. The relation between dynamic isomerism and selective absorption has been very carefully studied by Lowry and Desch,[2] who were able to trace the extent to which isomeric change determines the existence of a banded spectrum.

Nitrocamphor and bromonitrocamphor are known to exist in two isomeric forms, which, under certain conditions, pass into one another, forming an equilibrium mixture. The change, which can be accurately followed in the polarimeter by noting the change in rotation, is termed mutarotation, and is discussed on p. 367.

[1] *Ber.*, 1908, **41**, 2580.
[2] *Trans. Chem. Soc.*, 1909, **95**, 807, 1340; 1910, **97**, 900.

Lowry has shown that by altering the solvent it is possible to vary at will the period of change, to accelerate or retard it, or to stop it altogether. He concludes from his observations that 'in spite of the wide range of velocities, no great alteration was seen in the form of the absorption curve. Each spectrum showed a 'step out', but no band. . . . It is clear then that the isomeric change of nitrocamphor, even although it involves actual transference of a mobile hydrogen atom and takes place with high velocity in both directions, can proceed incessantly without production of a band.' On addition of alkali ($NaOC_2H_5$) a deep band was developed, but according to polarimetric observations the compound was purely enolic, and no intensification of the band could be detected on addition of a further quantity of alkali.

Precisely similar results were obtained with bromonitrocamphor. Thus, no special feature was observed in the spectra of the pseudo compounds to distinguish them from the normal modifications, until alkali was added, when the same band was developed in both modifications. This result was expressed as follows:



Normal nitrocamphor. Pseudo nitrocamphor. Sodium salt.

In the case of α-bromocamphor, which rapidly enolises on the addition of a trace of alkali, but not in neutral solution, no change is produced in the absorption band. Again, a definite band may be produced in a compound from which all possibility of isomeric change is removed, as in ω- and α-bromomethyl camphor.

ω-Bromomethyl camphor. α-Bromomethyl camphor

Thus, reversible isomeric changes cause no selective absorption, and in the simpler camphor derivatives the band is produced with equal facility, whether the substance is undergoing isomeric change or not.

There appear, from what has been stated, to be two kinds of absorption bands, namely, those produced by the addition of alkali and not by the parent substance, and which must therefore be due to a definite structure, and those which are developed indifferently in a neutral or alkaline solution. For the latter no complete explanation is forthcoming, and the authors suggest that it may be

caused by residual affinity of certain unsaturated atoms or groups, such as have been shown to give rise to exaltation of refractivity (p. 29) and magnetic rotation (p. 54).[1]

Hantzsch[2] has arrived at much the same conclusions in regard to acetoacetic ester and its derivatives ; that inasmuch as the pure keto and enol forms exhibit general absorption, though of varying intensity, whereas the alkaline solutions show a banded spectrum, the latter must be regarded as possessing a different structure from the other two.

This difference of structure between the enol form and its metallic derivatives is attributed to the residual valency of the metal (Me) and is represented thus.

$$CH_3 . C . OH \qquad\qquad CH_3 . C . OMe$$
$$\| \qquad\qquad\qquad \| \; \vdots$$
$$HC . CO . OR \qquad\qquad HC . CO . OR$$

Hantzsch[3] has explained the effect of solvents on absorption spectra by dividing them into two classes; namely, those solvents which may form loose complexes with the dissolved substance, whereby the general absorption is scarcely affected, and those solvents (generally containing oxygen, such as water, alcohol, ether, &c.) which either enter into definite chemical union or bring about dynamic isomerism when the character of the absorption is materially changed. From the fact that the organic acids and salts show similar absorption effects in certain dissociating solvents, but differ materially from those of the acids and their esters in non-dissociating solvents, he concludes that the structure of the acids and salts in ionising media must be represented by the co-ordinate formulae

$$R . C \begin{matrix} O \\ O \end{matrix} \Big\} H \qquad\qquad R . C \begin{matrix} O \\ O \end{matrix} \Big\} Me \qquad\qquad Me = \text{metal}$$

which he terms the *true* carboxyl form as distinguished from

$$R . C \begin{matrix} = O \\ \diagdown OR \end{matrix} \qquad\qquad R . C \begin{matrix} = O \\ \diagdown OH \end{matrix}$$

or *pseudo* carboxyl form. The weaker free acids show absorption curves pointing to mixtures of the true and pseudo forms, whereas the absorption of trichloracetic acid in water and ligroin is identical with that of its salts but different from its solution in alcohol and ether, which coincides with that of the ester. This view bears a certain analogy with that of Henri and Bielecki,[4] who made a com-

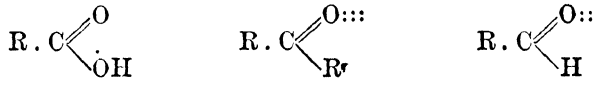
[1] Lowry and Southgate, *Trans. Chem Soc.*, 1910, 97, 899, 912.

[2] *Ber.*, 1910, 43, 3049; 1911, 44, 1771; see also Stewart, *Trans. Chem. Soc.*, 1913, 103, 406; and Bielecki and Henri, *Compt. rend.*, 1914, 158, 866.

[3] *Ber.*, 1917, 50, 1422.

[4] *Ber.*, 1913, 46, 1804, 3649.

parison of the absorption spectra of the aldehydes, ketones, and acids represent the three groups thus:



Baly's Theory of Absorption. Baly[1] has replaced the theory of isorropesis by one of a more comprehensive character. Like Lowry and others, he bases his view on the existence of residual affinity. In a molecule the residual affinities of the separate atoms will tend to neutralise one another with a certain loss of energy; but the whole of the free affinity will not necessarily disappear, and what remains forms the residual affinity of the molecule, and lends to it its basic or acid character.

This breaking down of the neutralised free affinities of the atoms, or, as the author expresses it, 'the unlocking of the condensed lines of force emanating from the secondary valency electrons', may give rise to a variety of effects. The unlocking process may be brought about by adding energy to the system in the form of heat or light. Among the effects produced are, in the first place, selective absorption or the absorption of those rays which correspond to the disposition of the electrons in the system upon which the light falls. Where no such absorption occurs, it is assumed that the closed system remains intact. The effect of the solvent, which may produce selective absorption where the pure substance fails to do so, is determined by the residual affinity of the solvent, which can in the same way unlock the closed system. The solution can now absorb light, and consequently exhibits a banded spectrum. This union of solvent and solute (solvate) may explain the deviations from Beer's law and the existence of Kundt's rule.[2] The combination may be regarded as the initial stage in a true chemical union. If this union is sufficiently active it will pass to a second stage; a rearrangement of electrons will take place, and a chemical reaction occur.

For example, some organic compounds which exhibit certain bands in alcohol solution, combine on warming with sulphuric acid, forming a sulphonic acid. It has been shown that the position of the bands is shifted on dissolving the substance in sulphuric acid, and is again displaced after combination with the acid has occurred.[3]

Stark's Theory of Absorption.[4] Stark recognizes three kinds of valency electrons: unsaturated, saturated, and loosened (*gelockert*). The unsaturated electron is confined to its own atom and is present in monatomic gases. The lines of force which emanate from the saturated electron are attached to other atoms; they are present in the molecules

[1] *Trans Chem. Soc.*, 1912, 101, 1469; *Zeit. f. Elektrochemie*, 1911, 17, 211.
[2] See footnote, p 75.
[3] Baly and Rice, *Trans. Chem. Soc.*, 1912, 101, 1475.
[4] *Die Prinzipien der Atomdynamik*, Part II, J. Stark. Hirzel, Leipzig, 1911.

of elements and compounds. The loose electron is not attached to another atom, but may be displaced under the influence of neighbouring electrons, as for example in ionisation. All the three varieties can be separated from compounds by adding energy; decomposition accompanies the removal of the saturated electron, but not that of the unsaturated or loosened electron. The valency electrons are the centres of emission and absorption spectra. By the partial separation of a valency electron from its positive atom and re-attachment, electro-magnetic waves are emitted, kinetic energy of the electrons being converted into electro-magnetic energy. The band spectrum of the unsaturated valency electrons lies in the ultra-violet region, that of the saturated electrons in the extreme ultra-violet region. If the saturated electron vibrates with its atom, absorption in the infra-red occurs. The absorption by the loosened electrons probably lies in the visible and ultra-violet (the rays have a wave length less than 700 $\mu\mu$). Chemical change, such as substitution, creates an increased loosening of the electron and consequent shifting of the absorption towards the red. Loosened electrons are present in carbon atoms of compounds with an aromatic nucleus (benzene, naphthalene, &c.), and also in carbon and oxygen (diketones, quinones) as well as in nitrogen (azobenzene and its derivatives). The chromophores, which will be presently referred to, contain these loosened electrons and are regarded by Stark as the centres of light absorption.

Nitro, azo and nitroso groups each contain a pair of such electrons, which may be regarded as synonymous with residual valency of these groups. The saturation of these electrons destroys selective absorption in the visible and ultra-violet region, and the source of colour disappears.

Absorption Spectra of Aliphatic Compounds. As these substances, with the exception of certain diketones, nitro, nitroso, and isonitroso compounds, are for the most part colourless, absorption where it occurs is in the ultra-violet region. Numerous observations have been made by Hartley and Huntingdon,[1] and by Henri and Bielecki,[2] from which it would appear that the addition of CH_2 causes a shifting of the absorption in the direction of the red and an increase in the depth of the curve. In the case of esters of the formula $C_nH_{2n+1}COOR$, the absorption appears to depend more upon the value of n and less on that of the alkyl group R. The carboxyl group has a marked effect, and differs from the carbonyl group in aldehydes and ketones, see p. 97.

Absorption Spectra of the Simpler Aromatic Compounds. The great bulk of compounds, which give a banded spectrum either in the visible or ultra-violet region, belong to the aromatic series.

A general feature of the absorption spectra of benzene derivatives is the remarkable change in the character of the spectrum produced

[1] Kayser's *Handbuch der Spektroskopie*, vol. III, 1905, article by Sir N. Hartley on 'Relation between Absorption and Constitution of Organic Compounds'.

[2] *Ber.*, 1912, **45**, 2819; 1918, **46**, 8627; *Compt. rend.*, 1912, **155**, 456.

by the introduction of even the simplest substituent.[1] Benzene dissolved in alcohol exhibits six or seven narrow bands lying within the oscillation frequencies of 3600 4400, as shown in Fig. 22.[2]

The introduction of alkyl groups causes merely a fusion of these bands. In toluene and the other monalkyl derivatives three of the bands are merged into one, and in *o*- and *m*-xylene only one band is left, whilst the para compound retains two.[3] From the absorption curves of twenty-two monosubstituted benzene derivatives Baly and Tryhorn[4] have shown that with few exceptions those compounds which yield meta disubstituted derivatives exhibit absorption bands of small persistence, whilst those that give ortho and para derivatives have bands of large persistence. It is an interesting fact that among the di-derivatives of benzene the para compounds usually retain more of the benzene bands, or, if the number is the same, the bands exhibit greater persistence than those of the other two isomers.[5] A similar fusion of bands is produced by the halogen derivatives, the persistence and shifting towards the red being increased with increase in atomic weight of the halogen, whilst the number of bands decreases from fluorine to iodine, the latter showing continuous absorption.

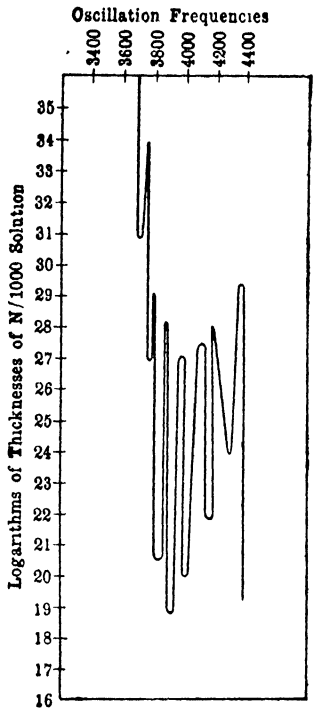


FIG. 22. Benzene.

It appears that the presence of unsaturated groups, or, in other words, residual affinity, plays an important rôle in modifying or obscuring the absorption bands of the nucleus, and shifting it towards the red. Unsaturated side-chains cause a shifting towards the red and obliteration of the benzene

[1] Hartley and Dobbie, *Trans. Chem. Soc*, 1898, 73, 695; Baly and Collie, *Trans. Chem Soc.*, 1905, 87, 1841.

[2] The vapour of benzene exhibits as many as 350 lines in the ultra-violet (Henri, *Compt rend.*, 1922, 174, 809).

[3] Hartley, *Trans. Chem Soc.*, 1885, 47, 685.

[4] *Trans. Chem. Soc.*, 1915, 107, 1058

[5] Baly and Ewbank, *Trans. Chem. Soc.*, 1905, 87, 1356.

bands. Styrene exhibits a broad band and stilbene general absorption. Among benzene derivatives conjugation shows greater absorption than isolated double linkages.[1]

An interesting case is that of amino compounds such as aniline, in which nitrogen is tervalent. The bands of benzene are here fused into one and shifted towards the red (3200–3800). When the nitrogen is saturated by conversion of the base into the hydrochloride some of the benzene bands reappear in their original positions.[2] Acetylation of the amino group has a similar effect in shifting the band towards the region of shorter wave length.

The spectrum of phenol in alcohol consists of a broad and deep band (3600–3800), which in its ethers divides into two. Conversion into the sodium salt causes the band to shift considerably towards the red (3400), whereas the spectrum of the phenol ethers is unaffected by the addition of alkali. Salt formation in the case of phenol has, therefore, the reverse effect of that of aniline when converted into the hydrochloride. On the other hand, the band which *p*-aminophenol shows at 3250 is shifted towards the ultra-violet (3600) on addition of acid, and behaves like aniline. The curve for phloroglucinol is shown in Fig. 18, p. 84. Benzyl alcohol and its ethyl ether show a broad and shallow band at about 3600.

The introduction of nitro groups generally produces a fusion of the benzene bands. Nitrobenzene shows strong general absorption and an undeveloped band at about 4000. Methyl groups develop in nitro compounds a distinct band slightly shifted towards the red, whilst the substitution of nuclear hydrogen by hydroxyl and amino groups brings about the appearance of well-developed bands strongly displaced towards the red. The bands of *m*- and *p*-nitraniline have their heads at about 2600–2800; that of *p*-nitrophenol in water or alcohol at about 3200. In the latter case the addition of alkali produces a marked displacement towards the red with the head at 2400–2600, and, in this respect, its behaviour resembles that of phenol. Both the nitranilines and nitrophenols have a yellow or orange colour when in the free state or in the form of salts. They will be referred to again when the question of the structure of coloured compounds is discussed (p. 95).

Benzoic acid shows a fusion of the benzene bands and displacement towards the red.[3] Salt formation produces a slight shifting back towards the ultra-violet. This is the reverse of the effect produced

[1] Crymble, Stewart, and Wright, *Trans. Chem. Soc.*, 1911, 99, 462, 1262; Macbeth and Stewart, *ibid.*, 1917, 111, 829.
[2] Baly and Collie, *Trans. Chem. Soc.*, 1905, 87, 1338.
[3] Hartley and Huntington, *Phil. Trans*, 1879, 170, 257.

with phenol, so that when the hydroxybenzoic acids are treated with alkali, sufficient to form the benzoate, displacement towards the ultra-violet is first produced, and is followed, when the hydrogen of the hydroxyl group is substituted, by a shifting towards the red.

Like unsaturated hydrocarbons, the presence in acids of an unsaturated side-chain, as for example in cinnamic acid, causes displacement towards the red and the appearance of a broad band. On reduction to hydrocinnamic acid three of the benzene bands reappear.

Benzaldehyde produces a shallow band at 3500, and benzonitrile two bands in a position slightly nearer to the red, whilst acetophenone produces weak general absorption.

Thus, the general effect of substitution, especially of groups possessing residual affinity, is to develop colour by shifting the absorption towards the visible region of the spectrum (p 119). The order of the different groups, beginning with those causing least displacement, would be roughly as follows :

$$CH_3 . CN . COOH . OH . ONa . NH_2 . NO_2$$

The reverse process is caused by salt formation in the case of amino compounds and carboxylic acids.

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Report of the British Association, 1916, p. 131, by Dobbie, Baly, and Stewart.

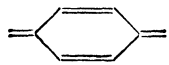
CHAPTER II

COLOUR AND STRUCTURE

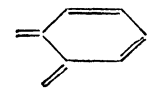
THE large number of brightly coloured organic compounds which have been discovered in recent years has naturally led chemists to speculate on the cause of colour, and to look for some general structural characteristics of these coloured substances which might determine their property of selective absorption.

The earlier theories translated colour into terms of structure without much regard to the physical cause which produces selective absorption in the visible spectrum. It is only within the last few years that the spectrograph has come into common use as part of a laboratory equipment, and the absorption spectra of organic compounds in the visible and ultra-violet region carefully studied and mapped. Thus, the field of view has been extended and attempts have been made to bring into line the older theories of structure with the more recent results of spectroscopic examination. How far these attempts have been successful will be briefly discussed in the following pages.

Theory of O. N. Witt.[1] One of the earliest theories connecting colour with structure is that of O N. Witt, who attributed colour to the presence of certain unsaturated groups or *chromophores*, of which the most important are the following: C=C, C=O, C=S, C=N, N=N, N=O, $N\begin{matrix}O\\ \diagup\\ \diagdown\\ O\end{matrix}$. To these the ortho- and para-quinoid radicals,



Para-quinoid.



Ortho-quinoid.

which may be regarded as compact assemblages of C=C groups, were subsequently added.[2]

On reduction or addition of halogens the unsaturation of the group disappears, and with it the colour. Hence unsaturation, as Graebe and Liebermann[3] first pointed out, seems to be correlated in some way with the attribute of colour. When the chromophore forms part of

[1] *Ber*, 1876, 9, 522; 1888, 21, 325

[2] Nietzki, *Organische Farbstoffe*, Springer, Berlin, 1888; Armstrong, *Proc. Chem. Soc.*, 1892, 8, 101; Green, *Proc. Chem. Soc*, 1892, 8, 195.

[3] *Ber*, 1868, 1, 104.

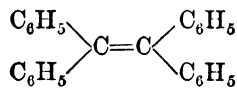
a carbon complex, the latter is known as a *chromogen*. The chromogen may or may not be coloured, but it constitutes the basis of the coloured substance. To convert the chromogen, if colourless, into a coloured substance, certain salt-forming groups, especially NH_2 and OH, are necessary, and these are known as *auxochromes*. Thus, benzophenone $C_6H_5 . CO . C_6H_5$, though colourless, is a chromogen by virtue of the presence of the chromophore C=O, but only becomes coloured on the introduction of the auxochrome NH_2. Aminobenzophenone is yellow and basic. In the same way the nitro group is the chromophore of the chromogen, nitrobenzene, and nitraniline the colouring matter.

Azobenzene is a coloured chromogen containing the chromophore N : N, whereas hydroxy- and amino-azobenzene are true dyestuffs, the one acidic and the other basic. By a true dyestuff is meant a colouring matter which can be used for dyeing, that is, one that can be attached directly or indirectly to the fibre. Whether this attachment is determined by chemical affinity, as some hold, or is a manifestation of some physical property, such as surface energy, as others think, cannot be discussed here.

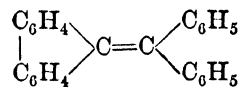
Chromophores. Colour appears to depend not only on the presence of the chromophoric group, but also on its reduplication in a compact form. A single C=C group, being a weak chromophore, produces colour, but, when multiplied, a coloured product results. Hydrocarbons of the ethylene series, such as diphenyl- and tetraphenyl-ethylene, are colourless, but diphenylhexatriene

$$C_6H_5 . CH : CH . CH : CH . CH : CH . C_6H_5$$

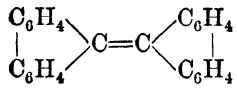
is yellow. Ring structure, with its compact arrangement of double linkages, appears to promote absorption in the visible spectrum and produce colour. Whereas tetraphenylethylene and diphenyldiphenylene ethylene are colourless, the corresponding bisdiphenylene and dinaphthylene diphenylene derivatives are coloured.



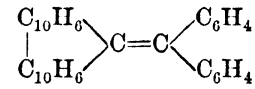
Tetraphenylethylene.
Colourless.



Diphenyldiphenylene ethylene.
Colourless.

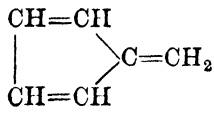


Bisdiphenylene ethylene.
Red.

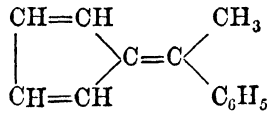


Dinaphthylene diphenylene ethylene.
Red-violet.

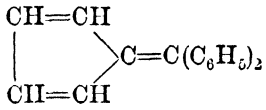
The same compact grouping of double linkages is present in the interesting series of coloured hydrocarbons, known as fulvenes, which were discovered by Thiele.[1]



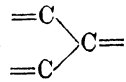
Fulvene.
Yellow liquid.



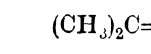
Methylphenyl fulvene.
Orange liquid.



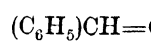
Diphenyl fulvene.
Dark red prisms.

By analogy it might be expected that benzene, which is isomeric with fulvene and contains the same number of double linkages, would be coloured. The absence of visible colour may be accounted for by the slight difference of grouping of the double bonds which cause the absorption bands to shift within the ultra-violet region of the spectrum (see p. 92). It seems very certain that the group  is a potent factor in colour production.

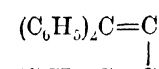
Other examples of coloured substances associated with the group C=C are the fulgenic acids and their anhydrides (the fulgides) of Stobbe.[2] The parent substance is unknown, but would probably be colourless like the methyl derivative; the introduction of phenyl groups deepens the colour, that is, shifts the absorption towards the red, as in the case of the fulvenes:



Tetramethylfulgenic acid.
Colourless.



Triphenylfulgenic acid.
Yellow.



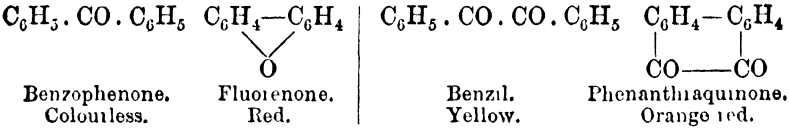
Tetraphenylfulgenic acid.
Orange.

The colour effect of the chromophore, CO, is not apparent in the simple aldehydes and ketones, which are colourless, nor in the compounds such as acetylacetone $CH_3 . CO . CH_2 . CO . CH_3$, in which the CO groups are separated, but the continguity of two or more of these groups produces colour. Whereas acetone and benzophenone are colourless, diacetyl $CH_3 . CO . CO . CH_3$ and benzil $C_6H_5 . CO . CO . C_6H_5$ are

[1] *Ber.*, 1900, **33**, 666, 851, 8895; *Annalen*, 1901, **319**, 226.
[2] *Annalen*, 1906, **349**, 333.

yellow, the anhydrous triketone $CH_3 . CO . CO . CO . CH_3$ is orange, and the tetraketone $C_6H_5 . CO . CO . CO . CO . C_6H_5$ is orange-red.[1]

Ring structure in deepening colour is evident in fluorenone, which is red, whilst benzophenone is colourless, and in phenanthraquinone, which is orange-red, whereas benzil is yellow.

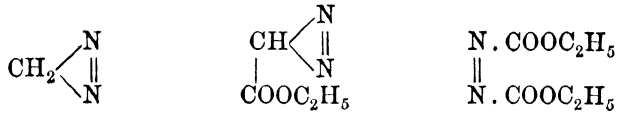


Benzophenone. Colourless. | Fluorenone. Red. | Benzil. Yellow. | Phenanthraquinone. Orange red.

In all these cases reduction, replacement of oxygen by chlorine, and, in some cases, hydration of the CO group removes the colour.

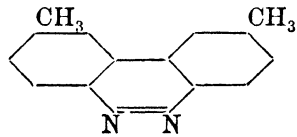
The group C : S seems to be a stronger chromophore than C : O, for both thiacetophenone and thiobenophenone are blue liquids and tetramethyldiaminothiobenzophenone $CS[C_6H_4N(CH_3)_2]_2$ is yellow, whereas the corresponding ketones are all colourless.

The large number of azo dyes furnishes countless examples of the colour effect due to the presence of the chromophore, N=N, in the aromatic series and its effect is also exhibited among aliphatic compounds in the yellow colour of diazomethane, diazoacetic ester, and azodicarboxylic ester,[2] and in the simpler aromatic azo compounds, such as azobenzene, which is red, and ethane azobenzene $C_6H_5N : N . C_2H_5$, which is yellow.



Diazomethane. | Diazoacetic ester | Azodicarboxylic ester.

Ring structure in the case of the azo group seems to diminish the intensity of the colour, tolazone being only slightly coloured.



Tolazone.

The blue or green colour effect, characteristic of most nitroso

[1] Sachs and Barschall, *Ber.*, 1901, 34, 3047.

[2] It is a curious fact that the azo compound derived from isobutyric ester is colourless.

compounds, is attributed to the chromophore, NO. Its absence in certain nitroso derivatives is explained by their bimolecular structure and the consequent saturation of their valencies.

The nitro group occupies a somewhat anomalous position as a chromophore. Whilst certain nitro compounds, especially in the aromatic series, are yellow or orange in colour, others, such as the nitro-paraffins, are colourless. The group is apparently a weak chromophore, and is dependent for its colour effect on its association with other groups. Other chromophores, as a rule, reinforce one another; but the reverse is the case with the nitro group (see p. 110). Nitrobenzene and nitronaphthalene are pale yellow, but dinitro- and trinitro-benzene are colourless.

The union of chromophores, in deepening the colour, such as an unsaturated ring structure presents, has already been indicated. Numerous examples of coloured substances containing mixed chromophores might be cited in illustration. Staudinger's ketenes (Part I, p. 141) which contain the group $>C=C=O$, are yellow.

$(CH_3)_2C:CO$ Dimethylketene. $(C_6H_5)_2C.CO$ Diphenylketene.

Phorone and chalcone are also coloured.[1]

$(CH_3)_2C.CH.CO.CH:C(CH_3)_2$ Phorone. $C_6H_5.CH:CH.CO.C_6H_5$ Chalcone.

On the other hand, though its solutions in strong acids are coloured, dibenzalacetone, $C_6H_5.CH:CH.CO.CH:CH.C_6H_5$, is colourless.[2] Dianisalacetone and similar derivatives are yellow.

The colour effect of the group HC : N is shown in such substances as benzylidene aniline, $C_6H_5CH:NC_6H_5$, and auramine, $HN:C[C_6H_4N(CH_3)_2]_2$, which are yellow, and certain ring compounds, such as quinoline yellow, in which the group forms part of the ring.

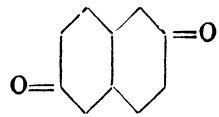
It appears from the foregoing that certain chromophores, such as N : N and NO groups, produce colour independently of the nature of their environment, whilst others, such as CO and CH : CH, only act in conjunction with other groups. On this account Kauffmann has separated them into two classes, called *dependent* and *independent* chromophores.

Nietzki's Quinoid Theory. In 1888 Nietzki[3] added the quinone

[1] Haller and v. Kostanecki, *Ber.*, 1897, 30, 2947.
[2] Stobbe, *Annalen*, 1909, 370, 93.

structure to the list of chromophoric groups. Its introduction has marked a great advance in the theory of colour; for, although it cannot be regarded by any means as a complete generalization, it is supported by a weight of evidence which is of the greatest significance and may ultimately lead to the solution of at least a part of this involved problem. It has, moreover, one important attribute which most of the other theories lack; it lends itself readily to experimental proof or disproof and is accountable for a valuable extension of our knowledge of dyestuffs.

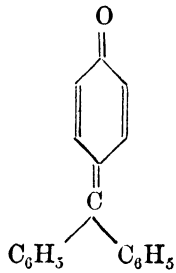
Ring compounds, like the quinones, in which the CO group forms part of the nucleus, and is consequently closely associated with the C:C group, are generally coloured. The ortho- and para-benzoquinones are orange and yellow respectively,[1] and the α- and β-naphthaquinones are orange and red. Amphi-naphthaquinone,



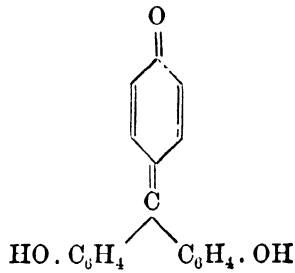
Amphi-naphthaquinone.

in which the CO groups are distributed between the two nuclei, is also coloured.

For the same reason fuchsone[2] and aurin, which may be regarded as quinone derivatives and are related to the triphenylmethane dyes, are coloured.



Fuchsone.



Aurin.

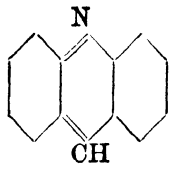
[1] Colourless and labile o-quinones have been isolated by Willstätter (*Ber.*, 1904, 37, 4744), which are monomolecular like the coloured compounds and rapidly change into the latter. They may be represented by the superoxide formula, and therefore contain no chromophore.

[2] Bistrzycki and Herbst, *Ber.*, 1903, 36, 2335.

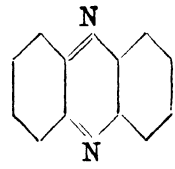
Tetraphenyl-*p*-xylylene, like fulvene, is orange.

$$(C_6H_5)_2C : C_6H_4 : C(C_6H_5)_2.$$

Acridine and phenazine may be regarded as ortho-quinoid compounds and placed in this category,

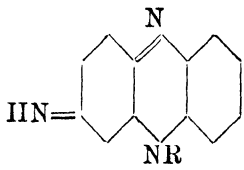


Acridine.

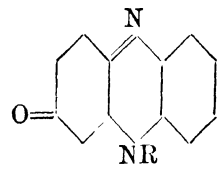


Phenazine.

whilst the indulines and indones belong to the para-quinoid series.



Induline.



Indone.

An attempt to extend the quinoid theory by making it the general basis of colour in organic compounds, though not entirely successful,[1] has thrown new light on certain structural anomalies and afforded a plausible interpretation of some of them.

A remarkable fact connected with the quinoid compounds is the absence of colour in the simplest quinonimines and their salts.

$HN : C_6H_4 : NH$ Quinone-diimine. $O : C_6H_4 : NH$ Quinonimine.

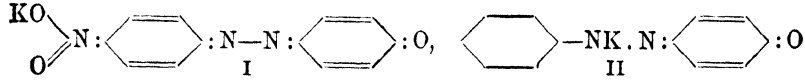
The dimethyl derivative of quinone-diimine is colourless in the solid state and pale yellow in solution. Quinone-phenyldiimine is, however, red, and the diphenyldiimine is reddish brown.[2]

Not only are certain quinoid substances colourless; but, on the other hand, there is a long and varied list of coloured substances, which are incapable of being represented by a quinoid structure. Such, for example, are diacetyl, α and β nitronapthalene, and nitrodimethylquinol, which are yellow; the two benzalnitroanilines, which are yellow and orange; acenaphthylene and azobenzene, which are red; and the nitroso compounds, which are blue. Furthermore,

[1] Armstrong, *Proc. Chem Soc*, 1892, 8, 101, 143, 189.
[2] Willstätter, *Ber.*, 1904, 37, 1494, 4605.

as Baly has pointed out,[1] there are many substances (such as the nitroanilines, which can be formulated as quinoid compounds, but possess an identical absorption spectra with others, such as nitrodimethylaniline) which cannot have that structure. In addition to these are the molecular quinhydrone compounds referred to on p. 126, and many compounds of ketones with acids.

Nietzki's theory has undergone various extensions and modifications. Hewitt,[2] from observations on a series of azo-colours, formulated the rule that the colour is deeper the longer the chain of conjugate linkages, to which E. R. Watson[3] added the further qualification that the conjugate chain must possess a quinoid structure. Substance of formula I has a deeper colour (crimson) than that of formula II (orange).



I II

A further modification of Nietzki's theory has been proposed by E. R. Watson,[4] namely, that only those dyes which are quinoid in all tautomeric forms exhibit a deep colour, but those which can be represented by a single quinoid or non-quinoid formula are paler in shade. For example, aminobenzene-azophenol is quinoid in both tautomeric forms and has a deep blue colour,

$$O : C_6H_4 : N . C_6H_4 NH_2 \rightleftarrows HO . C_6H_5N : C_6H_4 : NH$$

whereas benzene-azophenol has a yellow colour and can only exist in the single quinoid form,

$$O : C_6H_4 : N . NH . C_6H_5 \rightleftarrows HO . C_6H_4 . N : N . C_6H_5.$$

In the latter case the stability of the quinoid form will tend to deepen the colour. Moreover, it appears that dyes with long conjugate chains of alternate quinoid linkages, so disposed that isomerisation may occur between quinoid forms, are generally more deeply coloured. Although a considerable amount of valuable experimental evidence is adduced by Watson in support of this view, it is naturally subject to the same criticism as the simpler quinoid theory of Nietzki, in that it fails to afford a general explanation of the cause of colour in organic substances.

Colour and Configuration. That slight differences in configuration may have a marked effect on colour is proved in the case of certain stereoisomers, such as the two dibenzoyl ethylenes, $C_6H_5 . CO . CH : CH . CO . C_6H_5$, and the two benzaldesoxy-benzoins, $C_6H_5CO . C(C_6H_5) : CH . C_6H_5$, one of each pair being colourless and the other yellow, and the two diazobenzene sulphonates, which are yellow and orange respectively.

The Auxochromes. It has already been stated that the chromophore may or may not produce colour, which in the latter case appears on the introduction of the auxochrome. Substances containing a chromophore, in which colour is manifested by the introduction of an auxochrome, are called chromogens. The effect of the auxo-

[1] *Journ. Soc. Chem. Ind.*, 1915, 34, 393. [2] *Trans. Chem. Soc*, 1907, 91, 1251.
[3] *Trans. Chem. Soc*, 1914, 105, 764.
[4] *Trans. Chem. Soc.*, 1914, 105, 759, 1915, 107, 1567.

chrome is not only to produce colour in a colourless chromogen, but to intensify it if coloured. Benzalacetone is colourless, but the *p*-dimethylamino derivative is orange-yellow, and both amino derivatives of anthraquinone and phenanthraquinone are more deeply coloured than the unsubstituted compounds. Similarly the nitranilines are more deeply coloured than nitrobenzene. Of the two chief auxochromes, OH and NH_2, the latter appears to be the stronger, as may be seen on comparing *p*-nitrophenol with *p*-nitraniline. The former is colourless and the latter deep yellow. As a rule, however, the difference in the colour effect produced in analogously constituted compounds is only slight. Picric acid and trinitraniline are dark yellow, amino- and hydroxy azobenzene are yellow, alizarin and triaminoanthraquinone are red or violet, rosaniline and rosolic acid red, &c. It may be pointed out that both groups possess residual affinity and are therefore highly reactive, like the chromophores. It has been suggested that the residual affinities of the two kinds of groups, auxochromes and chromophores, may interact in some way so as to produce a banded spectrum when light energy is absorbed (see p. 129).

The replacement of hydrogen in NH_2 by alkyl and aryl radicals strengthens the auxochrome (deepens the colour) and with increasing molecular weight of the radical the absorption is shifted towards the red.

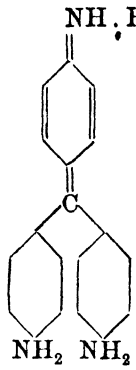
The auxochrome character of hydroxyl may be illustrated by numerous examples. Colourless dibenzalacetophenone gives a yellow ortho-hydroxy derivative, yellow anthraquinone yields an orange-red para-hydroxy compound and a red dihydroxy compound (alizarin), and orange phenanthraquinone a violet trihydroxy derivative. By replacing the hydrogen of the hydroxyl group by alkyl groups the auxochrome may be affected either way, in some cases the depth of colour being increased, in others diminished.

Ortho-nitrophenol, which is deep yellow, gives a pale yellow methyl ether; but the pale yellow nitroquinol gives a deep yellow methyl ether.

The relative position of auxochrome and chromophore might be expected to manifest itself clearly in its effect on colour; but this is so far from being the case that the vicinity of auxochrome and chromophore as frequently destroys as it intensifies the colour. Kauffmann[1] concludes that, as a rule, the auxochrome deepens the colour when it is attached indirectly to the chromophore by an aromatic nucleus, which can function as a chromophore. The subject is further considered under the auxochrome theory (p. 129).

[1] *Farbe und Konstitution*, by Dr. H. Kauffmann, Ahrens' *Vorträge*, 1904, **9**, 277.

This relation of auxochrome to chromophore is illustrated by pararosaniline hydrochloride, in which a quinoid group is attached by benzene nuclei to two auxochromes and which has a deep magenta colour.



Pararosaniline hydrochloride.

An interesting point in this connection is the effect of position of the NH_2 groups on the colour tint, which changes from para to ortho, the former being violet and the latter blue-green.

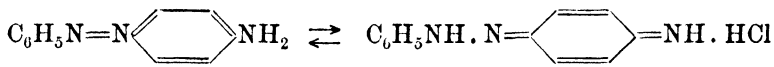
Now the auxochrome introduces an acidic or basic character into the compound, which can consequently function as an acid or base and form salts. Salt formation is a process of the greatest interest from the point of view of colour; for it may affect it either by intensifying or destroying it.

Para-nitrophenol is colourless, but its sodium salt is deep yellow or orange. Ortho aminobenzophenone and the nitranilines are deep yellow or orange, and their salts are colourless. The same result is produced by acetylation of the amino group. Acetyl derivatives of the above compounds are colourless. The formation of quaternary compounds is also attended by loss of colour. Meta-nitrodimethylaniline, which is deep yellow, becomes colourless when combined with an alkyl bromide. As no structural change is possible in many of these compounds, it must be inferred that salt formation alone is responsible for removing the auxochromic character of the amino group. But in other cases where salt formation affects the chromophore rather than the auxochrome the reverse is the case. Acridine is colourless, but its salts are yellow; phenazine is yellow and its salts are red. Aminoazobenzene, which is orange, forms salts which dissolve with a red colour. Many colourless substances, such as dibenzalacetone and certain aromatic hydrocarbons, dissolve with a bright colour in strong mineral acids. The latter belong, however, to a different category and cannot

be regarded as salts in the ordinary sense. They will be referred to again (p. 124).

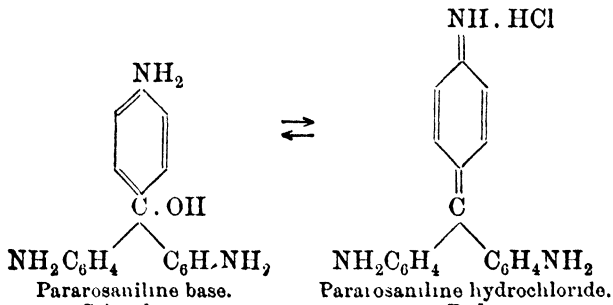
It must be remembered that, in dealing with salt formation in the case of an unsaturated compound, isomeric change may occur and the salt may possess a structure very different from that of the original compound. An example of this kind is *p*-aminoazobenzene, referred to above, which is orange in the free state, but forms a hydrochloride crystallising in steel-blue needles and dissolving in water with a bright red colour. *P-p*-diaminoazobenzene behaves in the same way. This is not a normal case of salt formation, seeing that the meta compound is dark orange and its salts bright yellow in colour. The explanation is that the meta compound, unlike the ortho and para compounds, cannot undergo isomeric change to the quinoid form, and therefore yields normal salts of a similar colour.

The relation of *p*-aminoazobenzene to its hydrochloride is represented as follows:



Normal form of free compound. Quinoid form of hydrochloride.

A difficulty is met with in the fact that, whilst the substance dissolves in dilute acid with a red colour, its solution in strong sulphuric acid is brown. According to Kauffmann the red solution represents the quinoid form, the brown the reversal to the azo compound, and this view is supported by observations of Auwers.[1] The change of colourless base to salt in the triphenylmethane dyes, to be presently referred to, is regarded as an illustration of the same kind of isomeric change from the saturated carbinol to the quinoid form (p. 81).

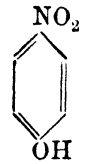


Pararosaniline base. Colourless. Pararosaniline hydrochloride. Red

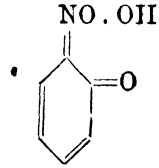
The formation of orange and red salts from colourless or pale yellow nitrophenols has been ascribed in the same way to isomeric change. Armstrong[2] was the first to suggest a quinoid structure for

[1] *Ber.*, 1900, 33, 1314. [2] *Proc. Chem. Soc.*, 1892, 8, 103.

the yellow *o*-nitrophenol in order to explain the difference between it and the colourless para compound.

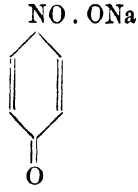


p-Nitrophenol.



o-Nitrophenol.

When alkali is added to *p*-nitrophenol it yields a salt of a deep yellow colour and the change is therefore ascribed to a change to the *p*-quinoid form:



Sodium *p*-nitrophenate.

Kauffmann has objected to this view on the ground that all three isomers behave similarly with alkali, including the *m*-nitrophenol which cannot give a quinoid form, and to the fact that the dihydroxy nitro compounds show an increased depth of colour when a second molecule of alkali is added, although only one nitro group is present. In the case of nitroresorcinol, however, the second molecule of alkali removes the colour of the mono sodium compound.

Seeing that most of the artificial dyes belong to the aromatic series, it might appear that an increase in the number of benzene nuclei or molecular weight on the one hand and of auxochromes on the other would lead to a deepening of the colour, that is, a colour change from yellow to blue. The deepening of colour with increase of molecular weight is known as *Nietzki's rule*, to which, however, there are many exceptions.

Many attempts have been made in this direction with the object of discovering some general law; but so far without any great success.

In the following series increasing molecular weight leads to a deepening of the colour:[1]

[1] The increase in depth of colour follows the following order: yellow, orange,

$C_6H_5N:N.C_6H_4(ONa)$ — Orange.

$C_6H_5N:N.C_{10}H_6(ONa)$ — Red.

$NaSO_3C_6H_4\overset{(4)}{N}:\overset{(1)}{N}C_{10}H_6\overset{(1)}{O}H\overset{(2)}{}$ — Orange.

$NaSO_3C_{10}H_6\overset{(4)}{N}:\overset{(1)}{N}C_{10}H_6\overset{(1)}{O}H\overset{(2)}{}$ — Red.

$$NaSO_3C_6H_4\overset{(4)}{N}:\overset{(1)}{N}.C_6H_4.\overset{(1)}{N}:\overset{(2)}{N}.C_{10}H_5(\overset{(6)}{O}H).SO_3Na$$

Scarlet.

$$NaSO_3C_6H_4\overset{(4)}{N}:\overset{(1)}{N}.C_{10}H_6\overset{(4)}{N}:\overset{(1)}{N}.\overset{(2)}{}C_{10}H_5(\overset{(6)}{O}H).SO_3Na$$

Violet.

$C(C_6H_4NH_2)_2$, $C_6H_4:NH_2Cl$ — Magenta.

$C[C_6H_4N(CH_3)_2]_2$, $C_6H_4:N(CH_3)_2Cl$ — Violet.

$C(C_6H_4NHC_6H_5)_2$, $C_6H_4:NHC_6H_5Cl$ — Blue.

That molecular complexity is alone not sufficient to deepen colour is seen from the dye known as alizarin yellow.

$$OH.C(C_6H_4N:N.C_6H_3(OH).COOH)_2$$
$$C_7H_6N\quad N.C_6H_3(OH).COOH$$

Alizarin yellow

Again, the nature of the auxochrome has a marked effect. The following two substances have practically the same molecular weight, the same aromatic nuclei, and the same position of the auxochrome groups, yet possess very different shades of colour.

$$CH_3.C_6H_3.N:N.C_{10}H_5(NH_2)SO_3Na$$
$$|$$
$$CH_3.C_6H_3.N:N.C_{10}H_5(NH_2)SO_3Na$$

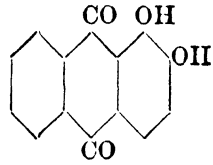
Red.

red, violet, blue, green, and the terms *hypsochrome* and *bathychrome* have been introduced to indicate those groups which lighten (hypsochromes) and those which deepen (bathychromes) the colour. By introducing one or more methyl, phenyl, and diphenyl groups into the amino group of certain meriquinoids (p 126) derived from benzidine, Piccard has succeeded in deepening the colour beyond the green, and has obtained what he terms yellow and red colours of the *second order*. (*Ber.*, 1913, **46**, 1847: *Rec. trav. chim. Pays-Bas*, 1922, **41** (4), 581.)

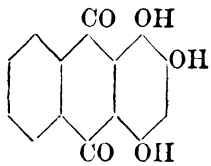
$$\begin{matrix} CH_3 . C_6H_3 . N : N . C_{10}H_5(OH)SO_3Na \\ | \\ CH_3 . C_6H_3 . N : N . C_{10}H_5(OH)SO_3Na \end{matrix}$$

Violet.

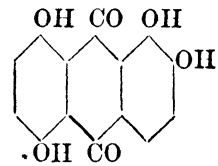
The number as well as the position of the auxochromes is also a matter of great importance. Anthraquinone is yellow, the monohydroxy-compound is deep orange, but of the ten possible dihydroxyanthraquinones only alizarin is a red dye.



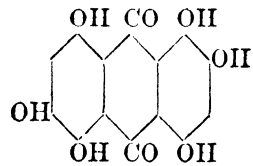
By increasing the number of hydroxyl groups the colour is deepened. The polyhydroxy-anthraquinones give the following colours when dyed with a chromium mordant:



Red-brown

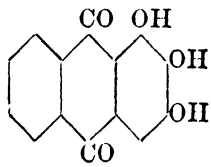


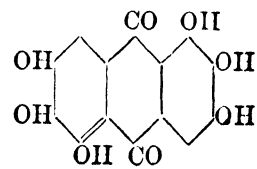
Violet-blue.



Blue

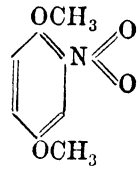
whereas the two following, containing respectively 3 and 6 hydroxyl groups, but differently attached from the foregoing, give brown shades:





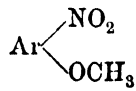
It therefore follows that both the number and position of the auxochromes is of importance in determining the shade of colour; no rule has yet been formulated which will with certainty foretell the character or colour of a dye from the structure of the compound.

H. von Liebig's Theory of Colour. From the fact that the fulvenes (p. 97) possess no quinoid structure, von Liebig suggested that the essential chromophore must be assigned to three adjacent unsaturated atoms A—Ä—Ȧ. This grouping is, however, not the only essential condition which may also require the closing of a ring. Although the colour of such a substance as nitroquinol dimethyl ether is explained in this way, the theory fails to account for the absence of colour of other compounds having this general structure.

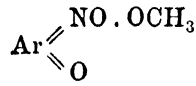


Theory of Chromoisomerism. In opposition to Kauffmann, and following Armstrong's suggestion, Hantzsch[1] has advanced what is known as the theory of chromoisomerism. It owes its origin to the discovery of coloured, in addition to the well-known colourless nitrophenol ethers.

In 1906 Hantzsch and Gorke found that red coloured nitrophenol ethers could be obtained by the action of alkyl iodides on the silver salts of the phenols. Colourless and coloured ethers of *o*- and *p*-nitrophenol, 2 . 4 dinitrophenol, picric acid and trinitrophenylmalonic ester were prepared, and the two series of compounds were represented thus:



True nitro ether.
Colourless.



Aci-nitro ether.
Coloured.

Ar = Aromatic nucleus.

[1] *Ber.*, 1906, **39**, 1073.

The first was called a *true* nitro ether and the second, coloured modification, was termed an *aci*-nitro ether, corresponding to the pseudo acid and acid forms of phenylnitromethane (p. 340).

Now, according to Witt's theory, the chromophore NO_2 is alone too weak to produce colour until reinforced by the auxochrome OH, the chromogenic character of which is intensified by conversion into the salt. By multiplying nitro groups the colour should be intensified, but, as already mentioned, this is not always the case. Hantzsch takes the view that all true nitro phenols and their derivatives are colourless[1] and that it is only by conversion into the aci form that colour is manifested. This was embodied in the following general rule: 'every appearance of colour or change of colour in salt formation with a colourless metallic atom is due to isomeric change.' Dinitroethane is colourless, but the sodium salt is deep yellow, and the change is denoted thus:

$$CH_3CH(NO_2)_2 \qquad CH_3C(NO_2)NO.ONa$$

Mercury nitroform exists in a colourless and yellow variety. The first will represent the true nitro compound, and the second the aci form.

$$\underset{\text{Colourless.}}{hg.C(NO_2)_3} \qquad \underset{\text{Yellow.}}{hgO.ON.C(NO_2)_2} \qquad hg = \frac{Hg}{2}$$

Another example is *m*-nitrophenylnitromethane, which exists in the form of a colourless and yellow isomer. Although nitromethane and ethylnitrolic acid, as well as their sodium salts, are colourless, the latter have a different ultra-violet absorption from the former and reveal in this way a difference of structure.

This kind of isomerism which shows itself in change of colour is termed *chromoisomerism*, and the process of isomeric change *chromotropism*.

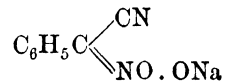
But the attempt to extend the theory by further experimental observation has only rendered the issues more complex and the explanations more involved. A comparison between the yellow *o*-nitrophenol and its ether shows that the latter is much the more deeply coloured. Hantzsch has therefore suggested that the free nitrophenol is not a pure *aci* compound, but a solid solution or

[1] A notable exception is nitroquinol methyl ether, $NO_2C_6H_3(OCH_3)_2$, which is yellow. It is colourless in a solution of ligroin, but dissolves in other solvents with a yellow colour, the depth of which is found to increase with the molecular weight of the solvent.

mixed crystal of both nitro and *aci* forms. Such an equilibrium mixture is called a *merochrome* compound. The view is supported by the observation that the orange sodium salt of tribromo *m*-dinitrophenol can be separated by anhydrous solvents into a yellow and red variety, each of which in aqueous solution reverts more or less rapidly to the same orange-coloured mixture. A yellow and red thallium picrate and several such pairs of salts are known.

We are thus confronted with the existence of two salts, a yellow and a red, in addition to the colourless, free nitro compound. How are they all to be formulated?

A further complication is presented by the salts of the mononitroparaffins, which are colourless, whilst those of the dinitro compounds are coloured, like the salts of the nitrophenols. The colour is not due to the additional electronegative nitro group, for its replacement by a different electronegative group is without effect, the sodium salts, for example, of phenylcyanonitromethane and bromonitromethane being colourless.[1]



Phenylcyanonitromethane sodium salt

Hantzsch concludes that the second nitro group plays a part in the production of colour by virtue of the linking of the subsidiary valency or residual affinity of the metal with that of the nitro group. It is, in short, an adaptation of Werner's theory of *valency isomerism*. Though its exact significance in colour production is not easily defined, it can be represented in the following way (Part I, p. 94):

Me = Metal.

in which the dotted line represents the subsidiary valency linkage.

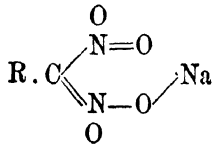
Hantzsch's theory of valency isomerism applied to the nitro compounds receives an interesting confirmation from certain recent observations on the absorption spectra of a number of aliphatic nitro compounds;[2] he concludes that the nitro group may appear in three forms, each of which possesses its own characteristic absorption. These three forms are described as a *true nitro group*, which shows faint absorption and a shallow band at about 3413; secondly a simple *aci-nitro group* >C : NOOH, present in the salts of mononitro-

[1] Hedley, *Ber*, 1908, 41, 1195. [2] *Ber.*, 1912, 45, 85.

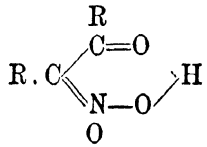
paraffins and exhibiting general absorption of about the same intensity as the first; and thirdly an aci-nitro group associated with a negative radical, which is termed a *conjuguted aci-nitro group* $R.C\begin{matrix}X\\ \\ NOOH\end{matrix}$ in which X stands for a strongly negative radical (NO_2, NOH, CO.COOH, $C_6H_5.CN$, &c.). It is characterised by strong selective absorption. The effect of the negative radical, which alone does not influence the absorption, is explained by chemical combination in which the residual affinity of the metal, hydrogen, or ester radical, as the case may be, of the aci-group enters into union with the unsaturated negative group, forming a closed chain.

$$R.C\begin{matrix}X\\ \\ NO.O\end{matrix}(Na.H.CH_3)$$

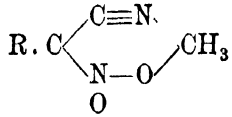
With the negative groups, NO_2, CO.R, CN, the molecular structure will take the following forms:



Aci-dinitro compound.



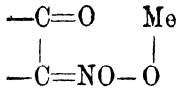
Aci-nitro ketone.



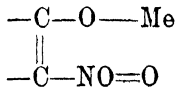
Cyan-aci-nitro compound.

This selective absorption is so strong that it is neither affected by additional chromophores nor by ionisation of the free acid or its salts.

From the optical properties it appears that nitro ketones can only exist in the aci-conjugated form, and therefore chromoisomeric compounds, such as the colourless and yellow salts of nitrobarboluric acid and *p*-nitrophenol and its derivatives, are represented by the following keto and enol forms:



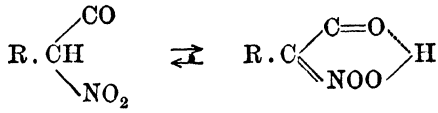
Aci-nitro ketone.



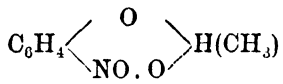
Nitro enol.

and both forms may exist in solution in equilibrium. Equilibrium may also occur (especially in the case of aliphatic nitro-derivatives)

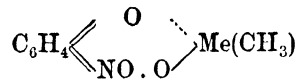
between the true nitro- and the aci-conjugated form of the nitro-ketones.



As *p*-nitrophenol is optically identical with the yellow stable esters, whereas the salts and red-coloured labile esters absorb much more strongly, a further modification in the formula is found necessary to distinguish them.



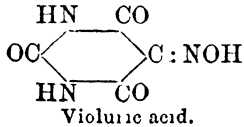
p-Nitrophenol and stable esters.



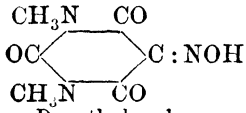
p-Nitrophenates and labile esters.

Chromoisomerism has also been observed in the case of unsymmetrical metallic compounds of 1·3 diketones of the general type $R.CO.CH_2.CO\ R'$, which are formulated as valency isomers.[1]

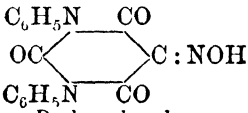
Still more complex are the coloured salts of the oximino ketones containing the group CO . C : NOH, which have been studied by Hantzsch [2] and his collaborators. Violuric acid and its dimethyl and diphenyl derivatives, together with some of their esters, are colourless or faintly coloured, but yield brightly-coloured salts.



Violuric acid.



Dimethyl violuric acid.



Diphenyl violuric acid.

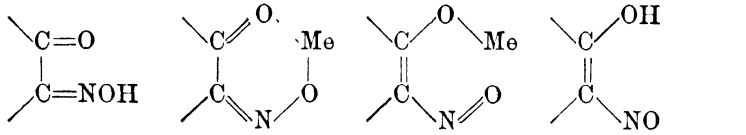
Not only do different metals and organic bases produce differently coloured salts, but the same metal yields differently coloured salts and solutions according to the solvent employed. The phenomenon

[1] *Ber*, 1915, 48, 158, 167, 785, 797.
[2] *Ber*, 1899, 32, 3101; 1910, 43, 32.

of one salt existing in differently coloured varieties is termed by Hantzsch *pantochromism*.[1] Potassium, rubidium, and caesium diphenyl violurate can each exist in blue and red modifications, and lithium diphenyl violurate gives both red and yellow salts. The results have been summarized as follows all the salt solutions contain monomolecular isomers; the colour of the salt changes from yellow to orange, red, violet, and blue with increasing positivity of the metal and also with increasing residual affinity of the solvent; the absorption curve of the yellow salt solutions are most closely related to that of the free oximino ketone, whilst that of the blue salt solutions resembles the aliphatic nitroso compounds. Assuming that the pure oximino and nitroso compounds are represented by the formulae,

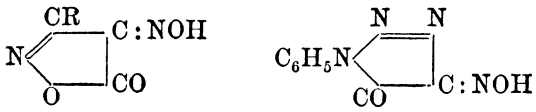
Yellow. Blue.

the yellow and blue salts are denoted as inner complexes derived from these two formulae in which residual valencies are brought into play, whilst the intermediate orange and violet salts are regarded as mixtures.



Colourless oximino ketone. Yellow. Red. True nitroso compound Blue.

Similar observations have been made with oximino-oxazolone and oximino-phenyltriazolone and its derivatives, each of which forms a series of coloured salts.



Oximino-oxazolone. Oximino-phenyltriazolone.

[1] *Ber.*, 1909, **42**, 966; 1910, **43**, 45. 68, 82.

Among other groups of compounds which exist in coloured modifications and form differently coloured salts are the following:

Hydroxyazobenzene, $C_6H_5N_2C_6H_4 . OH$, and its derivates are usually yellow and orange and the alkali and silver salts orange and red. Several of the silver salts also exist in both yellow and red modifications. The nitrobenzene-azophenols show similar changes of colour between the free compound and its salts.

Dihydroxyazobenzene (azophenol) exists in two modifications, each forming a series of yellow, red, and green salts. Many aminoazo compounds are known to form two series of differently coloured salts.[1] The orange salts, which resemble azobenzene (also azobenzene trimethyl ammonium salts, which cannot undergo isomeric change) in colour as well as in their absorption spectra, were formerly represented by the azo formula,

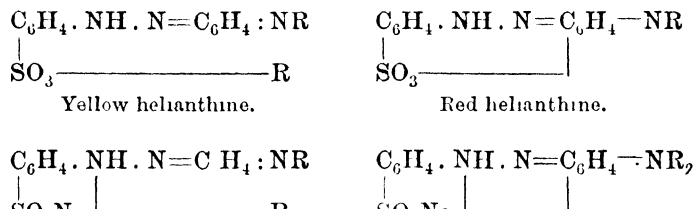
$$C_6H_5N : NC_6H_4NR_2 . HX$$

whilst the red salts were regarded as having the quinoid structure,

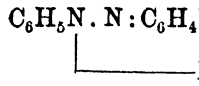
$$C_6H_5NH . N : C_6H_4 \quad NR_2X$$

Hantzsch[2] has since shown that both the yellow and red modification have the characteristic quinoid absorption band similar to that of rosaniline and that it is not modified in aqueous solutions of the salts. The yellow modification, moreover, exists not only in aqueous solution in presence of hydroxyl ions, but in neutral alcohol and acetone solutions, whereas the red modification depends on the presence of hydrogen ions. There is a third graphite-like salt of both aminoazobenzenes and helianthines, which, however, only exists in the solid form, and changes to the red or yellow modification in solution.

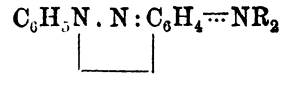
The following are the formulae proposed by Hantzsch for these various chromoisomeric compounds:



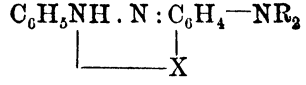
[1] Hantzsch and Hilscher, *Ber.*, 1908, 41, 1171.
[2] *Ber.*, 1913, 46, 1537; 1915, 48, 174.



Yellow aminoazobenzene.



Red aminoazobenzene (unknown).



Red aminoazobenzene (acid salt).

In addition to the above is a fourth yellow quaternary alkyl halide of dimethylaminoazobenzene which, from its optical similarity to azobenzene, must be regarded as a true 'azoid' compound, and is therefore represented thus:

$$C_6H_5N:N.C_6H_4N(CH_3)_3X$$

The red and blue solutions of congo red, like the above, do not, as was formerly supposed, depend on the presence of hydroxyl or hydrogen ions, but rather upon the solvent, for the free acid and alkali salts are optically identical, although in the case of congo red, the blue and red solutions do not give identical absorption spectra.

Hantzsch points out incidentally the untrustworthiness of colour as indicative of structure; for dimethyl *o*-toluidine-azo-benzene and its sulphonic acid, which so closely resemble the alkyl aminoazobenzenes and helianthines, and, like them, gives yellow and red solutions, possesses, nevertheless, an 'azoid' absorption spectrum.

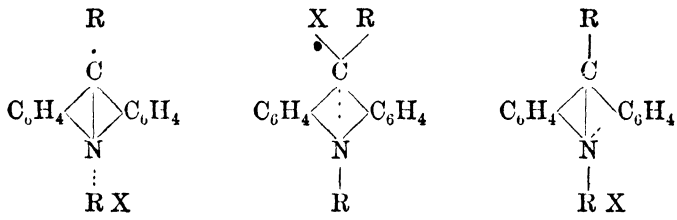
The same colour relationships were observed in the helianthines (aminoazobenzene sulphonic acid series and their sodium salts), such as methyl orange, which exists in red and yellow modifications.

Hexanitrodiphenylamine also yields both an orange and violet methyl ether.

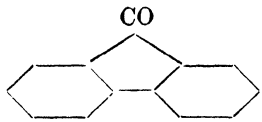
Hantzsch[1] has also obtained chromoisomers in the pyridine, quinoline, and acridine series. Phenylacridinium hydrogen sulphate exists in a yellow, red, and green, and the sulphite in four, yellow, red, green, and brown, modifications. The various modifications give identical solutions, but the colour of the solution depends upon the solvent, and in the case of the sulphite may vary from red in ethyl alcohol to green in acetylene tetrachloride.

[1] *Ber.*, 1910, 44, 1783; 1916, 49, 2169; see also Lifschitz and Kritzmann, *Ber.*, 1917, 50, 1719.

The modifications are represented as valency isomers having the following formula :



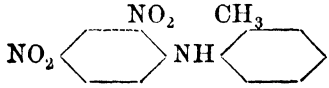
An interesting example of chromoisomerism is that of fluorene-ketone, which exists according to Stobbe [1] in a yellow and red



modification both in solution and in the fused state, the latter being converted into the former by means of strong sulphuric acid. Although the absorption spectra of the two are similar, both structural and stereo-isomerism seem excluded, and the difference has been attributed to some different disposition of the residual valencies of the oxygen atom.

A further complication is introduced by the observation that different structural modifications may possess the same colour and give identical absorption bands in solution, a phenomenon which has been termed *homochromoisomerism*.[2] It is found to exist in certain nitranilines, in the coloured syn- and anti-benzaldoximes, chlorotoluquinone-oximes, and other stereoisomers.

A good example is furnished by 2.4 dinitrophenyltolylamine ; for it gives, according to the solvent and temperature, two yellow and



Dinitrophenyltolylamine.

two orange salts, all of which are unimolecular in solution. The

[1] *Ber.*, 1911, 44, 1481.
[2] Hantzsch, *Ber.*, 1910, 43, 1910 ; 1911, 44, 2001.

two yellow salts, though different crystallographically, are optically identical in solution.[1]

In explaining the great variety of coloured substances derived from the same compound, it seems unnecessary to have recourse in all cases to isomerism. The existence of solid, crystalline modifications of different colours which give identical solutions is almost certainly due in some cases to polymorphism, which crystallographic examination should reveal.[2] In other cases the effect of one substance dissolving in different solvents with different colours may, as Hantzsch himself has suggested, be accounted for by the formation of a solvate or union of solvent and solute.

Absorption Spectra and Colour. Before discussing other theories of colour, we will consider briefly the structure of coloured substances in the light of their absorption spectra. The value of the method for determining constitution has already been referred to (p. 79), and its direct connection with the phenomenon of colour renders it peculiarly applicable to the study of the relationship of colour to structure.

The fact, observed by Baly, Edwards, and Stewart,[3] that *p*-nitrophenol and *p*-nitroanisole show similar absorption curves in the ultra-violet, but that the addition of alkali to the nitrophenol solution entirely alters its character by shifting the bands to the red, was first considered as supporting Hantzsch's quinoid formula. But a similar shifting to the red, observed on the addition of alkali to phenol, and the appearance of bands of nitro compounds at quite different concentrations from those of quinones (but very similar to those of nitrodimethylaniline, &c., which cannot possess a quinoid form) furnished strong arguments against a quinoid structure. It seems more probable that the NO_2 group produces its colour effect like the NH_2 and OH groups by causing displacement towards the visible spectrum, an effect which is augmented by conversion of the phenol into its salt.[4]

The same result has been arrived at in regard to the nitrobenzene azophenols and their salts, which have very similar spectra and, moreover, resemble the spectra of *m*- and *p*-nitrobenzeneazodimethylaniline, which cannot give a quinoid form. Chemical evidence, on the other hand, is in favour of the quinoid structure, for the re-

[1] Hantzsch, *Ber.*, 1910, 43, 1651, 1662.
[2] Bulmann, *Ber*, 1911, 54, 827; Pfeiffer, *Ber.*, 1915, 48, 1777.
[3] *Trans. Chem Soc.*, 1906, 89, 514.
[4] Baly, Tuck, and Marsden, *Trans. Chem. Soc.*, 1910, 97, 571.

actions of the nitrophenols are distinct in certain respects from those of phenols,[1] whilst Hantzsch, as we have seen (p. 111), regards *p*-nitrophenol as a conjugated *aci*-nitro compound.

Hartley's Theory of Colour. It has already been stated[2] that benzene exhibits a series of narrow absorption bands in the ultra-violet, and that these bands become displaced towards the visible region by the introduction of certain groups. The displacement is effected by substituents such as Witt's auxochromes, OH and NH_2, and certain other groups, or by condensing two or more benzene rings. Hartley[3] has advanced the theory that the fusion of benzene nuclei, as well as the introduction of certain groups, causes a retardation in the period of molecular vibration or damping down of their oscillation; in other words, a shifting of the absorption bands towards the red.

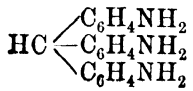
He regards a chromogen as an 'invisibly' coloured substance and a chromophore as an atom or group capable of reducing the rate of molecular vibration so as to absorb rays within the region of visibility. The effect of linking together two or more benzene nuclei by carbon atoms does not necessarily produce visible colour, but reduces the rate of vibration. Thus, triphenylmethane, though colourless or pale yellow when fused, produces a broad band of the same general character as benzene, but of greater intensity and much nearer the margin of the visible spectrum. It is therefore a chromogen. A comparison of the absorption spectra of triphenylmethane with a number of typical triphenylmethane dyes shows that they differ mainly in the position of the bands but neither in the character nor intensity of absorption Para nitrophenol, though apparently colourless, absorbs faintly in the violet and possesses a green tint. Its conversion into the sodium salt causes a shift in the absorption curve towards the visible region. There is no indication of change of structure. The relation of azobenzene to its derivatives, the azo-colours, is of the same kind. There is a change in position of the bands in each case, but not in the character of the absorption. An interesting observation derived from the examination of these substances was the predominating influence exhibited by the chromophore N=N in comparison with the small relative effect of the benzenoid radical.

[1] Hewitt, *Trans. Chem. Soc.*, 1912, 101, 1770.
[2] *Trans Chem. Soc.*, 1887, 51, 152.
[3] Kayser's *Handbuch der Spectroscopie*, vol. iii, p. 170. S. Hirzel, Leipzig.

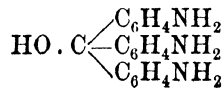
Hartley concludes, therefore, that colour is not necessarily accompanied by change of structure, nor by the presence of a quinoid nucleus. Similar views which have been advanced by Tuck[1] and by Meyer and Fischer[2] have been criticized by Watson and Meek.[3]

Formánek,[4] who has made a very complete investigation of the relation of structure to absorption of a large number of dye stuffs, has formulated a series of rules which may be embodied in the following general summary: colouring matters which have an analogous structure possess similar absorption spectra, and the same is true of those which have the same chromogen and the same number of auxochromes, $C_6H_4NR_2$ or C_6H_4OH groups. The absorption curve is different if the chromophore is different or if, with the same chromophore, the number of $C_6H_4NR_2$ groups varies, or if the position of the auxochrome varies in its relation to the fundamental element; finally, the absorption curve is modified by the substitution of hydrogen by alkylphenyl or phenyl groups in the amino group.

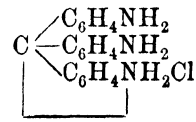
The Structure of the Triphenylmethane Dyes (Chemical Evidence). When the synthesis of pararosaniline by E. and O. Fischer in 1878 established the nature of the dye as a derivative of triphenylmethane, the relation of leucobase, colour base, and dye (hydrochloride) were very simply interpreted by the following formulae:



Leucobase.
Colourless.

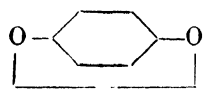


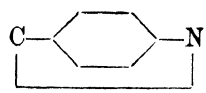
Colour base
Colourless.



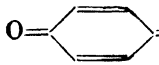
Dye-stuff.
Magenta.

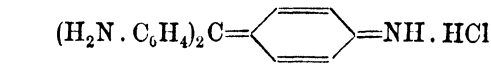
In other words, one of the basic radicals in the hydrochloride was built upon Graebe's superoxide formula for quinone.





This view was afterwards modified by Nietzki in 1888 by substituting Fittig's quinone formula and thus, by introducing what is known as the quinoid structure, this colouring matter and its congeners were brought into line with Witt's theory.

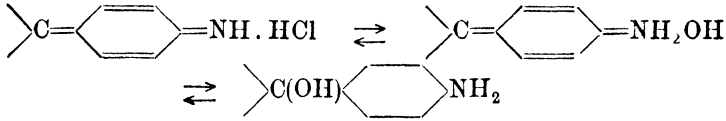




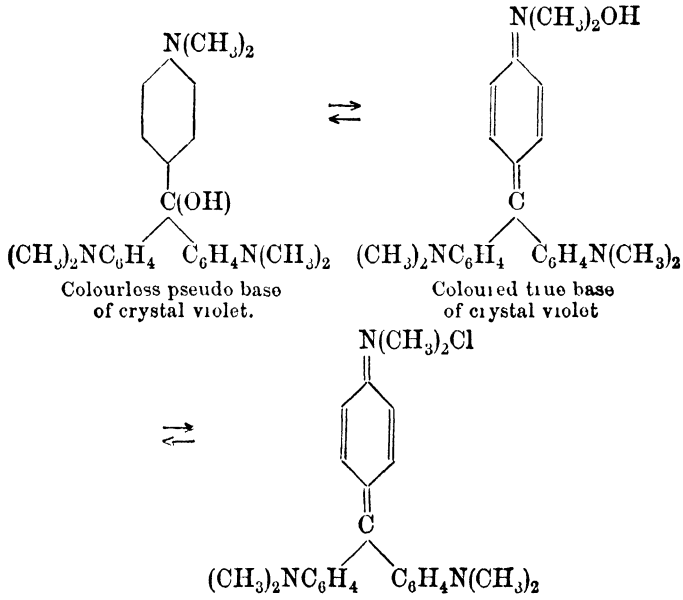
The mechanism of the change whereby the colour base is converted into the hydrochloride and vice versa was explained later by

[1] *Trans. Chem. Soc*, 1907, **91**, 449; 1909, **95**, 1809. [2] *Ber.*, 1913, **46**, 82.
[3] *Trans. Chem. Soc.*, 1915, **107**, 1573. [4] *Zeit. Farben- und Textil Chemie*, 1903, **2**, 7.

Hantzsch. According to Hantzsch the isomeric change of true base to pseudo base and the reverse process is brought about by the wandering of a hydroxyl between the quinoid carbon and nitrogen (see p. 866). The addition of alkali to the coloured salt first produces a labile and coloured ammonium base, which rapidly passes by a process of tautomeric change into the colourless and saturated carbinol base. The process can be reversed, and a colourless salt of the leucobase can be obtained under certain conditions, followed by a change to the coloured salt constituting the colouring matter.[1]



The change of colour and conductivity run parallel, indicating thereby a change of structure (for the true base is like ammonia, whereas the pseudo base corresponds to an alcohol [2]). The following represents the process of transformation of colour base to salt in the case of crystal violet.



Colourless pseudo base of crystal violet.

Coloured true base of crystal violet

Coloured salt of crystal violet.

Thus, the colour of the hydrochloride is readily accounted for on the chromophore theory. If more hydrochloric acid is added, the colour changes again owing to the union of the acid with the amino groups

[1] *Ber.*, 1900, 33, 278, 752.

[2] Muller, *Ber.*, 1910, 43, 2609.

of the other benzene nuclei and the removal of the influence of the auxochrome.

Another theory which was advanced by Rosenstiehl in 1880 explained the formation of the hydrochloride from the carbinol as follows:

$$HO \cdot C(C_6H_4NH_2)_3 + HCl = ClC(C_6H_4NH_2)_3 + H_2O$$

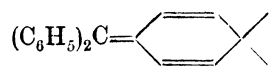
Here the hydroxyl is simply replaced by the halogen and no chromophore is present. This view of the structure is supported by the fact that, assuming no intramolecular rearrangement occurs in the process, pararosaniline can be prepared with carbon tetrachloride; but, on the other hand, the existence of a colourless pararosaniline cyanide is difficult to explain, if the structure is the same as that of the chloride.

Rosenstiehl's theory was long discarded, until the discovery of triphenylmethyl by Gomberg in 1900 introduced new features into the problem.

The constitution of triphenylmethyl and its existence in solution in a coloured form has already been referred to (Part I, p. 60). Shortly after its discovery Norris and Sanders[1] found that the colourless triphenylmethyl chloride and carbinol dissolve in strong sulphuric acid with a yellow colour. On dilution, the yellow colour disappears and the colourless carbinol is precipitated. If the sulphate and chloride are similarly constituted as salts of triphenylmethyl they will have the following structure, in which *no* chromophore is present:

$$C(C_6H_5)_3Cl \qquad C(C_6H_5)_3O \cdot SO_3H$$

In addition to the colourless compound a yellow chloride can be obtained in acetic acid solution by adding strong hydrochloric acid, which, like the sulphuric acid solution, loses its colour on the addition of water. The colourless chloride also dissolves in liquid sulphur dioxide with a bright yellow colour. Triphenylmethyl also forms a coloured perchlorate $(C_6H_5)_3C \cdot ClO_4$, which has been isolated, and a series of coloured double salts with $AlCl_3$ and $SnCl_4$. It thus appears that the salts of triphenylmethyl form two series, which Kehrmann and Wenzel explain by giving to the coloured variety a half-quinoid or quinole formula,



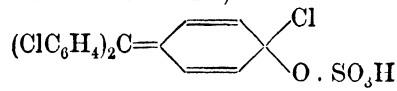
(X = acid radical)

and to the colourless compounds the simple salt structure described above. In agreement with this view Walden and Gomberg found

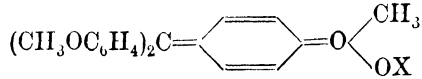
[1] *Amer. Chem. Journ.*, 1901, 25, 54.

that the yellow solution of the chloride in liquid sulphur dioxide conducts, and therefore, it is to be presumed, undergoes ionisation. On the other hand, Hantzsch and Meyer[1] observed that the colourless bromide in pyridine and other solvents also conducts, though it shows no absorption in the visible spectrum.

Baeyer's Theory. Baeyer and Villiger, from a careful study of the problem, have arrived at a different explanation. If the coloured salts of triphenylmethyl have a quinoid structure, the para-chloro-derivative should possess the structure,



in which the one (quinoid) chlorine atom is differently situated from the other two and should consequently be more easily removable with silver solution. But an acetic-sulphuric acid solution of the substance gives no silver chloride after standing for twenty-four hours with a solution of silver acetate, from which it may be inferred that there is no difference in the stability of the three halogen atoms. The quinoid structure is therefore dismissed. Other facts point in the same direction. On increasing the basicity of the triphenyl-methyl radical by the introduction of methoxy groups into the nucleus, moderately stable coloured salts have been isolated. Trianisyl nitrate $(CH_3OC_6H_4)_3NO_3 + 1\frac{1}{2}\,HNO_3$ is deeply coloured. On the quinoid hypothesis these salts should have the formula:



from which the quinoid methyl group should be easily detached in conjunction with the acid radical. Moreover, the trianisyl compound should behave differently from the isomers with the methoxy groups in the ortho and meta position; but no such difference has been observed. Baeyer therefore concludes that the coloured substance is not quinoid in structure, and that the difference between the coloured ionisable substance and the colourless non-ionisable compound must be formulated in another fashion. Carbon may function like nitrogen in ammonium salts or phosphorus and arsenic in the phosphonium and arsonium salts, that is, when saturated with basic radicals it may act like a metal, forming salts having the nature and structure of metallic salts. In order to indicate the difference between the colourless and coloured salts and the ionisation of the latter in solution, he has recourse to a difference in the character of the attachment of

[1] *Ber.*, 1910, 43, 886.

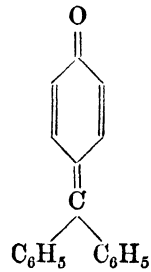
the *carbonium* carbon to the acid radical, which is represented by a straight bond in the colourless salts and by a wavy or 'carbonium valency' in the coloured salts. The coloured double salt with stannic chloride and the sulphate will appear thus:

$$(C_6H_5)_3C\sim Cl\,.\,SnCl_4$$
$$(C_6H_5)_3C\sim O\,.\,SO_3H$$

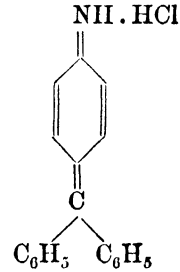
It must not be supposed that the use of two kinds of bonds is anything more than a system of notation. It affords as much explanation as if the acid radical were underlined or written in red ink in one case and not in the other.

The main point is that Baeyer, like Hartley, whose views he shares, does not regard the quinoid structure as affording an explanation of colour in this group of colouring matters. Many other colourless substances when dissolved in mineral acids give intensely coloured solutions. Dibenzalacetone and allied substances show this behaviour, and, according to the nature of the substituted phenyl radical, give coloured products with hydrochloric acid ranging from red to violet, which contain from 1 to 2 molecules of acid.[1] This property of forming coloured salts from colourless or feebly coloured compounds has been termed by Baeyer *halochromy* (see p. 104).

Baeyer does not entirely discard the quinoid structure, which is recognised as the basis of colour in certain triphenylmethane dyes, so that the cause of colour is twofold. It thus receives at his hands a wider, but at the same time a much less definite structural interpretation. In studying the properties of triphenylcarbinol derivatives Baeyer found that all hydroxy and amino compounds are colourless, and only become coloured on removal of the elements of water. In the mono-substituted derivatives only the para group can contribute to the loss of water. Thus, *p*-hydroxytriphenylcarbinol yields fuchsone, while fuchsonium chloride is obtained from *p*-aminotriphenylcarbinol.



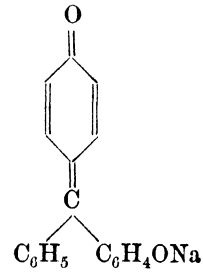
Fuchsone.



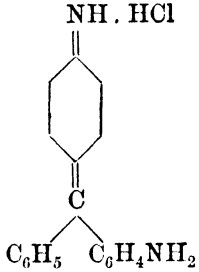
Fuchsonium chloride (fuchsonimine chloride).

[1] Stobbe, *Annalen*, 1909, 370, 93.

Now both these substances have an orange colour; but the full depth of colour of the triphenylmethane dyes, as well as the characteristic absorption bands, are not developed until at least two amino or two hydroxyl groups occupy the para position to the quinoid carbon. A comparison of the spectrum of the sodium salt of benzaurin with the hydrochloride of Doebner's violet showed identity in the absorption bands. It follows that the usual formulae cannot represent the true structure of these two substances, seeing that salt formation is quite differently represented.



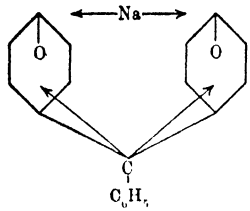
Sodium benzaurin.

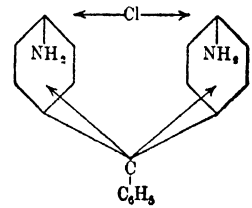


Doebner's violet

The source of colour in such a case is, according to Baeyer, not due to the damping of the oscillations and consequent shifting of the bands of the parent hydrocarbon to the visible region, but rather to the character of the oscillations, which are determined by the rhythmical effect produced by the structure of the molecule.

This rhythmical movement is caused by the oscillation of the metal or halogen atom between the two oxygen atoms or two nitrogen atoms respectively. The benzene nuclei must be represented as alternately possessing the structure of Graebe's superoxide formula, whilst the fourth carbon valency executes, as it were, a pendulum motion between the two oxygen or nitrogen atoms. The effect may be represented by the following formulae:



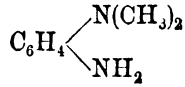


Similar views have been applied to phenolphthalein, to the tetramethylamino derivatives of diphenylphthalide,[1] to aurin, and to parafuchsin, but in the latter cases the three benzene nuclei are assumed to take part in the process.

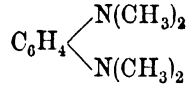
[1] Green, *J. Soc. Chem. Ind.*, 1909, 28, 638.

The same idea underlies the theory of colour put forward by Baly, Desch, and Stewart, and also by Willstätter, in which intermolecular or intramolecular change is made the active agent in producing molecular or electronic oscillations and so causing selective absorption.

Willstätter's Theory. After showing that the simplest quinonimines are colourless or faintly coloured (p. 101), Willstätter[1] examined the coloured compounds obtained by Wurster in 1879 by the action of bromine on *p*-aminodimethylaniline and tetramethyl-*p*-phenylenediamine.



p-Aminodimethylaniline.

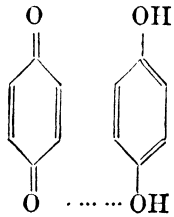


Tetramethyl-*p*-phenylenediamine.

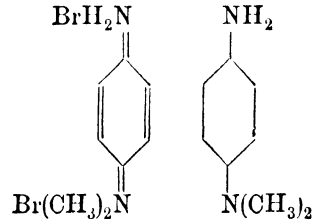
The first gives a red compound of the formula $C_8H_{11}N_2Br$ and the second a blue compound of the formula $C_{10}H_{15}N_2Br$. The red compound, which was regarded by Nietzki as a quinonimine,

$$HN=C_6H_4=N(CH_3)_2\,Br,$$

was found by Willstätter to be a semi-quinonimine (meriquinoid), the full quinonimine (holoquinoid), obtained by oxidation of aminodimethylaniline, being colourless. It was then found that the red semi quinonimine could be obtained either by the partial reduction of the quinonimine or by the union of the original base with the quinonimine; in other words, the coloured substance belongs to the class of quinhydrones Willstatter explains the colour of the quinhydrones by the saturation of the partial valencies of the oxygen atoms of the quinone and quinol, or of the nitrogen atoms of the quinonimines.



Quinhydrone.



Wurster's compound.

The difference between ordinary quinhydrone, which dissociates into its colourless constituents in aqueous solution, and Wurster's compound, which retains its red colour, is attributed to the greater stability

[1] Willstätter and Piccard, *Ber.*, 1908, 41, 1465.

of the latter and a form of isorropesis (p. 87) or make and break in the linking of the residual valencies, which sets up molecular oscillations.[1] The same thing may also occur between parts of a molecule (that is, between a quinoid and aromatic nucleus) and explains the similarity of Wurster's red and fuchsine both in the colour of the aqueous solution and in that of the acid solutions of the imino compound.

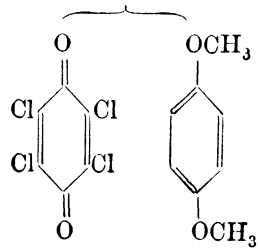
In this way the colour of the meriquinoids is referred to the same cause as that assumed by Baeyer in the di- and tri-phenylmethane colouring matters, the difference in the two cases being that in the fuchsonimines there is a state of isorropesis, which is restricted to the quinoid nucleus, whereas in the salts a meriquinoid condition prevails.

Many similar coloured compounds of quinones, quinonimines, chlorimides, and dichlorimides with amines and phenols have since been prepared,[2] and Werner[3] regards the coloured picrates of the hydrocarbons and aromatic bases as belonging to the same type, in which the residual affinity of the nitro group plays the part of the quinoid oxygen.

These views on colour have encountered strong opposition, both on theoretical and experimental grounds.

Kehrmann[4] considers that the triphenylmethane bases and their coloured salts differ fundamentally in structure, whereas in the meriquinoids and holoquinoids the structure of the chromophore is the same in both, and the colour is only developed on the introduction of a second molecule containing the auxochrome, NH_2 or OH.

But a more serious objection is that raised by Schlenk,[5] who prepared coloured compounds consisting of two molecules in which there is no possibility of intermolecular oscillation. Such, for example, is the blue compound of chloranil and quinolmethyl ether.



[1] Willstätter and Piccard, *Ber.*, 1908, 41, 1458, 3245, Schlenk, *Annalen*, 1908, 363, 313, Decker, *Annalen*, 1908, 362, 305.

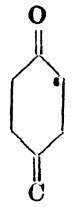
[2] K H Meyer, *Ber*, 1909, 42, 1149, 1910, 43, 157.

[3] *Ber*, 1909, 42, 4321; see also Sudborough and Beard, *Trans. Chem. Soc.*, 1910, 97, 773; Hofmann and Kimmeuther, *Ber.*, 1910, 43, 1761.

[4] *Ber.*, 1908, 41, 2340.

[5] *Annalen*, 1909, 368, 271.

Moreover, he has obtained *p*-tetramethyldiamino fuchsone,



$(CH_3)_2NC_6H_4 \quad C_6H_4N(CH_3)_2$

Tetramethyldiamino fuchsone.

which is a true dye, though oscillation of the kind suggested by Baeyer is impossible. Thus, the oscillation theory of colour must at present remain in abeyance. At the same time it is remarkable how frequently loose molecular combinations are attended by the appearance of colour. In this connection attention may be drawn to Vorländer's compounds (Part I, p. 164), which pass from a coloured labile to a colourless stable condition.

The same thing has been observed in many other cases. Triphenylmethyl, for example, combines with *p*-benzoquinone to form an unstable orange additive compound, $C_6H_4O_2 + 2(C_6H_5)_3C$, which rapidly changes into the stable and colourless triphenylmethyl ether.

$(C_6H_5)_3CO \quad OC(C_6H_5)_3$

Pfeiffer's Theory of Colour.[1] This theory of colour applies more particularly to the coloured molecular compounds of the quinhydrone type; but which includes also the halochrome combinations of ketones with inorganic salts and acids already referred to and of nitro compounds with aromatic hydrocarbons, with their auxochrome derivatives, and with acids and salts. These compounds belong to the following types:

$C_6H_4O_2$, C_6H_6	R_2CO, $Me\,X_n$	RNO_2, C_6H_6	Me = metal
$C_6H_4O_2$, $(C_6H_6)_2$	R_2CO, HX	RNO_2, HX	X = acid radical
Quinhydrones.	Halochromes.	Molecular nitro-compounds.	

They contain a group possessing, what Pfeiffer terms, one-sided saturation—that is, the doubly-linked oxygen of the quinone, ketone, or nitro group, which serves as the point of attachment for the other half of the molecule (benzene ring, acid or salt), is more saturated than the adjoining carbon.

[1] *Annalen*, 1914, 404, 1; 1916, 412, 253; *Organische Molekülverbindungen*, by P. Pfeiffer: Enke, Stuttgart, 1922; see also Sudborough, *Trans. Chem. Soc.*, 1916, 109, 1339.

—C=O · C=C,	C=O HX,
Quinone or ketone + ar. hydrocarbon.	Ketone + salt or acid.
RN=O C=C,	RN=O··· HX
Ö	Ö
Nitro-compound + ar. hydrocarbon.	Nitro-compound + salt or acid.

This one-sided saturation produces its chromogenic effect by rendering the carbon or nitrogen less saturated.

Baly's Theory of Colour.[1] Baly's explanation of absorption has already been outlined on p. 90. It is assumed to depend upon the fields of force surrounding the molecules. These may be closed or partially closed when they come together, but are capable of being opened up either by the action of the solvent or by the energy of the light waves to which they respond and which they absorb. This process of opening up may occur in stages and will be called into play by the use of different solvents, the effect of which will be recognized by varied selective absorption. There is, therefore, no occasion to postulate a new structure, as Hantzsch does, for each definite absorption spectrum, which according to Baly is derived from one unaltered primary structure. The existence of this primary structure is confirmed by 'proportionate representation' in the infra-red region of the spectrum. When a substance exhibits an absorption band energy is being absorbed, and if no photochemical change is thereby produced the whole of the absorbed energy is again radiated as heat (in the infra-red). The absorption bands in the violet and ultra-violet have frequencies which are integral multiples of the frequency of a band in the infra-red. This is in harmony with the quantum theory, since if the quantum of energy is the product of the frequency into a constant, one single quantum absorbed at one frequency can be radiated as an exact number of quanta at a smaller frequency if the first is an integral multiple of the second. The theory is not, however, limited to one band in the infra-red, so that, as Watson has pointed out,[2] considering the indefinite character of most absorption bands and the difficulty of determining accurately the positions of maxima, the theory may account for the presence of almost any band.

Kauffmann's Auxochrome Theory. Very different from the foregoing is the theory of Hugo Kauffmann,[3] sometimes described as the *auxochrome theory.*

The vapours of many substances at low pressures absorb Tesla radiations (high-frequency-current discharge) and become luminous, generally with a blue or violet and, occasionally, with a green or yellow light. As the pressure is increased the luminescence in most cases disappears, but not in all, and those that retain the property at atmospheric pressure have in common certain characteristics, which are supposed to form the basis of colour, fluorescence, and phosphorescence. A comparison of luminescent compounds indicates that they are mainly benzene derivatives and contain certain groups

[1] *Journ. Soc. Chem. Ind.*, 1915, 34, 396; *Phil. Mag.*, 1914, 27, 632; 1915, 29, 223; *Nature*, 1921, p. 312. [2] *Trans. Chem. Soc.*, 1915, 107, 1575.
[3] *Die Auxochrome*, Ahrens' *Vorträge*, 1908, 12, 1.

which Kauffmann terms *luminophores*. Benzene is therefore regarded as the seat of luminescence in these compounds. But benzene itself is only feebly luminescent. The effect may be intensified in various ways: in the first place by the introduction of an auxochrome (an amino or hydroxyl group); in the second place by the multiplication of aromatic nuclei, especially condensed nuclei, such as naphthalene, anthracene, &c., and thirdly by the linking of nuclei with unsaturated carbon chains, as in stilbene and diphenylbutadiene.

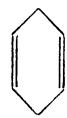
$C_6H_5 . CH : CH . C_6H_5$ — Stilbene.

$C_6H_5 . CH : CH . CH : CH . C_6H_5$ — Diphenylbutadiene.

This property of luminescence appears to run parallel with certain other chemical and physical attributes. Strongly luminescent compounds, such as aniline and *p*-aminophenol, show a tendency to oxidise and form quinoid products, to undergo substitution and, generally, to exhibit unusual reactivity. They show, moreover, anomalous magnetic rotation (p. 54), and to a smaller extent anomalous molecular refractivity (p. 29).

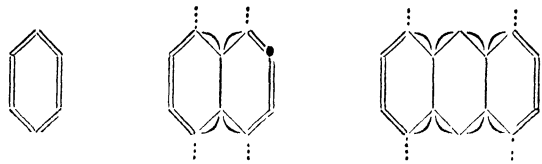
Other groups (NO_2, CH_3CO) produce a precisely opposite series of effects. These facts, according to Kauffmann, appear to indicate that in benzene, the seat of the phenomena, the energy of the molecule is differently distributed in its various derivatives, which may be represented by a difference of structure, and that there exists an ideal limiting condition of the nucleus towards which the most strongly luminescent compounds tend.

This limiting or 'D condition' is best represented by the Dewar benzene formula, or at least by that portion of it which consists of the pair of parallel double bonds. It is found that those physical and chemical characters which are most simply expressed by this structure are precisely those which favour luminescence. It may be represented by the following grouping:

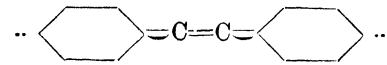


Assuming Thiele's theory of partial valencies (Part I, p. 147), Kauffmann's idea may be put in this way: that auxochromes and those groups which act as auxochromes are such as, by their manner of linking to the benzene ring, demand more than a whole valency.

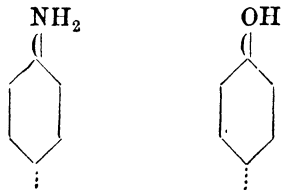
This will explain the feeble luminescence of benzene as compared with that of naphthalene and anthracene,



the luminescence produced by an unsaturated carbon chain,



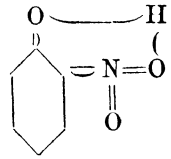
and by the introduction of amino and hydroxyl groups.



These views are more fully developed in the section on fluorescence (p. 140).

The auxochrome theory, contrary to that of Hantzsch (of isomeric change accompanying change of colour) makes no assumption as to interaction of auxochrome and chromophore, except in so far as residual affinity of the auxochrome tends to produce a D condition of the nucleus. Benzene is optically coloured, for it produces a banded spectrum in the ultra-violet. If auxochromes are introduced, the effect is to shift the absorption towards the red and thus produce visible colour. By passing from benzene to naphthalene and anthracene the bands shift more and more towards the red. Some of the absorption bands of nitrobenzene lie just within the visible spectrum, so that a weak auxochrome is sufficient to produce visible colour. These are precisely the views of Hartley; but Kauffmann explains in addition the cause of the shifting, which Hartley does not define. The latter considers that both auxochromes and chromophores produce their effect by virtue of their residual affinities, which correspond to Thiele's partial valencies. The greater the residual affinity binding auxochrome and chromophore to the nucleus, the more intense the colour.

How then does it come about that the free nitrophenols are often more deeply coloured than their ethers, in spite of the fact that alkyl groups often enhance the auxochrome effect? In the case of ortho nitrophenol neither Hantzsch's theory of isomeric change nor that of solid solution nor of dissociation is free from objection. Kauffmann explains it as follows: the oxygen and nitro group are conjugated to the nucleus, leaving the oxygen with a residual valency, whilst the ionisable hydrogen is simultaneously joined to both,



which implies a division of the hydrogen valency. The larger, therefore, the amount of hydrogen valency absorbed by the oxygen of the nitro group, the more of it will be at the disposal of the benzene ring for binding the hydroxyl oxygen, so that the latter derives an increased activity as auxochrome. As more valency is at the same time free for linking the nitro group to the nucleus, the two groups, auxochrome and chromophore, will combine to deepen the colour. Metals may behave like hydrogen, but the distribution of valency will probably be of a different character, and so the colour effect may vary from salt to salt. Alkyl groups, on the other hand, are less mobile, and mutual reinforcement of auxochrome and chromophore does not take place.

Indicators. Ostwald,[1] in applying the ionic theory to analysis, advanced a new theory of indicators, which may be explained as follows: an indicator is a substance which forms coloured salts and has a weak basic or acid character; that is, it is slightly ionised in solution and its organic ion has a different colour from that of the non-ionised molecule. Its sensitiveness will depend upon the amount of ionisation. The fewer the number of ions, the more delicate will be the indicator on addition of base or acid. For, supposing the indicator to be the salt of a weak acid, it will ionise into coloured organic and metallic ions. The addition of a rather stronger acid introduces a number of hydrogen ions and, according to the mass law, will diminish the amount of ionic dissociation of the organic molecule and so cause a change of colour. But a weak acid must be used in conjunction with a strong base; otherwise hydrolytic

[1] *Zeit physik Chem.*, 1892, 9, 579; see also *The Foundations of Analytical Chemistry*, W. Ostwald Macmillan.

decomposition may occur and the change will be indistinct. A good example af a weak acid is phenolphthalein, which is nearly colourless in the non-ionised state, but whose ion, according to Ostwald, is red. A solution of the sodium salt contains the coloured organic and sodium ions. The addition of a strong acid, such as hydrochloric acid, which is highly ionised will diminish the amount of ionic dissociation of the indicator and the phenolphthalein will pass into the colourless non-ionised condition. Phenolphthalein is more serviceable for acidimetry than for alkalimetry, for in the latter case it can only be used in conjunction with the stronger bases for the reason given above.

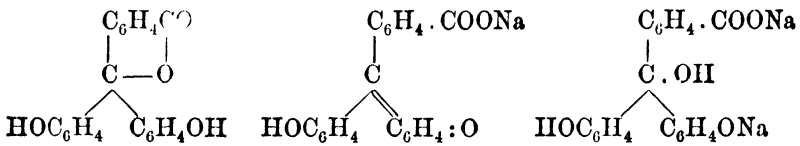
Methyl orange, on the other hand, is a moderately strong acid whose ion is yellow, whereas the non-ionised molecule is red. The aqueous solution of the free acid is perceptibly ionised, but, on addition of a trace of strong acid, ionisation is diminished and the red colour of the non-ionised molecule appears. But if the acid is weak, that is, slightly ionised, sufficient ions are not produced to visibly affect the number of organic ions, and an excess of acid will be required to produce a change of colour; in other words, the end-point will be indistinct. The selection of the indicator will therefore depend upon the nature of the base or acid to be estimated.

This view of ionic dissociation receives substantial support from the fact that the salts of a coloured acid with a series of colourless bases gives the same coloured solution, and similarly with the salts of a coloured base with different acids. That the colour of an ion is intimately associated with its ionic change seems to follow from the colour of ferrous and ferric salts, which contain the differently coloured ferro and ferric ions, from that of the ions of manganates and permanganates, and from the colour of the halogens and their colourless ions present in the halogen acids. In the last case the halogen is molecular in one case and atomic in the other, and the two are therefore not strictly comparable On the other hand, little difference in absorption in the ultra-violet has been observed between the slightly dissociated acetic acid and the highly dissociated salts. Further, many colouring matters retain their colours in the solid state. This applies to the alkali salts of phenolphthalein and *p*-nitrophenol. Nor does the ionic theory explain the disappearance of colour when a solution of phenolphthalein in alkali is made more strongly alkaline and its reappearance on neutralisation of the free alkali.

The discharge of the colour of certain indicators by the addition of ionising solvents, such as alcohol, is out of all proportion to the de-ionising effect and, further, the non-ionising solvents will often

produce less decolourisation than those which are known to produce ionisation. If colour is due to ionisation, depth of colour should not follow Beer's law, that is, it should not vary proportionately with dilution, and an ionising solvent should produce a different effect on dilution from that of a non-ionising solvent; but neither conclusion is supported by experimental evidence.[1]

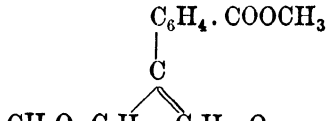
The other theory of indicators is a chemical one. The notion that change of colour is accompanied by a change of structure has been suggested by many observers: by Bernthsen and Friedländer, and more recently by Stieglitz,[2] Hantzsch, Kremann,[3] and Bredig.[4] The change of structure of aliphatic and aromatic nitro compounds on the addition of alkali has been very fully discussed (p. 106). The same reasoning has been applied to the colourless and coloured pseudo and true bases of the triphenylmethane series (p. 120). The chief evidence against such a view is of a physical rather than of a chemical nature, and is mainly based upon the absorption spectra of the parent substances and their derivatives (p. 118). Assuming that change of colour, at least in certain cases, is an indication of change of structure, the fact will explain among other things the slow colour change of certain indicators. Change of structure implies a time reaction, whereas ionisation should be instantaneous. This is very strikingly seen in the case of phenolphthalein. With caustic soda it gives a red solution which becomes colourless on further addition of alkali. The loss of colour, which takes place slowly with dilute alkali but does not occur on the addition of a neutral salt containing a common metallic ion, is difficult to explain on the ionisation hypothesis. Moreover, the colourless alkaline solution may be neutralised with acetic acid in the cold without apparent change, and the colour only returns on heating, as Green and Perkin have shown.[5] These results may be very simply explained by change of structure from the colourless lactone to the coloured quinoid form. On further addition of alkali the coloured quinoid passes into the colourless carbinol salt and its colourless acid.



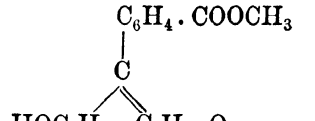
Colourless lactone. Coloured quinoid. Colourless carbinol.

[1] *Ber.*, 1906, 39, 4159; 1908, 41, 1161.
[2] *J. Amer. Chem. Soc*, 1903, 25, 112.
[3] *Zeit. anorg. Chem.*, 1903, 33, 87.
[4] *Zeit. anorg. Chem.*, 1903, 34, 202.
[5] *Proc. Chem. Soc.*, 1904, 20, 50.

The change has been followed by Hantzsch and Meyer[1] by observing the conductivity. Moreover, Green and King[2] have obtained the methyl ester of phenolphthalein and of its methyl ether, which are orange or red and are therefore assumed to correspond in structure to the sodium salt.

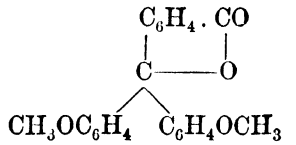


Orange.



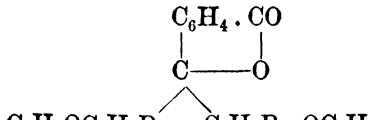
Red.

This view explains also the fact that whereas alcohol decolourises the ammonium salts of phenolphthalein, it has no such effect on its ester, for lactone formation can occur in the one case, but not in the other.[3] A further proof of the above structural differences is the existence of a lactone methyl ether, isomeric with the ester, which is colourless.

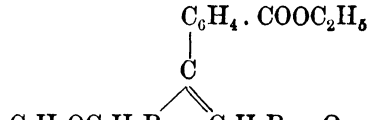


This should, according to the former view, form a coloured alkali salt, whereas the addition of caustic soda gives a colourless solution, which is taken to be the carbinol compound.

A very similar series of observations have been made by Meyer and Marx,[4] who obtained by the action of ethyl iodide on the silver salt of tetrabromophenolphthalein a yellow diethyl ester which easily passes into the colourless isomer.



Colourless.



Yellow.

[1] *Ber*, 1907, 40, 3480.
[2] *Ber.*, 1906, 39, 2365; *J. Soc. Chem. Ind.*, 1908, 27, 4
[3] Meyer and Spengler, *Ber.*, 1905, 38, 1318.
[4] *Ber.*, 1907, 40, 1414.

FLUORESCENCE

When light falls upon a substance, some of it may be reflected unchanged, some may be converted into heat, and some may be emitted in the form of light waves. According to Stokes (1852) the emitted waves have a longer period than those which are absorbed (Stokes's Law), but this has proved not to be invariably the case. Ultra-violet light, for example, will cause a solution of quinine sulphate to fluoresce with a blue colour, that is, with one of longer wave length, but, on the other hand, fluorescein, eosin, &c., emit light of shorter wave length,[1] whilst the absorption and fluorescent spectra of iodine vapour are the same.

If the effect ceases as soon as the source of light is withdrawn, the phenomenon is known as *fluorescence*; if it continues for a longer or shorter period after the stimulus ceases, it is called *phosphorescence*. The two merge into one another, and there is no sharp line of demarcation, as Becquerel showed by means of his phosphoroscope.

Fluorescence may be observed in many substances, solid, liquid, and gaseous. Fluor-spar and uranium salts are familiar examples of solids which become self-luminous with characteristic colours under the influence of light; paraffin oil and an acid solution of quinine give out a blue light; solutions of fluorescein emit green light, and eosin and chlorophyll red. Iodine, sodium, anthracene, indigo, &c., in the form of vapour also fluoresce. It will be seen that fluorescence is not restricted to any physical state nor confined to any particular position of the spectrum. The emitted light was naturally observed first in the visible spectrum, but Stark has shown in the case of several aromatic hydrocarbons that it may occur in the ultra-violet region and will probably be found also in the infra-red. Moreover, there exists a limited range of waves peculiar to each

[1] Nichols and Merritt, *Physical Review*, 1904, 19, 18.

fluorescent substance which can excite fluorescence, and a comparatively small range of waves is emitted having a well-marked maximum of intensity. This maximum corresponds to a maximum in the absorption curve; but, as there is a shift in the emission spectrum, the curves do not overlap, but lie side by side and dovetail into one another. Selective absorption of waves of definite wave length by fluorescent substances is readily demonstrated by directing a beam of light on to the surface of a quinine solution. It is only at the surface that the blue colour is perceived. The light is there robbed of the vibrations which produce the effect; for on entering a second layer of the same solution no fluorescence is visible. But if the second solution is replaced by one of eosin a green fluorescence will be produced at the surface as these waves have been transmitted by the first solution.

The nature of the solvent has a definite effect on fluorescence. Under its influence, fluorescence may be intensified, diminished, or made to vanish. Fluorescein fluoresces strongly in alkaline solution, and there is a gradual diminution of fluorescence with the solvents taken in the following order: methyl alcohol, pyridine, and acetone, disappearing completely in the last.

o-Aminocinnamic ester fluoresces with a violet colour in ligroin, blue in benzene, and green in alcohol; that is, with a longer wave length the higher the dielectric constant of the solvent. Concentration also affects fluorescence, which may be intensified or weakened by dilution. The action of the solvent has received no complete explanation.

It has been stated that the absorption of light is associated with the vibration of the valency electrons by a process which may be compared with that of resonance; but it is not easy to see why a particular set of light waves should give rise to vibrations of a different period such as occurs in fluorescent substances. Moreover, the fact that phosphorescence is only a special kind of fluorescence makes the notion of resonance improbable; for it implies that the vibrations of the electrons are continued sometimes for hours after the stimulus is removed. It seems more probable, as Wiedemann[1] suggested, that under the stimulus of the absorbed light an actual chemical change is effected by a temporary displacement of the atoms within the molecule or of a group of atoms. Hallwachs, who in 1888 observed that ultra-violet is capable of discharging a negatively charged metallic plate or producing in

[1] Wiedemann, *Annalen*, 1895, **56**, 201.

a neutral plate a positive charge, gave the clue to the present explanation.[1]

In terms of the electronic theory, the violent vibration excited by the absorbed light may detach an electron from one kind of atom and transfer it to another.[2] The new arrangement may be stable and produce a new substance (see p. 90), or unstable, when a more or less rapid change to the original position may occur.

This reversion will set up vibrations having a characteristic period, which will cause fluorescence if the reversion is rapid, or phosphorescence if the process is prolonged. It might be supposed that such a transition would be assisted by rise of temperature, and numerous cases are known in which it will revive or intensify the luminosity of phosphorescent substances, such as calcium sulphide, but it is also found that many compounds—acetophenone, benzophenone, diphenyl, &c.—which do not fluoresce at the ordinary temperature will do so when cooled in liquid air (−180°). It is possible that the phenomenon associated with differences of temperature may depend on exothermic or endothermic changes.

The Relation of Fluorescence to Structure. We have now to try and discover if any relation subsists between fluorescence and structure. From the similarity in the nature of selective absorption and fluorescence such a relationship seems highly probable, and there is little doubt that it exists.

Like banded absorption, fluorescence reveals a banded spectrum, which has been chiefly observed among members of the aromatic series and affords further evidence of close relation between the two phenomena.

A very full list of such substances is given by Kauffmann[3] It includes an extraordinary variety of compounds, the greater number consisting of condensed homo- or hetero-cyclic complexes, often containing certain characteristic groups.

A number of theories, both statical and dynamical, have been suggested by different observers, which, if they do not throw any very clear light on the phenomenon itself, serve at least as useful generalisations under which a very large number of fluorescent substances may be classified. It should be pointed out that the

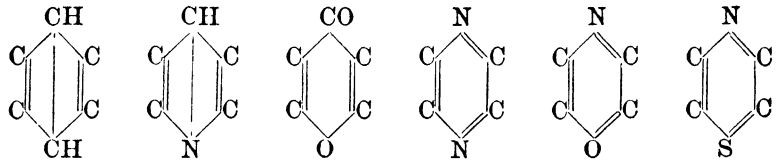
[1] Drude, *Zeit. f. Electrochemie*, 1904, **14**, 677, 936

[2] It was found later (Stark and Steubing) that organic compounds, including fluorescent substances, behaved similarly, and a current was set up by illuminating a sensitive electrode in a conducting liquid. Light cells have been constructed on this principle.

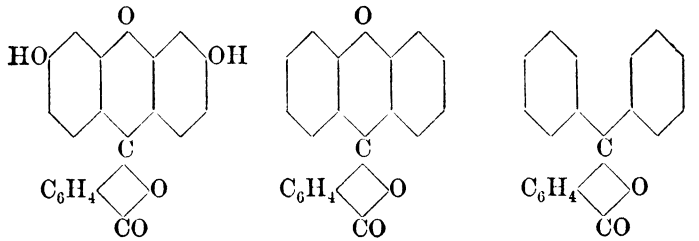
[3] *Die Beziehungen zwischen Fluorescenz und chemischer Konstitution*, Ahrens' *Vorträge*, 1907, 11, 1. Enke, Stuttgart.

theories are essentially qualitative in character. There is no attempt at connecting the nature, position, or intensity either of absorption or emission spectra with any particular atomic grouping. It follows, therefore, that the reverse process of ascertaining structure by a study of fluorescence is at present out of the question.

R. Meyer's Theory of Fluorescence and Structure. Liebermann (1880) was the first to attempt to correlate fluorescence with structure. The subject was then taken up by R. Meyer.[1] Fluorescence, according to the latter, is determined by the presence of certain groups which are termed *fluorophores.* They are ring complexes of the following types:

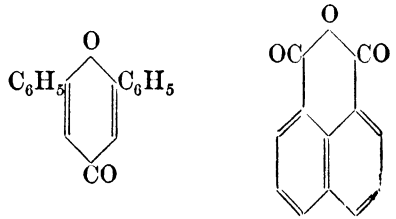


such as are found in anthracene, acridine, pyrones, azines, oxazines, and thiazines. The fluorophore is not, however, sufficient to produce fluorescence. It must be associated with dense atomic complexes, an arrangement which may be illustrated by the following examples:



Fluorescein. Fluorane Phenolphthalein.

Diphenylpyrone in strong sulphuric acid and naphthalic anhydride are also fluorescent for the same reason.



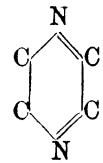
Diphenylpyrone. Naphthalic anhydride.

[1] *Zeit. physik. Chem.*, 1897, 24, 468.

The theory, it will be seen, resembles Witt's chromophore theory of colour, in which the fluorophore, like the chromophore, is not itself responsible for the particular phenomenon of which it is the seat, but only becomes so in association with other groups.

The theory is, however, complicated by the fact that the fluorescence is greatly influenced by the nature and position of the substituents in the nuclei associated with the fluorophore. The fluorescence of fluorane is diminished by introducing two hydroxyl groups into the two benzene nuclei in the meta position to the pyrone oxygen, and completely destroyed by their introduction into the para position. Chlorine atoms, nitro and methyl groups in the meta and para positions also diminish or remove fluorescence. Moreover, fluorophores are not essential to fluorescence. Diphenyl has a weak fluorescence, *p*-diphenylbenzene is stronger. The theory is obviously lacking in essential details.

Kauffmann's Theory. These details have been supplied by Kauffmann,[1] who has modified Meyer's theory in the following way. Kauffmann finds that Meyer's fluorophores have the property of luminescence ; that is, they can be excited when vapourised by the Tesla discharge, or in the solid state by exposure to β rays,[2] so as to emit light. The nature of the substances possessing this property has already been discussed (p. 129). It is usually associated with cyclic structures, but is occasionally found among carbonyl compounds. The luminescent substance is termed a *luminophore.* In order that the property of luminescence may be transformed into that of fluorescence, other atomic groups, *fluorogens,* are necessary. The fluorogens correspond roughly with the chromophores, and include carboxyl, carbonyl, cyanogen, and acrylic acid groups, the ethylene bond and conjugated ethylene bond, the benzene ring and the ortho- and para-quinoid ring, the azomethine group and conjugated azomethine ring, &c.



Azomethine ring.

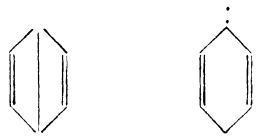
To return to the luminophore or luminescent substance. Benzene, though the seat of luminescence, is not of itself a luminophore.

[1] *Die Auxochrome,* Ahrens' *Vorträge,* 1908, 12, 35.
[2] *Ber.,* 1904, 37, 2946; *Annalen,* 1906, 344, 81.

It requires the introduction of auxochromes, that is, of amino and hydroxyl groups, alone or modified by the introduction of alphyl and aryl radicals. Acyl groups and salt formation destroy the effect of the amino group, and a metal in place of hydrogen that of hydroxyl, but ring formation, of which the auxochrome forms part, does not. Fundamental types of luminophores are aniline and quinol, which luminesce strongly. The same result may be produced by multiplying the number of benzene nuclei, as in diphenyl, and more especially of compact groups of nuclei, as in naphthalene, anthracene, &c., which are strongly luminescent, though not so active as the single nucleus with its auxochrome. Pyridine and tetrahydroquinoline carboxylic acid are luminescent, and so are many other simple ring compounds.

The fundamental idea underlying Kauffmann's theory has already been referred to (p. 129). The property of luminescence, and consequently of fluorescence, is dependent on a peculiar state of the benzene nucleus which is the seat of the phenomenon. In every benzene derivative the ring is supposed to be in a condition peculiar to that compound, but certain ideal extreme conditions may be imagined which give rise to characteristic properties. One of these ideal limits may be represented by Dewar's formula for benzene, where the substance is said to be in the 'D condition' and is then characterised by (1) maximum reactivity, (2) maximum tendency to form quinoids by oxidation, (3) maximum anomalous magnetic rotation,[1] and (4) maximum luminescence. This state is highly developed in dimethyl-*p*-phenylenediamine and nearly absent in nitrobenzene.

The limiting D condition is then Dewar's benzene formula with a mobile para bond, such as Thiele's theory of partial valencies might present.



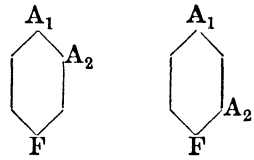
Dewar's formula. Thiele's formula

Admitting that luminophores are in the D condition, a number of empiric rules may be laid down in regard to the effect of auxochromes in producing this condition. Amino and hydroxyl groups tend to do so, depending on the strength of the auxochrome. If more than one is present, they only reinforce one another when

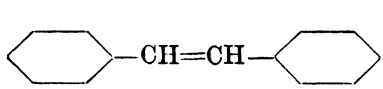
[1] *Zeit physik. Chem.*, 1906, 55, 547.

in the para position, as, for example, in dimethylquinol. This possesses the highest luminescence of all hydroxy derivatives. When the auxochromes are in the ortho or meta position they act in opposition, and consequently the action of auxochromes is not necessarily additive. The strongest luminophores contain para auxochromes. In these compounds weak fluorogens can excite fluorescence. This fact explains why derivatives of quinol, *p*-aminophenol, and *p*-phenylenediamine are so frequently fluorescent.

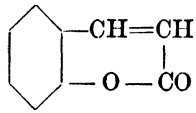
Suppose the fluorogen F to occupy the para position to one of the auxochromes A_1 and there is a second auxochrome A_2, two arrangements of the three groups are possible.



The fluorogen may tend to produce or suppress the D condition; but it is only in the former case that fluorescence is possible. These empiric propositions have been laid down by Kauffmann under the term 'the law of distribution of the auxochrome.' The ethylene bond promotes this state like an auxochrome. Hence stilbene and the coumarins are fluorescent.

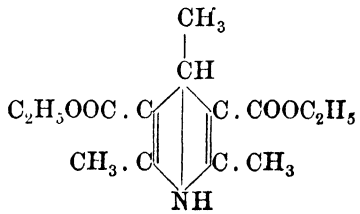


Stilbene.



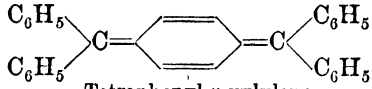
Coumarin.

Carboxyl has the reverse effect when in the para position, but produces fluorescence in the ortho position to the auxochrome. Anthranilic acid fluoresces, but not the para compound. That the parallel double linkage of the Dewar formula is responsible for luminescence, and therefore for fluorescence, is seen in certain hydropyridine carboxylic esters such as dihydrocollidinedicarboxylic ester, which has a strong and characteristic fluorescence.



Dihydrocollidinedicarboxylic ester.

Other examples of the same thing are succinosuccinic ester and its imide, $\Delta^{1,4}$ dichlorodihydroterephthalic ester, tetraphenyl-*p*-xylylene, &c.

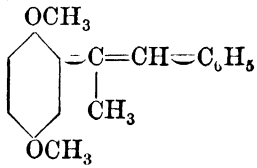


Tetraphenyl-*p*-xylylene.

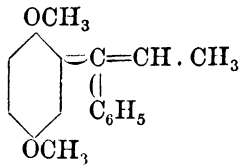
Thus, the D condition of the nucleus corresponds to Meyer's fluorophore (p. 139).

Some compounds, such as the quinones, which contain parallel double bonds and yet do not fluoresce, have not yet received any satisfactory explanation; but it may be that the light energy is for some reason utilised in producing colour rather than fluorescence.

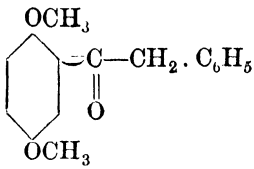
Kauffmann has made a large number of experiments on derivatives of quinol dimethyl ether, containing a side-chain, in order to determine in what respect substitution in the side-chain affects fluorescence. He explains the results by Thiele's theory, namely, that the stronger the partial valency which attaches the side-chain to the luminophore, the greater the fluorescent intensity. The following examples will make this clear:



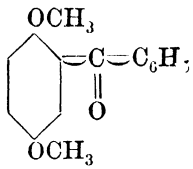
Fluorescent.



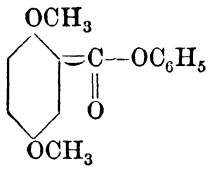
Non-fluorescent.



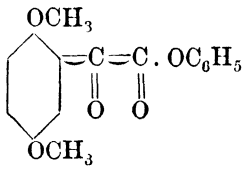
Fluorescent.



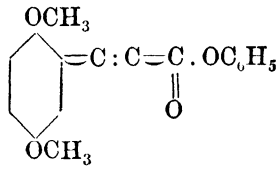
Non-fluorescent.



Fluorescent.



Non-fluorescent.



Fluorescent.

In reviewing the foregoing it will be seen that whereas benzene is the seat of fluorescence, the latter is only excited by the presence of two kinds of groups—the auxochrome and fluorogen—which must be introduced in certain positions. The luminophore, or that which produces luminescence, is determined by the insertion of an auxo-

chrome; finally, the subsequent introduction of a fluorogen causes fluorescence. The fluorogen appears at times to play the part of an auxochrome, and it is difficult to differentiate clearly the functions of the two; but it is assumed that the general tendency of both is to create a particular condition of the benzene ring, which is represented by the Dewar formula.

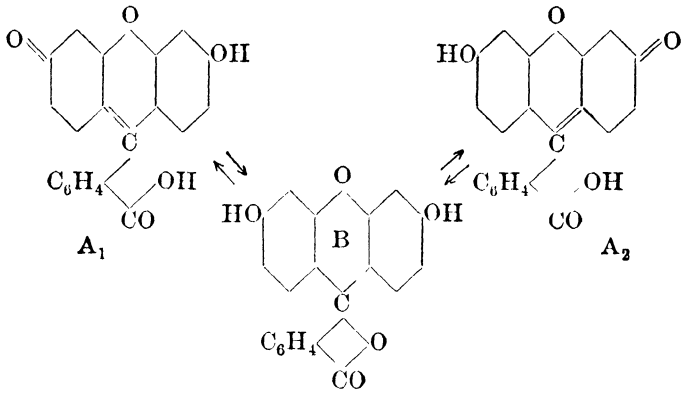
Since Stark's discovery [1] that benzene fluoresces in the ultra-violet, experiments have been instituted by Stark and Meyer, Ley and others [2] with the object of tracing the influence of substituents by observing the change in the character and position of the fluorescence in this region of the spectrum. Francesconi and Barghellini have shown that every substituent modifies the spectrum and shifts it towards the visible region. At the same time the intensity is affected by the substituents, which may either increase it (auxoflores) or diminish it (bathoflores). Among the auxoflores are the two auxochromes and their alphyl and aryl derivatives. Alkyl groups act as auxoflores without shifting the position of the bands. The other auxoflores, OH, OCH_3, NH_2, CN, COOH, CH : CH, shift the bands towards the visible region. Among the bathoflores are nitro groups, which entirely destroy fluorescence, as others had previously observed, and also the halogens, CH_3, CO, and N . N, which weaken it. The effect of salt formation has been studied in the same manner. The line of investigation, by connecting absorption and fluorescence with structure, has a special interest, but has thrown little fresh light on the phenomenon. According to Stark [3] the auxoflores loosen the valency electrons, the bathoflores produce the opposite effect.

Hewitt's Theory. Finally, Hewitt's theory [4] should be mentioned. Like Baly's theory of banded spectrum, which is an indication of oscillatory motion or electronic activity within the molecule, or Baeyer's theory of colour, it is based upon dynamic isomerism. Fluorescence is conditioned by a process of oscillatory tautomerism, or rapid vibration between tautomeric forms, of a peculiar kind, found among a certain class of substances capable of exhibiting what has been termed *double symmetrical tautomerism.*

The two modifications absorb and emit alternately light rays of different period. The operation may be compared to the swing of a pendulum, which once displaced would in the absence of friction continue to swing indefinitely. Thus, fluoresceein can be represented

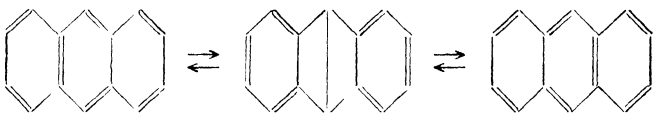
[1] Stark and Meyer, *Physik Zeit*, 1907, 8, 250
[2] *Zeit physik. Chem.*, 1910, 74, 1; *Ber*, 1908, 41, 2988.
[3] *Zeit physik. Chem*, 1900, 34, 1
[4] *Trans. Chem. Soc.*, 1907, 91, 1251; *Zeit. physik. Chem.*, 1900, 34, 1.

in two tautomeric forms—a lactone and quinone form—between which oscillation is supposed to take place.

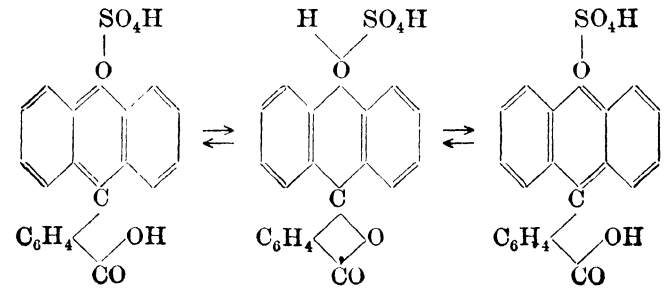


The phases are represented by the formulae A_1 B A_2. Each swing passes from A_1 through B to A_2 and back again, and at A_1 and A_2 energy is alternately absorbed and emitted. The process differs from ordinary dynamic isomerism inasmuch as the substances causing fluorescence are identical at the beginning and end of the swing, and moreover the intermediate position must present a symmetrical complex, otherwise one might expect all dynamic isomers to show fluorescence; for in a state of equilibrium they may be supposed to oscillate between the two forms.

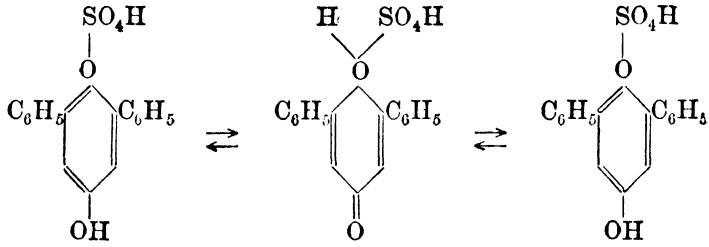
Many fluorescent compounds, already referred to, will be found to fulfil these conditions. Anthracene, for example, will oscillate between the following phases:



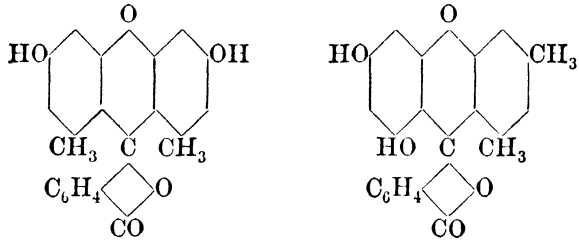
Fluorane, which does not fluoresce in alcoholic solution, is found to do so when dissolved in strong sulphuric acid.



The fluorescence of diphenylpyrone, which appears when the substance is dissolved in strong sulphuric acid, has received the same explanation.

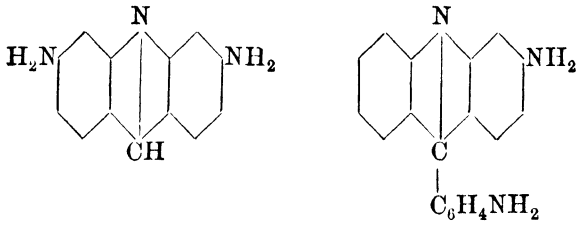


In case the intermediate phase does not represent a symmetrical structure, fluorescence is not produced, and this is supposed to account for the absence of fluorescence in the unsymmetrical dimethylfluorescein, whereas the symmetrical compound fluoresces.



Fluorescent. Non-fluorescent.

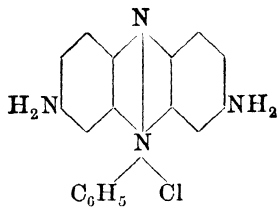
Similarly, acridine yellow fluoresces strongly, whilst chrysaniline produces only a feeble effect.



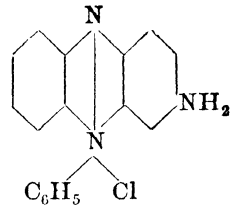
Acridine yellow. Chrysaniline.

The intermediate phase will have a symmetrical structure in the first case, but only half symmetrical in the second.

Phenosafranine hydrochloride gives a yellowish red fluorescence in alcohol; but aposafranine hydrochloride, in which one of the amino groups is absent, does not.



Phenosafranine HCl
(intermediate phase).



Aposafranine HCl
(intermediate phase).

The theory is not without its weak points. There are, for example, substances which fulfil the conditions required by the theory and which nevertheless do not fluoresce. There is no apparent reason why phenolphthalein should not, for it can exist as lactone and quinone and has a perfectly symmetrical structure, and the same applies to tetranitrofluorescein. Then again, it has been shown that if the mobile hydrogen is replaced by an alkyl group and tautomerism thereby suspended, fluorescence may still remain.

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PHOTOCHEMISTRY OF ORGANIC COMPOUNDS[1]

It has already been pointed out that the absorption of light is accompanied by the production of heat, fluorescence, or phosphorescence, or may go further and bring about definite chemical changes. There seems little doubt that these phenomena are closely correlated and may be explained by a temporary or permanent redistribution of the electrons. Before discussing more fully the principles which underlie photochemical action it may be convenient to consider the nature of the change.

The action of light as a bleaching agent has long been recognised, as well as its effect in changing the colour of certain minerals. The earliest definite record of its chemical action seems to have been made by Schultze in 1727, who noticed its effect on silver salts. The subject was taken up again and more fully investigated by Senebier in 1782. Its application to the pictorial reproduction of objects was utilised by Davy and Wedgwood in the early part of the

[1] An excellent summary on 'The Chemical Action of Light', by W. A. Davis, is published in *Science Progress*, 1912, 26, 251.

nineteenth century, who thus laid the foundations of the photographic process. The absorbing technical possibilities of this process, its remarkable success and widespread application, diverted attention from the wider and more purely scientific aspect of the phenomenon, and it is only in recent years that its systematic study has claimed proper attention. Apart from the records of its effects and an examination into the dynamics of a few special reactions, the theory of photochemical change has not advanced very far. Certain generalisations of fundamental importance have, however, been reached. In the first place, it must be recognized that the action of light is not confined to the visible spectrum, but covers a range extending from the shortest Rontgen rays to the long electrical Hertz waves.

Plotnikow in his *Photochemie*[1] postulates the following three photochemical laws The first was discovered by Theodor v. Grotthus[2] in 1818, who showed that those bodies must act most strongly on a given coloured light (or vice versa) which, in their natural condition, exhibit the complementary colour. Twenty-four years later the same law was enunciated by Draper, and is known as 'Draper's absorption law'. In referring to the union of hydrogen and chlorine under the action of light he says: 'The quality gained by chlorine arises from its having absorbed thitonic rays, corresponding in refrangibility to the indigo It is not transient but a permanent property, the rays absorbed becoming latent and the effect lasting an unknown time.' Herschel in 1842 confirmed it by the observation that paper stained with different vegetable colours was bleached most rapidly in the part of the spectrum which showed the complementary colour.

The second law states that photochemical action is proportional to the amount of light absorbed and is independent of the wave length. Timiriazew found in 1869 that the amount of carbon dioxide assimilated by green leaves corresponded to the region of largest absorption, namely, the orange portion of the spectrum; but the experimental proof was furnished by Lasareff,[3] who was able to measure with the aid of a thermocouple the light energy absorbed and determine by means of a spectrum photometer the rate at which colours were bleached in different parts of the spectrum.

The third or summation law was formulated by Plotnikow in 1906. This observer found that hydrogen iodide is oxidised differently in the dark and in the light and was able to follow the reactions

[1] *Photochemie*, by J. Plotnikow Knapp, Halle, 1910.
[2] Ostwald's *Klassiker*, No 152, p. 101. [3] *Ann d Physik*, 1907, 24, 661.

independently. He concluded from his results that when the substance is exposed to the light the two effects, that in the light and in the dark, are superimposed.

Photochemical changes vary enormously in character; for it will be easily understood that the absorption of light may act in many ways. It may increase the energy of the system or it may act, as it were, catalytically, setting free a certain amount of energy. In the first case a labile and reversible system will be produced; in the second, one of greater stability which is irreversible. Photochemical reactions may therefore be divided broadly into two classes, the irreversible or catalytic light reactions, and the reversible reactions the result of which consists in the shifting of the equilibrium point, which in the dark reverts to its original position. The system, in this way, increases its internal energy in the light and loses it again in the dark. Theoretically, such a process could be utilised for doing work at the expense of the light energy absorbed, and is in fact continually taking place when coal is burnt.

There is a third class of reactions which may be termed false or apparent photochemical equilibria, and may be illustrated by the following example: Luther and Plotnikow[1] found that if a solution of hydriodic acid and phosphorous acid is exposed to the light it turns yellow, from the separation of free iodine. In the dark the colour disappears, but reappears again on exposure to light, and so forth. The explanation is that two reactions are going forward; the first, which takes place rapidly in the light and is practically stationary in the dark, is due to the oxidation of the hydriodic acid to water and free iodine; the second, which is slower and uninfluenced by light, is due to the oxidation of the phosphorous acid by the iodine and its conversion into phosphoric acid and hydriodic acid.

$$2HI + O = H_2O + I_2$$
$$H_3PO_3 + H_2O + I_2 = H_3PO_4 + 2HI$$

Consequently there is an apparent reversion of the process in the dark, but as it depends on the presence of phosphorous acid is not strictly a reversible reaction. All three classes of reactions cover the photochemistry of organic compounds, to which we propose to confine our attention.

It should be stated at the outset that light is capable of influencing every kind of chemical change, oxidation and reduction, addition and substitution, isomeric change and polymerisation, hydrolytic and electrolytic decomposition, precipitation and coagulation, &c.

[1] *Zeit. physik. Chem.*, 1908, **61**, 513.

It may be asked, in what respect, if any, does the action of light differ from that of heat or other form of energy? In the first place, photochemical changes, especially of the reversible order, are usually associated with small energy changes, for the products differ little from the original substances in their heats of formation or combustion. Moreover, photochemical changes have, as a rule, much smaller temperature coefficients than ordinary chemical reactions.[1] Whereas in ordinary chemical reactions a rise of 10° will increase the velocity 2 to 3 times or more, the same interval will, as a rule, only accelerate a photochemical change from 1 to 1·4 times. Dewar found, for example, that a photographic plate is sensitive to light at the lowest temperatures so far obtained. Then again, the course of photochemical reactions as well as the end products are different from those of ordinary chemical reactions. The equilibria of reversible photochemical reactions are also different, seeing that they only persist by absorption of light energy, whereas ordinary equilibria are produced in a closed system, and, finally, the catalysts of light reactions are distinct from those which are effective in the dark. A fundamental difference must therefore be recognized in the nature of light and dark reactions. It is now generally conceded that this difference is due to the detachment of electrons under the influence of light. The energy of the electron is much greater than that produced by heat alone; for it is clearly recognized that it is only at high temperatures that heat reactions simulate those of light, a fact which also accounts for the small temperature coefficient of light reactions.

Without entering into the dynamics of these reactions, which are treated elsewhere in this volume (Part I, p. 372), we will consider a few of the more interesting cases of photochemical change.

Addition. Among the earlier observations connected with the effect of light on organic compounds are those which have reference to the formation or decomposition of halogen derivatives. The union of chlorine and carbon monoxide to form phosgene was first observed by Edmund Davy[2] in 1812. As change of volume accompanies the combination, the course of the reaction is easily followed.

$$\underset{1\text{ vol.}}{CO} + \underset{1\text{ vol.}}{Cl_2} = \underset{1\text{ vol.}}{COCl_2}$$

Wildermann[3] investigated the process in 1903 and found that, like hydrogen and chlorine, it exhibited an induction period and was

[1] Goldberg, *Zeit. physik Chem.*, 1902, 41, 1. [2] *Phil. Trans.*, 1812, 30, 144.
[3] *Zeit. physik. Chem.* 1903. 42. 259.

highly sensitive to impurities. Moisture accelerates and oxygen retards the change. In the same year Dyson and Harden[1] independently arrived at similar conclusions. Weigert[2] took up the problem again in 1907 and found that the gases combine in the dark, but at a high temperature, and there is no shifting of the equilibrium on exposure to light, which appears to influence equally the velocity of both reactions.

This example may be taken as the first of a series of reactions in which the addition of halogens is influenced by light.

Bauer and Moser found that certain ethylene derivatives, such as stilbene and methyl stilbene, *o*-nitrocinnamic acid and cinnamic nitrile, absorb bromine more rapidly when exposed to light than in the dark. They also noticed that the heavier the radical attached to the unsaturated carbon, the less bromine is taken up.

The union of benzene and *o*-xylene with chlorine and bromine in sunlight to form the hexachloride and bromide is another example. The dynamics of the reaction with benzene has been carefully studied by Slator,[3] who found that the velocity is proportional to the square of the concentration of the chlorine.

Michael[4] examined the products of bromination of cinnamic and allocinnamic esters in the dark and light with interesting results. In the light 13 per cent. of the lower melting dibromide of the methyl ester was obtained, whereas in the dark the quantity increased to 37 per cent.

Many of the olefines, ethylene, propylene, &c., react with chlorine in the dark, but more rapidly in the light.[5] Acetylene unites slowly with chlorine, but only in the light, to form $C_2H_2Cl_2$; the absorption then proceeds more rapidly, with the formation of acetylene tetrachloride.

A very interesting observation was made by J. Wislicenus[6] in studying the geometrical inversion of angelic and tiglic acids (see p. 266). He found that unless bromination of angelic acid is conducted in darkness, it undergoes inversion into the bromide of tiglic acid, an equilibrium mixture resulting which contains angelic and tiglic dibromide in the proportion of 1 : 9. This introduces the subject of light as an agent in promoting isomeric change, which will be considered presently.

Substitution. The effect of sunlight in assisting substitution of hydrogen by halogens is a very general observation, which in a few cases has been carefully examined.

[1] *Trans. Chem. Soc.*, 1903, 83, 201.
[2] *Ann. d Physik*, 1907, 24, 55.
[3] *Zeit. physik. Chem*, 1903, 45, 553.
[4] *Ber*, 1901, 34, 3663.
[5] Römer, *Annalen*, 1886, 233, 172.
[6] *Annalen*, 1892, 272, 55.

The paraffins, the aromatic hydrocarbons, and such substances as acetic acid, ethyl ether, alcohol, &c., undergo rapid chlorination in the light.

The action of halogens on benzene and toluene has been the subject of repeated study, and, although the process has not yet been fully explained, a number of important facts have come to light, of which the following is a brief record.

In the case of benzene, as we have just seen, addition occurs in sunlight in the absence of a catalyst; on the other hand, substitution takes place in presence of a catalyst both in the light and dark. It has long been known that toluene undergoes substitution either in the side-chain or nucleus according to the conditions. Schramm[1] found that when chlorine or bromine act upon toluene side-chain substitution takes place in sunlight at 0° and at higher temperatures; in diffuse daylight and in the dark a mixture of *o*- and *p*-chloro- and bromo-toluene results, and a similar effect is produced among the higher homologues. According to Schramm[2] the most active rays are not the blue and violet, as one might expect, but the yellow and green. Side-chain substitution also takes place in the dark at the boiling-point of toluene.[3] On the other hand, the presence of catalysts (metals, metallic chlorides, iodine, &c.) induce nuclear substitution. Recent experiments of a quantitative character by Holleman[4] and Bruner[5] have shown that the relative proportion of bromine which enters the side-chain is not only increased by light, but in the dark is increased by rise of temperature and by dilution of the reacting bromine. It appears, moreover, that at the boiling-point of toluene (110°) moist chlorine in the dark produces nuclear substitution to the extent of nearly 90 per cent., whereas dry chlorine in the light increases side chain substitution, yielding on the average about 94 per cent. of benzyl chloride.[6] Various explanations have been offered of this truly remarkable phenomenon, but it must be confessed that nothing definite is known about the mechanism of the process. Nor has the complexity of the phenomenon been simplified by Bruner's[7] observation that side-chain substitution may continue after the light has been withdrawn. The action in this case has been traced to the presence of a catalyst, probably an oxidised bromine compound which can be destroyed by heat or by the addition of

[1] *Ber*, 1885, 18, 350, 606, 1272; 1886, 19, 212
[2] *Bull Acad. Scient. Cracow*, 1898, p. 61
[3] Cannizzaro, *Compt. rend*, 1855, 41, 517
[4] *Rec. trav. chim*, 1908, 27, 435
[5] *Bull. Acad. Scient Cracow*, 1907, p. 693
[6] Cohen, Dawson, Blockey, Woodmansey, *Trans. Chem. Soc*, 1910, 97, 1623.
[7] *Bull. Acad. Scient Cracow*, 1910, pp. 516, 560.

iodine. In view of this fact it is easily understood that side-chain substitution should be promoted by the presence of ozonised oxygen in the dark, which may serve as halogen carrier; but it appears to contradict the observations of Luther and Goldberg,[1] who state that ordinary photochemical substitution is greatly retarded by the presence of oxygen.

Light can not only cause substitution, but may have the reverse effect, and assist in separating the halogen from halogen compounds. The discoloration which is so commonly seen when alkyl bromides and iodides are exposed to light is due to the separation of bromine and iodine. Kastle and Beatty[2] have investigated the dihalogen derivatives of benzenesulphonamide and found that not only do they lose halogen when exposed to light, but the chlorine, set free from the dichloro compound, can displace bromine and iodine from the other substituted products, such as iodoform, *p*-iodobenzoic acid, *p*-dibromobenzene, &c. This replacement, except in the case of easily decomposable substances like iodoform, takes place only in the light and is little influenced by temperature. Chloroform and iodoform occupy a special position, since the action of light is largely determined by the presence of oxygen, which brings about simultaneous separation of halogen and oxidation of the residue. Chloroform yields carbonyl chloride, hydrogen chloride, and some free chlorine, whilst iodoform behaves similarly, losing iodine and undergoing oxidation.[3]

Oxidation. The destruction or bleaching of colouring matters in presence of air and light is a common example of photochemical oxidation. That it is a direct or indirect effect of the action of atmospheric oxidation is proved by the fact that certain basic dyestuffs, which have been transformed into their colourless leucobases by reduction, exhibit their original colours on exposure to light and air. The velocity of the change may be increased by the presence of moisture and the addition of certain metallic salts, and the process is sufficiently rapid to be applied to colour photography. By making a suitable mixture of leucobases and exposing them to the light a coloured photograph is produced.[4]

But the dyestuff on further exposure loses its colour and then undergoes more fundamental chemical changes. It is a curious fact that the dye itself may act as catalyst, as Gros[5] has shown, and assist the oxidation.

[1] *Zeit. physik Chem.*, 1906, 56, 43. [2] *Amer. Chem. Journ*, 1897, 19, 139.
[3] Hardy and Willcock, *Zeit physik Chem*, 1903, 57, 317.
[4] König, *Zeit. anorg Chem.*, 1904, 17, 1623. [5] *Zeit. physik. Chem*, 1901, 37, 157.

Another interesting case of photochemical oxidation is that of quinine. It has long been known that it not only fluoresces when exposed to ultra-violet rays, but undergoes conversion into quinidine. A solution of quinine sulphate exposed to light also reduces chromic acid, and, as both solutions absorb light, the question arises as to which is the active agent. Recent experiments seem to point to quinine rather than to chromic acid, as was first supposed.[1]

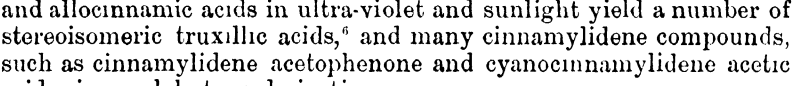
An example of an apparently simple oxidation process is furnished by oxalic acid, which from its regular action has been utilised as an actinometer. On exposure of the aqueous solution to air and light it breaks up into carbon dioxide and water. The process is not quite as simple as it might appear, for Richardson[2] noticed the formation of hydrogen peroxide, which, in presence of excess of oxygen, is derived from the oxalic acid and in turn becomes the active oxidising agent.

$$C_2H_2O_4 + O_2 = 2CO_2 + H_2O_2.$$

The change is produced by light of short wave length and is accelerated by metallic salts, whereas red light is without action. Oxidation has been observed in the case of hydroxy-acids[3] and alcohols.[4]

Many other organic compounds, formaldehyde, acetaldehyde, benzaldehyde, amyl alcohol, ether, turpentine oil, &c., undergo oxidation in the light, especially in violet light, more slowly in yellow and green, and most slowly in the dark. These reactions are frequently associated with the formation of hydrogen peroxide.

Polymerisation. A very common effect of light is to produce polymerisation of the organic compound, and many examples might be quoted. Ethylene and cyanogen undergo polymerisation in ultra-violet light, as Berthelot and Gaudechon have shown.[5] In ordinary light acetylene yields benzene, bromacetylene gives tribromobenzene, stilbene $C_{14}H_{12}$ forms parastilbene $C_{28}H_{24}$, cinnamic and allocinnamic acids in ultra-violet and sunlight yield a number of stereoisomeric truxillic acids,[6] and many cinnamylidene compounds, such as cinnamylidene acetophenone and cyanocinnamylidene acetic acid, give cyclobutane derivatives.

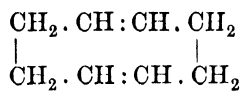


Truxillic acid. Dicinnamylidene acetophenone.

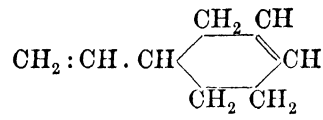
The subject has been studied by Reimer,[7] Stobbe and Rucker,[8] Macleod,[9] Riiber,[10] and Dziewonski and Paschalski.[11]

[1] Goldberg, *Zeit. physik. Chem.*, 1902, **41**, 9. [2] *Zeit. physik. Chem.*, 1894, **15**, 505.
[3] Boeseken and Cohen, *Chem. Centralbl.*, 1915, 1, 1375.
[4] Ciamician and Silber, *Ber.*, 1913, **46**, 1558. [5] *Compt. rend*, 1910, **150**, 1168.
[6] Stobbe, *Ber.*, 1919, **52**, 666; Stoermer and Foerster, *Ber.*, 1919, **52**, 1255; 1920, **53**, 497, 1921, **54**, 77.
[7] *Amer. Chem Journ.*, 1911, **45**, 417. [8] *Ber*, 1911, **44**, 869
[9] *Amer. Chem. Journ*, 1910, **44**, 331. [10] *Ber.*, 1902, **35**, 2908, 1913, **46**, 335.
[11] *Ber.*, 1913, **46**, 1986; 1914, **47**, 2680.

Harries has examined other unsaturated compounds. such as divinyl $CH_2:CH.CH:CH_2$ and isoprene $CH_2:C(CH_3).CH:CH_2$, and finds that under the action of light at low temperatures they polymerise, forming eight-carbon ring complexes, but at high temperatures derivatives of cyclohexene are produced. Divinyl, under these conditions, may give either of the following compounds:



Cyclo-octadiene.



Vinylcyclohexene.

The most interesting example of polymerisation produced by light is that of anthracene, which in certain solvents, especially in boiling anisole, phenetole, and xylene, is very sensitive to light and is partially converted into the insoluble dimeric form of dianthracene. The latter is insoluble, and its presence is readily seen by the liquid becoming cloudy. The change has been carefully examined by Luther and Weigert,[1] who found that the reaction is reversible and in the course of six to eight hours remains stationary. When the light is shut off the solution becomes clear and the dianthracene passes completely into the unimolecular form. One of the main results of this interesting investigation is the proof that the velocity of the change is directly proportional to the absorbed energy, whereas most reversible chemical changes follow the mass law.

Isomeric Change. The earliest observations on the action of light in inducing isomeric change are those of Wislicenus,[2] who noticed the conversion of maleic acid into fumaric acid in presence of bromine or iodine, and of Fittig,[3] who found that when citraconic acid is dissolved in ether and chloroform and a few drops of bromine added, exposure to sunlight will cause a rapid precipitation of crystals of mesaconic acid. Many similar changes have since been observed, and the following may be briefly enumerated. Sudborough and Thompson[4] found that both α- and β-bromallocinnamic acids and their barium salts are partially transformed into the trans modification under the influence of sunlight. Liebermann discovered the transformation of allocinnamylidene acetic acid into the isomeric form. Ciamician and Silber and Riiber and Schetely[5] showed that maleic passes into fumaric acid without a catalyst. Stoermer[6] found that

[1] *Zeit. physik. Chem.*, 1905, 51, 297, 327; 1906, 53, 385; *Ber.*, 1909, 42, 850.
[2] *Ber.*, 1896, 29, 1080; see also L. Brunel, *Bull Acad. Scient. Cracow.*
[3] *Annalen*, 1877, 188, 73. [4] *Trans. Chem. Soc.*, 1903, 83, 685, 1166.
[5] *Zeit. physik. Chem.*, 1904, 48, 345. [6] *Annalen*, 1905, 342, 1.

the short ultra-violet rays of the mercury vapour (uviol) lamp brought about the conversion of a series of high-melting and stable ethylene derivatives into their low-melting and labile isomers. The earlier experiments were made with diphenylethylene $(C_6H_5)_2C:CH_2$ and its derivatives:

$$\begin{array}{l} C_6H_5 . C . R \\ \quad\quad \| \\ X . C . H \end{array} \longrightarrow \begin{array}{l} C_6H_5 . C . R \\ \quad\quad \| \\ H . C . X \end{array}$$

in which R = *o*- and *p*- $C_6H_4OCH_3$, C_6H_4OH, C_6H_4Br, $C_{10}H_7$; X = Cl, Br.

Similar results were afterwards obtained with other geometrical isomers, the change being as a rule from the stable to the labile compound.[1] For example, the high-melting methylcoumaric acid, its amide, acetylcoumaric acid, and nitrocoumaric ester give the low-melting isomer. Cinnamic acid, *p*-methoxycinnamic acid and its amide, *β*-phenyl-*β*-anisylacrylic acid, its ester and amide were all transformed into the corresponding allo compounds. The reactions are mainly reversible, and the reverse process may be induced in some cases by exposure to ordinary light, in others by the addition of bromine. They thus furnish interesting examples of photochemical increase of energy with the production of a labile system. The transformation appears so general that Stoermer has suggested its use in discovering whether isomers are stereochemically related.

A different type of stereoisomeric change has been recorded by Ciamician and Silber. They found that solutions of the three isomeric anti-nitrobenzaldoximes in benzene are converted, when exposed to light, into the more stable syn compounds. Ciusa[2] observed the opposite change with tribromodiazobenzene cyanide, in which the syn was transformed into the anti compound in the light and a reversal of the process took place in the dark. This does not necessarily contradict the previous observations, seeing that the stability of the diazo cyanides, as Hantzsch has shown (see p. 315), is greatly modified by the introduction of halogens into the nucleus.

Lowry and Courtman[3] have observed isomeric change under the action of ultra-violet light of aminomethylene camphor and benzoyl camphor.

We will conclude with the following examples of ordinary photo-isomeric change: *o*-nitrobenzaldehyde dissolved in indifferent solvents passes into *o*-nitrosobenzoic acid,[4]

$$NO_2 . C_6H_4 . CHO \longrightarrow NO . C_6H_4 . COOH,$$

[1] *Ber.*, 1909, 42, 4865; 1911, 44, 637. [2] *Atti R. Accad Lincei*, 1907, 15, ii, 126. [3] *Trans. Chem. Soc*, 1913, 103, 1214. [4] Ciamician and Silber, *Atti R Accad. Lincei*, 1901, 10, i, 228; 1902, 11, i, 281; *Ber.*, 1901, 34, 2041; 1902, 35, 1992; Bamberger and Elger, *Annalen*, 1910, 371, 319.

and *o*-nitrobenzylidene aniline into *o*-nitrosobenzanilide,[1]

$$NO_2 . C_6H_4CH : NC_6H_5 \longrightarrow NO . C_6H_4CO . NHC_6H_5$$

Generally a nitro group in the ortho position to a CH group loses an atom of oxygen, which then attaches itself to the side-chain.

Diazo-compounds. That diazo-compounds are sensitive to light is well known to those who have attempted to prepare diazonium salts in bright sunlight. The phenomenon has received certain technical applications.

Feer found that diazo-sulphonates mixed with sodium phenate or an aromatic amino-compound yield the azo colour on exposure to light, and has utilised the reaction for photographic copying (Feer's diazotype process) Green, Cross, and Bevan[2] found that the diazo-compound from primulin is decomposed in the light and no longer produces azo dyes with phenols. Patterns or photographs may thus be produced by shading a portion of the material, or exposing it through a photographic negative.

Diazocarbazol, diazonaphthalene,[3] and many other diazo-compounds[4] are sensitive to light and undergo decomposition in the same way.

Phototropism. This term has been applied to reversible isomeric changes in solid substances produced by light and accompanied by change of colour. One of the earliest examples of this special kind of photochemical transformation is the change of benzaldehyde phenylhydrazone from yellow to red. Chattaway[5] explained the process by isomeric change from the hydrazone to the azo-compound.

$$C_6H_5NH . N : CH \ C_6H_5 \longrightarrow C_6H_5N : N . CH_2 \ C_6H_5$$

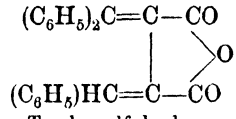
The β-naphthylhydrazones are also phototropic, but none of the α series. Many other examples of the same thing have been observed by Padoa and Graziani,[6] who contributed the additional observation that the rate of conversion is greatly increased by the addition of an isomorphous substance which is not itself phototropic. For example, anisaldehyde phenylhydrazone with one per cent. of anisylidene

[1] Sachs and Kempf, *Ber.*, 1902, **35**, 2704; 1904, **37**, 3425.
[2] *Chem. News*, 1890, **62**, 680 [3] Ruff, Stein, *Ber.*, 1901, **34**, 1668.
[4] *Proc. Chem. Soc.*, 1905, **21**, 168, 296.
[5] *Trans. Chem. Soc*, 1906, **89**, 462; see also Baly and Tuck, *Trans. Chem. Soc.*, 1906, **89**, 982.
[6] *Atti R. Accad. Lincei*, 1909, **18**, ii, 269, 676; 1910, **19**, ii, 190, 193, 302; 1913, **22**, i, 623; see also Torrey and Brewster, *J. Amer. Chem. Soc*, 1913, **35**, 426.

benzylamine is more rapidly and intensely coloured than the pure substance.

Senier and Shepheard[1] found that salicylidene *m*-toluidine $HO.C_6H_4CH:NC_6H_4CH_3$ and several similar compounds change from yellow to orange on exposure to light, the violet rays being most active. A reversal takes place in the dark, but replacement of hydroxyl by methoxyl destroys the phototropic effect entirely. α-Naphthylamino camphor is also phototropic.[2]

One of the most interesting examples of phototropism is furnished by the fulgides of Stobbe.[3] Triphenylfulgide is orange-red, but, on



Triphenylfulgide.

exposure to light, changes to brown; placed in the dark it resumes its original colour. The change only appears in the substance when in the solid state and is apparently reversible. Frequent repetition, however, produces less and less effect, until ultimately a new light yellow product is formed; in other words, the first reaction is accompanied by a second non-reversible change. The effect is also dependent on the nature of the light, for blue rays promote the transformation, whereas orange and red light produce the reverse effect. Stobbe has followed the changes by means of the spectrograph by exposing the substances, smeared over glass surfaces, to different parts of the spectrum. He concludes that there are two substances, an orange compound *A* which is sensitive to blue and violet light, and a brown compound *B* which is affected by yellow and red, and they are interconvertible. *A* is only stable in the dark, *B* in blue and violet light, and all other shades observed are mixtures of these two. The change from *A* to *B*, which is characteristic of many phototropic reactions, may be represented graphically in the following way:

$$A \underset{\text{long waves}}{\overset{\text{short waves}}{\rightleftharpoons}} B$$

The result confirms in an interesting manner the law of Grotthus (p. 148) that only those rays are active which are absorbed. This view of Stobbe accords also well with that of Luther[4] on the action

[1] *Trans. Chem. Soc.*, 1909, 95, 441, 1943; 1914, 105, 2162; 1915, 107, 452.
[2] Singh, *J. Amer. Chem. Soc.*, 1921, 43, 333
[3] *Annalen*, 1908, 359, 1; *Ber.*, 1913, 46, 1226.
[4] *Zeit. physik. Chem.*, 1899, 30, 628; see also Schlenk and Herzenstein, *Ber.*, 1910, 43, 3545, and Weigert and Kruger, *Zeit. physik. Chem.*, 1913, 85, 679.

of light on silver chloride and anthracene, both of which represent equilibria depending on wave length and light intensity.

$$2AgCl \underset{\text{dark}}{\overset{\text{light}}{\rightleftharpoons}} Ag_2Cl + Cl, \quad \text{Anthracene} \underset{\text{dark}}{\overset{\text{light}}{\rightleftharpoons}} \text{Dianthracene}$$

Similar phototropic changes have been recorded by Marckwald in the case of the yellow hydrochloride of quinoquinoline, which changes to green in light and reverts to the original colour in the dark, in that of tetrachloroketonaphthalene, which is colourless in the dark and reddish violet in the light, of benzilosazone, which changes from yellow to red, of benzaldehydephenylhydrazone, which passes from pale yellow to yellowish green, &c.

Light increases the energy of the system, which in the dark it loses again. Plotnikow compares it to a fountain, the waste water from which, if continually pumped back again, will represent the light energy absorbed. It affords a parallel with phosphorescence, which may be expressed in a similar way, light being absorbed and phosphorescence emitted.

$$A + \text{light} \longrightarrow B \qquad B \longrightarrow A + \text{phosphorescence.}$$

Photochemical Decomposition and Synthesis. Our knowledge of photochemical decompositions and syntheses is mainly due to the researches of Ciamician and Silber,[1] who have examined with remarkable results the behaviour of a variety of single organic compounds, as well as mixtures of them, on exposure in closed vessels to the influence of light. The reactions are, as a rule, highly complex, and a number of different substances are formed which are rarely produced by ordinary chemical methods.

We shall limit ourselves to naming the principal products obtained in some of these reactions, but before describing them two gas reactions of great interest must be referred to; the first is the conversion of carbon monoxide and oxygen under the influence of ultra-violet rays into carbon dioxide and ozone,[2] and the second that of carbon monoxide and hydrogen, which yield under similar conditions formaldehyde.[3] The latter reaction especially has a direct bearing on vegetable assimilation.

Aqueous acetone is stable under ordinary conditions, but breaks upon exposure to light into methane and acetic acid.

[1] G. Ciamician, *Soc. Chim de France*, June 6, 1908; see also Ciamician and Silber, *Atti R. Accad Lincei*, 1908, 17, i, 579, 1911, 20, ii, 673; 1912, 21, i, 547, 619, 1913, 22, i, 127, 540, ii, 339, 469; 1915, 24, i, 90; and Sernagiotto, *Gazz. chim*, 1917, 47, i, 153, 1918, 48, i, 52

[2] Chapman, Chadwick, and Ramsbottom, *Trans.*, 1907, 91, 942.

[3] Berthelot and Gaudechon, *Compt. rend*, 1910, 150, 1690.

This is a very general type of reaction where oxygen is excluded, the one molecule becoming oxidised or reduced at the expense of the other.

Aldehydes and ketones in alcohol are usually reduced and the alcohol oxidised. Thus, polyhydric alcohols yield corresponding sugars, glycerol gives dihydroxyacetone, erythritol forms erythrose, mannitol, mannose, and dulcitol, galactose.

Benzaldehyde forms hydrobenzoin, and benzoin also yields hydrobenzoin. Quinone forms quinol,[1] benzo- and aceto-phenone form pinacones. Pinacoline breaks up into acetaldehyde and butylene,

$$(CH_3)_3CO \cdot CH_3 = CH_3CHO + CH_3 \cdot CH_2 \cdot CH : CH_2$$

in which case the decomposition takes place in two directions.

A similar result was obtained with cyclic ketones, such as cyclohexanone and menthone. In the former case hexoic acid and an unsaturated aldehyde $CH_2 : CH \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CHO$ were obtained, and in the latter decylic acid and a hexene aldehyde, identical with either citronellal or rhodinal (Part III, p. 274).

Many organic compounds undergo condensation. Acetone and methyl alcohol unite and form isobutylene glycol, but with methyl ethyl ketone under similar conditions the product is

$$CH_3 \cdot CO \cdot CH(CH_3) \cdot CH(CH_3) \cdot CO \cdot CH_3$$

that is, a simple condensation of two molecules of the ketone.[2] Another example of the action of light on a ketone is that of carvone, which in aqueous alcoholic solution yields carvone camphor.[3]

$$CH_3 \cdot CO \cdot CH_3 + CH_3OH = \begin{matrix} CH_2 \\ \diagdown \\ \quad C(OH) \cdot CH_2OH \\ \diagup \\ CH_3 \end{matrix}$$

Quinone and benzaldehyde give *p*-dihydroxybenzophenone ; phenanthraquinone and aldehyde give acetylphenanthraquinone.

$$\begin{matrix} C_6H_4 \cdot CO \cdot COCH_3 \\ | \quad\quad\quad \| \\ C_6H_4 \cdot C(OH) \end{matrix}$$

Acetylphenanthraquinone.

The latter reaction represents a general type [4] and may be formulated thus :

$$\begin{matrix} CO \cdot CO \\ | \quad | \end{matrix} + CHOR' = \begin{matrix} C - C \\ | \quad | \\ OH \; OCOR' \end{matrix}$$

The action of benzaldehyde on nitrobenzene takes place in the first instance by the oxidation of the aldehyde and reduction of the nitrobenzene ; but other reactions occur simultaneously, and the

[1] Klinger, *Annalen*, 1888, 249, 137.
[2] Ciamician and Silber, *Abstr.*, 1912, i, 537.
[3] Ciamician and Silber, *Abstr.*, 1908, i, 555 ; Sernagiotto, *Abstr.*, 1915, i, 425, 1918, i, 414
[4] *Ber*, 1911, 44, 1280, 1351.

result is a mixture of a variety of products among which mono- and di-benzoylphenylhydroxylamine, mono- and di-benzoyl-*p*-aminophenol, azoxybenzene, and hydroxyazobenzene have been isolated.[1] This furnishes a good example of the complexity of some of these reactions.

Among other reactions effected by the action of light is the formation of esters by the action of alcohol or acids in presence of ultra-violet light[2] and the formation of anilinobutyric acid by the combined action of crotonic acid, aniline, and ammonia.[3]

Mention should also be made of the action of hydrocyanic acid on aldehydes and ketones, which is interesting from the point of view of plant assimilation. Acetone and hydrocyanic acid give ammonium oxalate and acetonyl urea, α-aminoisobutyric acid and probably α-hydroxyisobutyramide; acetaldehyde has little action, and benzaldehyde has none. The presence of metallic salts (iron and uranium) often accelerate these processes, and many interesting cases of the kind have been recorded.[4]

Assimilation of Carbon Dioxide by Plants. The photochemical change produced during the assimilation of carbon dioxide is not only one of fundamental importance for vegetable life, but indirectly also for animal existence, for it is during this process that the principal animal foodstuffs, the carbohydrates, are manufactured. In 1771 Joseph Priestley[5] discovered the action of growing vegetation on impure air (that is, air which had been vitiated by breathing or combustion) in restoring it to its original purity. He writes, 'I have been so happy as by accident to have hit upon a method of restoring air which has been injured by the burning of candles and to have discovered at least one of the restoratives which Nature employs for this purpose. It is vegetation.' Later, when 'dephlogisticated air' or oxygen was discovered, Priestley was able to identify it with the gas evolved from the surface of the growing plant. But his experiments in this direction were not always successful, and frequently the air was worse instead of better. It was only after Ingenhousz[6] had investigated the subject in 1779 that the essential part played by sunlight was clearly established. 'I was not long engaged in this enquiry', says Ingenhousz, 'before I saw a most important scene open to my view; I observed that plants not only have a faculty to correct bad air in six or ten days by growing in it, as the experiments of Dr. Priestley indicate, but that they perform this important office in a compleat manner in a few hours, that this wonderful operation is by no means owing to the vegetation of the plant; but to the influence of the sun upon the plant.'

[1] *Ber.*, 1905, **38**, 1176, 1671.
[2] Stoermer and Ladewig, *Ber.*, 1914, **47**, 1803.
[3] Stoermer and Robert, *Ber.*, 1922, **55**, 1030.
[4] Neuberg, *Biochem. Zeit.*, 1908, **27**, 271; 1910, **29**, 279; Benrath, *J. prakt. Chem.*, 1907, **73**, 383, *Zeit. physik. Chem.*, 1910, **74**, 115; Pfaltonius and Korn., *Ber.*, 1910, **43**, 2744.
[5] *Experiments and Observations*, by J. Priestley, vol. i, p. 86.
[6] *Experiments on Vegetables*, by J. Ingenhousz, London, 1779.

This was followed by the observation of the concurrent formation of starch by de Saussure, and of the necessary presence of chlorophyll by Engelmann.

It is only in comparatively recent times that the numerous problems suggested by the above experiments have been systematically pursued. Among the most important of these problems is the one having reference to the nature of the chemical changes whereby the carbon dioxide is converted into starch, for this process represents a reaction, or more probably a series of reactions, which chemists have so far failed to reproduce artificially. Other questions which present themselves are the proportion of carbon dioxide absorbed to the oxygen evolved; the relation of the rate of absorption of carbon dioxide to the quantity present in the air and to the temperature; the kind of light which is photochemically most active and its relation to that absorbed by the chlorophyll; the proportion of the solar energy utilised; the chemical nature of chlorophyll, and the changes, if any, which the latter undergoes during assimilation, and so forth. Many of these questions have been answered more or less completely. Draper examined the effect on assimilation of the different parts of the visible spectrum and found the maximum activity to lie in the yellow-green region. Timiriazew found in 1869 that the amount of carbon dioxide decomposed was directly related to the absorption, and was greatest in the orange, where the absorption was greatest. By the aid of a more delicate method, depending on the growth of certain bacteria in the oxygen evolved during assimilation, Engelmann was not only able to locate accurately the position of the actinic rays, but succeeded in proving, as Timiriazew had previously done, that the maximum activity runs parallel with the kind of light absorbed by the chlorophyll, and that a maximum is reached in the red region between the Fraunhofer lines *B* and *C*, a second maximum in the blue at *F*, and a minimum in the green at *E*. In thicker layers, when the absorption is nearly complete the maximum is shifted, as Draper found, towards the yellow-green region. Many observers have estimated the rate of carbon dioxide absorption under different conditions and found it to increase with the partial pressure of the carbon dioxide, as well as with the temperature, until a maximum is reached. In this connection the observations of H. T. Brown[1] are of special interest. He was able to show that, with increase in the partial pressure of the carbon dioxide in the surrounding air, the rate of assimilation increased from the normal amount up to five or six times the quantity.

[1] *Proc. Roy. Soc.*, 1905, 76 B, 29.

The variation in the rate of assimilation with the temperature has been examined by various experimenters. Miss Matthaei[1] found that, corresponding to each temperature, there is a certain definite amount of assimilation, which is termed *maximum assimilation* for that temperature, provided light and carbon dioxide are supplied in sufficient quantity. This maximum increases rapidly with rise of temperature, but at high temperatures an individual leaf can only maintain its maximum for a short time: the higher the temperature the sooner the decline in the rate of assimilation. The results were obtained by estimating the assimilation from the amount of carbon dioxide absorbed in unit time by unit leaf surface. Similar results are recorded by Kanitz.[2] He gives the following figures for the assimilation at different temperatures, results which concord well with van 't Hoff's rule, that a reaction velocity is doubled with a rise of 10° in temperature.

Temp.	*mg* CO_2 *absorbed.*	*Coefficient of temp. per* 10°.
0°	1·75	—
10°	4·2	2·4
20°	8·9	2·12
30°	15·7	1·76
37°	23·8	1·81

The amount of light energy utilised by the leaf has been measured by Pfeffer by estimating the amount of starch produced in 1 sq. cm. of leaf surface per second of exposure and comparing the heat of combustion of the starch with the calorific effect of radiation on the same surface. According to his results only 0·6 per cent. of the total energy was absorbed, but, as the method is affected by certain serious errors, no great reliance can be placed upon the result. A very different result was obtained by H. T. Brown,[3] who, in place of measuring the total solar energy falling on the leaf, estimated only that which was absorbed by the chlorophyll and was consequently photochemically and otherwise active. The amount of solar radiation taken up by the leaf was determined by means of a Callendar radiometer before and after transmission through the leaf. The energy thus absorbed was found to vary in different leaves between 64 and 77 per cent. Omitting the temperature changes in the leaf, which are negligible, he found that the absorbed energy Ra is divided between the amount used in vaporisation of water W, that in photosynthesis w, and a quantity r due to radiation from the leaf surface, which may be positive or negative according to the thermal conditions

[1] *Phil. Trans.*, 1905, 197 B, 85. [2] *Zeit. f. Elektrochemie*, 1905, 11, 689.
[3] *Phil. Trans*, 1900, 193 B, 223; *Proc. Roy. Soc.*, 1905, 76 B, 29.

existing between the leaf and its environment. When thermal equilibrium is established the balance between solar radiation received and expended is given by the equation

$$Ra = (W + w) \pm r$$

Three of these factors, *Ra*, *W*, and *w* per unit area of leaf surface in unit time, can be ascertained. *Ra* was found in the manner described above; *W* was determined from the weight of water lost by the leaf multiplied by the latent heat of water-vapour; *w* was estimated from the amount of carbon dioxide absorbed calculated as hexose and having a heat of combustion of 3760 cals.

The following is the record of an experiment:

Ra	solar energy absorbed		0·1762 cals.
W	0 000209 grm water × 592 6 cals.	0 1243	
w	0 000355 c c CO_2 × 5 02 cals.	0 0017	0 1260 ,,
r	by difference		0 0502 ,,
			0 1762 ,,

In this case $\frac{1260}{1762} \times 100 = 70$ per cent. of the absorbed solar energy was utilised by the leaf.

The actual rate of photosynthesis remains constant for wide limits of insolation, due to the fact that the special rays which produce photosynthesis are present in solar radiation of even moderate intensity far in excess of the demands of assimilatory centres for dealing with carbon dioxide which reaches them by diffusion. The proof of this is afforded, in the first place, by the enhanced assimilatory effect which is produced by increasing the partial pressure of the carbon dioxide in the air round the leaf, and secondly, by the fact that the intensity of ordinary summer daylight can be reduced to a very considerable extent by using revolving radial sectors placed in front of the leaf without affecting the rate of photosynthesis.

But the subject of chief interest to the chemist is the various phases which the carbon dioxide undergoes in its conversion into carbohydrate.

Baeyer[1] was the first to suggest that the carbon dioxide underwent reduction and that the first product of the assimilation process was formaldehyde. Supposing formaldehyde to be produced, its conversion into carbohydrate may be readily explained on the ground of its well-known property of polymerising and yielding fructose (Part III, p. 19). But, on the other hand, formaldehyde acts as a powerful poison on vegetation, and it is clear that if produced it must be formed under conditions which would render it innocuous.

[1] *Ber.*, 1870, 3, 66.

The first definite indication that formaldehyde can yield starch on assimilation was obtained by Bokorny.[1] Using the sodium bisulphite compound of formaldehyde which is non-poisonous, he found that, on immersing the green filaments of *Spirogyra* in a weak solution (0·1 to 1 per cent.) of the bisulphite compound, starch is produced. Later Bouilhac and Tréboux[2] found that in very dilute solutions of formaldehyde, plants would remain alive and form starch.

The observations of Berthelot and Gaudechon[3] that carbon dioxide in presence of hydrogen, or water in presence of carbon monoxide, when exposed to ultra-violet light, yield formaldehyde; of Loeb[4] on the decomposition of carbon dioxide in presence of water by the silent electric discharge, are interesting, but have at present no very direct bearing on the photosynthetic process. The same may be said of Fenton's reduction of carbon dioxide to formaldehyde by amalgamated magnesium,[5] and of Usher and Priestley's[6] observation on the formation of formaldehyde by the action of rays from radium emanation and the quartz-mercury lamp on a solution of carbon dioxide in water, and of a similar observation of Stocklasa on the production of formaldehyde by radium acting on a mixture of hydrogen and carbon dioxide.[7]

A more interesting statement is that made by Bach,[8] that, by passing carbon dioxide through a 1·5 per cent. solution of uranium acetate in sunlight, formaldehyde and uranium peroxide are formed. Here the uranium salt, having an absorption spectrum similar to that of chlorophyll, may act as sensitizer in the manner of chlorophyll and bring about the decomposition of the water, the hydrogen reducing the carbon dioxide to formaldehyde and the oxygen causing the oxidation of the uranium salt, possibly through the intermediate formation of hydrogen peroxide. Although doubt has since been thrown on the correctness of this observation,[9] it led Usher and Priestley[10] to take a similar view of the action of the chlorophyll in producing, in presence of light, double decomposition between the carbon dioxide and the water, yielding formaldehyde and hydrogen peroxide.

$$CO_2 + 2H_2O = CH_2O + H_2O_2 + O.$$

More recently Moore[11] has obtained formaldehyde by passing

[1] *Ber*, 1891, **24**, 103.
[2] *Flora*, 1903, p 73.
[3] *Compt. rend.*, 1910, **150**, 1890.
[4] *Zeit. f Elektrochemie*, 1905, **11**, 749.
[5] *Trans. Chem Soc.*, 1907, **91**, 687.
[6] *Proc. Roy Soc.*, 1911, **84 B**, 101.
[7] *Compt rend.*, 1913, **156**, 646.
[8] *Compt rend*, 1893, **116**, 1145.
[9] Euler, *Ber.*, 1904, **37**, 3415.
[10] *Proc Roy Soc*, 1906, **77 B**, 369; **78 B**, 318.
[11] *Proc. Roy Soc.*, 1913, **87 B**, 163; 1918, **90 B**, 168; 1920, **91 B**, 201; *Trans. Chem. Soc.*. 1921. **119**. 1555.

carbon dioxide into colloidal solutions of uranium and ferric oxides and other substances in presence of bright sunlight or the 'uviol' lamp. He also found that formaldehyde in concentrated solution exposed to the uviol lamp gave a reducing product, possibly sugar. Baly[1] has since shown that under the stimulus of light of short wave length (200 $\mu\mu$) carbon dioxide dissolved in water can be readily converted into formaldehyde without chlorophyll. Ordinary light can produce the same result in the presence of a photocatalyst such as methyl orange or malachite green. The formaldehyde, according to Baly, Heilbron, and Hudson,[2] activated by light of short wave length (290 $\mu\mu$) reacts in the form of H—C—OH and can then undergo polymerisation, yielding reducing sugars or, in presence of a nitrite, formhydroxamic acid

$$H.C.OH + O:N.OK = H.C(:NOH)OK + O$$

which condenses with other molecules of formaldehyde to produce organic bases (methylamine, pyridine, and piperidine).[3] Formaldehyde has now been detected in the growing plant by Schryver,[4] Curtius and Franzen,[5] and others, and although its presence may not necessarily indicate that it is formed by the reduction of carbon dioxide, it is at least an interesting and suggestive observation.

Other problems of interest connected with the subject of carbon dioxide assimilation are the nature of formaldehyde condensation and the chemical structure of chlorophyll. The stages in the process which ultimately lead to the appearance of starch in the leaf take place with enormous rapidity, and it has been estimated that starch grains may be detected within two minutes of the exposure of the leaf to sunlight.

According to Brown and Morris[6] the first product of assimilation is cane-sugar, which then breaks up into glucose and fructose, the former undergoing synthesis to maltose and starch, which is stored up in the leaf or transferred as glucose to other parts of the plant. Other observers have adopted the view that glucose or maltose are first formed. Whichever carbohydrate first makes its appearance, it would seem that the condensation of formaldehyde takes place in contact with some active material, probably chlorophyll, in order that an asymmetric synthesis may be accomplished, seeing that the

[1] *Trans Chem Soc.*, 1921, 119, 1025.
[2] *Trans. Chem. Soc.*, 1922, 121, 1078.
[3] *Trans. Chem. Soc*, 1923, 123, 185
[4] *Proc. Roy. Soc.*, 1910, 82 B, 226; 1918, 90 B, 168.
[5] *Ber.*, 1912, 45, 1715.
[6] *Trans. Chem. Soc.*, 1893, 63, 604.

sugars and starch are optically active; but of the actual mechanism of the process we are at present profoundly ignorant. The subject has been submitted to a prolonged and careful investigation by Willstätter and Stoll, and their results have been collected and published in book form.[1] It would be impossible to do justice to this important monograph in a few sentences; but it may be stated that according to these observers assimilation of carbon dioxide and its conversion into formaldehyde takes place in the first instance by the addition of carbon dioxide and water to the atom of magnesium present in the chlorophyll molecule (see Part III, p. 189), from which it is detached in the form of oxygen and formaldehyde. The study of the structure of chlorophyll, although an extraordinarily complex problem, is one which can be conducted independently of the life process and involves merely the methods and appliances of the laboratory. The work, which is now gradually approaching finality, has been carried out with remarkable skill and patience by a number of workers among whom the names of Schunck, Marchlewski, and Willstatter stand out most prominently.

It would be beyond the scope of the present chapter to give in detail the methods by which this intricate problem has been attacked and the various cleavage products obtained and examined. The subject is discussed in Part III, p. 186. It must suffice to state that one of its final cleavage products is haemopyrrole $C_8H_{13}N$, which is almost certainly a dimethyl ethyl pyrrole. A fact of even greater interest is the existence of the same substance among the decomposition products of haemoglobin or red colouring-matter of the blood.

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Lehrbuch der Photochemie, by A. Bernath. Winter, Heidelberg, 1912.

[1] *Untersuchungen über die Assimilation der Kohlensäure*, by Willstatter and Stoll. Springer, Berlin, 1918.

CHAPTER III

ISOMERISM AND STEREOISOMERISM

Historical. It is scarcely a matter of surprise that, in the early history of the science, inorganic chemistry, the older and more highly developed branch, should have bequeathed to organic chemistry its formulas and doctrines. Every inorganic substance had, or was assumed to have, its own distinctive composition, and the principle was tacitly applied to organic compounds.

That two substances might have the same composition and yet possess different properties was first clearly recognized by Faraday. It appears that in 1820 Dalton obtained (by the distillation of certain fatty oils) a hydrocarbon which combined with chlorine like olefiant gas, and he drew the shrewd conclusion that 'most probably the atom of the new gas consists of two of olefiant gas'. This suggestion was afterwards confirmed by Faraday, who in 1825 undertook an investigation into the nature of the oil gas, which was being manufactured by the Portable Gas Company compressed into metal vessels and distributed among consumers. This compressed gas contained a considerable quantity of a liquid of low boiling-point, from which Faraday isolated a hydrocarbon which had the same composition as olefiant gas but twice its density. It was on the same memorable occasion that benzene was discovered. Of the former hydrocarbon Faraday wrote: 'In reference to the existence of bodies composed of the same elements and in the same proportion, but differing in their qualities, it may be observed that now we are taught to look for them they will probably multiply.'

He pointed out the existence of a similar example in the case of the fulminates of Liebig and the cyanates and cyanurates of Wöhler.

In 1828 Wöhler obtained urea which possessed the same composition as ammonium cyanate but different properties. The existence of substances of this character aroused a lively interest; for Berzelius, in his *Jahresbericht* for 1829, after describing the artificial preparation of urea, proceeds: 'This fact opens the door to clearer views and indicates that the number of simple atoms may be distributed in the compound in various ways, and thereby give rise

to compounds with different properties, as we have already begun to discover in other cases.'

Two years later Berzelius, in studying an acid which had been found in the mother liquors from the manufacture of tartaric acid by Kastner, a manufacturer of Thann,[1] showed that it possessed the same composition as tartaric acid, but different properties, and named it racemic acid (*Traubensäure*). It is an interesting fact that, although Berzelius at first accepted the principle of isomerism with the greatest reserve, he should himself have been the discoverer of that notable example which was in later years to give rise to the modern conception of stereoisomerism, or the different arrangement of atoms in space.

In reference to his discovery of racemic acid in the *Jahresbericht* for 1831, Berzelius writes: 'The absolute identity in composition of two compounds possessing different properties has now been positively established by the analysis of racemic acid, an acid of organic origin. This acid has the same composition, contains the same elements in the same atomic proportion, and possesses the same saturation capacity as tartaric acid.' He proceeds to explain it by a different arrangement of the atoms, and points out that Mitscherlich's discovery of isomorphism must undergo a further extension; for as isomorphous bodies consist of different atoms similarly arranged in the crystalline state, so the same atoms may be grouped in such a way as to produce different crystalline substances, which is the case with tartaric and racemic acid. In order to distinguish these substances he proposes to use the word 'isomeric', from ἰσομερής, composed of equal parts. In the following year[2] he added the terms *polymerism* (πολύς, several) to indicate compounds possessing the same proportion but a different total number of atoms, and *metamerism* (μετά, used in the sense of metamorphosis) to denote isomeric compounds so nearly related that they can undergo reciprocal conversion like cyanic and cyanuric acid.

Thus the principle of isomerism became an established fact in organic chemistry, and, as Faraday had foretold, examples soon began to multiply.

Isomerism of the Paraffins. One case of isomerism long and strenuously upheld was opposed to the new system laid down by

[1] Racemic acid had been previously examined by Gay-Lussac without definite results. Kastner never succeeded in reproducing this acid. The story of Pasteur's pilgrimage in 1852 in the search for the source of the acid is one of the veritable romances of chemistry: *Vie de Pasteur*, p. 70, by Vallery-Radot.

[2] *Jahresb.*, 1832, 12, 63.

Kekulé, and was eventually shown to rest on insecure experimental data. This was the two series of hydrocarbons known as the free alcohol radicals and their hydrides.

Reference has already been made to the experiments instituted by Frankland and Kolbe to isolate the radicals. It was there stated that by the action, first of potassium on the cyanide, and later of zinc on the iodide of the radical, the radical itself was set free. From methyl iodide, methyl (CH_3) was supposed to be liberated, and from ethyl iodide, the radical ethyl (C_2H_5). Subsequently by the action of zinc and water on ethyl iodide Frankland obtained a hydrocarbon, which he called ethyl hydride $C_2H_5 . H$. The formulae given to the hydrocarbon radicals, methyl (CH_3), ethyl (C_2H_5), &c., were contrary to the law of even numbers of Gerhardt and Laurent, who doubled them. Many other chemists, notably Hofmann, Brodie, and Kopp, took the same view, pointing out that the physical properties—vapour density, boiling-point, and molecular volume—demanded the double formula. This was subsequently conceded, and methyl appeared as $(CH_3)_2$, ethyl as $(C_2H_5)_2$. But the question was then raised as to the identity of methyl with ethyl hydride. Frankland maintained that they were isomeric, an opinion which he based on the behaviour of the two hydrocarbons towards chlorine. He alleged that by the action of two volumes of chlorine on one volume of the hydrocarbons a gas was obtained from methyl without change of volume, according to the equation

$$2CH_3 + 2Cl_2 = 2CH_2Cl + 2HCl;$$

but in the case of ethyl hydride two volumes of hydrochloric acid were formed, and at the same time a liquid was produced which probably had the formula $C_2H_4Cl_2$. These statements were afterwards contested by Schorlemmer[1] (1867), who by a careful repetition of Frankland's experiments and by his own original investigations demonstrated the incorrectness of Frankland's results. He showed conclusively that both hydrocarbons yield the same products, ethyl chloride and ethyl alcohol, and at the same time established the identity of other chlorides and alcohols, obtained from the natural paraffins, with those prepared from the synthetic hydrocarbons, which he obtained by the action of sodium on the iodides of the radicals.

Isomerism of the Lactic Acids. A special interest centres round the constitution of lactic acid which represents an early example of isomerism. It was discovered in 1780 by Scheele in

[1] *Proc. Roy. Soc.*, 1864, 13, 225 et seq.; *Trans. Chem. Soc.*, 1864, 17, 262.

sour milk. In 1807 Berzelius isolated a lactic acid from the juice of flesh, without however having a clear conception of its nature.[1] It was not until Liebig and Mitscherlich reinvestigated the subject in 1832 that the individuality of the sour milk acid was definitely established. In 1847 Liebig[2] further drew attention to the character of the salts, notably the zinc and calcium salts of the acid from the juice of flesh, which he considered to be identical with the sour milk acid, until Engelhardt,[3] in the following year, pointed out the difference between them.

The theme was by no means exhausted, for between the years 1858 and 1860 the basicity of lactic acid became the object of a lively controversy. Although Liebig had determined the formula to be $C_3H_6O_3$, Gerhardt regarded the acid as dibasic and the formula was doubled. Strecker's synthesis of alanine from aldehyde and the conversion of the former into lactic acid led to the re-adoption of the older formula. The correctness of this view was subsequently confirmed by Wurtz, who prepared the acid by the oxidation of propylene glycol.[4] Kolbe and Wurtz were, however, divided on the question of its basicity. Wurtz held it to be dibasic by reason of its connection with propyl glycol (to which it stands in the same relation as alcohol to acetic acid), a view which he expressed by the following typical formulae:

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

Alcohol. Acetic acid.

$$\left.\begin{matrix}C_3H_6\\H_2\end{matrix}\right\}O_2 \qquad \left.\begin{matrix}C_3H_4O\\H_2\end{matrix}\right\}O_2 \qquad \left.\begin{matrix}C_3H_4O\\Cl_2\end{matrix}\right\}$$

Propylene glycol. Lactic acid. Lactyl chloride.

With phosphorus chloride it yields lactyl chloride. Both reactions indicated the presence of two *typical* hydrogen atoms. Kolbe, on the other hand, regarded it as monobasic and called it oxypropionic acid, which expressed the same relation to propionic acid that glycollic bears to acetic or oxybenzoic to benzoic acid. In support of his view he pointed out that glycocoll, alanine, and amidobenzoic acid are converted in the same manner by nitrous acid into the respective oxyacids. Moreover, the glycols, he alleged, were not alcohols, but oxyhydrates, as they neither yielded nor, according to his formulae,

[1] *Treatise*, vol ix, 573; *Jahresb.*, 1823, 2, 73; *Annalen*, 1832, 1, 1.
[2] *Annalen*, 1847, 62, 326.
[3] *Annalen*, 1848, 65, 359.
[4] *Compt. rend.*, 1858, 46, 1228; *Annalen*, 1858, 107, 192.

could yield aldehydes on oxidation.[1] He wrote the formulae as follows:

$2HO\left.\begin{matrix}C_4H_5\\H\end{matrix}\right\}C_2O_2$ $HO(C_4H_5)C_2O_2,O$ $HO\left(C_4\left\{\begin{matrix}H_4\\O_2H\end{matrix}\right.\right)C_2O_2,O$

Propylene glycol. Propionic acid. Oxypropionic acid.

Lactyl chloride was explained as chloropropionyl chloride, for the two chlorine atoms possess different functions, one only being acted upon by water, forming chloropropionic acid, or by alcohol, giving chloropropionic ether.[2]

Fresh proofs were now brought forward by Wurtz in favour of the dibasic nature of the acid. Brüning had obtained dibasic tin salts of the acid, and Wurtz had prepared, by the action of sodium ethylate on chloropropionic ether, the diethyl ether of lactic acid.

The reduction of lactic acid to propionic, which had recently been accomplished by Ulrich, and the fact that Wurtz's diethyl ether only lost one alcohol radical on boiling with caustic soda, were adduced by Kolbe in support of his view.[3] So the discussion continued, new facts being advanced by both disputants.[4] Wurtz had meantime introduced the distinction between atomicity and basicity: whereas basicity is determined by the number of hydrogen atoms replaceable by a metal, the atomicity is conditioned by the valency of the radical. Although glycol contains two typical hydrogen atoms neither is basic, whilst in glycollic acid one of the two is basic and in oxalic acid, both.

But the distinction found no expression in Wurtz's typical formula, and it was left to Wislicenus[5] to show that the two views might be very simply reconciled by translating Kolbe's formula into the *typical* notation, which meant the subdivision of the type into smaller types. Wislicenus' formulae for propionic and lactic acid appeared as follows:

$\left.\begin{matrix}C''O\\C_2H_5\\H\end{matrix}\right\}O$ $\left.\begin{matrix}C''O\\C_2H_4\left\{\begin{matrix}O\\H\end{matrix}\right.\end{matrix}\right\}O$

Propionic acid. Lactic acid.

The inner water type represents alcoholic, the outer one, acid properties; or, as Wislicenus expressed it, the diatomic and negative

[1] On this one point Kolbe was, of course, in error, for he did not admit Debus' glyoxal to be the aldehyde of glycol.

[2] *Annalen*, 1859, **109**, 257.

[3] *Annalen*, 1860, **113**, 223.

[4] *Annalen*, 1861, **119**, 369.

[5] *Annalen*, 1868, **125**, 41.

radical, carbonyl, is half neutralized by the positive alcohol radical, whilst the second half retains its monobasic acid character. These relations were more clearly emphasized when Kekulé's graphic formulae came into general use, which followed shortly after the publication of his textbook.[1]

The structure of the second lactic acid from flesh, called by Heintz *paralactic* acid and by Strecker *sarcolactic* acid, was still unexplained, as well as the connection subsisting between these two and a new isomeric acid which shortly appeared on the scene.

In 1863 Wislicenus[2] effected the synthesis of lactic acid by the action of potassium cyanide on ethylene chlorhydrin, which yielded the cyanhydrin, and this, on hydrolysis, formed the new or ethylene lactic acid.[3] At first he pronounced the product to be identical with Liebig's paralactic acid; but, on reinvestigating the matter, he recognized Liebig's acid as a mixture of an optically active acid with a small quantity of his own acid.[4] There were therefore three acids. A fourth isomeric acid was stated by Beilstein to be formed by the action of silver oxide and water on β-iodopropionic acid, and named by him hydracrylic acid, from its ready decomposition into acrylic acid by heat; but its identity with ethylene lactic acid was subsequently established by Wislicenus.[5]

The existence of more than two structurally different acids at the time Wislicenus published his final paper on the subject in 1873 could not be explained by any current hypothesis, and in reviewing his results he draws attention to the necessity for extending the conception of atomic grouping. 'If it is once granted that molecules can be structurally identical and yet possess dissimilar properties it can only be explained on the ground that the difference is due to a different arrangement of their atoms in space.'[6]

Isomerism of the Tartaric Acids. Many years before the appearance of the first memoir of the German chemist a partial solution of a similar problem had been offered by the French chemist, Louis Pasteur. Pasteur did not range far into the field of chemistry, but during the few years (1848–54) that he laboured at the subject he struck so rich a vein of scientific wealth that, after the lapse of half a century, it still remains unexhausted. The fascinating story of his discovery is told in two lectures on 'Molecular Asymmetry' delivered before the Chemical Society of Paris in 1860.[7]

[1] *Lehrbuch der organischen Chemie* (1866).
[2] *Annalen*, 1863, 128, 1.
[3] *Annalen*, 1863, 128, 1.
[4] *Ber.*, 1869, 2, 550.
[5] *Ber.*, 1870, 3, 809.
[6] *Annalen*, 1873, 167, 343.
[7] *Alembic Club Reprints*, No. 14.

The investigation in question concerns the nature of the two isomeric compounds, tartaric and racemic (paratartaric) acid, to which reference has already been made.

To understand the steps which led to the remarkable results achieved by Pasteur it is necessary to revert to the year 1808 when Malus discovered the phenomenon of the polarization of light. At his death, which took place at the early age of thirty-seven, his pupils Arago and Biot continued his investigations on the subject. Biot (1815) observed the peculiar property which a section of quartz crystal exhibits, when cut parallel to the axis and viewed by polarized light, of producing rotatory polarization. He found, moreover, that there exist two kinds of crystals which rotate the beam of light in opposite directions. Some years earlier Hauy, the mineralogist, had noticed two kinds of quartz crystals possessing hemihedral facets on opposite sides of the crystal, constituting what are known as enantiomorphous forms. In 1820 Sir John Herschel suggested in a paper read before the Royal Society a possible link between the opposite kind of polarization and the reversed position of the facets.

The suggestion of Herschel recurred to Pasteur when in 1848 he discovered hemihedral facets on tartaric acid, which was known to be dextro-rotatory. He recalled at the same time a statement which Mitscherlich had communicated to the Academy of Sciences, and which had greatly puzzled him at the time of its publication, to the following effect: 'The sodium ammonium double salt of racemic and tartaric acids have the same chemical composition, the same crystal form, and the same angles, the same specific gravity, double refraction, and consequently the same angles between the optic axes. The aqueous solutions have the same refraction, but the dissolved tartrate turns the plane of polarization and the racemate is indifferent, as Biot has found for the whole series of salts, yet here the nature and number of the atoms, their arrangement and distances are the same in the two substances.'

If, thought Pasteur, the racemate should possess no hemihedral facets and Herschel's supposition is correct, it will account for its optical indifference.

He forthwith crystallized sodium ammonium racemate, but found that the crystals exhibited the hemihedral facets of the tartrate. On further examination it was observed that the facets were differently situated on the different crystals, some being disposed on the inverse side to others. The forms were enantiomorphous. They were separated, and the one proved to be the salt of ordinary or right-

handed tartaric acid, whereas the other was that of a new left-handed acid, and the presence of the two kinds in equal quantities produced inactivity in the solution.

In reviewing his results, Pasteur pointed out that the hemihedral facets in the crystal mark the property of rotatory polarization, but, whereas the property is present in crystalline quartz and absent in the amorphous variety, it is absent in solid tartaric acid, but present in the fused or dissolved state.

The asymmetry must therefore be a function of the structural arrangement of the *molecules* in quartz, and of the *atoms* in the molecules of substances which rotate the plane of polarization in the gaseous and liquid state or in solution. In the latter the molecules are asymmetric. Now where asymmetry exists in an object, such as a hand or foot, the only other object which is symmetrical with it is its reflected image, i. e. the corresponding hand or foot which cannot, however, exactly overlap. The object and image are said to be non-superposable. How is this asymmetry of the molecule, which may exist as object and image, produced? 'Are the atoms of right-handed tartaric acid,' asks Pasteur, 'arranged along the spiral of a right-handed screw, or are they situated at the corners of an irregular tetrahedron, or have they some other asymmetric grouping? We cannot answer these questions. But of this there is no doubt, the atoms possess an asymmetric arrangement having a non-superposable image. Equally certain is it that the atoms of the left-handed acid possess just the inverse asymmetric arrangement. Lastly, we know that racemic acid results from the juxtaposition of these two inversely asymmetric atomic groupings.'[1]

Thus, the paths pursued by the French and German chemists, though they lay so far apart in point of time and differed so widely in their character, converged ultimately towards the same end, the conception of atomic space arrangement.

Whilst the closing words of Wislicenus' memoir were taking root in the mind of the brilliant young Dutch chemist, van 't Hoff, Pasteur's views were being moulded into definite shape by his countryman Le Bel. Almost simultaneously van 't Hoff and Le Bel published their theories of space- or stereo-chemistry. Van 't Hoff's paper appeared in September, 1874,[2] whilst Le Bel's memoir was published in November of the same year.[3]

[1] *Alembic Club Reprints*, No. 14; Ostwald's *Klassiker*, No. 28.

[2] 'Voorstel tot Uitbreiding der Structuurformules in de Ruimte,' Brochure, 1874.

[3] *Bull. Soc. Chim.*, 1874, 22, 337.

Optical Activity and Asymmetry. The theory of van 't Hoff and Le Bel connects optical activity with molecular structure. Substances which are optically active in the fused state or in solution contain within the molecule at least one multivalent atom united to different elements or groups forming an *unsymmetrical space arrangement.* As four is the minimum number of material points demanded by any space arrangement in three dimensions, the multivalent atom which unites the elements or groups must be at least tervalent. In the majority of carbon compounds the multivalent atom is carbon; but optically active compounds are known in which the central element of the system is nitrogen, sulphur selenium, silicon, phosphorus, or tin (pp. 326, 327).[1]

Optical Isomerism. Object and Mirror Image. As Pasteur pointed out, every asymmetrical object, like a hand or foot, has its fellow, but they do not precisely overlap; they are non-superposable. A left hand will not fit a right-hand glove. In the same way a substance containing a carbon atom, round which four different groups are distributed in three-dimensional space, is capable of existing in two forms which correspond to a left and right hand, or to an object and its reflected image.

The chief point of difference between two substances, having a space arrangement or *configuration* of their atoms corresponding to object and image, lies in their action on polarized light, the one turning it to the right (right-handed or dextro-rotatory), and the other, precisely the same amount, to the left (left-handed or laevo-rotatory) when in the dissolved or liquid state. In all other physical properties—density, molecular volume, boiling-point, melting-point, solubility, conductivity, refraction, &c.—and in their chemical behaviour the two substances are identical. There are numerous observations which support this conclusion. The two complementary active forms are variously termed *active components, antipodes,* or *enantiomorphs.* The term enantiomorph, though applied originally to crystal forms (p. 174), appears on the whole the most suitable and convenient. It conveys the idea of object and image, and it can moreover be used both in the singular and in the adjectival form of *enantiomorphous.* The dextro- or laevo-rotation of a substance is indicated by the letters *d* or *l* or by the plus or minus sign. So far the theories of van 't Hoff and Le Bel substantially agree, but in points of detail they present certain differences.

[1] Werner (*Ber*, 1914, 47, 3087) has prepared an active cobaltamine compound containing no carbon, namely, dodecamine hexol tetra-cobaltibromide

$$Co[(OH)_4Co(NH_3)_4]_3Br_6.$$

Van 't Hoff's Theory. Van 't Hoff regards the carbon atom as possessing four valencies or bonds directed towards the summits of a tetrahedron, of which it occupies the centre.[1] If the groups represented by *a*, *b*, *c*, *d* attached to these four bonds (Fig. 23) are different, such a grouping is present in substances, which, like active amyl alcohol or paralactic acid, exhibit optical activity.

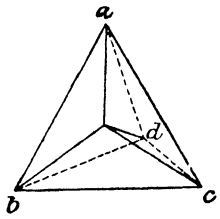
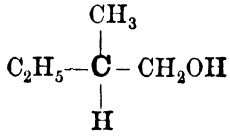
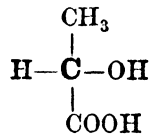


FIG. 23.

In amyl alcohol the central carbon atom is linked to the groups H, CH_3, CH_2OH, and C_2H_5; in paralactic acid to H, OH, CH_3, and COOH:



Amyl alcohol.



Paralactic acid.

Represented by space formulae (Figs. 24 and 25) the grouping is unsym-

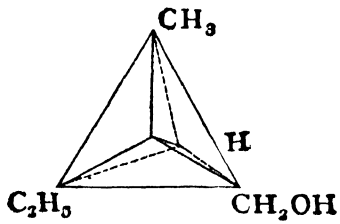


FIG. 24.

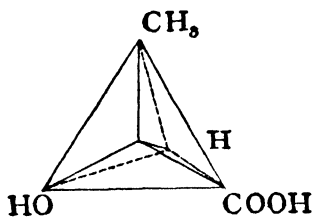
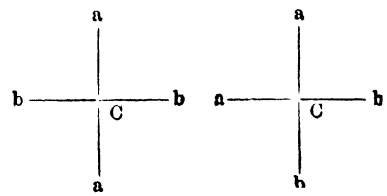


FIG. 25.

metrical, or asymmetrical in the sense that it forms a figure which cannot be divided in any direction into exactly similar halves.[2]

[1] This view has received important experimental confirmation in the structure of the diamond (W. H. Bragg, *Proc. Roy Soc.*, 1913, 89 A, 277). The atoms of carbon are there found to be grouped in the manner described by vant 't Hoff (see p. 390).

[2] Van 't Hoff points out the necessity of some such space arrangement if we desire to explain the absence of isomerism in cases where carbon is attached to two pairs of similar groups Ca_2b_2; for if the arrangement is represented in one plane the two following forms should exist, and no such case of isomerism is known. The same is true of the compound Ca_2bc, which should form two structural isomers, but is represented by only one individual.



The central carbon atom of the group is termed the *asymmetric carbon* atom.

Such an asymmetrical group has a complementary form or mirror-image possessing the reverse rotation. The two forms of lactic acid will appear as in Fig. 26. The one is the mirror-image of the other and they cannot be turned so as to coincide. This can only be effected by interchanging two of the groups in one of the figures.

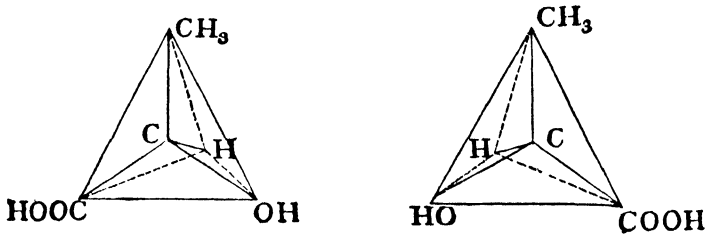


FIG. 26.

Van 't Hoff used a tetrahedron to denote the distribution of the four groups, but did not postulate any special shape of tetrahedron, which may be regular or not, and will probably depend on the relation of the groups. The molecular dimensions in no way affect the main conclusions, and may for the present be disregarded. It is not, however, essential to make the asymmetric carbon the centre of a tetrahedral figure as van 't Hoff proposed. The principle is in no way affected if the tetrahedron is replaced by a sphere on which the four groups are distributed in three-dimensional space, or if the groups are attached to four carbon linkages not lying in one plane, thus:

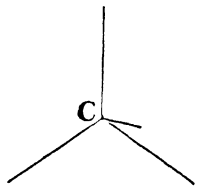


FIG. 27.

Le Bel's Theory. As already stated, in its fundamental idea Le Bel's theory agrees with that of van 't Hoff. Both recognize the existence of asymmetry produced by a space arrangement of four different groups or radicals surrounding the central carbon atom, its effect in producing rotatory polarization, and the necessary consequence of a complementary form or mirror-image having the

reverse rotation. They differ in regard to the nature of valency. Le Bel does not recognize the structural conditions laid down by Kekulé's theory of the quadrivalency of carbon or van 't Hoff's added hypothesis that the bonds are directed towards the summits of a tetrahedron. 'The asymmetry of the molecule,' says Le Bel,[1] 'can only be manifested by the asymmetric distribution of four atoms or radicals united to a single carbon atom, and this asymmetry will necessarily exist if these four radicals are different, whatever be the geometrical form of the molecule.' Thus, a pyramid on a square base with the carbon at the apex and the four groups arranged at the corners of the base would satisfy this condition. As van 't Hoff's theory is in stricter conformity with modern conceptions of structural chemistry, we shall proceed to develop his view of stereoisomerism.

Nature of the Space Arrangement. The theory, as we see, involves the conception of fixed material points. Such a conception, according to van 't Hoff, is not inconsistent with that of atomic motion, for, as the possibility of dissociation diminishes with decreasing temperature, the state of things at absolute zero is only to be explained by atomic mechanics; for intramolecular motion then ceases and the atoms must retain their positions by some force of repulsion which, he says, may possibly be electricity.[2]

The internal motion of the atoms may therefore be disregarded, and the centres about which they oscillate considered as a statical system of material points. How far the modern views of valency fit in with the idea of material points, whether the valency of carbon takes the form of a force acting in four directions or of one evenly distributed over the atom, whether it is determined by a tetrahedral figure of the carbon atom or depends upon the subdivision of the atom into smaller parts, it is not our intention to discuss. We are at present concerned with the experimental evidence upon which the theory rests.

Optically Active Compounds contain Asymmetric Carbon. According to the theory all optically active compounds contain an asymmetric carbon atom.[3]

The following are well-known examples of naturally occurring optically active substances containing one or more asymmetric carbon atoms, denoted in the formulae by heavy type:—

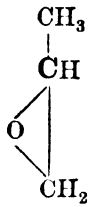
[1] *Bull. Soc. Chim.*, 1875 (2), **23**, 338; 1882 (2), **37**, 300; 1892 (3), **7**, 164; see Freundler's *Stereochimie*, p. 10.

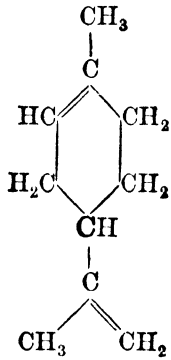
[2] *Arrangement of Atoms in Space*, by J. H. van 't Hoff, trans. by A. Eiloart (Longmans), p. 6.

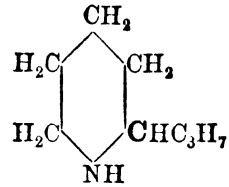
[3] Excluding for the present derivatives of other elements than carbon.

Amyl alcohol	$CH_3(C_2H_5)$. **C**H . CH_2OH
Lactic acid	CH_3 . **C**H(OH) . COOH
Malic acid	COOH . **C**H(OH) . CH_2 . COOH
Alanine	CH_3 . **C**H(NH_2) . COOH
Asparagine	COOH . **C**H(NH_2) CH_2 . $CONH_2$
Aspartic acid	COOH **C**H(NH_2) . CH_2 . COOH
Leucine	C_4H_9 . **C**H(NH_2) . COOH
Mandelic acid	C_6H_5 **C**H(OH) . COOH
Tyrosine	OH . C_6H_4 . CH_2 . **C**H(NH_2) . COOH
Tartaric acid	COOH . **C**H(OH) **C**H(OH) . COOH
Mannitol	CH_2OH . (**C**H . OH)$_4$. CH_2OH
Saccharic acid	COOH . (**C**H . OH)$_4$. COOH
Glucose	CH_2OH(**C**H . OH)$_4$. CHO.

The asymmetric carbon atom may also form part of a ring as in propylene oxide, limonene, and conine.


Propylene oxide.


Limonene.


Conine.

The supposed activity of a few compounds like propyl alcohol, CH_3 . CH_2 . CH_2OH, and styrene, $C_6H_3CH : CH_2$, which contain no asymmetric carbon, has been traced to inaccurate observations.

Whether every solid compound, which is active in solution, crystallizes in a hemihedral form, as Pasteur supposed, is a question about which opinions at present differ, and until fresh evidence is forthcoming judgment must be suspended.[1] Another question, however, suggests itself. Does activity of a substance in a liquid state or in solution necessarily involve activity of the solid? It appears to be rather the exception than the rule to find a substance active in both states. It has been observed in the case of certain tartrates,[2]

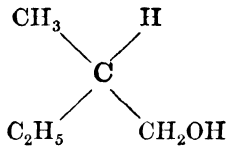
[1] This question has been discussed at length by F. M. Jaeger, *Lectures on the Principle of Symmetry*, p 256.

[2] The relation of the activity of the crystallized tartrate, which is laevorotatory, to that of its solution, which is dextrorotatory, has been explained by W. H. Bragg (*Trans Chem. Soc.*, 1922, 121, 2766) and by W. T. Astbury (*Science Progress*, 1923, 67, 401).

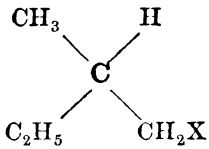
strychnine sulphate, zinc bimalate, and camphor. There is, however, no necessary connection between the activity of the two states, and it must be carefully borne in mind that stereoisomerism is concerned with the activity of the liquid or dissolved substance, and not with that of the solid.

Optical Activity and Asymmetry disappear together. According to the theory, activity should disappear with the removal of asymmetry, that is to say, when all the four groups are no longer dissimilar; when, for example, the compound Cabcd becomes Ca_2bc.

Amyl alcohol,

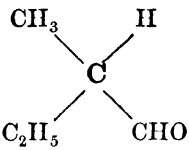


which is active in its esters, in the chloride, bromide, iodide, in amylamine and its salts, having the general formula:

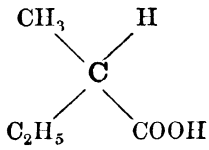


Amyl derivatives.

also in the aldehyde, valeric acid, and numerous other derivatives,

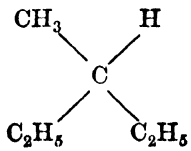


Valeraldehyde.

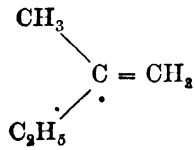


Valeric acid.

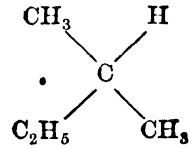
becomes inactive, as Le Bel and Just have shown, in methyl amyl, amylene, and amyl hydride, wherein the asymmetric carbon is lacking.



Methyl amyl.

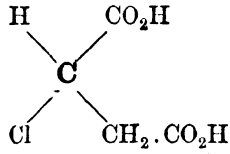


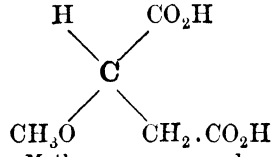
Amylene.

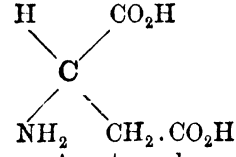


Amyl hydride.

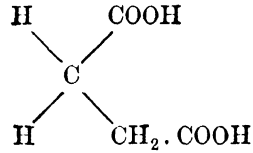
Active malic acid, which can be converted into active chlorosuccinic, methoxy-succinic, and aspartic acid,


Chlorosuccinic acid.

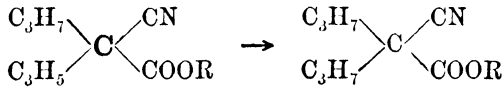

Methoxy-succinic acid.


Aspartic acid.

yields inactive succinic acid on reduction,



Again, active allyl propyl cyanacetic ester on reduction yields inactive dipropyl cyanacetic ester.[1]



Even living organisms which exhibit a tendency to form active substances never do so in the absence of an asymmetric carbon. Succinic acid, which often accompanies fermentative processes, is never active. It should be pointed out that where one group replaces another so that asymmetry is preserved, the product is not always active. The fact is accounted for by the compound undergoing during the process what is known as *racemisation*, which will be explained later (p. 194). Thus, an active chloro-succinic acid was obtained by Walden[2] from malic acid and phosphorus pentachloride, but the bromo compound prepared in a similar way was inactive The same thing occurred with *l*-mandelic acid, which gave inactive phenylbromacetic acid. Observations of a similar character have frequently been made.

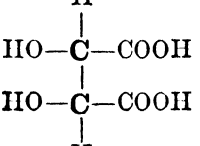
Optical Inactivity may exist with Asymmetry. We have now to discuss the converse of our first proposition. Is the presence of an asymmetric carbon atom always associated with optical activity? This is not necessarily the case. In the first place, the compound may consist of equal quantities of the two optically active varieties, in which case the activities will be neutralized, and hence the substance will appear inactive.

[1] Fischer and Brieger, *Ber.*, 1915, 48, 1517.
[2] *Ber.*, 1893, 26, 214; 1895, 28, 1287.

The Inactive Divisible Type. Thus, lactic acid from sour milk is inactive owing to the presence of equal quantities of the dextro- and laevo-compounds. Proof of this has been given by resolving the inactive acid into its two active components by methods to be presently described, and recombining the latter so as to reproduce the inactive substance. Inactive racemic acid is produced in the same way by dissolving equal quantities of the dextro and laevo tartaric acids. There exist a host of similar examples, which it is unnecessary to reproduce. In certain cases the two active varieties or enantiomorphs crystallize together, forming a product which has physical properties distinct from those of either constituent. Such a compound is called *racemic*. The term is derived from racemic acid, which in itself and its salts differs in crystalline form, water of crystallization, solubility, density, refraction, melting-point, &c., from either of the single active acids or their salts. Such differences disappear in solution, and the substance then behaves like a mixture. The distinction between racemic compounds and inactive mixtures is discussed more fully on p. 214. The two kinds of inactive substances are distinguished by the letters *r* and *dl*.

The Inactive Indivisible Type. There is another kind of inactivity which has quite a different origin. It depends upon the presence in the molecule of an even number of similar asymmetric carbon atoms, that is to say, carbon atoms to each pair of which a similar set of groups is attached. This inactive type was first observed by Pasteur in the case of tartaric acid which, in addition to inactive racemic acid, exists in the isomeric form of mesotartaric acid, and is obtained by heating ordinary tartaric acid with water or alkalis. The two are distinguished by different physical properties, but more especially by the fact that mesotartaric acid cannot be resolved into active components.

If we examine the structural formula of tartaric acid it will be seen that it possesses two asymmetric carbon atoms, denoted in the figure by thick type.



Each asymmetric carbon atom is attached to similar groups. Let us suppose that each asymmetric carbon with its associated groups produces a certain rotation in a given direction. We may imagine the following combinations of two similar asymmetric groups. Both produce dextro-rotation, or both produce laevo-rotation. They will represent the dextro- and laevo-enantiomorphs, and the mixture of the two will produce inactive racemic acid. Racemic acid is said to

be inactive by *external compensation*. Suppose, finally, that the two asymmetric groups produce rotation in opposite directions.

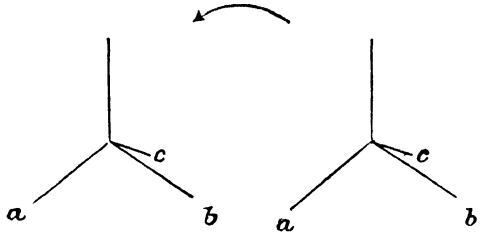


Fig. 28.

They will neutralize one another. The result will be a compound which is inactive by *internal compensation*. Such a compound cannot be resolved by any process into its active components. The last arrangement represents mesotartaric acid, which is permanently inactive or indivisible.[1] The explanation is more easily followed by means of models. Suppose that Fig. 28 represents the two asymmetric carbon atoms and that the bonds lettered *a*, *b*, *c*, stand for the three groups H, OH, and COOH, for which coloured sticks may be employed. Join together two identical models by bringing the one on the top of the other (Fig. 29).

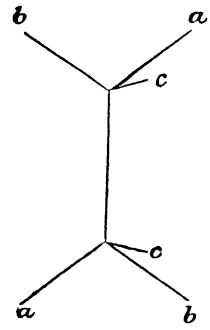


Fig 29.

If we suppose each model to be dextro-rotatory, the combination will also be dextro-rotatory, and will stand for the dextro-acid, Fig. 30 (I).[2] The mirror-image of this is shown in Fig. 30 (II), and will represent

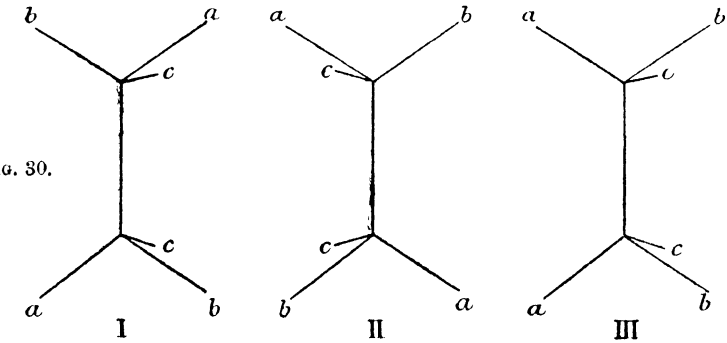


Fig. 30.

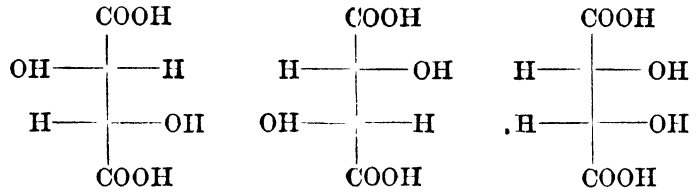
the laevo-acid. The mixture of the two will give inactive racemic

[1] The acid methyl ester of mesotartaric acid is not internally compensated and has been resolved by crystallization of its strychnine salt (see p. 190). Marckwald and Karezag, *Ber.*, 1909, **42**, 1518.

[2] It may be stated at once that there is no means of ascertaining the absolute relation of configuration to rotation.

acid. Finally, if the top and bottom asymmetric groups standing in the relation of object and image are combined, the rotations are opposed and neutralized and mesotartaric acid, Fig. 8 (III), is produced. It is identical with its mirror-image, for by revolving either of them in the plane of the paper through 180° they will coincide.

Instead of models, projection formulae can be used, and if the asymmetric carbon atom, instead of being represented by C, is merely denoted by a cross line, the above configurations will assume the following simple form:

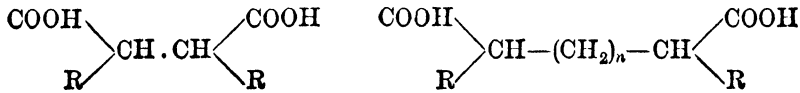


d. Tartaric acid. *l.* Tartaric acid. Mesotartaric acid.

The formulae unavoidably depict a fixed relative position of the two sets of groups surrounding the asymmetric carbon atoms; but it must be remembered that the above theoretical results would follow, if either or both carbon atoms revolved on a vertical axis into any other position, or continued permanently in a state of oscillation or rotation, provided the relative positions of the members of each asymmetric group were retained. The fixity, or otherwise, of the groups is a question which will be discussed later (p. 283).

The correctness of the explanation, which accounts for the inactive indivisible type, follows from the researches of E. Fischer,[1] who has shown that inactive and indivisible mucic acid, $CO_2H.(CHOH)_4.CO_2H$, gives, on reduction, galactonic acid, $CH_2OH.(CHOH)_4.CO_2H$. The symmetry of the molecule is thus disturbed, and the new substance, which now belongs to the divisible inactive type, can be resolved into its active enantiomorphs (p. 186).

The number of examples of the inactive and indivisible or meso type is not very large. In addition to mesotartaric acid and mucic acid already mentioned, erythritol $CH_2OH(CHOH)_2CH_2OH$ and dulcitol $CH_2OH(CHOH)_4CH_2OH$ belong to the same class of inactive compounds, as well as the dialkyl derivatives of succinic acid and its homologues of the general formula:



[1] *Ber.*, 1892, 25, 1247, 1260.

The following few examples afford a comparison of racemic (*r*) and meso (*i*) forms, from which it will be seen that the differences in physical properties are in the majority of cases well marked.[1]

Substance.	*M. P.*		*Density.*		*Affinity constant.*	
	r.	*i.*	*r*	*i.*	*r.*	*i.*
Tartaric acid	204°	140°	1·697	1 666	0 097	0·06
Dimethyl succinic acid	127	195	1·329	1·314	0·0123	0·0191
Diethyl succinic acid	129	192	—	—	0 0245	0 0343
Diisopropyl succinic acid	171	226	—	—	0 0108	0·2255
Diphenyl succinic acid	183	229	—	—	0 020	0·026
Dimethyl glutaric acid	128	140	—	—	0·0055	0·0055
Dimethyl adipic acid	75	140	—	—	0 0042	0 0042

Where the identity of the racemic compound has not been directly ascertained by resolving it into its enantiomorphs, the division into racemic and meso is usually determined by analogy with the melting-points of a related compound of known configuration. In the present case, however, it would appear that the racemic forms of the dialkyl and diphenyl derivatives of succinic acid and adipic acid, unlike racemic acid, have the lower melting-point, and the same is true of the sym. dichloro- and dibromo-succinic acids.[2]

In the above table the racemic form has been ascertained in the case of dimethyl-[3] and diphenyl-succinic [4] acids and dimethyl adipic acid [5] by resolution into their active forms.

Chemical as well as physical differences in racemic and meso compounds have also been observed, depending on solubility and water of crystallization. Whereas the calcium salt of mesotartaric acid crystallizes with three molecules of water $CaC_4H_4O_6 + 3H_2O$, that of racemic and the *d*- and *l*-acids crystallize with four.

Again, mesotartaric and racemic acid crystallize with one molecule of water, whereas the active tartaric acids are anhydrous. Hydrobenzoin $C_6H_5.CH(OH).CH(OH).C_6H_5$ is anhydrous, whilst isohydrobenzoin, the racemic form, may contain water of crystallization.

Resolution of Externally Compensated Compounds. The best proof of the existence of a substance (racemic compound or mixture) which is inactive by external compensation is its separation or resolution into active enantiomorphs. A few substances such as asparagine and gulonic lactone separate spontaneously into their enantio-

[1] A more complete list will be found in Werner's *Lehrbuch der Stereochemie.*

[2] Holmberg, *Chem. Soc. Abstr.*, 1912, 1, 4, McKenzie, *Trans. Chem Soc*, 1912, 101, 1196 [3] Werner and Basyrin, *Ber.*, 1913, **46**, 3229.

[4] Wren and Still, *Trans Chem Soc.*, 1915, 107, 444; 1917, 111, 513; McKenzie, Drew, and Martin, *ibid*, 1915, 107, 26.

[5] Noyes and Kyriakides, *J. Amer. Chem. Soc.*, 1910, **32**, 1057.

morphs on crystallization. In most cases it is a matter of some difficulty owing to the fact that stereoisomerism is only manifested by optical and occasionally crystallographic properties, and by the relation of the two enantiomorphs to other asymmetric substances. In all other respects the stereoisomers are identical. The three principal methods at present in use for resolving externally compensated compounds were suggested and developed by Pasteur.

Resolution by Crystallization in Enantiomorphous Forms. The method has already been described in the case of sodium ammonium racemate (p. 174), and depends on the deposition of the two enantiomorphous crystalline forms of the *d*- and *l*-tartrates from solution,[1] which can be separated mechanically. The process has undergone an interesting development. Why, it may be asked, does not the salt of the original racemate crystallize? On evaporating solutions of sodium ammonium racemate Stadel[2] did, in fact, obtain crystals of the original racemate, and not those of the *d*- and *l*-tartrates as Pasteur had done. How were the results to be reconciled? Scacchi[3] solved the problem by showing that the formation of the one or other kind of salt is dependent on the temperature at which crystallization occurs. A high temperature favours the crystallization of the racemate, whilst at the ordinary temperature the two tartrates are chiefly formed. The temperature above or below which the transformation occurs was found by Wyrouboff[4] to be about 28°. Van 't Hoff and van Deventer[5] have since shown that the *transition temperature*, as it is now termed, lies between 26·7° and 27·7°, and is determined by the loss of water of crystallization from the tartrates and their conversion into the racemate according to the following equation:

$$2C_4O_6H_4NaNH_4 + 4H_2O = (C_4O_6H_4NaNH_4)_2 . 2H_2O + 6H_2O.$$

Above the transition temperature the tartrates lose water of crystallization and the racemate is formed; below this temperature water is absorbed and the tartrates are produced. The transition temperature has since been studied in the case of other substances,[6] and great accuracy has been introduced into the observations by the refined methods of van 't Hoff, which are described in text-books of physical chemistry. The following substances have been examined:

	Transition temp.		*Transition temp.*
Sodium potassium tartrate	3°	Ammonium bimalate	74°
Potassium tartrate	37·2°	Methyl mannoxide	8°
Rubidium tartrate	40·4°	Camphoroxime	103°

The resolution of inactive substances by crystallization in this way has had only a limited application, owing to the difficulty of obtaining well-crystallized enantiomorphous specimens capable of mechanical separation. It has, however, been used by Purdie[7] to

[1] Pasteur, *Ann Chim. Phys.*, 1848 (3), **24**, 442; 1850, **28**, 56.
[2] *Ber.*, 1878, **11**, 1752.
[3] *Rend. Accad Napoli* (1865), 250.
[4] *Bull. Soc. Chim*, 1884, **41**, 210; 1886, **45**, 52; *Compt. rend.*, 1886, **102**, 627.
[5] *Zeit phys. Chem.*, 1887, **1**, 165.
[6] Kenrick, *Ber.*, 1897, **30**, 1749.
[7] *Trans. Chem. Soc.*, 1893, **63**, 1143.

resolve inactive lactic acid by means of the zinc-ammonium double salt, by Erlenmeyer jun.[1] to separate racemic isohydrobenzoin, and by Körner and Menozzi[2] to break up inactive asparagine. As all the substances named can be prepared artificially in their inactive forms, their resolution into active constituents can be effected in this way spontaneously, and consequently without the direct intervention of vital, i. e. asymmetrical, influences, a view which is contrary to that upheld by Pasteur.

The other two methods of Pasteur are based on the different behaviour of the two enantiomorphs under what may be termed asymmetric conditions.

Resolution by the Biochemical Method. Pasteur (1860) observed that a solution of ammonium racemate containing a little potassium phosphate becomes laevo-rotatory after green mould (*penicillium glaucum*) has been grown in it. The rotation increased slowly until a maximum was obtained, when no more *d*-tartrate was left in solution. In other words, living organisms, which Pasteur regarded as asymmetric bodies, have the property of *selective assimilation*. The observation has been widely applied, and many of the lower vegetable organisms—bacteria, fungi, and yeasts—have been pressed into the service of the chemist. The process is usually conducted as follows:—A dilute and sterilized solution of the inactive substance in water is prepared, to which small quantities of nutrient materials, such as phosphates and ammonium salts, are added, and finally a pure culture of the organism. After keeping the solution at a suitable temperature for the growth of the organism, a portion is withdrawn from time to time and examined in the polarimeter until a maximum rotation is reached.

The curious observation has been made by P. Frankland and MacGregor,[3] that, although fresh cultures of *bacillus ethaceticus* act only upon the dextro-salts of glyceric acid, they can, by cultivation in a solution of calcium glycerate, be gradually induced to assimilate the laevo-enantiomorph as well, but this is an exception to the general rule. The different kinds of organisms which have been used for resolving inactive substances in the manner described above do not always assimilate the same enantiomorph; on the contrary, they show the greatest diversity in their tastes, one organism attacking the dextro- and another the laevo-enantiomorph in an apparently arbitrary manner. The loss of the one enantiomorph, as well as the

[1] *Ber.*, 1897, 30, 1531. [2] *Gazz. chim.*, 1887, 226.
[3] *Trans. Chem. Soc.*, 1898. 63. 1034.

usually small yield of active material, constitute the chief disadvantages of the process. On the other hand, the method can be applied to a great variety of compounds, such as acids, alcohols, and sugars, and is frequently used for finding if an inactive substance is capable of resolution. Examples of its application are very numerous, lists of which will be found in papers by Winther,[1] McKenzie and Harden,[2] and in Werner's *Lehrbuch der Stereochemie*, p. 63.

Substance	*Organism.*	*Destroyed.*
Racemic acid	penicillium	*d.*
	schizomycetes	*l.*
Lactic acid	penicillium	*d.*
	bacteria	*l.*
Mandelic acid	penicillium	*d.*
	aspergillus mucor	*l.*
	yeast	*d.*
	bacterium termo	*l.*
Glyceric acid	penicillium, bac. Fitzianus	*l.*
	bac. ethaceticus	*l.*
	bac. coli, bac. acidi lactici	*l*
	bac. pyocyaneus	*l*
	aspergillus niger	*l*
Ethoxy succinic acid	penicillium	*d.*
Methyl ethyl carbinol	penicillium	*d.*
Methyl propyl carbinol	penicillium	*d*
	aspergillus niger	*d.*
Phenyl dibromopropionic acid	aspergillus fumigatus	*l.*
Amyl alcohol	fungus	*l.*
Propylene glycol	fungus	*d.*
	bacterium termo	*d*
	bacterium from cheese	*d*
Glucose, mannose, galactose, and fructose	yeast	*d*
Asparagine	penicillium	*d.*
Aspartic acid	penicillium	*l.*
Tyrosine	aspergillus niger	*l.*
	penicillium	*d.*
Leucine	penicillium	*l.*

The power of selective assimilation by living organisms finds a parallel in the different physiological action of enantiomorphs on the animal body and of the animal body on enantiomorphs. For instance, Piutti[3] found that *d*-asparagine has a sweet taste, whereas that of the laevo enantiomorph is insipid ; the same difference subsists between *d*- and *l*-histidine, *d*- and *l*-leucic acid, and *d*- and *l*-glutamic acid,[4] the former being sweet and the latter tasteless ; *l*-nicotine, according to Pictet and Rotschy,[5] and *l*-adrenaline, according to

[1] *Ber.*, 1895, **28**, 3022.
[2] *Trans. Chem. Soc.*, 1903, **83**, 424.
[3] *Ber.*, 1886, **19**, 1691.
[4] Kodama, *Abstr.*, 1920, **i**, 471.
[5] *Ber.*, 1904, **37**, 1233.

Abderhalden,[1] are far more poisonous than the *d*-compounds ; *l*-adrenaline has, at the same time, a greater effect on the blood pressure. Chabrié[2] showed that *l*-tartaric acid, when administered to guinea-pigs, was found to be twice as poisonous as the *d*-acid, whilst Cushny[3] found that *l*-hyoscyamine has about 100 times the mydriatic action of the *d*-enantiomorph and *l*-hyoscine fifteen to eighteen times the activity of the dextro-compound on the nerve endings. The power of the human body to assimilate and excrete certain optically active substances belongs to the same order of phenomena. Laevo-tyrosine, for example, is more easily destroyed in the animal body than the dextro-compound.[4] The discovery of the optical activity of certain mineral oils by Neuberg and the conversion of chaulmoogra oil by distillation with zinc dust into an active paraffin (Lewkowitsch) lends support to the theory of the organic origin of petroleum.

Resolution by means of Active Substances. The third method of Pasteur is the one most commonly employed. Pasteur[5] found that when racemic acid is combined with the active (laevo) base cinchonine and the solution left to crystallize, the cinchonine salt of *l* tartaric acid is the first to separate. In order to explain the fact we must assume that if sufficient cinchonine is present two salts are formed, one of the alkaloid with the laevo-acid and the other with dextro-acid. If we denote the acid by A and the base by B, we obtain the following two combinations:—

$$dA + lB, \quad lA + lB.$$

The two compounds are not enantiomorphs, for the two acids of opposite rotation are united to the same active base. They consequently exhibit different properties, more especially different solubilities. It is thus possible to resolve, by fractional crystallization of their salts, inactive acids (e.g. racemic acid) when combined with the same active base (e.g. cinchonine), or inactive bases (e.g. conine) when united to the same active acid (e.g. tartaric acid). There are certain practical difficulties connected with the operation which are occasionally encountered, such as small differences in the solubility of the two salts or lack of crystallizing power.[6] The first may be overcome by substituting an active reagent of higher rotatory power, which usually enhances the differences in physical properties; the

[1] *Zeit. physiol. Chem*., 1909, 59, 129. [2] *Compt. rend.*, 1893, 116, 1410.
[3] *Lancet*, 1916, p. 459, *J. Pharm. Exp. Ther.*, 1921, 17, 41
[4] Dakin, *J. Biol Chem.*, 1910, 8, 25, see also Pyman, *Trans Chem. Soc.*, 1917, 111, 1105.
[5] *Ann. Chim. Phys*, 1853 (3), 38, 437; *Compt. rend.*, 1853, 37, 162.
[6] Marckwald, *Ber.*, 1896, 29, 42.

second by inoculating the solution with a crystal of a similarly active salt, so as to induce crystallization. The bases commonly used are the active alkaloids, quinine, quinidine, cinchonine, cinchonidine, strychnine, morphine, and brucine, and also phenylethylamine, methyl and hydroxy hydrindamine and Werner's triethylene diamine cobalti-bromide, which has a very high rotation and was used to resolve $\alpha\alpha$-dimethylsuccinic acid.[1] The usual active acids are tartaric, camphorsulphonic, and bromocamphorsulphonic acid. There are some acids, like the amino acids, alanine, leucine, tyrosine, &c., which are too weak to form stable salts with the alkaloids, and cannot therefore be submitted to the process of fractional crystallization. E. Fischer[2] found a simple solution of the difficulty by introducing the strongly acid radicals benzoyl, nitrobenzoyl, or formyl into the amino group, thereby converting a weak acid into a strong one. The acyl derivatives readily form crystallizable salts with the alkaloids, from which, after resolution into their enantiomorphs in the usual way, the acyl group is removed by hydrolysis. It does not necessarily follow that because an inactive acid can be resolved by a certain active base, the corresponding inactive base may be as readily resolved by the corresponding active acid.[3]

Recent Methods of Resolution. The methods of Pasteur, which depend upon the differences exhibited by the components of an inactive substance under the influence of asymmetric (physical, chemical, or biochemical) reagents, have undergone expansion in various directions. Among the physical methods is that of Kipping and Pope,[4] who crystallized sodium ammonium racemate from solutions containing *d*-glucose, and obtained on the average an excess of the dextro-enantiomorph, and Ostromisslensky[5] found that if an inactive and supersaturated solution of sodium ammonium tartrate at 6° was seeded with a crystal of *l*-asparagine only the dextro-tartrate was deposited. Similar results were obtained with other salts. Even an inactive substance such as glycine may cause the separation of active asparagine from a solution of the mixture. Attempts to induce separation of the enantiomorphs by crystallization in a strong magnetic field, that is, under conditions which ordinarily produce rotatory polarization in inactive materials, were

[1] *Ber.*, 1913, **46**, 3229

[2] *Ber.*, 1899, **32**, 2451, 3638; 1900, **33**, 2370, *Ber.*, 1905, **38**, 3997. See also Gibson and Simonsen, *Trans. Chem. Soc.*, 1915, **107**, 798

[3] Kipping, *Trans. Chem. Soc.*, 1909, **95**, 408

[4] *Proc. Chem. Soc.*, 1898, **14**, 113, *Trans.*, 1909, **95**, 103.

[5] *Ber.*, 1908, **41**, 3035.

made by Pasteur, and have since been repeated, but without success. Chemical methods have been employed by E. Fischer, Walden and Marckwald, and McKenzie. Fischer[1] examined the rate of hydrolysis of cane-sugar by *d*- and *l*-camphoric acid with negative results. A similar process has been studied with more success by Walden,[2] and Marckwald and McKenzie.[3] The method is based on the different behaviour of the two enantiomorphs of an acid with the same active alcohol or of an alcohol with the same active acid, more especially in the effect on the rate of hydrolysis and esterification. The ester of the one combination is more easily formed or hydrolysed than the other, and therefore incomplete hydrolysis or esterification of the inactive material leads to a partial resolution of the enantiomorphs. If, for example, inactive mandelic acid is incompletely esterified with *l*-menthol, the dextro-acid being more rapidly esterified, the unesterified portion is laevo rotatory.

Erlenmeyer, jun.,[4] has separated isodiphenyl hydroxyethylamine

$$\begin{matrix} C_6H_5CH(OH) \\ | \\ C_6H_5CH.NH_2 \end{matrix}$$

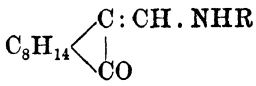
by combining it with active helicin. The compounds of the formula

$$C_6H_5.CH(OH).CHC_6H_5.N:CHC_6H_4.OC_6H_{11}O_5$$

formed by the two enantiomorphs are not mirror images, and can be separated by fractional crystallization, and Neuberg[5] has succeeded in resolving racemic arabinose by crystallizing the hydrazone formed with *l*-menthylhydrazine. In this case nearly pure *d*-arabinose *l*-menthylhydrazone crystallizes from the alcoholic solution.

An ingenious method for resolving alcohols has been devised by Pickard, and consists in forming the acid ester of a dibasic acid (succinic or phthalic acid) with the alcohol, combining it with an active alkaloid and then submitting it to fractional crystallization. In this way a large number of alcohols have been resolved (see p. 235). For resolving primary amines Pope and Read[6] use the two active hydroxymethylene camphors obtained from *d*- and *l*-camphor (see Part III, p. 265), which unite readily with bases to form compounds of the general formula

[1] *Ber.*, 1899, **32**, 3617.
[2] *Ber.*, 1899, **32**, 2703.
[3] *Ber*, 1899, **32**, 2130; 1901, **34**, 469; 1920, **117**, 680.
[4] *Ber*, 1903, **36**, 976
[5] *Ber*, 1903, **36**, 1192.
[6] *Trans. Chem. Soc*, 1909, **95**, 171; 1913, **105**, 444.



After separation by crystallization, the bases are recovered in the form of the hydrobromides by decomposing the compound with bromine.

Votoček and Vesely [1] have succeeded in resolving racemic sugars by combining them with active amyl mercaptan.

Another method for preparing active compounds, which cannot be obtained by any of the ordinary methods of resolution, is to synthesize them from active materials.

McKenzie and Wren [2] have converted *l*-mandelamide by the aid of the Grignard reagent (Part I, p. 245) into *l*-benzoin:

$$C_6H_5 . CH(OH) . CONH_2 + 2C_6H_5MgBr \rightarrow C_6H_5CH(OH) . C(OMgBr)(NHMgBr)C_6H_5 + 2H_2O \rightarrow C_6H_5CH(OH) . CO . C_6H_5 + MgBr_2 + Mg(OH)_2 + NH_3$$

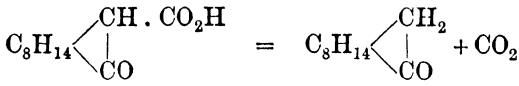
and also certain active glycols from active esters by the aid of the same reagent, whilst Fischer has succeeded in preparing an active *l*-methyl succinic acid from *l*-bromopropionic ester by Bone and Sprankling's method (Part I, p. 220).

An interesting case of partial resolution of potassium racemate was observed by McKenzie [3] on adding sufficient *l*-malic acid to form the acid potassium salt, which was found to be dextro-rotatory.

Among the methods which are related to Pasteur's biochemical method are the hydrolytic resolution of glucosides by enzymes (emulsin and maltase), which was investigated by E. Fischer,[4] and is treated more fully in Part III, p. 41, and the hydrolysis of the esters of an inactive acid by the fat-splitting enzyme *lipase*, which was studied by Dakin.[5] Both observers found that the enzymes in question exhibit the power of selective hydrolysis. Thus Dakin showed that the partial hydrolysis of the inactive esters of mandelic acid results in the production of the dextro-rotatory free acid and a laevo-rotatory residue of unchanged ester. He explains it by the union of enzyme and ester previous to hydrolysis. As the enzyme is an active substance, the rate of hydrolysis of enzyme + *d*-ester will be different from that of enzyme + *l*-ester.

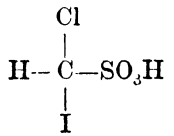
[1] *Abstr*, 1916, i, 308.
[2] *Trans. Chem. Soc*, 1908, 93, 309; 1909, 95, 1583; 1913, 103, 112.
[3] *Trans. Chem. Soc.*, 1915, 107, 440.
[4] *Zeit. phys. Chem.*, 1898, 26, 61.
[5] *Journ. of Phys.*, 1904, 30, 253; 1905, 32, 199.

An observation not unconnected with the partial hydrolysis of esters by an enzyme is that of Bredig and Fajans,[1] who found that *l*-nicotine used as a solvent for *d*- and *l*-camphocarboxylic acid had the effect of inducing more rapid decomposition of the dextro acid into camphor and carbon dioxide than the laevo acid



whereas in inactive solvents there was no apparent difference between the two enantiomorphs.

Substances which have not been resolved. Whilst a certain number of inactive externally-compensated compounds like asparagine, isohydrobenzoin, and certain lactones of saccharic acid show no tendency to form racemic compounds and separate spontaneously on crystallization into their enantiomorphs, and others again can be resolved more or less readily by the methods described, there still exists a class of substances which up to the present have defied all attempts to divide them. It was supposed at one time that no substance containing less than two carbon atoms united to the asymmetric carbon could be obtained in an active form, and until recently all attempts to resolve them failed.[2] Pope and Read[3] have now succeeded in resolving chloriodomethane sulphonic acid,



by crystallization with *d*- and *l*-hydroxyhydrindamine, brucine, or strychnine. The ammonium salt of the dextro-isomer shows a rotation of [M]. = +43·7°.

Racemisation. In the foregoing paragraphs the resolution of inactive substances has been described. The reverse process, whereby an active substance is rendered inactive, is frequently observed. It is termed *racemisation*, and is brought about by the conversion of one half of the active material into its enantiomorph. That the change

[1] *Ber.*, 1908, **41**, 752, *Zeit. physik Chem.*, 1910, **73**, 25.

[2] See van 't Hoff's *Arrangement of Atoms in Space*, trans. by Eiloart, p. 25; Pope and Read, *Trans. Chem Soc*, 1908, **93**, 794.

[3] *Trans. Chem. Soc*, 1914, **105**, 811; see also Franchimont and Backer, *Rec. trav. chim. Pays-Bas*, 1921, **39**, 751.

is due to this cause, rather than to the formation of some structurally different and inactive compound, has been shown repeatedly by resolving the product of racemisation into its originally active constituents.

Racemisation is usually effected by rise of temperature. It was first observed by Pasteur,[1] who obtained both racemic and mesotartaric acid by heating cinchonine *d*-tartrate to 170°. Jungfleisch[2] modified and improved the method, heating tartaric acid with ten to fifteen per cent. of water in sealed tubes to 175° for several hours, and obtained considerable quantities of racemic and mesotartaric acid. The same process has been found to bring about the racemisation of aspartic, mandelic, isopropylphenylglycollic, and camphoric acid. Active pinene, limonene and phellandrene, active amyl alcohol, and many of its derivatives are rendered inactive by heating. Active lactic acid is converted at 150° into inactive lactide, and active quinic acid into inactive quinide. The presence of foreign substances frequently produces racemisation. *d*-Tartaric acid is easily converted into racemic and mesotartaric acid when boiled with a concentrated solution of caustic soda.[3] Caustic potash racemises active amyl alcohol, lactic acid, mandelic acid, and amygdalin. Active leucine, glutamic acid, and pyrrolidine carboxylic acid, when heated with baryta water, and *d*-valeric acid, limonene, and pulegone, heated in presence of strong sulphuric acid, lose their activity. The racemising action on tartaric acid of the oxides of iron and aluminium has been attributed to the catalytic action of these substances.[4] Racemisation seems to occur more readily when substances are in the act of formation than when already formed. In this connection the racemising of a substance during the replacement of one group by another, as Walden observed when malic acid is converted into bromosuccinic acid (p. 182), can be readily understood. It is well known that acids with asymmetric carbon in the α-position are readily racemised by alkali, if one hydrogen is present in the asymmetric group, but not otherwise. Mandelic and phenyl *p*-tolyl acetic acid are readily racemised, but not atrolactic acid nor β-phenyl methyl propionic acid.

$C_6H_5 . CH(OH) . COOH$
Mandelic acid.

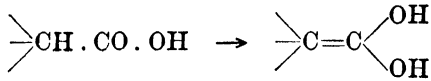
$(C_6H_5)(C_7H_7)CH . COOH$
Phenyltolyl acetic acid.

$(C_6H_5)(CH_3) . C(OH) . COOH$
Atrolactic acid.

$(C_6H_5)(CH_3) . CH . CH_2 . COOH$
Phenylmethyl propionic acid.

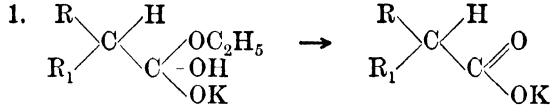
[1] *Compt. rend.*, 1853, 37, 162
[2] *Bull. soc. chim.*, 1872, 18, 201
[3] Meissner, *Ber.*, 1897, 30, 1574.
[4] Jungfleisch, *Compt. rend.*, 1877, 85, 805.

The reason advanced here is a tautomeric change (p. 330) in which the hydrogen in the asymmetric group attaches itself to the double-linked oxygen of the carboxyl group under the action of the alkali, when the asymmetric carbon atom momentarily loses its activity.

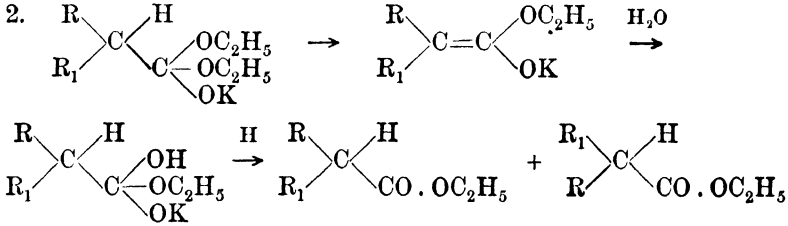


This can only occur in mandelic and phenyltolyl acetic acid, but not in atrolactic acid, which has no available hydrogen in the α-position, nor in phenylmethyl propionic acid, in which asymmetry is confined to the β-carbon group.[1]

In view of the fact that alcoholic potash has a much greater racemising action on the active esters than aqueous potash, McKenzie and Wren have suggested the following mechanism for the two reactions. With aqueous potash the change does not necessarily affect the asymmetric carbon atom.



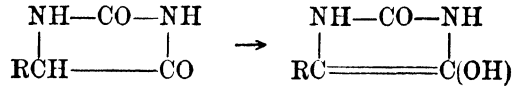
With alcoholic potash the asymmetric carbon atom is involved.



This explains the observation that racemisation of certain esters occurs before hydrolysis.[2]

There are many grounds for assuming that such a change occurs in other chemical reactions.[3]

The production of racemic amino acids when proteins are hydrolysed with alkalis (but not with acids) may be ascribed to the same cause, for Dakin[4] has shown that active hydantoins with a hydrogen atom in α-position to the CO group readily racemise, but not otherwise.

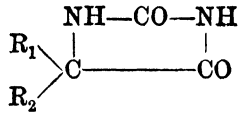


(racemises)

[1] Rothe, *Ber.*, 1914, 47, 843; McKenzie and Widdows, *Trans. Chem. Soc.*, 1915, 107, 702; McKenzie and Wren, *ibid.*, 1919, 115, 602.

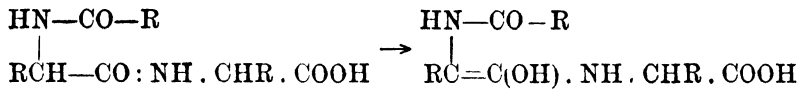
[2] Wren, *Trans. Chem. Soc*, 1918, 113, 210. [3] O. Aschan, *Ber.*, 1913, 46, 2162.

[4] *Amer. Chem. Journ.*, 1910, 44, 48.

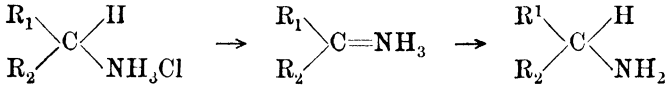


(does not racemise)

As the protein molecule consists of chains of amino acid groups, the analogy is readily understood.



The racemisation of active compounds containing the group $CH(NH_2)R'R''$, such as occurs in tetrahydro β-naphthylamine, which so frequently become inactive when acylated or liberated from their salts, is attributed by Pope and Harvey [1] to a transitory intermediate stage yielding an inactive compound.

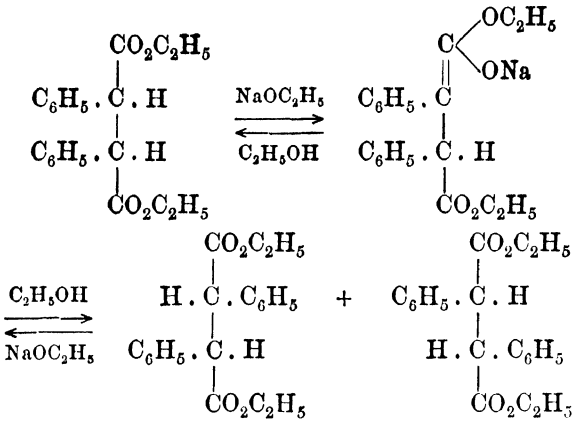


The temperature of racemisation of some substances is quite low, and the change known as *autoracemisation* has even been found to take place spontaneously at the ordinary temperature. Walden [2] observed a gradually decreasing rotation in the esters of *d*-bromosuccinic acid and *d*-phenyl bromacetic acid when kept for three or four years. During this period a few of the substances were completely racemised.

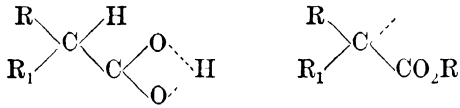
In other cases, such as the polyhydroxy-acids, where more than two asymmetric carbon atoms are present, racemisation on heating with water is never complete, but only a single asymmetric group is affected, and the process is known as *partial racemisation*.[3] The subject, which is of special interest in relation to the formation of synthetic sugars, is more fully discussed in Part III, p. 6.

In this connection it is interesting to learn from the investigations of Winther [4] that the racemisation of active tartaric acid by the action of alkalis takes place in two stages; one asymmetric carbon is first affected and then the other; in other words, the change is from the active acid to the meso form and from the meso to the racemic compound, a condition of equilibrium being finally established between the two latter. The same thing occurs with symmetrical diphenylsuccinic acid, the change from racemic to meso form being reversible, the first being effected by hydrochloric acid and the second by barium hydroxide.[5] The esters of these two acids are also interconvertible under the action of alkalis. The explanation is similar to that given by McKenzie and Widdows (p. 196).

[1] *Trans Chem. Soc*, 1901, 79, 85. [2] *Ber.*, 1898, 31, 1416.
[3] For examples of racemisation see Chr. Winther, *Zeit. phys. Chem*, 1906, **56**, 466. [4] *Zeit. phys Chem.*, 1906, **56**, 466, 720.
[5] Wren and Still, *Trans. Chem. Soc.*, 1917, **111**, 1019; 1918, **113**, 210.



so that racemisation appears to precede hydrolysis. The same occurs with the optically active esters. The greater difficulty experienced in racemising the active free acids may be due to the existence of the hydrogen ion in the acid, whereas the ester according to Hantzsch represents a pseudo-acid from which the hydrogen of the asymmetric carbon by the action of hydroxyl ions may become detached.



From experiments by James and Jones[1] it seems not improbable that racemisation in the case of both malic acid and tartaric acids on heating is due to the removal and subsequent addition of a molecule of water, malic acid yielding fumaric acid, tartaric acid, and hydroxyfumaric acid as intermediate products.

The mechanism of the process is capable of various interpretations. Van 't Hoff[2] points out that in the conversion of one stereoisomer into the other, where the stability is slight, equilibrium will be attained when the inactive mixture is formed; for it follows from the complete mechanical symmetry of the two isomers that the tendency to conversion is equal in both, and consequently the one present in larger quantity will always be converted in larger quantity until equal quantities of each are present. Werner[3] has suggested an ingenious mechanical device for representing the phenomenon, which disposes of certain difficulties, such as a readjustment of the bonds, or the actual separation of the groups from the asymmetric carbon during the rearrangement.[4] He constructs a model consisting of two circular wires or discs soldered at right angles at the two

[1] *Trans. Chem. Soc.*, 1912, 101, 1158. [2] *Ber.*, 1877, 10, 1620.

[3] Werner's *Stereochemie*, p. 48

[4] There seems no reason to assume that groups cannot become detached in view of Phillips's researches on the Walden inversion (p. 210) and those of Wedekind on the autoracemisation of pentavalent nitrogen compounds (*Ber.*, 1906, 38, 3488; 1908, 41, 2659).

ends of a common axis. Four differently coloured balls, pierced with holes, slip along each of the four wire semicircles into which the model is divided, and are retained in any position by elastic threads, which attach each ball to the centre of the common axis. The balls are arranged at the corners of an imaginary tetrahedron *a*, *b*, *c*, *d*, Fig. 31 (I). Racemisation is supposed to be effected by increasing the amplitude of the vibrations of each ball, that is, by moving it farther on each side of its original position along the wire semicircle. Each pair of balls may be supposed to eventually swing so far that at one moment they lie in the same horizontal plane, (Fig. 31 (II). From this position, when the racemising agent is removed, the balls may return to their original, or pass over into opposite, hemispheres, as shown in Fig. 31 (III). As there is an equal chance of both changes occurring, an equal number of molecules of both kinds, that is, equal quantities of

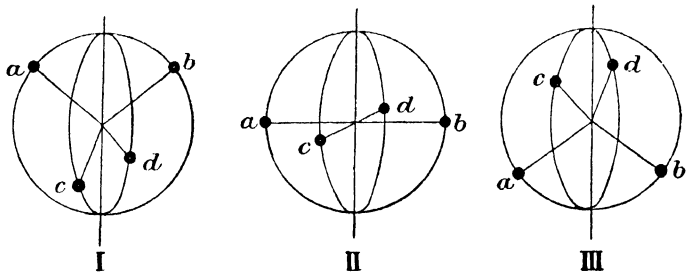
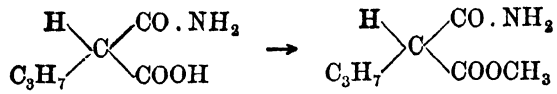


FIG. 31

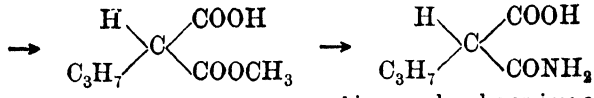
the two enantiomorphs, will be formed. That the second arrangement is the mirror-image of the first is easily demonstrated by turning the model Fig. 9 (III) upside down on its vertical axis.

Conversion of Active Compounds into Active Derivatives. The possibility of converting an active compound into an active derivative, provided molecular asymmetry is maintained, has already been advanced in support of the present theory (p. 181). The activity of the derivative is not, however, a necessary consequence of the change, seeing that racemisation may occur during the process, in which case an inactive derivative results.

It is possible, as Fischer and Brauns have shown, to interchange two groups in an active molecule and so convert one active form into its enantiomorph. This has been effected with *d*-isopropyl malonaminic acid, which by successive conversion into the aminic ester, the acid ester, and the aminic acid gives the *l*-compound.



d-isopropyl malonaminic acid.



l-isopropyl malonaminic acid.

Such a process of inversion is readily understood; but there is another form of inversion brought about by the replacement of one group by another in an active compound, giving rise to a derivative of opposite sign, and is not so easily explained.

Optical or 'Walden' Inversion.[1] When studying the action of reagents on the active chlorosuccinic acids P. Walden[2] found that by replacing chlorine by hydroxyl in the laevo compound, using a strong base (potassium hydroxide or ammonia), *d*-malic acid is formed, but if silver oxide or water is employed the *l*-acid is obtained. The same thing occurs if the dextro-chlorosuccinic acid is used, that is to say, potassium hydroxide gives a malic acid of opposite sign and silver oxide one of the same sign. Walden has studied the action of a variety of metallic oxides in the same way, and has shown that they form a series, the end members of which produce diametrically opposite effects in the character and amount of rotation, whilst the intermediate members form products which in sign and value lie between the two extremes. The hydroxides of the strong bases, rubidium, potassium, ammonium, copper, cadmium, barium, lead, and sodium, cause inversion of sign in different degrees, whereas those of silver, thallium, and mercury produce a malic acid having the same sign as the original malic acid.

Further, phosphorus pentachloride converts *l*-malic acid into *d*-chlorosuccinic acid and *d*-malic acid into *l*-chlorosuccinic acid. Pasteur[3] had previously shown that nitrous acid converts *l*-asparagine into *l*-malic acid, whilst Tilden and Marshall[4] found that nitrosyl chloride yields *l* chlorosuccinic acid.

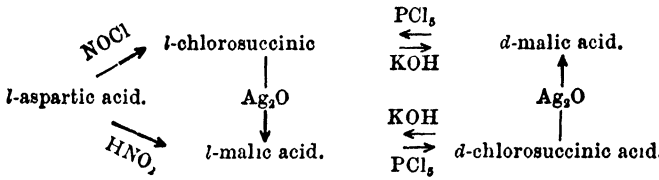
The following scheme, taken from Walden's memoir, shows the cycle of changes described above, from which it follows that the

[1] An excellent summary of the subject is given in the *Annual Reports of the Chemical Society*, 1911, p 60; the *British Assoc. Report*, 1912, p 687, by A. M'Kenzie; and the Presidential Address to the Chemical Society, by P. Frankland; *Trans Chem. Soc*, 1913, 103, 717.

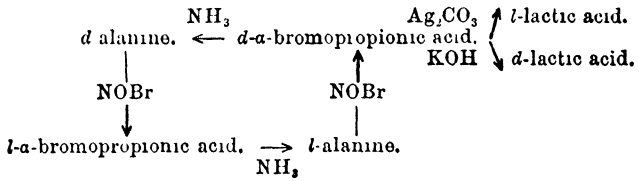
[2] *Ber.*, 1895, 28, 1287; 1896, 29, 133; 1897, 30, 2795, 3151; 1899, 32, 1841.

[3] *Ann. Chem. Phys.*, 1852. 34, 46. [4] *Trans. Chem. Soc.*, 1895, 67, 494.

sign of rotation of the active chlorosuccinic and malic acids may be interchanged at will, and that *l*-aspartic acid may be transformed into either *l*- or *d*-chlorosuccinic or malic acids.



Now it does not follow that a change of sign of rotation represents an abnormal reaction, for there are numerous cases where such a change occurs without assuming change of configuration. For example, the active amyl alcohols, when heated with halogen and other acids, yield halide derivatives and esters of opposite sign, and the introduction of acyl groups into malic and tartaric ester produce derivatives of opposite rotation from those of the unsubstituted ester. On the ground that the strong bases probably interact by ionisation, producing direct substitution of hydroxyl for halogen, whereas the weak bases are likely to form additive compounds, Walden concluded that the action of potassium hydroxide and also of phosphorus chloride represent a normal and silver oxide an abnormal change. This view has not been supported by the later experience of Fischer [1] and McKenzie [2] and their collaborators, who have studied many examples of optical inversion. Fischer observed the following cyclic series of changes:



Here it will be seen that potassium hydroxide yields a lactic acid of the same sign, and silver carbonate one of opposite sign to that of the halogen acid, whilst the action of ammonia on the halogen acid, or on its ester, produces an amino acid of the same sign, and that of nitrosyl bromide, on the free alanine, a halogen acid of opposite sign. All these reactions exhibit the reverse changes to those shown in Walden's table. Fischer regards the action of silver carbonate on

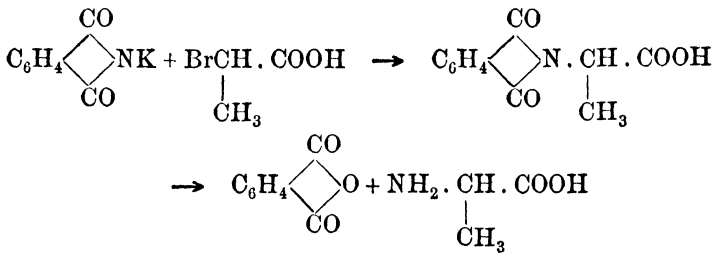
[1] *Ber.*, 1907, 40, 489. [2] *Trans. Chem. Soc.*, 1908, 93, 811.

the halogen acid as abnormal, since, if the latter is first combined with glycine to form *l*-α-bromopropionyl glycine, and then treated with the silver salt and hydrolysed, the lactic acid thus obtained is the laevo compound.

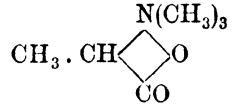
$$l.\ CH_3.CHBr.CO.NHCH_2.COOH \rightarrow l.\ CH_3.CHOH.COOH$$

l-α-Bromopropionyl glycine. *l*-Lactic acid.

For similar reasons Fischer considers the action of nitrosyl bromide on the free amino acid to be abnormal, but that of ammonia to be normal, for when nitrosyl bromide acts upon alanine ester in place of alanine, the bromopropionic acid thus prepared shows no change of sign; there is also no change of sign if α-bromopropionic acid is converted into alanine by first uniting it with potassium phthalimide and then hydrolysing the product.



Moreover, when trimethylamine acts upon *d*-α-bromopropionic acid it yields the same *l*-betaine as that obtained from the action of methyl iodide on *d*-alanine,[1]

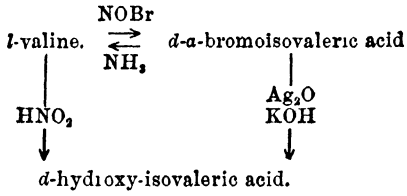


l-Trimethyl propiobetaine.

and therefore the action of ammonia by analogy should give a similar result.

Parallel results have been obtained with *l*-bromosuccinic acid, which with ammonia gives *d*-aspartic acid, whilst *l*-aspartic acid with nitrosyl bromide gives *l*-bromosuccinic acid; *l*-aspartic ester, on the other hand, gives *d*-bromosuccinic acid. From this it might be inferred that nitrosyl bromide always reacts abnormally, and that silver and potassium hydroxide act in a contrary sense. That this is not so will be seen from the following table:[2]

[1] *Ber.*, 1907, 40, 5000.
[2] Fischer and Scheibler, *Ber*, 1908, 41, 889, 2891.

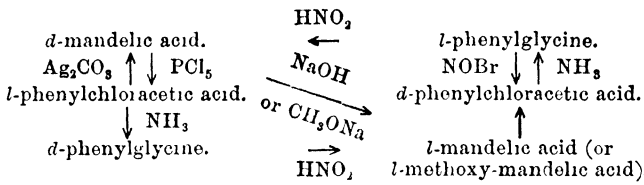


Here nitrosyl bromide and ammonia on the one hand, and potassium hydroxide and silver hydroxide on the other, act in the same sense. If, however, *d*-α-bromoisovaleric acid is first converted into the glycine derivative, the reverse changes are produced, indicating that both the former are abnormal.

d-α bromoisovalerylglycine. $\xrightarrow{NH_3}$ *d* valylglycine. $\xrightarrow{H_2O}$ *d*-valine.

Thus, as Fischer[1] has shown, the successive action of nitrosyl bromide and ammonia on *l*-valine gives the original product, from which it follows that the latter undergoes a double inversion during the process.

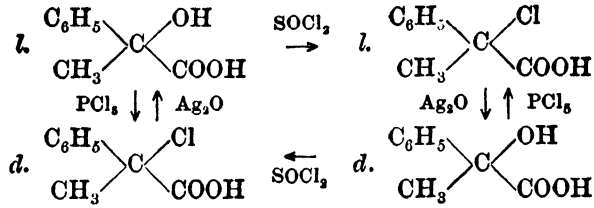
Phosphorus pentachloride, which was supposed at one time to act always normally, has been shown to produce, like the other reagents, varying results on the configuration of the product. The following scheme has been worked out by McKenzie and Clough:[2]



If the action of phosphorus pentachloride is normal (as originally suggested, seeing that the reagent produces the same result with the mandelic esters) that of silver hydroxide is also normal, whilst sodium methoxide and hydroxide behave abnormally. It should be stated that in most of the above changes a considerable amount of racemisation occurs.

If thionyl chloride is substituted for phosphorus pentachloride the opposite change occurs, that is to say, mandelic acid, as well as its ester, gives a chloro-acid of the same sign, and the same is the case with the α-hydroxy-β-phenylpropionic acid and the phenylmethyl glycollic[3] acids.[4]

[1] *Ber*, 1908, 41, 2891.
[2] *Trans. Chem. Soc.*, 1908, 93, 811; 1909, 95, 777.
[3] McKenzie and Barrow, *Trans. Chem Soc.*, 99, 1910
[4] McKenzie and Clough, *Trans. Chem. Soc.*, 1010, 97, 1016, 2566.



The fact that both acid and ester give chloro acids of the same sign, but in the inverse sense, with the two reagents (PCl_5 and $SOCl_2$) leaves it doubtful as to which represents the normal and which the abnormal reaction. It should be added that this difference in behaviour is not invariably true, for malic acid gives the same active chlorosuccinic acid with either reagent. We may therefore conclude that in all the above reactions, which include replacement of hydroxyl by halogen and the reverse, halogen by amino group and the reverse, and amino group by hydroxyl, it is impossible to predict the effect of the reagent on the configuration.

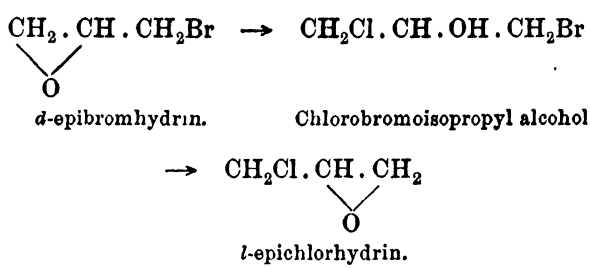
The only regularity which has resulted from the study of these changes is that recorded by Frankland and Garner,[1] namely, that the successive replacement of hydroxyl by chlorine and the latter by hydroxyl, using thionyl chloride followed by silver hydroxide, leads to inversion, and of the two alternative routes that represented by (2) has been shown to be followed by lactic acid; that is, where an alkyl group

$$\begin{array}{lll} & d.\ \text{X.Cl} \longrightarrow l.\ \text{X.OH} & (1) \\ d.\text{X.OH} \overset{(SOCl_2)}{\nearrow\searrow} & & \\ & l.\ \text{X.Cl} \longrightarrow l.\ \text{X.OH} & (2) \end{array}$$

is attached to the asymmetric carbon atom. If the change of sign represents change of configuration, then the final hydroxy compound will have the same sign and configuration as the halogen compound. A somewhat different case from any of the above is the reversal of sign produced when *d*-epibromhydrin is converted into *l*-epichlorhydrin through the successive action of hydrogen chloride, which gives chlorobromo-isopropyl alcohol, and potassium hydroxide, which eliminates hydrogen bromide.[2]

[1] *Trans. Chem. Soc.*, 1914, 105, 1101; see also Clough, *Trans. Chem. Soc.*, 1918, 113, 526, and Holmberg, *Abstr.*, 1916, i, 115; 1918, i, 309, 523.

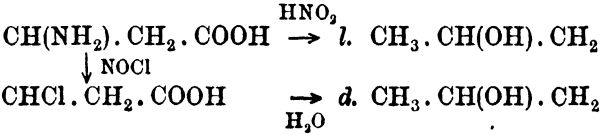
[2] Abderhalden and Eichwald, *Ber.*, 1915, 48, 1847; see also Hess and Fink, *Ber.*, 1915, 48, 1983.



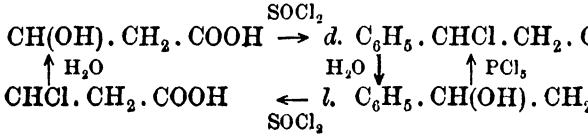
So far we have considered only those cases in which carboxyl is attached to the asymmetric carbon atom in the α-position, and the question arises as to whether a β-asymmetric carbon atom of an acid gives rise to the same kind of inversion.

Experiments have been carried out in this direction by Fischer and Scheibler[1] with l-β-hydroxybutyric acid and its methyl ester. Both give with phosphorus chloride a chloro-acid of opposite sign, which silver oxide and water convert into the original laevo acid. It may be assumed, therefore, that no inversion occurs. McKenzie and Humphries[2] found in the same way that d-β-amino-phenyl propionic acid and its ester yield with nitrous acid the same laevo acid.

But later experiments by Fischer and Scheibler[3] on the action of nitrous acid on β-amino butyric acid point in the opposite direction, as the following scheme shows :



This observation is confirmed by McKenzie and Barrow,[4] who found that d-β-hydroxy phenyl propionic acid yields with hydrochloric acid or phosphorus pentachloride a chloro-acid of opposite sign, which water reconverts into the original hydroxy-acid ; thionyl chloride has an opposite effect, and consequently in one of these changes inversion must occur.



[1] *Ber.*, 1909, **42**, 1219.
[2] *Trans. Chem. Soc*, 1910, **97**, 121.
[3] *Annalen*, 1911, **383**, 337.
[4] *Trans. Chem. Soc.*, 1911, **99**, 1915.

Among the more recent examples of inversion are those recorded by Holmberg[1] and Fitger.[2] The former converted *l*-bromosuccinic acid directly into *d*-xanthosuccinic acid by the action of potassium ethyl xanthate and indirectly by the action of the same reagent on *d*-malolactone which gave the *l*-xanthosuccinic acid, the first reaction taking place more rapidly than the second.

1. $COOH.CHBr.CH_2.COOH + SC\begin{matrix}SK\\OC_2H_5\end{matrix}$

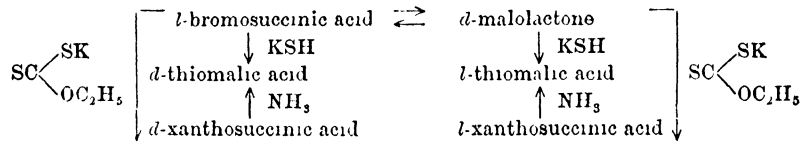
$= COOH.CH(S.CS.OC_2H_5).CH_2.COOH + KBr$

2. $COOH.CHBr.CH_2.COOH \xrightarrow{MOH} COOH.CH(O).CH_2.CO$

$\rightarrow COOH.CH(O).CH_2.CO + SC\begin{matrix}SK\\OC_2H_5\end{matrix}$

$= COOH.CH(S.CS.OC_2H_5)CH_2.COOK$

Holmberg was also able to show that the same changes could be effected by converting the same bromosuccinic acid and malolactone into the thiomalic acids by the action of potassium hydrogen sulphide

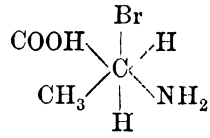


We have now to consider the theories which have been suggested to account for the phenomenon of optical inversion.

The fact that Fischer observed certain bromine additive compounds when nitrosyl bromide acted upon alanine and aspartic acid led him to view the initial stage in the action of a reagent as an additive process. Thus, by the residual affinity of the asymmetric carbon

[1] *Abstr.*, 1914, i, 139; 1916, i, 307; 1917, i, 115; 1918, i, 309, 523.
[2] *Ber.*, 1921, 54, 2948.

atom (or of some neighbouring atom), ammonia, for example, may dissociate and attach itself to bromopropionic acid in the manner indicated by dotted lines.



When hydrogen bromide is subsequently detached, the amino group may either take the place of the bromine atom (normal reaction) or there may be a rearrangement in which one of the other groups steps in with change of sign (abnormal reaction), or, finally, both reactions may occur, when more or less racemisation will be produced, such as has been observed in the case of mandelic acid and its derivatives (p. 195).

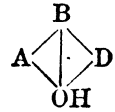
One objection which has been raised to Fischer's theory is the behaviour of trimethylamine with α-bromopropionic acid, previously described, in which the dissociation of the base, as formulated in the case of ammonia, is improbable. Moreover, the theory leaves unexplained the reason why the groups in an abnormal reaction should change their positions, a process which would appear to entail much more racemisation than is usually observed.[1]

Werner[2] offers a similar, but modified, view of the phenomenon. The reagent forms an additive compound, as explained by Fischer, by virtue of the residual affinity of the asymmetric carbon atom, which attaches it to the outer zone, and by whose attraction the new group tends to enter the inner zone. At the same time the formation of the additive compound loosens the attachment of the least stable of the original groups. The position taken up by the entrant group will be determined by the nature of the groups already present; but it does not necessarily follow that the former will take the place of the one expelled. Werner explains the case of the replacement of hydroxyl by a halogen by the formation of an additive compound with the halogen acid and subsequent removal of water.

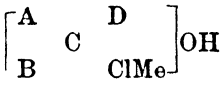
$$R_3C.OH + HX = [R_3COH_2]X$$
$$[R_3COH_2]X = R_3CX + H_2O$$

[1] Bülmann, *Annalen*, 1911, 388, 330.
[2] *Ber.*, 1911, 44, 878.

The attraction of the central carbon atom is exerted through the four planes of the tetrahedron ABD, AB(OH), AD(OH), BD(OH).



If the attraction for the halogen is exerted by one of the last three planes, the configuration of the halogen derivative will correspond to that of the original hydroxy-compound; but if the attraction is in the direction of the plane ABD then the mirror image of the first will result. Again, if the halogen is to be replaced by hydroxyl, by the aid of a metallic hydroxide, an additive compound of the structure



Me = metal

will first be formed, and the attraction of the central carbon atom for hydroxyl will depend on the nature of the metal which attaches itself to the halogen. If this attraction is exerted through one of the planes ABCl, ADCl, or BDCl, the hydroxy-compound will correspond in configuration to the halogen compound. Otherwise the enantiomorph will be formed.

Gadamer[1] has suggested a mechanism of the action of different metallic hydroxides on the halogen acids by which change of configuration may or may not occur without racemisation. When, for example, the chlorine is removed by silver hydroxide, the three residual groups, by their momentum, overshoot the equilibrium-point (which would otherwise bring them into the same plane as the carbon and so cause racemisation), and the hydroxyl group then attaches itself to the carbon so as to produce the opposite configuration. Moreover, the difference in the action of potassium and silver hydroxide is ascribed to the hydroxyl ions in the former case, producing an intermediate additive compound with the chlorine, with subsequent loss of chlorine and rearrangement without change of configuration; but to the silver ions in the latter case, which removes chlorine and produces the effect just described, with change of configuration. Other views have been put forward by Biilmann,[2] based upon Senter's investigation of the hydrolysis of halogen acids, in which it was shown that hydrolysis is dependent on the degree of dissociation of the acid. He explains the mechanism by a differ-

[1] *Chem. Zeit.*, 1912, 36, 1327 *Annalen*, 1912, 388, 330.

ence in the nature of the salts. Hydroxylation of the potassium salt is slow, and is effected by means of hydroxyl ions leading to a change of configuration, whilst with the silver salt it is rapid, and is produced by the silver ions, which unite with the halogen of the anion forming the unionised silver halide thus:

$$\begin{array}{l} CH_3 \\ | \\ CHBr \\ | \\ CO_2- \end{array} \quad \overset{+}{+Ag} = \begin{array}{l} CH_3 \\ | \\ CH+ \\ | \\ CO_2- \end{array} \quad +AgBr$$

The anion then combines with the hydroxyl ion of the water:

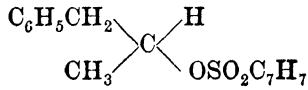
$$\begin{array}{l} CH_3 \\ | \\ CH+ \\ | \\ CO_2- \end{array} \quad \overset{-}{+OH} = \begin{array}{l} CH_3 \\ | \\ CHOH \\ | \\ CO_2- \end{array}$$

In this way no change of configuration is assumed to occur. The result is, therefore, the reverse of that required by Gadamer's theory. In the action of nitrous acid on an amino compound with replacement of the amino group by hydroxyl, direct substitution occurs, and there is no change of configuration; the action of the nitrosyl chloride and bromide is of the same character, whereas the effect of these reagents on the amino ester, which probably forms the intermediate diazo ester, may lead to a change of configuration. This view receives some support from an observation of Fischer,[1] on the one hand, and of Levene and La Forge[2] on the other. The former has shown that glucosaminic acid and its ester yield stereoisomeric hydroxy-acids; the latter has isolated from the benzal derivative of the ester the intermediate diazo compound. In other words, direct substitution is assumed to produce no change, indirect substitution a change of configuration. It is difficult to understand why racemisation does not occur in all these cases where the fourth asymmetric group is even momentarily detached, or where, as in the case of the diazo ester, asymmetry is removed.

Senter has recently shown that, in the hydrolysis of phenylchloracetic acid or the sodium salt in presence of water or alkali, it is the action of the water on the organic acid ion, and not the hydroxyl ions, which cause hydrolysis. That the solvent plays an important part in the process of inversion seems to follow from the observation

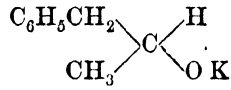
[1] *Annalen*, 1911, 381, 123; 1912 386, 374.
[2] *Journ. Biol. Chem.*, 1915, 21, 345.

of Senter and Drew,[1] who have examined the action of liquid ammonia and ammonia in different solvents (water, various alcohols, and methyl and phenyl cyanide) on active phenyl-chloracetic and phenyl-bromacetic acid. They find that the sign of rotation of the resulting phenyl-glycine varies; for example, active phenyl-chloracetic acid dissolved in liquid ammonia, in the first three alcohols of the series, and in methyl cyanide yields a product having the same sign, whereas butyl, heptyl, and benzyl alcohol induce a change of sign.[2] In the case of phenyl-bromacetic acid all the alcohols cause a change of sign, whilst liquid ammonia and methyl cyanide give a phenyl-glycine of the same sign. With phenyl-α-bromopropionic acid every solvent used produced a change of sign of the phenyl-alanine. Clough[3] has attempted to correlate optical activity and configuration on the assumption that the rotation of similarly constituted compounds possessing the same configuration are in general influenced similarly by changes in external conditions (solvent, dissolved salts, temperature) and also by the introduction of the same substituent into a given radical attached to the asymmetric carbon atom. Naturally occurring amino acids are also assumed to possess the same configuration for similar reasons. Thus *l*-lactic and *l*-glyceric acids, though opposite in sign to *d*-malic and *d*-tartaric acids, exhibit similar changes in rotation under different conditions and are therefore correlated in configuration, and for the same reason *d*-alanine and *d*-valine, though opposite in sign, are related to *l*-serine and *l*-leucine. A new light has been thrown on the subject by certain recent observations of Phillips.[4] He has been able to show that where a group attached to the asymmetric carbon atom is modified by substitution of part of the group no change in sign of rotation occurs, but may occur where the whole group is detached. The toluene-sulphonic ester of *d*-methyl-benzyl alcohol, when acted on by ethyl alcohol and potassium carbonate, gives an ethyl ether of opposite sign; but if the potassium compound of the alcohol is ethylated with toluene-sulphonic ester no change of sign occurs. The two changes are represented as follows:



C_2H_5OH

Laevo.

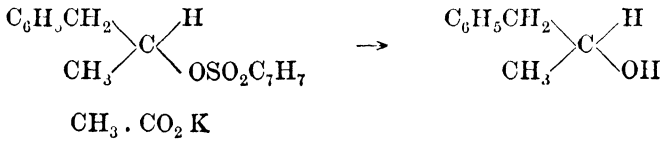


$C_2H_5.OSO_2.C_7H_7$

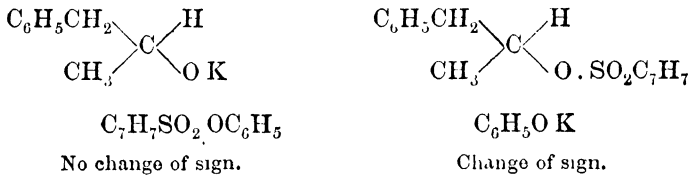
Dextro.

[1] *Trans. Chem. Soc.*, 1910, 97, 846; 1915, 107, 908.
[2] *Trans. Chem. Soc.*, 1915, 107, 638; 1916, 109, 690, 1091; 1918, 113, 140, 151.
[3] *Trans. Chem. Soc.*, 1918, 113, 526. [4] *Trans. Chem. Soc.*, 1923, 123, 44.

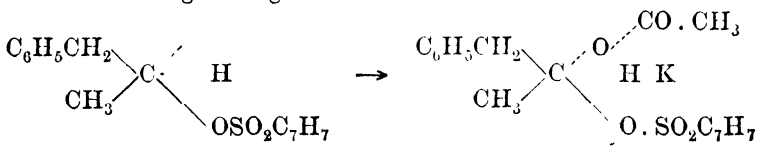
In the first case, therefore, a change of configuration is possible. Similarly the toluene-sulphonic ester of *d*-methyl-benzyl alcohol, on conversion into the acetic ester, suffers a change of sign, which is also exhibited by the alcohol derived from it,



whereas the acetic ester prepared by the action of acetic anhydride undergoes no such change, nor the alcohol which it yields on hydrolysis. In this connection it is interesting to note that on phenylating the sulphonic ester with phenyl-toluene sulphonate in which the phenyl group has a strong attachment to the oxygen atom [1] no change of sign occurs. It should, however, take place where the sulphonic ester is acted on with potassium phenate,



if the view advanced by Phillips is correct. It thus appears that where a member of the asymmetric quartet is completely detached during the reaction, the new group is forced to reverse the configuration in such a way that the inversion is complete. The mechanism of the inversion is explained by Phillips as due to the weakening effect exerted by the sulphonic ester radical on the hydrogen atom and its replacement, as in the case of potassium acetate, by the acid radical with change of sign.



[1] Lapworth and Ferns. *Trans. Chem. Soc*, 1912, 101, 273.

Asymmetric Synthesis. It was foreseen by the founders of the theory that asymmetric substances artificially produced from inactive materials would prove to be inactive. For it is clear from the identity in physical and chemical properties of the two enantiomorphs that there is no reason why a larger number of the one kind of molecules should be produced than of the other. This applies to the formation of an asymmetric carbon compound from a symmetric one, like bromopropionic acid from propionic acid, by substitution, or mandelic nitrile from benzaldehyde, by addition. It applies equally to the conversion of one asymmetric compound into another, such as inactive bromopropionic acid into lactic acid. Supposing, however, a new asymmetric carbon atom to be introduced into a compound which is already optically active, the question assumes another form. The new substance will be formed under asymmetric conditions, affording therefore the possibility of a product containing unequal quantities of the enantiomorphs relative to the new asymmetric carbon. E. Fischer was the first to show that this occurs in the formation of the synthetic sugars For example, *d*-glucose forms two cyanhydrins in very unequal quantities, whilst *d*-mannose yields only one of the two possible derivatives.[1]

Attempts were made by Cohen and Whiteley[2] to produce active substances under asymmetric conditions by reducing the pyruvic, mesaconic, and *a*-methyl cinnamic esters of *l*-menthol, and by brominating menthyl cinnamate, and then removing the active menthol by hydrolysis.

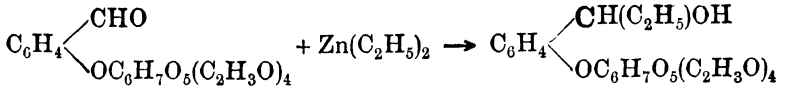
$$CH_3 . CO . COOC_{10}H_{19} \longrightarrow CH_3 . \mathbf{C}H(OH) . COOC_{10}H_{19}$$

$$C_6H_5CH : C(CH_3) . COOC_{10}H_{19} \longrightarrow C_6H_5CH_2 . \mathbf{C}H(CH_3) . COOC_{10}H_{19}$$

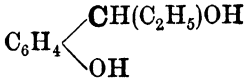
$$C_6H_5CH : CH . COOC_{10}H_{19} \longrightarrow C_6H_5\mathbf{C}HBr . \mathbf{C}HBr . COOC_{10}H_{19}$$

Fischer and Slimmer[3] attempted the same thing by introducing an asymmetric carbon atom into tetracetyl helicin by means of zinc ethyl,

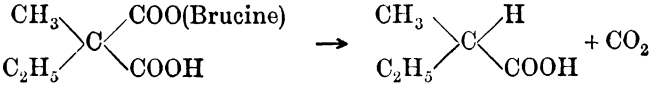
[1] Hartmann, *Annalen*, 1892, 272, 190.
[2] *Trans Chem Soc*, 1901, 79, 1305
[3] *Ber*, 1901, 34, 629; 1903, 36, 2575.



and then removing the glucose molecule; but again the results were negative.



Marckwald[1] later announced that he had accomplished an asymmetric synthesis by heating the acid brucine salt of methyl ethyl malonic acid to 170°, when carbon dioxide is split off and an active valeric acid is obtained, containing about 10 per cent. of the laevo compound.



It is clear that the brucine salt is already an asymmetric complex before carbon dioxide is removed, and can therefore exist in two active forms in the same way as the monoethyl ester of mesotartaric acid (p. 185); but seeing that the brucine is active, the two will not be strictly enantiomorphous. There is therefore the possibility of a partial resolution being effected before decomposition by the formation of unequal quantities of the two salts, in which case it would not represent a true asymmetric synthesis, but merely an ordinary process of resolution.

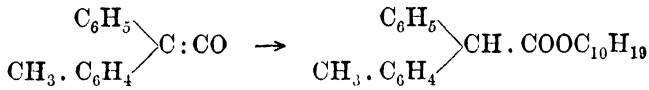
McKenzie and his co-workers,[2] using the methods suggested by Cohen and Whiteley, have been more successful. By the reduction of the *l*-menthyl or *l*-amyl esters of benzoyl formic acid and pyruvic acid they obtained on hydrolysis active mandelic and lactic acids. They also succeeded in converting menthyl benzoyl formate, by Grignard's method, into the ester of phenyl methyl glycollic acid, $C_6H_5C(CH_3)(OH)COOH$, which also gave an active acid on hydrolysis.[3] Further, by oxidising the bornyl esters of fumaric acid they obtained active tartaric acids, the *l*-borneol ester giving the *l*-acid and the *d*-borneol ester the *d*-acid.[4]

Other methods of asymmetric synthesis have been introduced by the use of enzymes. Rosenthaler[5] has shown that by combining aromatic aldehydes with hydrocyanic acid in presence of emulsin,

[1] *Ber.*, 1904, **37**, 349, 1368.
[2] *Trans. Chem. Soc.*, 1901, **79**, 1305; 1904, **85**, 1249; 1909, **95**, 544.
[3] *Trans. Chem Soc.*, 1906, **89**, 365. [4] *Trans. Chem. Soc*, 1907, **91**, 1215.
[5] *Biochem. Zeit*, 1909, **14**, 238; **17**, 257; 1909, **19**, 186; *Abstr.*, 1922, i, 480.

active cyanhydrins are formed, and Bredig and Fiske [1] have obtained similar results by effecting the union in presence of an active alkaloid. Quinine yields the cyanhydrin of *l*-mandelic and quinidine of *d*-mandelic acid. The alkaloid appears to act as a catalyst by entering into union with the compound.

Weiss combined *l*-menthol with phenyl *p*-tolyl ketene and obtained the menthyl ester of *d*-phenyl *p*-tolyl acetic acid.[2]



Physical methods have also been used for effecting the same purpose, but so far with only negative results. The fact that succinic, malonic, and cyanacetic acid lose carbon dioxide in presence of uranium salts when exposed to light led Henle and Haakh [3] to try the effect of polarized light, when passed through a magnetic field, on asymmetric derivatives of these acids, but without the desired result, and other photochemical reactions with circularly polarized light have been equally fruitless.[4]

In conclusion, it may be remarked that Pasteur's view, according to which asymmetric synthesis is to be regarded as a prerogative of life, has given rise to some discussion. Professor Japp, in his presidential address to the chemical section of the British Association in 1908, has adhered to Pasteur's view ; for, as he truly says, where the active substance is not directly elaborated by the organism, but produced by such methods as described above, 'a guiding power is exercised by the operator which is akin in its results to that of the living organism and is entirely beyond the reach of the symmetric forces of inorganic nature. Only the living organism with its asymmetric tissues, or the asymmetric products of the living organism, or the living intelligence with its conception of asymmetry, can bring about the isolation of the single asymmetric compound.'

Racemic Compounds and Mixtures. It has already been stated (p. 183) that there are two classes of inactive substances which can be resolved into their enantiomorphs, and which, in the solid form at least, present considerable differences in their properties. They are known as racemic compounds (*r*) and mixtures (*dl*). They usually differ in crystal form, in the amount of water of crystallization, in density, solubility, and melting-point. The best-known example is racemic acid, and the active tartaric acids and their salts. Racemic acid and the racemates crystallize in holohedral forms, the tartrates form hemihedral crystals. Racemic acid contains one molecule of water of crystallization ; the active tartaric acids are anhydrous. The solubility of racemic acid in water is greater than that of the tartaric acids.

[1] *Biochem Zeit.*, 1912, 46, 7.
[2] *Monatsh.*, 1919, 40, 891.
[3] *Ber.*, 1908, 41, 4261.
[4] Freundler, *Ber.*, 1909, 42, 233 ; Cotton, *J. Chim. Phys.*, 1909, 7, 81 ; Guye and Drouginine, *J. Chim. Phys.*, 1909, 7, 97.

As a rule the racemic compounds are less soluble, but it is not invariably so. *r*-Mandelic acid is more soluble than the active forms. The following are the melting-points and densities of some active and racemic types:

	Δ		*m. p.*	
	dl.	*r.*	*dl*	*r.*
Malic acid	1 595	1·601	100°	130–131°
Tartaric acid	1 754	1·666	170	140
Chlorosuccinic acid	1·687	1·679	176	153–154
Mandelic acid	1·341	1·300	130	118–119
Camphoric acid	1·186	1 228	187	202–203

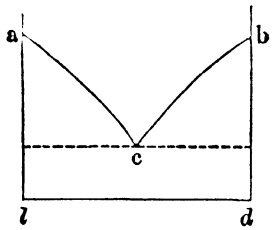
The evidence afforded by molecular weight determinations, both by the vapour-density and cryoscopic methods, as well as that derived from conductivity determinations, points to dissociation more or less complete of the racemic form into the inactive mixture on vaporisation or solution.

The criteria for distinguishing the two classes of compounds have been set forth in a very comprehensive manner by Bakhuis Roozeboom,[1] based on the phase rule. They are limited to the substances in the solid state. One method of Roozeboom consists in determining the melting-point of the substance under examination, and then adding a small quantity of one or other of the enantiomorphs. If a mixture is present, the melting-point will be raised; if the substance is racemic it will be lowered. This result will be clear from the following considerations.

The melting-point curve of the mixture of two enantiomorphs will be represented by a descending and ascending curve; for as the two substances do not combine, although they possess the same melting-point, they may be regarded as distinct individuals, and consequently the addition of successive small quantities of the one enantiomorph will lower the melting-point of the other until an equal quantity of each is present. When the quantity of the second enantiomorph exceeds that of the first, the reverse change will occur and the melting-point will rise until the original melting-point is reached. It the quantities of laevo and dextro compounds be marked off on the horizontal *ld*, and the melting-points of the mixtures on

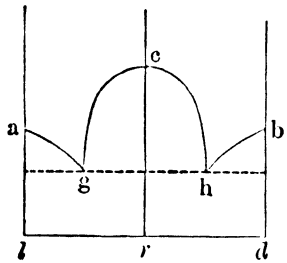
[1] *Zeit. phys Chem*, 1899, **28**, 494; see also *The Phase Rule*, p. 214, by A. Findlay, Longmans, 1904, and *Lectures on the Principles of Symmetry*, by F. M Jaeger, Camb. Univ. Press, 1917.

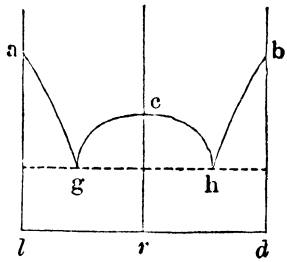
the verticals *l*a and *d*b, the curve will follow the lines ac, cb, the minimum c representing equal quantities of the two enantiomorphs, that is, the inactive mixture.



It therefore follows that the addition of one or other enantiomorph to the inactive mixture will raise the melting-point.

In the case of a racemic compound, the addition of either enantiomorph will produce melting-point curves of the following character:





For there are three individuals concerned, the dextro and laevo enantiomorphs which possess the same, and the racemic compound which has usually a different (higher or lower) melting-point. The curve may, therefore, be divided into two parts, each of which may be compared to the previous case of a simple mixture of two substances. If a represents the melting-point of the pure laevo compound, and c that of the racemic compound, and the percentages of the two be marked off on the horizontal *ld*, the curve will lie along ag, gc. The second half will be the counterpart of the first. By the addition of either enantiomorph to a racemic compound, the melting-point will consequently be lowered.[1]

It is obvious that the above methods cannot be applied to liquids which cannot be examined in the crystalline state, and the determination of the existence of a racemic compound or externally compensated mixture in such cases offers certain difficulties. Ladenburg[2] suggested that change of temperature on mixing the two enantiomorphs would indicate the existence of a racemic liquid, but such a view has been

[1] See also Bruni, *R. Accad. Lincei*, 1899, 8, i, 282; Bruni and Padoa, 1902, 11, i, 212.

[2] *Ber.*, 1894, 27, 3062, 1915, 28, 164.

shown to be untenable.[1] Other methods which have been suggested are molecular volume, viscosity values,[2] absorption power,[3] refractive index, magnetic rotation,[4] and molecular weight as determinated by Ramsay and Shield's surface tension method.[5] In most cases, however, the effect of dissociation or association leaves the result doubtful, and, in spite of the large accumulation of data, none of the methods employed can be said to have definitely established the existence of racemic liquids.

Pseudoracemic Mixtures. It is conceivable that the two enantiomorphs form neither a mixture nor a molecular complex, but are isomorphous and form mixed crystals. The effect on the melting-point produced by the addition of either enantiomorph will depend upon the composition of the mixed crystals which separate from the fused mass. If the crystals possess the same composition as the liquid mixture, the curve will be a horizontal line, and the addition of either enantiomorph will cause no change in the melting-point; otherwise it may produce a depression or rise, according to whether, on the addition of the active substance, the mixed crystals which separate from a mixture of the two enantiomorphs have a higher or lower melting-point than either constituent. Pseudoracemic mixtures were first observed by Kipping and Pope.[6]

Examples of all three kinds of mixed crystals are known.[7] Mixtures of dextro and racemic forms of 1-amyl 3-nitro and 2-amyl 3-nitro phthalic esters melt at the same temperature, the first at 116° and the second at 155°, and the same has been observed in the case of the active and inactive forms of the camphoroximes (M. P. 115°) and of the amyl phenyl carbamates (M. P. 31°). Mixed crystals showing a minimum melting-point are represented by the amyl carbamates and others showing a maximum melting-point by the carvoximes.

1-Amyl 3 nitro phthalic ester. Amyl carbamate. Carvoxime.

Melting-point curves of Pseudoracemic Mixtures.

[1] Adriani, *Zeit phys Chem*, 1900, 33, 453

[2] Dunstan and Thole, *Trans Chem. Soc*, 1908, 93, 1815; 1910, 97, 1249; 1913, 103, 19.

[3] Stewart, *Trans Chem. Soc*, 1907, 91, 1537.

[4] Pope and Peachey, *Trans. Chem. Soc*, 1899, 75, 1111; Bruhl, *Trans. Chem. Soc*, 1907, 91, 115.

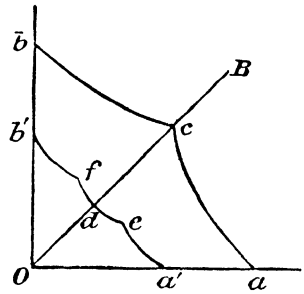
[5] Mitchell and Smith, *Trans. Chem. Soc.*, 1913, 103, 489; Gibb *Ber*, 1912, 45, 1441.

[6] *Trans. Chem Soc.*, 1897, 71, 973, 989.

[7] Marckwald and Nolda, *Ber*, 1909, 42, 1583.

An interesting case of a pseudoracemic mixture is presented by the four substances obtained by combining the two active tetrahydroquinaldines with the two active hydroxymethylene camphors (p. 192). Any two of these will crystallize together, and in this way two racemic and four pseudo-racemic mixtures are produced.[1]

A second method proposed by Roozeboom for determining the character of the two classes of inactive substances is based on solubility. The saturated solution and the inactive material in contact with it are in equilibrium at constant temperature. If the inactive substance is a mixture, the addition of either enantiomorph will not affect the number of phases, and no change in solubility will occur. If the inactive material is a racemic compound, the addition of one



of the enantiomorphs will introduce a new solid phase, and an alteration in the concentration of the solution will result.

In the figure above the vertical represents the concentration of the laevo and the horizontal that of the dextro enantiomorph; the upper solubility curve *acb* represents that of a mixture (above or below the transition point of the racemic compound). The point *c* will lie on the line *OB*, equidistant between the horizontal and vertical since the two enantiomorphs possess identical solubilities. The solubility curve for the pure racemic compound will also cut the line *OB* either above or below *c*, depending on the transition temperature, and, as in the former case, the point will be a maximum or minimum according to whether the solubility of the racemic compound increases or decreases in presence of excess of either

[1] Pope and Read, *Trans. Chem. Soc.*, 1913, 103, 1515.

enantiomorph. The curve $a'efb'$ represents the solubility curve for rubidium racemate, the transition point of which lies below that of the *dl* mixture. The addition of an excess of either enantiomorph by introducing a new phase will establish a new equilibrium, which will lie on *df* or *de* according to the enantiomorph added—in other words, the solution will be different from that of the pure racemic compound, and some of the active substance will pass into solution. This method may be combined with the use of the polarimeter. In the first case there is no change in the solution and it will remain inactive; in the second case the solution will contain a certain amount of active substance which will be revealed by the polarimeter.[1]

Partially Racemic Compounds. In addition to racemic compounds which are formed by the union of optical enantiomorphs, other active substances which are not structurally related may also crystallize together in the form of double salts. The phenomenon was first observed by Pasteur, who obtained crystals of the ammonium salt of *d*-tartaric acid in combination with an equimolecular proportion of the acid ammonium salt of *l*-malic acid. Another form of combination, to which Ladenburg[2] has given the name of *Partially Racemic Compounds*, has been observed in the case of pyrotartrate of quinine, which forms three series of salts, from one of which the *d*-acid, from a second the *l*-acid, and from the third the inactive acid was separated. The quinine in the third case must therefore have combined with the unresolved racemic acid. Strychnine also forms a racemate in the same way. Another partially racemic salt with an inactive base was prepared by Pope[3] from *r*-tetrahydropapaverine and *d*-tartaric acid, and Findlay and Hickmans[4] obtained a racemic mandelic ester of *l*-menthol. It naturally follows that the existence of partially racemic compounds may and, indeed, has been found to increase the difficulty of resolving certain inactive substances.[5]

[1] See Findlay's *Phase Rule*, p 273

[2] *Ber.*, 1898, 31, 524, 937, 1969; 1899, 32, 50.

[3] *Trans. Chem. Soc.*, 1898, 73, 902; see also Ladenburg and Fischl, *Ber.*, 1907, 40, 2279, and Ladenburg and Heimann, *Ber.*, 1908, 41, 966.

[4] *Trans. Chem. Soc.*, 1907, 91, 909.

[5] Pope and Read, *Trans Chem. Soc.*, 1910, 97, 987.

The Number of Stereoisomers. The number of possible stereoisomers increases with that of the asymmetric carbon atoms. We have seen that if one asymmetric carbon acid is present, two stereoisomers exist; if there is a second asymmetric carbon atom which is structurally dissimilar from the first, four stereoisomers are possible. Denoting the asymmetric carbon atoms by A and B, and the rotation by + and −, the following four combinations may be formed:

1.	2.	3.	4.
+A	+A	−A	−A
+B	−B	+B	−B

of which 1, 4, and 2, 3 are enantiomorphous pairs. The trihydroxyaldehydes (erythroses) furnish an example, although only three out of the possible four are actually known,

$$CHO.CH(OH).CH(OH).CH_2OH.$$

With three asymmetric carbon atoms A, B, C, eight stereoisomers are possible, which may be derived from the above four by adding +C and −C alternately to each member.

1.	2.	3.	4.
+A	+A	+A	+A
+B	+B	−B	−B
+C	−C	+C	−C
5.	**6.**	**7.**	**8.**
−A	−A	−A	−A
+B	+B	−B	−B
+C	−C	+C	−C

The enantiomorphous pairs in this case are evidently 1, 8; 2, 7; 3, 6; 4, 5.

With four asymmetric carbon atoms A, B, C, D, the number of stereoisomers is increased to sixteen, for each of the foregoing yields two derivatives by adding +D and −D, as follows:

A	+	+	+	+	+	+	+	+
B	+	+	+	+	−	−	−	−
C	+	+	−	−	+	+	−	−
D	+	−	+	−	+	−	+	−
	1	2	3	4	5	6	7	8

A	−	−	−	−	−	−	−	−
B	+	+	+	+	−	−	−	−
C	+	+	−	−	+	+	−	−
D	+	−	+	−	+	−	+	−
	9	10	11	12	13	14	15	16

Thus the number of stereoisomers, in which n represents that of the asymmetric carbon atoms, is given by the expression 2^n. Examples of stereoisomers with three and four carbon atoms are given in the chapter on sugars (Part III, p. 13), where the method of determining their configuration is also discussed.

If the asymmetric carbon atoms are not structurally distinct, as in the case of tartaric acid (p. 183), the above expression must be modified, for the inactive indivisible type is introduced and the number of active forms is consequently fewer. Thus, if A and A represent two similar asymmetric carbon atoms, the following combinations may occur:

1.	2.	3.	4.
+ A	+ A	− A	− A
+ A	− A	+ A	− A

It is obvious from what has been previously explained that 2 and 3 are identical and correspond to the meso type (p. 178). Thus, instead of four, the number of stereoisomers is reduced to three, namely, two active and one inactive, by internal compensation.

Pseudo-asymmetry. If there are two similar asymmetric carbon atoms attached to a central carbon, which, in addition, binds two different groups as in trihydroxyglutaric acid,

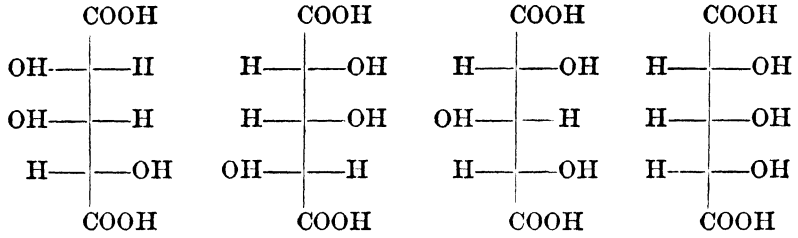
COOH . CH(OH) . CH(OH) . CH(OH) . COOH

the problem becomes more involved. If A and B represent as before the asymmetric carbon atoms and C the central carbon atom, the following combinations are possible. Let us assume, in the first place, that the end groups A and A have the same configuration, that is, are both + or both − ; they are identical, and the central carbon C possesses no asymmetry. Suppose, however, that the end groups have a different sign, two things happen; the activity of the end carbon groups is neutralized, but, at the same time, the central carbon atom becomes asymmetric and can exist in enantiomorphous forms. Four stereoisomers are thus possible, two active and two inactive, belonging to the meso type. They may be denoted by the following scheme,

in which O stands for absence of central asymmetry, and +C, −C for enantiomorphous configuration of the central carbon:

1.	2.	3.	4.
+A	−A	+A	+A
O	O	+C	−C
+A	−A	−A	−A

Experiment in the case of the trihydroxyglutaric acids supports this conclusion, for there are four stereoisomers, namely, two active and two inactive, which will probably have the following configurations:



m. p 127° *m. p.* 127° *m. p* 152° *m. p.* 170–171°

d- and *l*-Trihydroxyglutaric acids. *i*-Trihydroxyglutaric acids.

The case is a curious one, for, although the central atom C in the two inactive forms has no effect on the sign of rotation, it produces, by virtue of the difference in configuration, a change in the properties. This form of asymmetry is known as *pseudo-asymmetry.*[1]

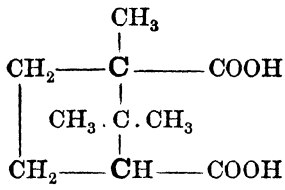
Stereoisomers with two pairs of Asymmetric Carbons. If the two end and two central carbon atoms of an open chain form two pairs of structurally similar asymmetric groups, A and B, as in the saccharic acids,

$$\underset{}{\text{COOH}}.\underset{\text{A}}{\text{CH(OH)}}.\underset{\text{B}}{\text{CH(OH)}}.\underset{\text{B}}{\text{CH(OH)}}.\underset{\text{A}}{\text{CH(OH)}}.\text{COOH}$$

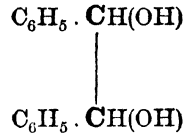
the number of isomers is no longer represented by the expression 2^n, which would give sixteen in the present case, but is reduced to ten. For when A, A and B, B have opposite signs inactive forms are produced of the meso type, which reduces the number by two, whilst each outer or inner pair may separately form a neutral group, which reduces it by four more. In the scheme on pp. 220, 221, configurations 4, 13 and 6, 11 become meso forms and represent two stereoisomers, whilst 2, 9; 3, 14; 5, 12; 8, 15 contain one neutral group and represent four instead of four pairs of stereoisomers.

[1] If n be the number of asymmetric carbon atoms in the molecule and all are different the number of possible active isomers is 2^n, if internal compensation occurs without pseudo-asymmetry the number is 2^{n-1}, and if there is pseudo-asymmetry it becomes $2^{n-1} - 2^{\frac{n-1}{2}}$ (F. M. Jaeger, *Lectures on the Principles of Symmetry*, p. 246).

Asymmetric Carbon in Cyclic Compounds. The optical activity of cyclic compounds has been traced to the same cause as that which determines the rotation of open chain compounds, namely, the presence of an asymmetric carbon atom. The asymmetric carbon may form part of the ring, as in camphoric acid, or be present in the side-chain as in hydrobenzoin.

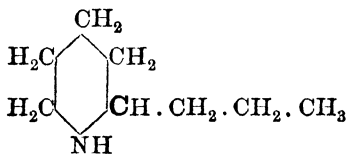


Camphoric acid.



Hydrobenzoin.

Stereoisomerism is manifested in the same manner as in open chain compounds, the only difference lying in the unusually larger rotation caused by the cyclic formation. If one asymmetric carbon atom is present as in conine, two optical enantiomorphs exist.

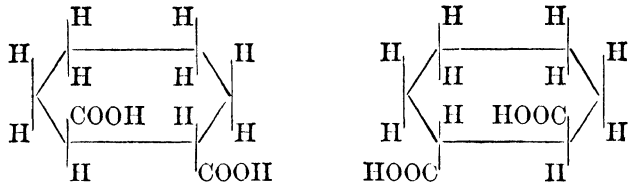


Conine.

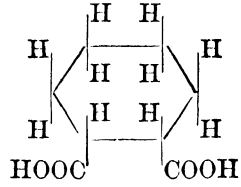
If two structurally different asymmetric carbon atoms are present, as in camphoric acids, two pairs of enantiomorphs (*dl*-camphoric and *dl*-isocamphoric acid (Part III, p. 265)) are produced. If the two asymmetric carbon atoms are structurally similar two active forms (*dl*-isohydrobenzoin) and one meso form (hydrobenzoin) can exist. The case is in fact precisely analogous to that of the tartaric acids. The symmetrical dialkyl succinic acids which exist in two inactive (racemic and meso) forms (p. 186) find a counterpart in the hexahydrophthalic acids (see p. 278). Like dimethylsuccinic acid, the racemic form of hexahydrophthalic acid[1] has been resolved into its enantiomorphs.

For simplicity the two enantiomorphs and the meso form of hexahydrophthalic acid are represented by hexagons, which must be viewed as if in perspective, that is, in a plane at right angles to that of the paper. The angles are occupied by the carbon atoms (omitted), to each of which two bonds are attached at right angles to the hexagonal surface.

[1] **Werner and Conrad, *Ber.*, 1899, 32, 3046.**

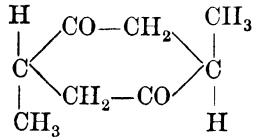


d- and *l*-Hexahydrophthalic acids.

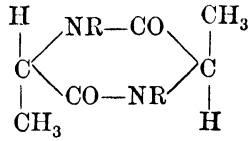


i-Hexahydrophthalic acid.

Pseudo-symmetry in Cyclic Compounds. A curious example of an inactive indivisible type is afforded by the diketohexamethylene derivatives and the diketopiperazines of the following formulae[1]:

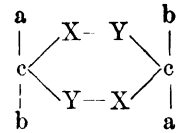


Dimethyl diketocyclohexane.



Dimethyl diketopiperazine.

They possess the general structure:



Now such a compound contains two structurally similar asymmetric carbon atoms, and, although strictly without any plane of symmetry, its reflected image is identical with it. Yet it does not accord with the meso type, since the two halves divided by the dotted line do not stand in the relation of object and image.

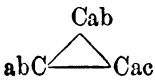
Attention was first drawn to the exceptional character of this configuration by Ladenburg,[2] who called the plane of symmetry *pseudo-symmetrical*, or, according to Groth, *compound symmetrical*. It divides the compound into halves, which become object and image when one half is revolved through 180°. It contains what

[1] The ring and the attached groups are assumed to be in planes at right angles to one another, as previously explained.

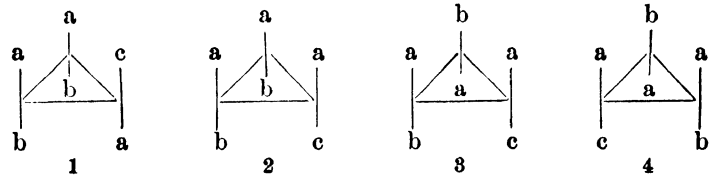
[2] *Ber.*, 1895, 28, 1996.

has been termed a *centre of symmetry*, or, in other words, a line drawn from one of the groups a or b through the centre will meet a similar group if produced beyond the plane of the ring. In the isomeric or *cis* dimethyl piperazine there is no such centre of symmetry, and consequently it exists in optically active forms.[1] Compounds which exhibit pseudo-symmetry in structure represent an inactive indivisible type.

Pseudo-asymmetry in Cyclic Compounds. Pseudo-asymmetry of the character of the trihydroxyglutaric acids (p. 222) is afforded by cyclopropane derivatives of the general formula:



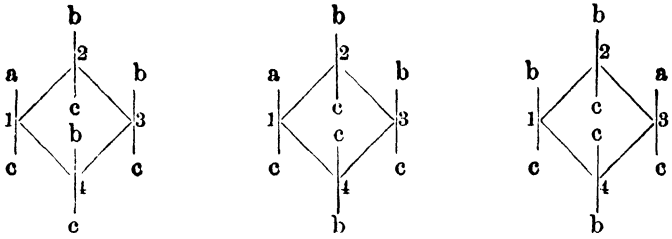
It may stand for the following configurations, in which the carbon atoms of the ring are represented as situated at the corners of a triangle lying at right angles to the plane of the paper:



Models illustrating these configurations may be easily constructed out of triangles of cardboard by thrusting pins through the corners. The head and point of the pin may stand for a, b, whilst c may be indicated by touching one point with coloured sealing-wax. Other cyclic configurations can be made in the same way from squares, pentagons, &c., of cardboard.

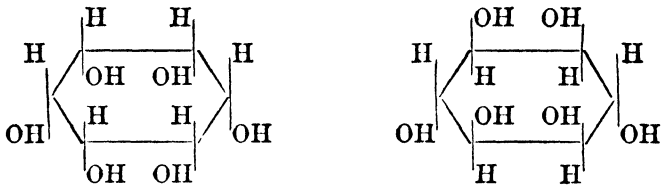
The first two of the above figures correspond to inactive meso compounds; the last two are optical enantiomorphs. The reasoning is the same as that which accounts for the existence of four trihydroxyglutaric acids. An example of this kind of isomerism is furnished by the three inactive 2.5-dimethylcyclopentane 1-carboxylic acids of J. Wislicenus,[2] which probably represent one racemic and two meso forms. Another curious example of stereoisomerism referred to by Werner[3] is furnished by a cyclobutane ring of the following types:

[1] Fischer, *Ber.*, 1906, 39, 467, 3981; Pope and Read, *Trans. Chem. Soc.*, 1912, 101, 2325; 1914, 105, 219; Barker and Marsh, *Trans. Chem Soc.*, 1913, 103, 837.
[2] *Ber.*, 1901, 34, 2572. [3] Werner's *Lehrbuch der Stereochemie*.

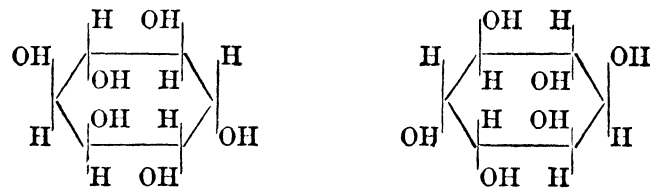


The cyclic carbon atoms 2 and 4 are asymmetrical *per se*; 3 is symmetrical though structurally identical with 2 and 4. It follows from what has been stated above that 1 and 3 are pseudo-asymmetric, that is to say, it is a case of a double trihydroxyglutaric acid, and there may consequently exist four inactive meso compounds by interchanging separately a and c and b and c in I, and also two racemic compounds derived from II and III by interchanging one of the groups a, c or b, c.

Optical Activity with Pseudo-asymmetry. Finally, a form of pseudo-asymmetry causing optical activity has been pointed out by van 't Hoff in the case of the inositols. Ordinary inositol from beans and flesh is a meso compound, and, therefore, has a symmetrical configuration of either of the following forms:

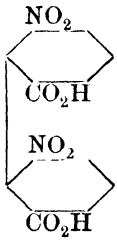


There are in addition *d*- and *l*-inositol $(\alpha)_D = \pm 65°$ obtained by Maquenne[1] from pinite (methyl *d*-inositol) and quebrachite (methyl *l*-inositol) to which van 't Hoff attaches the following space formulae, corresponding to a non-superposable object and image:

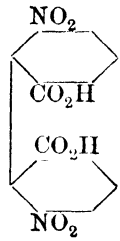


[1] *Ann Chim. Phys.*, 1891 (6), 22, 264; *Compt. rend.*, 1889, 109, 812.

A new kind of molecular asymmetry leading to optically active forms has been observed by Kenner and Stubbings [1] in the case of the dinitrodiphenic acids, the following structure being based on a suggestion of Kaufler.[2]



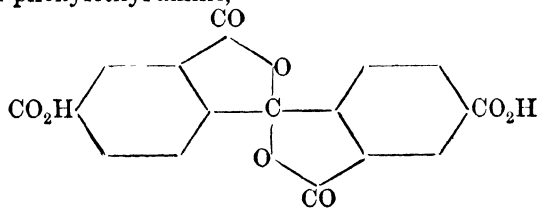
cis form.



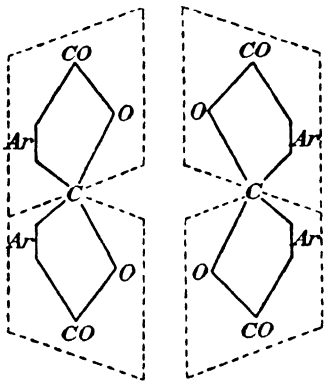
trans form.

The hexagons must be regarded as lying in a plane at right angles to the paper. According to this view, the second or *trans* form possesses no plane of symmetry and could therefore be resolved into its enantiomorphs by crystallization of the brucine salts.

Molecular asymmetry is also present in benzophenone tetracarboxylic acid lactone prepared by Mills and Nodder,[3] and was resolved by means of phenylethyl amine,



the stereoisomeric forms being represented as viewed in perspective by placing the rings in planes at right angles to one another.



Enantiomorphs of benzophenone tetracarboxylic lactone.

[1] *Trans. Chem. Soc.*, 1921, 119, 593; 1922, 121, 614; 1923, 123, 779, see also Cain and Micklethwaite, *ibid*, 1914, 105, 1438. [2] *Annalen*, 1907, 351, 151.
[3] *Trans. Chem. Soc.*, 1920, 117, 1407; 1921, 119, 2094.

The relation of cyclic compounds to what is known as 'geometrical' or 'cis-trans' isomerism is discussed in a later chapter (p. 252).

Activity of Benzene Derivatives. The question as to whether the unreduced benzene molecule, without asymmetric carbon in the side-chain, could under any conditions be rendered asymmetric, and consequently optically active, has frequently been the subject of experimental investigation. Le Bel[1] attempted to resolve *o*-toluidine; Lewkowitsch[2] has done the same with *m*-methylsalicyclic acid,

$$C_6H_3(\underset{1}{CH_3})(\underset{2}{COOH})\underset{3}{OH}$$

and *o*-methyl-*m*-hydroxybenzoic acid,

$$C_6H_3(\underset{1}{OH})(\underset{2}{CH_3})(\underset{3}{COOH})$$

whilst V. Meyer and Lühn[3] have employed nitro- and aldehydothymotic acids for the purpose.

$$C_6H.OH.COOH.CH_3.C_3H_7.NO_2$$
$$C_6H.OH.COOH.CH_3.C_3H_7.CHO$$

In no single case was the attempt successful. It may be further added that no simple benzene derivative showing optical activity has been found among the many products of this class elaborated by living matter.

NUMERICAL RELATION OF ROTATARY POWER TO STRUCTURE.

Determination of Rotatory Power.—The rotatory power of an optically active substance is determined by means of a polarimeter. One of these instruments known as Laurent's polarimeter is shown in Figs. 32 and 33.

The monochromatic light of a sodium flame is commonly used in these determinations, and is obtained by suspending in the flame of a Mekker burner a platinum wire basket containing fused sodium chloride or the more volatile bromide. The latter gives a brighter flame, but the basket requires replenishing more frequently. The light from the flame passes through a cell B, containing a solution of potassium dichromate (or a crystal of this substance), which deprives it of blue or violet rays. It then passes through the polarizing nicol prism P. A plate of quartz cut parallel to the optic axis covers half the opening D, and is of such a thickness that it

[1] *Bull. Soc. Chem.*, 1882 (2), **38**, 98.
[2] *Trans. Chem. Soc.*, 1888, **53**, 781; *Ber.*, 1888, **16**, 1576.
[3] *Ber.*, 1895, **28**, 2795.

produces a difference of a half-wave length (or an exact odd multiple of a half-wave length) between the two rays, which it gives by double refraction. The light then passes through the substance placed in the tube T and entering at E strikes the analysing nicol N. The telescope OH is focussed on the edge of the quartz plate at D. When N is turned, a pointer moves over the graduated circle C and its position can be read by means of the lens L.

The Theory of the Instrument may be explained as follows: If, after passing through the nicol P, the plane of vibration is in the

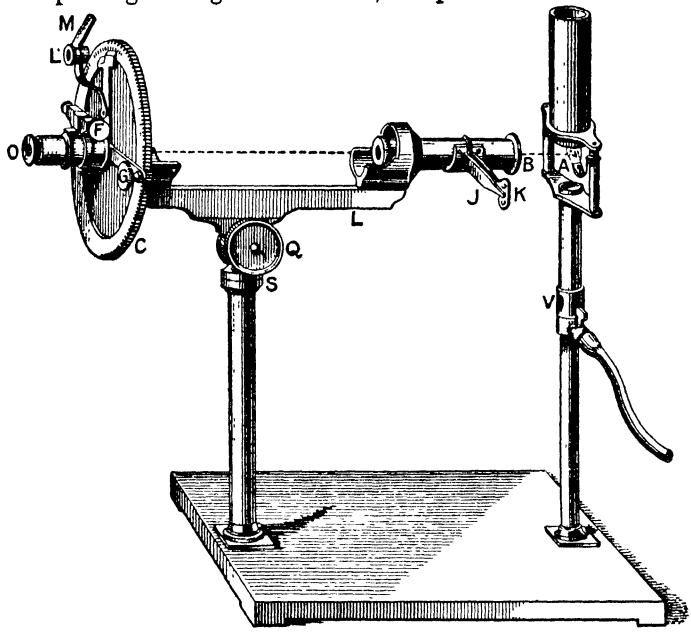


FIG. 32

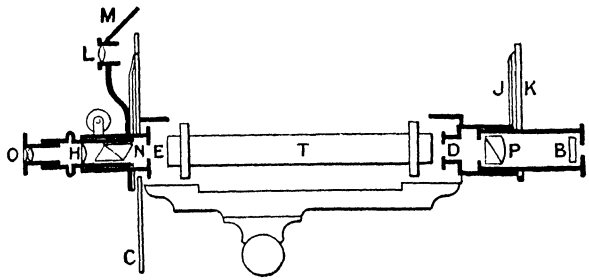


FIG. 33.

direction OB, Fig. 34*a*, then in the half of the field to the right, uncovered by the quartz plate, it passes on unchanged. When it

strikes the quartz the ray is broken up into the two components *Oy* and *Ox*. These traverse the quartz with different velocities, and since one ray is retarded half a wave-length in respect of the other, the vibration of one component will be represented by *Oy*, but the other must be represented by *Ox'* instead of *Ox*. These two combine on emerging to a plane polarized ray vibrating in the direction *OB'* so that the angle *AOB'* is equal to the angle *AOB*.

If now (the tube containing water or other non-rotating liquid) the nicol N be so placed that it is parallel to nicol P, then the light, in the half of the field to the right, will pass through unchanged, but only a portion of the light which has passed through the quartz diaphragm with its plane of vibration in the direction *OB'*, will pass through N, and consequently there will be different intensities of illumination in the two halves of the field, Fig. 34*b* (if the angle α is 45° then the angle *BOB* will be 90°, and the light in the left half of

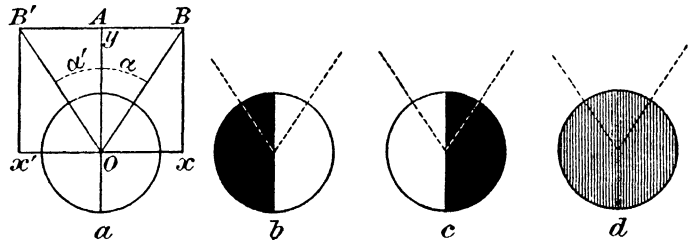


FIG. 34.

the field will be completely obscured). Similarly if the plane of the nicol N be made parallel to *OB'* there will be a greater intensity of illumination in the left half of the field, Fig. 34*c*. Between the two positions of the nicol N there must necessarily be one which gives uniform illumination of the whole field, and this is the zero point of the instrument, Fig. 34*d*.

If the tube T, containing the active substance, be interposed between the two nicols, then both rays *OB* and *OB'* will be rotated through equal angles, and to re-establish uniform illumination in the two halves of the field, the nicol N must be turned through an angle equal to the angle of rotation, which is then measured on the divided circle.

When the angle α is small, i.e. when the plane of vibration of the polarized light is almost parallel to the optic axis of the quartz, the greatest degree of sensitiveness is attained, for then a very small change in the position of N causes a great difference in the respective illuminations in the two halves of the field. As α increases, the

sensitiveness diminishes, but a greater total intensity of illumination is obtained. By moving J (Fig. 32) the position of the nicol P may be altered. For clear, colourless liquids the angle α may be made comparatively small; but in the case of coloured liquids it is necessary to have α larger, and so obtain a greater intensity of light at the cost of sensitiveness.

Calculation of Results; Homogeneous Liquids. The angle of rotation, represented by α_D (for sodium light), varies with the length of the column of substance through which the light passes. One decimetre has been chosen as unit of length. The angle also varies with the temperature, which must consequently be determined for each observation.

For the comparison of the rotatory power of different substances, use is made of the constant *specific rotation*, which may be defined as the angle of rotation, produced by 1 gramme of active substance in 1 c.c. by a layer 1 dm. in length. This is obtained by dividing the observed angle of rotation by the product of the length in decimetres l, and the density of the substance d at the temperature at which the observation was made. If a weighed quantity of the substance is examined in solution, d will stand for the weight in grammes in 1 c.c. of solution.

$$[\alpha]_D^t = \frac{\overset{t}{\alpha_D}}{l \times d}.$$

Molecular Rotation is the above quantity multiplied by the molecular weight M of the compound, and divided by 100 to avoid unwieldy numbers, and is represented thus:

$$[M]_D^t = \frac{[\alpha]_D^t \times M}{100}.$$

It expresses the angle of rotation of 1 mm. of active substance containing 1 gramme-molecule in 1 c.c.

For determining rotations at different, but constant, temperatures the polarimeter tube may be surrounded by a jacket resembling a Liebig condenser, through which water, or other liquid or vapour, may be passed at constant temperature.

Rotatory Dispersion.[1] It does not follow that the value for the specific rotation for the sodium D line is the same as that for other kinds of light, in fact, Biot found that the rotation is inversely as the square of the wave-length, or $[\alpha] = \kappa/\lambda^2$, so that by plotting the

[1] Lowry and Dixon, *Trans. Faraday Soc.*, 1914, 10, 54.

reciprocal of the rotation against the squares of the wave-lengths the values will generally be found to lie on a straight line. It has been usual to represent rotatory dispersion by what is termed the *dispersion coefficient*, that is, the ratio of the rotations for any two kinds of light conveniently wide apart in the spectrum, as, for example, the violet and green light of the mercury-vapour lamp.[1]

As Patterson[2] has shown, the rotations for different kinds of light are influenced to a different degree by concentration, solvent, and especially by temperature, and that the coefficient is subject to considerable variation. In order, therefore, to institute a satisfactory comparison it is necessary to select some fixed point as the zero, such, for example, as that of the intersection of the rotation curves for two different wave-lengths when the substance, or its solution, is examined under different conditions. This is termed the *rational zero*, and the ratio of the rotation values calculated from this zero will then be found to give a fairly constant dispersion coefficient.

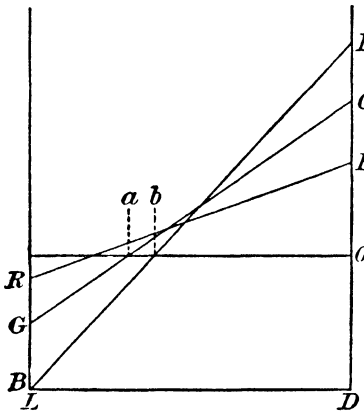


FIG. 35

It is also an interesting fact observed by Armstrong and Walker[3] that the rotation values for different wave-lengths, when plotted against that of some other wave-length as reference, generally lie on straight lines.

The rule laid down by Biot that the rotation varies inversely as the wave-length, which is termed *normal dispersion*, is not always true, for there are cases where, under certain conditions, the reverse obtains, that is to say, the rotation increases or decreases with increase or decrease of the wave-length. This is called *anomalous dispersion*.[4] Biot[5] himself has shown that anomalous dispersion may be produced artificially by mixing the substances of opposite sign and different dispersion, such as *d*-camphor and *l*-turpentine oil. If the rotations, say, for blue, green, and red, are plotted as ordinates against different proportions of the two ingredients as abscissae, the

[1] The ratio of a_v/a_g for normal dispersion varies between 1·8-2·0 and is not altered appreciably by rise of temperature or solvent. Biot's value, as Lowry has shown, is not quite correct, but is given more exactly by the Drude equation $a = k/(\lambda^2-\lambda_0^2)$, where k is the 'rotation constant' and λ_0^2 is the dispersion constant of the substance, λ_0 being the wave-length of the dominant absorption band, so that if the band were removed into the extreme ultraviolet λ_0^2 would become negligible and Biot's law would hold. The value of λ_0 cannot as a rule be directly determined, but can be ascertained experimentally from the Drude equation (*Trans. Chem. Soc.*, 1913, 103, 1067; 1919, 115, 800; 1922, 121, 532).

[2] *Trans. Chem. Soc.*, 1916, 100, 1176; *Science Progress*, 1922, 65, 60.

[3] *Proc. Roy. Soc.*, 1913, 88 A, 392.

[4] *Die anomale Rotations dispersion*, by H. Grossmann and M. Wreschner, Ahrens' *Vortrage*, 1921, 26, 259.

[5] *Ann. Chim. Phys*, 1852, 36, 405.

curves might intersect in their passage from the pure laevo-compound to the pure dextro-compound as shown in Fig. 35 in such a way that above the zero line at *a* the green and at *b* the blue might show a smaller rotation than the red and the dispersion coefficient would be a fraction instead of a positive integer, in other words, would be anomalous reaching $-\infty$ at the zero line.

Tschugaeff[1] has produced anomalous dispersion by forming the ester of *l*-menthol with *d*-β-camphorsulphonic acid. As these two substances, like the above mixture, have opposite signs of rotation and different dispersions, the rotation curve of the dissolved substance instead of steadily increasing from red to blue reaches a maximum between the green and blue.

Anomalous dispersion has also been observed in solutions of certain coloured substances, the effect appearing to depend on the vicinity of an absorption band in the visible region or in colourless substances, when it is associated with a band in the ultra-violet. These observations have been explained on Drude's theory of rotatory polarization depending on the spiral movement of electrons.[2] But there are other cases of anomalous dispersion, which have, as yet, received no satisfactory explanation. This is the case with the esters of tartaric acid, with naphthylmethyl- and naphthylhexyl-carbinols, and with a number of esters of secondary alcohols.[3] By comparing the rotation curves of various tartaric esters and their derivatives at different temperatures, also in different solvents and at different concentrations, Patterson[4] found that displacement of the curve took place in one direction or another, so that, by combining the effects, he was able to extend very considerably the length of the curve. In this way he showed that the esters exhibit well-marked maxima and minima, and, although the conditions under which these substances were examined differed, the actual value of the rotations at these points indicated a close correspondence. Moreover, by using different kinds of light he found that the curves for the different wave-lengths do not run parallel throughout the whole curve, but intersect at certain fixed points, and so produce anomalous dispersion. Thus, if the curve for red light having the lower rotation crosses that for violet with the higher rotation, in a region beyond the point of intersection, the relative value of the rotation will be reversed, and the phenomenon of anomalous dispersion will appear.

[1] *Ber.*, 1911, 44, 2026.

[2] *Anomalous Rotatory Dispersion*, by L. Tschugaeff, *Ber.*, 1909, 42, 2246; *Trans. Faraday Soc.*, 1914, 10, 28; see also *Annual Reports*, 1914, p. 17.

[3] Pickard and Kenyon, *Trans. Chem. Soc.*, 1914, 105, 830; Pickard and Hunter, *ibid.*, 1923, 123, 434.

[4] *Trans. Chem. Soc.*, 1916, 109, 1139.

Activity of Homogeneous Liquids. We will consider first the simple case, in which a solvent is unnecessary, and where the liquid or fused substance is directly examined.

Activity of Homologous Series.[1] The effect of the active radical in a homologous series seems, as a rule, to be influenced (raised or lowered) by the first term or terms and then to remain nearly constant in the succeeding members. Tschugaeff has made the following series of observations:

Menthol $[M]_D = -78{\cdot}0°$

	$[M]_D$		$[M]_D$
Menthyl formate	−146·3	Menthyl *n*-valerate	−157·3
,, acetate	−153·7	,, *n*-caproate	−157·[illegible]
,, propionate	−160·2	,, *n*-heptate	−157·7
,, *n*-butyrate	−159·6	,, *n* caprate	−155·8

In another series of esters of active amyl alcohol examined by Guye and Chavanne[2] the same thing has been observed.

That the active group is mainly affected by the group in its vicinity is further shown by the rotation constants of the amyl and menthyl esters of benzoic acid and its side-chain homologues, where the values drop to those of the aliphatic esters.

Ester.	Amyl $[M]_D$.	Menthyl $[M]_D$.
Benzoate	+9·52	−239
Phenylacetate	+7 91	−190·7
Phenylpropionate	+4·73	−161·9
Mean value of the aliphatic ester	+4·33	−157·8

Although the proximity of the phenyl group to the active radical usually raises the rotation, this is not always the case. The phenyl group in the esters of carvoxime produces the reverse effect.[3]

Menthyl ester.	$[M]_D$.
$C_{10}H_{14}$ NOH	
$C_{10}H_{14}$: NO . CO C_6H_5	81
$C_{10}H_{14}$ NO . CO . CH_2 . C_6H_5	77 7
$C_{10}H_{14}$ NO . CO . CH_2 . CH_2 . C_6H_5	77 9

[1] An excellent summary on the quantitative relation of rotation to structure is given by P. F. Frankland, *Trans. Chem. Soc.*, 1912, 101, 658.

[2] *Compt. rend.*, 1895, 120, 152.

[3] Rupe and Wolfsleben, *Annalen*, 1912, 395, 136.

Pickard and Kenyon[1] prepared three series of active secondary alcohols, namely, methyl R carbinols, ethyl R carbinols, and isopropyl R carbinols (R = alkyl) with the following results:

In the first (methyl) series the rotations of the homogenous liquids increase regularly with the molecular weights; in the third isopropyl series they increase rapidly to C_4H_9 and then remain nearly constant. In the second (ethyl) series there are sudden increments at the 5, 10, and 15 carbon radicals and also similar but smaller increments when the whole chain makes 5 or a multiple of 5 carbon atoms. The explanation suggested by Frankland[2] is that 'according to the commonly accepted views of stereochemistry a continuous chain of five carbon atoms will all but return upon itself and beyond this, further additions to the chain will lead to such interference as must necessitate a readjustment of the exact positions occupied by the carbon atoms in a shorter chain. It is surely highly probable that this stereochemical change should be betrayed by some irregularity in the rotatory manifestations, for example, by the exhibition of a maximum rotation in those series in which the ascent of the series leads to an increase in the rotatory power.[3] As the effect is emphasized in alcoholic solution, Pickard and Kenyon consider that it is important not to restrict observations to homogeneous liquids. As we shall see (p. 242) a solvent may produce a considerable extension of the rotation curve. Reviewing the results obtained by themselves and others, they conclude that there does not appear to be any simple numerical relation between the various values obtained for the molecular rotatory powers of the members of any homologous series.[3]

Activity of Unsaturated Compounds. A very large number of observations have been made on the effect of unsaturation on activity. Rupe[4] from the results of his earlier investigations laid down the general rule that unsaturated groups usually produce an enhanced rotation, which falls off with the increased distance of the unsaturated from the active radical.

The following table, where the saturated and unsaturated compounds are contrasted, illustrates the first part of this rule:

Menthyl ester.	$[M]_D$.	Menthyl ester.	$[M]_D$.
α Methyl acrylic acid	−205·5	Isobutyric acid	−162·9
Crotonic acid	−203·9	*n*-Butyric acid	−159·5
Angelic acid	−200·8	α Methyl butyric acid	−153·6
β Methyl crotonic acid	−210·9	β Methyl butyric acid	−153·7

[1] *Trans. Chem. Soc.*, 1911, 99, 45; 1912, 101, 620, 1427; 1913, 103, 1923; see also Clough, *Proc.*, 1913, 29, 357.
[2] *Trans. Chem. Soc.*, 1899, 75, 868.
[3] *Trans. Chem. Soc.*, 1913, 103, 1930.
[4] *Annalen*, 1908, 327, 157.

whilst the next table illustrates the second part, showing the increase in rotation with the proximity of the double bond:

Menthyl ester	$[M]_D$	Menthyl ester	$[M]_D$
$\alpha\beta$ Pentenic acid	−177·1	$\alpha\beta$ Hexenic acid	−172·4
$\beta\gamma$,,	−172·5	$\beta\gamma$,,	−164·1
$\gamma\delta$,,	−160·2	$\gamma\delta$,,	−153·5
		$\delta\epsilon$,,	−154·4

Further experience has shown that, although these rules hold good in the case of aliphatic compounds, the introduction of phenyl groups produce unaccountable irregularities depending on the position of the phenyl group in relation to the double bond, as may be seen from the following table, in which the unsaturated ester exhibits in some cases a higher, in others a lower, rotation than the corresponding saturated compound. This lowering of the rotation is especially noticeable in the unsaturated phenyl derivatives.[1]

Menthyl esters.	$[M]_D$	Menthyl esters	$[M]_D$
Muconic acid	−390·4	Piperic acid	−187·8
$\alpha\beta$ Hydromuconic acid	−372·8	$\alpha\beta$ Hydropiperic acid	−165·0
$\beta\gamma$ Hydromuconic acid	−339·3	$\beta\gamma$ Hydropiperic acid	−150·8
Adipic acid	−352·8	Piperonylbutyric acid	−136·8

Brucine salt.	$[M]_D$	Brucine salt	$[M]_D$
Muconic acid	− 90·4	Piperic acid	− 28·6
$\alpha\beta$ Hydromuconic acid	−359·0	$\alpha\beta$ Hydropiperic acid	−154·3
$\beta\gamma$ Hydromuconic acid	−356·5	$\beta\gamma$ Hydropiperic acid	−179·1
Adipic acid	−397·8	Piperonylbutyric acid	−170·5

Rupe[2] has examined aromatic menthyl esters which are unsaturated in the nucleus and others which are unsaturated in the side-chain, with the following results:

Menthyl ester	$[M]_D$	Menthyl ester	$[M]_D$
Terephthalic acid	−153·4	Benzoic acid	−239
$\Delta^{1,4}$ Dihydroterephthalic acid	−463·9		
Δ^1 Tetrahydroterephthalic acid	−308·6	Δ^1 Tetrahydrobenzoic acid	−200
Δ^2 Tetrahydroterephthalic acid	−338·9	Δ^2 Tetrahydrobenzoic acid	−159·2
Hexahydroterephthalic acid	−334·7	Hexahydrobenzoic acid	−159·6

[1] Hilditch, *Trans. Chem. Soc.*, 1908, 93, 700, 1388, 1618; 1909, 95, 289; 1910, 97, 223, 1091, 2110; 1911, 99, 218.

[2] *Annalen*, 1910, 373, 126.

In the case of those esters which are unsaturated in the side-chain considerable differences in rotation are noticeable in the position which an alkyl or aryl radical occupies in relation to the unsaturated carbon atoms. The corresponding saturated compounds are given for comparison:

Menthyl ester.	$[M]_D$	Menthyl ester	$[M]_D$
Cinnamic acid	−220·1	Hydrocinnamic acid	−168·5
α Methylcinnamic acid	−187·8	α Methylhydrocinnamic acid	−153·2
β ,,	−198·1	β ,,	−230·3
α Phenylcinnamic acid	−193·4	α Phenylhydrocinnamic acid	−313·2
β ,,	−137·3	β ,,	−224·7

Both Frankland and Rupe[1] are of opinion that unsaturation leads to an irregularity in the rotatory effect, though not necessarily to an increased rotation.[1]

Activity of Conjugated Compounds. The effect of conjugation on rotatory power has also been studied by Rupe[2] and Hilditch.[3] According to the former the effect of the two conjugated linkages increases the rotation. The following table illustrates the effect of a single double bond in the $\alpha\beta$ and $\beta\gamma$ positions and also of a conjugated double bond, as well as that of the saturated ester:

Menthyl ester.		$[M]_D$.
Caproic acid	$CH_3.CH_2\ CH_2.CH_2.CH_2.COOH$	−157·7
$\alpha\beta$ Hydrosorbic acid	$CH_3.CH_2.CH_2.CH{=}CH.COOH$	−172·3
$\beta\gamma$ Hydrosorbic acid	$CH_3.CH_2.CH{=}CH.CH_2.COOH$	−164·1
Sorbic acid	$CH_3.CH{=}CH.CH{=}CH\ COOH$	−221·4

Curiously enough this is not the case with dimethyl sorbic acid, as the following table shows:[4]

Menthyl ester.	$[M]_D$.
$(CH_3)_2C\ CH.C(CH_3){:}CH.COOH$	166·2
$(CH_3)_2CH\ CH{:}C(CH_3)\ CH_2\ COOH$	191·8
$(CH_3)_2CH.CH_2.CH(CH_3).CH_2.COOH$	161·8

The anomaly is explained by the attachment of the additional alkyl groups to the doubly linked carbon atom which is known to have a marked effect on the refractivity of such compounds (p. 28).

The effect of the replacement of the end methyl group by phenyl

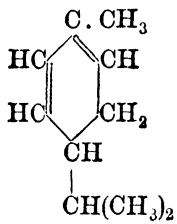
[1] Frankland, *Trans. Chem. Soc.*, 1912, 101, 661; Rupe, *Trans. Faraday Soc.*, 1914, 10, 5.
[2] *Annalen*, 1910, 369, 311. [3] *Trans. Chem. Soc*, 1909, 95, 1570.
[4] Rupe and Lotz, *Annalen*, 1909, 369, 344; 1915, 409, 330.

is seen in the following table, which includes for comparison the aliphatic esters:

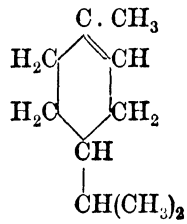
Menthyl ester.	$[M]_D$.	Menthyl ester.	$[M]_D$.
Acetic acid	−153·7	Benzoic acid	−239
Propionic acid	−160·2	Phenylacetic acid	−190·7
n-Butyric acid	−159·5	β-Phenylpropionic acid	−161·9
Caproic acid	−157·7	Phenylvaleric acid	−107·0
β γ-Hydrosorbic acid	−164·1	δ-Phenyl β γ-pentenic acid	−149·3
Sorbic acid	−221·4	Cinnamenylacrylic acid	−234·4

From the first three and the last member of the series it appears that the presence of phenyl raises the rotation, but with diminishing effect as the distance of the phenyl group from the menthyl radical increases. The low rotation of phenylvaleric and phenylpentenic esters is, however, as inexplicable as that of the unsaturated phenyl compounds referred to above.

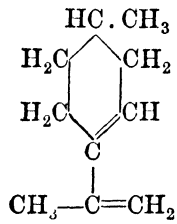
The effect of conjugation in increasing rotation is also apparent from a comparison of the rotations of phellandrene and carvomenthene and of *p*-menthadiene and *p*-menthene.



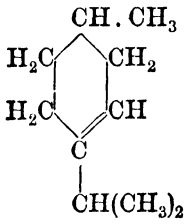
Phellandrene.
$[M]_D + 82·1°$



Carvomenthene.
$[M]_D - 2·9°$



p Menthadiene.
$[M]_D + 133·6°$



p-Menthene.
$[M]_D + 45·2°$

The high rotation of the menthyl ester and brucine salt of oxalic acid compared with those of other saturated dibasic acids has been ascribed by Hilditch[1] to conjugation of the group O : C − C : O, and

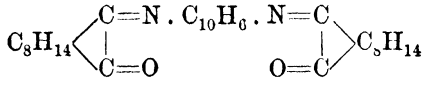
[1] *Trans. Chem. Soc.*, 1909, **95**, 1578; 1911, **99**, 224.

this increase has been shown to exist in other compounds containing the ketone group conjugated with an ethenoid linkage.

Some remarkably high rotations have been observed in the group O: C – C = CHR as the result of conjugation. Such substances have been obtained by the action of aldehydes on camphor and thujone.[1]

	$[M]_D$		$[M]_D$.
Benzylidene camphor	+1020·3	Benzylidene thujone	+1416·3
Piperonylidene camphor	+1236 5	Piperonylidene thujone	+2172·6
Cuminylidene camphor	+1397 8	—	—
Camphor	+ 67·2	Thujone	+ 113·2

By increasing the number of conjugated groups, as in 1·4 naphthylene-bis-imino camphor, B. W. and M. Singh [2] observed the remarkably high rotation of $[M]_D = 8175°$ in chloroform.[3]



1·4 Naphthylene-bis-imino camphor.

In the few instances where acetylene derivatives have been prepared it is found that the effect is not referable to any rule, since they sometimes fall below both the ethylenic and saturated compound and sometimes exceed them, as will be seen below [4]:

Ester of	Acid $[M]_D$.		
	β-Phenyl propionic.	Cinnamic.	Phenyl propiolic.
l-amyl alcohol	+ 5°	+ 16·4	+ 12·1
10 % benzene	−178·3	−235·5	−215·9
l-menthol 10 % chloroform	−171·5	−171·6	−166 7
10 % acetone	−162 6	−184·3	−157·6
d-borneol 10 % chloroform	+ 86 5	+ 82 5	+ 87·6
10 % acetone	+ 82·9	+ 82·6	+ 89·4
d-methyl hexylcarbinol	+ 82·1	+104·4	+131·1
l- ,,	− 32·8	−103·4	−130·9

Activity of Cyclic Compounds. It is perhaps difficult to institute a satisfactory comparison between open and closed chain compounds, but on the whole it may be affirmed that the latter show an enhanced rotation. Anhydrides and lactones show a

[1] Hilditch, *Trans. Chem. Soc*, 1909, 95, 333.

[2] *Trans. Chem. Soc.*, 1920, 117, 1599; see also Forster and Thornley, *ibid.*, 1909, 95, 942, and Forster and Saville, *ibid.*, 1921, 119, 791.

[3] Some of the active metalammine salts of Werner exhibit much higher rotations (*Ber.*, 1914, 47, 3087).

[4] Hilditch, *Trans. Chem Soc*, 1908, 93, 1; Pickard and Kenyon, *Trans. Chem Soc.*, 1911, 99, 46.

much higher rotation than the acids from which they are obtained. Lactide, $[\alpha]_D = -86°$, is obtained from lactic acid, $[\alpha]_D = +3°$. It is, therefore, scarcely surprising that the presence of a cyclic radical should produce a corresponding effect. Haller and Desfontaines[1] have converted a series of β-methyladipic esters into methylcyclopentanone carboxylic esters and found in each case a largely increased rotation:

$$\begin{array}{c} CH_2 . CH_2 . COOCH_3 \\ | \\ (CH_3)CH . CH_2 . COOCH_3 \\ [\alpha]_D = +3{\cdot}49° \end{array} = \begin{array}{c} CH_2 . CH_2 \\ | \quad \diagdown CO \\ (CH_3)CH . CH . COOCH_3 \\ [\alpha] = +91{\cdot}07° \end{array} + CH_3OH$$

Although it is generally recognized that ring structure increases rotatory power, this only occurs if the asymmetric atom forms part of the ring system. Otherwise only small and indefinite effects are produced.

Menthyl ester.	$[M]_D$	Menthyl ester.	$[M]_D$.
Cyclopropane dicarboxylic acid	−153·5	*n*-butyric acid	−159·6
Cyclobutane ,,	−164 4	*n*-valeric ,,	−157 3
Cyclopentane ,,	−171·3	*n*-hexoic ,,	−157·7
Cyclohexane ,,	−157·2	*n*-heptoic ,,	−157·7

Activity of Structural Isomers. No general rule determining the relation of activity to structural isomerism can be laid down, seeing that the sign and value of the rotation is influenced by the nature and, more especially, the position of the groups. This would follow from the facts contained in the paragraph on homologous series. The normal and iso-esters of active amyl alcohol, on the one hand, or active valeric acid, on the other, show very small differences:

Amyl *n*-butyrate	$[\alpha]_D = +2\,97°$	*n*-Butyl valerate	$[\alpha]_D = +10{\cdot}60°$
,, iso- ,,	,, $= +2\,83$	Iso- ,,	,, $= +10\,48$

But amylacetic acid differs considerably in rotation from amyl acetate, and methyl valerate from amyl formate:

Amylacetic acid	$[\alpha]_D = +8\,53°$	Methyl valerate	$[\alpha]_D = +16{\cdot}83°$
Amyl acetate	,, $= +2{\cdot}50$	Amyl formate	,, $= +2{\cdot}01$

[1] *Compt. rend*, 1905, 140, 1205.

Activity of Position Isomers. Conditions similar to those which determine the activity in an homologous series appear to obtain where the effect of the *o*-, *m*-, and *p*-positions on the rotation of the active radical is considered, that is to say, the group nearest to the active radical usually produces the largest effect. The following rule may be laid down: that the rotatory effect produced by an ortho-substituent in benzoic ester differs more from that of unsubstituted ester than do those of the meta and para substituents. The following table will illustrate this point:[1]

Menthyl ester.	$[M]_{D.}^{20}$		
	ortho	meta.	para.
Toluic acid	−231	−240	−246
Methoxybenzoic acid	−148	−247·5	−250 5
Propoxybenzoic acid	−170·5	−240·5	−250
Isoamyloxybenzoic acid	−186·5	−240·5	−247·5
Fluorobenzoic acid	−194·5	−236	−239
Chlorobenzoic acid	−195	−237	−237
Bromobenzoic acid	−205	−239	−239
Iodobenzoic acid	−237	−237	−237
Nitrobenzoic acid (65°)	−381	−251	−235

Menthyl benzoate $[M]_{D.}^{20} = -239$.

This effect is even more apparent in the disubstituted benzoic esters in which the 3.4, 3.5, and 2.6 derivatives are taken for comparison.

Menthyl ester.	$[M]_D$.		
	2.6	3.5	3.4
Dichlorobenzoic acid	−113	−233	−227·5
Chlorobromobenzoic acid	− 32·5	−237	−208 } Cl Br −221 } Br Cl
Dibromobenzoic acid	− 19·5	−228	−231
Chloronitrobenzoic acid at 100°	−237	−248	−207·5 } Cl NO_2 −229·5 } NO_2 Cl
Dinitrobenzoic acid (in benzene solution) at 20°	−612	−246	−470

It follows, therefore, that the ortho-substituent may either raise or lower the rotatory power; but whichever occurs the effect of the same substituent in the meta and para positions is insignificant.

Effect of Halogens on Rotatory Power. The rotations of halogen substituted menthyl esters of the aliphatic acids have been

[1] Cohen and Dudley, *Trans.*, 1910, 97, 1787 · Cohen, *Trans.*, 1911, 99, 1060.

examined by Tschugaeff,[1] Cohen,[2] and Hilditch,[3] with the result that the introduction of the halogen, as a rule, raises the rotatory value, which tends towards a constant in the higher members of the series. It is an interesting fact that the effect of the three halogens is in the inverse order of their atomic weights, a fact which is also noticeable in the substituted benzoic acids given in the above table.

Activity of Stereoisomers. In spite of similarity of structure and molecular dimensions the effect on the rotation of the same optically active substance by the introduction of stereo- or geometrical-isomeric radicals[4] is very marked. Walden[5] has made a series of observations on the active amyl esters of fumaric and maleic acid and their derivatives, of racemic and mesotartaric acid and of *r*- and *i*-dimethylsuccinic acid.

	$[\alpha]_D$.		$[\alpha]_D$.
Fumaric ester	+5·93	Bromofumaric ester	+5·99
Maleic ,,	+4 62	Bromomaleic ,,	+4·58
Chlorofumaric ester	+5·78	Mesaconic ,,	+5 93
Chloromaleic ,,	+4 03	Citraconic ,,	+4 14
Racemic ,,	+3·37	Dimethyl succinic (*r*)	+3 66
Mesotartaric ,,	+4 77	,, ,, (*i*)	+3 42

It will be seen from the foregoing summary of the relation of rotatory value to constitution that, although certain regularities appear among the more closely related compounds, nothing in the way of a broad generalization has yet been drawn from the data at present available.

Activity of Solutions. The part which the solvent plays in modifying the activity of the dissolved substance is frequently very marked and difficult to interpret; but the recent work of T. S. Patterson on the relation of solvent to active solute promises to throw new light on the problem.[6]

Non-electrolytes. Some substances, like turpentine oil and nicotine, seem to be very little affected by the presence of a solvent. The specific rotation, calculated from observations of the pure liquid or of the solutions of different strengths in alcohol, acetic acid, and benzene, gives the same result. In other cases the influence of the

[1] *J. Russ. Phys. Chem Soc.*, 1902, 34, 606.
[2] *Trans. Chem. Soc*, 1911, 99, 1061. [3] *Trans Chem Soc.*, 1912, 101, 202.
[4] Geometrical isomerism is explained on page 238, et seq.
[5] *Zeit. phys. Chem.*, 1896, 20, 377.
[6] *Trans. Chem. Soc.*, 1916, 109, 1139.

solvent is very great. For example, ethyl *l*-mandelate in acetone, $[\alpha]_D = -90{\cdot}6°$, in chloroform $-180°$, although the molecular weight in both solvents is normal. Still larger differences have been observed with ethyl tartrate, which shows a rotation $[\alpha]_D = +65°$ when dissolved in α-nitronaphthalene and $[\alpha] = -19°$ in ethylene bromide.[1] The effect of the solvent on the magnitude of the rotation depends also on both temperature and concentration. Biot[2] observed that an aqueous solution of tartaric acid shows an increase in specific rotation, with decreasing concentration, and he found later that camphor in alcohol or acetic acid exhibits the reverse phenomenon. Landolt[3] says, 'this has since been substantiated for a very great number of substances. . . . So far we do not recognize any connection between the direction of this variation and the chemical nature of the active substance.' Since this paragraph was written the observations on the effect of both temperature and concentration on the rotation of active substances in different solvents have

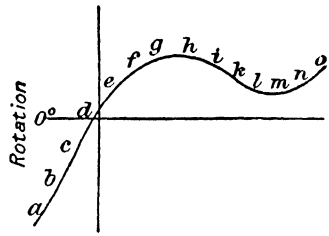


FIG. 86.

accumulated, and brought us a little nearer to a satisfactory interpretation of what have, until now, seemed somewhat confusing data. Patterson[4] has shown that the effect of temperature, solvent, and concentration on tartaric ester and its derivatives is merely to shift the position of the rotation curve. By taking the maximum point as the fixed point for comparison, for example, *g* in the ideal curve, Fig. 86, he observed that the substitution of the ethyl ester by the propyl ester causes a slight displacement of the maximum. Again, the effect of solution in the case of ethyl tartrate is to displace this maximum towards a lower temperature and a higher value in certain solvents, and towards a higher temperature and a lower value in others. Finally, it was noticed that certain derivatives of the tartaric

[1] Patterson, *Trans*, 1908, 93, 1836.
[2] *Mém. de l'Acad*, 15, 93; *Ann. Chim. Phys.*, 1844 (3), 10, 385.
[3] *Optical Activity and Chemical Composition*, p 20.
[4] *Trans. Chem Soc*, 1916, 109, 1139; *Proc. Roy Soc. Ed*, 1919, 39, 18; see also *Science Progress*, 1922, 65, 60.

esters had minimum values at definite temperatures, which in certain solvents moved in the same direction as the maximum in ethyl tartrate. Thus, in the above Fig. 36, the temperature-rotation curve for ethyl tartrate is represented by the section *c–h*; in a solvent such as nitrobenzene the portion of the curve *g–k* comes into view with increasing dilution; if quinoline is used as solvent the section *i–m* appears. On the other hand, if acetylene tetrabromide is the solvent, the curve alters in the opposite direction, towards *c–f*. In this way the different points on the curve may be moved about as regards temperature by the use of different solvents. For example, the maximum $[M]_D = 30{\cdot}9°$ for the homogeneous ester which occurs at about 175°, is found at about 30° in a 20 per cent. nitrobenzene solution having $[M]_D = 51°$. By using other derivatives of tartaric ester in different solvents, and at different concentrations and temperatures, a further extension of the curve has been obtained.

Although at present no explanation is forthcoming of the relation of solvent and temperature to activity, that such a relation exists is in itself a fact of great significance, and seems much the most valuable achievement in this line of research.

The sensitiveness of an active compound to the influence of small differences of structure in a solvent has attracted the attention of many observers. The view originally advanced by Patterson of a relation existing between the rotation of the solute and the molecular solution volume, due to variations in internal pressure produced by the solvent, is now regarded as untenable;[1] but, although there is an absence of agreement between the two values, it does not exclude the correlation of rotation and internal pressure. Another view which has been suggested to explain the effect of different solvents on the activity of the solute is the existence of compound molecules of solvent and solute. In neither case is the evidence conclusive. Nevertheless, a number of interesting observations have been made on the nature of dynamic isomerism and of position isomerism by observations on changes of rotation produced by the solvent on the active substance.[2]

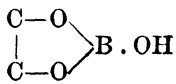
Electrolytes. The observation of Oudemans and Landolt, that the solutions of salts of active acids and bases attain a constant value with dilution, is a natural consequence of the theory of electrolytic dissociation to which Hädrich[3] first drew attention. Lan-

[1] *Trans. Chem. Soc*, 1910, 97, 2112.
[2] Patterson, *Trans. Chem. Soc*, 1907, 91, 504; 1909, 95, 822; 1910, 97, 2110; 1912, 101, 26.
[3] *Zeit. phys Chem*, 1893, 12, 476.

dolt[1] found that equivalent quantities of different tartrates in dilute solution possess the same rotation independently of the metal present, whilst Oudemans[2] obtained the same result with salts of the active alkaloids. From this generalization, which is known as the law of Landolt-Oudemans, it naturally follows that the rotation of an active salt, composed of both active acid and base, depends upon the combined activity of the two ions, a result which has been confirmed by Walden from the behaviour of the α-bromocamphor-sulphonates of morphine and cinchonine.

The change of sign in the rotation of malic and tartaric acids on dilution cannot be explained in this way, and it has been attributed to the presence of molecular aggregates in the concentrated solution of opposite rotation, just as crystal aggregates of a compound have been found which differ in sign from their solutions. Imperfect electrolytes, like the organic acids, exhibit in solution a series of changes which depend generally on the degree of dissociation. The extent of dissociation is increased by dilution and by rise of temperature, with a corresponding numerical change in rotation. The effect of different solvents may also be accounted for on the dissociation hypothesis.

Influence of Added Substances. The presence of inactive inorganic compounds sometimes influences the rotation of an active substance in a very sensible degree. It may be due to various causes, to an alteration in the degree of dissociation, to dynamic isomerism (see p. 329), to the formation of new compounds, or to some unexplained change in constitution. The activity of tartaric acid is increased three to four times by the addition of boric acid, and many of the polyhydric alcohols are affected in the same manner. The change in this case is attributed to the formation of a ring structure which corresponds with its chemical and physical behaviour, and its enhanced rotation.[3] The ring formation will be of the following type, in which the hydrogen atoms of two hydroxyls are replaced by attachments to the boron atom:



The increased activity which tartaric acid and the tartrates undergo

[1] *Ber*, 1878, 6, 1077.

[2] *Annalen*, 1879, 197, 48; 1881, 209, 38; *Rec. Trav. Chim. Pays Bas*, 1884, 1, 18; 1886, 4, 166. Tykociner, *Rec. Trav. Pays Bas*, 1, 144.

[3] *Zeit. phys. Chem.*, 1890, 6, 58; 1892, 9, 280.

on conversion into tartar emetic, and the alkali boryl and arsenyl tartrates, is accounted for in the same way. The addition of molybdates, tungstates, and uranyl salts[1] greatly increases the rotation of malic and tartaric acid, and is probably due to the formation of complex acids depending apparently on the presence of a CH(OH) group, for no increase occurs in the chloro- and bromo-succinic acids where the group is absent. The increased conductivity of boric acid in presence of active tartaric acid is referred to on p. 264.

Mutarotation.[2] It has long been known that freshly prepared solutions of certain sugars change in rotation on standing. The specific rotation of glucose sinks to one-half before becoming constant. The phenomenon was therefore termed *birotation.* But when the rotation of other sugars was found to diminish to a less extent than one-half, whilst that of maltose was observed to increase on standing, the name was changed from birotation to *multirotation.* As the latter term implies some simple ratio between the original and final values, the word *mutarotation* recently adopted by Lowry, which postulates neither increase nor decrease in any special ratio, but merely indicates a change in either sense, is to be preferred. The following table shows the initial and final rotations of a series of natural sugars:[3]

Substance.	*Initial* $[\alpha]_D$	*Final* $[\alpha]_D$
d-Glucose	110°	52·5°
d-Fructose	−140·0	−93·0
d Mannose	−14°	14°
Galactose	140°	80·4
Lactose	86°	55·3°
Maltose anhydride	118·7	137·0
Arabinose	184°	104·5
Xylose	100°	19·2
Rhamnose	−7°	+9·4
Fucose	−112·0	−77·0
Melibiose	171°	143°

The change, which frequently takes several hours to complete, may be hastened by boiling the solution, or by adding certain reagents, such as ammonia or other alkali. Many other groups of substances exhibit this change of rotation, which is clearly indicative of an alteration in the structure or configuration of the molecule.[4] It is a subject of the greatest possible interest and is more fully discussed in the chapter on isomeric change (p. 329) and on the sugars (Part III, p. 54).

[1] Walden, *Ber*, 1897, 30, 2889.
[2] C. S. Hudson, *J. Amer. Chem. Soc.*, 1910, 32, 889.
[3] Parcus and Tollens, *Annalen*, 1890, 257, 160.
[4] Pope and Read, *Trans. Chem. Soc.*, 1909, 95, 171.

Optical Superposition. According to van 't Hoff the optical effect of each asymmetric group is retained independently of the other asymmetric groups present in the compound, so that the total effect is the sum of the activities of all the asymmetric groups. This relation has been termed by Guye and Gautier[1] *optical superposition.* It has been experimentally tested by Guye and by Walden[2] in the following way, which on reflection will be seen to afford no proof of van 't Hoff's proposition. Suppose the rotation of an ester, composed of an active alcohol A and an inactive acid B, is known, and also that of a second ester, composed of the inactive variety of the same alcohol A with one of the active acids of B, the two compounds will be represented as follows:

(1) A (Active.) + B (Inactive.)

(2) A (Inactive.) + B (Active.)

On summation of the results the inactive alcohol and acid cancel and leave

(3) A (Active.) + B (Active.)

In other words, if two liquids (1) and (2) are mixed, the observed rotation will be due to the compound of active alcohol A with active acid B. The problem may be viewed in another way: (1) is a mixture of two esters, namely, active alcohol, which we will suppose to be the dextro enantiomorph, with *d*- and *l*-acid, and (2) is also an assumed mixture of *d*-acid with *d*- and *l*-alcohol:

(1) dA, dB + dA, lB

(2) dA, dB + lA, dB

Now adding the two specific rotations is equivalent to mixing equal quantities of the two liquids. The compounds dA, lB and lA, dB are strictly enantiomorphous according to the theory, and will produce inactivity, leaving the active compound dA, dB, which comprises half of each original mixture (1) and (2), so that the combined effect gives the rotation dA, dB, that is, the sum of the rotations (1) and (2).

The following observations of Walden confirm the above theoretical deduction:

[1] *Compt rend.*, 1894, 116, 740, 952.
[2] *Zeit. phys Chem.*, 1895, 17, 721.

	l. i.	i l.	l. l.	Calculated
Amyl lactate	−6 38	+2 64	−3·93	−3·74
Amyl mandelate	−96 46	+2·76	−94·02	−93 70
Amyl malate	−9·92	+3·50	−6 88	−6·42
	d. i.		d. l.	
Amyl phenylchloracetate	+23·31	+3·23	+26·79	+26·54
Amyl chlorosuccinate	+21·56	+3·75	+25·15	+25·31
Amyl tartrate	+14·10	+3·37	+17·73	+17 47

It is clear that the result does not touch the question of the optical value of a particular group. In point of fact there is very definite evidence that the optical activity of a group is determined by its environment in the molecule and has no fixed value.[1]

Rosanoff has deduced this from Walden's own observations. If the configurations of the asymmetric groups in *l*-amyl *d*-tartrate $[M]_D = +50\ 66°$ and *l*-amyl *l*-tartrate $[M]_D = -31{\cdot}12°$ do not influence one another's rotation, the two esters should show the same differences in regard to the rotation of *l*-amyl mesotartrate, which Walden found to be $[M]_D = +13{\cdot}83°$, but the differences are far from being identical.

In the same way Patterson and Kaye [2] have shown that the menthyl esters of the three diacetyl tartaric acids have respectively the rotations $[M]_D = -226°$ (dextro), $-382°$ (laevo), and $-280°$ (meso), showing differences of 54° between dextro and meso and 102° between laevo and meso form. Tschugaeff[3] has attacked the problem in a somewhat different fashion. By combining the three tartaric esters with *l*-menthyl carbimide $C_{10}H_{19}N{:}CO$, and with *l*-fenchyl carbimide, $C_{10}H_{17}N\ CO$, he has produced urethanes in which the asymmetric groups in the two combined compounds have different rotations and dispersions, thus producing what Tschugaeff terms compounds of intramolecular abnormal dispersion. Here the difference between the observed and calculated values in chloroform and acetone solution only varies by 1 to 5 per cent. He considers that 'the superposition rule is valid at least to a first approximation'.

Theory of Guye and Crum Brown. Assuming optical activity to be a function of the asymmetry of the molecule, we are still ignorant of any direct connection between the two whereby the magnitude of the rotation may be measured in terms of the dimensions of the radicals composing the asymmetric molecule. Crum Brown[4]

[1] Rosanoff, *J. Amer. Chem Soc*, 1906, 28, 528.
[2] *Trans. Chem. Soc.*, 1907, 91, 705. [3] Tschugaeff and Glebko, *Ber.*, 1918, 46, 2752.
[4] *Proc Roy Soc. Edinb.*, 1890, 17, 181.

suggested that if each of the radicals possesses a function K which determines its rotation, the differences between these functions will give the rotation of the molecule. He concluded from experimental evidence that the function increases with the size of the radical. Guye [1] has approached the subject from a similar, but broader, standpoint. The amount of asymmetry is determined by the displacement of the centre of gravity of the regular tetrahedron from its six planes of symmetry. The six values are measured by the distances of the six perpendiculars drawn from the centre of gravity to these six planes of the regular tetrahedron, and when multiplied together form what he terms the *product of asymmetry.* If $d_1 \ldots d_6$ denote these distances, the product of asymmetry P is given by the expression:

$$P = d_1 \times d_2 \times d_3 \times d_4 \times d_5 \times d_6.$$

As a first approximation Guye assumed the tetrahedron to be regular, and estimated the values of $d_1 \ldots d_6$ from the difference of the masses m_1, m_2, m_3, m_4 of the four radicals located at the summits. If $m_1 > m_2 > m_3 > m_4$ represent the order of magnitude of the masses the above expression becomes:

$$P = \frac{(m_1 - m_2)(m_1 - m_3)(m_1 - m_4)(m_2 - m_3)(m_2 - m_4)(m_3 - m_4)}{(m_1 + m_2 + m_3 + m_4)^6}.$$

This expression satisfies the following essential conditions, that if two groups are identical it equals zero, that is, the substance becomes inactive; also, if two groups are interchanged, it becomes negative, which signifies a change of sign, that is, the formation of the enantiomorph. The results of the above expression may be stated as follows:

1. If the masses of any two radicals become equal, $P = 0$, that is, optical activity will vanish.

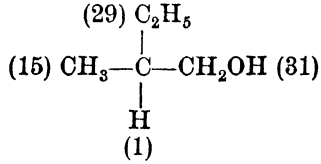
2. If m_1 increases or m_4 diminishes in value, P increases, and consequently the rotation will rise. Other relative changes will produce a rise or fall in rotation.

3. If there is a change of sign of 1, 3, or 5 of the factors, it will be followed by a change of sign of P. For example, when m_2 becomes greater than m_1, the first factor becomes negative, and the compound, which we may suppose was originally dextro-rotatory, now becomes laevo-rotatory, the amount depending on the differences between the masses of the groups in question.

To test his theory, Guye compared the rotatory power of forty-three compounds derived from active amyl alcohol.

[1] *Compt. rend*, 1890, 110, 714; 1891, 111, 745; 1892, 114, 478; 1893, 116, 1133, 1378, 1451, 1454; 1894, 119, 906; 1895, 120, 157, 452, 632, 1274, &c.

Active amyl alcohol has the formula:

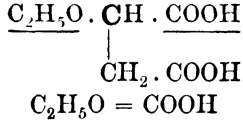


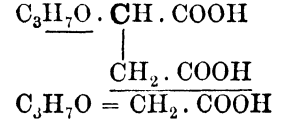
in which the masses of the radicals are in the order $CH_2OH(31) > C_2H_5(29) > CH_3(15) > H(1)$. On increasing the mass (m_1) of the carbinol radical (R) there should be a corresponding increase in rotatory power. The following are some of the numbers obtained:[1]

R.	m_1.	Rotation.
CH_2CN	40	1° 16′
CH_2SH	47	1° 7′
CH_2Cl	49·5	1° 6′
$CH_2 . CO_2H$	59	3° 20′
CH_2Br	94	4° 24′
CH_2I	142	8° 20′

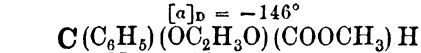
The numbers agree well with the theory. Nevertheless the hypothesis in its original simplicity has not been supported by the results of subsequent research. Guye himself soon discovered that two different groups of equal mass did not destroy optical activity.

If active amyl alcohol is oxidised to the aldehyde, there are present in the molecule an ethyl ($C_2H_5 = 29$) and an aldehyde group ($CHO = 29$), both of which represent equal masses, yet the compound is active. Purdie[2] has shown the same thing in the case of ethoxy- and propoxy-succinic acids,

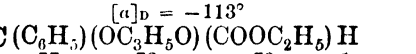




and Walden has produced many similar examples, thus:



Acetyl mandelic (methyl) ester.



Propionyl mandelic (ethyl) ester.

Walden[3] has subjected the theory to a still more searching criticism. He found that the acyl derivatives of the malic esters have a nearly equal rotation irrespective of the mass of the acid radical.

[1] *Ann. Chim. Phys.*, 1893 (6), 25, 146. [2] *Trans. Chem. Soc.*, 1895, 67, 946.
[3] *Zeit. phys. Chem.*, 1894, 15, 638; 1895, 17, 245, 705.

Acyl radical in dimethyl malate.		$[\alpha]_D$.
CH_2BrCo	= 122	−22·40°
C_4H_9CO	= 85	−22·39
CH_2ClCO	= 77·5	−23·30
C_3H_7CO	= 71	−22·40

The mono-halogen derivatives of the succinic esters, on the other hand, have a nearly equal dextro-rotatory activity irrespective of the alcohol radical. Walden finds that the following two substances, with groups of nearly equal masses, have nearly equal *but opposite* rotatory power:

n-butyryl malic diisobutyl ester

$$m_1 = 115,\ m_2 = 101,\ m_3 = 87,\ [\alpha]_D = -26\,68°,$$

bromosuccinic diisobutyl ester

$$m_1 = 115,\ m_2 = 101,\ m_3 = 80,\ [\alpha]_D = +23\,56°.$$

Equality of the masses does not therefore produce inactivity, nor does inequality necessarily cause a change of rotation. Just as little does a reversal in the masses give rise to a change of sign.

Mandelic acid $\underset{77}{C}(\underset{77}{C_6H_5})(\underset{45}{COOH})(\underset{17}{OH})\underset{1}{H}$ $[\alpha_D] = -153°$

Mandelic isobutyl ester $\underset{77}{C}(\underset{77}{C_6H_5})(\underset{101}{COOC_4H_9})(\underset{17}{OH})\underset{1}{H}$ „ -100

Acetyl mandelic ester $\underset{77}{C}(\underset{77}{C_6H_5})(\underset{45}{COOH})(\underset{59}{OC_2H_3O})\underset{1}{H}$ „ -156

Perhaps the most striking case showing the effect of equal masses is that of propyl, isopropyl cyanacetic acid, which in spite of the close similarity of the two alkyl groups has been resolved into its active components.[1]

REFERENCES

See end of Chapter IV.

[1] Fischer and Flatau, *Ber.*, 1909, 42, 2981.

CHAPTER IV

STEREOCHEMISTRY OF UNSATURATED AND CYCLIC COMPOUNDS (*GEOMETRICAL ISOMERISM*)

A FORM of isomerism which cannot be explained by ordinary structural relations, nor yet by molecular asymmetry, has long been observed among the unsaturated compounds of the ethylene series.

The earliest example is that of maleic and fumaric acid, both unsaturated dibasic acids of the formula $C_2H_2.(CO_2H)_2$. They are obtained from malic acid by distillation, when maleic acid in the form of its anhydride sublimes, whilst fumaric acid remains in the retort.

Fumaric acid sublimes at 200° without melting, is but slightly soluble in water, and crystallizes in needles; maleic acid melts at 130°, dissolves readily in water, crystallizes in rhombic prisms, and forms an anhydride at a temperature a little above its melting-point. The close similarity in structure follows from the fact that they both yield succinic acid on reduction, both regenerate malic acid on heating in a closed vessel with water, and each can be readily transformed into the other by means which will be presently described. The kind of isomerism was foretold by van 't Hoff in *La Chimie dans l'Espace*, published in 1877. The importance of the theory then advanced has been brought into prominence by the experimental researches of J. Wislicenus, which were embodied in a brochure bearing the title *Die Lagerung der Atome im Raume*, and published in 1887. Van 't Hoff's conception of a simple unsaturated compound like ethylene is that of two regular tetrahedra united by a common edge with the four remaining summits occupied by hydrogen (Fig. 37).

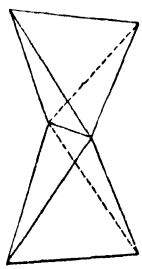


FIG. 37.

The same idea is presented by the four-bond carbon models by supposing the carbon atoms to be united by two pairs of bonds, and the remaining two pairs to be linked to hydrogen atoms.

If the bonds diverge at equal angles from the central carbon atom,

and retain their positions when the carbon atoms are doubly linked, the space arrangement of ethylene, viewed in perspective, will appear as in Fig. 38.

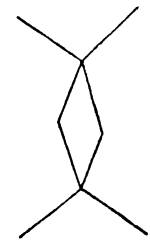


Fig. 38.

It follows from this space conception that the hydrogen *atoms lie in one plane*, and at the same time the *free rotation of the carbon atoms is suspended*, that is, the hydrogen atoms are fixed. If now the hydrogen atoms are replaced by two pairs of unlike groups ab, ab, or by groups ab, ac or ab, cd, the system will offer possibilities of space isomerism. By interchanging one pair of groups, which may be conveniently represented by projection formulae, the following pairs of isomers will be formed:

$$\begin{array}{cc|cc|cc} a-C-b & a-C-b & a-C-b & a-C-b & a-C-b & a-C-b \\ \| & \| & \| & \| & \| & \| \\ a-C-b & b-C-a & a-C-c & c-C-a & c-C-d & d-C-c \end{array}$$

Fumaric and maleic acid will have the following space formulae:

$$\begin{array}{ll} COOH-C-H & COOH-C-H \\ \quad\quad\| & \quad\quad\| \\ H-C-COOH & COOH-C-H \end{array}$$

Since the two pairs of groups lie in one plane, asymmetry is excluded, and with it both optical activity and enantiomorphous crystalline structure.

Le Bel's conception differs in a fundamental point from van 't Hoff's. It neither assumes the tetrahedral grouping of van 't Hoff nor the spatial distribution of four carbon bonds, so that it is left undecided whether the two pairs of groups attached to the carbon atoms lie in the same or in different planes; in other words, it does not wholly exclude asymmetry, and isomerism may manifest itself by optical activity.

The few cases of supposed activity of ethylene derivatives have been traced to errors of observation. The activity of a solution of citraconic acid[1] produced by the growth of fungi was found to arise from the formation of methyl malic acid, probably by the activity first of water and then of the organism.

$$\underset{\text{Citraconic acid.}}{CH_3 . C(COOH) : CH(COOH)} \rightarrow \underset{\text{Methyl malic acid.}}{CH_3C(OH)(COOH) . CH_2(COOH)}$$

The supposed activity of styrene $C_6H_5CH : CH_2$ and of chlorofumaric and chloromaleic acid $CO_2H . CCl : CH . CO_2H$[2] belong to the

[1] Le Bel, *Bull. Soc. Chim.*, 1894 (3), 11, 292.
[2] Perkin, *Trans. Chem. Soc.*, 1888, 53, 695.

same category of inaccurate observations. It is significant in this connection that among the many unsaturated compounds found in nature, such as oleic, fumaric, coumaric (*cis* and *trans*), piperic acid, &c., not one is active. Even unsaturated compounds derived from active substances, like fumaric and maleic from active malic acid, bromocinnamic acid from active cinnamic acid dibromide, &c., are inactive:

$$C_6H_5CHBr \cdot CHBr \cdot COOH = C_6H_5CBr : CH(COOH) + HBr$$

Cinnamic acid dibromide. Bromocinnamic acid.

Although all the facts support van 't Hoff's theory which disposes of asymmetry in ethylene derivatives, it should be pointed out that where two ethylene linkages occur of the form Cab : C : Ccd, asymmetry is possible, for the two pairs of groups now lie in planes at right angles to one another (Fig. 39).[1]

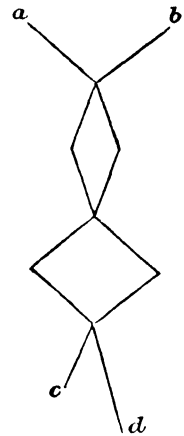
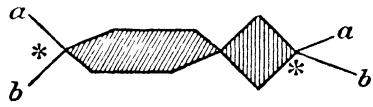


FIG 39.

Such substances should exist in enantiomorphous forms and exhibit optical activity, but as they are difficult to prepare, experimental confirmation is still wanting.[2] A case very similar to the above is presented by replacing one of the double bonds by a ring structure. Two different groups attached to one of the carbon atoms of the ring would throw the two pairs of groups into different planes, and thus produce molecular asymmetry. Supposing the hexagon in the following diagram to lie in a plane vertical to the surface of the paper, the two pairs of groups *a*, *b*, will lie in opposite planes,



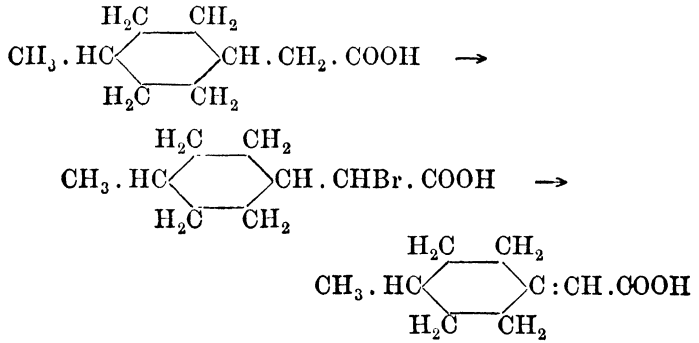
and the one configuration will not be superposable on its mirror image. Thus, molecular asymmetry is produced without the four groups being necessarily different. As to whether the carbon atoms indicated by asterisks are asymmetric or not, seems to be rather a matter of definition than of principle, and provided the molecule presents no plane of symmetry, it should exist in optically active forms.[3] Compounds of this character have been recently prepared

[1] See Perkin and Pope, *Proc. Chem. Soc.*, 1906, **22**, 107, and Marckwald and Meth, *Ber.*, 1906, **39**, 1171, 2035.

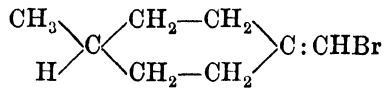
[2] Lapworth and Wechsler, *Trans. Chem. Soc.*, 1910, **97**, 38.

[3] Everest, *Proc.*, 1911, **27**, 285; Marsh, *Proc.*, 1911, **27**, 317; Perkin, Pope, and Wallach, *Trans. Chem. Soc.*, 1909, **95**, 1785.

and resolved by Perkin, Pope, and Wallach.[1] One of the substances in question was prepared from hexahydro *p*-tolyl acetic acid by bromination and removal of hydrobromic acid.



The compound was resolved by crystallization with brucine into its enantiomorphs. Optically active forms of the compound



were also obtained.[2] By a simple extension of the theory to trebly linked carbon atoms a compound like acetylene would be represented by two tetrahedra with two faces in contact, or by a pair of carbon models attached by three bonds of each (Figs. 40 and 41).

It is clear that a spatial arrangement of this character offers no possibility of space isomerism, a prevision which is fully attested by experience.

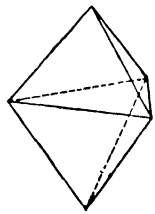


FIG 40.

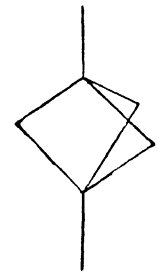


FIG. 41.

Properties of the Isomers. The theory of van 't Hoff propounds a condition of things which bears a much closer resemblance to our conception of structural than of the optical isomerism. In fumaric and maleic acid the molecular dimensions and attractions are obviously

[1] *Trans Chem Soc*, 1909, 95, 1785.
[2] Perkin and Pope, *Trans. Chem. Soc.*, 1911, 97, 1510.

different, and isomerism might therefore be expected to manifest itself by such properties as distinguish structural isomers. This view is confirmed by experience. The isomers differ in crystalline form, solubility, density, melting- and boiling-point, conductivity, or affinity constant; also in stability, which shows itself in chemical behaviour and heat of combustion; finally, in molecular dimensions, which determine certain aspects of chemical activity known as *steric hindrance* (I. 381). The spatial relations of the compounds not depending on structural differences, which distinguish them from structural isomers, are manifested by the ease with which they undergo mutual conversion on heating or by the action of reagents, recalling, in this respect, the process of racemisation or optical inversion.

Geometrical Isomers. In order to distinguish this kind of isomerism from that of optical isomers, on the one hand, and of structural isomers, on the other, the term *geometrical isomerism* has been introduced. It constitutes a special case of stereoisomerism. Among the characteristic groups which exhibit geometrical isomerism are the following:[1]

Dimethylethylene	$CH_3 . CH : CH . CH_3$
Stilbene	$C_6H_5 . CH : CH . C_6H_5$
Dichloroethylene	$ClCH : CHCl$
Dibromoethylene	$BrCH : CHBr$
Dichlorobromethylene	$CHCl : CClBr$
Diiodoethylene	$ICH : CHI$
α-Chlorobutylene	$CH_3 . CH : CCl . CH_3$
α-Bromobutylene	$CH_3 . CH \cdot CBr . CH_3$
Chlorostilbene	$C_6H_5 . CH : CCl . C_6H_5$
Tolanedichloride	$C_6H_5CCl : CClC_6H_5$
Tolanedibromide	$C_6H_5CBr : CBrC_6H_5$
α-Bromostyrene	$C_6H_5CH : CHBr$
β-Bromostyrene	$C_6H_5CBr : CH_2$
Diiodostyrene	$C_6H_5CI : CHI$
o- and *p*-Dinitrostilbene	$(NO_2)C_6H_4CH : CHC_6H_4(NO_2)$
Nitrostilbene	$C_6H_5C(NO_2) : CC_6H_5$
ω-Nitrostyrene	$C_6H_5CH : CH(NO_2)$
o-Aminostilbene	$(NH_2)C_6H_4CH : CHC_6H_4(NH_2)$
Crotonic and Isocrotonic Acid	$CH_3 . CH : CH . COOH$
Tiglic and Angelic ,,	$CH_3 . CH : C(CH_3) . COOH$
Gaïdic and Hypogæic ,,	$C_{13}H_{27}CH : CH . COOH$
Oleic and Elaïdic ,,	$C_8H_{17}CH : CH(CH_2)_7COOH$

[1] A more complete list will be found in Werner's *Lehrbuch der Stereochemie*, p. 189.

Erucic and Brassidic Acid	$C_8H_{17}CH:CH(CH_2)_{11}COOH$
α-Chlorocrotonic ,,	$CH_3.CH:CCl.COOH$
β-Chlorocrotonic ,,	$CH_3.CCl:CH.COOH$
β-Bromoacrylic ,,	$CHBr:CH.COOH$
β-Iodoacrylic ,,	$CHI:CH.COOH$
Cinnamic and Allocinnamic ,,	$C_6H_5CH:CH.COOH$[1]
α-Chlorocinnamic ,,	$C_6H_5CH:CCl.COOH$
α-Bromocinnamic ,,	$C_6H_5CH:CBr.COOH$
β-Chlorocinnamic ,,	$C_6H_5CCl:CH.COOH$
β-Bromocinnamic ,,	$C_6H_5CBr:CH.COOH$
α-Iodocinnamic ,,	$C_6H_5CH:CI.COOH$
β-Iodocinnamic ,,	$C_6H_5CI:CH.COOH$
α-Methylcinnamic ,,	$C_6H_5CH:C(CH_3).COOH$
α-Phenylcinnamic ,,	$C_6H_5CH:C(C_6H_5).COOH$
Isosafroles	$CH_2O_2:C_6H_3.CH:CH.CH_3$
Coumaric Acid	$(OH)C_6H_4CH:CH.COOH$
Fumaric and Maleic ,,	$COOH.CH:CH.COOH$
Mesaconic and Citraconic ,,	$COOH.CH:C(CH_3)COOH$
Phenylitaconic and phenylaticonic Acid	$C_6H_5CH:C(CH_2COOH).COOH$

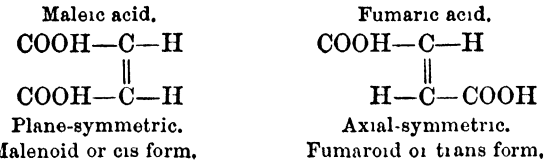
and numerous halogen, aryl, and alkyl derivatives of fumaric and maleic acid.

Determination of Configuration. Before discussing the methods which are used for determining the configuration of the geometrical isomers, the system of nomenclature must be briefly indicated. In the simplest case of two pairs of groups abC:Cab the first of the two isomers

[1] Allocinnamic acid presents an interesting example of trimorphism. Three substances are known possessing different crystalline forms and melting at 42°, 58°, and 68° respectively. That they represent one substance is shown in various ways; by fusion and supercooling and then introducing one of the modifications, the substance assumes the melting-point of that modification (Liebermann and Trucksass, *Ber.*, 1909, **42**, 1027, 4659; 1910, **43**, 411; Bülmann, *Ber.*, 1909, **42**, 1443), they all possess the same conductivity in solution (Bülmann and Bjerrum, *Ber*, 1910, **43**, 568), they exhibit the same selective absorption in the ultra-violet (Stobbe, *Ber.*, 1910, **43**, 504), the same refractivity (Stobbe, *Ber*, 1911, **44**, 2735), and the same solubility in the fused state (J. Meyer, *Ber.*, 1911, **44**, 2966).

The α-methyl cinnamic acids (*m. p.* 82° and 74°) which present a similar case of dimorphism are *trans* compounds and can be converted by means of ultraviolet rays into the *cis* compound *m. p.* 92° (Stoermer, *Annalen*, 1915, **409**, 13, 20). Erlenmeyer (*Biochem. Zeit.*, 1919, **97**, 198) professes to have prepared by what he terms a process of induction optically active cinnamic acids.

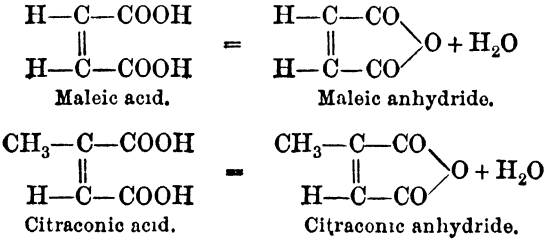
is distinguished by having the same groups on the same side of the molecule. It exhibits lateral symmetry, and is known as the *plane-symmetric*, or, more commonly, as the *cis* or *malenoid* form. The second isomer has its similar groups diagonally opposite, and is known as *axial-symmetric*, *trans* or *fumaroid* form. The terms malenoid and fumaroid have, of course, reference to maleic and fumaric acid, the configurations of which have been ascertained and correspond to the cis and trans forms:



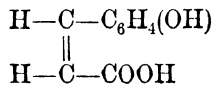
Where only one pair of similar groups is present, the terms cis and trans apply to that pair; where all the groups are different the terms cannot be used, and the difference is indicated in some other way.

The general principle which underlies the methods used in determining configuration is one which has long lent itself to this kind of inquiry, namely, the interpretation of a chemical change as a mechanical process in which spatial relations of the original molecule persist in the new product, an assumption which, it may be said in passing, is not always supported by experience. The method has its limitations and must be used with caution, since such changes are not always simple and do not invariably proceed in what one is accustomed to call a normal fashion.

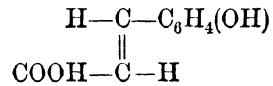
First Method. Formation of Cyclic Structures. Among the isomeric dibasic and hydroxy acids one member of the pair is usually found to yield an anhydride more readily than the other. Maleic and citraconic acids give anhydrides on heating, and are converted into the original acids when dissolved in water. This is taken as an indication of the proximity of the two carboxyl groups. Maleic and citraconic have therefore the cis configuration:



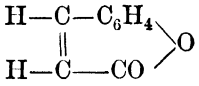
It is true that fumaric and mesaconic acid pass into anhydrides on heating, though less readily than the isomers, but the anhydrides are those of maleic and citraconic acids. That the above interpretation of the facts is correct follows from independent evidence afforded by the character of the stereoisomeric tartaric acids, which maleic and fumaric acid yield on oxidation, and which will be referred to presently (p 262). Having determined the configuration in this way, it is possible to fix that of related compounds. Thus the two iodoethylenes have been converted into fumaric and maleic acid respectively and their configuration ascertained.[1] The conversion of the two coumaric acids, $OH.C_6H_4CH:CH.COOH$, into lactones may be used in the same way to distinguish the *cis* from the *trans* isomer. One acid passes at once into the lactone, coumarin, when liberated from its salts by the addition of acid, whereas the second coumaric acid is much more stable and requires an active reagent like hydrobromic acid to effect the change. The lactone passes into the sodium salt on the addition of sodium hydroxide, from which it is again liberated by acids, but if the strongly alkaline solution is boiled the second isomer is formed, which acids no longer precipitate as lactone. The first or labile acid will therefore have the hydroxyl and carboxyl in closest proximity.



Coumaric acid (labile).



Coumaric acid (stable).

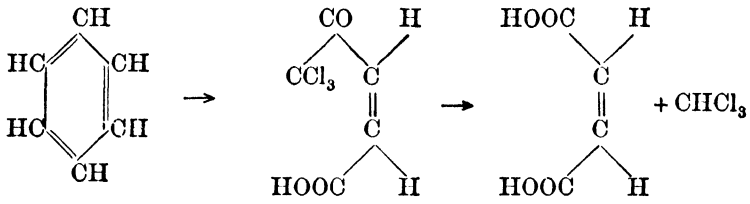


Coumarin.

The above examples will serve to illustrate the principle of the anhydride method for distinguishing geometrical isomers. The reverse of this process has been occasionally utilized for ascertaining configuration, but as the conversion of a ring into an open chain compound requires more drastic treatment than the former process, isomeric change may occur, and the results cannot be relied on with the same security. It is found, for example, that benzene and its

[1] Keiser and Macmaster, *Amer. Chem. J*, 1911, 46, 518.

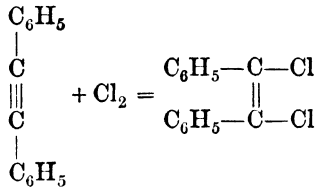
derivatives usually give derivatives of maleic and not of fumaric acid. Benzene itself was converted by Kekulé[1] into trichloracetyl acrylic acid, which breaks up in turn into maleic acid and chloroform:



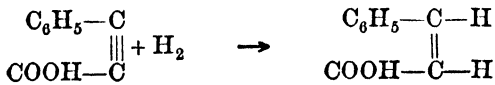
Trichloracetyl acrylic acid. Maleic acid.

Zincke[2] obtained dichloromaleic acid by the action of chlorine on *p*-aminophenol in alkaline solution. Derivatives of other ring compounds—furfurane, thiophene, and pyrrole—likewise yield derivatives of maleic acid.[3]

Second Method. Conversion of Acetylene into Ethylene Derivatives. When tolane $C_6H_5C:CC_6H_5$ combines with two atoms of chlorine and passes into the dichloride $C_6H_5CCl\cdot CClC_6H_5$, it might be supposed that the formation of a *cis* compound would produce the least disturbance in the molecular arrangement and would therefore be formed in the largest amount.



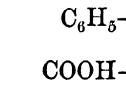
Consequently the tolane dichloride (*m. p.* 143°) obtained in this way may be regarded as the *cis* compound, whilst that obtained from the tolane tetrachloride by removal of chlorine (*m. p.* 63°) will represent the *trans* configuration. This principle, which was laid down by J. Wislicenus,[4] has been applied in a variety of cases. Phenylpropiolic acid is converted on reduction with colloidal palladium and hydrogen into allocinnamic acid.



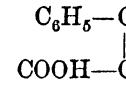
Phenylpropiolic acid. Allocinnamic acid.

[1] *Annalen*, 1884, 233, 170. [2] *Ber.*, 1891, 24, 912.
[3] Ciamician and Silber, *Ber.*, 1887, 20, 698, 2594; Ciamician and Angeli, *Ber.*, 1891, 24, 77, 1847. [4] *Die räumliche Anordnung der Atome*, p. 24.

β-Bromocinnamic acid, obtained by the addition of hydrogen bromide to phenylpropiolic acid, and its reduction product, allocinnamic acid, must have the following configuration:

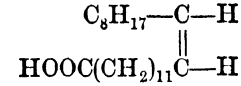


β-Bromocinnamic acid.



Allocinnamic acid.

Behenolic acid $C_{19}H_{39}C{:}C.COOH$ gives on reduction brassidic and not erucic acid, and has the configuration:



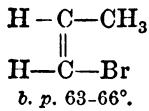
Brassidic acid.

In these cases the accuracy of the conclusions cannot be supported by independent proof. It is otherwise with acetylene-dicarboxylic acid COOH.C C.COOH, for the configuration of the additive compounds with bromine are known, and the product, which, according to the above argument, should consist mainly of dibromomaleic acid, contains, even under the most favourable conditions, a larger proportion of dibromofumaric acid. The presence of the *trans* isomer was ascribed by Wislicenus to a secondary process, brought about by the action of bromine or hydrogen bromide on bromomaleic acid, but the explanation has been rendered untenable by Michael,[1] for hydrochloric, hydrobromic, and hydriodic acid yield in the same way chloro-, bromo- and iodo-fumaric acid,[2] which cannot be ascribed to the action of the halogen acid on the *cis* compound, seeing that bromo-maleic acid remains unchanged in presence of hydrobromic acid.

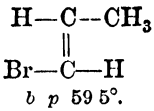
Other reactions of the same nature are the addition of hydrogen chloride to tetrolic acid $CH_3.C{:}C.COOH$, which yields *trans* chlorocrotonic acid.[3]

The method has consequently lost its value.[4] The reverse process of converting an ethylene into an acetylene derivative has also been proposed by Wislicenus, but appears to be open to the same disadvantage as the former one. Bromopropylene (*b. p.* 63-66°) is more slowly decomposed by alcoholic potash than its isomer (*b. p.* 59·5°), and the former might therefore be assumed to have the hydrogen and bromine atoms in the *trans* position, whilst the latter would represent the *cis* compound.

[1] *J. prakt. Chem.*, 1892, 46, 210; 1895, 52, 352.
[2] Bandrowski, *Ber.*, 1882, 15, 2694. [3] Friedrich, *Annalen*, 1883, 219, 370.
[4] P. F. Frankland has offered an explanation of these anomalous results (*Trans. Chem. Soc.*, 1912, 101, 678).

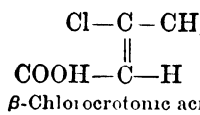


b. p. 63-66°.

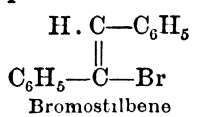


b p 59 5°.

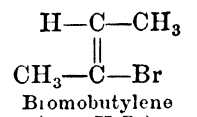
But it is found that β-Chlorocrotonic acid, bromostilbene, and bromobutylene lose hydrogen chloride or bromide more readily from the *trans* than from the *cis* positions.



β-Chlorocrotonic acid (*trans* H,Cl).



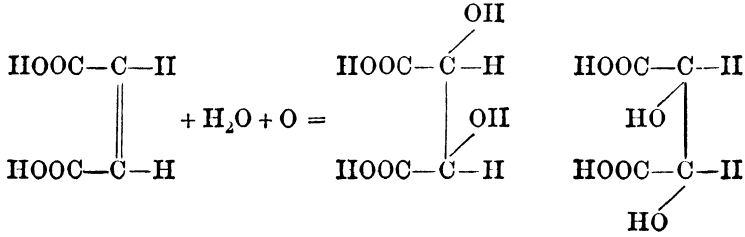
Bromostilbene (*trans* H,Br).



Bromobutylene (*trans* H,Br).

Moreover, dibromofumaric ester is more easily transformed by zinc into acetylene dicarboxylic ester than its isomer, and the same is true of bromo- and chloro-fumaric acid.[1] In short, it seems to be the general rule that elimination of both halogen and halogen acid from the *trans* position is more easily accomplished than from the *cis*.[2]

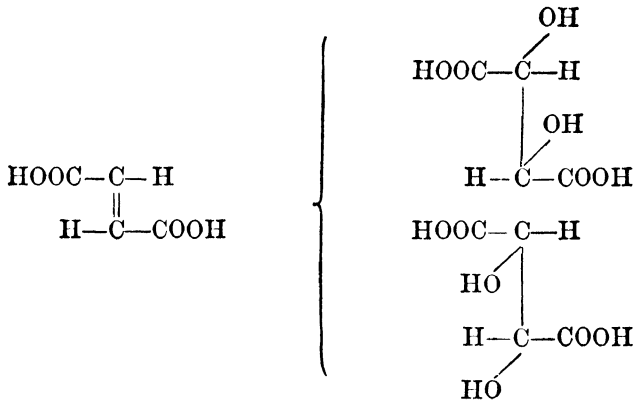
Third Method. Conversion of Ethylene Derivatives into Saturated Compounds. The method is perhaps best explained by taking, by way of illustration, an actual experiment. It has been found that when maleic and fumaric acid are oxidised with potassium permanganate, they take up two hydroxyl groups and yield inactive tartaric acids, but whereas maleic acid gives the meso-acid, fumaric acid yields racemic acid.[3] This result agrees precisely with the configuration of the two geometrical isomers ascertained by the first method. The mechanism of the change will be evident from the following considerations. Assuming, in the case of maleic acid, that the carboxyl groups and hydrogen atoms have the *cis* configuration, it follows that if either link of the double bond is broken, by the addition of hydroxyl groups, the same product must result, namely, meso-tartaric acid, in which the two halves of the molecule stand in the relation of object and image.



Maleic acid. Meso-tartaric acid.

[1] Michael, *J. prakt. Chem*, 1892, **46**, 230; 1895, **52**, 307.
[2] P. F. Frankland, *Trans. Chem. Soc.*, 1912, **101**, 681, *et seq.*
[3] Kekulé and Anschutz, *Ber.*, 1880, **13**, 2510; 1881, **14**, 713.

If fumaric acid is oxidised the effect is otherwise, for the *trans* configuration will permit of the hydroxyl groups occupying two different positions according to which of the ethylene bonds is ruptured.



Fumaric acid. *d*- and *l*-tartaric acid.

Now these two configurations stand in the relation of dextro and laevo tartaric acid, and, since they must be formed in equal quantity, racemic acid results (p. 183).

Cinnamic and allocinnamic acid can also be oxidised in the same way, each yielding a different phenylglyceric acid, but, as the latter contains two dissimilar asymmetric carbon atoms, they can both be resolved into optically active forms,[1]

$$C_6H_5 . CH : CH . COOH \longrightarrow C_6H_5CH(OH) . CH(OH) . COOH$$

It is a curious fact that the dibromosuccinic acid which is obtained by the action of bromine on fumaric acid yields, on hydrolysis, chiefly meso-tartaric acid, and that isodibromo succinic acid from maleic acid gives mainly racemic acid. Seeing that isodibromo succinic acid is the racemic form (for it has been resolved), inversion must occur on bromination (p. 268).[2]

The course of a reaction involving the use of bromine is, obviously, subject to influences which may produce abnormal results, for it appears to form *trans* additive compounds by preference, that is to say, it has a tendency to generate the more stable form.

The reversal of the process just described, that is, the conversion of asymmetric (meso and racemic) into ethylene compounds may be

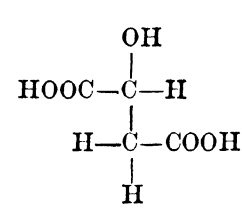
[1] Ruber, *Ber.*, 1915, 48, 823.
[2] M°Kenzie, *Trans. Chem. Soc.*, 1912, 101, 1196; Holmberg, *Abstr. Chem. Soc.*, 1912, 1, 4.

reckoned among the methods for ascertaining configuration, provided that the configuration of the original stereoisomers is known and the reaction proceeds in a normal fashion. The meso compound should yield the *cis* derivative and the racemic compound the *trans*. Experiment in this direction has not been attended with any great success. The removal of hydrogen bromide from the meso and racemic dibromosuccinic acids yields chiefly bromofumaric acid in both cases.

If the saturated compound is not of the asymmetric type, but is one like tolane tetrachloride $C_6H_5CCl_2 . CCl_2C_6H_5$, which, by the action of zinc, can be converted into the unsaturated dichloride $C_6H_5CCl : CClC_6H_5$, the configuration of the product depends as before on that of the original substance. But there is no direct method for ascertaining the configuration of the original substance, and an entirely new problem is introduced.

Fourth Method. Action of Ultraviolet Light. Stoermer has utilized the action of the ultraviolet rays, which are found to convert the more stable into the less stable isomer, in order to ascertain the configuration of a number of substances (see p. 266).

Are the Atoms attached to singly linked Carbon fixed? Do the different atoms or groups in a saturated compound of singly linked carbon atoms assume a fixed configuration relatively to one another, or are they in a state of oscillatory motion or rotation round the singly linked carbon? If, as Wislicenus and others suppose, the former is the case, and that the groups arrange themselves in positions of greatest stability, the difficulty of fixing these positions has still to be solved. Wislicenus proceeds in the following fashion: as fumaric acid is formed from malic acid at a temperature of 140–150°, whereas the anhydride of maleic acid only appears at a much higher temperature, he concludes that the favoured or more stable configuration of malic acid is represented by the following space formula:

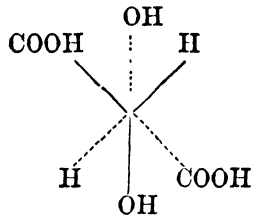


The hydrogen atom and hydroxyl group occupy *cis* positions, since in forming fumaric acid they are removed together. As the effect of heat is to counteract chemical attraction, rise of temperature may alter the original conditions and the two carboxyls may swing round into *cis* positions, giving rise to the anhydride. Wislicenus has attempted to test the principle quantitatively.[1]

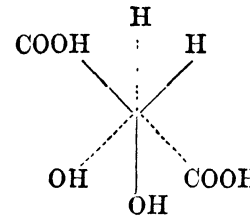
Boeseken[2] and Coops[3] have, however, discovered a method for determining the relative positions of the hydroxyl groups, namely, by the increased conductivity of a solution of boric acid, which seems to be manifested wherever in polyhydroxy compounds the pairs of hydroxyl groups are grouped on the same side of the molecule. Now, as active tartaric acid increases, whilst mesotartaric decreases the conductivity, it would appear that the carboxyl groups

[1] Blank, *Annalen*, 1888, 248, 27.
[2] *Rec. trav. chim. Pays-Bas*, 1921, 40, 553, 568, 578; 1922, 41, 199.
[3] *Kon. Akad. Wetench. Amsterdam*, 1920, 29, 868.

tend to repel one another. The arrangement of the groups round the two asymmetric carbon atoms, as seen in looking along the bond joining the two latter, may be represented in the following way:

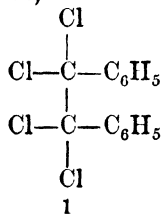


Mesotartaric acid
(hydroxyl groups opposite).

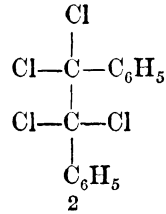


Tartaric acid
(hydroxyl groups adjoining).

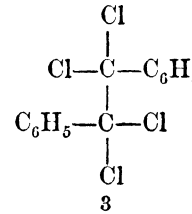
Suppose in tolane tetrachloride the three configurations in which two chlorine atoms occupy *cis* positions to exist side by side in equal amounts, or, in other words, to offer no favoured configuration, a condition which might be supposed to obtain at a high temperature,



1

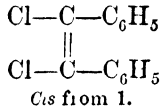


2

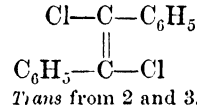


3

the removal of two atoms of chlorine by zinc would give only two tolane dichlorides, since 2 and 3 generate the same product.



Cis from 1.



Trans from 2 and 3.

It therefore follows that under conditions wherein all three configurations are equally stable, one-third of the *cis* form along with two-thirds of the *trans* isomer will be produced. Under conditions in which one of the three forms alone can exist, either the *cis* or *trans* form, but not both, would appear.

The first condition is fulfilled at 80°, and only one-third of this *cis* compound is formed; at lower temperatures the *trans* form predominates to the extent of considerably more than two-thirds. The question of fixity of configuration of saturated compounds is discussed more fully on p. 283.

Geometrical Inversion. A passing reference has been made to the mutual conversion of geometrical isomers or *geometrical inversion* and the resemblance which it bears to the process of racemisation or optical inversion. Transformations of this character, produced both by physical and chemical agencies, were first observed with fumaric

and maleic acid. It has already been stated that fumaric acid is converted into the anhydride of maleic acid on heating, and the same result is obtained with many of its derivatives; maleic chloride passes into fumaric chloride on standing; the methyl ester of β-bromocinnamic acid (*m. p.* 147°) is converted into the isomer (*m. p.* 159°) on distillation; angelic acid passes into tiglic acid on heating for several hours. In many cases only one product results; in others, the process is reversible, for the same mixture of isomers is obtained whichever compound forms the starting-point. In a few cases light produces geometrical inversion. Paal and Schulze[1] found that sunlight converts yellow *trans* dibenzoylethylene into the colourless *cis* form, and Wislicenus has shown that angelic acid dibromide under these conditions passes into tiglic acid dibromide. A very interesting method of affecting geometrical inversion is by the use of light rich in ultraviolet rays, such as is furnished by the mercury-vapour lamp. Stoermer[2] has found that by exposure to these rays certain high-melting and stable ethylene derivatives may be converted into their low-melting and labile isomers. *Trans* cinnamic and coumaric acid and their derivatives may be converted into the *cis* compounds. By the aid of this reaction Stoermer has succeeded in showing the relation between *cis*-coumaric and allocinnamic acid in the following way. Ordinary or *trans* *o*-nitrocinnamic acid is exposed to ultraviolet rays and converted into the *cis* isomer. This is reduced to the amino compound, and then diazotised to coumaric acid. The amino group can be replaced by hydrogen by means of phosphorus acid, and the product is allocinnamic acid, *m. p.* 58°.[3] The process has also been applied to the nitro-α-phenylcinnamic acids which are converted in the same way into the *cis* and *trans* α-phenylcinnamic acids. When these are heated with barium oxide they lose carbon dioxide and yield the corresponding stilbenes.[4]

$$C_6H_5CH:C(C_6H_5)COOH \longrightarrow C_6H_5CH:CH.C_6H_5 + CO_2$$

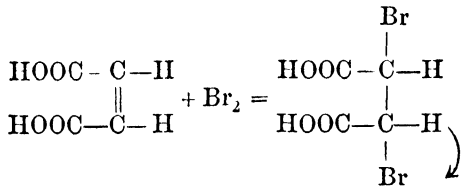
Isostilbene corresponds to the *cis* and stilbene to the *trans* configuration. The solvent in the process of crystallization is known to effect the same thing. Iodoacrylic acid (*m. p.* 65°) is converted on recrystallization into the isomer (*m. p.* 139–140°). Turning now to chemical reagents, maleic acid is converted into fumaric acid on heating with water under pressure; but the most effective reagents

[1] *Ber*, 1902, 35, 168.
[2] *Ber*, 1909, 42, 4865; 1911, 44, 637; 1912, 45, 3099; 1914, 47, 1786, 1795, 1863; 1917, 50, 959, 1921, 54, 77; 1922, 55, 1232.
[3] *Ber.*, 1912, 45, 3099.
[4] Stoermer and Heymann, *Ber.*, 1912, 45, 3099; *Annalen*, 1915, 409, 13.

are the halogens and halogen acids. A trace of bromine or iodine converts maleic ester into fumaric ester. The action of the halogens is usually promoted by sunlight; the change of citraconic acid dissolved in ether into mesaconic acid, by the addition of a few drops of a chloroform solution of bromine, is very rapid on exposure to bright sunlight, and is readily observed. Iodine has a similar action on yellow dibenzalsuccinic acid, which passes into the colourless modification. Hydrochloric, hydrobromic, and hydriodic acid convert maleic into fumaric acid; nitrous acid converts oleic into elaïdic, and hypogaeic into gaïdic acid; also nitric acid can be used for transforming citraconic into mesaconic acid. Finally, caustic alkalis convert maleinaminic acid, $NH_2OC \cdot CH \cdot CH \cdot COOH$, into fumaric acid and citraconic into mesaconic acid.

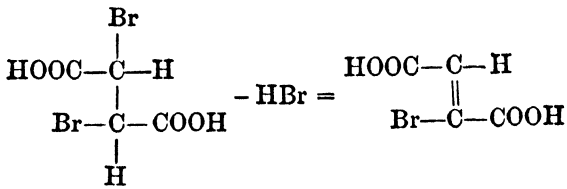
With few exceptions the conversion is complete, and probably follows the line of least resistance, that is, from the labile to the stable configuration, unless energy in the form of ultraviolet light is introduced into the system, when the reverse change occurs, as explained above. All these processes probably follow the law which governs isomeric change in general, and are cases of completed or incompleted reversible reactions accelerated by the intervention of a catalyst (see p. 371).

The mechanism of these changes, as originally suggested by Wislicenus,[1] must, for various reasons, be abandoned. It is well known that bromine combines with maleic acid to form dibromosuccinic, which, on boiling with water, yields bromofumaric acid, and that fumaric may be converted in the same way into bromomaleic acid. Wislicenus supposed that an additive compound is first formed, namely, meso-dibromosuccinic acid (1); one carbon group then rotates on its axis until the hydrogen atom attached to the lower carbon comes opposite the bromine of the upper carbon group, as indicated by position (2), when hydrogen bromide is removed and bromofumaric acid results.



Meso-dibromosuccinic acid (1).

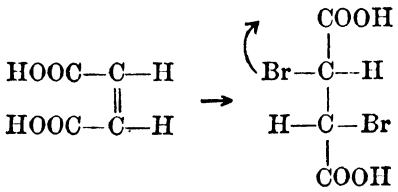
[1] *Räumliche Anordnung der Atome.* J. Wislicenus, Leipzig, 1889.



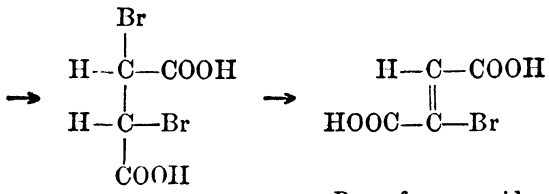
Meso-dibromosuccinic acid (2). Bromofumaric acid.

Fumaric acid, in the same way, was assumed to give racemic dibromosuccinic acid, lose hydrogen bromide, and so pass into bromomaleic acid.

This explanation is confronted with the difficulty that maleic acid forms not the meso, but the racemic dibromo derivative, for it has been resolved into its active components,[1] and that fumaric forms the meso compound (see p. 263).[2] It necessarily follows that both bromine addition and hydrogen bromide elimination must take place in both cases in the *trans* position thus:



Maleic acid.



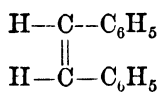
Bromofumaric acid.

Various views have been advanced to explain *trans*-addition and elimination, such as steric hindrance (Part I, p. 383), the proximity of certain groups in loosening the attachment of the atoms which are removed, and the strength of the acid as determined by the relative

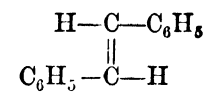
[1] McKenzie, *Trans. Chem. Soc.*, 1912, 101, 1196.
[2] Michael, *J. prakt. Chem.*, 1892, 46, 222; 1895, 52, 352.

position of the two carboxyl groups.[1] The fact that the elimination of halogen by zinc from the two dibromosuccinic acids and the reduction of bromomaleic and bromofumaric acids yield in all cases the same fumaric acid, must be explained on the ground that the most stable arrangement of the carboxyl groups is that in which they are oppositely situated.

Similar changes to the above have been observed in the case of tiglic and angelic acids, which are converted into the dibromides, and finally into unsaturated bromo acids of opposite configuration; in that of erucic and brassidic acid, which pass into chlorobrassidic and chloroerucic acid respectively. The process is not limited to acids. Stilbene (*trans*, *m. p.* 124°) yields the meso dibromide (*m. p.* 237°) and bromoisostilbene (*cis*, *m. p.* 19°), which, on reduction, changes back to *trans*-stilbene (*m. p.* 124°), whilst isostilbene (*cis*, liquid) yields the racemic dibromide (*m. p.* 110°) and bromostilbene (*trans*, *m. p.* 31°).



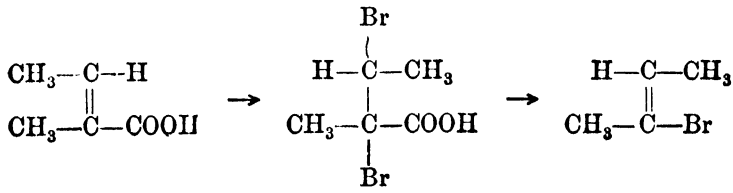
cis-Stilbene (liquid).



trans-Stilbene (*m. p.* 124°).

Cis-butylene is converted into butylene bromide (*b. p.* 93·5) and *trans*-bromobutylene (*b. p.* 93·5), whereas *trans*-butylene yields butylene bromide (*b. p.* 161°) and *cis*-bromobutylene (*b. p.* 85°). An interesting connection has been established between angelic and tiglic acid and the two bromobutylenes.

Angelic acid gives a dibromide by *trans* addition. On boiling a solution of the sodium salt in water, carbon dioxide and sodium bromide are removed by *trans* elimination, and *trans*-bromobutylene, *b. p.* 93°, is formed.



Angelic acid

Angelic acid dibromide.

trans-Bromobutylene (*b. p.* 93·5).

[1] P. F. Frankland, *Trans. Chem. Soc.*, 1912, 101, 679.

The isomeric *cis*-bromobutylene is obtained from tiglic acid in precisely the same manner.

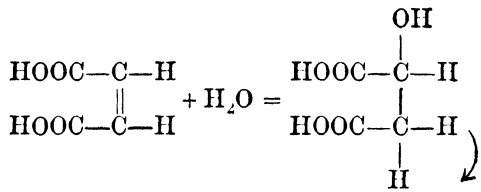
The formation of the two butylenes from tiglic and angelic acid has been effected and their relation determined on similar lines. Briefly stated, the process consists in forming the additive compound of the acid with hydrogen iodide and boiling the latter with caustic soda solution.

$$CH_3 . CH : C(CH_3) . COOH + HI = CH_3 . CHI . CH(CH_3) . COOH$$

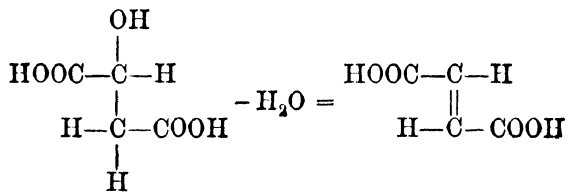
$$CH_3 . CHI . CH(CH_3) . COONa = CH_3 . CH : CH . CH_3 + NaI + CO_2$$

The two butylenes which boil at 1—1·5 and 2—2·7° respectively can be identified by means of their dibromides.

Wislicenus' Theory. The difficulties which Wislicenus' mechanical conception, so ingeniously applied to the action of bromine in causing geometrical inversion, has encountered, have already been referred to. Nor has it met with greater success in explaining other manifestations of the same phenomenon. The action of water in converting maleic into fumaric acid might be explained by the intermediate production of malic acid, followed by rotation into the favoured configuration and elimination of water.



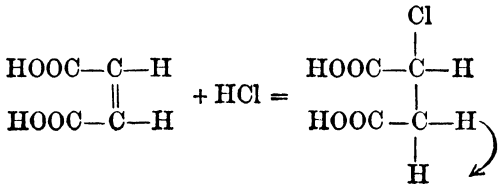
Maleic acid. Malic acid (1).



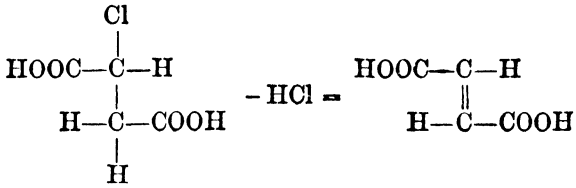
Malic acid (2). Fumaric acid.

This theory of the transformation cannot be sustained, for Skraup[1] failed to convert malic acid by heating it with water into fumaric acid under conditions in which geometrical inversion readily succeeds.

Traces of the halogen acids convert maleic acid into fumaric acid. Wislicenus explains the change in the usual way by the formation of an additive compound, followed by rotation into the stable configuration and the final separation of hydrogen halide.



Maleic acid. Chlorosuccinic acid (1).

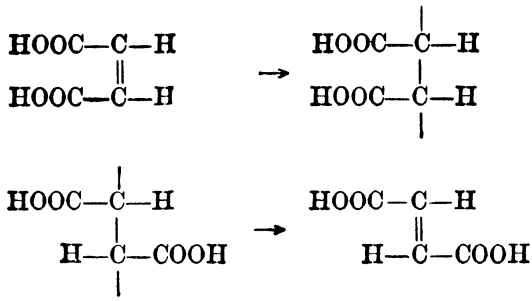


Chlorosuccinic acid (2). Fumaric acid.

The difficulty encountered in this assumption arises from the fact that the intermediate monohalogen succinic acids are actually stable at the temperature at which the conversion takes place. Anschütz has shown that whilst strong hydrochloric acid at 10°, and hydrobromic acid at 0°, convert maleic into fumaric acid, monochloro- and monobromo-succinic acid are perfectly stable at these temperatures, and exhibit no tendency to lose hydrogen chloride or bromide. The action of iodine in converting maleic into fumaric acid is explained as follows. Iodine is supposed to yield a diiodo additive compound of maleic acid, from which hydrogen iodide separates and reduces the iodofumaric acid to fumaric acid. In the conversion of maleic into fumaric acid by heat, the double bond connecting the carbon atoms in the former is loosened so as to permit of free rotation of the carbon atoms into the more stable configuration.

It follows that when the double linking occurs on cooling, fumaric acid is formed.

[1] *Monatsh.*, 1891, 12, 108.



The reader is reminded of the action of alkalis and of nitrous and nitric acid in effecting optical inversion, which, according to the theory of Wislicenus, would necessitate the formation of intermediate additive compounds with these substances. Still more striking are the facts discovered by Skraup of the partial inversion of metallic salts of maleic acid by precipitation of the metal by hydrogen sulphide. The same observer has also found that, although hydrogen sulphide and sulphur dioxide acting separately on a solution of maleic acid produce no effect, their united action causes partial inversion. In conclusion it should be mentioned that exposure to light alone is sufficient to cause inversion. It is clear from the examples given that the mechanical theory of Wislicenus cannot be indiscriminately applied and that in many cases it is either contrary to fact or manifestly improbable. A variety of attempts have been made to throw light on this complex change. Skraup suggests that an exothermic reaction, such as the combined action of hydrogen sulphide and sulphur dioxide in a solution of the isomer, or the incipient formation of an additive compound which may occur in certain cases, acts catalytically by setting up vibrations which he compares to the physical phenomenon of resonance or the chemical effect of an explosion wave. The theory possesses one convenient attribute. Like the old vibration theory of fermentation it stands beyond the reach of direct experimental disproof.

The same may be said of Werner's theory, which postulates the even distribution of affinity or valency over the surface of the carbon atom, which may take the form of a sphere. The four radicals of a saturated carbon atom occupy positions corresponding to the summits of a tetrahedron as the result of a tendency to neutralize most effectively their mutual attractions. In doubly linked carbon atoms the affinity which binds the pair of radicals to each of the two carbon atoms may be represented by two segments of a carbon sphere (unshaded in Fig. 42), the remainder, which is shaded in the

figure, being used for binding the two carbon atoms together. Of the latter, the segments corresponding to the more deeply shaded portions *a* do not prevent free rotation, which is entirely controlled by the mutual attractions of the smaller surfaces *b*. The latter act like elastic bands attached one on each side of the sphere, thereby keeping the atoms in position.

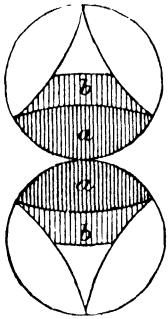


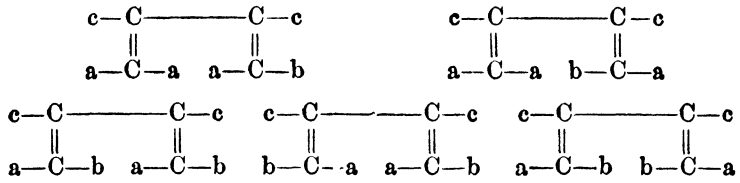
FIG. 42.

This small fraction of affinity is easily neutralized by rise of temperature or chemical action, and the spheres will then be free to revolve through 180°, that is, into the opposite configuration.

Geometrical inversion is clearly the result of a variety of different conditions at present imperfectly understood. The conditions which determine the formation of additive compounds—the basis of Wislicenus' hypothesis—furnish a problem which still awaits exhaustive treatment; so much at least may be said; the additive process is greatly modified by the nature of the groups attached to the unsaturated carbon atoms.

At present we must leave the subject of geometrical inversion without the embellishment of a theory which embraces all the phenomena.

Geometrical Isomers with more than one Ethylene Linkage. Few examples of isomers containing two ethylene linkages are known. Compounds of the formula aaC:Cc.Cc:Cab may exist in two stereoisomeric forms, whilst in the case of abC:Cc.Cc:Cab the number is increased to three.



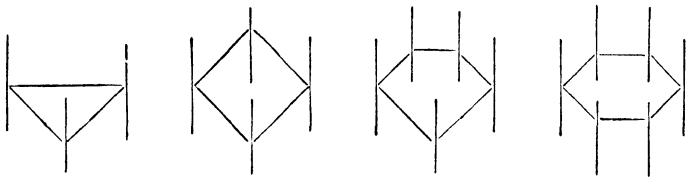
Stobbe[1] has obtained not only three isomeric dibenzalsuccinic acids of the formula $C_6H_5CH:C(COOH).C(COOH):CHC_6H_5$, but an additional anhydride which is formed by the action of light on the anhydride of one of the other three acids. The configuration of none of these compounds has been ascertained, and the existence of the fourth isomer remains unexplained.

[1] *Gesell. Naturforscher and Aerzte*, München, 1899, 88.

Stereoisomerism of Cyclic Compounds. A short account has already been given (p. 223) of the optical isomerism of cyclic compounds containing asymmetric carbon in the nucleus. The stereochemistry of this class of compounds must now be developed a little more fully.

In his original pamphlet van 't Hoff discussed the subject of the stereoisomerism of cyclic compounds, although the only example known at the time which fulfilled the necessary conditions was Baeyer's hydro- and isohydro-mellitic acids, $C_6H_6(COOH)_6$. Van 't Hoff's conclusions have since been amply verified by the researches of Baeyer, Baumann and Fromm, Buchner, W. H. Perkin, jun., and others.

If the carbon atom is represented in the usual way with four bonds directed to the four corners of a tetrahedron, and then three or more carbon atoms be joined by single bonds in the form of a ring or closed chain, the arrangement drawn diagrammatically may be represented as follows; the pairs of available bonds, for the sake of simplicity, are rendered by vertical lines at right angles to the contour orbit of the ring, and the ring itself lies in a plane vertical to that of the paper and must be viewed as if in perspective, as previously explained (p. 225).



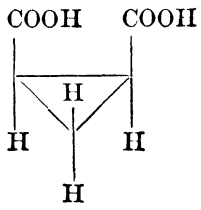
Each carbon atom, therefore, possesses two residual linkages, which may be joined to different pairs of atoms or groups. As the power of free rotation of the carbon atoms is suspended by the fact of their being linked in a ring, the space arrangement should bear some analogy to that of the doubly linked carbon atom and should manifest characteristics of *cis-trans* isomerism; in other words, the isomers should exhibit the differences in properties which distinguish compounds of the fumaric and maleic acid type.

Thus, a derivative of trimethylene with two pairs of groups *a*, *b*, should possess the following configurations:

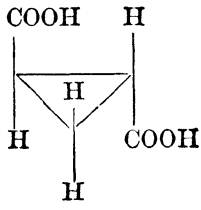
Examples of this kind of isomerism are now very numerous and embrace a variety of different groups of compounds. They include the dicarboxylic acids of cyclo-propane, -butane, -pentane, and -hexane. The isomers are distinguished as *cis* and *trans* for reasons to be presently discussed.

Name.	Melting-point.	
	Cis.	*Trans.*
1 2 Cyclopropane dicarboxylic acid	139°	175°
1 3 Cyclobutane ,, ,,	135-136	170-171
1 2 ,, ,, ,,	137-138	131
1 2 Cyclopentane ,, ,,	140	159-160
1 3 ,, ,, ,,	120-121 5	87-88 5
Cyclopentane tricarboxylic acid	169-170	184-185
Hexahydrophthalic acid	192	215
Δ^4 Tetrahydrophthalic acid [1]	174	218
$\Delta^{3,5}$ Dihydrophthalic acid	173-175	210
Hexahydroisophthalic acid	161-163	118-120
Δ^4 Tetrahydroisophthalic acid	165	227
Hexahydroterephthalic acid	161-162	300
Δ^2 Tetrahydroterephthalic acid	150-155	about 200
$\Delta^{2,5}$ Dihydroterephthalic acid	—	—
Camphoric acid	188	170 (iso)
Caronic acid	174-175	212
Truxillic acid [2]	α = 274	γ = 228

Taking one example from the above list, the two cyclopropane dicarboxylic acids will appear as follows:

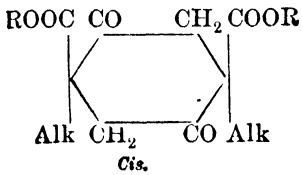


Cis.

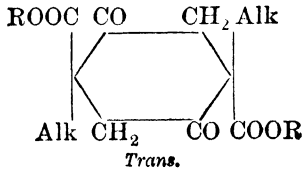


Trans.

A series of dialkyl succino-succinic esters are known in isomeric forms[3], which probably have the following structure:



Cis.



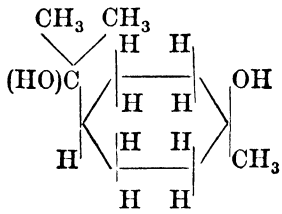
Trans.

Dialkyl succino-succinic esters.

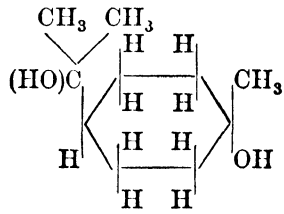
[1] The use of the symbol Δ is explained on p. 419. [2] See p. 154.
[3] Baeyer, *Ber*, 1893, 26, 232.

Also a number of substances belonging to the terpene group:

	Cis.	*Trans.*
Terpin (anhydrous)	102 105°	156-158°
Dipentene dihydrochloride	25	50
Limonene nitrosochloride	103-104	105-106
Menthylamine	207-208	209 210



Cis. Terpin.



Trans. Terpin.

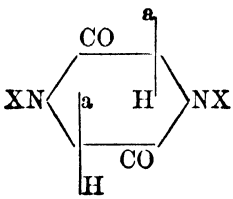
and a variety of cyclohexane derivatives.

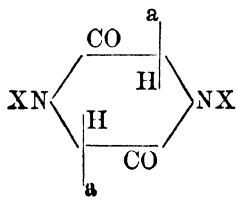
	m. p.	*m. p.*
Quinitol	139°	100-102°
Dimethyldiketo cyclohexane	93	115-117
1 4 Dibromo cyclohexane	113	liquid
Benzene hexachloride	310	157
Benzene hexabromide	253	212

Several of the alkaloids exist as cis and trans isomers.

	Cis.	*Trans*
Tropine	61 2°	108°
Ecgonine	198	257
Cocaine	98	46-47

The heterocyclic compounds are represented by diketopiperazines of Bischoff[1] and Fischer[2] of the general formulae:

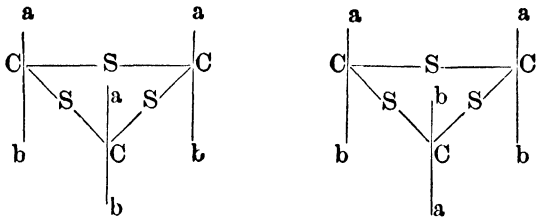




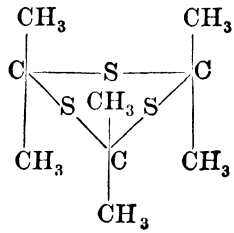
[1] *Ber.*, 1892, 25, 2950.

[2] *Ber.* 1906, 39, 3981.

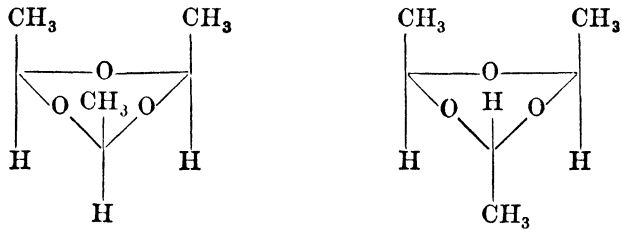
whilst a series of isomeric trithiomethylene derivatives have been obtained by Baumann and Fromm[1] by the polymerisation of thio-aldehydes and thiacetones. They are substances which may be represented by the general formulae:



It is significant that when the groups *ab* are identical, as in trithiacetone derived from thiacetone, and when, according to the theory, isomerism is impossible, only one form is known.



It is probable that paraldehyde and metaldehyde belong to the same type of *cis-trans* isomerism.

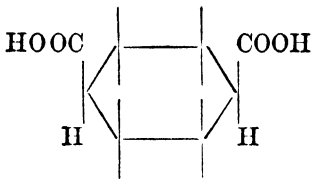


Determination of Configuration. The isomeric dibasic acids may generally be divided into a *cis* or malenoid and a *trans* or fumaroid type, exhibiting the distinctive characteristics of maleic and fumaric acid. The *cis* or malenoid form is distinguished by its greater solubility in water, its lower melting-point, its affinity constant (which is usually, though not invariably, higher), also by its anhydride formation (which is more readily effected than that of its isomer) and its conversion into the *trans* isomer by the aid of hydrochloric acid. The *trans* or fumaroid form is much less soluble in water; it has

[1] *Ber.*, 1891, **24**, 1419.

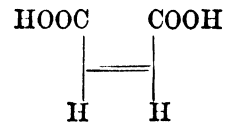
a higher melting-point, and occasionally yields an anhydride on heating with acetyl chloride, which, on more prolonged heating, passes into the anhydride of the *cis* form.

The following comparison between *cis* and *trans* hexahydroterephthalic acid and fumaric and maleic acid will illustrate the parallelism existing between the two pairs of compounds.



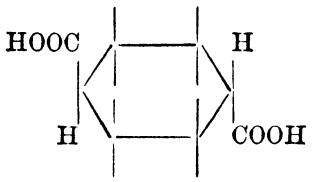
Cis Hexahydroterephthalic acid.

Crystallizes in large plates (*m. p.* 161-162°). Much more soluble in water than the trans form. Transformed into the trans form when heated with hydrochloric acid.



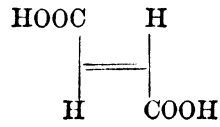
Maleic acid.

Crystallizes in large plates (*m. p.* 130°). Much more soluble in water than fumaric acid. Transformed into fumaric acid when heated with hydrochloric acid.



Trans Hexahydroterephthalic acid.

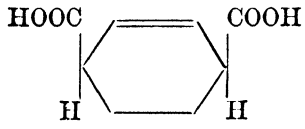
Crystallizes in short prisms, sublimes when heated, and melts at 300°. Forms no anhydride.



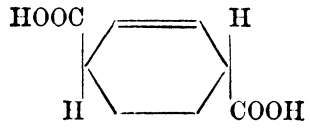
Fumaric acid.

Crystallizes in small prisms, sublimes at 200°. Forms the anhydride of maleic acid on heating.

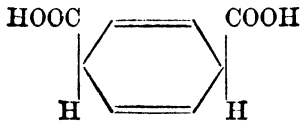
The partly saturated di- and tetra-hydrobenzene dicarboxylic acids also furnish examples of geometrical isomers and show similar differences in properties (see p. 275).



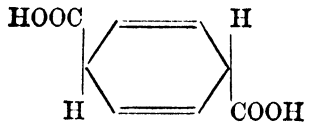
Cis Δ^2 Tetrahydroterephthalic acid.



Trans Δ^2 Tetrahydroterephthalic acid.



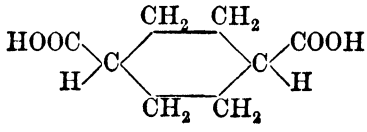
Cis $\Delta^{2,5}$ Dihydroterephthalic acid.



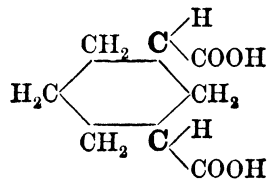
Trans $\Delta^{2,5}$ Dihydroterephthalic acid.

Thus in the case of the dibasic acids there is little difficulty in ascertaining the configuration of the isomers. In other cases the criteria are less satisfactory. It is generally assumed that the compound of higher melting-point corresponds to the *trans* form, but this distinction cannot be implicitly accepted. Occasionally the experience derived from steric hindrance (Part I, p. 383) will give some information.

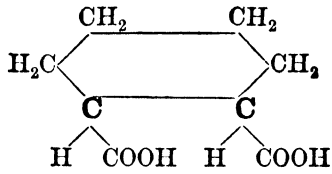
Absolute and Relative Asymmetry. From the list of dibasic acids on p. 275 it will be seen that the three hexahydrophthalic acids are represented by *cis* and *trans* isomers, but there is an important distinction between the para compound and the other two, for the latter contain asymmetric carbon atoms whilst the former does not. This is seen by reference to the space formulae



Hexahydroterephthalic acid.

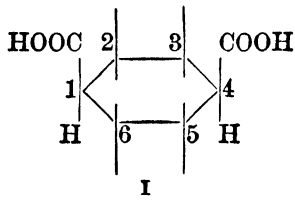


Hexahydroisophthalic acid.

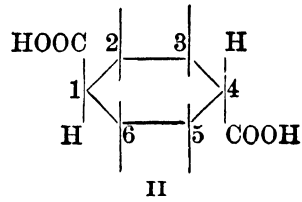


Hexahydrophthalic acid.

But there is a distinction between hexahydroterephthalic acid and an ordinary symmetrical open-chain compound, to which Baeyer has drawn attention. For if a person is represented as floating on his side in the orbit of the ring, with his face to the centre and his hands outstretched at right angles to the plane of the ring; further, supposing his feet to be at 1, and his head at 2, he will on reaching 4 in formula I (*cis* form) see carboxyl on his right and hydrogen on his left, whereas if he starts with head at 6 and feet at 1, he will see on arriving at 4 carboxyl on his left and hydrogen on his right. The same is true of formula II (*trans* form). The structure as a whole is therefore unsymmetrical, and to this Baeyer has given the name *relative asymmetry*.

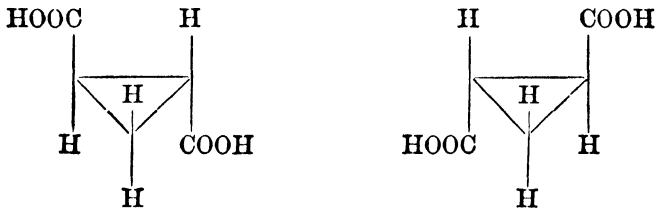


I



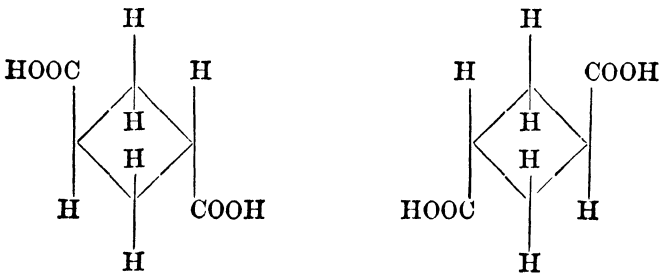
II

Hexahydro-phthalic and -isophthalic acids should therefore be separable into optical enantiomorphs, but not the hexahydroterephthalic acid. The resolution of hexahydrophthalic acid has in fact been accomplished by Werner and Conrad[1] (p. 223). The same principle is applicable to the other cyclic isomers. Thus 1 . 2 cyclopropane dicarboxylic acid contains two asymmetric carbon atoms and the two *trans* forms are non-superposable, and the same is true of 1 . 2 cyclobutane dicarboxylic acid, whereas *cis* and *trans*



Trans 1 . 2 Cyclopropane dicarboxylic acid.

1 . 3 cyclobutane dicarboxylic acids are examples of relative asymmetry, and each form is identical with its mirror-image. The conditions



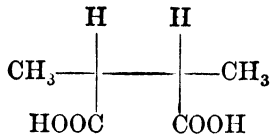
Trans 1 . 3 Cyclobutane dicarboxylic acid.

of asymmetry may be conveniently studied by means of the cardboard models described on p. 225.

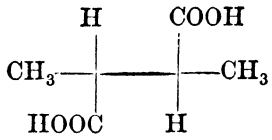
Combined Optical and Geometrical Isomerism. The question now arises: which of the two geometrical isomers containing

[1] *Ber.*, 1899, **32**, 3046.

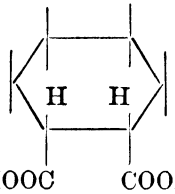
asymmetric carbon is inactive by internal, which by external compensation? A little reflection will furnish the answer, for the cyclic orthodibasic acids stand midway in configuration between the dialkyl succinic acids and the unsaturated acids of the maleic-fumaric type. The relationship will be evident from the following formulae:



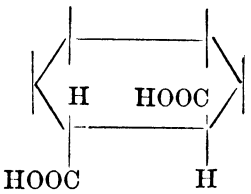
i-Dimethyl succinic acid.



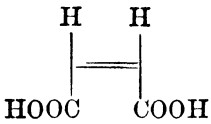
r-Dimethyl succinic acid.



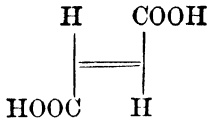
Cis Hexahydrophthalic acid.



Trans Hexahydrophthalic acid.



Maleic acid.



Fumaric acid.

The *cis* configuration represents the meso compound, the *trans*, the racemic form. This has been proved, as already stated, by Werner and Conrad, who succeeded in resolving the trans compound into its optical enantiomorphs.

The correspondence between each pair of the three types of dibasic acids described above is not one of configuration only, for it is exhibited in a very striking fashion by a close resemblance in physical and chemical properties. The following scheme will make this clear.

i-Dimethyl succinic acid.

m. p. 120°. Readily forms an anhydride (*m. p.* 87°); more soluble in water than its isomer, into which it is converted by strong hydrochloric acid.

Cis Hexahydrophthalic acid.

m. p. 192°. Passes readily into the anhydride (*m. p.* 32°); is more soluble in water than its isomer, into which it is transformed by heating with strong hydrochloric acid.

r-Dimethyl succinic acid.

m. p. 192°. Forms an anhydride with acetyl chloride (*m. p.* 38°), which when heated forms the anhydride of the meso compound.

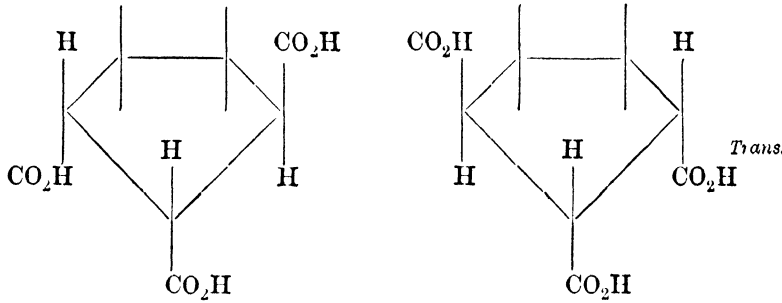
Trans Hexahydrophthalic acid.

m. p. 215°. Treated with acetyl chloride it forms an anhydride (*m. p.* 140°); when heated it is transformed into the cis anhydride.

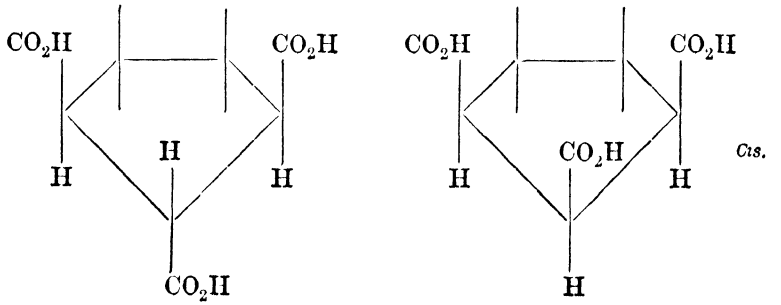
Maleic acid.	*Fumaric acid.*
m. p. 130°. Readily forms an anhydride on heating; more soluble in water than its isomer, and is converted by hydrochloric acid into fumaric acid.	*m. p.* 286-287°. Sublimes at 260°; forms the anhydride of the cis form on continued heating or with acetyl chloride.

It will be seen that in all three cases the malenoid form has the lower melting-point, and is the more soluble and the less stable isomer.

Another example of combined optical and geometrical isomerism is furnished by the cyclopentane tricarboxylic acids which Perkin and Robinson [1] obtained by the action of disodium malonic ester on $\alpha\alpha'$-dibromoadipic ester. Now there are two dibromoadipic acids (m.p. 193° and 139°), a meso (*cis*) and a racemic (*trans*) form, and it is the latter only which, when transformed into the cyclopentane derivative, could be resolved into its optical enantiomorphs. At the same time the meso acid must exist in a *cis* and *trans* form, as may be seen from the following formulae :



Racemic acid (dextro and laevo forms).



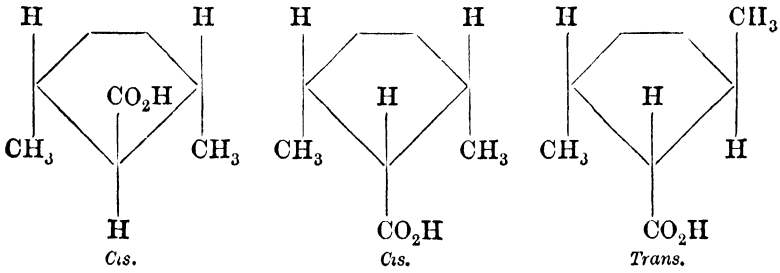
Meso acid (*cis* and *trans* forms).

It is the *trans* form of the cyclopentane acid derived from the dibromoadipic acid (m. p. 193°), which was resolved by crystallization of the brucine salt, thus determining the configuration of the dibromoadipic acid.

Three isomers of 2 . 5 dimethyl cyclopentane 1-carboxylic acids

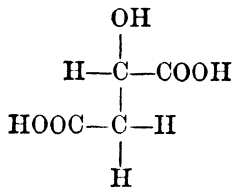
[1] *Trans. Chem. Soc*, 1921, 119, 1392.

had been previously obtained by J. Wislicenus,[1] two *cis* and one *trans* form, but the latter was never resolved.

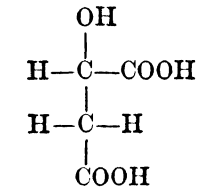


Cis. *Cis.* *Trans.*

Fixed Configuration of Open-chain Compounds. Several interesting questions arise out of the stereochemical relations subsisting between saturated and unsaturated open-chain compounds and the saturated or partly-saturated cyclic compounds, which, as we have seen, stand midway between them. For the latter exhibit many of the characteristic properties of geometrical isomers of the ethylene series, whilst they frequently resemble the open-chain compounds in their manifestation of optical activity. This dual character is seen concurrently where two similar asymmetric and nuclear carbon atoms adjoin one another as in the orthodibasic acids. The resemblance in certain physical and chemical properties between the *cis* and *trans* hexahydrophthalic acids and the two dimethyl succinic acids, on the one hand, and of fumaric and maleic acid, on the other, has been described, and its significance is unmistakable. It clearly indicates the fixed configuration of the groups in the dimethyl succinic acids, since they possess the distinguishing characteristics of geometrical isomers. This question has already been referred to on p. 264. According to Aberson[2] the third active malic acid found by Schmidt and Meyer in certain species of *Echeveria* can only be explained on the assumption of a fixed configuration of the radicals in these acids, to which Aberson attaches the following formulae:



Ordinary malic acid.



Aberson's acid.

Hantzsch[3] suggests that the two $\alpha\beta$-dibromopropionic acids, $CH_2Br.CHBr.COOH$, of Linnemann, which are readily interconvertible, and the three α-phenyl hydrocinnamic acids,

$$C_6H_5CH_2.CH(C_6H_5).COOH$$

[1] *Ber.*, 1901, 34, 2572.
[2] *Ber.*, 1898, 31, 1432.
[3] *Grundriss der Stereochemie*, p. 99.

of von Miller are to be accounted for in the same manner. The conversion of geometrical isomers of the *cis-trans* type, like fumaric and maleic acid, into the same product on reduction (succinic acid) appears at first sight to contradict this view, but it is readily explained by supposing that singly linked carbon atoms will in the majority of cases assume, by free rotation, the most stable configuration, and consequently no second compound is formed. There appears to be no direct means of ascertaining this favoured configuration, and the various proposals which have been suggested partake more or less of a speculative character. A certain amount of information has been derived from the behaviour of the alkyl succinic acids. It is well known that the facility with which they pass into anhydrides increases with the number of alkyl groups present. Succinic acid itself demands a higher temperature for conversion into the anhydride than mono- and di-methyl succinic acid, whilst tetramethyl succinic acid, even in aqueous solution, passes spontaneously into the anhydride. This property of anhydrisation seems to change concurrently with conductivity. Whereas succinic acid has a dissociation constant, K = 0·0068, which is nearer to fumaric acid, K = 0·09, than to maleic, K = 1·2, the methyl succinic acids have the following constants[1]:

	K
Monomethyl succinic acid	0 0085
s-Dimethyl succinic acid	0 0123 (cis), 0 0196 (trans)
Trimethyl succinic acid	0 0194
Tetramethyl succinic acid	0 0314

As it is usually found that the proximity of acid groups, such as the ortho-nitro substituted acids of the benzene series, increases the conductivity, it is fair to presume that the tendency in the methyl succinic acids is for the carboxyl groups to be driven into juxtaposition by increasing the number of methyl groups. The tendency of succinic acid will consequently be towards the *trans* configuration, that of tetramethyl succinic acid towards the *cis* configuration. It must be confessed that such a line of reasoning leads to no very satisfactory conclusion, but the subject is one of great interest and would repay further study.

[1] Walden, *Zeit. phys. Chem.*, 1891, 8, 433; Bone and Sprankling, *Trans. Chem Soc.*, 1899, 75, 864; Bethmann, *Zeit. phys. Chem.*, 1890, 5, 404.

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CHAPTER V

STEREOCHEMISTRY OF NITROGEN

Historical. In 1883 Goldschmidt,[1] working under the direction of V. Meyer, discovered an isomer of benzildioxime. It was found on investigation that the two were structurally identical, and consequently stereoisomeric. This unexpected result opened out a new and, as it has since proved, remarkably fertile field of research in stereochemistry. The first, or α-benzildioxime, is obtained by digesting equivalent weights of benzil dissolved in alcohol and hydroxylamine hydrochloride on the water-bath. It melts at 237°.

$$C_6H_5 . C(:NOH)C(:NOH) . C_6H_5$$

Benzildioxime.

The second, or β-compound, is prepared by heating an alcoholic solution of benzil with an excess of hydroxylamine hydrochloride in a sealed tube at 170°. It is colourless, like the first, but melts at 206–207°, and is more soluble in the ordinary solvents. In 1889 V. Meyer and Auwers[2] discovered a third, or γ-dioxime, which is obtained from the dioxide (see below) by reduction, and melts at 164–166°.[3] Each substance has the normal molecular weight, and gives a parallel series of ethers and esters of the general formula :

$$C_6H_5 . C(:NOR)C(:NOR) . C_6H_5$$

Each is decomposed with hydrochloric acid into the original benzil and hydroxylamine, yields dibenzyl on reduction, and a dioxide on oxidation[4].

$$\begin{array}{l} C_6H_5 . C : N . O \\ \quad\quad | \quad\quad | \\ C_6H_5 . C : N . O \end{array}$$

Benzildioxime-dioxide.

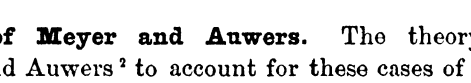
The α-compound is the least stable ; for, when heated with alcohol to 170°, or with water to 200°, it passes into the β-modification, and there are other ways of effecting the same result.[5]

[1] *Ber.*, 1883, 15, 1616, 2176. [2] *Ber*, 1889, 22, 705.
[3] Atack and Whinyates (*Trans. Chem. Soc*, 1921. 119, 1184) have discovered a fourth benzildioxime. [4] Koreff, *Ber.*, 1886, 19, 183.
[5] Auwers, *Die Entwicklung der Stereochemie*, p. 88.

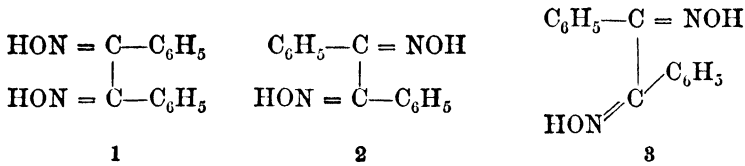
In 1888 V. Meyer and Auwers[1] obtained two isomeric benzil-monoximes; one (α) of melting-point 137–138°, was obtained by the action of free hydroxylamine on benzil in the cold alcoholic solution, and the other (γ) of melting-point 113–114°, by digesting an aqueous alcoholic solution of benzil with hydroxylamine hydrochloride on the water-bath. They are also structurally identical, and, like the dioximes, form a parallel series of alkyl and acyl derivatives. The first may be readily converted into the second by heating with alcohol to 100°, or by passing hydrochloric acid gas into the α-compound dissolved in a mixture of acetic acid and anhydride (Beckmann's method).

By the action of free hydroxylamine on the second or γ-monoxime, the γ-dioxime, referred to above, is obtained.

Theory of Meyer and Auwers. The theory proposed by V. Meyer and Auwers[2] to account for these cases of isomerism had reference to the linking of the carbon atoms. Different space arrangements of the molecule were produced by the carbon atoms becoming fixed, that is, losing their power of rotation, and so occupying a different relative position. The two monoximes were represented thus:



The three dioximes appeared as follows:



1 2 3

In formula 3 the two pair of groups are situated in two planes, at right angles.

Such a theory was contrary to van 't Hoff's conception of stereo-isomerism, which postulates no second form in singly linked carbon compounds unless the carbon group is asymmetrical; it was opposed to previous experience, and, in addition, there seemed no reason why the number of either monoximes or dioximes should be restricted to two in one case and three in the other. On the same principle it would be possible to construct two additional monoximes and a fourth dioxime.

[1] *Ber.* 1888, **21**, 784, 3510. [2] *Ber.*, 1890, **23**, 594.

When, therefore, isomeric *p*-chlorobenzophenoneoximes,

$$ClC_6H_4 . C(:NOH) . C_6H_5$$

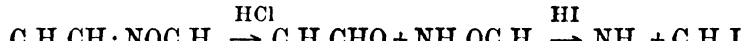
and other unsymmetrical ketoximes appeared without the requisite pair of singly linked carbon atoms, the theory could no longer be upheld, and it was forthwith abandoned.

About this time Beckmann [1] announced the discovery of a second oxime of benzaldehyde.

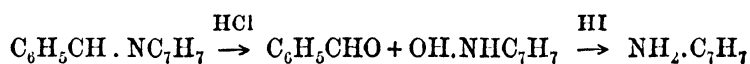
The ordinary or α-compound (*m. p.* 35°) is obtained by adding hydroxylamine hydrochloride gradually to a mixture of benzaldehyde and strong caustic soda solution, from which, after passing in carbon dioxide, the oxime is extracted with ether [2]; the β-compound is obtained in the form of the hydrochloride by passing hydrogen chloride into an ethereal solution of the α-compound. The addition of soda liberates the β-compound, which melts at 130°, and readily reverts to the α-form on standing. Beckmann [3] represented the two forms by different structural formulae on the following grounds:

α-Benzaldoxime. β-Benzaldoxime.

Both compounds form benzyl ethers, which decompose with hydrochloric acid into benzaldehyde and benzylhydroxylamine; but, whereas the benzylhydroxylamine from the α-aldoxime yields, with hydriodic acid, benzyl iodide, the β-benzylhydroxylamine forms benzylamine. Consequently the benzyl group in the ether of the β-oxime, and therefore the hydrogen atom in the β-oxime itself, is linked to nitrogen thus:



α-Benzaldoxime benzyl ether. Benzyl iodide.



β-Benzaldoxime benzyl ether. Benzylamine.

The same explanation served for the isomeric ketoximes. But the argument could not be sustained. In the first place, Auwers and others found that benzaldoxime exhibits tautomerism (p. 330), and

[1] *Ber.*, 1889, 22, 429, 1531.
[2] *Ber.*, 1890, 23, 1684.
[3] *Ber.*, 1889, 22, 1531.

the constitution of the aldoxime could not be inferred from that of its benzyl ethers.

Moreover, three methyl ethers of a number of aldoximes have been obtained. For example, in the case of *m*-nitrobenzaldoxime the action of methyl iodide on the sodium salt of the α-oxime gives an oxygen methyl ether and on the sodium salt of the β-oxime a nitrogen methyl ether together with a small quantity of a second oxygen methyl ether. Thus there are three ethers the existence of which is unexplained by Beckmann's formulae. Semper and Lichtenstadt[1] have recently obtained two O-methyl ethers and two N-methyl ethers from α- and β-phenyltolylketoxime.

In the second place, Goldschmidt[2] obtained from both benzaldoximes by the action of phenyl carbimide, $C_6H_5N:CO$, under precisely similar conditions, carbanilide compounds, one of which, the β-derivative, is converted into the α-compound by a trace of hydrogen chloride, and both are decomposed by dilute alkalis with equal ease. A compound having the formula of the α-aldoxime would give a carbanilide of the following structure:

$$C_6H_5CH:N.O.CO.NHC_6H_5$$

whilst, according to Beckmann, the β-oxime would yield a stable urea derivative of the formula:

$$C_6H_5CH.N.CO.NHC_6H_5$$
$$\quad\quad\quad

or they may be drawn together by mutual attraction, causing the bonds to be bent along the edges of a tetrahedron. In this case they will no longer lie in the same plane with the nitrogen atom but form an unsymmetrical space arrangement, and stereoisomerism becomes possible (Fig. 44).

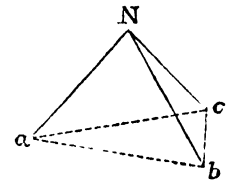


FIG. 44.

Attempts to resolve substituted ammonias[1] like benzylethylamine, *p*-tolylhydrazine, methylaniline, tetrahydroquinoline, &c., by crystallization of their salts with active acids, have invariably failed, and the conclusion seems inevitable that the nitrogen bonds in these compounds lie in one plane with the nitrogen atom.

The experiments are, however, so far inconclusive that partially racemic compounds might be formed, or hydrolytic dissociation of the salts might occur in process of crystallization. In the former case the two enantiomorphous bases would crystallize with the same active acid in equivalent amounts, and, in the second, optical inversion of the nitrogen groups might occur, producing racemisation.

Another suggested cause of failure of the above method is the change of valency of the nitrogen atom in the union of the tervalent bases with acids which might displace the original directions of the bonds. These possible causes of failure have to some extent been avoided by crystallizing the salts from non-hydroxylic solvents, and by using substituted hydrazines of the general formula $\begin{matrix}\mathrm{a}\\\mathrm{b}\end{matrix}\!\!>\!\mathrm{N.NH_2}$, in which the valency of the asymmetrical tervalent group is undisturbed;[2] but in neither case has any resolution of the bases been effected.

Evidence, but of another kind, of the plane arrangement of the nitrogen bonds has been furnished by Kipping and Salway.[3] They have fractionally crystallized the amide resulting from the union of an externally compensated acid chloride, for example, *dl*-benzyl-methyl-acetyl chloride with an unsymmetrical secondary amine (e. g. methylaniline). If the amine is externally compensated, two enantiomorphous pairs of compounds should result, namely, *d*A*d*B and *l*A*l*B; *d*A*l*B and *l*A*d*B, which would form two inactive salts separable by crystallization. As the product was homogeneous, the

[1] Kraft, *Ber.*, 1890, 23, 2780; Behrend and König, *Annalen*, 1891, 263, 184; Ladenburg, *Ber.*, 1893, 26, 864.

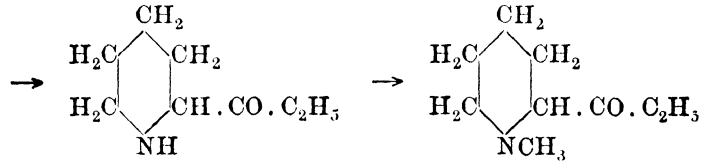
[2] Reychler, *Bull. Soc. Chim*, 1902 (3), 27, 979; Jones and Millington, *Proc. Camb Phil. Soc.*, 1904, 2, 489.

[3] *Trans. Chem. Soc.*, 1904, 85, 438.

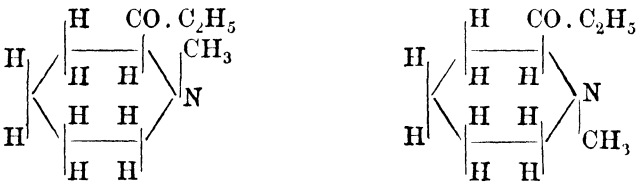
evidence is in favour of a plane configuration of the tervalent nitrogen compounds.

Attempts to resolve such compounds have been more successful where the nitrogen forms part of a ring. Hess[1] has been able to show that racemic methyl isopelletierine obtained from isopelletierine of pomegranate (see Part III, p. 345) is stereoisomeric with the racemic compound of methyl conhydrinone obtained synthetically from picolinic acid by distilling the calcium salt with calcium propionate, reducing the product with hydrogen in presence of colloidal platinum, and finally methylating with formaldehyde in presence of formic acid.

$$C_5H_4N.COOCa' + Ca'OOC_2H_5 = C_5H_4N.CO.C_2H_5 + CaCO_3$$

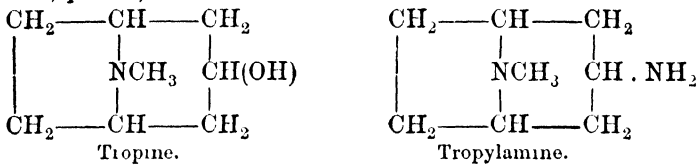


Conhydrinone. Methyl conhydrinone.



Stereoisomeric forms of methyl isopelletierine and methyl conhydrinone.

The existence of the two tropines and tropylamines of Willstätter and Müller,[2] can only be explained by a change in the configuration of the NCH_3 group relatively to the substituted methylene group (Part III, p. 336).



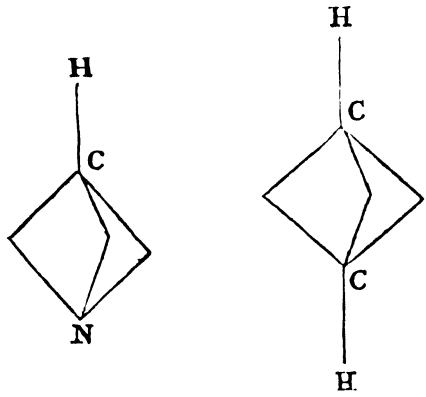
Tropine. Tropylamine.

Theory of Hantzsch and Werner. The theory of Hantzsch and Werner,[3] which was put forward to explain the existence of the isomeric oximes, appeared in 1890, and, in spite of some adverse criticism, has successfully held its ground.

[1] *Ber.*, 1919, **52**, 964, 1622; 1920, **53**, 129.
[2] *Ber.*, 1896, **29**, 936, 1636, 2228; 1898, 31, 1212, 2655; see also Hess, *Ber.*, 1919, **52**, 1622.
[3] *Ber.*, 1890, 23, 11.

Based on recognized stereochemical principles, it afforded at the time of its publication a simple explanation of existing facts, and has since become a fruitful source of new discoveries.

Hantzsch and Werner point out that in compounds like hydrocyanic acid, cyanogen, pyridine, thiazole and other cyclic nitrogen compounds in which nitrogen is linked to carbon, if the carbon bonds are directed towards the summits of a tetrahedron, a corresponding bending of the nitrogen linkages is probable (Fig. 45).



Hydrocyanic acid. Acetylene.

Fig. 45.

A configuration of this character will correspond to acetylene and cannot furnish isomeric derivatives (p. 255); but supposing that whilst the direction of the carbon and nitrogen bonds in hydrogen cyanide is preserved one pair is severed, the nitrogen and carbon become doubly linked as in ethylene and its derivatives. Represented by tetrahedral models (nitrogen occupies the summit of one tetrahedron), the two space arrangements will be represented thus:

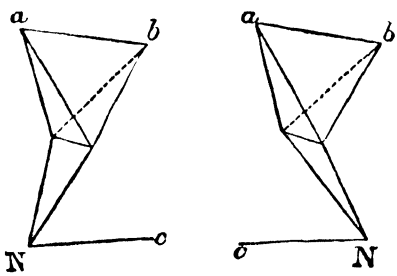


Fig 46.

If the Kekulé models are substituted, the formulae will appear as follows:

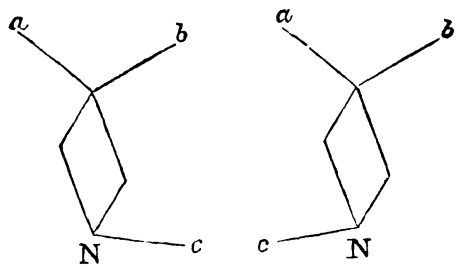


FIG. 47.

Just as geometrical isomerism may occur in ethylene derivatives when the doubly linked carbon atoms are united to a different pair of groups, so in the present case two substances are conceivable, in which doubly linked nitrogen and carbon are present. The configurations may be conveniently represented in the following way:

Precisely these conditions obtain in the unsymmetrical oximes.

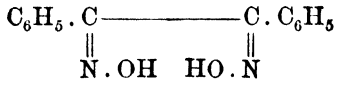
The two benzaldoximes may be represented by the following configurations, which are distinguished by the prefix *syn* and *anti*, which correspond to *cis* and *trans* respectively in the ethylene series.

Benz*syn*aldoxime. Ben*zanti*aldoxime.

In the case of the aldoximes and monoketoximes the term *syn* precedes the name of the group occupying the cis position to the hydroxyl of the oximino group, whilst *anti* indicates the reverse arrangement. The two *p*-chlorobenzophenoneoximes will appear thus:

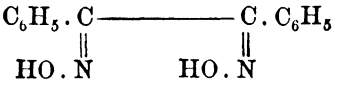
Syn-Chlorobenzophenoneoxime. *Anti*-Chlorobenzophenoneoxime.

The three benzildioximes are distinguished by the terms *syn*, *anti*, and *amphi*.



Syn-Benzildioxime.

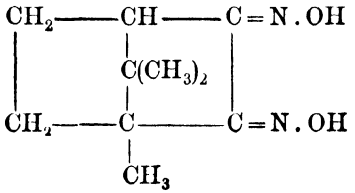
Anti-Benzildioxime.



Amphi-Benzildioxime.

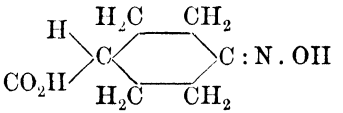
The number of actual isomers in each of the above examples corresponds exactly to that required by the theory.

Camphor dioxime should exist in four different configurations:



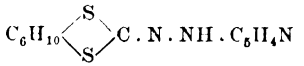
All four are known.

The theory of Hantzsch and Werner receives strong support from the observation of Mills and Bain,[1] who succeeded in resolving the oxime of cyclohexanone carboxylic acid into two optically active forms.



This could only occur if the molecule were rendered asymmetric by the oxime-hydroxyl occupying a different plane from that of H and CO_2H as explained on p. 254.

[1] *Trans.*, 1910, **97**, 1866. Further confirmation that the three valencies of nitrogen are not coplanar is afforded by the fact that Mills and Schindler have resolved the pyridylhydrazone of cyclohexylene dithiocarbonate

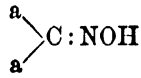


into two optically active forms (*Trans. Chem. Soc.*, 1923, **123**, 312).

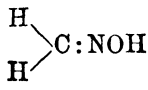
Properties of the Isomers. The isomers are not characterized by optical differences, but by those physical and chemical properties which distinguish the geometrical isomers of the ethylene series (p. 255). In addition they are readily convertible into one another, and, most significant of all, isomerism disappears where theory demands it. Thus, the benzaldoximes give the same benzyl hydroxylamine on reduction,

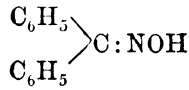
$$C_6H_5CH_2 . NHOH$$

and isomeric ketoximes of the formula,



like formaldoxime and diphenylketoxime, have never been prepared,





whilst acetaldoximes and propionaldoximes as well as a variety of aldoximes and unsymmetrical ketoximes of the aromatic series are known. In short, the experimental facts satisfy all the essential conditions of geometrical isomerism.

The impulse which the theory of Hantzsch and Werner has given to the search for new examples of stereoisomerism among this class of compounds has rapidly added to the number, and the list has grown to formidable proportions. The following are among the better known examples:[1]

Aldoximes.

o- *m-* and *p*-Nitrobenzaldoxime	Anisaldoxime
o- *m-* and *p*-Chlorobenzaldoxime	Cuminaldoxime
m- and *p*-Bromobenzaldoxime	Piperonaldoxime
p-Iodobenzaldoxime	Furfuraldoxime
m- and *p*-Tolylaldoxime	Thiophenaldoxime

Ketoximes.

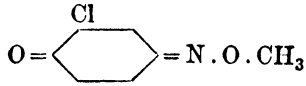
p-Methoxybenzophenoneoxime	*p*-Propylbenzophenoneoxime
m- *p*-Chlorobenzophenoneoxime	Xylylbenzophenoneoxime
m- *p*-Bromobenzophenoneoxime	*p*-Aminobenzophenoneoxime
o- *p*-Tolylphenylketoxime	*m-p*-Hydroxybenzophenoneoxime
p-Ethylbenzophenoneoxime	Thienylphenylketoxime

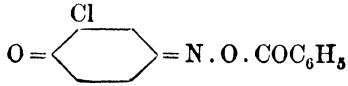
[1] A more complete list will be found in Werner's *Lehrbuch der Stereochemie.*

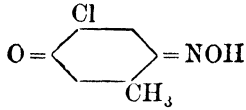
Dioximes.

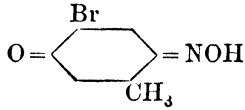
Benzildioxime	Nitrobenzildioxime
Anisildioxime	Phenylglyoxime
Cuminildioxime	Glyoximedicarboxylic acid
Tolildioxime	Camphordioxime

Quinoncoximes.

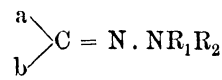
Methyl *m*-chloroquinoneoxime 

Benzoyl *m*-chloroquinoneoxime 

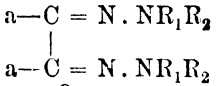
p-Chlorotoluquinoneoxime 

p-Bromotoluquinoneoxime 

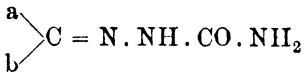
In addition to the oximes of aldehydes, ketones, diketones, and quinones, isomers belonging to the class of hydrazones, osazones, anil-compounds, chlorimides, and diazo-compounds, all of which contain the requisite doubly linked carbon-nitrogen or nitrogen-nitrogen complex, are now known:



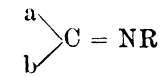
Hydrazones.



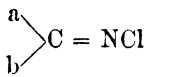
Osazones.



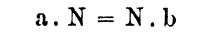
Semicarbazones.



Anil compounds.



Chlorimides.

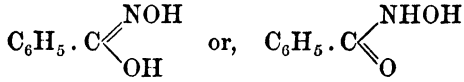


Diazo-compounds.

Lossen's Benzhydroximic Acid and its Derivatives. The theory has, moreover, accounted for some of the mysterious *physical*

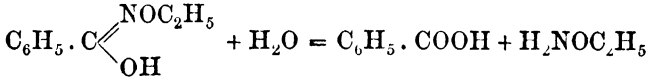
isomers which Lossen[1] found among the derivatives of benzhydroxamic acid.

Benzhydroxamic acid, or benzhydroximic acid, as Werner[2] prefers to call it, is obtained by the action of benzoyl chloride or benzoic ester on hydroxylamine



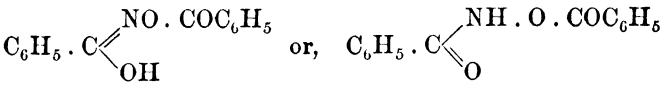
Benzhydroximic acid.

The ethyl ether, prepared by the action of ethyl iodide on the potassium salt, has the following formula, since it is decomposed by dilute acids into benzoic acid and ethoxylamine:

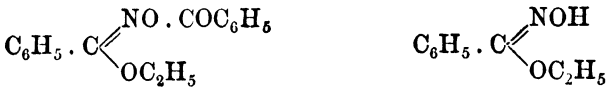


Benzhydroximic ether. Benzoic acid Ethoxylamine.

The hydrogen of the hydroxylamine-hydroxyl may also be replaced by acid radicals, such as benzoyl, as well as by alkyl groups. The compounds with acid radicals are acids and form salts. The formula of the benzoyl derivative will be one of the following:



If now the replaceable hydrogen is substituted by an alkyl group, by the action of alkyl iodide on the silver salt, the product (as well as that obtained by its hydrolysis, namely, ethyl benzhydroximic acid) is found to be a mixture of two isomers:



Ethyl benzhydroximic benzoyl ester. Ethyl benzhydroximic acid.

Both of the ethyl benzhydroximic acids decompose on hydrolysis into benzoic ester and hydroxylamine.

Werner has pointed out that these compounds are strictly oximes, and offer a striking analogy in chemical behaviour to the isomeric ketoximes. The reason for this becomes apparent on making a slight alteration in the manner of writing the formula:

[1] *Annalen*, 1872, 161, 347; 1875, 175, 271; 1877, 186, 1; 1889, 252, 170; 1891, 265, 176; 1894, 281, 169.

[2] *Ber.*, 1892, 25, 27; 1893 26, 1561; 1896, 29, 1155.

$C_6H_5 . C . OC_2H_5$ / $C_6H_5CO . O . N$
Ethyl syn-benzhydroximic benzoyl ester.

$C_6H_5 . C . OC_2H_5$ / $N . O . COC_6H_5$
Ethyl anti-benzhydroximic benzoyl ester.

$C_6H_5 . C . OC_2H_5$ / $HO . N$
Ethyl syn-benzhydroximic acid.

$C_6H_5 . C . OC_2H_5$ / $N . OH$
Ethyl anti-benzhydroximic acid.

The following are the names of some of the hydroximic acids which exist in isomeric forms:

Hydroximic acids.

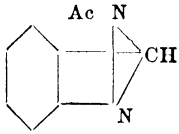
Propylbenzhydroximic acid	$C_6H_5 . C(:NOH)OC_3H_7$
Ethyl *p*-tolylhydroximic acid	$CH_3C_6H_4C(:NOH)OC_2H_5$
Ethylanishydroximic acid	$CH_3OC_6H_4C(:NOH)OC_2H_5$

Hydroximic esters.[1]

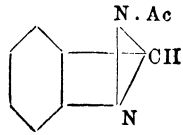
Propylbenzhydroximic benzoyl ester	$C_6H_5C(:NOCOC_6H_5)OC_3H_7$
Ethyl *p*-tolylhydroximic benzoyl ester	$CH_3C_6H_4C(:NOCOC_6H_5)OC_2H_5$
Ethylanishydroximic benzoyl ester	$CH_3OC_6H_4C(:NOCOC_6H_5)OC_2H_5$
Ethylanishydroximic anisyl ester	$CH_3OC_6H_4C(:NOCOC_6H_4OCH_3)OC_2H_5$
Ethylbenzhydroximic anisyl ester	$C_6H_5C(:NOCOC_6H_4OCH_3)OC_2H_5$.

Determination of Configuration. We have now to consider the methods adopted by Hantzsch for determining the configuration of the isomeric oximes The methods, like those applied to ethylene derivatives, are based on some marked difference in chemical behaviour, and especially on intramolecular changes such as the formation of anhydrides.

[1] A curious case of stereoisomerism is that observed by Auwers and Lange (*Ber.*, 1919, **52**, 1330, 1920, 53, 1211, 1179, 1922, 55, 1139) If indazole and its derivatives are converted into the acyl derivative with the acid anhydride, one set of stereoisomers is obtained, whereas acid chlorides in presence of pyridine or when allowed to react with the silver compound of indazole give rise to a second series. They are represented as follows:



Anti (stable).



Syn (labile).

Configuration of the Aldoximes. It is found that derivatives of one of the isomeric aldoximes decomposes into a nitrile more readily than the other. This property is taken to indicate the *syn* configuration. Thus benzsynaldoxime forms benzonitrile and water,

$$\begin{matrix} C_6H_5C\,.\,H \\ \| \\ N\,.\,OH \end{matrix} = \begin{matrix} C_6H_5C \\ \| \\ N \end{matrix} + H_2O$$

The reaction is generally performed by warming the aldoxime with acetic anhydride at a temperature not above 35° (when the acetyl derivative is formed), cooling, adding solid sodium carbonate, and finally a solution of caustic soda. Under these conditions the acetyl derivative of the anti-oxime is hydrolysed, and dissolves as the oxime in the alkaline solution, whilst the nitrile from the syn-compound remains undissolved and is readily detected by its strong and characteristic smell:[1]

$$\begin{matrix} C_6H_5CH \\ \| \\ NO\,.\,COCH_3 \end{matrix} = C_6H_5\,.\,CN + CH_3\,.\,COOH$$

The two phenyloximino-acetic acids[2] may be distinguished by the same process. The acetyl derivative of the one yields benzonitrile, that of the other is hydrolysed and gives the original oximino compound. The first has therefore the syn configuration:

$$\begin{matrix} C_6H_5\,.\,C\,.\,COOH \\ \| \\ N\,.\,O\,.\,COCH_3 \end{matrix} = \begin{matrix} C_6H_5C \\ \| \\ N \end{matrix} + \begin{matrix} CO_2 \\ + \\ HO\,.\,COCH_3 \end{matrix}$$

Antiglyoxime dicarboxylic acid behaves in the same manner and gives carbon dioxide, water, and cyanogen:

$$\begin{matrix} COOH\,.\,C{-}C\,.\,COOH \\ \| \quad \| \\ HO\,.\,N \quad N\,OH \end{matrix} = \begin{matrix} CO_2 \\ + \\ H_2O \end{matrix} \begin{matrix} C{-}C \\ \| \quad \| \\ N \quad N \end{matrix} \begin{matrix} CO_2 \\ + \\ H_2O \end{matrix}$$

Goldschmidt[3] has suggested the use of phenyl carbimide for determining the configuration of the oximes, depending on the formation of the carbanilide derivatives. On hydrolysis they were supposed to behave like the acetyl derivatives of the oximes, giving in one case the original substance and in the other the nitrile; but Brady and Dunn[4] have shown that the method is untrustworthy, as in some cases inversion of the carbanilide takes place.

Another method of distinguishing syn and anti aldoximes depends on an observation of Comstock[5] that only the former unite with cuprous chloride and bromide, forming compounds of the general formula $(R\,.\,CH\ NOH)_2CuX$.

Configuration of the Ketoximes. In determining the configuration of the ketoximes Hantzsch employs what is known as Beckmann's reaction. When the ketoximes are treated with strong sulphuric acid, hydrochloric acid, or phosphorus chloride, a molecular change occurs whereby the oxime is converted into an amide. To prevent conversion of one isomer into the other during the process, it is found

[1] Wentworth and Brady, *Trans. Chem. Soc.*, 1920, 117, 1015
[2] Hantzsch, *Ber.*, 1891, **24**, 41
[3] *Ber.*, 1889, **22**, 3112; 1890, **23**, 2136; 1891, **24**, 2546; 1893, **26**, 2087.
[4] *Trans. Chem. Soc.*, 1916, **109**, 650. [5] *Amer. Chem. J.*, 1897, **19**, 485.

advisable to use phosphorus pentachloride in preference to the other reagents, and to add it to the compound in a cold solution of benzene or petroleum spirit. The reaction has been explained in the following manner. The hydroxyl group attached to the nitrogen atom changes place with the radical attached to the carbon atom in the cis position. This is followed by the shifting of the hydroxyl-hydrogen from the oxygen to the nitrogen (p. 338). The character of the product will consequently depend on the relative positions of the hydroxyl group and radical in the oxime. If a and b denote the two radicals the changes will proceed as follows:

1. $\begin{matrix} a\text{—}C\text{—}b \\ \| \\ HO.N \end{matrix} \rightarrow \begin{matrix} HO.C\text{—}b \\ \| \\ a\text{—}N \end{matrix} \rightarrow \begin{matrix} O:C\text{—}b \\ | \\ a\text{—}NH \end{matrix}$

2. $\begin{matrix} a\text{—}C\text{—}b \\ \| \\ N.OH \end{matrix} \rightarrow \begin{matrix} a\text{—}C.OH \\ \| \\ N\text{—}b \end{matrix} \rightarrow \begin{matrix} a\text{—}C:O \\ | \\ HN\text{—}b \end{matrix}$

The amine and acid obtained by decomposing the amide will be different in the two cases.

Thus, there are two isomeric *p*-methoxybenzophenoneoximes *m. p.* 137° and 115°. The one phenylanisylketoxime yields anisic anilide and finally anisic acid and aniline, and is therefore the syn-compound, whereas the other is converted into benzoic aniside and then anisidine and benzoic acid, and is consequently the anti-compound:

$\begin{matrix} C_6H_5.C.C_6H_4OCH_3 \\ \| \\ HO.N \end{matrix} \rightarrow \begin{matrix} O:C.C_6H_4OCH_3 \\ | \\ C_6H_5HN \end{matrix} \rightarrow \begin{matrix} HOOC.C_6H_4OCH_3 \\ + \\ C_6H_5NH_2 \end{matrix}$

Syn-phenylanisylketoxime. Anisic anilide. Anisic acid and aniline.

$\begin{matrix} C_6H_5.C.C_6H_4OCH_3 \\ \| \\ N.OH \end{matrix} \rightarrow \begin{matrix} C_6H_5.C:O \\ | \\ NHC_6H_4OCH_3 \end{matrix} \rightarrow \begin{matrix} C_6H_5COOH \\ + \\ NH_2C_6H_4OCH_3 \end{matrix}$

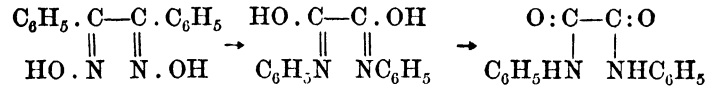
Anti-phenylanisylketoxime. Benzoic aniside. Anisidine and benzoic acid.

Configuration of the Hydroximic Acids. The same reaction may be used for identifying the ethylbenzhydroximic acids, for the *α*-acid (syn) changes into phenylurethane, whereas the *β*-acid (anti) is undecomposed and combines with the phosphorus to form an ester:

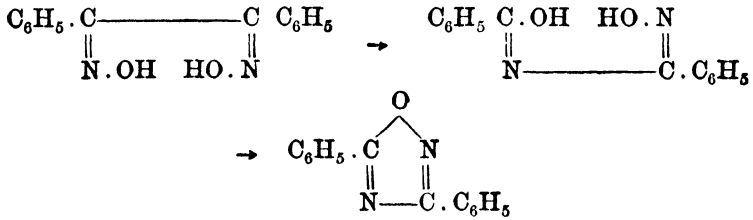
$\begin{matrix} C_6H_5.C.OC_2H_5 \\ \| \\ HO.N \end{matrix} \rightarrow \begin{matrix} HO.C.OC_2H_5 \\ \| \\ C_6H_5.N \end{matrix} \rightarrow \begin{matrix} O:C.OC_2H_5 \\ | \\ NHC_6H_5 \end{matrix}$

Ethyl syn-benzhydroximic acid. Phenylurethane.

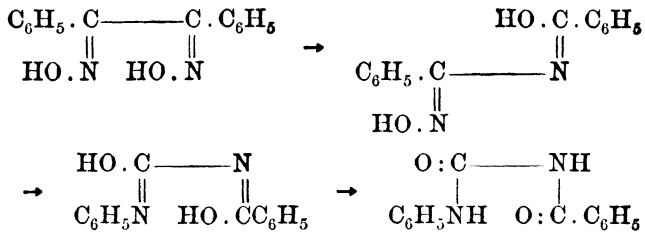
Configuration of the Dioximes or Glyoximes. The behaviour of glyoximedicarboxylic acid has already been mentioned (p. 299). The benzildioximes and analogous compounds can be differentiated by the aid of Beckmann's reaction. The most stable (β) of the benzildioximes, since it yields oxanilide, is the anti-compound:[1]



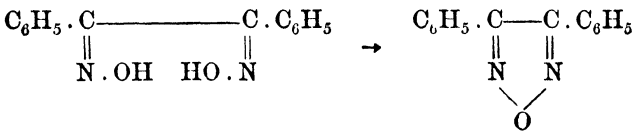
The α-compound gives dibenzenylazoxime and is therefore the syn-compound:



whilst the γ-dioxime is converted into benzoylphenylurea and represents the amphi-compound:



The syn-dioximes are further characterized by the formation of anhydrides or furazanes:

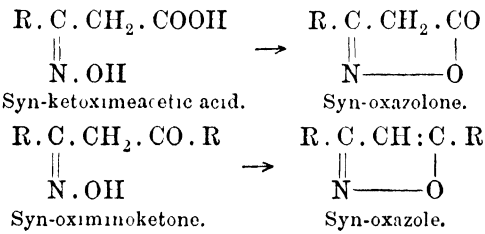


Syn-benzildioxime. Diphenylfurazane.

The same property can be utilized to determine configuration in such

[1] From experiments by Meisenheimer and Weibezahn (*Ber*, 1921, **54**, 3195, 3208) the β-compound must be represented by the syn configuration and the α-compound by the anti configuration; for the β-monoxime is undoubtedly the syn compound, and moreover the β-dioxime is most easily transformed into the anhydride. It is, however, difficult to reconcile this view with the results of the Beckmann reaction.

cases as the β-ketoximic acids of the formula R . C(NOH) . CH_2 . COOH and β-oximinoketones R . C(NOH) . CH_2 . CO . R, even though no second isomer is known. Both groups of compounds form anhydrides more or less readily, and possess, therefore, a syn configuration:



Tschugaeff[1] finds further that it is possible to distinguish the syn dioximes by the compounds which they form with various metallic salts, such as those of nickel, cobalt, palladium, platinum, iron, and copper.

Inversion of the Oximes. The manner in which the oximes undergo conversion into one another has already been illustrated in the case of the benzaldoximes and benziloximes (pp. 286, 288). Light[2] will sometimes effect the change, but hydrogen chloride is the most common and effective reagent for transforming the anti-aldoxime into the syn-isomer through the formation of a hydrochloride. The methods that can be employed are passing hydrogen chloride into a solution of the anti-oxime in an inert organic solvent, preferably warm, or suspending the oxime in concentrated hydrochloric acid and saturating the suspension with hydrogen chloride.[3] The hydrochloride obtained by the former method is filtered, and decomposed by adding it to an excess of sodium carbonate solution, or preferably by dissolution in sodium hydroxide and precipitating the oxime with ammonium chloride; in the latter method the whole reaction mixture is slowly poured into excess of sodium carbonate solution. The syn-oxime so obtained is generally impure and requires recrystallization.

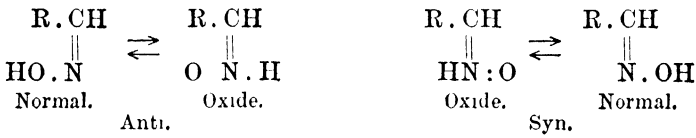
In general aldoximes which exist in the anti and syn forms yield two hydrochlorides. The one is obtainable from the anti-oxime at low temperatures and regenerates anti-oxime on treatment with alkali. The other yields syn-oxime on treatment with alkali and can be obtained from the anti-oxime at higher temperatures, from

[1] *Ber*, 1908, 41, 1678; see also Atack, *Trans. Chem. Soc*, 1913, 103, 1317.
[2] Ciamician and Silber, *Ber.*, 1902, 35, 4128, 1903, 36, 4268; Brady and Dunn, *Trans. Chem. Soc.*, 1913, 103, 1619.
[3] Dunstan and Thole, *Proc. Chem Soc* 1911, 27, 233.

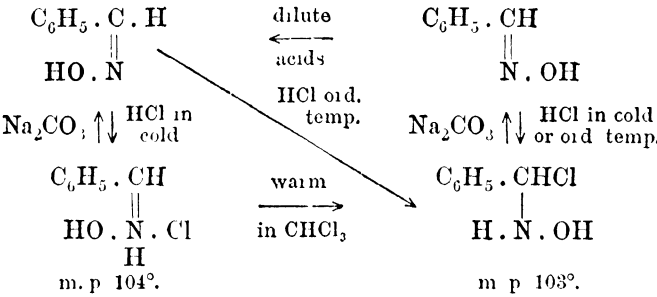
the syn-oxime, or by heating the former hydrochloride in neutral organic solvents, such as chloroform or benzene.[1]

Dilute hydrochloric acid converts the syn-oxime into the anti-isomer; the hydrochlorides are decomposed by moist air, sometimes very rapidly, and, in the case of the syn-forming hydrochloride, the acid so formed converts the syn-oxime, which is liberated at the same time, into the anti-isomer. In the case of benzaldoxime, Luxmoore[2] claimed to have obtained two hydrochlorides; one melted at 104° and regenerated anti-oxime on treatment with alkali, and the other melted at 67° and gave the syn-oxime. Brady and Dunn have now shown that the hydrochloride, m. p. 67°, is a hydrate of the syn-forming hydrochloride, which they find melts at 103°.

Brady and Dunn[3] suggest that these changes occur in the following way. They assume that each oxime may exist in tautomeric forms.



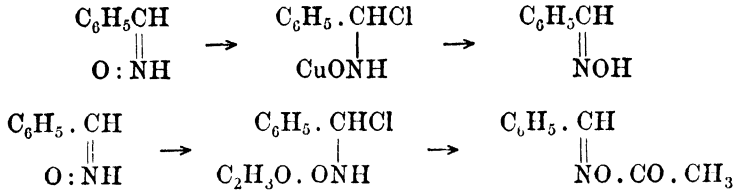
and that the formation of the hydrochlorides may occur in two ways as follows:



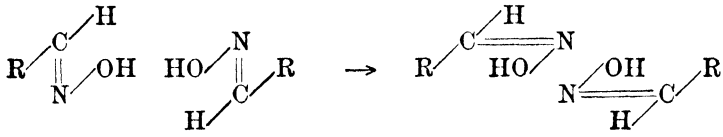
The anti-oxime with hydrogen chloride at the ordinary temperature passes into the tautomeric form and adds on a molecule of the acid, whereby the nitrogen becomes linked by a single bond to the carbon atom so that the former is free to swing round into the syn position on losing the molecule of hydrogen chloride.

Other facts such as the conversion of the anti into the syn compound by the action of cuprous chloride and acetyl chloride may be explained in the same way.

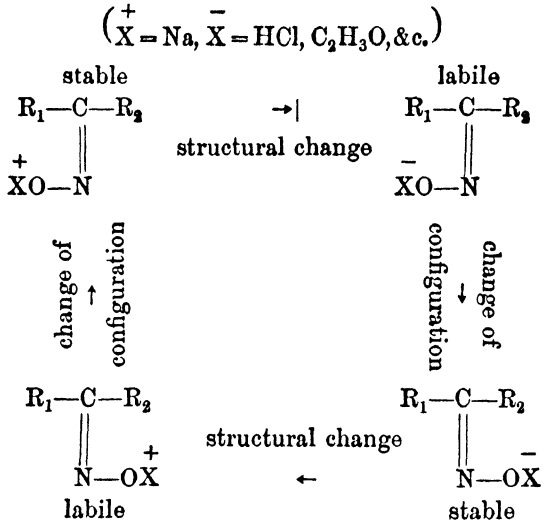
[1] Brady and Dunn, *Private Communication.*
[2] Luxmoore, *Trans Chem. Soc*, 1896, **69**, 181.
[3] *Trans Chem Soc.*, 1913, 103, 1620; 1914, 105, 824, 2104; 1915, 107, 1858; 1916, 109, 650.



The spontaneous reversal of the syn- into the anti-oxime is not so easily accounted for. Brady and Dunn adopt Stewart's [1] suggestion that a temporary union of two molecules of the syn-compound and subsequent fission along a horizontal plane



Hantzsch [2] divides the oximes into the *acid stable* and the *alkali stable* and formulates the general scheme :



All the dioximes such as the dioximes of benzil, phenylglyoxal, glyoxal dicarboxylic acid, as well as the oximes of *p*-hydroxybenzophenone and phenylglyoxylic acid, exhibit this behaviour, which explains, among other things, the formation of the one isomer by

[1] *Proc. Chem. Soc.*, 1905, 21, 73.
[2] *Grundriss der Stereochemie*, 2nd ed., p. 130.

the action of free hydroxylamine in the presence of alkali, and the other by the use of the hydrochloride (p. 288).

The instability of the anti-compounds in presence of acids, especially hydrochloric acid, accounts for the action of acetyl chloride, which, by producing traces of hydrogen chloride, converts benzanti-aldoxime into the acetyl derivative of the syn-compound; hence the substitution of acetic anhydride in the method described for determining configurations. It explains also the use of carbon dioxide for liberating the anti-benzaldoxime from its sodium salt (p. 288).

It is readily conceivable from what has been stated that the formation of the particular isomer is dependent on the chemical or physical conditions of the experiment, and that it is rather the exception than the rule to find both isomers in the product. Nevertheless, isomeric ketoximes of the aromatic series frequently appear together when the oxime is formed in alkaline solution by Auwers' method,[1] and they can then be separated by fractional crystallization. The simultaneous formation of the two aldoximes has been observed in the process of decomposing the bisnitrosylbenzyl compounds.[2] The latter are formed by oxidizing the β-benzylhydroxylamines,

$$2C_6H_5CH_2 . NHOH + O_2 = (C_6H_5CH_2NO)_2 + 2H_2O$$

and with sodium ethylate yield a mixture of the two geometrical isomers:

$$(C_6H_5CH_2NO)_2 = 2C_6H_5CH : NOH \text{ (syn and anti).}$$

But in other cases the two compounds are derived from different materials, one oximino-succinic ester, for example, being prepared by the action of nitrous acid on succino-succinic ester, and the other by the action of hydroxylamine on oxaloacetic ester[3]:

$$HOOC . C(:NOH) . CH_2 . COOH$$

Oximino-succinic ester.

Stability of the Isomeric Oximes. It must not be supposed that in all cases the number of isomers corresponds to that demanded by the theory. The unsymmetrical monoximes do not always exist in two forms. In many cases the isomer is missing. Among the aromatic aldoximes only one, namely the anti-oxime of the three hydroxybenzaldoximes, o-methoxybenzaldoxime, and the oximes of vanillin, bromo- and nitro-vanillin, &c.,[4] is known, whilst, with the exception of acetaldoxime, oenanthaldoxime, and possibly propion-

[1] *Ber*, 1889, 22, 604. [2] Werner's *Lehrbuch der Stereochemie*, p 270.
[3] Ebert, *Annalen*, 1885, 229, 65; Piutti, *Ber*, 1891, 24, 2287
[4] Brady and Dunn, *Trans. Chem. Soc*, 1914, 105, 821, 2409; 1915, 107, 1858; 1916, 109, 667; Wentworth and Brady, *ibid.*, 1920, 117, 1040

aldoxime, no stereoisomeric representatives of the aliphatic aldoximes exist. The single aromatic aldoximes mentioned above are anti-aldoximes; the majority of aliphatic aldoximes, on the other hand, are syn compounds. This result is significant when combined with the fact, already discussed, that oximes in the free state frequently exhibit marked differences in stability. Hantzsch attributes the difference to the nature of the radicals attached to the doubly-linked carbon atom, which may attract or repel the oxime-hydroxyl in its vicinity. Working on this basis and from a careful study of a variety of aldoximes and ketoximes, Hantzsch has drawn up a table of radicals which are arranged in the order of decreasing attraction for the hydroxyl group. The principal members are:

1. $COOH.CH_2$; 2. $COOH$; 3. C_6H_5; 4. C_6H_4X; 5. C_4H_3S; 6. C_nH_{2n+1}; 7. CH_3.

It follows from this table that the syn configuration will exhibit greater stability in the case of compounds containing radicals which attract the hydroxyl group, whilst in those in which the radical repels the hydroxyl, the anti configuration will be the more stable. If the instability of the second isomer is such as to prevent its existence under ordinary conditions, the absence of the anti configuration of the oxime of benzoylacetic acid and of the syn configuration of acetophenone is readily accounted for:

$$C_6H_5.C(=N.OH).CH_2COOH$$

Oxime of Benzoylacetic acid.

$$C_6H_5.C(=HO.N).CH_3$$

Acetophenoneoxime.

The absence of one isomer is more likely to occur where the radicals are drawn from the extremes in the scale, whilst oximes containing radicals drawn from the middle would appear to have a better chance of a stereoisomeric existence. Experience seems to justify this conclusion. Ketoximes $C_6H_5.C(NOH).C_6H_4X$, containing the aromatic radicals 3 and 4, form sufficiently stable syn and anti configurations to be isolated without difficulty and present the greatest variety of examples of this kind of isomerism. The relative stability of these compounds is also subject to variation depending on the nature as well as on the position of the radical X.

A word must be added on the position of hydrogen in the scale. Its behaviour seems capricious. Whilst in aldoximeacetic acid, hydrogen, by its strong attraction for hydroxyl, appears at the opposite end of the scale to methyl

$$\begin{matrix} H.C.CH_2.COOH \\ \| \\ HO.N \end{matrix}$$

it shows the very reverse behaviour in the benzaldoximes, in which, especially in the ortho series (p. 305), it has strong proclivities for the aromatic radical.

The order of attraction of the radicals for the hydroxyl will naturally make its influence felt in the process of chemical change, and it is scarcely surprising that such decomposition as the formation of nitriles from the aldoximes and ketoximecarboxylic acids, as well as the production of anhydrides, should vary with the nature of the radicals.

Syn-aldoximes and carboxylic acids of the aliphatic series, such as acetaldoxime and the oxime of pyruvic acid,

$$\begin{matrix} CH_3.C.H \\ \| \\ N.OH \end{matrix} \qquad \begin{matrix} CH_3.C.COOH \\ \| \\ N.OH \end{matrix}$$

Acetaldoxime. Oxime of pyruvic acid.

form acetyl derivatives which spontaneously yield the nitriles, whilst if the alkyl is replaced by an aryl radical the decomposition is retarded.

Sufficient has been said to indicate how much less decisive are the methods available for studying the configuration of the oximes than is the case in the ethylene series.

Hydrazones. Stereoisomeric hydrazones of the general formula

$$\begin{matrix} a \\ b \end{matrix}\!\!>\!C=N.NHR$$

frequently appear together in the course of preparation by the ordinary process from ketones and hydrazines, and can then be separated by fractional crystallization. In other cases the one is transformed into the other by the action of reagents.[1] Fehrlin[2] observed that the hydrazone of *o*-nitrophenylglyoxylic acid yields an isomer on dissolving it in alkalis, and the two compounds have different melting-points, crystalline appearance, and solubilities, but form the same product on reduction. Different materials may occasionally give rise to the two isomers. One of the isomeric phenylhydrazones of anisylphenylketone is obtained from the ketone

[1] Lockemann and Liesche, *Annalen*, 1905, 342, 14; Laws and Sidgwick, *Trans. Chem. Soc.*, 1911, 99, 2085. [2] *Ber.*, 1890, 23, 1574

chloride, whilst the second is derived from the ketone itself.[1] They differ in appearance and solubility, and one is slowly transformed in alcoholic solution into the other. The subsequent discovery of two diphenylhydrazones of anisylphenyl ketone, which were obtained in the same way, excluded the probability of structural differences in the two series of isomers.

Anschutz and Pauly obtained from dihydroxy-tartaric ester three isomeric diphenylhydrazones, two of which pass into the third by heating the solution, or by the action of traces of iodine or sulphur dioxide. Two hydrazones of benzoyl-formaldehyde were prepared by Bamberger and Schmidt, and isomeric hydrazones of aldehydes have also been obtained from benzaldehyde, nitroformaldehyde, salicylaldehyde, and protocatechuic aldehyde.

In addition to these the following important hydrazones exist in stereoisomeric forms:

Hydrazones.

Acetaldehydephenylhydrazone
Benzoinphenylhydrazone
Cyanacetic ester phenylhydrazone
Cyanacetic ester *o*-and *p*-tolylhydrazone,

and other substituted phenylhydrazones of cyanacetic ester.

Osazones. Stereoisomeric osazones are also known. Geldermann obtained an osazone of glyoxal dicarboxylic ester, *m. p.* 120–121°, by the action of phenylhydrazine in alcoholic solution. Two other isomers, making up the theoretical number, were subsequently prepared by Anschutz and Pauly.[2]

$$ROOC.C(:N.NHC_6H_5).C(:N.NHC_6H_5).COOR$$

Osazone of glyoxal dicarboxylic ester.

Semicarbazones. Isomeric semicarbazones of camphorquinone, from which structural isomerism is excluded, have been obtained by Forster and Zimmerli,[3] and also of phenylstyryl ketone and mesityloxide by Wilson and Heilbron.[4]

Chlorimido Compounds. A number of stereoisomeric compounds of the general formula

$$\begin{array}{c} a-C-b \\ \| \\ NCl \end{array}$$

[1] Hantzsch and Kraft, *Ber.*, 1891, 24, 3511; Hantzsch and Overton, *Ber*, 1893, 26, 9.
[2] *Ber*, 1895, 28, 64. [3] *Trans Chem Soc*, 1910, 97, 2156.
[4] *Trans. Chem Soc*, 1912, 101, 1482; 1913, 103, 377.

have been obtained by Stieglitz and his co-workers. The simplest is that derived from *p*-chlorobenzophenone, which yields two chlorimides.[1]

$$C_6H_5.C(=NCl).C_6H_4Cl \qquad C_6H_5.C(=ClN).C_6H_4Cl$$

Chlorimido ethers have further been prepared from the amides of *m*- and *p*-nitrobenzoic and naphthoic acid by the action of sodium hypochlorite. The chlorimides obtained in this way are converted into ethers with diazomethane.[2]

$$Ar.CO(NH_2) \xrightarrow{NaOCl} Ar.CO(NHCl) \xrightarrow{CH_2N_2} Ar.C(OCH_3)(=NCl)$$

Each of these exists in two stereoisomeric forms.

Anil Compounds. Few stereoisomeric anil compounds of the formula

$$a—C(=NR)—b$$

have been prepared, but examples of them are known.[3]

Stereochemistry of the Diazo-compounds. Many years ago Griess found that when a concentrated solution of caustic potash is added to diazobenzene chloride, a colourless crystalline potassium diazotate is deposited, which, in conformity with Kekule's formula for diazobenzene, appeared as follows:

$$C_6H_5N:N.OK.$$

In 1894 Schraube and Schmidt[4] made the curious observation that if diazobenzene chloride and strong potash solution are heated to 130–140° a new crystalline compound of great stability is formed, which is isomeric with Griess's salt. Two isomeric derivatives of *p*-nitrodiazobenzene were obtained in a similar way. Not the least remarkable of the characteristics of the new and stable isodiazotates is their inability to give azo-colours when added to an alkaline solution of a phenol, a property which is entirely contrary to the ordinary behaviour of diazobenzene salts. This property is, however, regained

[1] *Ber.*, 1910, 43, 782.
[2] Stieglitz and others, *Amer. Chem J.*, 1903, 30, 399; 1908, 40, 152.
[3] Straus and Ackerman, *Ber.*, 1910, 43, 596; Hicks, *Trans. Chem Soc.*, 1910, 97, 1032; Manchot and Furlong, *Ber.*, 1909, 42, 3030.
[4] *Ber.*, 1894, 27, 514.

if the potassium salt is first acidified and then brought into the alkaline solution of the phenol. Further investigation showed that if the isodiazotate of potassium is acted on with an alkyl iodide or acyl chloride, a phenylnitrosamine derivative is formed of the formula $C_6H_5NR.NO$, and for this reason Bamberger regarded the new compound as the potassium salt of phenylnitrosamine:

$$C_6H_5NK.NO.$$

The insufficiency of this deduction was shortly afterwards pointed out by von Pechmann, who, by using the silver salt in place of the potassium compound, prepared the isomeric ethers, having the formula:

$$C_6H_5.N:N.OR.$$

The case is precisely parallel to that of the amides and aldoximes and many other compounds which exhibit tautomerism (p. 330). Hantzsch, without, it must be admitted, any very clear evidence, explained the isomerism of the two diazotates by a space arrangement of the ethylene or oxime type. The unstable potassium compound represented the syn, the stable salt, the anti configuration:

C_6H_5N	C_6H_5N
$\|\|$	$\|\|$
$KO.N$	$N.OK.$
Syn-diazotate of potassium.	Anti-diazotate of potassium.

But the view very soon received substantial support from Hantzsch's discovery of a second diazobenzene sulphonate and diazobenzene cyanide; for, unlike the diazotates, these substances possess no mobile hydrogen atom, and do not admit of tautomeric change.

By the action of potassium sulphite on diazobenzene chloride Fischer had prepared potassium diazobenzene sulphonate:

$$C_6H_5N:N.Cl + K_2SO_3 = C_6H_5N:N.SO_3K + KCl.$$

By performing the same reaction at a low temperature and in presence of sodium carbonate, the new and highly unstable sulphonate is obtained. The production of the two cyanides is effected in a similar manner.

Hantzsch expressed the constitution of these compounds as follows:

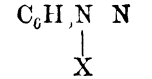
C_6H_5N	C_6H_5N
$\|\|$	$\|\|$
$KO_3S.N$	$N.SO_3K$

Potassium Diazobenzenesulphonates.

C_6H_5N	C_6H_5N
$\|\|$	$\|\|$
$NC.N$	$N.CN$

Diazobenzene cyanides.

This view was strenuously opposed by Bamberger, who adhered to the opinion that structural and not stereoisomeric differences underlie the constitution of the two series of compounds. After a long controversy a partial *rapprochement* between the views of Hantzsch and Bamberger was at length reached. Both observers are now disposed to accept, at least as regards the salts of diazobenzene with the stronger acid radicals, which do not exhibit isomerism, the formula proposed in 1875 by Blomstrand. These compounds behave like ammonium salts, inasmuch as they form neutral salts and appear from their electrical conductivities to be dissociated in aqueous solution. They probably contain, like the ammonium salts, quinquevalent nitrogen, and have the following general formula (X = acid radical):



Blomstrand's formula.

From their analogy with the salts of ammonium they received the name of *diazonium* salts, and the group C_6H_5N N was called the diazonium group. But whilst Bamberger explains the two series of isomeric diazo-compounds by the diazonium and diazo formulae, that is, as differing in structure, Hantzsch retains for the alkaline diazotates, the diazosulphonates, and cyanides their former stereoisomeric relations.

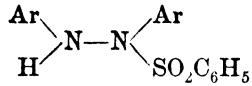
Structural Identity of the Diazo-compounds. The reasons advanced by Hantzsch for regarding each pair of the series of isomeric diazo-compounds as structurally identical are briefly as follows; the alkaline diazotates are colourless salts resembling those of the oximes of the general formula $>C:N.OK$. Though more or less hydrolysed in aqueous solution, like salts of the oximes, it is unlikely that either salt is the alkaline derivative of diazonium hydrate, which is a strong base like potassium hydroxide. Moreover, both diazotates behave chemically alike; they are reduced to hydrazines, give with benzoyl chloride, nitrosoacylanilides, and yield nitramine salts on oxidation (Ar = *aryl*):

$Ar.N(COC_6H_5)NO$	$Ar.N_2O_2K$
Nitrosobenzoylanilide	Potassium nitramine

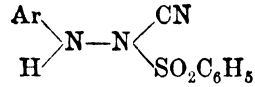
The diazosulphonates dissociate into two ions, K' and ArN_2SO_3', which are yellow or reddish yellow in colour. They are, therefore, not diazonium salts, for they should then break up into the colourless ions ArN_2', SO_3'', and K'. As alkalis do not form sulphonates, but sulphites, which are decomposed by acids, it is unlikely that

either substance in question is a diazonium sulphite, seeing that in addition to being coloured they fail to give the ordinary sulphite reactions.

The isomeric diazocyanides differ from alkaline cyanides in being sparingly soluble in water and in showing little tendency to evolve hydrocyanic acid on the addition of acids, but, like azo-compounds, they are coloured and dissolve in the common organic solvents. They both yield diazoamino-compounds and diazoimino-ethers with the elimination of cyanogen, and like azobenzene form additive compounds with benzenesulphinic acid :



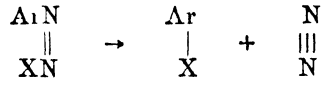
Azobenzene-benzenesulphinic acid.



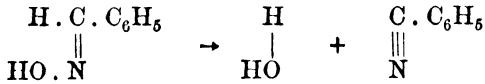
Diazobenzenecyanide-benzenesulphinic acid.

Configuration of the Diazo-compounds. The distinction between the syn and anti configuration of the diazo-compounds does not appear to be so sharply defined as between the syn- and anti-oximes, nor are the examples of isomerism as numerous.

Hantzsch assumes similar relations to exist between these two series of diazo-compounds as between the stereoisomeric ethylenes and oximes, that is to say, the syn-compounds, being the less stable, are the more reactive; they contain more available energy. It follows that the isomer, which is the more easily reduced and oxidised, the more readily converted into the nitrosamide, and the more quickly combined with phenol to form an azo-colour, is the syn-compound. It is probably the syn-compound also which undergoes the ordinary decompositions in which nitrogen is eliminated, although Hantzsch considers that the diazonium salts are directly susceptible of the same change :



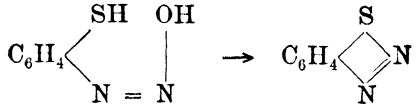
The reaction is parallel to the breaking up of the syn-aldoxime :



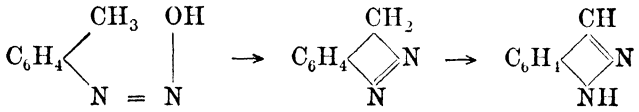
It is also the syn-compounds which, like the cis ethylenes and syn-oximes, have the lower melting-point and the greater solubility. The syn-diazotates, sulphonates, and cyanides all behave similarly.

The anhydride formation so characteristic of cis- and syn-compounds

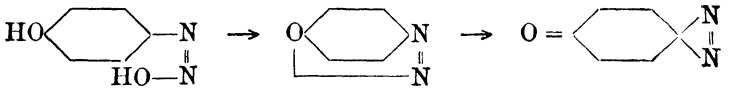
has its probable counterpart in the production of Jacobsen's diazosulphide,



of Bamberger's indazole,



and of Wolff's [1] and Hantzsch's [2] quinone diazides,



Analogous anti-reactions are unknown.

Isomeric Change of Diazo-compounds. The syn-compounds follow Ostwald's rule, according to which the more labile compound of two isomers is first formed, but as most syn-compounds pass spontaneously into the anti configuration, and as the change is not reversible in the ordinary sense, their isolation requires special conditions. It is usually effected by the action of caustic potash, potassium sulphite, or potassium cyanide on the diazonium salts in alkaline solutions and at low temperatures. It should be added that the greater lability of the syn-compound is not an invariable rule, for tribromodiazobenzene cyanide, $Br_3C_6H_2 . N_2 . CN$, can only with difficulty be converted into the anti form. The result must be ascribed to the presence of bromine in the nucleus, a fact which introduces the interesting question, to be presently considered, of the effect of nuclear substitution on the stability of the isomers.

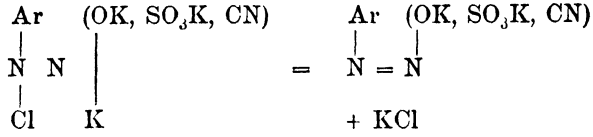
There appears to be a close connection between the diazonium salts and the syn-diazo-compounds, a relation which Hantzsch characterizes by describing the syn-compounds as pseudo-diazonium compounds. The term is intended to imply a kind of 'isomeric change', or 'ionic isomerism', such as nitro-compounds and many other substances exhibit in aqueous solution when they pass from the normal to the pseudo condition (see p. 340):

$$-CH:NO.OH \rightleftarrows -CH_2.NO_2.$$

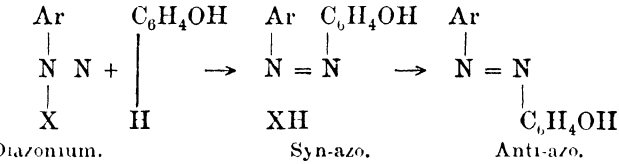
Pseudo form. Normal form.

[1] *Annalen*, 1900, **312**, 126. [2] *Ber.*, 1902, **35**, 888.

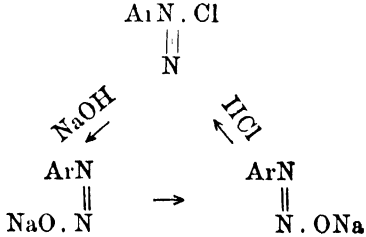
This isomeric change of diazonium to syn-diazo or pseudo-diazonium salts may be represented as follows :



The diazonium or normal salts are stable in presence of acids, but pass into the syn-diazo configuration in presence of alkalis, alkaline sulphites, or cyanides. The reverse change is effected by acids. Translated into electrolytic parlance, the first change is accelerated by hydroxyl ions, the second by hydrogen ions. In dilute aqueous solution both compounds may be present and give rise to equilibrium mixtures. As the diazonium salts are colourless, whilst the diazo-sulphonates and cyanides are coloured, the change may be observed from the colour of the solution. Anisdiazocyanide in dilute aqueous solution partially dissociates into the colourless diazonium cyanide; in stronger solutions the coloured diazocyanide is present. In the process of azo-colour production or coupling, Hantzsch considers that the syn-compound is first formed, and passes into the anti configuration.



In the light of this explanation many obscure changes become clear: It has been stated that the anti-diazotates lose the power of coupling with phenols until the solution has first been made acid and then alkaline. The acid converts the anti-compound into the diazonium salt, which in alkaline solution passes into the labile syn-diazo configuration. Indirectly, therefore, the anti may pass into the syn configuration, thus completing a cycle of changes represented by the following scheme :



In conclusion, a word may be added on the effect of different

elements or radicals in determining the stability of the above three forms of diazo-compounds.

Hantzsch points out that the more positive the character of X in $Ar.N_2.X$ the greater is the tendency towards the formation of the diazo complex. Thus, whilst the chlorides are colourless, the diazo-bromides, thiocyanates, and iodides in the solid state are coloured, the colour increasing in intensity in the order of the salts given. Positive groups in the nucleus, on the other hand, favour the diazonium type, negative groups the diazo type. Thus, trimethyl syn diazo-benzene cyanide exhibits a tendency to dissociate into a diazonium ion, whilst the tribromo-derivative has the opposite effect, and forms a stable diazo-compound. In the same way the conversion of syn into anti diazo-compounds is retarded by positive and accelerated by negative groups.

Azo-compounds which should exhibit isomerism of the diazo type are not known with certainty. It is still doubtful whether the two trinitro-azotoluenes and *p* azoxytoluenes of Janovsky[1] owe their existence to stereoisomeric differences.

Diazo compounds of the aliphatic series, which have been studied by numerous observers, appear to be represented by the general formula, $R_2N{=}N$, and exhibit no stereoisomerism.[2]

STEREOCHEMISTRY OF QUINQUEVALENT NITROGEN

The discovery of stereoisomers among unsymmetrical derivatives of carbon has naturally directed attention to the derivatives of quinquevalent nitrogen and furnished chemists with an attractive theme for experimental inquiry. In constructing a space formula for quinquevalent nitrogen compounds, two conditions must be kept in view. By analogy with the tetrahedral form applied to carbon, the geometrical figure should be of a simple, symmetrical type. Further, it must be remembered that the quinquevalent nitrogen compounds are usually derived from tervalent compounds by addition of two groups (of which one is acidic), and, from what has been previously stated, the three groups in tervalent compounds are in one plane with the nitrogen atom.

Van 't Hoff[3] represented quinquevalent nitrogen by a cube, of which the nitrogen atom occupies the centre; the five bonds or valency directions being indicated by lines drawn from the centre to five corners of the cube. The linkages are all equal in length, but the angles which 1, 2, 3 make with 4 are smaller than with 5. Although these three linkages do not lie in one plane with the

[1] *Ber.*, 1889, 22, 40, 1172.

[2] Hantzsch and Lehmann, *Ber.*, 1902, 35, 901, Curtius and others, *J. prakt. Chem.*, 1905 (2), 44, 182, 537; Staudinger, *Ber.*, 1916, 49, 1884; *Hel. Chim. Act.*, 1921, 4, 887; 1922, 5, 87.

[3] *Ansichten uber die org. Chem.*, 1878, 1, 80.

nitrogen atom, being, according to van 't Hoff, displaced by the influence of the acid radical 5, they are supposed to take up this position when the nitrogen becomes tervalent. The remaining two linkages 4, 5 lie along a diagonal of the cube (5 = acid radical).

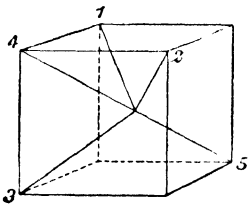


Fig. 48.

Willgerodt[1] suggests that the bonds of quinquevalent nitrogen are directed towards the summits of two superposed tetrahedra, represented by Fig. 49 or more simply by Fig. 50. The original valency directions 1, 2, 3 of the tervalent nitrogen are unaltered and lie in the plane

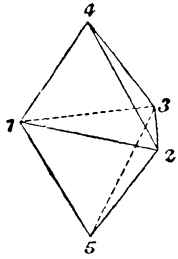


Fig 49.

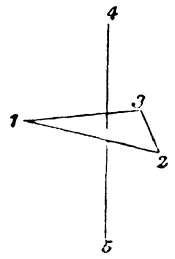


Fig 50.

of the two contiguous faces of the double tetrahedron. The fourth and fifth groups (which include the acid radical) are attached to 4 and 5.

A third arrangement, that of a four-sided pyramid, in which nitrogen occupies the centre, has been proposed by Bischoff,[2] Fig. 51.

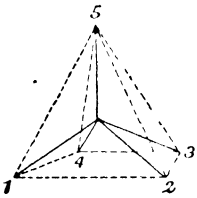


Fig. 51.

The acid radical is supposed to occupy the apex of the pyramid, and the other four radicals are grouped round the four corners of the square base. The pyramidal formula may be conveniently denoted by a plane projection of the following form:

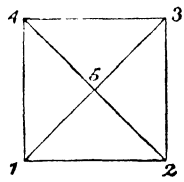


Fig. 52.

A difficulty arises in attempting to derive the pyramidal formula

[1] *Journ. prakt. Chem.*, 1890, 41, 291. [2] *Ber.*, 1908, 23, 1197.

from a tervalent nitrogen group with three linkages in one plane without some alteration in the valency direction. An attempt has been made to prove the correctness of one or other of the two alternative formulae of Willgerodt and Bischoff by introducing the same active alkyl group, in one case into the tertiary base, and in the second case into the quaternary base.[1] As the active radical in these two cases would be differently situated in regard to the nitrogen atom and the other radicals, according to Willgerodt's formula, a difference in rotation should be produced; but none was observed. Consequently Bischoff's pyramid formula, in which all four radicals are similarly situated, corresponds with the evidence so far as it goes. We will turn now to the experimental data.

A quaternary ammonium salt of the formula Na_3bX may be formed in two ways, either from $Na_3 + bX$ or from $Na_2b + aX$.

The cube and double tetrahedron formulae, which may practically be considered as one, require that the two compounds should be isomeric (Fig. 53),

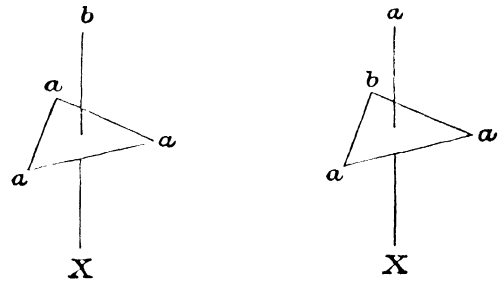


FIG. 53.

whereas the pyramidal formula demands that they should be identical (Fig. 54).

The experimental evidence is somewhat conflicting. V. Meyer and Lecco[2] found that trimethylethylammonium iodide prepared from trimethylamine and ethyl iodide and from dimethylethylamine and methyl iodide were identical and not isomeric. Le Bel,[3] on the other hand, obtained two different crystalline chlorides and chloroplatinates of trimethylisobutylammonium by combining the radicals in a different order. In other cases, such as the chloroplatinate of benzyl triethylammonium, trimethylpropylammonium, trimethyl-

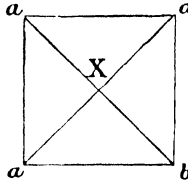


FIG. 54.

[1] Cohen, Marshall, and Woodman, *Trans. Chem Soc.*, 1915, 107, 887.
[2] *Ber.*, 1874, 7, 1747; 1875, 8, 233, 936.
[3] *Compt. rend.*, 1890. 110. 145: 1891. 112. 725: *Bull. Soc. Chim.*, 1890 (3). 4. 104.

ethylammonium,[1] &c., prepared in two different ways, no difference in crystalline form was observed. As the chlorides and chloroplatinates of primary and secondary amines, as well as of quaternary bases containing the same four radicals, frequently exhibit dimorphism in their salts, it is possible that the differences noticed by Le Bel are due to the same cause. A considerable number of experiments have been made in the attempt to obtain stereoisomers of the type Na_2bcX. The double tetrahedron requires three isomers, of which one is asymmetric and should yield optical enantiomorphs (Fig. 55):

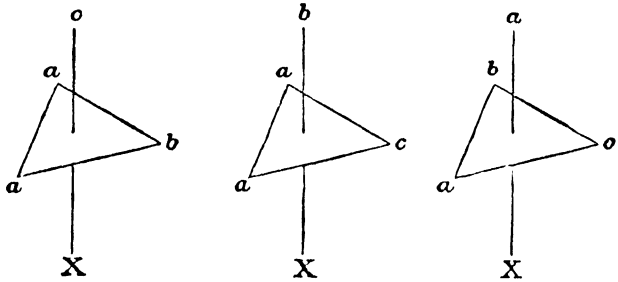


FIG. 55.

The pyramid formula should yield two isomers, one of which is asymmetric and divisible (Fig. 56):

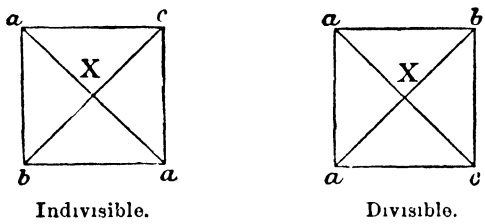


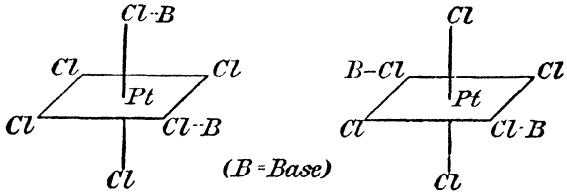
FIG. 56.

Among the first attempts to obtain quinquevalent compounds of this type are those of Schryver and Collie,[2] who succeeded in preparing dimethylethylisoamylammonium chloroplatinate by introducing the radicals in three different ways. When the process was conducted in the cold, two crystalline modifications—rhombic and monoclinic—were obtained. The monoclinic readily changes into the rhombic form on warming. As in the cases already described, there is no evidence that the phenomenon is not due to dimorphism.

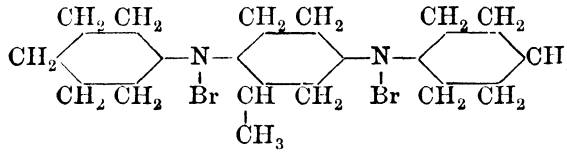
[1] *Proc Chem Soc.*, 1891, 7, 39

[2] Schryver and Collie, *Proc Chem. Soc.*, 1891, 7, 39.

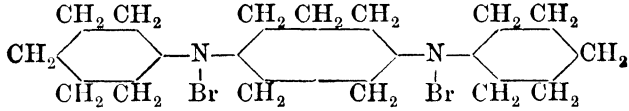
It is possible that the crystalline forms may represent stereo-isomeric platinum salts



A more comprehensive examination of this type of quaternary compound has been made by H. O. Jones,[1] who found that even when the combination of the tervalent group with the alkyl iodide was effected in the cold only one product was formed. This product could not be resolved into active enantiomorphs by Pope and Peachey's method (to be presently described in detail), which consisted in recrystallizing the *d*-camphorsulphonate or *d*-bromo-camphorsulphonate of the base. Other attempts in this direction by different observers[2] have been equally unsuccessful, with the exceptions of those of Aschan,[3] who obtained two isomers of ethylene-propylene-dipiperidinium dibromide, and also of ethylene-trimethylene-dipiperidinium dibromide and diiodide, by combining piperidine with alkylene bromide in two ways:



Ethylene-propylene-dipiperidinium dibromide.

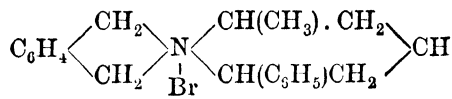


Ethylene-trimethylene-dipiperidinium dibromide.

As these compounds have not been resolved, it is possible that it is not a question of asymmetric nitrogen, but of *cis-trans* isomerism in which the bromine atoms linked to nitrogen are situated on the same and on opposite sides of the plane of the rings.

On the other hand Scholtz[4] has obtained two isomers by combining *o* xylylene dibromide with α-phenyl α′-methylpiperidine,

[1] *Trans. Chem. Soc.*, 1903, 83, 1400.
[2] Menschutkin, *Zeit. phys. Chem.*, 1895, 17, 226; Evans, *Trans. Chem. Soc.*, 1897, 71, 522, Wedekind, *Ber.*, 1899, 32, 527.
[3] *Ber.*, 1899, 32, 988; *Zeit. phys. Chem.*, 1903, 46, 804.
[4] *Ber.*, 1910, 43, 2121.



which cannot be accounted for in this way.

We come now to the type NabcdX, which on the whole affords the most interesting and conclusive results. The number of possible isomers is much increased. The double tetrahedron requires four, the pyramid three, isomers, all of which are asymmetrical and should be divisible into optical enantiomorphs. Some of the first members of this type were obtained by Wedekind,[1] who prepared phenyl-ethyl-methyl-allyl ammonium iodide in three ways. Nevertheless, only one product was obtained. The alleged difference between phenyl-benzyl-allyl-methyl ammonium iodide, obtained by the action of methyl iodide on benzyl-allyl-aniline, and that produced by combining allyl iodide with methyl-benzyl-aniline, or benzyl iodide with methyl-allyl-aniline, has now been traced to an error of observation, the first of the two being actually phenylbenzyldimethyl ammonium iodide.[2] Several other products which at first appeared dissimilar have since proved either to be identical or to have a different composition.[3]

The first successful attempt to resolve a compound of the type NabcdX into its enantiomorphs was made in 1891 by Le Bel,[4] who submitted a solution of methyl-ethyl-propyl-isobutyl ammonium chloride to the action of the mould *penicillium glaucum*, when the solution became feebly laevo-rotatory, $[\alpha]_D = -7°$ to $-8°$.

The active chloride was isolated as chloroaurate and chloroplatinate and analysed and converted into the acetate, which was also active, but the activity disappeared when the platinum or mercury double salt was decomposed by hydrogen sulphide. Doubt was thrown upon the result by Marckwald and Droste-Huelshoff, but it was reaffirmed by Le Bel, who announced that he had succeeded in preparing active solutions of other compounds by the same method. The results achieved by Pope and Peachey,[5] by Pope and Harvey,[6] and by H. O. Jones[7] are of a much more decisive character. Pope and Peachey succeeded in resolving Wedekind's α-phenyl-benzyl-allyl-methyl ammonium iodide by converting it, by means of the silver salt, into the *d*-camphorsulphonate, and fractionally crystallizing the

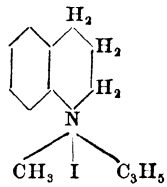
[1] *Ber.*, 1903, 36, 3791. [2] H. O. Jones, *Trans Chem Soc.*, 1905, 87, 1721.
[3] *Ber*, 1902, 35, 178. [4] *Compt. rend.*, 1891, 112, 724
[5] *Trans. Chem Soc.*, 1899, 75, 1127. [6] *Trans. Chem. Soc*, 1901, 79, 828.
[7] *Trans. Chem. Soc.*, 1903, 83, 1400; 1904, 85, 223; 1905, 87, 135, see also Wedekind, *Ber.*, 1905, 38, 3933, and Scholtz, *Ber.*, 1905, 38, 595, 1289.

latter from acetone and ethyl acetate, solvents which prevent dissociation and therefore diminish the chances of racemisation, to which the ammonium salts are very prone.

The two camphorsulphonates were then decomposed with potassium bromide and iodide and converted into the corresponding bromides and iodides of the base. The bromides showed a rotation of $[\alpha]_D = +64{\cdot}1°$ and $-65\,0°$ and the iodides of $\pm 56\,8°$ in chloroform solution.

Since Pope and Peachey succeeded in resolving Wedekind's asymmetric nitrogen compound, a very large number of similar substances have been separated into their active components by Wedekind and H. O. Jones and their pupils, who have obtained a series of ammonium salts containing the following groups of radicals:

Phenyl, methyl, benzyl, and a series of alkyl radicals.[1,3]
Phenyl, methyl, allyl, and a series of alkyl radicals [1]
p-Methoxyphenyl, methyl, benzyl allyl.[2]
p-Ethoxyphenyl, methyl, benzyl allyl.[1,2]
p-Bromophenyl, methyl, allyl, and a series of alkyl radicals.[1]
Benzyl, methyl, allyl, and a series of aryl radicals.[1]
Allyl kairolinium iodide.[4]



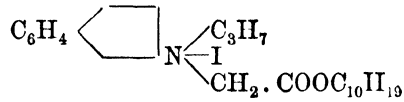
It is an interesting fact that in whatever order the radicals are introduced not more than one inactive pair of enantiomorphs has so far been produced.

Compounds have also been obtained containing both an asymmetric carbon and nitrogen atom, as well as two asymmetric nitrogen atoms. These should give two inactive externally compensated isomers; or, if one of the radicals is active, two active isomers should result. Examples of all these types have been prepared.

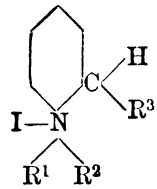
Jones[5] obtained two active isomers of phenyl, methyl, *l*-amyl, allyl ammonium iodide, Scholtz[6] the ethylallyl, benzylpropyl, and benzyl-

[1] Jones and Thomas, *Trans. Chem. Soc*, 1906, 89, 280; Jones and Hill, *Trans. Chem. Soc.*, 1908, 93, 295, Reilly, *Trans Chem. Soc.*, 1917, 111, 20.
[2] Wedekind and Frohlich, *Ber*, 1907, 40, 1001.
[3] E. Wedekind, *Ber*, 1905, 38, 3933.
[4] Buckney, *Trans. Chem. Soc.*, 1907, 91, 1821.
[5] E. and O. Wedekind, *Ber.*, 1907, 40, 4450; *Trans. Chem. Soc.*, 1905, 87, 135.
[6] *Ber.*, 1905, 38, 595, 1289; 1907, 40, 685.

butyl coninium iodide in two active forms, and Wedekind and Ney[1] the compound of N-ethyl- and N-propyl-tetrahydroisoquinoline with *l*-menthyl iodacetate.

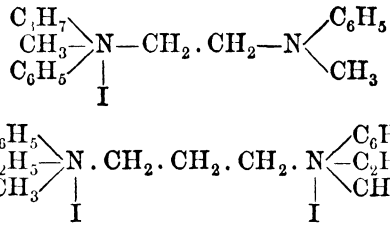


Scholtz[2] has observed that the formation of two isomers in the case of the quaternary iodides of a substituted alkyl piperidine which contains both an asymmetric carbon and nitrogen atom



appears to depend on the size of the α radical (R^3); for it is only in the case of the larger radicals that two isomers have been obtained.

Among the compounds containing two asymmetric nitrogen atoms Wedekind[3] has obtained the following:



The first was resolved; but, although two isomers of the second were obtained, they were both inactive, corresponding therefore to racemic and meso-tartaric acid. Fröhlich,[4] however, succeeded in resolving a benzidine derivative containing a symmetrical pair of asymmetric nitrogen atoms.

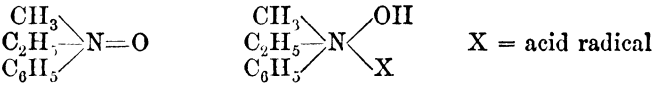
One phenomenon connected with the resolution of asymmetric nitrogen has given rise to some discussion, namely, the autoracemisation of the great majority of the active quaternary bromides and iodides in chloroform solution. The fluorides seemed less disposed to change, and the same is the case if alcohol is the solvent. From the fact that the two isomeric phenyl, methyl, *l*-amyl, allyl ammonium iodide change into the same active product on standing seems to

[1] *Ber.*, 1908, 41, 456; 1909, 42, 2138.
[2] *Ber.*, 1909, 42, 303; 1910, 43, 2707.
[3] *Ber.*, 1908, 41, 2005.
[4] *Ber.*, 1911, 44, 1057.

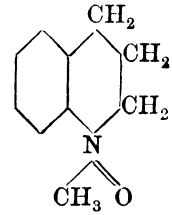
point to dissociation and reunion of the alkyl iodide; at least this is the view taken by Pope and Harvey, Jones and others, and appears to be supported by the greater weight of evidence.[1]

Before concluding an account of optically active nitrogen compounds, mention must be made of a remarkable member of this group of substances.

In 1908 Meisenheimer[2] resolved methylethylaniline oxide, by the aid of *d*-camphorsulphonic acid, into its active enantiomorphs. The structural relation of the base to the salt has been shown to be the following:

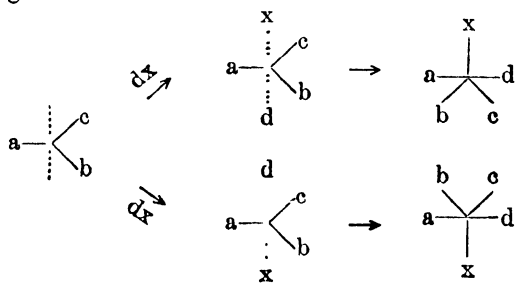


The enantiomorphs are crystalline substances and dissolve in benzene, from which it follows that the base is present rather as the oxide than the hydrate. Methylethyl-β-naphthylamine and kairoline oxide have also been obtained and resolved in the same manner.



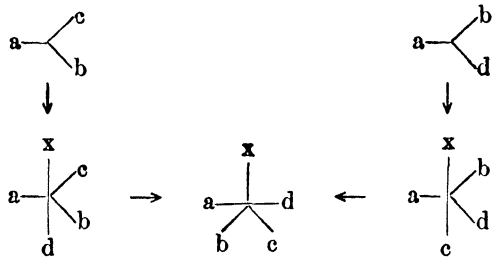
Kairoline oxide.

The formation and configuration of quinquevalent nitrogen compounds have been placed in a clear light by H. O. Jones.[3] Adopting Bischoff's pyramidal configuration as the most symmetrical and affording the smallest number of possible isomers, and further assuming the plane arrangement of tervalent nitrogen groups, the passage of tervalent to quinquevalent compounds is represented by the following scheme:



[1] *Annual Reports*, 1907, p 195; 1908, p. 109.
[2] *Ber*, 1908, 41, 3966; 1909, 42, 303; *Annalen*, 1911, 385, 117; 1922, 428, 286.
[3] *Trans. Chem. Soc.*, 1905, 87, 1728.

The process represents an unstable intermediate stage which changes to the stable pyramidal form, and, by the addition of the groups dX in the two possible ways, gives enantiomorphous configurations. It is easy to explain also why the formation of the compound NabcdX from Nabc and dX, or from Nabd and cX, &c., should always give one product, since there must be one arrangement more stable than the others, and equilibrium would be established in this position during the intramolecular change. Considering only one of the enantiomorphs, the process would probably take place as follows:



It is easy to understand also, from this point of view, the absence of isomers of the type Na_3bX or Na_2bcX, each of which may be supposed to assume an arrangement which does not admit of resolution into enantiomorphs. Using the projection formulae, in which the dotted lines denote the plane of symmetry, the arrangement will appear thus:

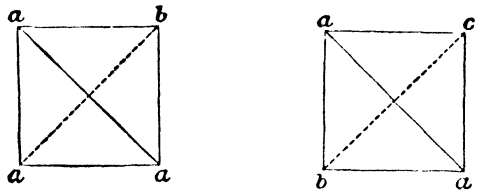


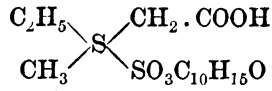
FIG. 57.

STEREOCHEMISTRY OF OTHER ELEMENTS

Optically Active Sulphur and Selenium Compounds. Pope and Peachey's discovery of optically active nitrogen compounds was soon followed by that of optically active sulphur, selenium, and tin compounds. The active sulphur compounds were obtained from methylethylthetine.[1] The bromide was decomposed by silver

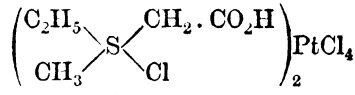
[1] *Trans. Chem. Soc*, 1900, 77, 1072.

d-camphorsulphonate, and the salts so obtained repeatedly crystallized from alcohol and ether.



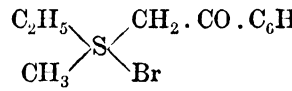
Methylethylthetine camphorsulphonate.

A fraction was obtained which melted at 118–120° and showed a rotation of $[M]_D = +68°$, whereas that of the *d*-camphorsulphonic acid is $[M]_D = +52°$. With the *d*-bromocamphorsulphonate the fraction melted at 166–168°, and gave a rotation $[M]_D = +290°$ instead of $[M]_D = 275°$, the rotation of the acid. The salt was decomposed by platinic chloride in an alcoholic solution containing hydrochloric acid, and yielded a platinum salt,



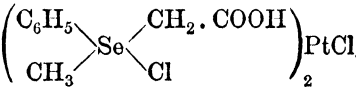
which gave a rotation of $[M]_D = +30{\cdot}8°$.

About the same time Smiles[1] obtained the methylethyl sulphine compound of ω-bromacetophenone,



which he succeeded in resolving into its active enantiomorphs by Pope and Peachey's method of crystallization of the *d*-bromocamphorsulphonate. The *l*-compound is less soluble than the *d*-enantiomorph and separates out first. From the alcoholic solution the sulphines were precipitated as picrates, and showed a rotation in acetone solution of $-9{\cdot}2°$ and $+8{\cdot}1°$. The observations have since been revised by Pope and Neville, who obtained much higher rotations.

Active selenium compounds were obtained by Pope and Neville[2] from phenylmethyl selenetine bromide, which was converted into the *d*-bromocamphorsulphonate and submitted to fractional crystallization. Two salts were obtained melting at 168° and 151°, which, when converted into the chloroplatinates, showed a rotation of $[M]_D = +55°$ and $-54{\cdot}3°$ in acetone solution.



From both *d*-bromocamphorsulphonates mercuric iodide gave the same inactive mercuric iodide double salt, and precipitation with potassium mercuric iodide also produced racemisation.

[1] *Trans. Chem. Soc.*, 1900, 77, 1174. [2] *Proc. Chem. Soc*, 1902, 18, 198.

Optically Active Tin Compounds. Active tin compounds were obtained by Pope and Peachey,[1] by the method of Cahours and Ladenburg, by the following series of reactions:

$$2Sn(CH_3)_3I + Zn(C_2H_5)_2 = 2Sn(CH_3)_3C_2H_5 + ZnI_2$$
$$Sn(CH_3)_3C_2H_5 + I_2 = Sn(CH_3)_2C_2H_5I + CH_3I$$
$$2Sn(CH_3)_2C_2H_5I + Zn(C_3H_7)_2 = 2Sn(CH_3)_2(C_2H_5)(C_3H_7) + ZnI_2$$
$$Sn(CH_3)_2(C_2H_5)(C_3H_7) + I_2 = Sn(CH_3)(C_2H_5)(C_3H_7)I$$

The product is an oil which boils at 270°. With silver *d*-camphorsulphonate it yields the corresponding salt, which, after fractional crystallization, melts at 126°. It shows a rotation in dilute solution of $[M]_D = +95°$, which corresponds to a rotation of $[M]_D = +45°$ for the radical $Sn(CH_3)(C_2H_5)(C_3H_7)$.

Potassium iodide precipitates the iodide of the tin compound from a solution of the *d*-camphorsulphonate as an oil, which shows an unaccountable variation in rotatory power, the highest observed rotation being $[\alpha]_D = +23°$ in ethereal solution.

The solution of the *d*-camphorsulphonate exhibits a remarkable phenomenon on evaporation, depositing only the *d*-salt and none of the *l*-salt. This is accounted for by the rapid racemisation of the *l*-salt, in consequence of which the less soluble *d*-salt, as it is deposited, is accompanied by a further racemisation of *l*-salt, until the whole is converted into dextro-salt. The salt of the *d*-bromocamphorsulphonate showed a similar behaviour.

Optically Active Silicon Compounds. In 1904 Kipping, using Grignard's reagent, obtained an asymmetric silicon derivative $Si(C_6H_5)(C_2H_5(C_3H_7)Cl$, but failed to resolve it.[2] A second asymmetric derivative, phenyl benzyl ethyl propyl silicane, was prepared later.[3] On treatment with strong sulphuric acid it loses the phenyl group in the form of benzene and yields the sulphonic acid of benzyl ethylpropyl silicyl oxide,

$$SO_3H.C_6H_4.CH_2.\underset{\displaystyle C_3H_7}{\overset{\displaystyle C_2H_5}{Si}}-O-\underset{\displaystyle C_3H_7}{\overset{\displaystyle C_2H_5}{Si}}.CH_2.C_6H_4.SO_3H$$

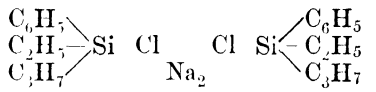
which contains two asymmetric silicon atoms. The salts of this acid with *d*-methylhydrindamine was resolved by crystallization into two components, the sodium salts of which showed the specific rotatory powers of + 3·3° and — 4·5° respectively.

[1] *Proc. Chem. Soc.*, 1900, 16, 42, 116. [2] *Proc. Chem. Soc.*, 1904, 20, 15
[3] *Trans. Chem. Soc.*, 1907, 91, 209.

The above compound was afterwards more easily obtained by the action of water on benzyl ethyl propyl silicon chloride, which gives the corresponding silicol, and this, on treatment with sulphuric acid, forms the above sulphonic acid of the oxide. The sodium salts of this product after resolution showed rotations of + 5·8 and − 5·9.[1]

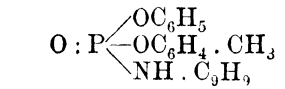
The sulphobenzyl ethyl isobutyl silicon oxide was afterwards prepared in the same way,[2] and after resolution the sodium salts showed specific rotations of ± 10·5°. Finally the monosulphonic acid of dibenzyl ethyl propyl silicane has been prepared by sulphonation and resolved by means of brucine. Although the rotations are small ($[\alpha]_D = 1°$), there was good evidence that resolution had been effected.[3] Attempts to resolve other asymmetric silicane sulphonic acids were unsuccessful, partly, no doubt, owing to their feeble activity and rapid racemisation.[4]

Other asymmetric silicon compounds have been obtained by Kipping[5] by the action of sodium on phenyl, ethyl propyl, and benzyl ethyl propyl silicon chloride, and converting the products into the sulphonic acids,



but were not resolved.

Optically Active Phosphorus Compounds. Kipping and Luff[6] prepared an asymmetric phosphorus compound in the form of phenyl *p*-tolyl phosphoric acid, and although it was found impossible to resolve it into its enantiomorphs, a very clear indication was given of their existence. It was found by combining the acid chloride with *d*-methylhydrindamine that the resulting amide

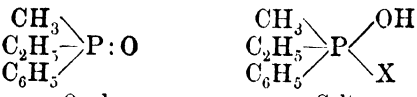


was a mixture, and by fractional crystallization yielded two isomeric substances, one of which melted at 127° and had $[\alpha]_D$ − 17·4°, and the other melted at 82–86° and had $[\alpha]_D$ − 21·2°. A similar result was obtained with *l*-menthylamine. The *l*-menthylamide of phenyl-*β*-naphthyl hydrogen phosphate was separated in the same way,

[1] *Trans. Chem. Soc.*, 1908, **93**, 465. [2] *Trans. Chem. Soc.*, 1908, **93**, 2004, 2090.
[3] *Trans. Chem. Soc.*, 1910, **97**, 149, 755.
[4] *Trans. Chem. Soc.*, 1907, **91**, 717; 1909, **95**, 69.
[5] *Trans. Chem. Soc.*, 1921, **119**, 647. [6] *Trans. Chem. Soc.*, 1909, **95**, 1993.

giving two isomers of different melting-points and different specific rotations.[1]

In the meantime Meisenheimer and Lichtenstadt had prepared phenyl methyl ethyl phosphoric oxide,



Oxide. Salt. (X = acid radical)

from which the dextro-enantiomorph was separated by crystallizing the salt of *d*-bromo-camphorsulphonic acid from ethyl acetate solution. It melts at 94–95°, and in aqueous solution gives $[\alpha]_D$ + 67·4°. By passing dry ammonia into the benzene solution the oxide was separated and showed a rotation of $[\alpha]_D$ + 23·1° in water and + 33·8° in benzene.[2]

Burrows and Turner[3] prepared various derivatives of asymmetrical arsine oxides and tertiary arsines, of which the following:

$$(C_6H_5)(\alpha C_{10}H_7)(C_6H_5 \cdot CH_2)(CH_3)AsBr$$

was converted into the bromo-camphor-sulphonate, crystallized, and then transformed into the iodide, which showed a small dextro-rotation. Lederer[4] has obtained asymmetric tellurium compounds but did not succeed in resolving them. Iodonium compounds of the formula have also refused to separate into active components, from which it is concluded that the three bonds, like those of tervalent nitrogen, lie in one plane with the iodine atom.[5]

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Die Entwicklung der Stereochemie, by K. Auwers. Winter, Heidelberg, 1890.
Brit Assoc. Reports, 1904, p 170, by H O Jones.
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Lectures on the Principle of Symmetry, by F. M. Jaeger. Cambridge Univ. Press, London, 1917.

[1] Kipping and Challenger, *Trans. Chem Soc*, 1911, 99, 626.
[2] *Ber*, 1911, 44, 356; see also Radcliffe and Brindley, *J. Soc. Chem. Ind.*, 1923, 42, 64.
[3] *Trans. Chem. Soc.*, 1921, 119, 426
[4] *Ber.*, 1916, 49, 1615.
[5] *Trans. Chem. Soc.*, 1902, 81, 1350.

CHAPTER VI

ISOMERIC CHANGE

ALTHOUGH our views on isomerism have of late years received a much wider interpretation than formerly owing to the recognition of the space arrangement of atoms, experience has taught us that among some classes of compounds structural isomerism is subject to certain limitations which were not foreseen by the original theory.

For example, attempts to prepare propylene alcohol from β-bromopropylene by the usual methods always result in the production of acetone:

$$CH_3 . CBr : CH_2 \longrightarrow CH_3 . C(OH) : CH_2 \longrightarrow CH_3 . CO . CH_3$$

and in the same way vinyl bromide invariably yields acetaldehyde instead of the isomeric alcohol:[1]

$$CH_2 : CHBr \longrightarrow CH_2 : CH(OH) \longrightarrow CH_3 . CHO$$

This result appeared so general that Erlenmeyer,[2] who carefully studied the reaction, concluded that 'all secondary alcohols in which two bonds of the radical are saturated by two bonds of a carbon atom are transformed at the moment of their formation into the aldehyde, &c.'

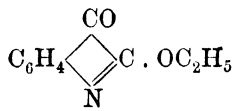
The change may be represented by the transference of a hydrogen atom from the oxygen to the carbon:

$$\begin{array}{l} C \\ \| \\ C . OH \end{array} \longrightarrow \begin{array}{l} CH \\ | \\ C : O \end{array}$$

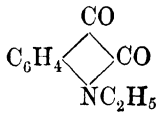
The same idea was utilized by Baeyer to explain the non-existence of the second isomer of isatin.[3] Baeyer obtained two alkyl isatins, one of which gave potassium isatin on hydrolysis (alcohol being at the same time removed), and the other the potassium salt of ethylaminophenylglyoxalic acid. They were termed respectively

[1] *Annalen*, 1878, 192, 119. [2] *Ber.*, 1880, 13, 309.
[3] *Ber.*, 1882, 15, 2093; 1883, 16, 2193; see also Pummerer, *Ber.*, 1911, 44, 338.

ethyl isatin and ethyl pseudoisatin, and were distinguished as the *normal* or *lactim* form and the *pseudo* or *lactam* form :

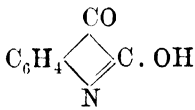


Ethyl isatin (lactim).



Ethyl pseudoisatin (lactam).

There is, however, only one isatin, to which Baeyer somewhat arbitrarily assigned the formula :

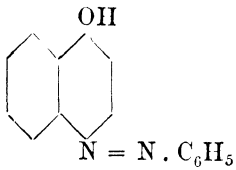


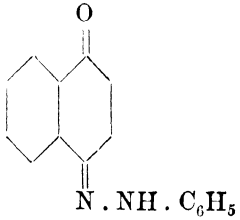
The non-existence of the second or pseudo form was accounted for by the wandering of the hydrogen atom from the nitrogen to the more stable position beside the oxygen atom.[1]

Similar observations were made in the case of other nitrogen ring structures, such as oxindole,[2] hydroxy-nicotinic acid,[3] γ-hydroxyquinaldine,[4] and carbostyril.[5]

Tautomerism. In a paper 'Ueber die Moglichkeit mehrerer Strukturformeln für dieselbe chemische Verbindung' Laar[6] drew attention to the phenomenon of one substance doing duty for two structural isomers and proposed for it the name *tautomerism* (ταὐτό, the same , μέρος, a part).[7]

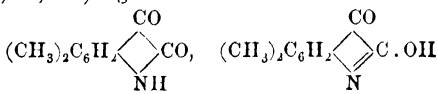
He refers to the case of isatin ; to the identity of two substances which might be expected to possess different formulae, one of which is formed by the action of diazobenzene chloride on α-naphthol and the other by that of phenylhydrazine on α-naphthaquinone ;





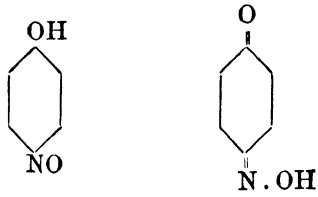
also to the twofold character of nitrosophenol or quinoneoxime, which on the one hand behaves like a phenol and gives nitrophenol and

[1] Both lactim and lactam forms of dimethyl isatin have been isolated by Heller (*Ber* , 1919, 52, 437) together with two other modifications :



[2] Baeyer and Comstock, *Ber* , 1883, 16, 1704, 2188.
[3] v Pechmann, *Ber* , 1884, 17, 2387.
[4] Knorr and Antrick, *Ber.*, 1884, 17, 2873
[5] Friedländer and Weinberg, *Ber.*, 1885, 18, 1528
[6] *Ber.*, 1885, 18, 648.
[7] Various other names, such as *pseudomerism*, *merotropism*, *desmotropism*, *tropomerism*, have been applied to the same or a similar phenomenon.

aminophenol by oxidation or reduction, and on the other is converted by hydroxylamine into a dioxime after the manner of a ketone.



He also discusses the structure of acetoacetic ester, which has now become the classical example of tautomerism.

The question as to whether acetoacetic ester should be represented by Geuther's formula as β-hydroxycrotonic ester or by Frankland's formula as a ketone has been one of the long-debated problems of organic chemistry.

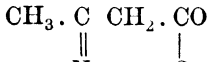
$CH_3 . C(OH) : CH . COOC_2H_5$ — Geuther's formula.

$CH_3 . CO . CH_2 . COOC_2H_5$ — Frankland's formula.

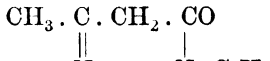
The evidence, which is derived from its chemical behaviour, will be seen to be very conflicting. The facts adduced in favour of Frankland's formula are as follows:

Acetoacetic ester with its alkyl derivatives is decomposed by dilute alkalis into acetone or its homologues; nitrous acid converts it into isonitroso acetone; it gives the usual reactions for ketones, forming hydroxybutyric acid on reduction and yielding additive compounds with hydrogen cyanide and sodium bisulphite.

Moreover, it combines with hydroxylamine to form β-oximinobutyric ester, and with phenylhydrazine to form a hydrazone, both of which lose alcohol and pass into their respective anhydrides, methyl oxazolone and phenylmethyl pyrazolone.



Methyl oxazolone.



Phenylmethyl pyrazolone.

By the action of iodine on the sodium compound diacetosuccinic ester is formed, although it has since been shown that this is not the only product of the reaction (p. 351).

Diacetosuccinic ester.

Again, acetic anhydride yields so small a quantity of an acetyl

derivative that the presence of a hydroxyl group seems very improbable, whereas acetyl chloride acting upon the sodium compound of the ester gives mainly diacetoacetic ester. Finally, Claisen has shown that the behaviour of acetoacetic ester is different from that of certain unsaturated alcohols of the type of Geuther's formula which readily react with acetic anhydride, &c. (p. 349).

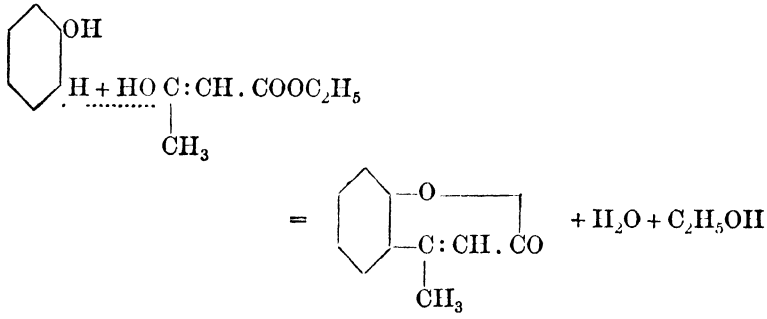
One fact which is strongly in favour of Geuther's formula is the acidic character of the ester, which enables it to form a sodium salt, a well-defined and crystalline copper salt and a violet coloured ferric salt. Although it is true that acetylene forms metallic derivatives in which the metal is associated with carbon, it is not very probable that this will occur when the much more electronegative oxygen is available for salt formation. Again, the action of chloroformic ester on the sodium compound, instead of yielding wholly acetyl malonic ester, gives mainly a carbonic ester of the formula[1]:

$$CH_3 . C(O . COOR) : CH . COOC_2H_5$$

and although, as previously stated, acetyl chloride acting on the sodium compound gives diacetoacetic ester, if the acid chloride and the ester react in presence of pyridine, the acetyl derivative of hydroxycrotonic ester is formed.[2] Furthermore, ammonia and amines yield amino and alkylamino crotonic esters of the general formula:

$$CH_3 . C(NR_2) : CH . COOC_2H_5$$

The union of acetoacetic ester with other organic compounds in which water is eliminated is often more simply represented by the hydroxyl than the ketone formula, as, for example, the formation of methyl-coumarin from phenol[3]:



[1] Michael, *J prakt Chem*, 1883 (2), 37, 473; 1891, 45, 580; 1892, 46, 189.
[2] Claisen, *Ber.*, 1888, 21, 3397, 3567; 1892, 25, 1760; Claisen and Haase, *Ber.*, 1900, 33, 1242, 3778
[3] V. Pechmann and Duisberg, *Ber.*, 1883, 16, 2119.

Although the alkyl groups, which are introduced by the action of alkyl iodides and acetyl chloride on the sodium compound of acetoacetic ester, attach themselves to the carbon of the methylene group, the reaction does not necessarily imply a ketonic structure of the sodium compound, for, as Michael has suggested, it may be represented equally well by the following scheme,[1] in which an additive compound with the alkyl iodide is first formed and is succeeded by the separation of sodium iodide:

$$CH_3 . C(ONa) : CH . COOC_2H_5 + CH_3I$$

$$= CH_3 . \underset{\displaystyle I}{\overset{\displaystyle ONa}{\overset{|}{\underset{|}{C}}}} - - CH(CH_3) . COOC_2H_5 = CH_3 . CO . CH(CH_3) . COOC_2H_5 + NaI$$

Another and more probable explanation is that proposed by Robinson,[2] in which the oxygen attaches the iodine by its residual valency.

$$CH_3 . \underset{\displaystyle Na\ I}{\overset{\displaystyle O}{\overset{..}{\underset{/\ \backslash}{C}}}} - CH(CH_3) . COOC_2H_5 = CH_3 . CO . CH(CH_3) . COOC_2H_5 + NaI$$

These are some of the arguments which have been advanced in support of the two formulae.

The question has been finally set at rest by the separation of the two isomeric compounds and by a careful examination of their chemical and physical properties. Knorr[3] has succeeded in freezing out the pure keto form of acetoacetic ester by cooling a concentrated solution of the liquid in different solvents to $-78°$. The keto form separates in crystals which melt at $-39°$ and give no coloration with ferric chloride. To obtain the enol form the sodium compound is treated with dry hydrogen chloride at $-78°$. It solidifies in liquid air to a glassy mass, and gives an intense ferric chloride reaction. Both substances, at the ordinary temperature, form the same equilibrium mixture, which, from the difference in refractive indices of the two components, has been estimated as containing 2 per cent. of the enol form and 98 per cent. of the keto form. Other tautomeric compounds, such as benzoylacetic ester, have been isolated in the same way; but in the case of the methyl ester it is the crystalline enolic form which separates.

K. H. Meyer[4] has succeeded in isolating the pure enol form by fractional distillation at 10 mm. pressure. The mixture was first distilled from a Jena glass vessel, the distillate (which contained 90 per cent. of the enol isomeride) being collected in a quartz receiver. It was then immediately refractionated from a silica vessel, the first fraction being the pure enol compound. Similar results were obtained with benzoylacetic ester and acetylacetone.

[1] Michael, *J. prakt. Chem.*, 1883, 37, 487, 1892, 46, 205; 1899, 60, 316, *Ber.*, 1905, 38, 3217; see also Nef, *Annalen*, 1891, 266, 59, and Paal, *Ber.*, 1906, 39, 1436. [2] *Trans. Chem. Soc.*, 1916, 109, 1040. [3] *Ber.*, 1911, 44, 1147.
[4] Meyer and Schoeller, *Ber.*, 1920, 53, 1410; Meyer and Hopff, *Ber.*, 1921, 54, 579.

Since Laar drew attention to the subject in 1885 cases of tautomerism have rapidly multiplied. Before discussing the later development of the subject a short account will be given of a few of the principal types of tautomeric compounds, that is to say, compounds which possess a double function, but are commonly represented by only one substance.

If we examine the examples of tautomerism which have been given, we shall find that the structure of the compounds is such that it allows of the formation of isomers by the transference of a hydrogen atom from one polyvalent element to another, accompanied by a corresponding change in the linkages. This structure depends, therefore, on the presence of certain groups.

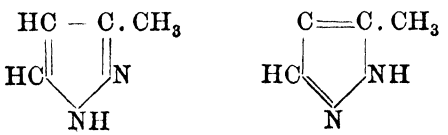
A convenient plan of classifying the greater number of tautomeric compounds has been proposed by Laar, who divides them into *dyads*, consisting of two polyvalent elements linked together, from one to the other of which the hydrogen atom may be supposed to travel; *triads*, in which the original two polyvalent elements are separated by a third (which is of necessity at least tervalent), so that the hydrogen has now to travel from the first to the third element in the chain, and so forth.

Dyads. Hydrogen cyanide may be taken as representative of a dyad group and its structure denoted by one of the following formulae:

$$N{:}C.H \text{ or } C{:}N.H \text{ or } C{\vdots}N.H$$

For whilst only one hydrogen cyanide is known, there are two series of alkyl derivatives, the cyanides or nitriles and the isocyanides or carbamines The sulphinic acids or sulphones are also dyads, for the one substance forms two series of compounds[1] derived from the two forms:

Methyl-pyrazole, described on p. 327, may also be included in the class of dyads, for the one compound gives rise to two N-phenyl derivatives, and must be represented by the formulae[2]:



Methyl-pyrazole.

[1] Otto and Rössing, *Ber.*, 1892, 25, 230. [2] Knorr, *Annalen*, 1894, 279, 192.

Triads. The following are the common types of triad grouping, in which the central atom of the triad is carbon or nitrogen and the end atoms carbon, nitrogen, oxygen, or sulphur. These types furnish the most numerous and familiar examples of tautomerism. The symbols X and Y stand for radicals and (S) for sulphur.

XC—C—CY ↖ H ↗	N—C—O (S) ↖ H ↗	N—N—O ↖ H ↗
C—C—O (S) ↖ H ↗	XN—C—NY ↖ H ↗	N—N—C ↖ H ↗
C—C—N ↖ H ↗	C—N—O (S) ↖ H ↗	XN—N—NY ↖ H ↗

Only the more important examples of the above types will be described.

Unsaturated Hydrocarbon Type. The type may be formulated thus:

$$\begin{array}{l} XC:C.CHY \\ \quad|\quad|\quad| \end{array} \qquad \begin{array}{l} XHC.C:CY \\ \quad|\quad|\quad| \end{array}$$

This form of change is not, as a rule, included among examples of tautomerism for the reason that both isomeric forms are usually stable substances and can be easily isolated, whereas the original conception of tautomerism was associated with one substance forming two derivatives. The interconversion of the isodibutylenes described by Butlerow[1] and discussed on p. 371 is one example of this change.

$$(CH_3)_2C:CH.C(CH_3)_3 \rightleftarrows CH_2:C(CH_3).CH_2.C(CH_3)_3$$

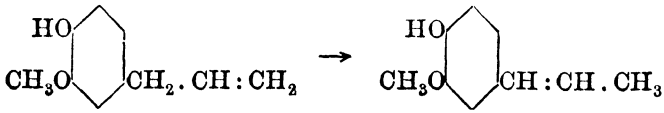
The conversion in hot alkaline solution of $\beta\gamma$ unsaturated acids into $\alpha\beta$ unsaturated acids observed by Fittig[2] and others furnishes another example.

$$RCH:CH.CH_2.COOH \longrightarrow RCH_2.CH:CH.COOH$$

Other cases of the same kind are the conversion of β- into α-phenylpropylene, of eugenol into isoeugenol, of dihydrocarvone into carvenone, Δ^2-dihydro- into Δ^1-dihydro-naphthalene,[3] &c.

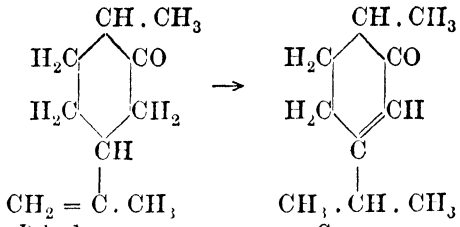
$$C_6H_5CH_2.CH:CH_2 \longrightarrow C_6H_5CH:CH.CH_3$$

β-Phenylpropylene. α-Phenylpropylene.

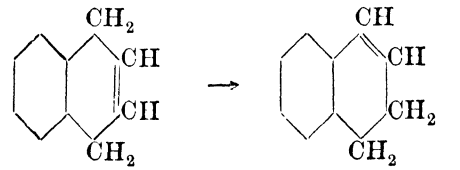


Eugenol. Isoeugenol.

[1] *Annalen*, 1877, 189, 76. [2] *Ber.*, 1891, 24, 82; 1894, 27, 2677; *Annalen*, 1894, 283, 129; 1896, 299, 1. [3] Bamberger and Lodter, *Annalen*, 1895, 288, 75; Rowe, *Trans Chem. Soc.*, 1920, 117, 1574, 1921, 119, 2021; *J Soc. Chim. Ind*, 1920, 39, 241.



Dihydrocarvone. Carvenone.



Δ^2 Dihydro naphthalene. Δ^1 Dihydro naphthalene.

Also certain acetylene derivatives yield allene derivatives when heated with alcoholic potash.[1] $R.CH_2.C:CH \rightarrow RCH=C=CH_2$

The above changes, which for convenience may be described as tautomeric, have in certain cases been shown to be reversible,[2] and are usually ascribed to the intervention of water which is alternately added and removed (p. 371).

$$XC:C.CHY + H_2O \rightleftarrows XCH.C(OH).CHY \rightleftarrows XCH.C.CY + H_2O$$

It should be recognized that this type may furnish cases of real tautomerism like benzene, as formulated by Kekulé, which yields only one instead of two ortho di-derivatives, or the glutaconic acid of Thorpe,[3] the α and γ methyl derivatives of which are not isomeric but identical (Part I, p. 80).

Keto-Enol Type. This type includes acetoacetic ester and most of the more carefully studied examples of tautomerism. The two forms may be represented by the general scheme:

$$O=C—CH< \qquad HO—C=C<$$

Keto form. Enol form.

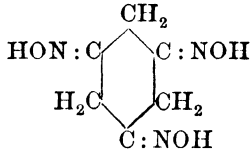
In accordance with a suggestion of Brühl the one is called the *keto form* and the other the *enol form*. The number of examples of this type is very large and embraces the 1.3 diketones like acetylacetone $CH_3.CO.CH_2.CO.CH_3$, the β aldehydic and ketonic esters, like formyl and acetoacetic ester, and substances like malonic and cyanacetic ester,[4] the sodium salts of which are probably represented by the formulae: RO.CO.CH:C(OR)ONa CN.CH:C(OR)ONa.

It also includes numerous cyclic compounds like phloroglucinol,[5]

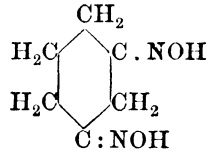
[1] Jegorowa, *Journ russ. phys.-chem. Ges*, 1912, 43, 1116. [2] *Annalen*, 1894, 283, 47.
[3] *Trans Chem Soc*, 1905, 87, 1669. [4] Thorpe, *Trans. Chem. Soc.*, 1900, 77, 923.
[5] Baeyer, *Ber.*, 1885, 18, 3454, 1891, 24, 2687.

dihydroresorcinol,[1] succino-succinic ester,[2] phenanthrone,[3] and camphor,[4] which function both as phenols and ketones.

Thus, phloroglucinol yields a trioxime and dihydroresorcinol a dioxime and a bisulphite compound.[5]

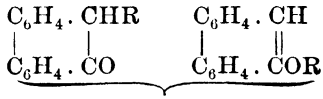


Phloroglucinol-trioxime.

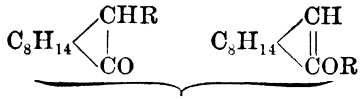


Dihydroresorcinol-dioxime.

Phenanthrone and camphor form derivatives of both the ketonic and enolic type:



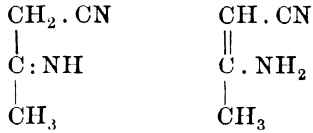
Phenanthrone.



Camphor.

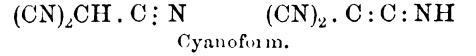
Cyanide-Imide Type. Examples of the third type on the list (p. 335) are not numerous:

but E. von Meyer's[6] diacetonitrile which exists in two modifications may, if it is not a case of geometrical isomerism, represent one:



and cyanocamphor and cyanoform[7] others:

Cyanocamphor.



Cyanoform.

Here again both isomers are known and the change from one to the other is reversible.

[1] Merling, *Annalen*, 1893, 278, 20. [2] Baeyer, *Ber.*, 1889, 22, 2168.
[3] Japp and Findlay, *Trans. Chem Soc.*, 1897, 71, 1115.
[4] Forster, *Trans. Chem. Soc.*, 1901, 79, 987.
[5] Fuchs and Elsner, *Ber.*, 1920, 53, 886; Fuchs and Stix, *Ber.*, 1922, 55, 658.
[6] *J. prakt. Chem.*, 1895, 52, 83. [7] Hantzsch and Osswald, *Ber*, 1899, 32, 641.

Amide-Imidol Type. The two structures may be denoted by the general formulae

$$O = \underset{|}{C}—\underset{|}{NH} \qquad HO—\underset{|}{C} = \underset{|}{N}$$

The simplest example is that of cyanic acid, which according to E. A. Werner forms an equilibrium mixture, and he explains in this way the conversion of ammonium cyanate into urea.

$$NH_4OCN \rightleftarrows NH_3 + \begin{matrix} HO.CN \\ \downarrow\uparrow \\ HN:CO \end{matrix} \rightleftarrows HN:C\begin{matrix}NH_3\\|\\O\end{matrix} \rightarrow NH:C\begin{matrix}NH_2\\OH\end{matrix}$$

Urea and its derivatives also exhibit the same type of tautomerism:

$$HN:C\begin{matrix}NH_2\\OH\end{matrix} \rightleftarrows H_2N.CO.NH_2$$ [1]

Substances like isatin, which also belong to this group of triads, are usually distinguished as amide and imidol or normal and pseudo forms, or in the case of cyclic structures as lactam and lactim forms. The earliest examples of this class are isatin, indoxyl, and oxindol, which form stable derivatives of both types, but in the free state are represented by only one substance. The simple amides have similar properties. They have been studied by Tafel and Enoch,[2] Comstock,[3] and Claisen.[4] For example, the silver salts of formanilide and benzamide when treated with ethyl iodide yield ethyl derivatives which are isomeric with the compounds obtained in a similar manner from the sodium salts.

As the latter yield the ethyl derivative of the amine on hydrolysis they will possess the amide structure, those from the silver salt the imidol structure.

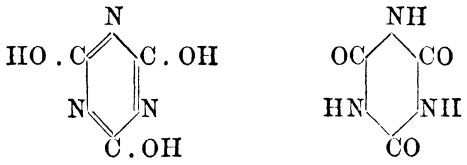
	From the sodium salt.	From the silver salt.
Ethyl benzamide . .	$C_6H_5CO.NHC_2H_5$	$C_6H_5C(OC_2H_5).NH$
Ethyl formanilide .	$C_6H_5N(C_2H_5).CHO$	$C_6H_5N:CH(OC_2H_5)$

It would be natural to conclude that in the sodium salts the metal is attached to nitrogen, and in the silver salts to oxygen; but if alkyl substitution takes place by addition of alkyl iodide, as Michael suggested in the case of acetoacetic ester (p. 333), it is not necessarily the case. The observations of Lander[5] on the simultaneous produc-

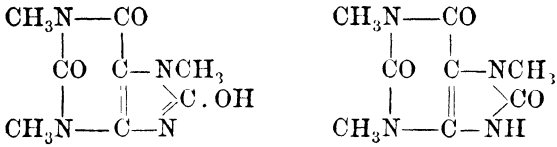
[1] *Trans. Chem. Soc.*, 1913, 103, 1010, 2275; 1914, 105, 923; 1915, 107, 715; 1918, 113, 694; 1919, 115, 1093.
[2] *Ber.*, 1890, 23, 1550
[3] *Amer. Chem. J.*, 1892, 13, 514
[4] *Annalen*, 1895, 287, 361.
[5] *Trans Chem. Soc.*, 1903, 83, 418

tion of both alkyl derivatives by the action of alkyl iodide on the silver compound, or by the combined action of alkyl iodide and silver oxide, make it probable that both silver compounds are present (p. 386).[1]

There are numerous cyclic compounds which exhibit a similar behaviour to the amides. Familiar examples are cyanuric acid and hydroxycaffeine, which exist as single substances, but yield two series of isomeric esters derived from the following structural forms :

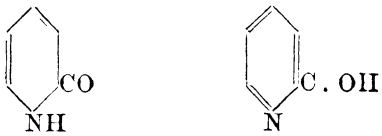


Cyanuric acid.



Hydroxycaffeine.

Examples might be multiplied.[2] To the same type also belong the α- and γ-hydroxy derivatives of pyridine, which react both as hydroxypyridines and pyridones, and form two series of alkyl derivatives.



α-Hydroxypyridine or α-Pyridone.

γ-Hydroxypyridine or γ-Pyridone.

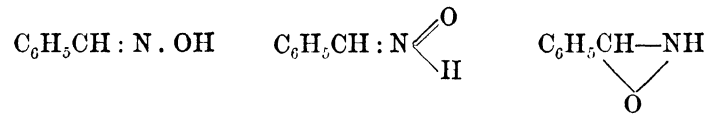
[1] Titherley, *Trans. Chem. Soc*, 1897, 71, 468 ; 1901, 79, 407.
[2] Marckwald, *Ber*, 1892, 25, 2354 ; Dixon, *Trans. Chem. Soc.*, 1899, 75, 375.

Thioamide-Thioimidol Type. The thioamides, both in open-chain and cyclic structures, commonly exhibit tautomerism like the amides,[1] and in some cases both isomeric forms are known.[2]

Thioamide. Thioimidol.

Oxime-Iso-oxime and Nitrone Type. Many oximes are known in two stereoisomeric forms (p. 295); but in addition they occasionally exhibit tautomerism. Benzaldoxime and its derivatives form alkyl compounds in which the alkyl group may be attached to oxygen or to nitrogen.[3] Meta-nitrobenzaldoxime forms two oxygen ethers and one nitrogen ether, whilst two oxygen ethers and two nitrogen ethers have been obtained from phenyltolylketoxime (p. 289).

Three structural formulae are possible, known as the oxime, iso-oxime, and nitrone formulae,

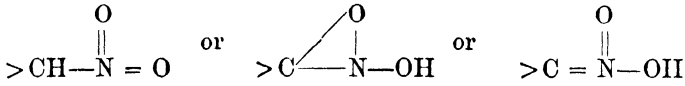


Oxime Nitrone. Iso-oxime.

the oxygen ethers being derived from the first and the nitrogen ethers from either of the other two. According to Brady and Dunn and to Semper and Lichtenstadt the nitrogen ethers are represented by the nitrone formula, and the existence of compounds of this type has been clearly demonstrated by Staudinger and Miescher.[4]

Tautomerism has also been observed among nitroso compounds, which are sometimes interconvertible with oximes.[5]

Nitro-Pseudonitro Type. Tautomerism is represented by the forms:



Hantzsch and Schultze[6] found that the ordinary liquid phenyl-

[1] Marckwald, *Ber.*, 1896, 29, 2920. [2] Hugershoff, *Ber.*, 1899, 32, 3649.
[3] Scheiber, *Annalen*, 1909, 365, 215. [4] *Helv. Chim Act.*, 1919, 2, 554
[5] Schmidt, *Ber*, 1902, 35, 2323, 2336, 3727; Piloty and Steinbock, *Ber*, 1902, 35, 3114, Bamberger and Pemsel, *Ber*, 1903, 36, 57, 85.
[6] *Ber*, 1896, 29, 699, 2251.

nitromethane dissolves in a solution of sodium hydroxide. From this solution acids precipitate in the cold a solid isomer, which gives a reddish-brown coloration with ferric chloride, combines with phenyl carbimide, dissolves in sodium carbonate, and in the free state changes spontaneously into the liquid modification, which exhibits none of the foregoing reactions. The two isomers are represented by the following formulae:

$C_6H_5CH_2 . NO_2$	$C_6H_5CH . NO . OH$
Normal phenylnitromethane.	Isophenylnitromethane.

Similar results have been obtained with other nitro compounds.[1]

As the one is a strong acid and the other a neutral compound they may be distinguished by the difference in electrical conductivity (see p. 365).

Nitrosoazo-Azoxy Type. Two formulae have at different times been proposed for this group of compounds.

$$Ar{-}N = N . Ar \quad (O) \qquad \text{or} \qquad ArN{-}N{-}Ar \quad (O)$$

From a mass of evidence which has been collected by Angeli and others[2] it seems clear that the majority of these substances must be represented by the nitrosoazo formula.

For example, by the oxidation of *p*-bromazobenzene with hydrogen peroxide in glacial acetic acid two isomeric *p*-bromazoxybenzene compounds are formed,

$$BrC_6H_4N : NC_6H_5 \quad (O) \qquad BrC_6H_4N : NC_6H_5 \quad (O)$$

which would not be possible if the other formula were used. There are many other examples of isomerism which might be quoted.[3]

A similar form of tautomerism is applicable, as Bamberger has found, to the arylazohydroxyanil compounds.[4]

$$C_6H_5N(OH)N : NC_6H_5 \rightleftarrows C_6H_5N . N . NHC_6H_5 \quad (O)$$

[1] Holleman, *Rec. trav. chim. Pays-Bas*, 1895, 14, 129; 15, 356; 16, 162; 33, 2913; Konowaloff, *Ber.*, 1896, 29, 2193, Hantzsch, *Ber.*, 1899, 32, 607, 1900, 33, 2542.

[2] Angeli, *Abstr.*, 1913, i, 658; *Ueber die Konstitution der Azoxyverbindungen*, by A. Angeli, Ahrens' *Vorträge*, 1912, xix, 447.

[3] *Abstr.*, 1921, i, 364, 624.

[4] *Annalen*, 1920, 420, 137.

Nitrosamine-Diazo Type. The geometrical isomerism exhibited by the diazo-compounds has already been discussed (p. 312), but in addition the isomers are capable of undergoing tautomeric change of the triad type:

$$—N = N—OH \qquad HN—N = O$$

Schraube and Schmidt,[1] for example, showed that the stable sodium salt of *p*-nitrodiazobenzene and methyl iodide gives nitrophenylmethyl nitrosamine, whereas von Pechmann,[2] by using the silver salt, obtained the isomeric nitrodiazobenzene methyl ether.

$(NO_2)C_6H_4N : NOCH_3$	$(NO_2)C_6H_4N(CH_3) . NO$
Nitrodiazobenzene methyl ether.	Nitrophenyl methyl nitrosamine.

The case resembles very closely that of the two series of alkyl anilides (p. 338).

Azo-Hydrazone Type. This is another example of a triad type of tautomeric compound, and may be represented as possessing either a hydrazone or azo structure.

$>C = N—\underset{\vert}{N}H$	$>CH—N = N—$
Hydrazone.	Azo-compound.

Reference has already been made to the fact that diazobenzene chloride and α-naphthol give the same product as that obtained by the action of phenylhydrazine on α-naphthaquinone (p. 330). R. Meyer[3] has shown that the compound obtained by combining diazobenzene chloride with malonic ester and then hydrolysing the product is the same as that which is formed by the action of phenylhydrazine on mesoxalic acid, and it may therefore be formulated either as a hydrazone or azo-compound.

$C_6H_5NH . N : C(COOH)_2$	$C_6H_5 . N : N . CH . (COOH)_2$
Hydrazone	Azo-compound.

Whichever formula is selected, one reaction must involve a tautomeric change. The choice of the formula has been the subject of much discussion, but the weight of evidence seems to be on the side of the

[1] *Ber.*, 1894, 27, 518.
[2] *Ber.*, 1894, 27, 672.
[3] *Ber.*, 1888, 21, 118; 1891, 24, 1241.

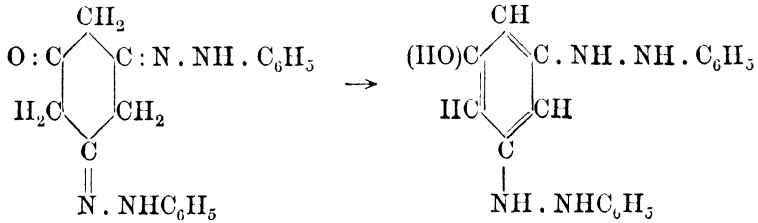
hydrazone structure.[1] That the non-appearance of the second form is due to its instability seems probable from Fischer's observation[2] that azophenylethyl $C_6H_5N:N.C_2H_5$, which is prepared by the oxidation of symmetrical phenylethylhydrazine $C_6H_5NH.NHC_2H_5$ with mercuric oxide, is readily converted into the isomeric acetaldehyde phenylhydrazone by the action of mineral acids, and also, as Bamberger[3] showed, by sodium ethoxide. The reverse change is produced by light.[4]

The action of nitrous acid on aldehyde hydrazones may give rise to two types of compounds:

$$\begin{array}{ccc} & \text{R.CH:N.NHR} & \\ & \swarrow \quad \searrow & \\ \underset{\text{I.}}{\text{R.C(NO):N.NHR}} & \text{or} & \underset{\text{II.}}{\text{R.CH:N(NO)R}} \end{array}$$

Bamberger[5] adopts formula I, whereas Busch and Kunder,[6] from the fact that the ketohydrazones react with nitrous acid, forming nitrosamines, accept formula II.

A tautomeric change of a somewhat different type has been studied by Baeyer,[7] who brings evidence to show that the product of the action of phenylhydrazine on phloroglucinol and similar compounds is not a hydrazone of the keto form, but a hydrazide, and that tautomeric change is brought about by the wandering of a hydrogen atom from a carbon of the benzene nucleus to the nitrogen of the hydrazone radical, which he explains in the following way:



[1] Japp and Klingemann, *Annalen*, 1888, 247, 190; Fischer, *Amer. Chem. J.*, 1899, 21, 14, Thiele and Heuser, *Annalen*, 1896, 290, 1, Bulow and Ganghofer, *Ber.*, 1904, 37, 4169; see also K. H. Meyer and Zahn, *Annalen*, 1913, 396, 152, *Abstr.*, 1914, i, 599

[2] *Annalen*, 1879, 199, 328; *Ber.*, 1896, 29, 793

[3] *Ber.*, 1903, 36, 56.

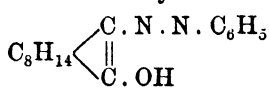
[4] Chattaway, *Proc. Chem. Soc.*, 1906, 22, 36.

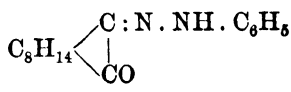
[5] *Ber.*, 1903, 36, 57, 359.

[6] *Ber.*, 1916, 49, 317.

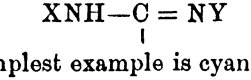
[7] *Ber.*, 1891, 24, 2688.

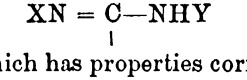
A similar case is that of the hydrazone of camphor quinone, which has been obtained by Betti [1] in both isomeric forms.





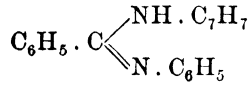
Amidine Type. In this type of tautomeric compound the hydrogen is transferred from one nitrogen atom to another.

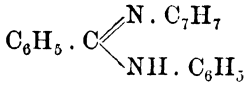




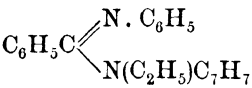
The simplest example is cyanamide, which has properties corresponding to both the formulae $NH_2 . C . N$ and $NH : C : NH$. [2]

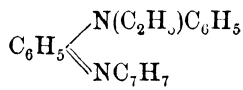
Other examples are the amidines. By combining benzanilidoiminochloride with *p*-toluidine, von Pechmann [3] obtained the same product as that from benz-*p*-toluidiminochloride and aniline, instead of two different compounds of the formulae:





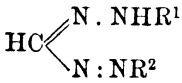
Although the same phenyl-*p*-tolylbenzamidine is produced in the two reactions, it nevertheless gives rise to two different ethyl derivatives of the formulae:

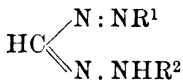




which von Pechmann identified by comparing them with the compounds obtained from the corresponding iminochlorides by the action of ethylaniline in one case and ethyl-*p*-toluidine in the other. In other cases only one alkyl derivative was obtained; methylnaphthylbenzamidine yields only one methyl derivative, from which von Pechmann concluded that tautomerism occurs only if the radicals are similar in character.

Other examples of the same kind are the formazyl derivatives of von Pechmann [4] and Wallach [5] of the general formula:

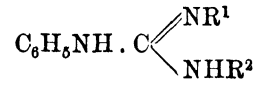


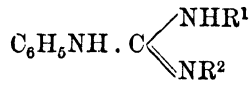


and the guanidine compounds of Forster, [6] Marckwald and Wolff, [7]

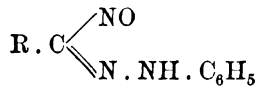
[1] *Ber.*, 1899, **32**, 1995; see also Lapworth, *Trans. Chem Soc*, 1902, **81**, 1508.
[2] E. A Werner, *Trans. Chem Soc*, 1915, **107**, 715
[3] *Ber.*, 1895, **28**, 869, 2362, 1897, **30**, 1779, 1783; see also Cohen and Marshall, *Trans Chem. Soc*, 1910, **97**, 328; Ingold and Piggott, *ibid.*, 1922, **121**, 2381; Pyman, *ibid*, 1923, **123**, 367.
[4] *Ber.*, 1894, **27**, 1679.
[5] *Annalen*, 1882, **214**, 209; *Ber.*, 1883, **16**, 147.
[6] *Annalen*, 1875, **175**, 85.
[7] *Ber*, 1892, **25**, 3116.

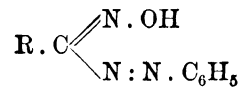
and Huhn,[1] which are represented in each case by only one substance:





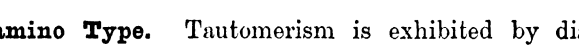
Very similar in character also are the nitroso-aldehydrazones of Bamberger and Pemsel,[2] which are very unstable, and pass spontaneously into the isomeric azoaldoximes.





Nevertheless, in a few cases, both isomeric forms have been isolated.

Diazoamino Type. Tautomerism is exhibited by diazoamino compounds, which contain the triad group.



When diazobenzene chloride acts upon toluidine a different product would be anticipated from that produced by the action of diazotoluene chloride upon aniline.

Benzenediazoaminotoluene. Toluenediazoaminobenzene.

Meldola and Streatfeild[3] have proved that the compounds obtained in this way are not isomeric but identical.

Virtual and Functional Tautomerism. Where tautomerism is expressed by two structural forms denoting similar chemical properties, such as the amidine, formazyl, guanidine, and diazoamino types just described, von Pechmann employs the term *virtual* to distinguish it from *functional* tautomerism, in which the structure of the tautomeric forms expresses a difference of function, such as the tautomerism of the keto and enol, amide and imidol, nitroso and oxime compounds, and in fact the great majority of tautomeric compounds.

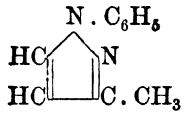
Tautomerism of Heterocyclic Compounds. The identity of the methyl pyrazoles obtained by Knorr[4] from 1-phenyl 3-methyl-

[1] *Ber*, 1886, 19, 2404. [2] *Ber.*, 1903, 36, 85.

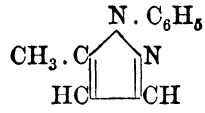
[3] *Trans. Chem. Soc*, 1887, 51, 102, 434; 1888, 53, 664, 1889, 55, 412; 1890, 57, 785; Ingold and Piggott, *Trans Chem. Soc.*, 1922, 121, 2381.

[4] *Annalen*, 1894, 279, 188.

and 1-phenyl 5-methyl-pyrazole, by removing the phenyl group, is a very interesting example of tautomerism.

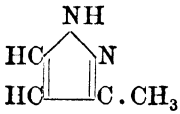


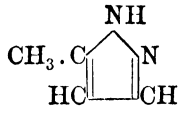
1-phenyl 3-methyl-pyrazole.



1-phenyl 5-methyl-pyrazole.

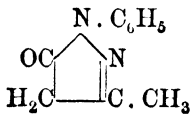
The removal of the phenyl group would be expected to yield two structural isomers.

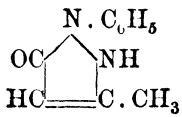


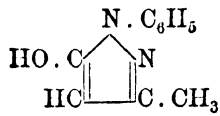


The existence of one substance can only be explained by the wandering of a hydrogen atom from one nitrogen atom to a more stable position beside the adjoining nitrogen atom, or, as Knorr has suggested, by the oscillation of the hydrogen atom between the two positions, which is practically synonymous with a mixture of the two forms. This view is supported by the fact that a mixture of two dimethyl pyrazoles is formed on methylation. The case is exactly parallel to the formation of two ethyl derivatives of phenyl-tolylbenzamidine (p. 344).

How complex cyclic tautomerism may become is seen from another case in which Knorr [1] obtained three methyl derivatives of phenyl methyl pyrazolone. They are regarded as derivatives of the following tautomeric forms:



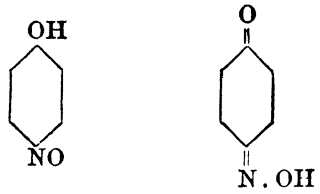




Quinone Type. A typical example is the compound nitroso-phenol already referred to, which is obtained both by the action of nitrous acid on phenol and of hydroxylamine on quinone,[2] and may therefore be represented by two structural formulae:

[1] *Ber.*, 1895, 28, 706. See also Fischer and Rigaud, *Ber.*, 1901, 34, 4202; Thiele and Buchner, *Annalen*, 1906, 347, 253.

[2] Goldschmidt, *Ber.*, 1881, 17, 213.

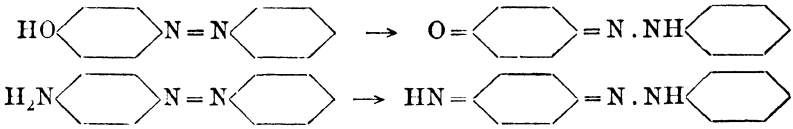


Nitrosophenol or Quinoneoxime.

It is customary to adopt the second of the two formulae, since the compound yields alkyl and acyl derivatives of the oxime type and a dioxime with hydroxylamine. Moreover, the green or blue colour, which is characteristic of true nitroso compounds, is absent in the solid which is brown, although it exhibits a green colour in certain solvents.

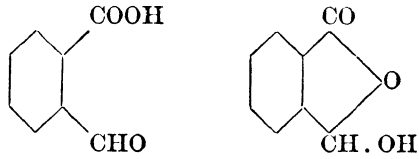
Both yellow and red modifications of oximes derived from orcinol and β-naphthol[1] have been described, but whether they represent the nitroso and oxime structure is uncertain.

The colour of the azo and other dyes is frequently referred to the quinonoid structure, which the hydroxy-azo and amino-azo compounds are supposed to assume by a process of tautomeric change.



The phenomenon of fluorescence is also ascribed to tautomerism of a special kind.[2] (See p. 144).

Lactone Type. Lactone tautomerism is applied to cases of tautomerism where an interchange of atoms may occur between groups in the ortho or, in open chain-compounds, in the γ-position. Liebermann[3] found that aldehydophthalic acid assumes the functions of a lactone or hydroxyphthalide,

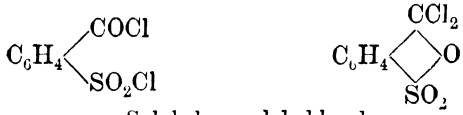


and it is well known that phthalyl chloride and *o*-sulphobenzoyl-dichloride behave in some cases as if both atoms of chlorine were

[1] Henrich, *Monatsh.*, 1897, 18, 142; Kehrmann and Zimmerli, *Ber.*, 1898, 31, 2417.
[2] Hewitt, *Proc. Chem Soc.*, 1900, 16, 6.
[3] *Ber.*, 1896, 29, 175, 2030.

attached to the same carbon.[1] Each compound must therefore be represented by two formulae:

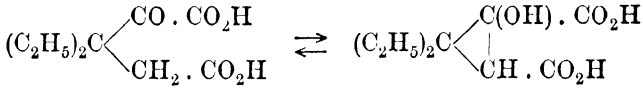
Phthalyl chloride.



Sulphobenzoyl dichloride.

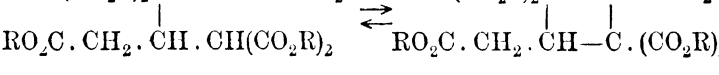
Phthalyl chloride has actually been prepared in two isomeric forms by Ott[2] and Csányi,[3] the symmetrical chloride being converted into the second by the action of aluminium chloride, and a simple method for distinguishing them has been devised by v. Braun and Kaiser,[4] who use the thiourethanes of piperidine and dimethylamine which yield different products with the two isomers.

An interesting case of tautomerism which has been described by Ingold, Thorpe, and Perren[5] has been termed by them ring-chain tautomerism, and may be illustrated by the following examples:



in which a cyclopropane ring is formed by a keto-enol change.

A similar process of ring formation may also be effected by what may be termed an intramolecular Michael condensation as follows:



Dynamic Isomers or Desmotropic Compounds. It will be seen from the foregoing examples of tautomerism that Laar's conception of one substance representing two structural isomers has not been consistently adhered to, for several cases are cited in which both

[1] Graebe, *Ber.*, 1883, 16, 860; Auger, *Ber*, 1888, 21, Ref. 610; *Ber*, 1891, 24, Ref 319, Remsen, *Amer Chem. J*, 1896, 18, 792; Liszt and Stein, *Ber.*, 1898, 31, 1648, R. Meyer, *Ber*, 1895, 28, 1577, Purdie and Young, *Trans. Chem. Soc*, 1910, 97, 1524, Scheibei, *Annalen*, 1912, 389, 121, Ott, *Annalen*, 1912, 392, 215; *Ber.*, 1912, 45, 2252.

[2] *Annalen*, 1912, 392, 245.

[3] *Monatsh*, 1919, 40, 81

[4] *Ber*, 1922, 55, 1305.

[5] *Trans. Chem. Soc.*, 1922, 121, 1765; 1923, 123, 113.

isomers anticipated by theory are known. The latter have been called *dynamic isomers* or sometimes *desmotropic compounds* to distinguish them from the single or tautomeric substance. Dynamic isomers differ in no respect from ordinary isomers but in the fact that they are more or less readily interconvertible. There is little doubt that this convertibility or metamorphosis of isomeric substances is the idea which Berzelius[1] had in mind when he introduced the term *metamerism*, although the example of cyanuric and cyanic acid, which he selected to illustrate it, is one, not of isomeric, but of polymeric change (p. 169).

Fresh light has been thrown on the subject of tautomerism by the discovery of both structural forms of the familiar and peculiarly labile (keto-enol) type of tautomeric compounds. Its immediate result has been to demonstrate the futility of the method hitherto adopted of attempting to ascertain the structural formula of a tautomeric compound from that of its derivatives or from the chemical behaviour of the compound itself. It has been shown that the extreme mobility of one or both of the isomers renders them liable to isomeric change, not only in presence of a reagent, but frequently by a rise of temperature, action of light, or the action of a solvent.

It may thus happen that the lower melting isomer may fuse, and as the temperature rises may again solidify and remelt when the equilibrium temperature is reached. That point will not be, as Claisen supposed, the true melting-point of the second isomer, but the fusion temperature of the equilibrium mixture (p. 363).

Both Claisen and von Pechmann had already pointed out the uncertainty of chemical reactions as indicative of structure. They adopted a method of comparison whereby they claimed to demonstrate by the behaviour of certain hydroxymethylene compounds, such as formylacetic ester, formylpropionic ester and hydroxymethylene camphor (Part I, p. 273), that they are true hydroxyl compounds, partaking partly of the character of alcohols, partly of that of acids. As in no case do the substances in question exhibit the characteristics of the acetoacetic ester type of compound, they concluded that the latter has a ketonic and not an enolic structure.[2]

Among the earliest examples of dynamic isomers are acetyldibenzoylmethane, tribenzoylmethane, and mesityloxide-oxalic ester discovered by Claisen.[3] The first two compounds were obtained by the action of benzoyl chloride on the sodium compounds of

[1] *Jahresb*, 1832, 12, 63.

[2] Wislicenus, *Ber.*, 1887, 20, 2930; Claisen, *Ber.*, 1892, 25, 1776; von Pechmann, *Ber.*, 1892, 25, 1040

[3] *Annalen*, 1893, 277, 184, 1896, 291, 25.

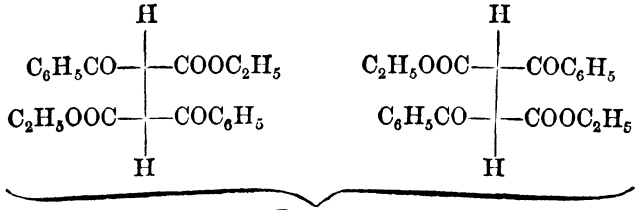
benzoylacetyl methane $C_6H_5CO.CH_2.COCH_3$ and dibenzoylmethane $C_6H_5CO.CH_2.COC_6H_5$, and the third by condensing mesityl oxide with oxalic ester in presence of sodium ethoxide. The following formulae, which are distinguished as 'enol' and 'keto', were assigned to the isomeric forms:

	Enol	Keto.
Acetyldibenzoylmethane	$C(OH).CH_3$ $C—CO.C_6H_5$ $CO\ C_6H_5$ *m. p.* 80-85°	$CO.CH_3$ $HC—CO.C_6H_5$ $CO.C_6H_5$ *m. p.* 150°
Tribenzoylmethane	$C(OH).C_6H_5$ $C—CO.C_6H_5$ $CO.C_6H_5$ *m. p.* 155°	$CO.C_6H_5$ $HC—CO.C_6H_5$ $CO.C_6H_5$ *m. p.* 245-250°
Mesityloxide-oxalic ester	$CO.CH.C(CH_3)_2$ $CH.C(OH).COOC_2H_5$ *m. p.* 21-22°	$CO.CH:C(CH_3)_2$ $CH_2.CO.COOC_2H_5$ *m. p.* 59-60°

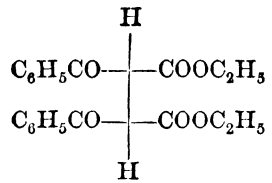
The compound obtained by precipitating acetyldibenzoylmethane from its cold solution in sodium carbonate with acetic acid melts at 101-102°, dissolves in alkalis with a yellow colour, gives a dark red coloration with alcoholic ferric chloride, and forms a crystalline copper salt. It is known as the *α*-compound. When heated it melts at 80-85°, solidifies again above 90° and melts a second time at 110°.[1] This is taken as indicative of a change into the second or *β*-form. (see p. 363). The new substance is not directly dissolved by sodium carbonate, copper acetate produces no immediate precipitate, and the coloration with ferric chloride is only slowly developed. The first or *α*-compound which readily forms metallic salts is assumed to contain a hydroxyl group and consequently represents the enol form; the second or *β*-compound is the keto form. The change of enol to keto may also be effected by certain solvents. Ligroin and benzene are without action, but when heated with alcohol on the water-bath the solution is found to contain about one-third of the keto form; if dilute alcohol is used a still larger proportion is produced. The reverse change of keto to enol may be effected by adding alkali, when the keto compound passes gradually into solution, and on acidifying

[1] The true melting-point of the keto form is 150°, the lower melting-point being due to small quantities of the enol form which is readily produced when traces of alkali are present (Dieckmann, *Ber*, 1916, **49**, 2203).

the well-cooled liquid with acetic acid the enol compound is precipitated. Similar observations have been made with tribenzoyl methane and mesityloxide-oxalic ester. The non-existence of ketonic forms of triacetyl methane $CH(COCH_3)_3$ and benzoyldiacetyl methane $CH(COCH_3)_2COC_6H_5$ is accounted for by the nature of the acyl radicals, for it is found that the presence of three benzoyl radicals, as in tribenzoylmethane, renders the ketonic form more stable.[1] This investigation was followed by many others on the same lines. Knorr[2] found that dibenzoylsuccinic ester, which is obtained by the action of iodine on sodium benzoylacetic ester, consists of two isomeric substances which could be separated by means of alcohol. As neither of them gave a coloration with ferric chloride, Knorr concluded that they were both ketonic, corresponding to the racemic and meso forms of tartaric acid.



Racemic.



Meso.

But if either of these compounds is dissolved in a solution of sodium ethoxide, and precipitated in the cold with dilute sulphuric acid, an oily product is obtained which gives the ferric chloride reaction, and unlike the other isomers dissolves in dilute alkalis. It is represented by the enolic formula:

$$C_6H_5 . C(OH) : C . COOC_2H_5$$
$$\quad\quad\quad

$$\begin{array}{c} CH_3 . CO . CH . COOC_2H_5 \\ | \\ CHR. \\ | \\ CH_3 . CO . CH . COOC_2H_5 \end{array}$$

with benzylidenediacetylacetone by Schiff,[1] who claims to have

$$\begin{array}{c} CH_3 . CO . CH . CO . CH_3 \\ | \\ CH . C_6H_5 \\ | \\ CH_3 . CO . CH . CO . CH_3 \end{array}$$

obtained no less than six structural or geometrical isomers, and by others.[2]

A further insight into the mechanism of tautomeric change is afforded by W. Wislicenus' discovery of the desmotropic forms of formylphenylacetic methyl and ethyl esters :[3]

$HCO . CH(C_6H_5) . COOC_2H_5$; $HC(OH)\ C(C_6H_5) . COOC_2H_5$

They are obtained by the condensation of formic ester with phenylacetic ester in presence of sodium (Part I, p. 264). Both isomers are found in the product, and since one is a liquid and the other a solid they can be separated by filtration. If precipitated by carbon dioxide from alkaline solution the enol form is obtained, if by sulphuric acid the keto form is produced. The liquid or α-ester gives the usual reactions for the enol form with ferric chloride and copper acetate. The solid or β-ester, which melts at about 110°,[4] gives no coloration with ferric chloride ; and though it forms both sodium and copper compounds, they are very unstable and pass into the corresponding derivatives of the α-ester. Whilst both esters remain unchanged in closed vessels for an indefinite time, exposed to the air the β-ester soon becomes liquid, producing some of the α-form. This change is more quickly effected at 70°. On the other hand the α-ester changes slowly but almost completely into the β-compound at the ordinary temperature on introducing a crystal of the latter substance.

Similar results have been obtained with the methyl ester, which exists in two forms, the enol or α-form melting at 40-41° and the β- or keto form at 91–93°.

Although the keto form of neither the methyl nor ethyl ester gives the characteristic ferric chloride reaction, nevertheless both keto and enol combine with a molecule of bromine, and are equally soluble

[1] *Annalen*, 1899, 306, 332 , 309, 206

[2] Knorr, *Annalen*, 1898, 303, 133 , Rabe, *Annalen*, 1907, 360, 289 ; Wislicenus and Ruthing, *Annalen*, 1911, 379, 229.

[3] *Annalen*, 1896, 291, 147 , 1900, 312, 62 ; 1912, 389, 270 ; 1916, 413, 206 ; *Ber* , 1899, 32, 2837 , see also Michael, *Annalen*, 1912, 391, 235, 275 ; 1914, 406, 137 ; K H. Meyer, *Ber.*, 1912, 45, 2863 ; Dieckmann, *Ber.*, 1916, 49, 2213.

[4] Traces of alkali, such as may be derived from the glass vessel, lower the melting point (Dieckmann, *Ber.*, 1916, 49, 2213).

in alkalis,[1] and it seems doubtful whether they are not in reality, as Dieckmann supposes, *cis* and *trans* enol forms.[2]

Both keto and enol forms appear to combine with a molecule of methyl alcohol, forming definite additive compounds which react neither with bromine nor ferric chloride.

Perhaps the most interesting result of this investigation is the discovery that in certain solutions a condition of equilibrium is reached between the two forms which is dependent upon temperature, concentration and the nature of the solvent. The equilibrium point was ascertained by observing the intensity of the coloration with ferric chloride.[3] If either α- or β-ester is dissolved in the same solvent, under the same conditions of temperature and concentration, the coloration produced by adding an alcoholic solution of ferric chloride to the one ester diminishes in intensity, whilst that of the other gradually increases until eventually the two solutions appear of the same tint.[4] The equilibrium point was found to change with temperature and concentration. Wislicenus observed further that whilst methyl alcohol and water favour the formation of the keto form, benzene favours that of the enol form, whereas in ether solution both forms are present, and he ascribed the effect, in accordance with a previous suggestion of Knorr, to the ionizing power of the solvent. In the present case the more strongly ionizing solvent determines the keto formation. A very interesting confirmation of Wislicenus' results on the action of the solvent is afforded by the observations of Brühl. He found that the dynamic isomers of Claisen's mesityloxide-oxalic ester showed well-marked differences in refractive and dispersive power, and was thus able, whilst avoiding the disturbing influences which might be introduced by the use of a chemical reagent, to follow the changes effected by the solvent. He found that chloroform had little action, whilst methyl and ethyl alcohol rapidly ketonize the dissolved enol form. Brühl, like Wislicenus, ascribed the change to the ionizing action of the solvent, which appeared also to be closely related to its dielectric constant. Without discussing at present the mechanism of the change, it is clear from the examples which have been given that the convertibility of dynamic isomers belongs to a class of reversible reactions of a peculiarly sensitive kind. Gault and Weick[5] have obtained both enol forms as well as the keto form of phenylpyruvic ethyl ester, $C_6H_5 . CH_2 . CO . COOC_2H_5$.

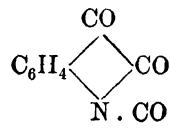
Determination of Structure, Chemical Methods. In view of

[1] W. Wislicenus, *Annalen*, 1917, 413, 208. [2] Dieckmann, *Ber.*, 1917, 50, 1375.
[3] *Annalen*, 1896, 291, 178 [4] See also Stobbe, *Annalen*, 1903, 326, 359.
[5] *Compt. rend.*, 1920, 171, 395.

the mobility of dynamic forms it may be well to consider to what extent chemical methods are available for determining structure. It is evident that many reagents are excluded from the simple fact that they produce isomeric change, a fact which applies equally to the formation of derivatives of the compounds in question. There is scarcely one of the reactions, discussed at length on pp. 331, 332, and formerly used as evidence in favour of the keto or enol structure of acetoacetic ester, which has withstood the test of subsequent experience. It is on this account that the action of bases and acids is generally excluded, and also the derivatives which are obtained by their aid. It has been shown that sodium compounds are mainly enolic, and in some cases, as Knorr found, the enolic form may be extracted by alkalis; but it does not always follow that the derivative obtained by the use of the sodium compound is a guide to the structure of the original substance. Much depends upon the rate of change. Where the change is slow it is possible, as in the case of phenylaminotriazole carboxylic ester, to estimate the acid form by titration with alkali (p. 359). Acetic anhydride cannot be employed to ascertain the presence of hydroxyl. Both forms of formylphenylacetic ester yield the same acetyl derivative. Acid chlorides act in the same way. Many ketones are known to yield enolic acyl derivatives.[1] Phenyl hydrazine and hydroxylamine are also excluded. Here again both isomers of formylphenylacetic ester give the same hydrazone and oxime. Among the few reagents which appear to have little effect upon the isomers is phenyl carbimide dissolved in a non-ionizing solvent. It reacts in the cold with hydroxy- and amino-compounds in the following way to form carbamic esters and carbamide compounds:

$$R\ OH + C_6H_5 . N . CO = RO . CO . NHC_6H_5$$
$$R . NH_2 + C_6H_5 . N : CO = R . NH . CO . NHC_6H_5$$

Isatin, for example, forms a carbanilide, and is therefore a lactam and not a lactim as Baeyer supposed.



Phenyl carbimide combines with phloroglucinol, but not with succinosuccinic ester, indicating that the former is enolic and the latter ketonic. It unites also with the pseudo but not with the normal forms of phenyl nitro methane and its derivatives.

[1] Michael and Smith, *Annalen*, 1908, 363 64.

Ozone is another reagent which can occasionally be employed for detecting and estimating the enolic form.[1] Its action is that described in Part I, p. 131, that is, it forms an ozonide with the doubly linked carbon atoms of the enol form with subsequent cleavage at that point. One advantage of the method is that, where there is a choice between two enol forms, such, for example, as that presented by benzoyl acetone, which may have either of the following formulae,

$$C_6H_5C(OH) = CH \cdot CO \cdot CH_3 \quad \text{or} \quad C_6H_5CO \cdot CH = C(OH) \cdot CH_3$$

the ozone method will differentiate them by the nature of the oxidation products. The method also furnishes a means of detecting a dienolic structure, which cannot be ascertained with certainty by the optical methods of refractivity and magnetic rotation, owing to the indeterminate effect of exaltation. In this way oxalacetic ester has been shown to consist of the di-enolic and one monoketonic form.

The tendency to produce enolisation (from the least to the greatest) appears to be in the order:

$$-COOC_2H_5, \quad -COCH_3, \quad -CO\ C_6H_5, \quad -CO \cdot COOC_2H_5.$$

An alcoholic solution of ferric chloride can also be used to determine the presence of the enolic form, and, as already pointed out, to follow the changes taking place between the two dynamic isomers.

Knorr and Schubert[2] have utilized the ferric chloride reaction to estimate the amount of enol by a colorimetric method, which depends on the fact that the greatest colour intensity is reached when equimolecular proportions of ferric chloride and enol compound are present, in accordance with the equation,

$$R \cdot OH + FeCl_3 = FeCl_2 \cdot OR + HCl$$

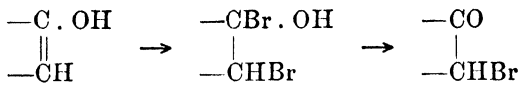
in which R . OH stands for the enolic compound. A standard solution of the pure enol and ferric chloride is prepared and the solution of the desmotropic mixture ascertained by adding the same quantity of ferric chloride and comparing the solution in a colorimeter with the standard. The amount of enolic constituent of mesityloxide oxalic ester in different organic solvents varies from 3 to 4·5 per cent.

The method, however, is open to the objection, which has been repeatedly pointed out, that the reagent may act as a catalyst,[3] and can only be employed in those cases where isomeric change is so slow as to be controlled and the extent of error ascertained.

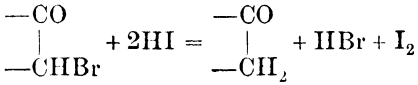
Another chemical method, devised by K. H. Meyer,[4] depends upon

[1] Scheiber and Herold, *Ber.*, 1913, 46, 1105; *Annalen*, 1914, 405, 295.
[2] *Ber.*, 1911, 44, 2772.
[3] Lowry, *Trans Chem. Soc*, 1899, 75, 230; K. H. Meyer, *Ber*, 1911, 44, 2725.
[4] *Annalen*, 1911, 380, 212; 1913, 398, 49, *Ber.*, 1911, 44, 2718; 1912, 45, 2843

the rapid union of the enolic, but not of the ketonic, form with bromine. The former is unstable, and is at once decomposed with the separation of hydrogen bromide and the formation of the bromoketone (see Part I, p. 369).



On adding potassium iodide the bromoketone is reduced, and the iodine set free is estimated by titration in the usual way. The amount of free iodine gives that of the enol form present.



A standard solution of bromine in alcohol is introduced in excess and β-naphthol immediately added in order to remove the uncombined halogen. On the addition of potassium iodide, iodine is liberated and estimated as described above.

Experiments carried out with acetoacetic ester show that about 7 per cent. of enol is present, a number which agrees with that of Auwers determined from the observed and calculated refractivity (p. 37); but is much higher than that which Knorr calculated from the refractive index of mixtures of the two pure substances (about 2 per cent.) obtained by fractional crystallization of acetoacetic ester at low temperatures (p. 333). Benzoylacetic ester was found to contain 29 per cent. of enol.[1] A source of error in the bromine method is the action of bromine in enolising the keto form,[2] a change which takes place very slowly, and which is to some extent obviated by the addition of β-napthol. In the case of acetoacetic ester it is estimated at about 1 per cent. per minute; but as the operation can be completed in half that time the error does not exceed 0·5 per cent.

The following table gives the percentage of enol determined by this method in different tautomeric compounds at the ordinary temperature:

Methyl acetoacetate	4·8	Benzoylacetic acid	98·0
Methyl methylacetoacetate	3·1	Methyl benzoylacetate	16·7
Acetylacetone	80 4	Ethyl ,,	29·2
Ethyl acetonedicarboxylate	16·8	Benzoyl acetone	98·0
Oxalacetic acid	100 0	Dibenzoyl methane	96·0
Methyl oxalacetate	100·0		

Many interesting results have been obtained by this method in observing the effects of different solvents and different dilutions on

[1] K H Meyer, *Ber.*, 1911, 44, 2730. [2] Part I, p. 127.

the proportions of enol and ketone. Dilution increases the amount of enol in all cases, and is least in alcohol and greatest in hexane (see p. 362).[1] K. H. Meyer[2] further finds that solid crystalline substances are always homogeneous, and do not form solid solutions or mixed crystals of enol and keto forms; but that the solvent may bring about fundamental changes. Benzene, for example, enolises acetyl dibenzoyl methane to the extent of 98 per cent., whilst the solid enol form of oxalacetic methyl ester is largely ketonised in solution.

Hieber[3] has introduced a method for estimating the amount of enol by adding copper acetate in alcohol-chloroform solution to the substance dissolved in alcohol. The liquid is then poured into water and the chloroform, which contains the enol compound in the copper salt, is separated and decomposed with dilute sulphuric acid. The copper is estimated by adding potassium iodide and titrating with sodium thiosulphate. The results of a number of estimations agree substantially with the method of K. H. Meyer.

The use of tertiary amines has been suggested as a reagent for distinguishing between enolic and ketonic structures,[4] as in many cases it is found to combine with the former, producing additive compounds from which the original substance may be reprecipitated unchanged; but experience has shown that it is not always trustworthy.[5]

To determine the presence of keto and enol form in acetoacetic ester, Schiff[6] conceived the device of bringing about a combination between the ester and a compound with which either enol or keto form will readily unite. The substance selected was benzalaniline $C_6H_5CH:N.C_6H_5$, which can combine with acetoacetic ester in the following ways:

$$CH_3.CO.CH(C_6H_5CH.NHC_6H_5).COOC_2H_5$$

In union with the *keto* form.

$$CH_3.C(OH)=C(C_6H_5CH.NHC_6H_5).COOC_2H_5$$

In union with the *enol* form.

A product was obtained melting at 95°, which was shown to be a mixture of the two forms. The individual substances were obtained separately either by adding to the mixture of acetoacetic ester and the reagent a few drops of piperidine, which ketonizes the ester, or a trace of sodium ethoxide, which converts it into the enol form. These two compounds melt at 78° and 104° respectively. Similar results have been obtained with benzoylacetic ester, and, by Francis,[7] with dibenzyl ketone and desoxybenzoin. The action of piperidine and sodium ethoxide is interesting. The small amount of reagent required led Schiff to infer that the action is catalytic. This view is clearly opposed to the general conception of a catalytic agent which can only accelerate equilibrium but not modify the proportions of the ultimate constituents. It is, moreover, contra-

[1] See Hantzsch, *Ber.*, 1906, 39, 1086; Knorr, *Annalen*, 1899, 306, 315.
[2] K. H Meyer, *Ber*, 1912, 45, 2847. [3] *Ber*, 1921, 54, 902.
[4] Michael and Smith, *Annalen*, 1908, 363, 36 [5] K H Meyer, *Ber.*, 1912, 45, 2844.
[6] *Ber.*, 1898, 31, 205, 601, 1304, 1388, 1899, 32, 332.
[7] *Trans. Chem. Soc.*, 1899, 75, 865; *Ber.*, 1903, 36, 937, *Trans. Chem. Soc.*, 1901, 87, 998.

dicted, as Schaum [1] has pointed out, on thermodynamical grounds as well as by his own experimental evidence. He showed that, by the displacement of equilibrium without adding energy to a system, one change is accelerated at the expense of the other, and consequently a certain amount of energy is used. If the catalyst is then removed, the original equilibrium is restored, and the energy set free can be utilized to perform work, so that by combining the two systems a perpetual motion is created. Experimentally he proved that neither reagent affects in the slightest degree the density or specific refraction when equilibrium is established. An explanation of the process has been given by Lowry.[2] He suggests that each reagent reacts with one form only, producing an additive compound, which then interacts with the benzalaniline, and at the same time liberates the reagent One of the isomers is thus removed from the mixture, equilibrium is restored, to be again disturbed by the reagent, and so the process continues until the whole undergoes change into the one product.

Physical Methods have afforded much valuable information about isomeric change. The methods utilized include solubility, density, optical properties, electrical conductivity, colour, and have been discussed in the chapter on 'Physical Properties and Structure'. A brief recapitulation of the results is therefore all that is necessary.

Action of Solvents. It has already been pointed out that solvents affect the equilibrium point of mixtures of enolic and ketonic forms. It was observed by Clausen in crystallizing the enol form of acetyldibenzoyl methane from alcohol, by Knorr in the case of diacylsuccinic esters, by Wislicenus in that of formylphenyl acetic ester, &c., by K. H. Meyer in the equilibria of acetoacetic ester in different solvents, &c. In these cases the dissociating solvents favoured the ketonic structure, the energy required to modify the equilibrium point being ascribed by Brühl to the solvent. Knorr[3] attributed the effect to the ionizing power of the solvent, a view which was also shared by Wislicenus, Bruhl,[4] and others. Moreover, those solvents with a high dielectric constant appeared to increase the velocity of the change. Brühl supposed that the enol form, which is a weak acid, undergoes dissociation, the hydrogen of the hydroxyl group

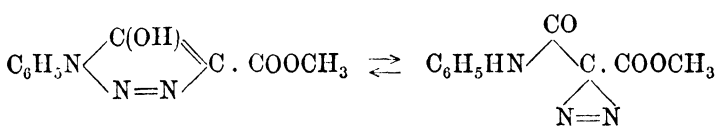
[1] *Ber.*, 1898, 31, 1964
[2] *Trans, Chem Soc*, 1899, 75, 241.
[3] *Ber.*, 1895, 25, 708.
[4] *Zeit. phys. Chem.*, 1899, 30, 1; *Ber*, 1899, 32, 2326.

forming an ion, which wanders to the adjacent carbon atom. It is obvious that, unless the process is a reversible one, the change from enol to keto must necessarily be complete.

The effect of solvents possessing different dielectric constants has been examined by Brühl from the refractivity and dispersivity constants for the two forms of mesityloxide oxalic ester (p. 39). He observed that the enolic form remains unchanged in chloroform, but is rapidly ketonised in methyl and ethyl alcohol. In the same way, by the aid of the absorption spectra Hantzsch showed that acetoacetic ester is ketonized in water and the alcohols, but enolised in hexane.

Stobbe,[1] using the ferric chloride reaction and different solvents, was able to slow down the change by conducting the process at a low temperature (− 78°), so that he could follow roughly its velocity. He found that alcohols accelerate the change keto-enol, and that the greater the molecular weight of the alcohol the greater the velocity. The action of the solvent is therefore the reverse of the foregoing. Non-dissociating solvents did not affect the keto form. Stobbe regards the solvent as acting the part of a catalyst in the first case and of an anti-catalyst in the second, and classifies all solvents under these two heads.

Dimroth's experiments led him at first to conclude that the action of the solvent in the case of phenylhydroxytriazole carboxylic ester is related to its dielectric constant, but is the reverse of that found by the earlier observers, inasmuch as the solvents with the smallest dielectric constants appeared to produce the maximum velocity by which the change is completed in the direction of the enol/keto transformation, whereas water and the alcohols cause a similar but incomplete change, which proceeds very slowly.[2] This reaction, although belonging to the category of isomeric changes, was subsequently found not to be tautomeric in the ordinary sense of the term, but to occur with the following change of structure:

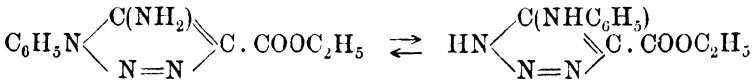


In the meantime Michael and Hibbert[3] investigated the action of a great variety of solvents on dibenzoylacetyl methane and diacetylsuccinic ester, and found that although the solvent with the higher

[1] *Annalen*, 1903, **326**, 859; 1907, 352, 132.
[2] *Annalen*, 1904, **335**, 1; 1905, 338, 143, 1910, 373, 336.
[3] *Ber.*, 1908, **41**, 1080.

dielectric constant lowers the velocity and vice versa, the more highly dissociating solvent produces a higher ketone content in the final mixture. They conclude that there is no simple relation between the rate of isomeric change and the dielectric constant, or indeed any other special character of the solvent, but that the velocity of the change is determined by the nature of the tautomeric compound, and that the solvent may be supposed to enter into loose complexes with the isomeric compounds undergoing change.

Dimroth's later results led him to modify materially his earlier conclusions. He determined the relation between the solubilities and the velocity of transformation of phenylhydroxytriazole carboxylic ester and its amino derivatives in a great variety of solvents.[1]



Neutral form. Acid form.

Phenylaminotriazole-carboxylic ester.

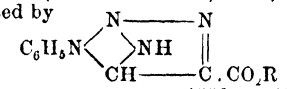
The second or acid form of the above modifications can be titrated with alkali and thus quantitatively determined in presence of the first or neutral form.[2] Dimroth found that the velocity of change is determined by the relative solubilities of the isomers, and is smaller the greater their solubility in the solvent, or, in other words, the velocities are approximately inversely proportional to the solubilities. This principle had already been arrived at on theoretical grounds by van 't Hoff in 1898.[3] Van 't Hoff regards the effect of the solvent on the velocity to be two-fold: the one is catalytic, and influences both reactions equally, whereas the other affects the two reactions differently, and depends upon some interaction between the reacting substance and the solvent. This influence of the solvent on the equilibrium is a function of the solubility of the reacting substances, and, according to Dimroth, may be expressed by the equation:

$$\frac{C_a}{C_b} = G \cdot \frac{L_a}{L_b}$$

where C_a and C_b are the concentrations of the two isomers, and L_a and L_b their solubilities, G being a constant which is independent of the nature of the solvent; in other words, the two substances undergoing isomeric change are in equilibrium in any solvent when their concentrations are proportional to their solubilities multiplied

[1] *Annalen*, 1911, 377, 127.

[2] According to P. K Dutt (*Trans Chem Soc*, 1923, 123, 265) the second compound must be represented by



[3] *Vorlesungen uber theoret. u. physik. Chemie*, 1898, 1, 217.

by the constant G, or when the ratio of their solubilities to the ratio of their concentrations reaches the value G, which is called the *absolute equilibrium constant.* The following values were obtained with the methyl and ethyl esters of phenylaminotriazole carboxylic ester:

Solvent.	D C.	$\frac{C_a}{C_b}$	$\frac{L_a}{L_b}$	G
Ether	4 6	20 7	8 4	2 4
Ethyl alcohol	26	4·56	2 1	2 3
Toluene	2 37	1 53	0 74	2 1
Benzene	2 25	1 2	0 6	2 4
Nitrobenzene	34	0·85	0·33	2 6
Chloroform	5	0 32	0 19	1·7

Solvent.	D C	$\frac{C_a}{C_b}$	$\frac{L_a}{L_b}$	G
Ether	4 6	21 7	53 0	0·4
Methyl alcohol	35 4	2 3	7·0	0 33
Toluene	2 37	1·8	4 3	0 33
Benzene	2 25	1 02	3 2	0 32
Nitrobenzene	34	0 8	2·2	0 36
Chloroform	5	0·32	1 1	0·32

D C. = dielectric constant.

It should be added that accurate experimental data in support of this relation between the velocity and solubility of reacting substances are still lacking.

A simple relation between the equilibrium ratio in different solvents of enol to keto form for different tautomeric substances has been established by K. H. Meyer.[1] Although the equilibrium ratio may vary greatly in the same solvent for different tautomeric substances, the ratios for the same series of solvents vary in the same way. An example will make this clear. The following table gives the ratio enol/ketone in different solvents for acetoacetic and benzoylacetic ester:

Solvent.	Acetoacetic ester.	Benzoyl-acetic ester.	D.
Water	0 004	0 008	2 0
Formic acid	0·011	0 028	2 5
Acetic acid	0 061	0 16	2·6
Methyl alcohol	0·074	0·16	2·2
Acetone	0 08	0·18	2·1
Chloroform	0·089	0·18	2·0

[1] *Annalen*, 1911, 380, 229; *Ber.*, 1912, 45, 2843; 1914, 47, 826.

Solvent.	Acetoacetic ester.	Benzoyl-acetic ester.	*E.*
Ethyl alcohol	0·13	0 32	2·5
Ethyl acetate	0·15	0·33	2 2
Benzene	0 22	0·45	2 1
Toluene	0·26	0·62	2·4
Ether	0·43	0 90	2 1
Carbon bisulphide	0·73	1 6	2 2
Hexane	1 0	2 2	2·2
		Mean	2·3

It will thus be seen that the equilibrium ratio for benzoylacetic ester in the different solvents is that of acetoacetic ester multiplied by a constant (E) which is about 2 3; in other words, knowing the constant and the values enol/ketone in one series of solvents it is possible to calculate approximately the ratios in the same solvents. This constant is resolved into two, one for the solute and the other for the solvent, so that the expression becomes

$$\frac{\text{Concentration of enol}}{\text{Concentration of ketone}} = K = E \,.\, L$$

Applying this to Dimroth's formula the expression becomes

$$E \,.\, L = G \,.\, \frac{L_a}{L_b}$$

The following are the mean values for E of a series of tautomeric substances, acetoacetic ester being taken as unity

Acetoacetic ester	1	Benzoyl acetone	120
Benzoylacetic methyl ester	2 3	Dibenzoyl methane	350
,, ethyl ester	2 6	Acetyl-camphor	8
Acetyl-dibenzoyl-methane	80	Benzoyl-camphor	12
Acetyl acetone	33	Acetoacetanilide	1 4

Other observations on the influence of solvents on the velocity of isomeric change have been made by Lowry and his co-workers in the case of nitro- and bromonitro-camphor, and are referred to on p. 367.

Temperature. K. H. Meyer[1] has also studied the effect of temperature on the equilibrium point for a variety of tautomeric substances between 0° and 40° in alcohol, and between 0° and 65° in toluene, and concludes that the ketone form is favoured by rise of temperature, and it is therefore this form which has the greater energy content.

[1] *Ber.*, 1914, 47, 833.

Solubility and Melting-point. Several cases have been referred to in which dynamic isomers have been isolated and their quantity estimated by differences of solubility. The method is, however, limited in its application, since, if crystallization proceeds slowly, isomeric change may occur, and equilibrium is re-established in the solution as soon as the less soluble isomer begins to separate. The second isomer will consequently not crystallize out. Lowry found that this was the case with nitro-camphor, which could only be obtained in one isomeric form. If the separation takes place quickly, or isomeric change is slow, the two isomers will behave like distinct substances and separate according to their solubilities. It is also clear that, if isomeric change occurs during solution, the substance will possess an apparent as well as a real solubility depending on the extent of the conversion. Lowry[1] has applied the principle to diagnosing cases of isomeric change by determining the solubility immediately following solution and after an interval has elapsed. As there is an apparent and a true solubility there will exist an apparent and a true melting-point, depending on isomeric change. These changes can best be followed by means of the freezing-point curves of the mixed isomers, as was done in the case of mixtures of enantiomorphs (p. 215).

In the diagram, Fig. 53, *ad* and *bd* represent the freezing-point curves of a mixture of two dynamic isomers *A*, *B*, and *c* the freezing-point of the equilibrium mixture after fusion. The true melting-points are represented by *a* and *b*. If isomeric change occurs on fusion the melting-point of the higher melting isomer *a* will fall and will become constant when the equilibrium temperature of fusion *c* is reached. Similarly the melting-point of *b* will follow the curve *bdc*, and, according to the rate of isomeric change, will indicate after fusion a lower or higher melting-point which eventually becomes constant at *c*. If the change is slow the two substances will behave like separate individuals, one of the components first separating, followed by the more fusible entectic mixture. The temperature above which isomeric change first sets in has been termed by Knorr[2] the *stability limit* of the substance. If it lies above the melting-point the true melting-point will be given. This is the case with both the keto

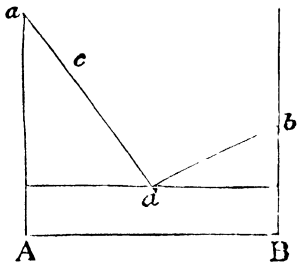


FIG 58

[1] *Trans. Chem. Soc.*, 1904, 85, 1541, 1551. [2] *Annalen*, 1896, 293, 88

forms of dibenzoylsuccinic ester (p. 351), which melt at 128–130° and 75° respectively, and show no ferric chloride reaction until heated to 170° in one case and to 160° in the other, and with that of mesityloxide oxalic ester, which melts at 59–60° and enolises at 130°. The stability limit, though obviously not a fixed point, is usually coincident with the fusion temperature, and in that case the melting-point will not be the correct one.

The same is true if the stability limit falls below the melting-point A very good example is Claisen's acetyldibenzoyl methane (p. 349), the enol form of which melts at 80–85°, and undergoes isomeric change above that temperature. At 110°, the second melting point, isomeric change has set in, and a mixture of keto and enol forms are present, after which it melts a second time.[1]

Density and Volume. Schaum[2] observed that freshly distilled acetoacetic ester acquires a different density after standing, and recognized the fact as evidence of isomeric change. The constants for molecular volumes (p. 14) are as yet too indeterminate to be usefully applied, but Traube has made a number of experiments on molecular solution volumes of tautomeric substances.[3] From the density of acetoacetic ester and its solutions in various solvents he showed that in the majority of the latter the molecular volume undergoes a gradual change which can only be explained on the assumption of the existence of two esters in equilibrium (p. 17).

Refraction and Dispersion. Brühl[4] has shown that molecular refraction and dispersion offer an excellent means of differentiating the enol and keto forms, and has determined the structure of a variety of compounds in this way (p. 37). To quote one or two examples, free acetoacetic ester was found to represent the keto form, whilst

[1] The behaviour of dynamic isomers on fusion is discussed from the phase rule standpoint by Findlay. *Trans. Chem. Soc.*, 1904, 85, 403.

[2] *Ber.*, 1898, 31, 1964.

[3] *Ber*, 1896, 29, 1715.

[4] *Ber*, 1892, 25, 366, *J. prakt. Chem.*, 1894, 50, 159; *Zeit. phys. Chem.*, 1900, 34, 31.

its sodium compound was enolic.[1] In other respects Claisen's rule that negative groups favour the enol formation is fully confirmed. Oxalacetic ester and acetylmalonic ester are enolic compounds, whilst acetone and pyruvic acid appear to be purely ketonic (see p. 38). Formylacetic ester and hydroxymethylene-camphor were shown to belong to the enolic type.

$HC(OH) : CH . COOC_2H_5$ — Formylacetic ester.

C_8H_{14} (C : CH(OH), CO) — Hydroxymethylene-camphor.

Magnetic Rotation. The results derived by W. H. Perkin[2] from observations of the magnetic rotation of acetoacetic ester and other ketones agree substantially with those of Brühl. Acetoacetic ester is a ketone, acetylacetone is probably a mixture of 80 per cent. mono- and 20 per cent. di-enol, whilst methylacetylacetone is about half ketonic and half enolic, from which it follows that the positive ethyl radical favours the ketonic structure and thus in a sense supports Claisen's rule (p. 351). The further interesting observation was made that those ketonic compounds which exhibit enolic structure are rendered more ketonic with rise of temperature—in other words, that the condition of equilibrium between the isomers changes with the temperature (see p. 362).

Electrical Conductivity. An interesting application of the ionization hypothesis to the study of tautomeric change has been elaborated by Hantzsch.[3]

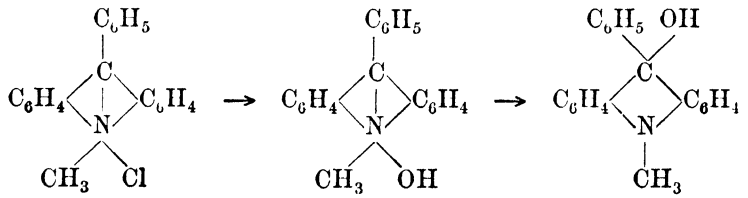
In 1896 Hantzsch and Schultze[4] obtained the two dynamic isomers of phenylnitromethane $C_6H_5CH_2NO_2$ (see p. 341). The product obtained by the action of silver nitrite on benzyl iodide is an oil which dissolves in soda solution and forms a sodium salt, from which hydrochloric acid precipitates in the cold a crystalline substance which melts at 84°. The latter, in contact with acids, passes gradually into the oily isomer, and the same thing occurs on warming the substance in ethereal or alcoholic solution. The two may be distinguished by the intense brown coloration which alcoholic ferric chloride gives with the crystalline modification.

The conversion of the one isomer into the other is explained by a tautomeric change of the following nature:

$$\underset{\text{Phenylnitromethane liquid.}}{C_6H_5CH_2 . NO_2} \rightleftarrows \underset{\text{Isophenylnitromethane. } m\ p.\ 84°}{C_6H_5CH : NO . OH}$$

[1] Brühl and Schroder, *Zeit. phys. Chem.*, 1904, 50, 1; 1905, 51, 1.
[2] *Trans. Chem. Soc.*, 1892, 61, 800.
[3] *Ber.*, 1899, 32, 575, 3066.
[4] *Ber.*, 1896, 29 699, 2251.

Whereas the liquid compound is a neutral substance and a non-electrolyte, the isomer is a strong acid and an electrolyte.[1] The presence of the second compound and its gradual change into the first may therefore be recognized by its decreasing conductivity in solution, whilst the passage of the first into the second may be followed by the reverse process or by observing the gradual neutralization of the solution on the addition of an alkali. These and other manifestations of tautomerism, such as the colour change of the liquid on the addition of an alkali, may be observed in compounds like the aliphatic and aromatic nitro-compounds, nitroparaffins, nitrophenols, and nitrolic acids, lactams, primary nitrosamines, oximinoketones, e.g. violuric acid, quinoneoximes, &c., which are unknown in desmotropic forms, owing, as a rule, to the instability of the free enol type. Such compounds have been named by Hantzsch *pseudo-acids*, by which term is implied the free compounds, which, not being acids themselves, exhibit by a change of structure the characteristic behaviour of acids, and the manifestation is termed *ionic isomerism*. Hantzsch also recognizes a group of basic substances corresponding to pseudo-acids which he terms *pseudo-ammonium bases*.[2] These substances are not in themselves bases, but exhibit ionic isomerism, inasmuch as they pass into true ammonium salts on the addition of an acid and thereby become strong electrolytes. Like the pseudo-acids they also show colour changes and 'abnormal neutrality'. These changes were first studied in the case of phenylmethylacridinium chloride. The addition to an aqueous solution of the salt of an alkali or silver oxide sufficient to unite with the acid liberates a strong base, which shows a degree of dissociation comparable with that of potassium hydroxide. Its conductivity then gradually diminishes until it reaches zero, and at the same time the solution becomes neutral and the pseudo-base is precipitated. The change is represented by the wandering of the hydroxyl ion to the carbon atom thus:

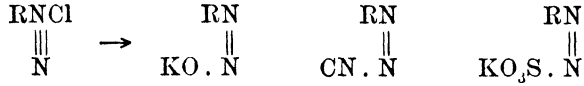


Phenylmethylacridinium chloride. True ammonium base. Pseudo-ammonium base or carbinol.

[1] Holleman, *Rec. trav. chim. Pays Bas*, 1895, 14, 129.
[2] *Ber.*, 1899, 32, 594, 3109, 3132; 1900, 33, 278.

The reverse changes occur on acidifying the pseudo-ammonium base, which passes into the true ammonium salt.

The theory has been used to interpret the changes which diazonium salts undergo when acted upon by solutions of alkalis, alkali cyanides, and sulphites (p. 310). Under these circumstances the diazonium salt is converted into the *syn* diazotate, diazocyanide, and diazosulphonate.



The theory has also been applied to explain the relation of dye-stuffs to their colour bases (see p. 105).

Electrical Oscillations. By the use of a specially contrived apparatus, Drude[1] examined the absorptive power of organic compounds for electrical oscillations, and found that whilst hydroxyl compounds absorb the oscillations readily, aldehydic and ketonic compounds do not. The method has been applied to the investigation of dynamic isomers, and the results are stated to be in substantial agreement with those of Brühl and Perkin.

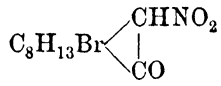
Acetoacetic ester does not absorb and is ketonic, oxalacetic ester absorbs strongly and is therefore mainly enolic. The change in absorption which accompanies the passage of the liquid to the solid form of formylphenylacetic ester agrees with the observations of Wislicenus. Many other compounds have been studied with similar results. K. H. Meyer, on the other hand, finds that the results do not conform with those obtained by the bromine method (p. 356), and consequently regards the method as untrustworthy.[2]

Optical Activity. The large differences in optical activity of many dynamic isomers have been turned to excellent account as a means of distinguishing the two forms, and of following the equilibrium changes which occur under different conditions. The method has been utilized by Lowry[3] in the study of nitrocamphor and π-bromonitrocamphor, and by Lowry and E. F. Armstrong[4] in that of the different glucoses and glucosides.

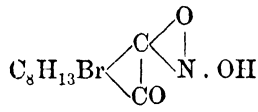
The dynamic isomers of π-bromonitrocamphor and pseudo π-bromo-

[1] *Ber.*, 1897, **30**, 940. [2] *Ber*, 1912, **45**, 2844.
[3] *Trans. Chem. Soc.*, 1899, **75** 235. See also Rupe and Lenzinger, *Annalen*, 1913, **398**, 372.
[4] *Trans. Chem. Soc*, 1903, **83**, 1314.

nitrocamphor are probably represented by the following formulae (see p. 88):



Normal.

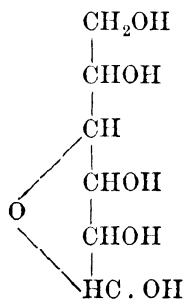


Pseudo.

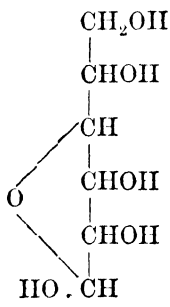
Both compounds have been isolated by crystallization from different solvents · the one, which from its high rotation is regarded as the pseudo form, melts at 142° and has a specific rotation of $[\alpha]_D = +188°$, and the other melts at 108° and has the value $[\alpha]_D = -51°$. When either substance is dissolved in various media an equilibrium mixture of the two isomers results. A 3 33 per cent. benzene solution at 15° reaches a constant rotation of $[\alpha]_D = -38°$, and consists then of an equilibrium mixture of one part of pseudo and seventeen parts of the normal compound. This change of rotation has been named by Lowry *mutarotation*. Nitrocamphor, though only known in one crystalline modification, *m. p.* 100°, nevertheless when dissolved in various solvents shows the same kind of change as the bromo-derivative, thereby indicating the existence of an equilibrium mixture of the two forms. Simon[1] suggested, and Lowry and E. F. Armstrong[2] have since shown, that the α, β, and γ modifications of glucose, which have the specific rotations

$$[\alpha]_D = +110°, \quad +52\,5°, \text{ and } +20°$$

respectively, consist in all probability of two stereoisomeric α- and γ-glucoses having the rotations $[\alpha]_D = +110°$ and $+20°$, which exhibit mutarotation by forming an equilibrium mixture having the intermediate value (Part III, p. 45).



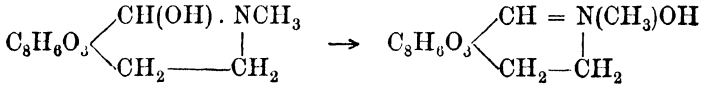
α glucose.



β-glucose.

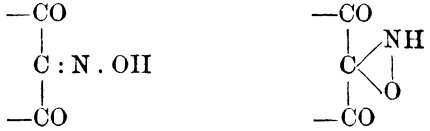
[1] *Compt. rend*, 1901, 132, 487. [2] *Trans. Chem. Soc.*, 1903, 83, 1305, 1314.

Absorption Spectra. The absorption spectra in the visible and ultra-violet region have been studied by Hartley, by Dobbie and Lauder, and by Baly and Desch, with results which possess considerable interest. Dobbie, Lauder, and Tinkler[1] were able to observe changes in the spectra of solutions of cotarnine and its derivatives which could only be explained by isomeric change.

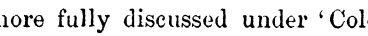


On the assumption that similarity in the absorption spectra denotes similarity of structure, Hartley and his co-workers were able to determine the structure of many tautomeric compounds by comparing their spectra with those of their tautomeric derivatives (see p. 79).

Colour. Examples of the differentiation of dynamic isomers by means of colour have already been given. There are many pseudo-acids possessing one colour which, on the addition of a base, are supposed to change into a salt of the normal acid having another colour. Colourless violuric acid, which is the pseudo form, gives pink or violet salts.[2] Colourless nitrolic acids form red salts. The green solution obtained by adding nitrous acid to phenol probably represents the nitroso compound, whilst the red sodium salt may have the oxime formula. Other examples are the colourless and yellow modifications of acetone dioxalic ester,[3] and the colourless and yellow mesoxamide oxime and its coloured salts,[4] which are represented as containing the following isomeric groups:



There are also the colourless and yellow silver compounds of the amides, and the colourless nitrophenols and their orange or red salts.



The subject is more fully discussed under 'Colour and Structure' (p. 95).

Theories of Tautomerism. Laar, who was the first to offer a theory of tautomerism, supposed that the mobile hydrogen atom

[1] *Trans Chem Soc*, 1903, 83, 598. [2] Hantzsch, *Ber.*, 1899, 32, 593.
[3] Willstätter and Pummerer, *Ber.*, 1904, 37, 3733.
[4] Whiteley, *Trans. Chem. Soc.*, 1900, 77, 1040; 1903, 83, 24.

in tautomeric compounds was in a state of constant oscillation, so that both compounds might be regarded as present in the substance in a labile state. This applied to solids as well as to liquids and solutions. The view received support from the observations of von Pechmann and others (p. 344). It has already been stated that phenyltolylbenzamidine forms with ethyl iodide two ethyl derivatives. The result is readily explained on the assumption that the substitution of hydrogen by ethyl occurred at opposite periods of an oscillation. A similar idea is embodied in Knorr's[1] theory of the *oscillating double-bond*, in which the rapid shifting to and fro of the double-bond and of the hydrogen atom associated with it, is made accountable for the identity of such substances as the two methyl pyrazoles referred to on p. 346.

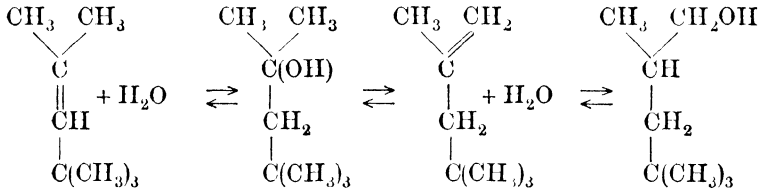
Allelotropism. Knorr[2] was the first to discuss the subject of tautomerism on a broad, philosophical basis In a paper on the tautomerism of the dibenzoyl- and diacetyl-succinic esters subsequent to that already referred to (p. 351), he lays down the principle that each substance has its own structure, that when heated above its stability limit it yields an equilibrium or *allelotropic* mixture, and that similar mixtures are formed in solution; the proportion of the isomer depending on the nature of the solvent, the temperature, and the dilution. Finally, he revives Butlerow's view of the nature of the change occurring between the two isodibutylenes to explain isomeric change in general, which he attributes to an intermolecular, and not, as Laar had done, to an intramolecular process. At the same time he recognizes that Laar's oscillation theory may explain very rapid isomeric changes, such as presumably exist in the case of hydrogen cyanide, benzene, the methyl pyrazoles, &c.

Thus Laar's tautomerism or oscillating structures, and Baeyer's pseudomerism or single, stable structures, are limiting cases of allelotropism or equilibrium mixtures of isomers.

[1] *Annalen*, 1894, 279, 188.
[2] *Annalen*, 1899, 306, 332.

Dynamic Isomerism. The theory which has been recently developed by T. M. Lowry [1] has been moulded on a still broader basis. In place of the word tautomerism and the various other names applied by different observers to indicate different views of the same phenomenon, he has introduced the single expression *dynamic isomerism*, which he defines as *reversible isomeric change*.

The principle of balanced actions between isomers had already been recognized by Butlerow [2] from the results of his inquiry into the action of sulphuric acid on trimethyl carbinol. Butlerow showed that the product consisted of two isomeric isodibutylenes, and he explained their formation on the assumption that equilibrium is established between the isodibutylenes and the corresponding alcohols by means of water.



Butlerow suggested that equilibrium might also exist in the absence of any reagent, and that hydrogen cyanide and cyanate might be equilibrium mixtures of cyanide and nitrile in the one case, and carbimide and cyanogen hydroxide in the other.

Dynamic isomerism includes every form of balanced action between isomers, and therefore embraces not only examples of labile isomeric change, like that of the two formylphenylacetic esters (which are readily interconvertible at ordinary temperatures), but others which are perfectly stable, and only undergo isomeric change on fusion, like ammonium thiocyanate and thiourea.[3]

$$NH_4CNS \rightleftarrows CS(NH_2)_2$$

These reactions therefore belong to the type of unimolecular reversible or balanced actions, and may be treated mathematically. According to the theory of reversible reactions a condition of equilibrium is attained when the quantities of the two substances are in a definite ratio, which is determined by the ratio of the velocity constants of the opposing reactions. If k_2 and k_1 are the velocity constants of the two isomeric changes taking place in

[1] *Trans. Chem. Soc.*, 1899, **75**, 211, *Brit. Assoc Reports*, 1904, p. 193.
[2] *Annalen*, 1877, **189**, 76.
[3] Waddell, *Journ phys. Chem.*, 1898, **2**, 523, Reynolds and Werner, *Trans. Chem. Soc.*, 1903, **83**, 1.

opposite directions, and x_0, x_t, and x_∞ the quantities of the original substance at times 0, t, and ∞, the reaction will proceed according to the equation,

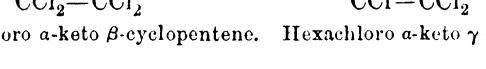
$$\frac{dx}{dt} = k_1(x_0 - x_t) - k_2 x_t,$$

which when integrated becomes,

$$k_1 + k_2 = \frac{1}{t} \log \frac{x_0 - x_\infty}{x_t - x_\infty}.$$

If the quantity of one of the substances is known at time t, the value of $k_1 + k_2$, that is, the sum of the velocity constants of the opposing reactions, can be determined and should give a constant. The velocity constant is only subject to variation with change of concentration in case one of the substances acts as a catalyst or undergoes some secondary change. The above equation has been used by Küster,[1] by Lowry,[2] and others, and the experimental results are in close agreement with the unimolecular law.

Küster applied the equation to the dynamic isomerism of two hexachloroketocyclopentenes.



Hexachloro α-keto β-cyclopentene. Hexachloro α-keto γ cyclopentene.

The process was conducted by suspending a small quantity of the substance in the vapour of boiling nitrobenzene for a certain length of time and then rapidly cooling. The substances were then converted into the anilides and separated by solvents. When equilibrium was established the mixture consisted of 61·4 per cent. of β- and 38·6 per cent. of γ-compound. Lowry studied the rate of change of solutions of nitro- and π-bromonitro-camphor by means of the polarimeter.

Every form of isomeric change may be studied from this standpoint, including such processes as optical and geometrical inversion (pp. 200, 265). The racemisation of tartaric acid and the transformation of the two tolane dibromides belong to the same order of phenomenon and are subject to the same law.

The existence of only one representative of two possible isomers such as isatin may be regarded as merely a limiting case in which the isomeric form is too labile to exist under the experimental conditions. The same may be said of those reactions which are

[1] *Zeit. phys Chem.*, 1895, **18**, 171. *Trans. Chem. Soc.*, 1899, **75**, 224.

apparently non-reversible, for the balance may then be assumed to shift so much to one side that little or none of the original substance can be detected. These one-sided or completed reversible reactions will be considered separately.

The Mechanism of Isomeric Change. It will be interesting to attempt to form some idea of the process by which isomeric change is brought about. Laar regarded the change as intramolecular, that is, as a change produced by a direct transference of the atoms in the molecule. Butlerow was of opinion that the process might either be spontaneous or depend on the presence of a catalyst. Lowry, on the other hand, considers that the aid of a third substance which plays the rôle of a catalyst is essential, just as the union of certain gases requires the presence of a trace of water.

In support of this view he points to the fact that nitrocamphor[1] and the enolic form of α-benzoyl camphor[2] in chloroform solution will remain unchanged for a long period, but that the dust of the laboratory or the soft glass of the polarimeter tube is sufficient to start the transformation

As we have seen, Knorr, Brühl, and others have suggested that certain solvents have an ionizing action on the dissolved substance, and the enolic form, being a weak acid and electrolyte, breaks up into a hydrogen ion and an organic ion, and the latter has a tendency to recombine with the hydrogen ion to form the non-ionized ketonic compound.

The objection to this view is that it implies a complete conversion of the enolic to the ketonic type, which is not always the case. Lapworth[3] has suggested that the change takes place in the negative organic ion through an alteration in the position of the free bond or affinity. In the case of bases the acceleration is due to the diminution of hydrogen ions by increasing the concentration of hydroxyl ions and at the same time increasing that of the organic ions.

The interconversion of the ketonic and enolic form of acetoacetic ester will be represented as follows :

$$CH_3 . CO . \dot{C}H . COOC_2H_5 + H \rightleftarrows CH_3 . C\dot{O} : CH . COOC_2H_5 + H$$

so that in a sodium ethoxide solution both ketonic and enolic forms will be present in equilibrium, a condition which is virtually equivalent to the presence of the two sodium compounds :

$$CH_3 . CO . CHNa . COOC_2H_5 \rightleftarrows CH_3 . C(ONa) : CH . COOC_2H_5$$

[1] Lowry, *Trans. Chem. Soc.*, 1899, 75, 219, Lowry and Magson, *Trans. Chem. Soc.*, 1908, 93, 128.

[2] Forster, *Trans. Chem. Soc.*, 1901, 79, 997. [3] *Trans. Chem. Soc.*, 1902, 81, 1503.

It should be noted that the structure of the sodium compound which separates from solution will depend on the relative solubilities of two isomeric forms, and, if equilibrium is rapidly established, will be independent of the composition of the equilibrium mixture in solution.

It frequently happens that acids have an opposite effect to bases and retard or suspend isomeric change, in other cases they act as catalysts and accelerate it.[1] When the latter occurs another explanation than that of the diminution of hydrogen ions must be found, and Lapworth has suggested that they may cause the change by forming a complex ion with the organic compound, which functions as a weak base like ammonia, and then undergoes internal rearrangement as follows, the dot indicating the temporary disposition of the free affinity:

$$HO-\dot{C}=\dot{C}+H \rightleftarrows HO-\dot{C}\cdot\dot{C}H$$

$$HO-\dot{C}\cdot\dot{C}H \leftrightarrows HO\cdot\dot{C}-\dot{C}H$$

$$HO\cdot\dot{C}-\dot{C}H \leftrightarrows O\cdot\dot{C}-\dot{C}H+H$$

Lowry[2] regards the ionisation theory as untenable, for reasons to be presently described, and has adopted the idea of Butlerow's catalyst, whereby the change is effected by the alternate addition and removal of the catalyst.

$$\begin{array}{l} -CH_2 \\ | \\ -CO \end{array} + KOH \rightleftarrows \begin{array}{l} -CH_2 \\ | \\ -C(OK)(OH) \end{array} \rightleftarrows \begin{array}{l} -CH \\ \| \\ -C\ OH \end{array} + KOH$$

He has shown that it is possible to accelerate or arrest the isomeric change of nitrocamphor described on p. 367 by the use of certain substances. Now it is just those substances which are capable of breaking up into an atom of hydrogen and a radical which accelerate the change. They include both acids and bases. Such are, for example, water H . OH, alcohol H . OC_2H_5, acetic acid H . OOC . CH_3, hydrogen chloride H . Cl, ammonia H . NH_2, piperidine H . NC_5H_{10}, potassium hydroxide H . OK, whereas benzene, ether, and chloroform, which do not break up in this way, have a very slow action The method employed was to determine the velocity constant for some solvent, such as benzene, ether, or alcohol, and then to add varying quantities of the catalyst. The following table gives some of the observations. The first column represents the nature of the solvent,

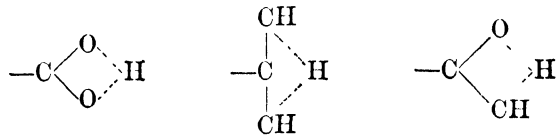
[1] Lapworth, *Trans. Chem Soc.*, 1902, 81, 1503; 1903, 83, 1123, 1904, 85, 30.
[2] Lowry and Magson, *Trans. Chem. Soc*, 1908, 93, 128.

the second the velocity constant (K) in minutes, the third the period occupied by the change, and the fourth the percentage change accomplished in each minute:

Solvent.	K	Period.	Percentage.
Alcohol (purified)	0 0048	8 hours	1·31
+ 1 per cent. H_2O	0 0096	4 ,,	2·61
+ N/10^5 $NaOC_2H_5$	0 0056	7 ,,	1 52
+ N/10^4 ,,	0·0101	$3\frac{1}{2}$,,	2 75
Ether	0 00149	26 ,,	0·405
+ 1 per cent. H_2O	0 0154	$2\frac{1}{2}$,,	4·18
Benzene	0·00013	12 days	0 035
+ N/10^4 NC_5H_{11}	0 23	10 mins.	62 6
+ N/10 CH_3 COOH	0 057	40 ,,	15 5
+ N/10^2 CCl_3 . COOH	0 0113	$3\frac{1}{4}$ hours	3·074

An interesting point in regard to these observations is that certain acid chlorides, such as carbonyl chloride and acetyl chloride, arrest the change in certain solvents, and this is attributed by Lowry to the neutralization of traces of basic impurities. Now ether belongs to the class of ionising solvents, since hydrogen chloride conducts in this liquid If, therefore, an ionising solvent caused isomeric change, it should be impossible to arrest the change by means of carbonyl chloride.

Lowry[1] has advanced a theory of dynamic isomerism based on the electronic theory of Lewis-Langmuir on the principle that the hydrogen atom passes easily from a condition of co-valency to that of electrovalency, or in other words may share its electron with other atoms or lose it and become an ion. In the latter state it is mobile. In this way the hydrogen ion in acids, in glutaconic acid, and in acetoacetic ester may be represented in a similar way based upon Hantzsch's conception of 'true acid' and 'pseudo acid' (see p. 366).



The isomerisation produced by the presence of a base, or sometimes of water or other solvent, has the function of an acceptor of the hydrogen ion and so effects its migration.

[1] *J. Soc. Chem. Ind.*, 1923, **42**, 43.

COMPLETED ISOMERIC CHANGE

Although it is generally recognized that the isomeric changes which appear to take place in only one direction may be merely limiting cases of reversible reactions in which the original substance virtually disappears, it is convenient, until these reactions have been more fully studied, to place them in a separate group by themselves.

An isomeric change which is completed in one direction is a unimolecular reaction, and, provided there are no disturbing by-reactions, represents the simplest type of chemical change. It follows a logarithmic law, and may be studied as a problem in chemical dynamics. According to the mass law the rate of change will be proportional to the concentration at any given time, or conversely, if the change follows the mass law and the quantity of substance present at any time is ascertained, the velocity constant k can be calculated from the well-known equation,

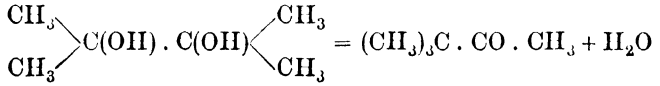
$$k = \frac{1}{t} \log \frac{a}{a - x},$$

in which t is the time, a the amount of substance at the beginning of the observation, and x the amount transformed after an interval of time t.

The velocity constant can of course only be determined where the change takes place sufficiently slowly for the composition of the mixture undergoing transformation to be ascertained, and where either the process can be suddenly arrested or the products quickly analysed. It is clear that these conditions render the study of many isomeric changes difficult or impossible, and the result has been that only a very few have been examined dynamically. In such cases as the transformation of acetochloranilide into *p*-chloracetanilide [1] (p 392), that of diazoaminobenzene into aminoazobenzene [2] (p. 397), of acetophenoneoxime into acetanilide [3] (p. 387), it has been found that the reaction follows the mass law. These reactions are fully considered in Part I, p. 322.

Generally speaking, these completed isomeric changes result not in the transference of a single mobile hydrogen atom, but in the interchange of groups, reactions which are usually, though not invariably, induced by the presence of strong acids. It would appear, therefore, that on the ionic theory the change is produced by the catalytic action of hydrogen ions. This view has been advanced by Goldschmidt and Reinders in the case of diazoaminobenzene, by observing that the velocity of isomeric change from diazoaminobenzene to aminoazobenzene increases with the proportion of catalyst (an aniline salt) and with the dissociation constant of the acid of the salt.[4] A similar view has been expressed by Beckmann in reference to the reaction which bears his name.[5]

Migration of Hydrocarbon Radicals (from Carbon to Carbon). The pinacone-pinacoline conversion is an example of the transposition of a radical from carbon to carbon; strictly speaking, it is not an isomeric change, for the process is accompanied by the loss of water; but the reaction may be conveniently discussed here. Fittig [6] found that when tetramethyl pinacone is distilled with dilute sulphuric acid it is converted into pinacoline, or tertiary butyl methyl ketone.



Pinacone. Pinacoline.

On reduction with hydriodic acid, pinacoline loses oxygen and yields

[1] J J. Blanksma, *Rec trav Pays-Bas*, 1902, 21, 366; 1903, 22, 290.
[2] Goldschmidt and Reinders, *Ber*, 1896, 29, 1369, 1899.
[3] Lobry de Bruyn and Sluiter, *Koninklijke Akad. van Wetenschappen*, 1904, 778.
[4] *Ber*, 1896, 29, 1905.
[5] *Ber.*, 1894, 27, 300; see also Michael, *J. Amer. Chem. Soc.*, 1920, 42, 787.
[6] *Annalen*, 1860, 114, 56.

tetramethylethylene, in which a methyl group wanders back to the original carbon. It would appear from this and from other observations that the reaction is, under certain conditions, reversible.[1]

$$(CH_3)_3C.CO.CH_3 \longrightarrow (CH_3)_3C.CH(OH).CH_3$$
$$\longrightarrow (CH_3)_2C:C(CH_3)_2$$

Precisely similar results have been obtained with benzpinacone.

Another curious change is that produced by oxidation which transforms tetraphenylethylene into benzoyltriphenylmethane.[2]

$$(C_6H_5)_2C:C(C_6H_5)_2 + O = (C_6H_5)_3C.CO.C_6H_5$$

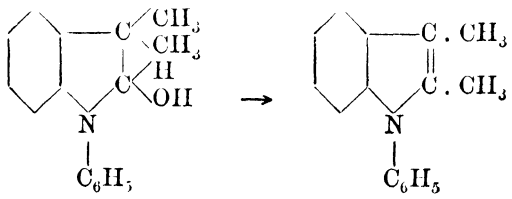
To the same class of reactions belong the conversion of hydrobenzoin into diphenylacetaldehyde and *as.* phenyl alkyl glycols into the corresponding aldehydes[3] under the action of sulphuric acid and of benzil into benzilic acid by fused potassium hydroxide.

$$C_6H_5CH(OH).CH(OH)C_6H_5 = (C_6H_5)_2.CH.CHO + H_2O$$
Hydrobenzoin. Diphenylacetaldehyde.

$$\begin{matrix} C_6H_5 \\ CH_3 \end{matrix}\!\!>\!C(OH).CH_2OH = \begin{matrix} C_6H_5 \\ CH_3 \end{matrix}\!\!>\!CH.CHO + H_2O$$
as. Phenyl methyl ethylene glycol. Phenyl methyl acetaldehyde.

$$C_6H_5.CO.CO.C_6H_5 + H_2O = (C_6H_5)_2.C(OH).COOH$$
Benzil. Benzilic acid.

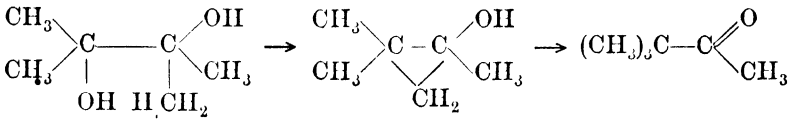
The same kind of change has been shown by Brumer,[4] Wolff,[5] and Knorr[6] to occur in ring compounds. To take one example, Brumer found that phenyldimethyl indolinol is converted by hydrogen chloride into a dimethyl indole with the loss of a molecule of water.



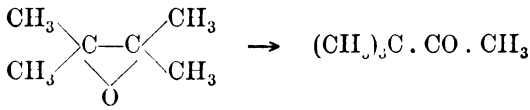
Although many chemists have attacked this problem, the mechanism of the change is still somewhat obscure.[7] Erlenmeyer, sen.,[8] sug-

[1] Levy, *Compt rend*, 1921, 172, 383
[2] Delacre, *Compt rend*, 1896, 122, 1202, 1896, 123, 215.
[3] Stoermer, *Ber*, 1906, 39, 2288.
[4] *Monatsh.*, 1896, 17, 276, 1900, 21, 156
[5] *Annalen*, 1902. 322, 351.
[6] *Ber*, 1903, 36, 1272.
[7] See Werner and Grob, *Ber*, 1904, 37, 2887.
[8] *Ber.*, 1881, 14, 322.

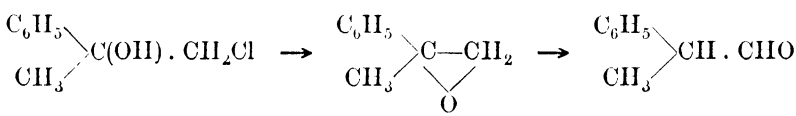
gested that the action took place by the elimination of the elements of water, thus :



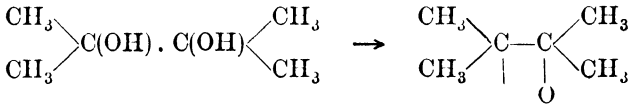
but apart from the improbability of alkyl and aryl radicals losing hydrogen in this way, the theory has been rendered untenable by the experimental work of Montagne[1] and Lindner.[2] A more plausible explanation, which is supported by a certain amount of evidence, is that, if an intermediate compound is produced, it will take the form of an anhydride.



Such anhydrides have been obtained by the action of sodium ethoxide on the chlor- and iod-hydrins of the glycols,



by the action of alcoholic potash on the glycol ethers, and in other ways, and are readily converted into aldehydes and ketones on heating with sulphuric acid.[3] As in the above example, it does not necessarily follow that migration of a radical always accompanies the change. Tiffeneau,[4] in the course of an elaborate inquiry, has determined the conditions under which migration occurs when halogen acid is removed from an iodhydrin or water from a glycol. He concludes that the process is determined by loss of water without the formation of an intermediate product.



which, being unsaturated, causes rearrangement of radicals.

[1] *Rec. trav. chim. Pays-Bas*, 1905, **24**, 105

[2] *Monatsh*, 1911, **32**, 403.

[3] Tiffeneau, *Compt. rend*, 1905, **140**, 1458, 1595 ; Klages, *Ber.*, 1905, **38**, 1969 ; 1906, **39**, 1753 ; Paal and Weidenkaff, *Ber*, 1906, **39**, 2062.

[4] *Ann. Chim. Phys*, 1907, **10**, 322, *Abstr. Chem. Soc*, 1908, **1**. 305.

The results of a very large number of observations appear to show that in the case of different radicals the nature of the radicals as well as that of the reagent determines the end product.[1] In the case of phenyl dimethyl glycol

$$C_6H_5CH\,.\,OH\,.\,C(OH)(CH_3)_2$$

with concentrated sulphuric acid, oxalic acid, or phosphorus pentoxide the methyl group migrates, giving phenyl dimethyl acetaldehyde

$$C_6H_5(CH_3)_2C\,.\,CHO$$

whereas with dilute sulphuric acid a certain amount of the polymerised product is also formed.

$$\begin{array}{l} C_6H_5\,.\,CH\text{—}C(CH_3)_2 \\ \quad\quad\quad\quad\quad\quad | \quad\quad | \\ \quad\quad\quad\quad\quad\quad O \quad\quad O \\ \quad\quad\quad\quad\quad\quad | \quad\quad | \\ (CH_3)_2C\text{—}\text{—}CH\,.\,C_6H_5 \end{array}$$

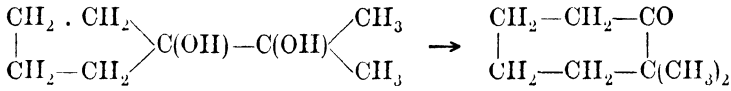
With phenyl ethyl phenyl glycol

$$C_2H_5\,.\,C_6H_5C(OH)\,.\,CH(OH)\,.\,C_6H_5$$

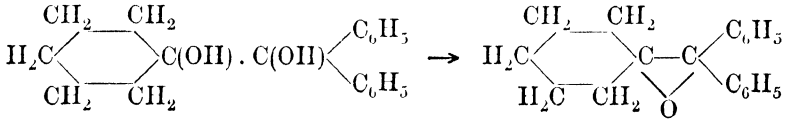
very dilute sulphuric acid causes the migration of the phenyl group attached to the tertiary carbinol, whereas 20 per cent. sulphuric acid brings about that of the second phenyl group, giving diphenyl ethyl acetaldehyde.

$$C_2H_5(C_6H_5)_2C\,.\,CHO$$

This view is also adopted by Meerwein,[2] who examined the following type of reaction in which the ring structure is altered:



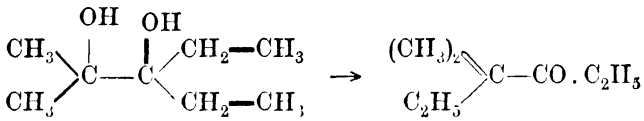
In the case of the diphenylcyclohexyl glycol, the ethylene oxide which is formed appears to be very stable.



Meerwein[3] has made the curious observation that in the case of dimethyl diethyl pinacone and diethyl dipropyl pinacone it is the ethyl group which is detached, or generally speaking the radicals with an even number of carbon atoms migrate. He explains it on Flürscheim's theory of the uneven distribution of valency, on the

[1] Tiffeneau and Orechow, *Compt. rend.*, 1920, 171, 400, 473; 1921, 172, 387.
[2] *Annalen*, 1910, 376, 152; 1913, 396, 200; 1914, 405, 122; 1918, 417, 255; 1919, 419, 123.
[3] *Annalen*, 1919, 419, 123.

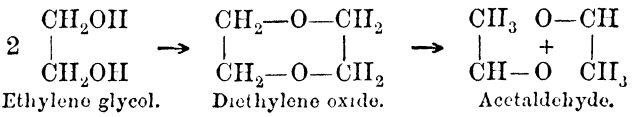
assumption that the bond is stronger between carbon and carbon than between carbon and hydrogen, so that the radicals with an odd number of carbon atoms are more firmly attached to the tertiary carbinol group than those with an even number.



The reaction does not proceed, however, wholly in the one direction, a certain quantity of the isomeric pinacoline being formed.[1]

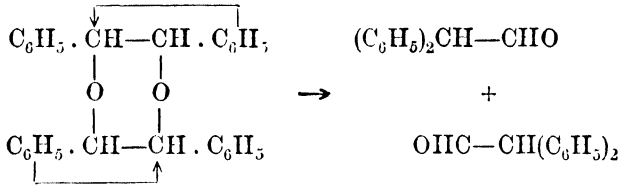
Like Tiffeneau, he regards the change as a simple intramolecular rearrangement in which migration is determined in the first place by instability caused by the unsaturated carbon and oxygen atoms and then by the nature of the radicals and the relative stability of the hydroxyl groups, so that in one case the pinacoline and in another the ethylene oxide may be formed.

Another view, which is favoured by Faworski[2] from observations on the action of sulphuric acid on ethylene glycol, is that, as the principal product is diethylene oxide, which readily breaks up into acetaldehyde, the initial stage may be one of polymerisation with loss of water, yielding a diethylene oxide.



Polymeric oxides of this type are often produced along with the simple oxides, and break up, like the latter, into aldehydes and ketones.

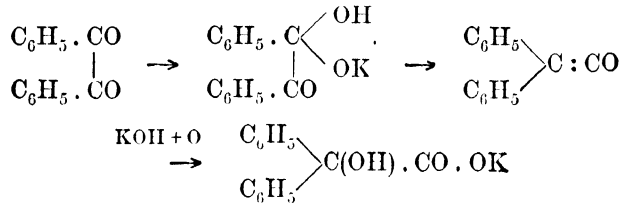
Hydrobenzoin, for example, isomerises in the following way:



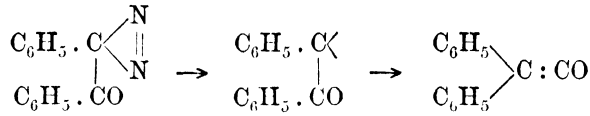
Schroeter[3] has attempted to explain the formation of benzilic acid from benzil on the principle advanced by Stieglitz and adopted by Tiffeneau, namely, that the unsaturation of an atom is a source of

[1] Nybergh, *Ber.*, 1922, 55, 1960.
[2] 1907, *Journ. Russ. Phys. Chem. Soc.*, 1906, 38, 741.
[3] *Ber.*, 1909, 42, 2335

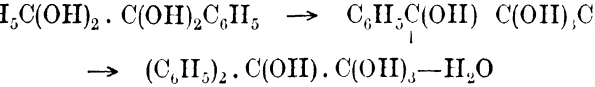
instability and consequently of atomic rearrangement, and that in the case of benzil the removal of an atom of oxygen produces diphenyl ketene, which then reunites with the oxygen and potassium hydroxide to form the salt of benzilic acid.[1]



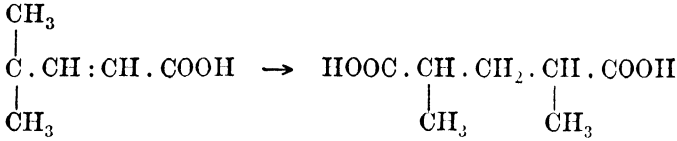
In order to test this view, he prepared azobenzil and found, as he anticipated, that on heating in benzene solution it loses nitrogen and gives diphenylketene, whilst in methyl alcohol solution benzilic ester is formed.



Lachman[2] explains the change by the addition of two molecules of water and a readjustment of the hydroxyl groups.



The wandering of a methyl group from one carbon atom to another is occasionally met with among other groups of compounds. Blaise[3] found that $\alpha\alpha$-dimethylglutaconic acid on reduction with hydrogen iodide gives $\alpha\alpha_1$-dimethylglutaric acid.



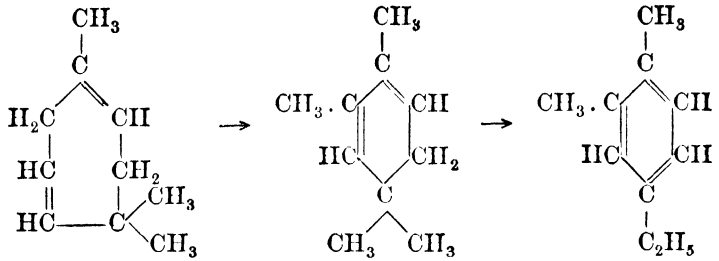
Among aromatic compounds a similar process has also been observed by Gillet. Baeyer[4] has shown that by exhaustive bromination of euterpene, isogeraniolene, and similar compounds, the methyl group changes its position in the ring. Euterpene gives ethyl *o*-xylene probably in the following steps:

[1] This view seems to be disproved by the fact that hydrogen peroxide either free or in presence of alkalis has no action on diphenyl ketene (Nicolet and Pelc, *J. Amer. Chem. Soc.*, 1921, 43, 935).

[2] *J. Amer. Chem. Soc.*, 1922, 44, 330.

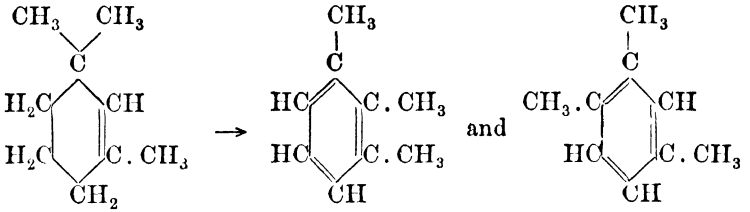
[3] *Compt. rend.*, 1903, 136, 381.

[4] *Ber.*, 1898, 31, 2067; 1899, 32, 2430.



Euterpene. Intermediate compound. Ethyl *o*-xylene.

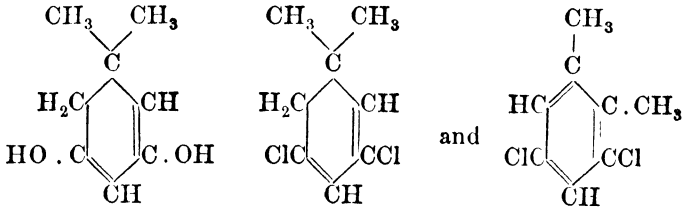
whilst isogeraniolene gives bromine derivatives of two trimethyl benzenes.



Isogeraniolene. *v*-Trimethylbenzene. Pseudocumene

Also Crossley and Le Sueur[1] have found that dimethyl dihydroresorcinol yields with phosphorus pentachloride a small quantity of an *o*-xylene derivative.

Similar isomeric changes have been observed by Auwers,[2] Bamberger,[3] and Kischner.[4]



Dimethyl dihydro-resorcinol. Dichloro-dimethyl dihydrobenzene. Dichloro-*o*-xylene

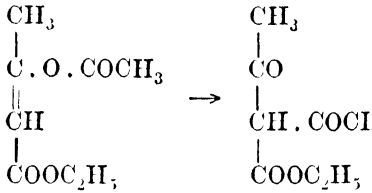
[1] *Trans. Chem. Soc.*, 1902, **81**, 827, see also Crossley and Renouf, *ibid*, 1914, 105, 166.
[2] *Annalen*, 1907, **352**, 44, *Ber*, 1911, **44**, 588.
[3] *Ber.*, 1903, **36**, 1625, 2028; 1907, **40**, 1893.
[4] *Journ. russ. phys.-chim. Ges.*, 1908, **40**, 676, 994.

Migration of Radicals (from Oxygen to Carbon). Claisen[1] found that isoacetophenone ethyl ether when boiled under pressure changes into phenylpropyl ketone.

$$C_6H_5C(OC_2H_5)\cdot CH_2 \longrightarrow C_6H_5\cdot CO\cdot CH_2\cdot C_2H_5$$

Isoacetophenone ethyl ether. Phenylpropyl ketone.

He also showed that the acetyl derivative of hydroxycrotonic ester (from acetoacetic ester, acetyl chloride, and pyridine) was transformed by means of potassium carbonate and a little acetoacetic ester, or by sodium acetoacetic ester into diacetoacetic ester.[2]

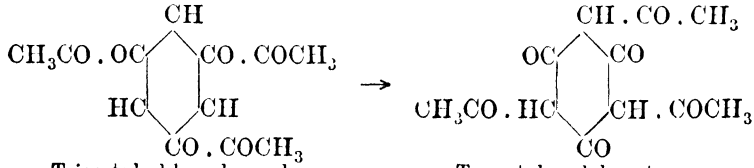


The corresponding alkyl derivatives do not undergo this conversion. Acetophenone O-benzoate,[3] on the other hand, is converted in much the same way by the action of metallic sodium and a little acetophenone into the sodium compound of dibenzoylmethane.

$$C_6H_5CO(CO\cdot C_6H_5)\ CH_2 \longrightarrow C_6H_5CO\cdot CH_2\cdot COC_6H_5$$

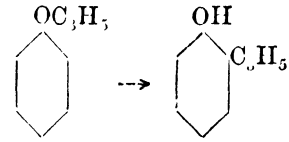
These reactions are attributed by Claisen to the displacement by the alkali metal of the acid radical, which is thereby thrust on to the adjoining carbon atom. He perceives in the above isomeric change the cause of the formation of diacetoacetic ester when acetyl chloride acts upon sodium acetoacetic ester. The unstable O-acetyl derivative which is first formed passes into the stable C-acetyl compound (p. 332). The theory fails, however, to explain the non-appearance of the very stable O-alkyl derivatives when the alkyl iodides react with the sodium compound.[4]

A reaction of a character similar to the foregoing is the conversion of the acetyl derivatives of the polyhydric phenols into acetyl derivatives of the cyclohexanones when heated with zinc chloride.[5]



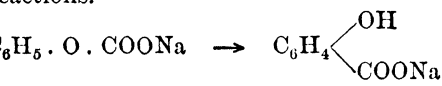
Triacetyl phloroglucinol. Triacetyl cyclohexatrione.

Claisen[6] has converted the allyl ethers of phenol by heating to a high temperature into the *o*-allyl phenol and by repeating the process into 1.2.4 triallyl phenol.

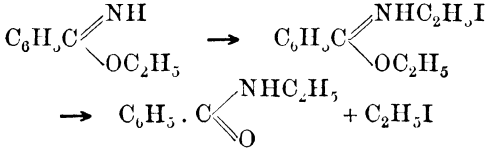


[1] *Ber.*, 1896, **29**, 2931. [2] *Ber.*, 1900, **33**, 3778. [3] Claisen and Haase, *Ber*, 1903, **36**, 3678. [4] See also Dieckmann and Stein, *Ber*, 1904, **37**, 3392. [5] Heller, *Ber.*, 1909, **42**, 2736; 1912, **45**, 418 [6] *Annalen*, 1919, **418**, 69, see also Powell and Adams, *J. Amer. Chem. Soc*, 1920, **42**, 646.

Kolbe's well-known salicylic process in which phenyl sodium carbonate is converted into sodium salicylate may be included in the same group of reactions.[1]

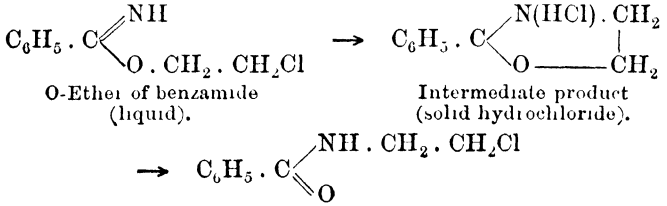


From Oxygen to Nitrogen. Examples of the transference of an alkyl group from oxygen to nitrogen are very numerous. Hofmann and Olshausen[2] and also Pomarew[3] found that normal cyanuric esters pass into the isocyanuric esters on heating. Wislicenus and Korber[4] found that the O-ether of hydroxycaffeine passes into the N-ether (Part III, p. 122), and Wheeler and Johnson[5] showed that imino ethers are converted into alkyl amides on heating with alkyl iodides. Benzimino ethyl ether, heated to 100° with ethyl iodide, yields ethyl benzamide.



That the reaction may be brought about by addition of alkyl iodide seems not improbable from the following observation of Wislicenus and Körber.[6]

These chemists observed that when an ethereal solution of benzimido chlorethyl ether (obtained from benzonitrile and ethylene chlorhydrin[7]) is evaporated on the water-bath an oil remains which on further heating momentarily becomes solid and then melts again. If this solid is removed and dissolved in water it gives a precipitate of silver chloride when silver nitrate is added. The liquids do not react in this way, and the solid is therefore the chloride of a base. This reaction is interpreted as follows:



O-Ether of benzamide (liquid).

Intermediate product (solid hydrochloride).

N-Ether of benzamide (liquid).

Wislicenus and Goldschmidt[8] noticed that in many cases (benzimino

[1] Sluiter, *Ber.*, 1912, **45**, 69.
[2] *Ber.*, 1870, **3**, 272.
[3] *Ber.*, 1885, **18**, 3269.
[4] *Ber.*, 1902, **35**, 199.
[5] *Amer. Chem. Journ.*, 1899, **21**, 187
[6] *Ber.*, 1902, **35**, 164.
[7] Gabriel and Neumann, *Ber.*, 1892, **25**, 2386
[8] *Ber.*, 1900, **33**, 1467.

ethyl ether is an exception) mere heating will convert the imino ether into the amide. The imino ether of formanilide slowly changes at 200° into ethylformanilide,

$$C_6H_5N : CHOC_2H_5 \longrightarrow C_6H_5N(C_2H_5)CHO$$

Lander,[1] who has repeated the experiments, finds this isomeric change, by heat alone, not easy to effect in any case, and does not regard it as a simple transformation; but adopts the view that addition occurs and takes the following form:

$$C_6H_5 . C(=NR^1)(OR^2) + R^3I \longrightarrow C_6H_5C(NR^1R^3)(:I)(OR^2)$$

$$\longrightarrow C_6H_5 . C(=O)(NR^1R^3) + R^2I$$

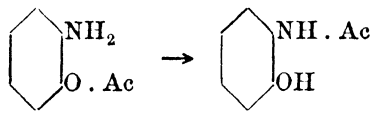
The formation of an intermediate ring structure, such as that which Wislicenus and Körber assumed to exist in the reaction just described, has been actually shown to occur in the conversion of O-benzoyl salicylamide into N-benzoyl salicylamide by McConnan and Titherley,[2] who have succeeded in isolating all three acyl derivatives,

$$C_6H_4(CO . NH_2)(O . COC_6H_5) \rightleftharpoons C_6H_4(CO . NH)(O—C(OH)C_6H_5)$$

$$\rightleftharpoons C_6H_4(CO . NH . COC_6H_5)(OH)$$

and the reaction is reversible.

Similar changes have been observed and very fully investigated by Auwers[3] in which acyl radicals of aminophenols migrate from oxygen to nitrogen.

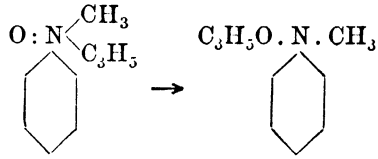


He finds that migration takes place spontaneously when the nitrogen is in the α, β, or γ position in an ortho side-chain, if the nitrogen group is sufficiently basic, but a diminution in the basic character of this group or in the acid character of the acyl group retards the migration but does not altogether arrest it. Further, the relative weight of the acyl group is a factor in the transformation, the lighter the group, the more easily, as a rule, is the migration effected,

[1] *Trans. Chem. Soc*, 1903, **83**, 411.
[2] *Trans. Chem. Soc*, 1905, **87**, 1207; 1906, **89**, 1318
[3] *Annalen*, 1909, **364**, 147; **365**, 278, 291 **369**, 209; *Ber.*, 1914, **47**, 1297. See also Stieglitz, *Amer. Chem. Journ.*, **31**, 458, Ransom, *Ber.*, 1900, **33**, 199.

provided the basic character of the nitrogen group is sufficiently pronounced.

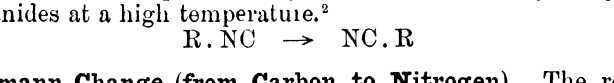
From Nitrogen to Oxygen. There are few examples of the reverse process. Meisenheimer[1] has, however, observed that methyl aniline oxide passes into N-methyl O-allyl phenyl hydroxylamine



From Nitrogen to Carbon. The interchange of radicals between nitrogen and carbon is presented by the conversion of alkyl isocyanides into cyanides at a high temperature.[2]

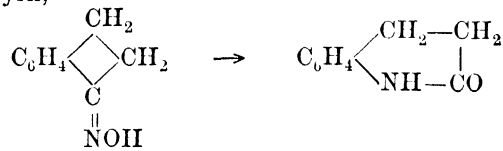
$$R.NC \rightarrow NC.R$$

Beckmann Change (from Carbon to Nitrogen). The reaction has already been described and consists of an interchange of organic radical and hydroxyl in the oximes (p. 299). A simple illustration is the conversion of acetophenoneoxime into acetanilide, which is usually explained in the following fashion:

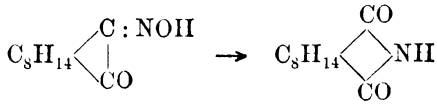


Acetophenoneoxime. Acetanilide.

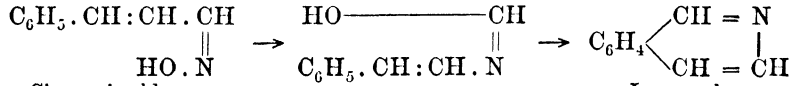
The change can be effected by numerous reagents, such as the chlorides of phosphorus and other organic and inorganic acid chlorides, sulphuric and hydrochloric acid, acetic acid, and anhydride and phosphorus pentoxide. The reaction can be applied not only to the oximes of open-chain aliphatic and aromatic ketones, but to those of cyclic structures like α-hydrindone-oxime which changes into hydrocarbostyril,[3]



and isonitrosocamphor which passes into camphorimide.[4]



Another curious manifestation of the Beckmann change is the conversion of cinnamic aldoxime into isoquinoline.[5]



Cinnamic aldoxime. Isoquinoline.

[1] *Ber.*, 1922, **55**, 513. [2] Wade, *Trans. Chem. Soc*, 1902, **81**, 1596.
[3] Kipping, *Proc. Chem Soc*, 1895, **9**, 240. [4] Angeli, *Real Accad. dei Lincei* (5). **1**, 441.
[5] Bamberger, Goldschmidt, *Ber.*, 1894, **27**, 1955.

The mechanism of the change in spite of careful study is still very obscure. The original reagent, phosphorus pentachloride, used by Beckmann, and the formation of benzanilide iminochloride from benzophenoneoxime, which was isolated in the course of the decomposition, rendered it probable that the hydroxyl was replaced by chlorine and then underwent rearrangement.

$$\begin{array}{lcll} C_6H_5.C(=NOH).C_6H_5 & PCl_5 & C_6H_5.C(=NCl).C_6H_5 & \rightarrow \\ C_6H_5.C(=N.C_6H_5)Cl & H_2O & C_6H_5.CO.NHC_6H_5 & \end{array}$$

But the action of other reagents like sulphuric acid cannot be explained in precisely the same way. The radical of the acid might, however, enter in place of hydrogen or hydroxyl and render the latter labile and more prone to rearrangement The behaviour of γ-benzilmonoxime towards benzenesulphonic chloride, with which it combines in pyridine solution, renders some such explanation probable. It is represented by Werner and Piguet[1] in the following way:

$$\begin{array}{l} C_6H_5.C(=HON).CO.C_6H_5 \rightarrow HO.C(=C_6H_5N).CO.C_6H_5 \\ \rightarrow C_6H_5SO_2.O.C(=C_6H_5N).COC_6H_5 \end{array}$$

If this is a correct interpretation it indicates that the process is not dependent in the first instance on the hydroxyl being replaced by a negative group, although there is nothing to show that the interchange precedes rather than follows combination with the sulphonic chloride.

The small quantity of phosphorus pentachloride or oxychloride necessary to convert benzo- and aceto-phenoneoxime into the corresponding anilide, and the trace of acid chloride required to transform benzaldoxime benzyl ether into benzylbenzamide,

$$\underset{\text{Benzaldoxime-benzyl ether.}}{C_6H_5.CH(O)N.C_7H_7} \rightarrow \underset{\text{Benzylbenzamide.}}{C_6H_5CO.NH.C_7H_7}$$

led Beckmann[2] to formulate the somewhat vague hypothesis that the process consists in the transposition of electrically charged radicals

[1] *Ber*, 1904, 37, 4295. [2] *Ber.*, 1894, 27, 800.

or ions, and that the reagent merely acts as a catalyst by increasing the velocity of the interchange.

Stieglitz[1] takes a very different view of the mechanism of the process. He groups together under one head the Hofmann method for converting amides into amines, $R.CONHBr \longrightarrow CO:NR + HBr$, Curtius' process for producing urethanes from azides,[2]

$$R.CO.N_3 + CH_3OH = NHR.COOCH_3 + N_2$$

including the formation of methylene phenylimine from benzyl azide, $C_6H_5CH_2N_3 = CH_2{:}NC_6H_5 + N_2$, the conversion of acyl hydroximic salts into carbimides,[3]

$$R.C(OK)=NO.COCH_3 = CO:NR + CH_3.COOK$$

and the Beckmann change. In all of these reactions the radical passes from carbon to nitrogen, and a general explanation has been furnished to include them all.

Stieglitz shows that the various changes described above are completely arrested if a radical is attached to the nitrogen atom, as for example in acetylchloriimino-amyl ether $CH_3.CO.NCl(C_5H_{11})$ and in the chloriimino ethers of the formula $RC(:NCl)OR^1$. This is scarcely surprising in view of the stability of the imino ethers (p. 225). Nevertheless, he infers that before the change can occur a univalent nitrogen atom must be present. The bromamide, azide, and acyl hydroximic salts yield $R.CO.N<$ and the oximes yield

$$\begin{matrix} R \\ R \end{matrix}\!\!>\!C.N<$$

The same view of the Beckmann change is taken by Schroeter,[4] who formulates the reaction as follows:

$$\begin{matrix} R \\ R^1 \end{matrix}\!\!>\!C:NOH \xrightarrow{HCl} \begin{matrix} R \\ R^1 \end{matrix}\!\!>\!C(Cl)(NHOH) \xrightarrow{-H_2O} \begin{matrix} R \\ R^1 \end{matrix}\!\!>\!C(Cl)N<$$

The experimental proof is afforded by heating the diazide (obtained from benzophenone dichloride and sodium azide) which at 150° loses nitrogen and gives a tetrazole derivative, whilst at the same time,

[1] *Amer. Chem. Journ.*, 1896, 18, 751; 1903, 29, 49, 289; 1903, 30, 399, 412; 1911, 36, 272.

[2] Curtius' reaction is as follows: The ester of the acid is combined with hydrazine hydrate and the resulting hydrazide treated with nitrous acid.

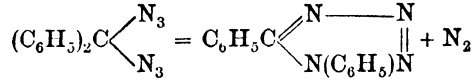
$$R.CO_2R \rightarrow R.CO.NH.NH_2 + HNO_2 \rightarrow R.CO.N\!<\!\!\begin{matrix} N \\ \| \\ N \end{matrix} + 2H_2O.$$

(*J. prakt. Chem.*, 1902, ii, 65, 20), see also Senter, *J. Amer. Chem. Soc.*, 1916, 38, 2718.

[3] Hantzsch, *Ber.*, 1894, 27, 1256.

[4] *Ber.*, 1909, 2336, 3356.

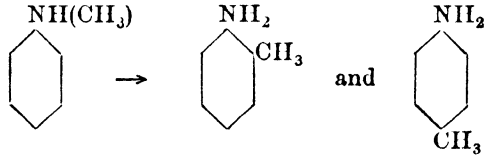
and this is the essential feature, the radical wanders from the carbon to the nitrogen atom.



The objection has been raised that in the case of two stereoisomeric ketoximes the above reaction would yield identical amides, seeing that according to the Hantzsch-Werner hypothesis the double bond, upon which the theory is based, disappears in the intermediate product.[1]

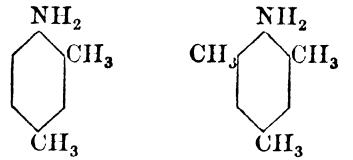
In the present incomplete state of the investigation it is scarcely profitable to pursue the argument further; but it may be pointed out that an explanation which includes only a few arbitrarily selected cases out of a large number of isomeric changes is not likely to lead to a satisfactory generalization.

Migration of Radicals from Side-Chain to Nucleus (from Nitrogen to Nuclear Carbon). This is a type of conversion which is most commonly experienced. It includes the reaction of Hofmann and Martius,[2] which consists in heating the hydrochloride of aromatic methylamino compounds to 250–350° when the methyl group is transferred from the nitrogen to the *o*- and *p*-carbon of the nucleus and the nuclear hydrogen to the nitrogen.



o-Toluidine. *p*-Toluidine.

The process may be repeated until a second or third methyl group is introduced, when it comes to an end.

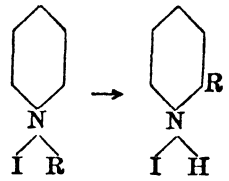


2 : 4 Xylidine. 2 : 4 . 6-Cumidine.

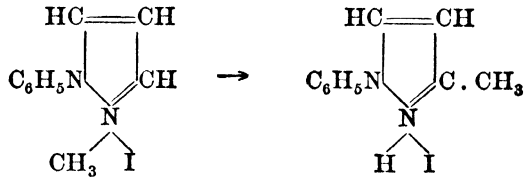
An analogous reaction is the formation of α-alkyl pyridines from the alkyl pyridinium iodides (Part III, p. 287),

[1] Montagne, *Ber*, 1910, 43, 2014; see also Schroeter, *Ber.*, 1911, 44, 1201.

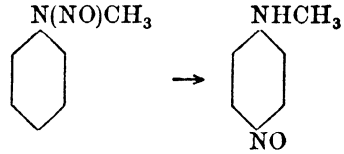
[2] *Ber*, 1871, 4, 742; 1872, 5, 704; 1874, 7, 526; see also Reilly and Hickinbottom, *Trans. Chem. Soc.*, 1920, 117, 103.



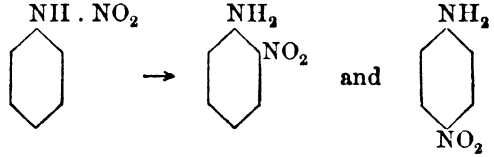
and phenylmethyl pyrazole from phenylpyrazole methyl iodide.[1]



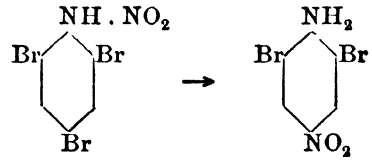
Fischer and Hepp[2] found that the nitrosamine of monomethylaniline when treated with hydrogen chloride in alcohol solution passes into *p*-nitroso-methylaniline.



Bamberger[3] discovered that phenylnitramine undergoes a similar change to *o*- and *p*-nitraniline in presence of mineral acids even in the cold.



A number of interesting observations have been made by Orton on the isomeric change of halogen substituted phenyl nitrames in which the nitro group may either remove the halogen in the nucleus and replace it,

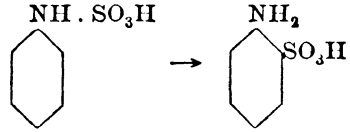


or merely cause it to shift its original position as in the case of the

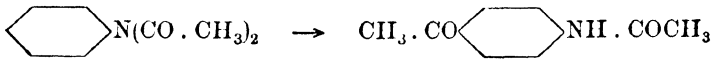
[1] Balbiano and Maschetti, *Real. Accad. Lincei*, 2, (1), 114. [2] *Ber.*, 1886, 19, 2991.
[3] *Ber.*, 1893, 26, 471, 482; 1894, 27, 359; 1897, 30, 1248.
[4] *Trans. Chem. Soc.*, 1905, 87, 889; 1908, 93, 725.

2·6 dibromo-phenylnitramine, which yields both the 2·6 dibromo 4 nitraniline and the 2·4 dibromo 6 nitraniline.

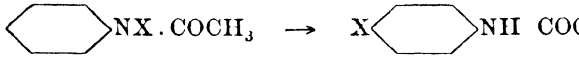
Phenylsulphamic acid, $C_6H_5NH.SO_3H$, which Bamberger and Hindermann [1] obtained by the action of sulphur dioxide on phenylhydroxylamine, changes in the cold into aniline *o*-sulphonic acid on the addition of acetic acid and a few drops of sulphuric acid.



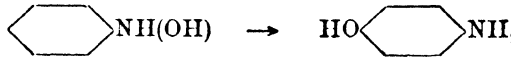
Bamberger and Kunz [2] further observed that on heating the ortho-compound to 180–190° with strong sulphuric acid the latter was converted into the para-compound (sulphanilic acid). The above changes may indicate the course of the reaction between sulphuric acid and aniline at a high temperature, which is the common method for preparing the sulphanilic acid. Similar to the changes studied by Bamberger are the conversion of diacylanilides into acylamino ketones [3] by means of zinc chloride,



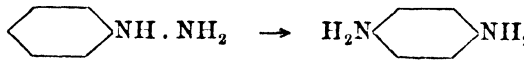
and the transformation which acylchloro- and bromo-anilides, &c., undergo in presence of glacial acetic acid [4] (X = halogen).



The formation of *p*-aminophenols from phenylhydroxylamine and its derivatives by the action of mineral acids [5]



and of *p*-phenylenediamine from phenylhydrazine [6] by heating with strong hydrochloric acid to 200°

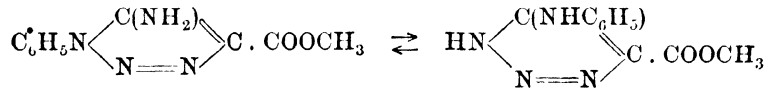


are examples of the same general process.

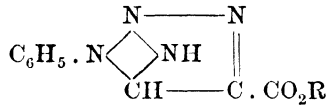
Migration between nucleus and side-chain (between nuclear nitrogen and side-chain nitrogen). Examples have already been given of radicals migrating from one carbon atom to another in the nucleus of a cyclic compound (p. 383). The same thing may occur where nitrogen atoms form part of a ring, or where one is in the ring

[1] *Ber.*, 1897, 30, 654 [2] *Ber.*, 1897, 30, 2276.
[3] Chattaway and Lewis, *Trans. Chem. Soc.*, 1904, 85, 386, 589.
[4] Chattaway and Orton, *Trans. Chem. Soc.*, 1899, 75, 1046.
[5] Bamberger, *Ber.*, 1894, 27, 1849; *Annalen*, 1921, 424, 283.
[6] Thiele and Wheeler, *Ber.*, 1895, 28, 1588.

and one in the side-chain. The latter may be illustrated by Dimroth's amino-triazole carboxylic esters referred to on p. 359. Here a phenyl group is assumed to wander between nuclear and side-chain nitrogen, and the process is reversible.[1]

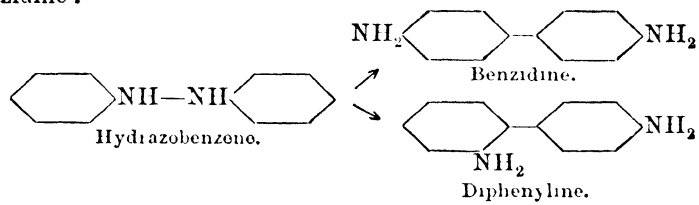


This interpretation has been shown by Dutt[2] to be wrong, the second compound being represented by the formula,



which involves no migration of the phenyl group, though the reversibility of the reaction is not affected.

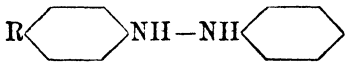
Benzidine Conversion. The well-known change of hydrazobenzene to benzidine on boiling with mineral acids, known as the benzidine conversion, is analogous in many respects to the foregoing reactions. Zinin[3] found that when azobenzene is reduced and boiled with sulphuric acid, benzidine or *p*-diamino-diphenyl is formed. Hofmann[4] subsequently showed that an intermediate product, hydrazobenzene, is produced during reduction, and that this is the substance which undergoes the transformation. Schultz[5] then took up the investigation and discovered a small quantity of a second isomer, called diphenyline, which is produced simultaneously with benzidine:

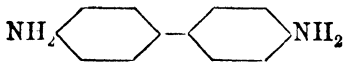


From the formulae it will be seen that the attachment between two nitrogen atoms in hydrazobenzene is substituted by that of two carbon atoms of the nuclei, the amino groups being transferred to the two para positions in benzidine or to one para and one ortho in diphenyline. A simple way of visualizing the change is to suppose the two nuclei in hydrazobenzene to separate, and in the one case to make half a complete revolution before joining up again, and in the other case for one nucleus to be turned through 180° and the other through 60° before joining.

[1] *Annalen*, 1909, **364**, 183.
[2] *Trans. Chem Soc.*, 1923, **123**, 265.
[3] *J. prakt. Chem.*, 1845, **36**, 93.
[4] *Jahresb.*, 1863, 424.
[5] *Annalen*, 1881, **207**, 311.

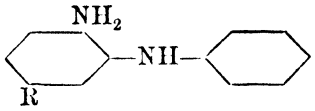
In a series of papers published by Jacobson and his pupils[1] the results of subjecting substituted hydrazobenzenes to the action of hydrochloric acid have been studied. If, for example, the para position to the nitrogen in hydrazobenzene is occupied in one or both nuclei, will the conversion into benzidine be prevented, or, if not, what will happen? The method employed by Jacobson was to reduce the azo-derivatives, which are readily obtained, with an alcoholic solution of stannous chloride and hydrochloric acid. The hydrazobenzene compound would thus be formed and simultaneously converted into the required products, which could then be separated, identified, and estimated. The following changes are possible, supposing one nucleus to be substituted in the para position by R:





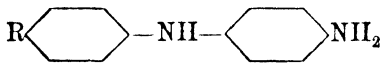
Benzidine (R being detached).

I



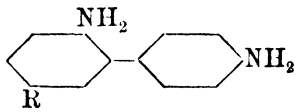
Ortho-semidine.

II



Para semidine.

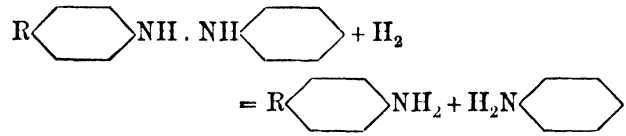
III



Diphenyl base.

IV

V. Decomposition of the compound into two molecules of base thus:



It has been shown that all these reactions may and occasionally do occur, but usually the principal changes are limited to one, or at most two, of the above, the others being subordinate.

The following table contains a summary of the results. In the first column are the elements or groups occupying the position R, and the signs 0, I, II, and III indicate roughly the extent of the changes denoted at the head of the column.

[1] *Annalen*, 1895, 287. 97, 1899, 303, 290, 1922, 427, 142.

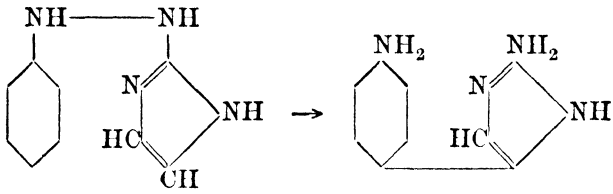
	Benzidine conversion. R displaced.	Ortho-semidine	Para-semidine.	Diphenyl base.
Cl	II	III	I	III
Br	I	III	I	III
I	?	II	0	III
OC_2H_5	0	III	II	0
$OCOCH_3$	II	0	0	III
$N(CH_3)_2$	0	I	0	III
NH $COCH_3$	0	0	III	0
CH_3	0	III	?	?
COOH	III	?	0	0

Jacobson, from the result of a large number of observations, has laid down the following rules: *p-p*-benzidine conversion occurs if both para positions are free, and may occur if one para position is occupied by a detachable group such as CO_2H, SO_3H, and as a secondary reaction if a halogen, -OR, and $-OCOCH_3$ are present. *O-o*-benzidine conversion never occurs in the benzene series, but occasionally in the naphthalene compounds, with free or occupied para positions. Diphenyline (*o p*-benzidine) conversion is the main reaction when a single para substituent consisting of halogen, acetoxy or dimethylamino group, or, if in one nucleus a para methyl, and in the other an *o* ethoxy group are present, and occasionally as secondary reaction when both para positions are free. Ortho-semidine conversion is the main reaction in the benzene series if the para position is occupied by a CH_3 or OR group. It may be modified or suppressed if ortho positions to the hydrazo group are filled. It takes place as secondary reaction in the benzene series where the para position is substituted by halogen or a dimethylamino group. Para-semidine conversion is the main reaction in the case of a single para substitution by NH_2 or NH. CO. CH_3. It accompanies the ortho-semidine change where para substitution is effected by OR, especially if substituents are present in the ortho positions. It accompanies the diphenyline change in the case of a single para substitution by halogens, and if one nucleus contains para-CH_3 and the other ortho-OR. It occurs with elimination of OCO. CH_3 if the group occupies the para position in one nucleus with a para-CH_3 or para-Br in the other.

The main points of interest to be derived from the above table are, firstly, that substitution of both *p*-positions determines decomposition into two molecules of base, and, secondly, that the presence of methyl groups in the ortho position to the azo group, irrespective of the nucleus, diminishes the ortho-semidine conversion. The latter

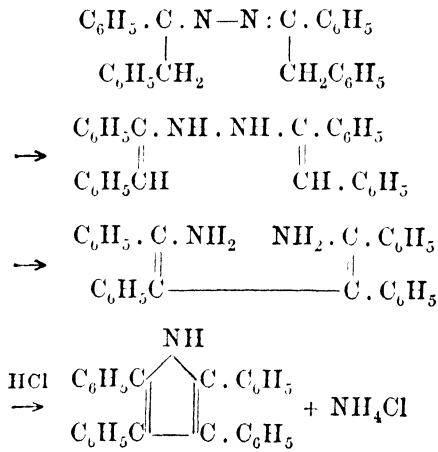
observation appears to be intimately connected with those anomalous reactions which are discussed under *steric hindrance* (Part I, p. 383).

Another example of the benzidine conversion is recorded by Pyman and Fargher [1] in the case of benzene azoglyoxaline, which on reduction yields the diamino compound.



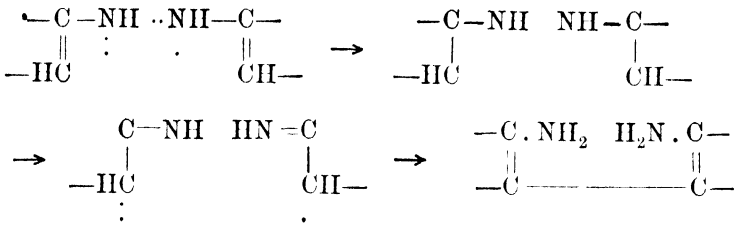
A change closely analogous to the benzidine conversion has been observed by Ingle and Mann [2] in the action of alkalis on dibenzalphenylhydrazone, which passes into benzilphenylhydrazone.

An explanation of this change has been proposed by G. and R. Robinson [3] from the observation that the hydrazone of deoxybenzoin on heating with dry hydrogen chloride to 180° is converted into tetraphenyl indole, a reaction which may be represented thus:



[1] *Trans. Chem. Soc.*, 1919, 115, 217, 1015. [2] *Trans. Chem. Soc.*, 1895, 67, 606.
[3] *Trans. Chem. Soc.*, 1918, 113, 639.

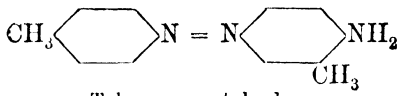
Dividing the single bond into two partial valencies, and making the thick bond represent three partial valencies, the following progressive dissolution of the nitrogen linkages and formation of carbon linkages occur as follows:



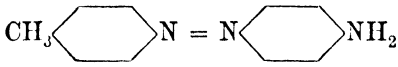
Diazoamino-Aminoazo Conversion. The conversion of diazoamino compounds into aminoazo derivatives by the action of a small quantity of hydrochloride of the aromatic base was discovered by Kekulé in 1866.

$$C_6H_5N:N.NHC_6H_5 \longrightarrow C_6H_5N:NC_6H_4NH_2$$

Nietzki[1] found that a similar reaction failed with *p* diazoaminotoluene and *p*-toluidine hydrochloride, but was successful if the toluidine salt were replaced by the hydrochloride of *o*-toluidine or aniline, giving rise to the following two products:

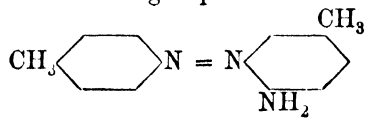


p-Tolueneazo-*o*-toluidine



p Tolueneazo-aniline

The failure of *p*-toluidine to combine was due to the fact that the azo nitrogen attaches itself by preference to the carbon para to the amino group, and in *p*-toluidine it is already appropriated. Nevertheless, the reaction with *p*-toluidine was subsequently found by Zincke and Jaenke[2] to yield a certain quantity of *p*-tolueneazo-*p*-toluidine, in which the azo nitrogen attaches itself to the carbon in the ortho position to the amino group.



p-Tolueneazo-*p*-toluidine.

[1] *Ber.*, 1877, 10, 666. [2] *Ber.*, 1888, 21, 548.

The same observers, in the course of the same investigation, made it quite clear that the conversion is the result not of an intramolecular, but of an intermolecular process, for they obtained aminoazo-*p*-toluene from diazoaminobenzene, and *p*-toluidine hydrochloride dissolved in *p*-toluidine.

$$C_6H_5N:N.NHC_6H_5 + 2CH_3C_6H_4NH_2.HCl = CH_3C_6H_4N:{}^{1}N.C_6H_3{}^{5}(CH_3)({}^{2}NH_2) + 2C_6H_5NH_2.HCl$$

A much more complete study of the change has been carried out by Goldschmidt and his collaborators[1] They have followed the course of the reaction, where interchange of radicals was effected, by determining the alteration of freezing-point and the nature of the products formed during the conversion. In this way they found that the interchange of radicals occurs in the diazonium stage, that is, before the aminoazo conversion sets in. They interpret the results as follows: the production of aminoazotoluene from diazoaminobenzene and *p*-toluidine hydrochloride dissolved in *p*-toluidine consists in the formation of an additive compound of hydrogen chloride with diazoaminobenzene, which is very unstable, and in which aniline residues are replaced by toluidine residues.

$$\begin{matrix} C_6H_5NH \\ \quad\backslash \\ \quad\ NCl \\ \quad/ \\ C_6H_5NH \end{matrix} + 2C_7H_7NH_2 = \begin{matrix} C_7H_7NH \\ \quad\backslash \\ \quad\ NCl \\ \quad/ \\ C_7H_7NH \end{matrix} + 2C_6H_5NH_2$$

The product in presence of a large excess of toluidine then unites with another molecule of *p*-toluidine,

$$\begin{matrix} C_7H_7NH \\ \quad\backslash \\ \quad\ N\ Cl \\ \quad/ \\ C_7H_7NH \end{matrix} + H\ C_7H_6NH_2 = \begin{matrix} C_7H_7NH \\ \quad\backslash \\ \quad\ N.C_7H_6.NH_2 \\ \quad/ \\ C_7H_7NH \end{matrix} + HCl$$

which breaks up into toluidine and aminoazotoluene. In subsequent papers, already referred to (p. 377), the velocity of the change diazoamino-aminoazo has been studied and shown to follow the mass law for unimolecular reactions.

[1] *Ber.*, 1892, **25**, 1347; 1896, **29**, 1369, 1899.

CHAPTER VII

THE BENZENE THEORY

At a time when the paraffins and their derivatives, known as 'the fatty compounds', formed a well ordered and compact group of closely related substances, there remained an unclassified collection of vegetable products, such as balsams, resins, essential oils, and their derivatives, which, from their pleasant perfume, received the name of 'aromatic compounds'.

A closer study of these aromatic compounds revealed a connection between certain members similar to that which had long been recognized among the derivatives of the paraffins. Thus toluene, C_7H_8, obtained by distilling tolu balsam, bore the same relation to oil of bitter almonds and benzoic acid as ethane to acetaldehyde and acetic acid.

C_7H_8	C_7H_6O	$C_7H_6O_2$
Toluene.	Oil of bitter almonds.	Benzoic acid.
C_2H_6	C_2H_4O	$C_2H_4O_2$
Ethane.	Acetaldehyde.	Acetic acid.

Cymene, $C_{10}H_{14}$, cuminol. $C_{10}H_{12}O$ (from Roman cumin oil), and cumic acid, $C_{10}H_{12}O_2$, prepared by oxidation of cuminol, showed a similar relationship. The first of each series was a stable hydrocarbon, the second exhibited the properties of an aldehyde, and the third was an acid.

But notwithstanding the parallelism which appeared among members of the aliphatic and aromatic groups, a sharp line divided them; indeed, many years elapsed before any direct synthesis of a member of the one group from that of the other served to establish a link between them.

Among the members of the aromatic group there existed a certain family resemblance which was easy to recognize. They contained a higher proportion of carbon than the fatty compounds, and on being broken up into simpler substances, it was found that the products, such as benzene, C_6H_6, phenol, C_6H_6O, picric acid,

$C_6H_3N_3O_7$, &c., contained 6 atoms of carbon. Any attempt to pass beyond this point and to form substances with 5 or fewer carbon atoms, generally resulted in the complete disintegration of the molecule.

Kekulé's Benzene Formula. Kekulé was the first to draw attention to these facts in his 'Chemie der Benzolderivate', published in 1867, and based upon them a theory which shed a new light on this obscure corner of chemistry. The rapid development of the aromatic group of compounds, which has now become the predominant partner in the two great divisions of organic chemistry, must be attributed in a great measure to this theory which Kekulé expounded in the following words:

'In order to determine the atomic constitution of the aromatic compounds the following facts must be considered:

'1. All aromatic compounds, even the simplest, are comparatively richer in carbon than the corresponding class of fatty compounds.

'2. Among the aromatic substances, as among fatty compounds, numerous homologous compounds exist.

'3. The simplest aromatic substances contain at least 6 atoms of carbon.

'4. All decomposition products of aromatic substances show a certain family resemblance; they belong to the group of aromatic substances. In more vigorous reactions a part of the carbon in the form of compounds of the fatty group is eliminated, but the main product is always aromatic and contains at least 6 atoms of carbon (benzene, quinine, chloranil, phenol, oxyphenic acid, picric acid, &c.). The decomposition stops with the formation of these products, unless complete destruction of the organic group ensues. These facts, which have been recognized as of general application, justify the supposition that in all aromatic compounds there is one and the same atomic group or common nucleus, which consists of 6 atoms of carbon. Within this nucleus the carbon atoms are in a certain closer connection or denser combination, from which it follows that all aromatic compounds are comparatively rich in carbon. More carbon atoms can then be added to this nucleus in the same manner and according to the same laws which govern the fatty compounds. In this way the existence of homologous compounds may be explained.'

Kekulé then proceeds to show how these 6 atoms of carbon may be so united as to leave 6 single combining units free. In conformity with his view of the constant valency of carbon, Kekulé

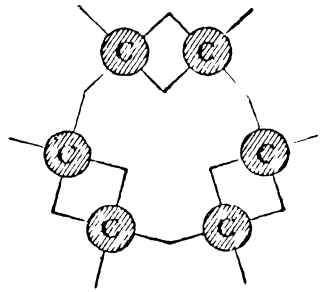
supposes that every alternate linkage is a double one. Six carbon atoms thus arranged in an open chain will have 8 free combining units,

$$—C = C—C = C—C = C—$$

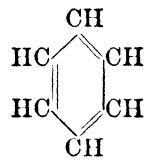
but if the two end carbon atoms are linked together, a closed chain of carbon atoms results with 6 free combining units,

$$\overline{C = C—C = C—C = C}$$

which he represented by the following graphic formula:



If each of the free linkages is attached to a hydrogen atom, the formula for benzene is obtained, and is usually represented in the following manner:



Kekulé's formula for Benzene.

This formula therefore postulates three ethylene linkages. Evidence in favour of such an unsaturated closed chain is afforded by the existence of additive compounds of benzene with 2, 4, or 6 atoms of hydrogen, chlorine, or bromine, and three molecules of hypochlorous acid, $C_6H_6(HClO)_3$, but no more. The isomeric hydrocarbon, *dipropargyl*, which is obtained from diallyl tetrabromide by removing hydrogen bromide with potassium hydroxide,

$$CH_2Br . CHBr . CH_2 . CH_2 . CHBr . CH_2Br + 4KOH$$

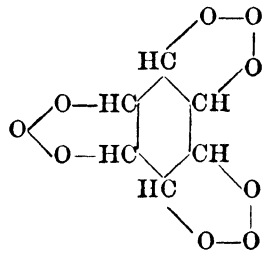
Diallyl tetrabromide.

$$= CH : C . CH_2 . CH_2 . C : CH + 4KBr + 4H_2O$$

Dipropargyl.

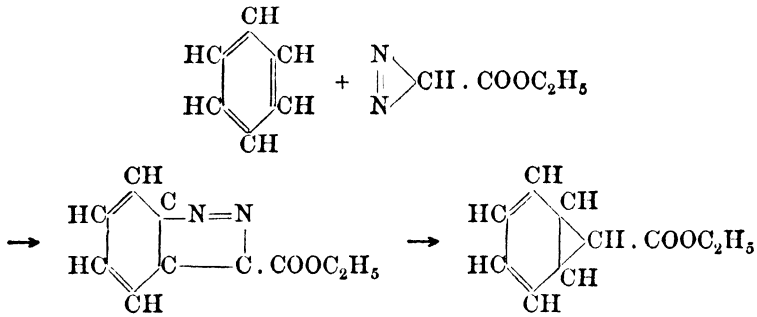
is undoubtedly an open-chain compound, since it requires 8 additional atoms of the above three elements for saturation. Dipropargyl also is very sensitive to oxidising agents, whereas benzene is marked by great stability, an indication in itself of some fundamental difference in structure.

Further evidence for the existence of ethenoid linkages in benzene is the formation of a triozonide (Part I, p. 133)



Benzene triozonide.

of a compound with diazoacetic ester according to the Buchner-Curtius reaction for unsaturated compounds (Part I, p. 241)[1]

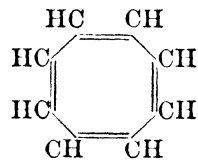


and the exaltation of molecular refractivity and magnetic rotation (pp. 31, 55) produced by an unsaturated side-chain when conjugated with benzene.

Non-Olefinic Character of Benzene. But, on the other hand, the affinity displayed by the olefinic hydrocarbons for the halogens is not exhibited to an equal degree by benzene and its homologues. The halogens form additive compounds with benzene only in presence of sunlight, and the hydrogen halides do not combine at all. There is consequently no strict analogy between the two classes of olefinic compounds. The difference is further emphasized by the action of oxidising agents upon benzene and its homologues. Benzene

[1] *Annalen*, 1908, 358, 1; 1910, 377, 259; *Ber.*, 1920, 53, 865.

itself is highly resistant, but if a side-chain is present it is attacked and converted into carboxyl, whilst the benzene nucleus is untouched. Thus methyl and ethyl benzene form benzoic acid on oxidation. The very opposite result might have been anticipated from the well-known behaviour of olefinic compounds, which, on oxidation, break down at the double link. Indeed, so commonly does this occur that the rapid reduction of an alkaline solution of permanganate in the cold was used by Baeyer [1] to ascertain the presence of an ethylene linkage in unsaturated acids. It is an interesting fact that cyclo-octatetrene, the unsaturated 8-carbon ring compound obtained by Willstätter,[2] though it exhibits points of similarity with benzene, behaves as a true ethenoid compound with 4 double bonds, forming additive compounds readily with 4 molecules each of hydrogen, hydrogen halides, and the halogens, and reducing permanganate in the cold (p. 30).



General Properties of Aromatic Compounds. We have now to consider the action of reagents in forming substitution products, and to compare those products with similar compounds of the aliphatic series. By the term 'aromatic' is usually denoted not only benzene and its derivatives, but other closed-chain compounds, such as naphthalene, anthracene, pyridine, thiophene, &c., which show the general behaviour of benzene. The terms *benzenoid* and *cyclic* are synonymous with aromatic.

An important characteristic of the aromatic compounds is the acidic nature of the nucleus. This is observed in the phenols, which correspond to tertiary alcohols in constitution, yet behave like weak acids, and dissolve readily in caustic alkalis; in the amines, which like aniline are weak bases whose salts redden litmus, or like triphenylamine, which forms no salts at all; in substances such as benzyl cyanide and desoxybenzoin, which contain a replaceable hydrogen in the methylene group, thus resembling the 1:3-diketones,

$C_6H_5.CH_2.CN$	$C_6H_5.CO.CH_2.C_6H_5$	$R—CO.CH_2.CO—R$
Benzyl cyanide.	Desoxybenzoin.	1:3-Diketone.

[1] *Annalen*, 1888, 245, 146. *Ber.*, 1912, 45, 1478.

and like the 1:3-diketones undergo condensation by Knoevenagel's method (Part I, p. 282). Characteristic, too, is the stability of the simple halogen derivatives of the aromatic hydrocarbons which are unchanged by caustic alkalis, and in fact by most reagents, excepting the alkali metals. By heaping up nitro groups in the nucleus, the acid character may be so far intensified that the halogen, like that in an acid chloride, can be removed by potassium hydroxide, giving a phenol, or by ammonia, forming an amino compound.

The formation of nitro compounds by the action of nitric acid, of sulphonic acids by the action of strong sulphuric acid, and the Friedel-Crafts reaction, have no exact parallel among the aliphatic compounds. To obtain the nitro derivatives of normal paraffins with nitric acid, dilute nitric acid at a high temperature must be employed,[1] although the iso-paraffins are readily attacked by the fuming acid,[2] and, for preparing the alkyl sulphonic acids, fuming sulphuric acid or the anhydride is necessary.[3]

Furthermore, whereas the aromatic sulphonamides readily combine with sodium hypochlorite to form chloramine salts,

$$Ar.SO_2NH_2 + NaOCl = ArSO_2NNaCl + H_2O$$

the corresponding aliphatic compounds seem incapable of doing so.[4]

We also find among the aromatic compounds diazo and azo compounds, which have only a very limited number of representatives in the aliphatic series. Here again the acidic character—carboxyl in the aliphatic and phenyl in the aromatic series—of the associated group seems to play a part in determining the formation of these compounds.

$C_6H_5N_2OH$ — Diazonium hydroxide.

$C_2H_5OOC.CHN_2$ — Diazo-acetic ester.

Position Isomerism. Whether or not Kekulé's benzene formula accounts for the distinctive characters of the aromatic compounds, is a question which will be discussed later; but the formula served another purpose. It was designed to explain the special kind of isomerism which is met with among these compounds and usually described as *position isomerism*.

The symmetrical distribution of the hydrogen atoms admits of only one mono-substitution product, and only one such product is known; among the di-derivatives of benzene it soon appeared that

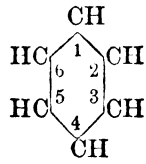
[1] Konowaloff, *Ber*, 1892, 25 R, 108.

[2] Francis and Young, *Trans. Chem. Soc.*, 1898, 73, 928.

[3] As Markwald points out, it is scarcely admissible to draw a comparison between benzene and the saturated aliphatic hydrocarbons. Analogies should be sought among the olefinic compounds of the series. Thus the hydroxymethylene compounds (Part I, p. 275) which contain the group $=CH(OH)$ have stronger acid properties than phenol, and halogen compounds of the type $CH:CHCl$ contain a more stable halogen than the alkyl chlorides. Also, a substance like cinnamic acid forms with nitric acid a dinitro compound $NO_2.C_6H_4.CH.C(NO_2).COOH$ in which one nitro group replaces hydrogen in the olefinic side-chain and corresponds to nitrobenzene.

[4] Cohen and Clutterbuck, *Trans. Chem. Soc.*, 1922, 121, 120.

many existed in three isomeric forms. If we denote the positions of the carbon atoms in Kekulé's benzene formula (omitting from it the double linkages) by the numbers 1–6,



it is obvious that two elements or groups replacing the hydrogen atoms 1 and 2 will produce a different compound from that formed by replacing those at 1 and 3 and at 1 and 4. As the six carbon and six hydrogen atoms are symmetrically disposed, the substitution of the hydrogen atoms at 1 and 5 will be equivalent to that at 1 and 3, and that at 1 and 6 to 1 and 2, so that three and not more than three di derivatives are possible. This was in strict agreement with the facts, although the direct proof of the symmetry of the molecule was not forthcoming until later.

Orientation. The necessity for assigning definite positions to the substituents in the different series of isomeric compounds was soon recognized, but it was only after repeated failures that trustworthy methods were at length evolved. The history of the development of the process, which is usually known as *orientation*, presents many features of interest, but cannot be fully discussed here.[1] The first attempts were based on pure assumptions, which being as often wrong as right, led to frequent confusion. Baeyer's view, that mesitylene being formed from acetone must therefore be symmetrical trimethyl benzene, has stood the test of time.

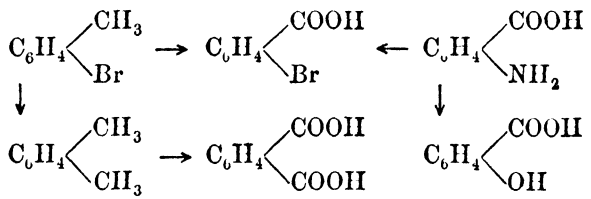
The proof of the symmetrical structure of mesitylene was supplied by Ladenburg in 1874.[2] He prepared dinitromesitylene which gave nitromesidine by the reduction of one of the nitro groups. The nitromesidine yielded, on nitration of its acetyl derivative, a dinitromesidine, from which, by elimination of the amino group, a dinitromesitylene was obtained, identical with the first. The positions occupied by the two pairs of nitro groups are therefore equivalent. If now the above nitromesidine is converted into nitromesitylene and the latter into mesidine and its acetyl derivative then nitrated a nitromesidine is formed which is identical with the original nitromesidine. As the interchange of nitro and amino groups gives the

[1] An excellent account is given in Roscoe and Schorlemmer's Treatise, vol. iii, part iii (Introduction), and also in the introduction by Richard Meyer to Erlenmeyer's *Lehrbuch der organischen Chemie*, vol. ii (Leipzig, 1882).

[2] *Ber.*, 1874, 7, 1133; *Annalen*, 1875, 179, 103.

same compound, these two positions must be equivalent, and therefore the three hydrogen atoms, and consequently the three methyl groups, are symmetrically arranged. As mesitylene can be converted into one of the xylenes and into isophthalic acid, the structure of the two latter as meta-derivatives follows. In 1870 V. Meyer converted sulphobenzoic acid, on the one hand, into hydroxybenzoic acid by fusion with potassium hydroxide, and on the other into isophthalic acid by fusion with sodium formate, and thus established these two as meta-derivatives. Salicylic and phthalic acids, since they yielded anhydrides, were assumed to be ortho compounds, and consequently the third hydroxy- and dibasic-acid (terephthalic) were para compounds.

The proof of the structure of the two last compounds was furnished by Ladenburg in 1869.[1] Hübner and Petermann[2] had observed that ordinary bromobenzoic acid, which is related to *m*-hydroxybenzoic acid, gives, on nitration, two isomeric nitrobromobenzoic acids. The latter, on reduction, yield the same aminobenzoic acid, i.e. anthranilic acid, which is related to salicylic acid. As both bromonitrobenzoic acids are derived from the same bromobenzoic acid, the bromine atom in both compounds must have the same relative position to the carboxyl group. The difference must therefore be due to the position of the nitro groups in the two compounds. But since both bromonitrobenzoic acids give the same aminobenzoic acid on reduction, the two nitro groups must also occupy the same relative position to the carboxyl group. This can only happen if the bromine atom or nitro group is not in the para position (see p. 411). Consequently, the third hydroxybenzoic acid, which is related to the third bromo- and amino-benzoic acid, must be a para compound, and as this acid and terephthalic acid are both related to the same bromotoluene, the constitution of terephthalic acid is also given.



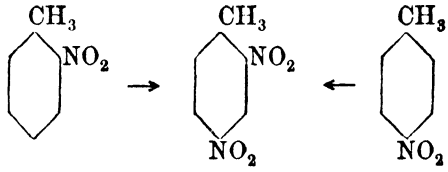
p. Xylene. Terephthalic acid. Hydroxybenzoic acid.

Two out of the three nitrotoluenes were brought into relation with the meta- and para-hydroxybenzoic acids by successively

[1] *Ber.*, 1869, **2**, 140. *Annalen*, 1869, **149**, 129.

oxidising, reducing, and diazotising each of the compounds; the third was consequently the ortho compound.

Petersen[1] pointed out that since ortho- and para-nitrotoluene give the same dinitrotoluene on nitration, the product must contain the two nitro groups in the meta position one to another,



and concluded that dinitrobenzene must also be a meta compound, a deduction which has since proved correct. As *m*-dinitrobenzene is related to a series of simple di-substituted benzene derivatives the structure of these is determined, whilst those of the ortho- and para-compounds are known by their relation to the corresponding dibromobenzenes.

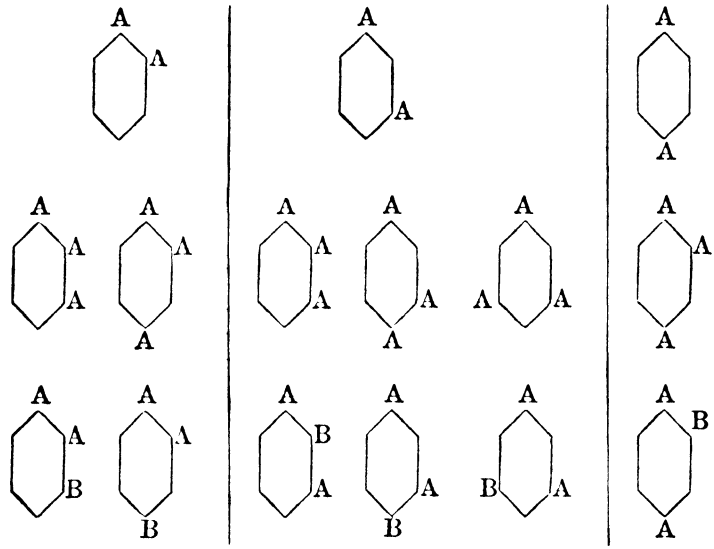
Körner's Absolute Method. The constitution of phthalic acid as an ortho compound was based upon two hypotheses—its relation to the formula for naphthalene and the structure of its anhydride; the formula for isophthalic acid was derived from its relation to mesitylene, the constitution of which was at the time purely hypothetical.

In an important paper published in 1874, 'On the Isomerism of Aromatic Compounds with six Carbon Atoms,' Körner[2] subjected the methods of orientation, then employed, to a very searching criticism. He pointed out that the structure of the three phthalic acids was too problematical, and their connection with the derivatives of benzene, prepared by direct substitution, too uncertain to serve as a basis of orientation. He held that since it was always open to question whether a reaction, which determined the relation between one compound and another, proceeded in a normal fashion, any method of orientation, to be entirely satisfactory, should be as far as possible independent of the course of chemical change.

Körner's method was based on a principle which assumed the equivalence of the six hydrogen atoms of benzene. A di-derivative of benzene containing similar groups, A A, in the ortho position, can

[1] *Ber.*, 1873, 6, 368; 1874, 7, 58.
[2] *Gazz chim. ital.*, 1874, 305, *Jahresb.*, 1875, 299.

only produce two tri-derivatives by the introduction of a third group, A or B. In the same way a meta compound can only produce three tri-derivatives and a para compound only one.



It will be seen from the above scheme that when the three groups in the tri-derivatives are the same, only three isomers are produced in all, whereas if the third group, B, is different from the other two, all the six tri-derivatives are isomeric Korner applied the principle to determine the constitution of the di- and tri-bromobenzenes. Solid dibromobenzene (m. p 89°) yields only one nitrodibromobenzene, the isomeric liquid modification is able to form two, and the third, three nitro derivatives. In the same way Körner obtained two tribromobenzenes from the first dibromobenzene, one from the second, and three from the third. The first compound is therefore para, the second, ortho, and the third, meta. In practice the method is difficult to carry out, as the complete series of derivatives is not always formed. The reverse process may sometimes be adopted with advantage. If the same di-derivative is obtained from two tri-derivatives, the product is an ortho compound; if from three tri-derivatives, it is meta; if from one only, it is para.

The constitution of the phenylene-diamines, $C_6H_4(NH_2)_2$, has been established by Griess [1] in this way. The six diaminobenzoic acids, all of which are known, yield, on distillation with lime, three

[1] *Ber.*, 1874, 7, 1228.

phenylenediamines. Three of them give the same phenylenediamine (m. p. 63°) which is consequently a meta compound, two yield a phenylenediamine (m. p. 99°) which is therefore the ortho compound, and the sixth diamino-benzoic acid forms a phenylenediamine (m. p. 140°) which must be the para compound.

Symmetrical Structure of Benzene. It has already been stated that Kekulé based his formula for benzene upon the general character of the aromatic compounds and upon the symmetrical distribution of the carbon and hydrogen atoms, indirect evidence of which was furnished by the existence of only one mono- and three di-derivatives. The direct proof of the symmetry of the molecule was supplied by the combined researches of Ladenburg, Wroblewsky and Hübner and Petermann. Ladenburg[1] showed that phenol may be converted by the action of phosphorus bromide into monobromobenzene, which in turn may be transformed, by the action of carbon dioxide and sodium, into the sodium salt of benzoic acid by Kekulé's method (Part I, p. 215).

$$C_6H_5OH \longrightarrow C_6H_5Br \longrightarrow C_6H_5 \cdot COOH.$$

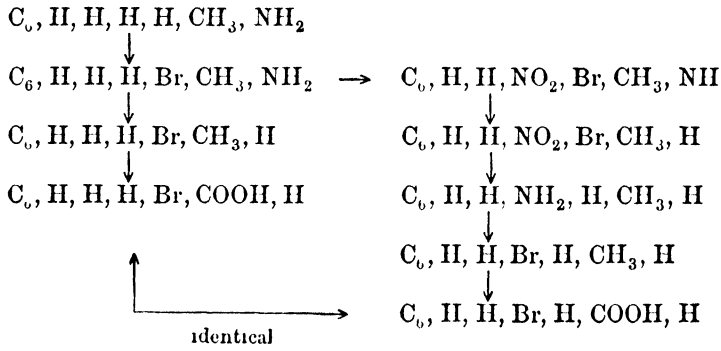
The carboxyl in benzoic acid may be assumed to occupy the same position as the hydroxyl in phenol. Now there are three hydroxybenzoic acids, which may be converted, on the one hand, into benzoic acid and, on the other, into phenol. The benzoic acid and phenol, thus obtained, are identical in every case. If we suppose position 6 to be occupied by carboxyl in the three hydroxybenzoic acids, the hydroxyls will assume three other positions, say 3, 4, and 5, and as the three phenols obtained by removal of carboxyl are identical, and the same as that from which benzoic acid in the first instance was derived, it follows that the positions 3, 4, 5, and 6 are symmetrical or equivalent.

	1	2	3	4	5	6
C_6,	H,	H,	H,	H,	H,	COOH
C_6,	H,	H,	(OH),	H,	H,	COOH
C_6,	H,	H,	H,	(OH),	H,	COOH
C_6,	H,	H,	H,	H,	(OH),	COOH
C_6,	H,	H,	H,	H,	H,	(OH)

[1] *Theorie der aromatischen Verbindungen*, by A. Ladenburg. Vieweg, Brunswick, 1876.

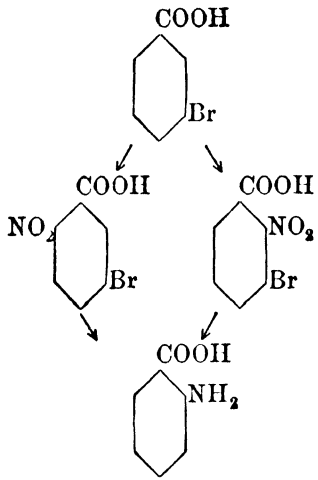
The same reasoning can be applied to the reduction of the three hydroxybenzoic acids to benzoic acid. The proof of the equivalence of the remaining two positions lies in the fact that there are two pairs of positions which are symmetrically situated with regard to a third pair. It has been shown, for example, that a bromine atom may be introduced into benzoic acid in two different positions relatively to the carboxyl, and yield the same bromobenzoic acid, and, in the same way, a nitro group may replace hydrogen in two other positions and form the same nitrobenzoic acid.

Starting from *m*-toluidine, Wroblewsky[1] prepared a bromotoluidine, and from this, in successive stages, bromotoluene and bromobenzoic acid. He then converted the above bromotoluidine into a nitro-compound, a nitrobromotoluene, a toluidine, and, finally, a bromo-toluene and bromobenzoic acid, which were identical with the first two. If direct replacement occurs in the various reactions, it necessarily follows that the first bromine occupies a different position from the second. This will be manifest from the following scheme in which the substituents are given arbitrary positions.



The existence of a second pair of symmetrical positions follows from the observations of Hübner and Petermann,[2] to which reference has already been made (p. 406). The bromobenzoic acid of Wroblewsky yields, on nitration, two isomeric nitrobromobenzoic acids, which, on reduction, form the same aminobenzoic acid (anthranilic acid).

[1] *Ber.*, 1872, 5, 30; *Annalen*, 1873, 168, 113; 1878, 192, 196.
[2] *Annalen*, 1869, 149, 131.



The two nitro groups, therefore, occupy a second pair of symmetrical positions in regard to the carboxyl. The six carbon and hydrogen atoms are therefore symmetrically grouped, and benzene is, as a whole, a symmetrical structure.

Ring Structure of Benzene. Direct evidence of the ring structure of benzene and its derivatives is afforded by the synthesis of hexahydrobenzene or cyclohexane, and certain of its derivatives from open-chain compounds, and by their identity with the products obtained by the direct reduction of benzene. Thus, Perkin[1] obtained cyclohexane by the action of sodium on hexylene dibromide, which is identical with hexahydrobenzene prepared from benzene by reduction.[2]

$$\begin{matrix} CH_2—CH_2—CH_2Br \\ | \\ CH_2—CH_2—CH_2Br \end{matrix} + 2Na = \begin{matrix} CH_2—CH_2—CH_2 \\ | \quad\quad | \\ CH_2—CH_2—CH_2 \end{matrix} + 2NaBr$$

Also the cis- and trans-hexahydro-isophthalic acid and hexahydro-terephthalic acid obtained by Baeyer by the reduction of iso- and terephthalic acid (p. 426) are identical with the synthetic compounds obtained by Perkin from disodium pentanetetracarboxylic ester and methylene iodide in the one case,[3] and from disodium butanetetracarboxylic ester and ethylene bromide in the other.[4] Many other examples of synthesis of cyclic compounds from open-chain com-

[1] *Ber.*, 1894, 27, 216.
[2] Sabatier and Senderens, *Compt. rend.*, 1901, 132, 1254.
[3] *Trans. Chem. Soc.*, 1892, 61, 172.
[4] *Trans. Chem. Soc.*, 1891, 59, 798.

pounds, identical with the reduction products of benzene derivatives, have been examined.

A further important piece of evidence is derived from the atomic structure of the diamond and graphite as determined by the X-ray reflection method of the Braggs,[1] which represents the substances as consisting of superimposed 6-carbon rings (Fig. 59). As graphitic acid obtained by the oxidation of graphite, as well as of wood charcoal,[2] give mellitic acid, a benzene derivative, on oxidation, the natural inference is that graphitic acid is produced by the breaking up of the graphite into entities containing 6-carbon groups. This evidence of ring structure is important, seeing that it is derived from an independent and purely physical source; indeed it constitutes the only definite experimental proof of the ring grouping of the atoms.

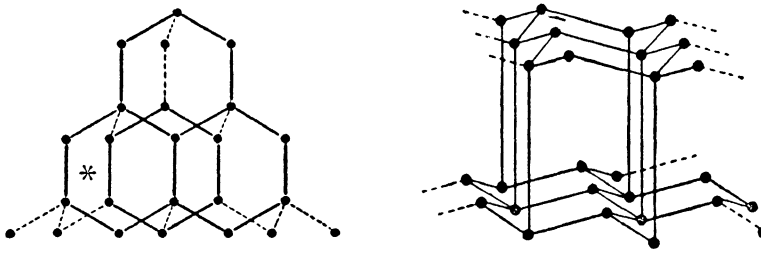


Fig. 59.

Structure of the diamond (Bragg). Structure of graphite (Hull).

The hexagons are indicated by continuous lines; the dotted lines merely complete the geometrical design. The hexagons have not flat contours, for, seen sideways on, as in the six carbon atoms round the asterisk, the top and bottom carbon atoms lie outside the plane.

The structure of graphite is derived from that of the diamond by shifting the relative positions of the hexagons which lie along the cleavage planes and separating the hexagons in these planes from those in adjoining planes by nearly double the distance (W. H. and W. L. Bragg, *X-Rays and Crystal Structure*, p. 227). According to Debye and Scherrer (*Phys. Zeitsch.*, 1917, 18, 291) the bonds in graphite across the cleavage planes represent residual valencies, and the carbon atoms of the ring will consequently possess a tervalent character, as in triphenylmethyl, &c. (see Part I, p. 59).

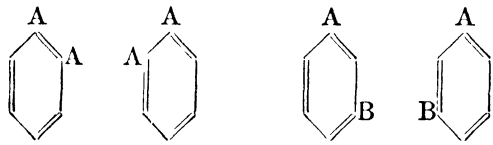
The symmetrical ring structure of benzene being thus satisfactorily established, the problem narrows itself down to ascertaining the fate of the fourth carbon bond. Much ingenuity has been displayed in devising formulae, both statical and dynamical, which should solve this problem.

Statical Formulae for Benzene. Ladenburg employed the proof of the symmetry of benzene to attack a vulnerable point in Kekulé's formula, which represents the carbon atoms as linked alternately by single and double bonds. On this assumption it necessarily follows

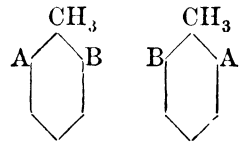
[1] *Proc. Roy. Soc.*, 89 A, 277; *Nature*, 1922, p. 115.

[2] Dimroth and Kerkovics, *Annalen*, 1913, 399, 120; Philippi, *Annalen*, 1922, 428, 286.

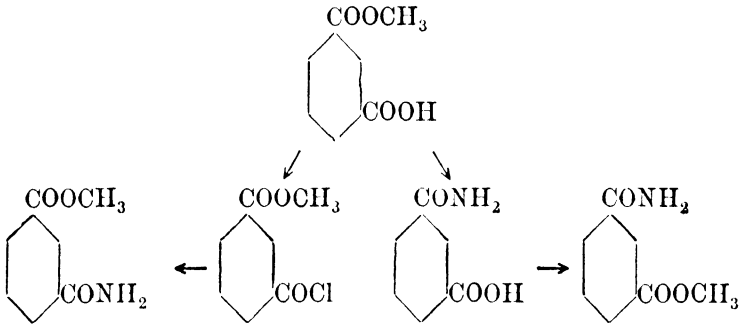
that in the di-derivatives two different ortho compounds 1, 2 and 1, 6 should exist, and, if the groups are different, two meta compounds also become possible.



No such differences have been observed. Noelting prepared a series of di-halogen derivatives from 2 6 dinitrotoluene, in which, in place of the nitro groups, two different halogens (A, B) were introduced in the inverse order, but he failed to detect any difference in the properties of the compounds.

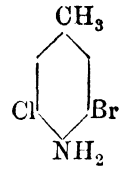


A similar process has been carried out by Wohl,[1] who converted the acid ester of isophthalic acid into the ester-amide in two ways, so that the ester and amide group were reversed; but the products were again identical.

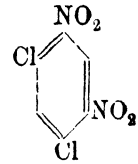


The author[2] has also prepared 3 5 chlorobromo *p*-toluidine by reversing the process of chlorination and bromination and obtained the same product.

[1] *Ber*, 1910, 43, 3474.
[2] *Trans. Chem. Soc.*, 1915, 107, 847.

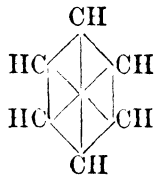


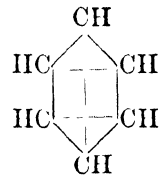
Borsche and Bahr,[1] on the other hand, assert that as only one chlorine atom in dinitro-dichlorobenzene,



reacts with ammonia and primary amines and at least readily with sodium acetoacetic and malonic esters (when the second chlorine atom is still reactive towards ammonia and amines) the two chlorine atoms are differently situated. Too much importance need not be attached to this conclusion, seeing that every new radical alters more or less the reactivity of the remaining atoms or groups, and consequently it could scarcely be expected that when one chlorine atom had been replaced the second one would exhibit identical properties.

To avoid the difficulty introduced by the double bonds, Claus proposed two formulae, which represent each carbon atom of the ring attached to three others, that is, to two in the ortho and one in the para position, or to two in the ortho and one in the meta position.



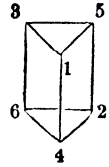


Claus[2] gave the preference to the first or *diagonal formula*, which appeared to suggest a reason for the simultaneous formation of ortho and para compounds, so often observed in reactions with benzene.

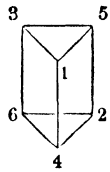
[1] *Annalen*, 1913, 402, 81.

[2] *Theoretische Betrachtungen und deren Anwendungen zur Systematik der organischen Chemie*, Freiburg, 1867, p. 207.

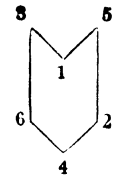
Ladenburg's Prism Formula. Ladenburg[1] adopted the second or prism formula. The six carbon atoms are placed at the corners of a regular prism, the edges of which denote the linkages.



The numbered positions correspond to the arrangement of the carbons in the hexagon, as determined by Körner's principle of orientation. The diagonal corners of the prism faces are ortho, those occupying the ends of the vertical edges are para, and those at the corners of the triangular faces are meta positions. Kekulé objected to Ladenburg's formula on the ground that it did not admit of the formation of additive compounds in a satisfactory manner. To convert benzene into cyclohexane it was necessary to have recourse to the doubtful expedient of breaking one para and two meta linkages:



Benzene, C_6H_6.



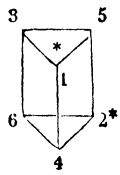
Cyclohexane, C_6H_{12}.

Moreover, the introduction of two different groups into the prism formula gives rise to molecular asymmetry, which implies the existence of optical enantiomorphs. All attempts to resolve such compounds have been fruitless (p. 228), and, what is even more significant, there is no single instance of an optically active compound of benzene, among the many derivatives found in nature, which owes its activity to the asymmetry of the nucleus. But the most complete refutation of Ladenburg's formula has been furnished by Baeyer. He showed that, of the three hexahydrophthalic acids, it is only the ortho compound which readily forms an anhydride, for the meta compound must be heated with acetyl chloride to give it, and the para compound under no conditions exhibits this change.

According to Ladenburg's formula, phthalic acid on reduction

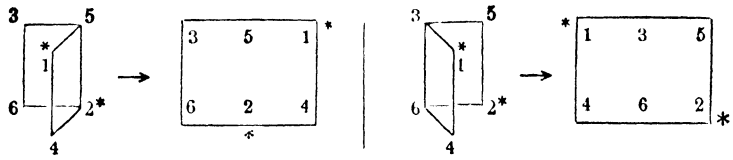
[1] *Ber.*, 1869, 2, 141, 272.

should produce a meta or a para cyclohexane derivative, depending upon which sets of bonds are removed. The process may be graphically represented in such a way that, after the three links are removed, the two prism faces are folded back like the covers of a half-open book.



* = COOH

Phthalic Acid.



Meta. Para.

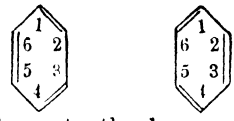
Hexahydrophthalic acid according to the prism formula.

It is difficult to reconcile these formulae with the existence of an anhydride, which is more stable than that produced by carboxyls in the ortho position, as denoted by Kekulé's formula.

In reply to Ladenburg's criticism of Kekulé's formula, V. Meyer[1] pointed out that the difference in the two ortho positions was not produced by any alteration in the relative positions of the atoms, as, for example, in the α- and β-derivatives of acrylic acid or propylene, but only by the more delicate distinction of single and double bonds, the exact significance of which is unknown.

Kekulé's Dynamic Hypothesis. Kekulé[2] took a similar view of the question. In order to account for the existence of only one ortho derivative, he brought forward his dynamic hypothesis. Valency, he suggested, may have a mechanical meaning, representing the number of contacts with other atoms experienced by an oscillating atom in unit of time. Two atoms of quadrivalent carbon, linked by one combining unit of each, will perform four complete oscillations, striking each other and also three other atoms in the unit of time, during which period the univalent atom of hydrogen will make a single oscillation. A doubly linked carbon atom will come in contact twice with its neighbouring carbon atom in the same period and also strike two other atoms.

[1] *Annalen*, 1870, 156, 265; 1874, 180, 24.
[2] *Annalen*, 1872, 162, 85.



Applying this hypothesis to the benzene formula, carbon 1 will strike carbon 2 twice, hydrogen once, and carbon 6 once in the following order:

2, 6, H, 2.

In the second period the order will become:

6, 2, H, 6,

in which carbon 6 is struck twice and carbon 2 once, to be followed in the third period by a recurrence of the first order and so forth. This will naturally take place with all the atoms of the ring. Kekulé supposes that if the first of the above formulae for benzene represents the contacts made during the first unit of time, constituting the first phase, the second formula will depict the second phase, and, as these phases are constantly alternating, there will be an equal number of molecules at any one moment in both phases. The difference between the two ortho positions is, therefore, more apparent than real. But this hypothesis would imply a more rapid motion of the carbon than of the hydrogen atom, which is opposed to the kinetic theory.[1] On the other hand, the observations which have been discussed under tautomerism (p. 369) make it conceivable that some such oscillatory motion of atoms or groups may occur.[2]

Baeyer's Researches on the Constitution of Benzene. In his classical research 'On the Constitution of Benzene', Baeyer[3] sought to decide between the two formulae of Claus and Kekulé, which had alone survived, by an exhaustive inquiry into the reduction products of the phthalic acids. Although this investigation has greatly extended our knowledge of the hydrocyclic compounds, and exhibited their striking analogy with the aliphatic compounds, it cannot be said that the main problem has approached much nearer to its solution.

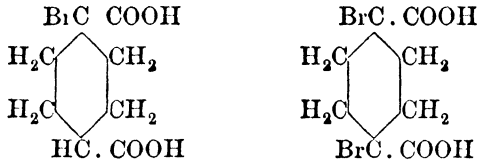
Baeyer himself has frankly admitted as much. 'The task,' he says, 'which I set before me on commencing these researches was to elucidate the constitution of benzene, and not to seek an experimental verification of any particular hypothesis. As a consequence of this resolution I have more than once changed my views, according as

[1] Michaelis, *Ber.*, 1872, 5, 463.

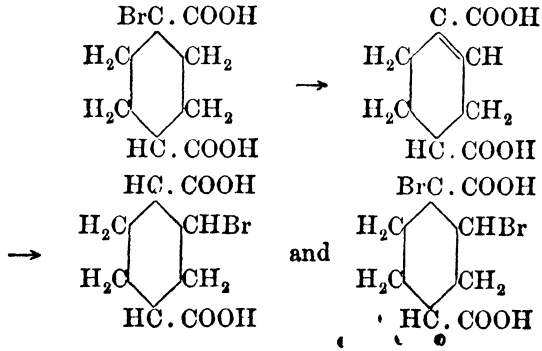
[2] In this connection Knoevenagel's theory of the atomic motion of unsaturated carbon atoms may be mentioned, *Ber.*, 1903, 36, 2803. In the case of benzene each of the carbon atoms is supposed to rotate in opposite directions to its neighbours, thus alternately making and breaking the double link.

[3] *Annalen*, 1887, 245, 103; 1889, 251, 257; 1890, 256, 1; 258, 1, 145; 1892, 266, 169; 269, 169.

the sum of experimental evidence appeared to favour one or another theory. And I would ask the reader not to be astonished because I now give prominence to a hypothesis which I have previously combated, nor to hold me inconsistent if I should chance in the course of time to transfer my allegiance to another theory. . . . No conclusion can be drawn as to the structure of benzene derivatives from their behaviour on reduction.'[1] Baeyer's attention was first directed to the diagonal formula of Claus, with the object of ascertaining whether diagonal or *para linkages* exist, and as a preliminary step he began by studying the conditions under which they might conceivably be formed. Terephthalic acid yields, on reduction, hexahydroterephthalic acid, and the latter, on treatment with bromine, is converted into a mono- and a di-bromo compound having the following constitution:

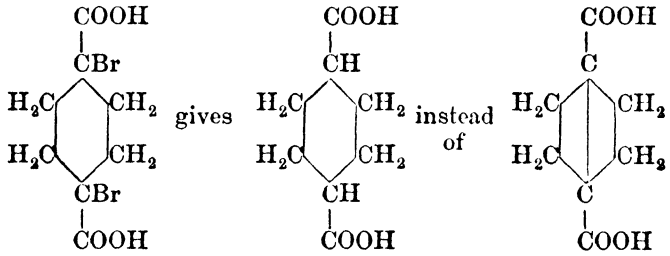


By analogy with the general behaviour of acids on bromination the bromine attaches itself to the α-carbon. The experimental verification of the above structure of the bromine derivatives is as follows: by the action of alcoholic potash on the monobromo compound hydrogen bromide is removed, and a tetrahydroterephthalic acid is formed which reunites with hydrogen bromide to give a different monobromo derivative from the original, and also with bromine to form a dibromo compound which is isomeric with that obtained by direct bromination. These changes can only be satisfactorily explained on the above assumption, namely, that the bromine enters the α-position.

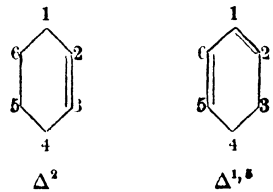


[1] *Annalen*, 1892, 269, 176; see also *Year-Book of Science*, 1898, 225.

The two dibromo compounds show a remarkable difference in their behaviour with zinc dust and acetic acid. Whereas the bromine is readily removed from the compound which contains the bromine atoms in the ortho position, re-forming tetrahydroterephthalic acid with a double link between the two ortho carbons, the effect on the bromine atoms in the para position is to replace them by hydrogen and form the original hexahydro acid. No para linkage is therefore produced where, according to Claus's formula, it would be most natural to expect its appearance.



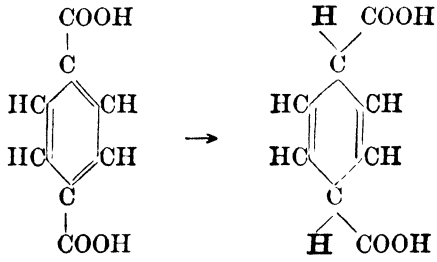
The diagonal formula was accordingly rejected, only to be reinstated later in a modified form. The change of view was the result of observations made by Baeyer in extending his experiments on the reduction products of the phthalic acids, which will now be briefly described. It should first be stated that the large number of products obtained by the reduction of phthalic,[1] isophthalic,[2] and terephthalic[3] acids has necessitated a special system of notation. The carbon atoms of the nucleus being numbered from 1 to 6 in the order of the figures on a clock face, the position of the double bond is indicated by the Greek Δ followed by the number of the initial carbon of the double linkage, as in the following two examples.



Baeyer found that on reducing the phthalic acids with sodium amalgam in alcoholic solution the hydrogen atoms attach themselves to the α-carbon, i.e. to the carbon which carries the carboxyl group.

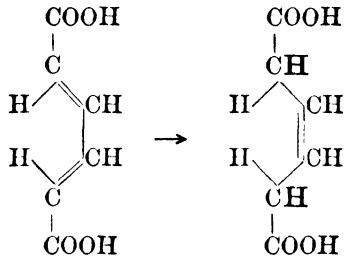
[1] *Annalen*, 1890, 258, 145; 1892, 269, 145.
[2] *Annalen*, 1893, 270, 255
[3] *Annalen*, 1888, 245, 103; 1889, 251, 257; 1890, 258, 1.

The same thing was observed in the case of unsaturated open-chain acids, like muconic and piperic acid, and was ascribed by Baeyer to the electro-negative character of the α-carbon.[1] For example, the first reduction product of terephthalic acid is the $\Delta^{2,5}$ dihydro acid,



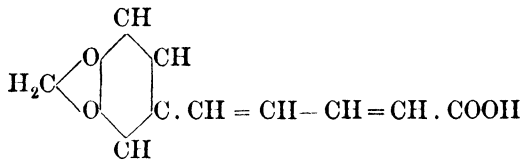
Terephthalic acid. $\Delta^{2,5}$ Dihydroterephthalic acid.

whilst muconic acid is converted into βγ-dihydromuconic acid,

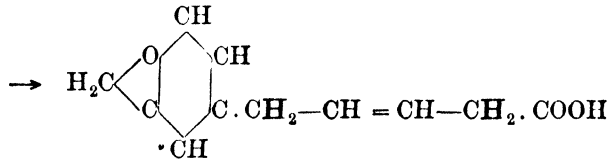


Muconic acid βγ-Dihydromuconic acid.

and piperic acid yields βγ-dihydropiperic acid.



Piperic acid.



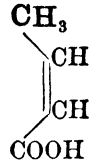
βγ-Dihydropiperic acid.

Baeyer explained the process as follows: 'Reduction only occurs if hydrogen ions can penetrate the molecule. The number is con-

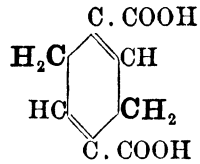
[1] *Annalen*, 1889, 251, 265.

ditioned by the number of negative groups, which makes reduction possible—in the present instance, by the carboxyl in conjunction with the double bond.'

If, however, the double bond is in proximity to a positive group—CH_2 or CH_3—as in crotonic or $\Delta^{1,4}$ dihydroterephthalic acid, reduction is very much impeded,



Crotonic acid.

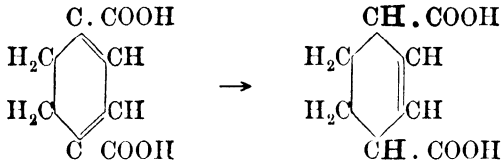


$\Delta^{1,4}$ Dihydroterephthalic acid.

whilst fumaric and $\Delta^{1,3}$ dihydroterephthalic acid readily undergo reduction to succinic and Δ^2 tetrahydroterephthalic acid respectively.

$$HOOC.CH=CH.COOH \longrightarrow HOOC.CH_2{-}CH_2.COOH$$

Fumaric acid. Succinic acid.



$\Delta^{1,3}$ Dihydro acid. Δ^2 Tetrahydro acid.

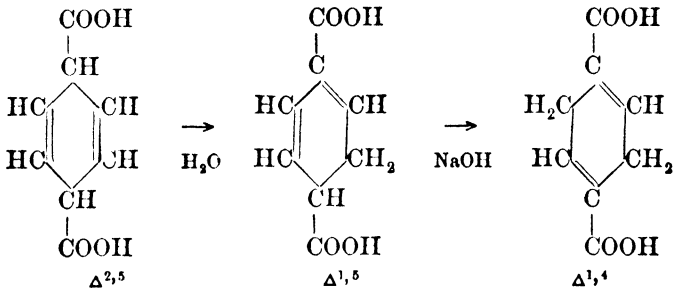
A very different explanation of the process has been advanced by Thiele[1] (Part I, p. 147), which will be briefly outlined, inasmuch as it forms the basis of a new view of the structure of benzene, to be presently discussed. Thiele supposes that each doubly linked atom, in addition to its ordinary bonds, is provided with a partial valency, and it is by means of this partial valency that union with other atoms is first effected. Moreover, the partial valencies of two adjoining atoms can unite or become 'conjugated', which causes them to lose their activity. Thus, in a system containing two pairs of doubly linked atoms separated by a single bond and known as a 'conjugated' system, the partial valencies of the middle pair can unite and thus become inactive, leaving the two end atoms free to combine. When this occurs, the bonds between the middle pair of atoms are transposed into an ordinary double bond. The stages in the process may be

[1] *Annalen*, 1899, 306, 125.

represented by the following scheme, in which the dotted lines indicate the partial valencies:

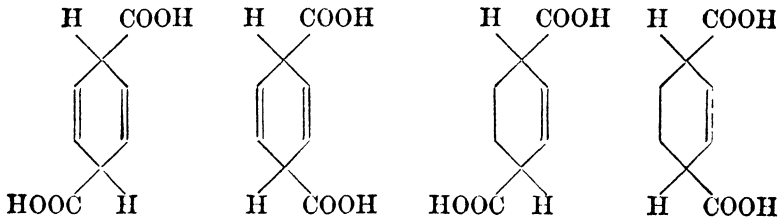
$$a = b—c = d \qquad a = b—c = d \qquad ax—b = c—dy$$

The theory explains the addition of only two hydrogen atoms and the positions which they occupy on reducing such compounds as muconic, piperic, and terephthalic acid, &c. To return now to the reduction of terephthalic acid, the first product is the $\Delta^{2,5}$ dihydro acid. No further reduction takes place until a double bond has been displaced towards the α-carbon, a process which has already been discussed (p. 420), and may be accomplished in the case of $\Delta^{2,5}$ dihydroterephthalic acid in two steps, the first by boiling with water which gives the $\Delta^{1,5}$ isomer, and the second by boiling with dilute solutions of caustic alkalis which transforms the latter into the $\Delta^{1,4}$ acid.



Tetrahydroterephthalic acids.

The $\Delta^{1,5}$ acid can now be reduced and yields Δ^{2} tetrahydroterephthalic acid. Both the $\Delta^{2,5}$ and Δ^{2} acids exist in stereoisomeric forms, each pair bearing a similar relation to one another as maleic acid bears to fumaric acid (p 264).

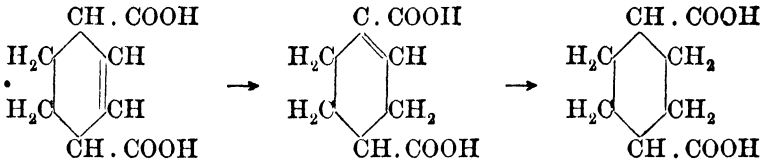


Trans. Cis. Trans. Cis.

$\Delta^{2,5}$ Dihydroterephthalic acid. Δ^{2} Tetrahydroterephthalic acid.

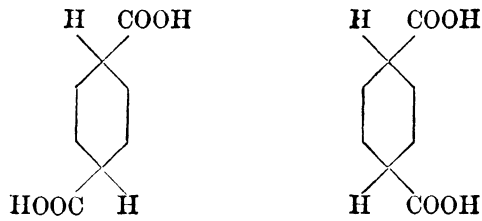
The action of caustic alkalis on the Δ^{2} acid causes the double

bond to shift to the Δ^1 position, and the acid, thus produced, yields hexahydroterephthalic acid on reduction.



Δ^2 Tetrahydro acid. Δ^1 Tetrahydro acid. Hexahydro acid.

The hexahydro acid also exists in stereoisomeric forms which may be represented by the following formulae (p. 278):

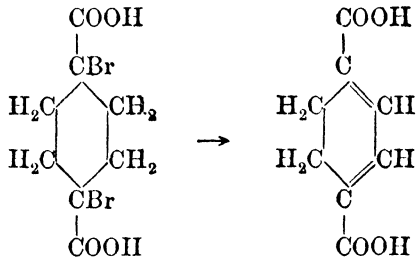


Trans. Cis.

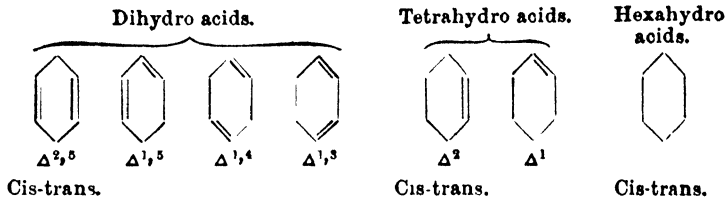
Hexahydroterephthalic acid.

The last of the series of possible isomers is derived from the $\alpha\alpha_1$-dibromohexahydro acid already described (p. 418), from which alcoholic potash removes two molecules of hydrogen bromide.

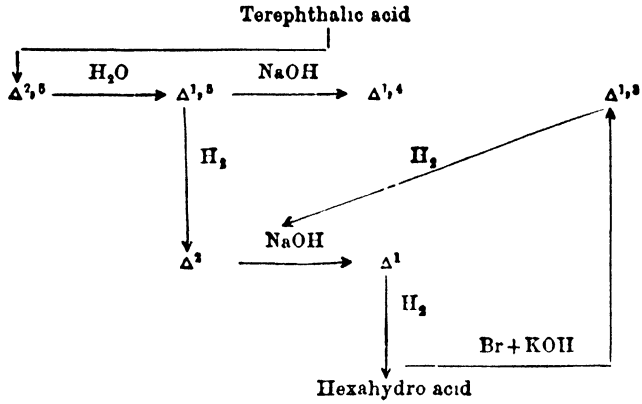
The product is $\Delta^{1,3}$ dihydroterephthalic acid



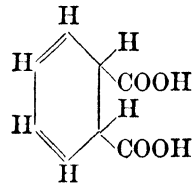
There are other ways in which reduction may be effected, such as the action of zinc dust and acetic acid on the hydrogen bromide additive compounds, but it is unnecessary to enter into further detail. It is sufficient for the present purpose to indicate the manner in which the complete series of reduced terephthalic acids have been prepared. They may be tabulated as follows:



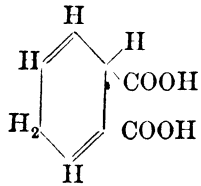
Their relation to one another is indicated in the following table.



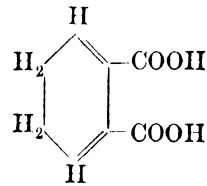
Similar results were obtained with phthalic and isophthalic acids, with α and β naphthoic acids, benzoic acid, &c., all of which form a series of hydro acids. Thus, phthalic acid, in accordance with the rule by which the hydrogen attaches itself to the α-carbon, gives in the first place a $\Delta^{2,5}$ dihydro acid, having the following structure:



This, by the shifting of the double bond, forms the $\Delta^{2,6}$ dihydro acid, the intermediate $\Delta^{2,5}$ acid being probably very unstable.[1]



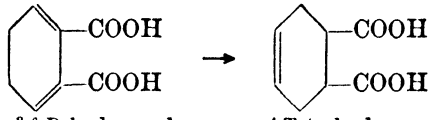
$\Delta^{2,5}$ labile.



$\Delta^{2,6}$ stable.

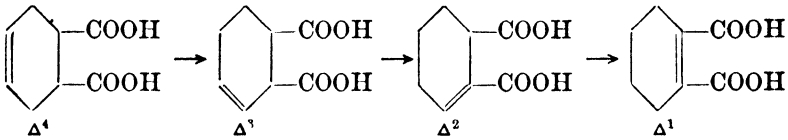
[1] See G. Abati, *Abstr. Chem. Soc.*, 1906, 1, 955; 1907, 1, 419.

The latter undergoes reduction, but in an abnormal fashion, the hydrogen probably attaching itself not to the α-carbons but to those in positions 3 and 6 according to Thiele's rule, and the double link shifts at the same time to the Δ^4 position.



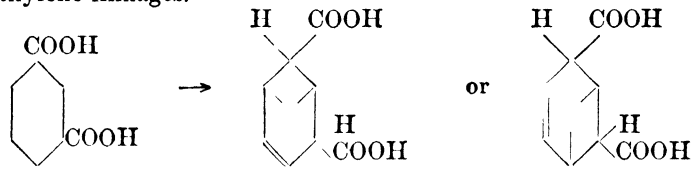
$\Delta^{2,6}$ Dihydro acid. Δ^4 Tetrahydro acid.

The latter on boiling with caustic soda solution may be converted successively into the Δ^3, Δ^2, and Δ^1 acids.[1]

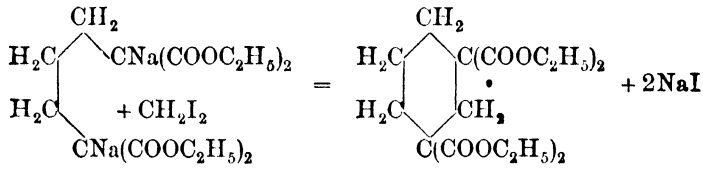


The symmetrically constituted acids exist, like the analogous terephthalic acids, as cis and trans isomers.

In the case of isophthalic acid great difficulty is experienced in effecting reduction, and Baeyer explains this by the fact that the attachment of the hydrogen to the α-carbons prevents the formation of ethylene linkages.

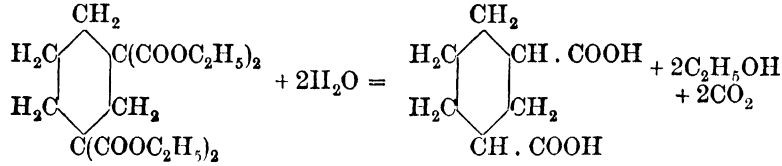


Nevertheless two tetrahydroisophthalic acids have been obtained by direct reduction[2], and also a hexahydro acid in cis and trans forms[3], whilst a dihydro acid and two other tetrahydro acids have been prepared by indirect methods. In this connection should also be mentioned the important synthesis of cis and trans hexahydro-isophthalic acid by Perkin, jun.,[4] from di-sodium pentane tetra-carboxylic ester and methylene iodide.



[1] *Annalen*, 1890, 258, 167, 212.
[2] Perkin, Pickles, *Trans. Chem. Soc.*, 1905, 87, 293, 841.
[3] Baeyer, *Annalen*, 1892, 269, 173, 195.
[4] Perkin, *Trans. Chem. Soc.*, 1891, 59, 808.

The latter on hydrolysis loses carbon dioxide and gives the hexahydro acids.



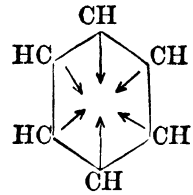
This synthesis, as previously mentioned, is a clear indication of the ring structure of benzene and its reduction products.

Aliphatic Character of Hydrocyclic Compounds. We have already perceived the close analogy which subsists between the hydrophthalic acids and the saturated and unsaturated acids of the aliphatic series, their behaviour on bromination, the position taken up by the hydrogen on reduction, the shifting of the double bond, &c. This analogy may be extended, for the double bond of the di- and tetra-hydro acids possesses the unsaturated character of true ethylene linkages. These compounds unite readily with hydrogen bromide, as well as with bromine, and the hydrogen bromide and bromine additive compounds lose hydrogen bromide on treatment with alcoholic potash and become unsaturated. Moreover the di- and tetra-hydro acids show the general behaviour of unsaturated fatty acids in rapidly decolourising alkaline permanganate in the cold. The olefinic character of the partly reduced acids is reproduced in the di- and tetra-hydro benzenes which resemble true olefines, whereas the saturated ring structures as represented by cyclohexane and other cycloparaffins possess the characteristic properties of the paraffins.

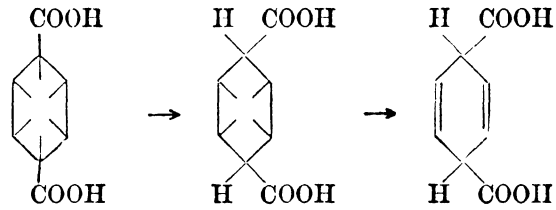
In marked contrast to these compounds stands benzene with many of its substitution products. Terephthalic acid, for example, unlike the di- and tetra-hydro acids, is neither oxidised by permanganate in the cold nor combines to form additive compounds with bromine or hydrogen bromide. How is this difference in chemical behaviour to be reconciled with the presence of three ethylene linkages in benzene? This is the question to which Baeyer has tried to find an answer in the results of his research on the reduction products of the phthalic acids. Adopting a suggestion of Armstrong,[1] he supposes that the fourth carbon valency is directed towards the centre of the benzene ring though not actually linked to its opposite neighbour in the para position, as represented in Claus's original

[1] *Trans. Chem. Soc.*, 1887, **51**, 264 (footnote).

formula. This *centric bond* is not a real but a potential bond exciting a directive force or pressure towards the centre of the molecule. The formula is known as the *centric formula*, and can be pictured by the following diagram, in which the centric bonds appear as arrows:

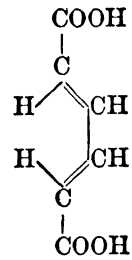


Baeyer does not regard this formula as representing the structure of all benzene derivatives. For certain compounds, such as phloroglucinol, which are readily oxidised by permanganate, the Kekulé formula is retained. 'The benzene nucleus,' he says, 'can exist in two forms which can be regarded as tautomeric in the sense that a definite structure is attached to each individual derivative.'[1] The centric formula enables the reduction of the phthalic acids to be represented by a simple mechanical device. Thus, the first two hydrogen atoms attach themselves to the two α-carbons, and thereby remove two centric bonds in the para position. The result is the linking up of the remaining two pair of bonds forming true ethylene linkages.

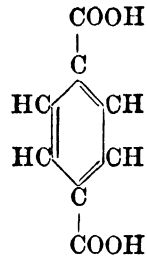


Baeyer nevertheless recognizes that the Kekulé formula is capable of expressing equally well the formation of $\Delta^{2,5}$ dihydroterephthalic acid; for the behaviour of muconic acid on reduction furnishes an exactly parallel case with that of the attachment of the two hydrogen atoms to the α-carbons in terephthalic acid and the consequent shifting of the double bond.

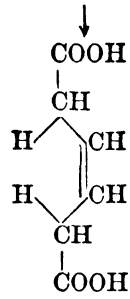
[1] *Annalen*, 1892, 269, 188.



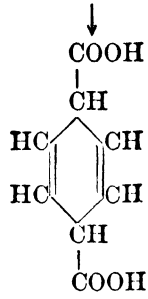
Muconic acid.



Terephthalic acid.

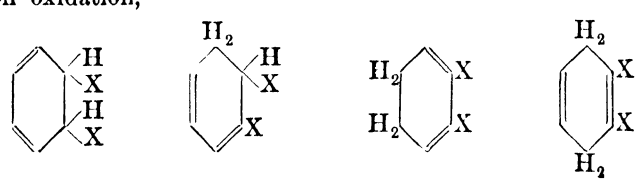


Dihydromuconic acid.



Dihydroterephthalic acid.

Baeyer[1] in fact admitted that the structure of benzene derivatives could not be determined by their behaviour on reduction. He therefore turned to the reverse process—the oxidation of the hydro acids—and sought for evidences of structure in the behaviour of these compounds. It must be confessed that the results of this inquiry appear incomplete and unconvincing. Baeyer perceives in the fact that the $\Delta^{1,5}$, $\Delta^{2,4}$, and $\Delta^{2,6}$ dihydrophthalic acids give benzoic acid on oxidation,

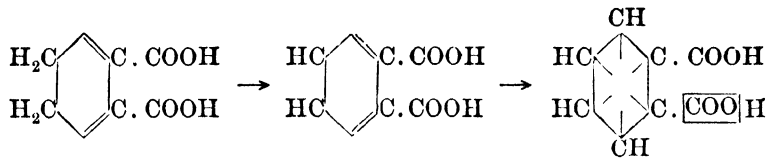


$\Delta^{1,5}$ $\Delta^{2,4}$ $\Delta^{2,6}$ $\Delta^{1,4}$

(X = COOH)

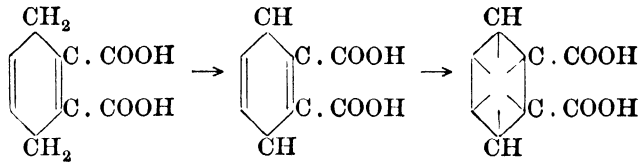
whilst the $\Delta^{1,4}$ acid gives phthalic acid, a shock (Erschütterung) to the α-carbon in the three former cases, which causes it to lose carbon dioxide, this effect being associated with the change from ethylene to centric linkages thus:

[1] *Annalen* 1892. 269. 178.



$\Delta^{2,6}$ Benzoic acid.

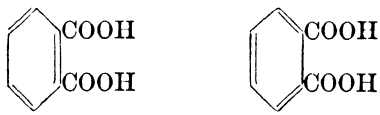
The formation of benzoic acid from the $\Delta^{3,5}$ dihydro acid, in which oxidation does not directly affect the α-carbons, is accounted for by the carbons in the para position to the α-carbons being involved in the change, whereas oxidation of the $\Delta^{1,4}$ acid neither directly nor indirectly touches the α-carbons.



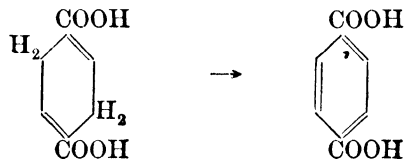
$\Delta^{1,4}$ Phthalic acid.

Brühl,[1] in a careful examination of this theory, asks why only one molecule instead of two molecules of carbon dioxide is removed from the $\Delta^{2,6}$ acid, and (he also might have added) from the $\Delta^{3,5}$ dihydro acid, both of which are symmetrical structures.

It might be urged in favour of Kekulé's formula that, of the two possible phthalic acids, only the first is stable.



This would be formed by the oxidation of the $\Delta^{1,4}$ dihydro acid, whilst the second should appear when the $\Delta^{2,6}$ acid is oxidised. The loss of carbon dioxide in the second case might be attributed to the shock attending the rearrangement of double linkages; but as $\Delta^{1,4}$ dihydroterephthalic acid yields terephthalic acid on oxidation, when likewise a change in the double bonds must be assumed to occur, this argument is untenable.



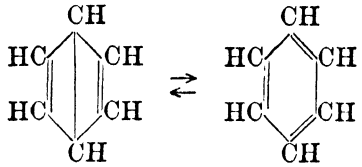
$\Delta^{1,4}$ Dihydroterephthalic acid. Terephthalic acid.

Brühl in his criticism has sought to explain the different chemical

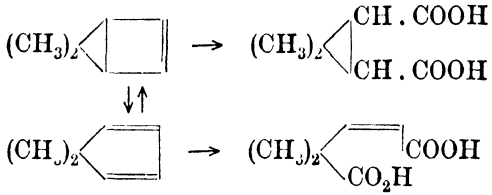
[1] *J. prakt. Chem.*, 1894 (2), 49, 299.

behaviour of the dihydro acids on the very simple basis of their difference of stability, and such a view has the advantage of being independent of any structural hypothesis. At the same time he apparently fails to perceive that by avoiding any reference to structure as affecting stability he is 'begging the question'.

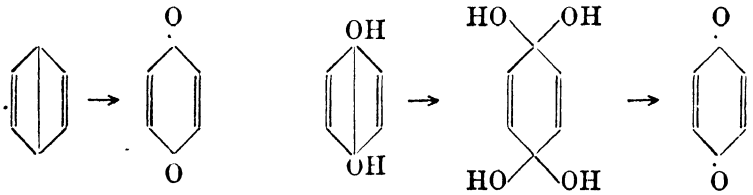
Dewar's Formula for Benzene. Latterly a suggestion has been made by Ingold [1] that the so-called Dewar formula might represent a tautomeric phase of benzene.



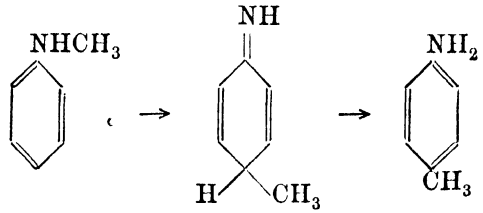
He bases it on a number of observations, such, for example, as the two oxidation products of a bridged cyclopentene ring,



the electrolytic oxidation of benzene to benzoquinone, of the oxidation of quinol to quinone,



of the tautomerism of phenol, of the conversion of methyl aniline to *p*-toluidine, &c.



[1] *Trans. Chem Soc.*, 1922, **121**, 1133.

This view has received some support from the crystal structure of benzene, which requires a fourfold symmetry, which according to Shearer[1] is best represented by the Ladenburg or Dewar formula.

Evidence of Physical Properties. The data afforded by the values of the melting-points and solubilities of phthalic acid and its anhydride appear to be the mean of those calculated by Baeyer[2] for the two formulae:

and have been used as evidence in favour of the centric formula; but when it is considered that the calculated constants are derived from the somewhat artificial analogies instituted between the isomeric di-, tetra-, and hexa-hydro acids, and that, in addition, we are profoundly ignorant of any connection between these physical constants and structure, the evidence cannot be regarded as entirely trustworthy. Of greater interest are the optical and thermo-chemical constants of benzene and its derivatives. From determination of the molecular refraction and dispersion of benzene and di-, tetra-, and hexa-hydrobenzene, Brühl has arrived at the conclusion that three double linkages are present in benzene, since benzene and its homologues give normal values for three double bonds, and diallyl, hexylene, and hexane show a corresponding increment for each double bond. The following table is taken from Brühl's paper:[3]

	Density d 20/4	*Refractive Index* at 20°	*Mol. Vol* at 20°	*Sp. Ref.* $\frac{n^2-1}{(n^2+2)d}$	*Mol. Ref.* $\left(\frac{n^2-1}{n^2+2}\right)\frac{M}{d}$	
					H_a	D
Benzene	0·8799	1 4967	88 65	0 3324	25 93	26·18
Dihydrobenzene	0 8478	1 4699	94 36	0 3291	26 33	26·51
Tetrahydrobenzene	0 8102	1 4435	101·21	0 3277	26 87	27 01
Hexahydrobenzene	0 790	1 426	107 2	0 3255	27·56	27 66[4]
Dipropargyl	0 8049	1 4402	96 91	0·3278	25·57	25 74
Diallyl	0 6880	1 3981	119 18	0 3509	28 77	28 96
Hexylene	0 6825	1 3939	123 08	0 3506	29 45	29·61
Hexane	0 6603	1 3734	130·25	0 3454	29 70	29·84

[1] *J. Soc Chem. Ind.*, 1922, 41, 562 R. [2] *Annalen*, 1892, **269**, 186.
[3] *J. prakt. Chem.*, 1894 (2), 49, 250.
[4] The value for hexahydrobenzene represents the mean of those calculated from three independent sets of data which fluctuate between 27·91 and 27·31.

In order to institute a comparison between the aliphatic and aromatic series we may either take differences between successive or between corresponding members of each series.

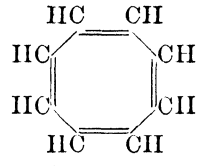
	M_D	Δ		M_D	Δ
Benzene	26 13				
		38			
Dihydrobenzene	26 51		Diallyl	28.96	
		50			.65
Tetrahydrobenzene	27.01		Hexylene	29 61	
		65			.23
Hexahydrobenzene	27 66		Hexane	29 81	

	M_D	Δ
Diallyl	28 96	
		2 45
Dihydrobenzene	26 51	
Hexylene	29 61	
		2 60
Tetrahydrobenzene	27 01	
Hexane	29 84	
		2 23
Hexahydrobenzene	27 66	

In examining the figures in the first of the above tables, it is clear that the differences among members of the same series are very small; for the molecular refractions are made up of two opposed factors, namely, the index of refraction which forms a decreasing series, and the molecular weights which form an increasing series from the less to the more hydrogenated compounds. When, in addition to this, it is considered that the difference between the minimum and maximum value calculated for hexahydrobenzene nearly covers the whole difference between tetra- and hexa-hydrobenzene, the significance of these figures becomes very small. The larger differences between the molecular refractions of members of the corresponding series is clearly due to ring formation. Very little reliance can therefore be placed on the direct evidence which molecular refractions afford of three double linkages in benzene. On the other hand, it seems clear that there is no sudden change of structure between benzene and its reduction products, such as occurs between hexane and hexahydrobenzene, or between dipropargyl with its two treble linkages, and diallyl with its pair of double bonds.

Later observations have introduced new features into the problem through the discovery of optical anomaly or increase (exaltation) of molecular refractivity in presence of conjugated double linkages

(p. 29). Hexatriene, $CH_2 : CH . CH : CH . CH : CH_2$, which is the open-chain analogue of benzene, has three conjugated double linkages and shows an increase of 2 06 units above the calculated value. Benzene, as stated above, exhibits no increase, and this is now taken to indicate the absence of double bonds.[1] Willstätter and Waser[2] have, however, obtained a cyclo-octatetrene,



Cyclo octatetrene.

which, while possessing all the properties of an unsaturated hydrocarbon with four double linkages (p. 30), exhibits at the same time normal refractivity like benzene (see p. 28). The evidence is very conflicting, and the conclusions which we are led to draw will depend upon the relative value which we attach to the chemical and physical behaviour of the hydrocarbon. It should, however, be pointed out that the greater reactivity of cyclo-octatetrene may very well depend on the less stable nature of the ring, for the benzene ring is subject to an even smaller strain of the carbon linkages (2° 35′) than a cyclohexane ring (5° 16′). Similar exaltation, produced by conjugated double linkages, has been observed in the case of magnetic rotation (p. 53), which, in the case of hexatriene, amounts to 3·776 units above that of diallyl, which is normal.

		M	Δ
Diallyl	$CH_2 : CH . CH_2 . CH_2 . CH : CH_2$	8 420	3 776
Hexatriene	$CH_2 : CH . CH \quad CH . CH : CH_2$	12·196	

Deducting from the magnetic rotation of hexatriene the value 0 982 for ring formation, the resulting number (11·214) is almost precisely that observed for the magnetic rotation of benzene (11·284). Benzene, therefore, exhibits the same magnetic-rotatory exaltation as hexatriene, and should therefore possess three double linkages.

From the results of molecular volume determinations (p. 13) Schiff[3] concluded that benzene contains nine single carbon linkages; but this view was subsequently opposed by Lossen and Zander,[4] and by Horstmann,[5] who gave their verdict in favour of Kekulé's formula from the results of a much more complete series of observations. For example, a comparison of the values for the double bond

[1] Smedley, *Trans. Chem. Soc.*, 1908, 93, 380. [2] *Ber.*, 1911, 44, 3423.
[3] *Annalen* 1883, 220, 303. [4] *Annalen*, 1884, 225, 109. [5] *Ber.*, 1887, 20, 766.

in open- and closed-chain compounds is much the same (about 7 units):

	V_m	Δ		V_m	Δ
Hexane	139 9	7·4	Cyclohexane	116·5	$\frac{20\,5}{3} = 6\,8$
Hexylene	132 5		Benzene	96 0	

but there is a large contraction in passing from an open to a closed chain, as observed in the case of cyclohexane, namely, 23·4 units (p. 13). If we compare in the same way the value calculated for tetrahydrobenzene, 96 + (2 × 6 8) = 109 6, with that of hexylene, 132·5 — 109·6 = 22 9, we find approximately the same contraction for the closed chain. There is no reason, therefore, for supposing that benzene possesses other than the Kekulé formula

The conclusions derived from thermo-chemical data are very conflicting. Thomsen's[1] determinations of the heats of combustion led him at first to conclude that benzene contains nine single bonds, a view which was also shared by Horstmann,[2] but he afterwards transferred his adherence to Kekulé's formula. Stohmann, on the other hand, from the evidence of a much more comprehensive series of observations, arrived at Thomsen's original conclusion that 'three equivalent double bonds cannot be present in the benzene nucleus. The bonds are most firmly attached in benzene itself, and more loosely in the di- and tetra-hydro compounds, reaching again a high degree of stability in hexahydrobenzene, which is, however, unequal to that of the original nucleus'. The following are the constants for the heats of combustion of benzene and its reduction products obtained by Stohmann and Langbein:[3]

	Mol grm. cals.	Δ
Benzene	779 8	68 2
Dihydrobenzene	848 0	44 0
Tetrahydrobenzene	892 0	41·2
Hexahydrobenzene	933·2	58 0
Hexane	991 2	

The differences correspond closely with those of terephthalic acid and its reduction products[4] (see p. 71).

	Δ
Terephthalic acid	
Dihydro acid	> 68 7 cals
Tetrahydro acid	> 45 3 ,,
Hexahydro acid	> 45·3 ,,
Sebacic acid	> 54·8 ,,

[1] *Ber*, 1880, 13, 1806; *Thermochem. Untersuch.*, 1886, vol. iv.
[2] *Ber*, 1888, 21, 2211. [3] *J. prakt. Chem.*, 1893 (2), 48, 447.
[4] The isomeric di and tetra-hydro acids differ slightly among themselves.

It seems not improbable, therefore, that benzene and terephthalic acid are similarly constituted.

As the heat of combustion of H_2 is 69 mol. grm. cals., it follows that during the graduated reduction of benzene 'the formation of dihydrobenzene utilizes almost the whole of the energy of the hydrogen molecule; in the second stage of reduction there is an excess of energy amounting to 25 cals. in the initial system, and in the third an excess of 27·8 cals., whereas in the final stage, where the benzene nucleus is dissolved, the energy of the initial system only amounts to 11 cals.'

From this Stohmann concludes that the 'jump' between the first and second terms of the series compared with the two following, as well as between the fourth and fifth, indicates a fundamental difference of structure between benzene and its di- and tetra-hydro derivatives, and also between tetrahydro- and hexahydro-benzene, which led him, as we have seen, to reject the Kekulé formula.

A careful redetermination of the values for the saturated and unsaturated aromatic hydrocarbons have led Roth and Auwers[1] to the following results, which differ somewhat from those of Stohmann. The differences (Δ) are given in mol. grm. cals.:

	Δ
Aromatic hydrocarbon and conjugated cyclohexadiene	64
Conjugated cyclohexadiene and cyclohexene	50
Cyclohexene and cyclohexane	45

In the case of the two dihydronaphthalenes, one being conjugated and the other not, there was a difference of 5 cals. less in the conjugated compound, or, in other words, it is the more stable. They consider that the nature of the conjugation and the symmetry of benzene would naturally produce greater stability and a smaller amount of free energy, and is not opposed to the presence of three double linkages.

Stohmann's conclusions have also been contested by Brühl,[2] who adopts an entirely different attitude in the interpretation of his results. He shows from Stohmann's own observations that substantial differences in heats of combustion are frequently found among isomeric and even stereoisomeric compounds, and that these effects mainly depend on the stability of the compounds in question. The unequal differences observed in the heats of combustion of the different states of hydrogenation of benzene depend on the stability of the individual compounds. When a body passes from a less to a

[1] *Annalen*, 1915, 407, 148. [2] *J. prakt. Chem*, 1894 (2), 49, 260.

more stable condition it loses heat energy, and, according to Brühl, the differences obtained by Stohmann are fully accounted for by the greater stability of benzene and hexahydrobenzene, compared with that of the intermediate compounds. This stability of the benzene molecule is attributed to the symmetry of the Kekulé formula. The argument might be applied with equal force to the diagonal formula, which is even more symmetrical.

But there are other reasons for doubting Stohmann's conclusions. In the first place, the value for the double bond varies greatly in different compounds, and even in compounds which are so closely related as geometrical isomers or the three dihydroterephthalic acids.

		Mol. grm. cals.	Δ
$\Delta^{1,4}$	Dihydroterephthalic acid	836 1	
$\Delta^{1,5}$	,,	842.7	6 6
$\Delta^{2,5}$	,,	845 8	9 7

The variation is still more manifest in the relation between conjugated and unconjugated double linkages. Conjugation means increased stability and consequently a relatively smaller heat of combustion. The conclusion is obvious that if there exists a difference between the highest and lowest value among isomeric dihydroterephthalic acids of 9 7 cals., it is impossible to foretell the effect of the additional double bond in terephthalic acid, except that it is almost certain to have a value very different from the mean of that which divides the di- and tetra-hydro acids.

The ultra-violet absorption of benzene both as liquid and vapour has been very carefully studied by Hartley[1] and Baly[2] (p. 90) and more recently by Stark[3] and Henri.[4] Stark, by means of a fluorspar spectrograph, has been able to examine the absorption spectrum of benzene vapour in a region beyond that previously observed. In this region there are indications of absorption by saturated hydrocarbons such as cyclohexane, as well as by unsaturated ring compounds such as cyclohexene and cyclohexadiene, which show well-marked broad bands The conjugation of linkages in the second case is indicated by the shifting of the bands towards the visible region and an intensification of the less refrangible band. Benzene shows an entirely different spectrum, and the conclusion is drawn that the character of the linking is of a special kind and different from the ethenoid type. It has yet to be shown that these marked differences in absorption

[1] *Phil. Trans*, 1908, A 208, 520. [2] *Phil. Mag.*, 1915, 30, 510.
[3] *Jahrb Radioaktive Elektrotechnik*. 1913, 10, 139, 175.
[4] *Comvt rend.*. 1922. 174. 809.

spectra are due to a difference in the character of the linkage and not to some other cause, seeing that wide discrepancies appear in the absorption bands of benzene and many of its simple derivatives (p. 91).

In conclusion it must be admitted that the evidence of physical properties has thrown little new light on the benzene problem.

Space Formulae for Benzene. Whatever view has been taken of the structure of benzene, it has sooner or later found expression in a space formula. Representing the carbon atoms by tetrahedra, Kekulé's formula will assume the following form:

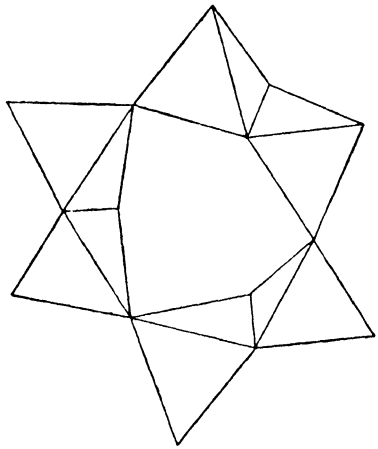


FIG 60. Kekulé's space formula.[1]

It will be noticed that the hydrogen atoms lie in the same plane with the carbon atoms, and consequently, however dissimilar the groups replacing hydrogen may be, no asymmetric molecule can be formed. Also, the breaking of a double bond by reduction obviously involves two carbon atoms.

In Baeyer's space formula[2] the tetrahedra are arranged in a compact ring, each with a face on the same horizontal plane, and with the hydrogen linkages pointing upwards, so that the hydrogen atoms lie in a parallel plane with the carbon atoms.

[1] This and the following figures are taken from Graebe, *Ber.*, 1902, 35, 526.
[2] *Annalen*, 1888, 245, 123; see also Erlenmeyer, jun., *Annalen*, 1901, 316, 57.

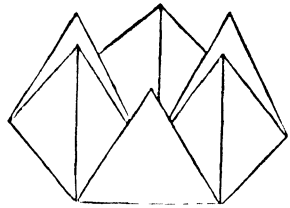


FIG. 61. Baeyer's space formula.

A similar arrangement to Baeyer's has been suggested by Marsh,[1] Vaubel,[2] and others.

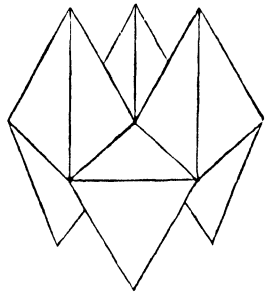


FIG 62. Vaubel's space formula.

In this formula the tetrahedra are arranged alternately above and below the middle plane so that three hydrogen atoms lie in one plane, three in another and the six carbon atoms occupy two parallel planes between them. In both Baeyer's and Vaubel's space formulae, hydrogenation does not necessarily involve more than one carbon atom at a time.

Another space formula of a very different type has been proposed by Sachse.[3] It is formed by cutting away two parallel faces of an octahedron and superposing tetrahedra on the remaining six faces.

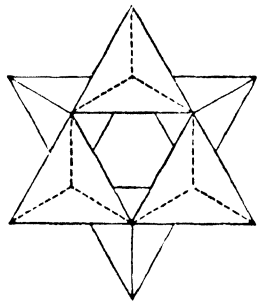


FIG. 63. Sachse's space formula.

[1] *Phil. Mag.*, 1888, 26, 426.
[2] *J. prakt. Chem.*, 1891, 44. 137; 1894, 49, 308; 50, 58.
[3] *Ber.*, 1888, 21, 2530; 1890, 23, 1363.

The model is easily made by cutting a piece of thin card of the following shape (Fig. 64), nicking it and bending it over where the dotted lines are drawn, and fastening the ends, when it will form an octahedron with two parallel faces missing.

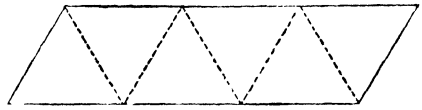


FIG. 64.

The tetrahedra are made in a similar way by cutting out and bending pieces of the following shape (Fig. 65).

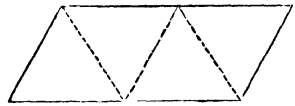
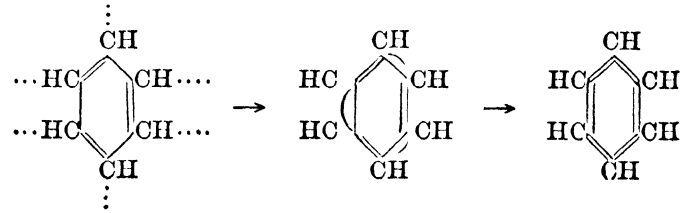


FIG. 65.

Each of the tetrahedra should be placed on one of the six faces of the octahedron, which will assume the form shown in Fig. 58, but each tetrahedron should be fastened only by an edge (with gummed paper) to the left-hand vertical edge of the face so as to enable the process of hydrogenation to be realized. In Sachse's model the hydrogen atoms lie in two parallel planes, whilst the carbon atoms occupy a parallel plane between them. Also, the hydrogenation of one carbon atom does not necessarily involve that of a second carbon atom.

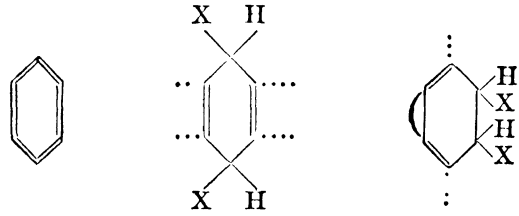
Sachse proposed the formula with the object of representing the most stable, compact, and symmetrical grouping of six tetrahedra, and it has received the support of Brühl [1] and of Thiele.[2]

On the theory of conjugated systems of double bonds, to which reference has already been made, Thiele [3] has pointed out that benzene represents a twofold conjugated system (Part I, p. 153). Supposing that each carbon atom of benzene possesses a partial valency, and that, as previously explained, adjoining partial valencies neutralize one another or become conjugated, the result will be equivalent to a potential double link between each pair of carbon atoms.



[1] *J. prakt. Chem.*, 1894 (2), 49, 236; *Zeit. phys. Chem.*, 1893, 11, 214.
[2] *Annalen*, 1901, 319, 136. [3] *Annalen*, 1899, 306, 125.

Such an arrangement will, according to Thiele, explain the stability of benzene, its difference from ordinary olefinic compounds with three double bonds, and, more especially, its behaviour on reduction; for if hydrogen is added in the ortho or para positions, as in the reduction of phthalic or terephthalic acid, the conjugated double bond is transformed into an ordinary olefinic linkage.



The first acquires four partial valencies, and can consequently unite with four atoms of bromine, whilst the second is endowed with two and can therefore only form a dibromo-derivative, which, as Thiele points out, is in complete agreement with Baeyer's observations. Various other arguments are brought forward in support of this formula for which the original paper must be consulted.

Thiele adopts Sachse's formula as the effective space representation of his view of the structure of benzene. When examined it will be observed that each carbon atom is linked by two pairs of bonds to its neighbours and by one to hydrogen. Each carbon is apparently provided with five bonds; but as two pairs are conjugated they are to be regarded, it is presumed, like centric valencies, that is, as modified in character.

It is not our intention to discuss the arguments for and against each of the above space formulae; but it may be observed that any formula to be satisfactory must represent in a simple fashion the symmetry of the molecule, the process of hydrogenation, the anhydride formation of ortho compounds and the relation to naphthalene and other multinuclear hydrocarbons. These points have been discussed in detail by Graebe,[1] who finds that Kekule's formula is the only one which meets the many demands made upon it. It may be stated also that, with the single exception of Kekulé's formula, there is one inherent defect in all. Unless the carbon and hydrogen atoms lie in the same plane, the replacement of two hydrogen atoms by different groups in the ortho or meta position leads at once to asymmetry and to the possibility of optical enantiomorphs. It has already been pointed out in connection with Ladenburg's formula (p. 415) that neither among artificial nor

[1] *Ber.*, 1902, 35, 526.

natural products have substituted benzene derivatives of this character been observed.

In reviewing the more important evidence which has been accumulated on the subject of the benzene formula there seems to be no statical representation which explains so large a number of facts as Kekulé's formula. When it has been proved that simple benzene derivatives can exist in optically active forms it will be time to reconsider the position.

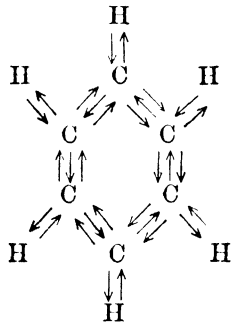
Dynamic Formulae for Benzene. At a very early period in the history of the benzene formula, Kekulé put forward a dynamic hypothesis to explain the equivalence of the two ortho positions (p. 416). This was followed by Knorr's oscillation formula, in which only the hydrogen atom was assumed to oscillate between each pair of carbon atoms. Knorr's view, which bears a close resemblance to Laar's theory of tautomerism, was the direct consequence of the observation establishing the identity of methyl pyrazole obtained from two different phenylmethyl pyrazoles, and has already been discussed (p. 346). In 1897 a new dynamic formula was proposed by Collie,[1] in which the carbon groups as a whole are supposed to rotate as well as change their relative positions. Without a model it is impossible to describe the evolutions of this mobile system; but it is claimed that it represents in turn the Kekulé and centric arrangement as phases of the one formula. Latterly, the study of the absorption bands in the ultra-violet region of the spectrum has led to views on the dynamical condition of benzene, which promise a very interesting development. According to Hartley,[2] six, or according to Baly and Collie,[3] seven, distinct absorption bands are produced by benzene. These bands are accounted for by synchronous oscillations of the molecule, in much the same way as a tuning-fork vibrates in response to a note of definite pitch. The nature of these molecular vibrations are, however, differently interpreted by the two observers. Hartley supposes the carbons to be rotating and alternately passing through a double and single (or centric) link phase. If the passage from single to double linking produces a band, the first phase which involves the making of three double links will produce three bands and the second phase another three bands, making six together, though it is not obvious why the same recurrent process should produce six sets of oscillation frequencies. Baly and Collie take a different view. The oscillations are connected with dynamic

[1] *Trans. Chem. Soc.*, 1897, 71, 1018. [2] *Trans Chem. Soc.*, 1905, 87, 1822.
[3] *Trans. Chem. Soc.*, 1905, 87, 1332.

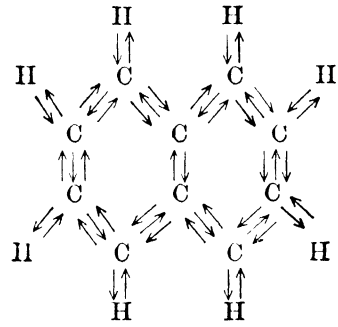
change involved in the making and breaking of the links between one or more pairs of carbon atoms.

Now, it is possible to produce from the six carbon atoms, constituting benzene, seven combinations of one, two, and three pairs of carbon atoms. If making and breaking of links occurs between these pairs, it will set up vibrations in the benzene ring which correspond to the seven absorption bands, and these vibrations are compared with an expanding and contracting elastic ring.[1]

Electronic Formulae for Benzene. One electronic formula for benzene, proposed by Fry in order to explain the process of substitution, has already been described (Part I, p 174). Another formula based on the theory of dual affinity (Part I, p. 101) has been suggested by Sir J. J. Thomson,[2] and takes the following form for benzene and naphthalene:



Benzene.



Naphthalene.

The formulae are derived from the accepted structural grouping of the atoms, and have contributed little to the solution of the benzene problem.

Structure of Crystalline Benzene. According to Bragg the unit

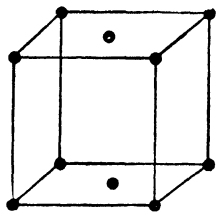


FIG. 66. Position of the benzene molecules in the unit cell.

[1] *Trans. Chem Soc.*, 1906, 89, 524; see also Wilnberg. *Ber.*, 1919, 52, 930.
[2] *Phil. Mag*, 1914, 27, 784.

cell contains a molecule at each of the four corners and one at each face, as in the figure.[1]

Moreover, the carbon atoms of the ring are disposed in two planes so that they lie alternately one in front and one behind.

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Lehrbuch der organischen Chemie, by V. Meyer and P. Jacobson, vol II, p. 41. Veit, Leipzig, 1902.

Rise and Development of Organic Chemistry, by C. Schorlemmer, edited by A. Smithells. Macmillan, 1894.

[1] In order to ascertain the arrangement of the molecules in a benzene crystal and their actual distances apart, it is necessary first to determine the crystal system to which the substance belongs. The system is given by the angle and length of the crystal axes. Benzene is orthorhombic, that is, the three axes are at right angles and of unequal length. It contains a certain number of planes of symmetry which are denoted by the symbols 1 and 0, by which is implied that in the first case (1) the plane touches the axis at unit distance from the centre, and in the second (0) it is parallel to that axis.

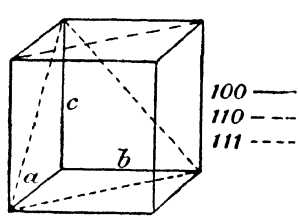

Fig. 67.

In the figure the three planes touching the *b* axis are indicated by 100, 110, and 111

b	*a*	*c*
1	0	0
1	1	0
1	1	1

and so on for the other two axes.

The relative length of the axes has been determined by ordinary crystallographic measurements to be $a : b : c = 0{\cdot}891 : 1 : 0{\cdot}799$

In order to ascertain the actual value of *b* and also *a* and *c* in Å.U. one proceeds as follows:

The volume is $0{\cdot}891 \times 0{\cdot}799 \times b^3$ in Å.U. ($= 10^{-24}$ c.c).

The density is 0·956.

Therefore the mass $= b^3 \times 0{\cdot}891 \times 0{\cdot}799 \times 0{\cdot}956$ Å.U. (10^{-24} gram).

The molecular weight of two molecules of benzene $= 2 \times 78$

The weight of a H atom = 1·662 Å.U. (10^{-24} gram).

Therefore $b^3 \times 0{\cdot}891 \times 0{\cdot}799 \times 0{\cdot}956 = 2 \times 78 \times 1{\cdot}662$.

From which $b = 7{\cdot}23$, $a = 6{\cdot}45$, $c = 5{\cdot}80$.

The calculated values for the spacings from the above values and those found when two molecules are present in the cell are :

	Calc	Found.	
100	3·22	3·12	weak
110	4 83	4·80	strong
111	3 72	3 67	strong

Now two molecules in the cell arranged according to these values must be placed one at each corner and one at the centre of the two horizontal faces as indicated above. At first sight it would appear as if there were ten molecules in the cell ; but it must be remembered that the eight at the corners are shared by eight contiguous cells and the two in the centre of each face by two other cells, so that each single cell only shares one-eighth of the corner molecules and one-half of the face molecules, or in other words there are on the average only two molecules to the cell.

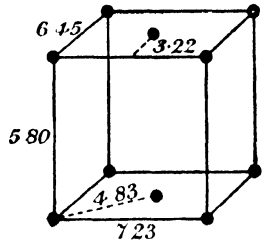

Fig. 68.

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