a concise text-book of organic chemistry

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preface

THIS book is an attempt to present in a handy format a concise account of organic chemistry, such as would be required for revision purposes by students preparing for the Advanced Level — General Certificate of Education examination (including the Special Paper) and for Ordinary National Certificate examinations. It will also be found helpful to students taking the first year Organic Chemistry courses in certain University scientific and related courses, e.g. agricultural, medical, pharmaceutical, etc., and in the corresponding courses in Colleges of Advanced Technology and Technical Colleges.

In view of the variations between the syllabuses, it may be found that a few of the sections appear to be beyond the scope of any particular examination, but this should not prove a disadvantage to the student. Indeed, it may well be helpful for students to realize that the scope of a subject is not limited to a narrow examination requirement.

It is believed that the subject has been approached in a logical and modern manner and that the student has been helped in his revision by the provision of flow-sheets and summary tables. Attention has been drawn to those relatively new industrial processes, which are so important to the economic development of our present-day society.

The authors acknowledge with gratitude the helpful criticism and much sound advice received from Dr. M. Gordon of the Constantine College of Technology, Middlesbrough, and Dr. J. Sharp, Headmaster of Christ College, Brecon. Their assistance has led to many improvements in the lay-out and presentation of the book.

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October, 1964 N. H. L.

a note to the student about how to use this book

IN REVISION you should try to make your own summaries, to compare them with those in this book, and then to continue *beyond* this stage by trying to condense the material still further. Such continued condensing of your information, leaving finally only the main skeleton of the subject, is essential if knowledge is really to be assimilated and if you are to grasp how the various pieces of the Organic Chemistry jig-saw puzzle are fitted together.

It is also a good idea to fix your knowledge by cross-references. Many such references occur in the text and it is well worth taking a little trouble to follow them up.

Tables of comparisons between aliphatic and aromatic compounds are also especially useful. You should try to make these yourself from memory and then compare them with those in this book and so discover if you have really learned the work.

It is hoped that you will find this book a useful guide to clarifying your ideas on Organic Chemistry.

1

the nature of organic chemistry

THE CHEMISTRY of those substances which are closely related to the metabolism of living organisms is, in general, much more complex than the chemistry of inorganic substances. A distinction was made between organic and inorganic chemistry in the early history of chemistry, the former being restricted to the study of the various chemical products obtainable from living sources. It was believed that these substances differed fundamentally from the compounds of inorganic chemistry by the possession of some "vital principle". In 1828 *Wöhler* showed that this was not true when he obtained a typical organic substance (urea) from an inorganic source (ammonium cyanate).

From that time, although it was realized that there was no fundamental difference between organic and inorganic compounds, the division of chemistry into two distinct branches has been retained as a matter of convenience. As now understood, organic chemistry refers to the chemistry of carbon, which forms a very much larger number of compounds than any other element. A century of research has revealed the reactions through which they are interconverted and has enabled the arrangements of the atoms within their molecules to be pictured accurately. The larger part of this book deals with these changes and structures.

Attention is now being paid to the understanding of the electronic arrangements within the molecules of organic compounds and their behaviour during chemical reactions. A general introduction to these aspects is given in the following paragraphs and some individual examples will be discussed in the later sections of this book.

Carbon is in the middle of the first short period of the Periodic Table of the elements and has four valency electrons. It forms compounds by co-valencies (electron-sharing) rather than by gaining or losing electrons through electro-valencies. Consequently, organic compounds are typically non-ionic and many of them are very complex since the covalent bond allows carbon atoms to combine together to an almost unlimited extent.

The reactions between organic compounds proceed more slowly than those between ionized substances. Often, they take place in a series of consecutive stages, and the overall reaction rate is controlled by that of the slowest process in the sequence. A step by step reaction sequence may operate even in those cases where the final products can be derived from the reactants using a single, simple equation.

Organic reactions involve the breaking of covalent bonds and the formation of new ones. A covalent bond may be broken in two ways, leading to the transitory formation of either two free radicals or two ions as reactive intermediates. In the first case, each atom separates with one of the bonding electrons (homolytic fission); in the other case, one atom retains both electrons and becomes a negative ion, the other atom becoming a positive ion (heterolytic fission). The environment may influence the method of disruption of a bond, e.g. in the vapour phase, homolytic fission usually occurs while heterolytic fission is favoured by reacting in solution in solvents with ion-solvating tendencies.

$$\mathrm{A:B \rightarrow A\cdot + \cdot B}$$

$$\mathrm{A:B \rightarrow \overset{-}{A}: + \overset{+}{B}} \quad \text{or} \quad \mathrm{\overset{+}{A} + :\overset{-}{B}}$$

The formation of a new covalent bond involves the reversal of these two processes. The course of a reaction sequence may be determined by the manner in which a bond is broken and the behaviour of the reactive intermediate so produced.

The course and/or the rate of a reaction may also be influenced by the electrical charges on the atoms which arise from the unequal sharing of the electrons of a covalent bond. When a covalent bond is formed between similar atoms, the electron pair is shared equally between them and the same equal sharing occurs when carbon is linked to hydrogen. But in most other cases, the sharing is unequal and the bond is not completely electrically neutral, e.g. in the C—Cl bond the electron pair is situated, on the average, slightly nearer to the chlorine nucleus than to the carbon nucleus; thus the atoms possess slight electric charges and constitute an electric dipole $(\rightarrow\!\!\overset{+}{\mathrm{C}}-\overset{-}{\mathrm{Cl}})$. Electrically charged reactants, such as ions, are attracted towards the oppositely charged atom of the covalent bond and may initiate a reaction with it. Correspondingly, the inactivity of the paraffin hydrocarbons towards the commoner laboratory reagents is correlated with the absence of polarity in the carbon–hydrogen bond, so that the reacting species are not attracted towards either atom.

In other cases, the reaction process may be influenced by the charges on covalent bonded atoms arising from movement of the shared electrons towards one atom under the stimulus of electrical forces arising from other parts of the molecule or from the influence of an approaching reactant. (This change may be represented by the symbol $\curvearrowright$, denoting the direction of electron movement.)

Side reactions. In practice, it is found that the main reaction in any organic reaction sequence is generally accompanied by side reactions and the chief products are, therefore, usually obtained in much less than the 100 per cent yields of ionic interactions. Correspondingly, the main products are usually obtained in impure conditions and need to be treated by such processes as crystallization or distillation before they are obtained as pure specimens. The physical constants of the samples, e.g. boiling point, melting point (including mixed melting point), refractive index, are valuable aids in confirming their chemical identities and their degrees of purity.

THE MOLECULAR FORMULAE OF ORGANIC COMPOUNDS

Almost all organic compounds contain hydrogen in addition to carbon; many also contain oxygen or nitrogen and, less commonly, sulphur, phosphorus or other elements. The first stages in establishing the formula of any compound are the quantitative determinations of the proportions of the constituent elements and the calculation of the empirical formula. The molecular weight is then determined (e.g. by the ebullioscopic or cryoscopic methods) and the molecular formula is derived by multiplying the empirical formula by a suitable integer which gives the correct molecular weight.

The Determination of Hydrogen and Carbon

This is carried out by the combustion of a measured weight of the substance in a stream of oxygen, followed by the weighing of the water and carbon dioxide formed after they have been respectively absorbed by a dehydrating agent (such as magnesium perchlorate), and an alkali (such as sodium hydroxide). If the percentages of carbon and hydrogen do not add up to 100 per cent the difference is taken to be the percentage of oxygen in the compound, if no other element is known to be present. (There is no simple experimental method for the direct determination of oxygen.)

The Determination of Nitrogen

This is carried out either by the *Dumas* or the *Kjeldahl* method. In the former, a weighed quantity of the substance is mixed with copper oxide and heated in a stream of carbon dioxide, which sweeps the products through a tube containing heated copper oxide (to complete the oxidation of the carbon and hydrogen) and a heated copper spiral (to reduce nitrogen oxides to nitrogen). After absorbing the carbon dioxide in potassium hydroxide solution, the nitrogen gas is collected and its volume is measured.

Kjeldahl's method involves heating the substance with concentrated sulphuric acid (often with selenium and/or mercuric sulphate as a catalyst and potassium sulphate to raise the boiling point). The substance is decomposed and the nitrogen is converted to ammonium sulphate, which is determined by diluting, rendering alkaline and distilling off the ammonia into a standard acid solution.

The Determination of Halogens and Sulphur

This is carried out by *Carius*' method where the substance is heated in a sealed tube with fuming nitric acid (and silver nitrate in the case of the halogens). Sulphur is converted to sulphuric acid which can be determined gravimetrically as barium sulphate; the halides are determined as the silver salts.

Example. *On combustion,* 0·300 g *of a compound yielded* 0·425 g *of carbon dioxide and* 0·260 g *of water. Calculate the percentage composition and the empirical formula. If the vapour density is* 31, *calculate the molecular formula.*

44 g of carbon dioxide contain 12 g of carbon. Hence, 0·425 g contain $\frac{12}{44} \times 0{\cdot}425 = 0{\cdot}116$ g of carbon.

18 g of water contain 2 g of hydrogen. Hence, 0·260 g contain $\frac{2}{18} \times 0{\cdot}260 = 0{\cdot}029$ g of hydrogen.

Therefore 0·300 g of the compound contains 0·116 g carbon, 0·029 g hydrogen, and 0·155 g oxygen (by difference) and the percentage composition is

$$\begin{array}{lll} \text{Carbon} & \frac{100}{0{\cdot}300} \times 0{\cdot}116 = & 38{\cdot}7\% \\ \text{Hydrogen} & \frac{100}{0{\cdot}300} \times 0{\cdot}029 = & 9{\cdot}7\% \\ \text{Oxygen} & \frac{100}{0{\cdot}300} \times 0{\cdot}155 = & 51{\cdot}7\% \end{array}$$

Ratios of atomic weights (C:H:O) = 12:1:16.

Therefore ratios between the numbers of atoms

$$= \frac{38{\cdot}7}{12} : \frac{9{\cdot}7}{1} : \frac{51{\cdot}7}{16}, \text{ i.e. } 3{\cdot}23 : 9{\cdot}7 : 3{\cdot}23$$

Hence the empirical formula is CH_3O.

Molecular weight = 2 × vapour density.

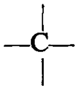
Hence the molecular weight of the compound is 2 × 31 = 62 and the molecular formula is $C_2H_6O_2$.

THE CONSTITUTIONAL FORMULAE OF ORGANIC COMPOUNDS

Owing to the complexity of the molecules of organic compounds, molecular formulae are inadequate representations of their chemical behaviour. The arrangements of the atoms within the molecules are as important as the total numbers of the various atomic species present and it is necessary to set out the arrangements if the whole chemical behaviour is to be understood.

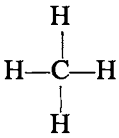
Graphic formulae reveal how each atom is chemically united, each univalent bond between the atoms being represented by a stroke on the paper. Thus the quadrivalent carbon atom with four equal covalencies, and the simplest hydrocarbon (methane) are represented thus (I and II)

(I)



$$\begin{array}{ccc} & | & \\ - & C & - \\ & | & \end{array}$$

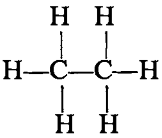
(II)



$$\begin{array}{ccccc} & & H & & \\ & & | & & \\ H & - & C & - & H \\ & & | & & \\ & & H & & \end{array}$$

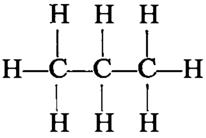
Actually, the arrangements are three-dimensional (as shown by the phenomena of stereochemistry cf. p. 133) and the four valencies of the carbon atom are directed towards the corners of a regular tetrahedron, but two-dimensional representations suffice to illustrate most of the properties of organic compounds.

The next simplest hydrocarbon (ethane) has the molecular formula C_2H_6 and the only arrangement of the atoms in the ethane molecule which is consistent with the quadrivalent carbon atom and the univalent hydrogen atom is represented by the following formula, which shows that the two carbon atoms are linked together. This formula has been verified experimentally.



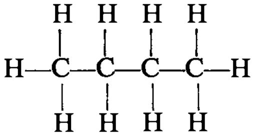
$$\begin{array}{ccccccc} & & H & & H & & \\ & & | & & | & & \\ H & - & C & - & C & - & H \\ & & | & & | & & \\ & & H & & H & & \end{array}$$

The higher members of the paraffin series are also formed by linkage of carbon to carbon; e.g. propane (C_3H_8) and butane (C_4H_{10}) are represented by the formulae



$$\begin{array}{ccccccc} & H & & H & & H & \\ & | & & | & & | & \\ H - & C & - & C & - & C & - H \\ & | & & | & & | & \\ & H & & H & & H & \end{array}$$

Propane



$$\begin{array}{ccccccccc} & H & & H & & H & & H & \\ & | & & | & & | & & | & \\ H - & C & - & C & - & C & - & C & - H \\ & | & & | & & | & & | & \\ & H & & H & & H & & H & \end{array}$$

Butane

These formulae reveal that *chains* of carbon atoms can be built up by the bonding of carbon to carbon and such chains are important in most organic compounds. This fact enables the writing of the graphic formulae to be simplified by writing the atoms attached to each carbon atom immediately after its symbol (C) and representing the carbon–carbon bond by a point (·) instead of a stroke. Thus the formulae of the compounds mentioned above become

CH_4	$CH_3{\cdot}CH_3$	$CH_3{\cdot}CH_2{\cdot}CH_3$	$CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CH_3$
Methane	Ethane	Propane	Butane

Formulae of this type which show, in adequate detail, the arrangement of the different atoms in the molecule are called *constitutional formulae or structural formulae.* The constitutional formula of a compound is deduced (after the molecular formula has been determined) from a study of its reactions, which indicate which functional groups are present in the molecule. The deduced constitutional formula is usually confirmed by synthesis (cf. p. 157).

HOMOLOGOUS SERIES: FUNCTIONAL GROUPS

The molecular formulae of the above four hydrocarbons differ from one another in the lengths of the carbon chains; each differs from its neighbours by CH_2. These hydrocarbons constitute an example of a *homologous series,* which is defined as: *A series of organic compounds possessing similar chemical properties, whose* *molecular formulae show a constant difference of* CH_2 *from member to member as the series is ascended.*

The members of a homologous series are said to be *homologues* of one another.

While the physical properties of the members of a homologous series change steadily as the molecular weight increases, the chemical properties vary relatively little (except that the first member, i.e. the substance with the simplest formula, commonly differs to some extent from the others). This lack of variation in the chemical properties is correlated with the fact that the carbon–carbon and carbon–hydrogen bonds are not very reactive chemically, and the addition of $\cdot CH_2 \cdot$ groups to lengthen a carbon–carbon chain contributes little new chemical reactivity to the molecules. Also it is relatively infrequent for the carbon chain to take part in the reactions of the substance and so the chemical behaviour of all the members of a homologous series is determined by whatever other atomic grouping is present.

The study of organic chemistry is greatly simplified by the existence of homologous series of closely related and similar substances, each series being characterized by the presence of a particular reactive group of atoms (the functional group).

A functional group is a particular arrangement of atoms which confers its own characteristic chemical behaviour on all organic substances whose molecules contain the group.

When a compound contains more than one functional group in the molecule, it usually exhibits the properties of, and takes part in the reactions characteristic of, all the different functional groups present. It is prepared by suitable modifications of the general methods of preparation for the particular groups.

ISOMERISM

In organic chemistry, a large number of cases is known where two or more different substances have exactly the same molecular formula. These substances are said to be *isomeric.* They are *isomers* of one another. The differences can be attributed to the different arrangements of the various atoms within the molecule, and there are different classes of isomerism in accordance with the various ways of obtaining different arrangements of the atoms (cf. p. 243). The simplest type is called *branched-chain isomerism* to describe the way in which it arises.

The formula of ethane can be derived from that of methane by the substitution of a $\cdot CH_3$ group for a hydrogen atom, and the formula of propane can be derived in the same way from that of ethane. The same process gives rise to chain lengthening in any

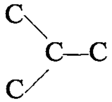
$$\underset{\text{Methane}}{CH_4} \qquad \underset{\text{Ethane}}{CH_3{\cdot}CH_3} \qquad \underset{\text{Propane}}{\overset{1}{CH_3}{\cdot}\overset{2}{CH_2}{\cdot}CH_3}$$

homologous series. When this substitution is made in the molecules of methane and ethane, only one product is possible, since each hydrogen atom is identically arranged within the molecule. But when the propane molecule is so substituted, two products are possible, depending on whether a hydrogen atom 1 or 2 is replaced giving either

$$CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CH_3 \quad \text{or} \quad CH_3{\cdot}CH(CH_3)_2$$

Of these two products of formula C_4H_{10}, one has a straight* (or open chain) of carbon atoms, the other has a formula with a branched chain —

$$C—C—C—C$$



They are called *normal* and *iso* butane respectively, and the term *normal* is reserved for substances containing open chain molecules. By replacing a hydrogen atom in these butane molecules by a $CH_3\cdot$ group, three isomeric pentanes of formula C_5H_{12} are obtained and the number of possible isomers increases very rapidly as the chain length increases —

$$CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_3 \qquad (CH_3)_2CH{\cdot}CH_2{\cdot}CH_3 \qquad C(CH_3)_4$$

---

* The carbon atoms in the chain form a zig-zag arrangement (cf. p. 135).

2

the aliphatic hydrocarbons

THE SUBSTANCES formed by the union of carbon and hydrogen are called *hydrocarbons*. There is a very large number of these compounds formed by the union of the two elements in different proportions, but they fall naturally into classes. All the members of a class resemble one another in their chemical properties, and their molecular formulae are closely related.

The hydrocarbons of the methane series (the *paraffin* hydrocarbons or the alkanes) occupy an important position in organic chemistry. They, and their derivatives, whose properties are described in the succeeding chapters, are the *aliphatic* or fatty compounds. The hydrocarbons of the benzene series and their derivatives (the *aromatic* compounds) are described later.

THE PARAFFIN HYDROCARBONS (GENERAL FORMULA C_nH_{2n+2})

Methane, a hydrocarbon of the formula CH_4, is the simplest member of a homologous series of hydrocarbons of which ethane (C_2H_6), propane (C_3H_8), butane (C_4H_{10}), and pentane (C_5H_{12}) are the members immediately following methane. The members after butane are named in accordance with the number of carbon atoms in their molecule (e.g. pentane C_5H_{12}, hexane C_6H_{14}, etc.) and the series extends up to $C_{80}H_{162}$.

The derivatives formed by replacing hydrogen by other atoms or groups are named from the parent hydrocarbon, e.g.

1 atom of hydrogen replaced — ending *ane* becomes *yl*;
2 atoms of hydrogen replaced — ending *ane* becomes *ylene.*

For example:

CH_4 methane, CH_3 methyl, CH_2 methylene;

C_2H_6 ethane, $CH_3{\cdot}CH_2$ or C_2H_5 ethyl, C_2H_4 ethylene;

C_3H_8 propane, $CH_3{\cdot}CH_2{\cdot}CH_2$ or C_3H_7 propyl, C_3H_6 propylene.

The term *alkyl* (abbreviated to alk) is used generally to represent any of the groupings methyl (Me), ethyl (Et), propyl (Pr), butyl (Bu), etc.

Occurrence and Extraction of Paraffin Hydrocarbons

Methane is present in natural gas (an inflammable gas issuing from the earth in various localities), in the gases escaping from coal in mines (fire-damp), and in the gases rising from the decomposing vegetable matter in marshes (marsh-gas). It is also an important constituent of commercial coal-gas and coke-oven gas.

Petroleum distillation. A large number of paraffin hydrocarbons occur naturally in petroleum, which probably originated from the action of pressure on decomposing organic matter. American petroleums consist chiefly of a mixture of these hydrocarbons, including the open and branched chain types. The products obtained from other oilfields also contain hydrocarbons of other series (e.g. the cycloparaffin series).

The various constituents of crude petroleum oil are partially separated by fractional distillation. The first distillation results in the following fractions:

(1) *Gases* (methane, ethane, propane and butane). The first two are separated for use as a fuel gas, either directly or after incorporation into town gas. Propane and butane are marketed as liquefied petroleum gases.

(2) *Light distillates* used for motor and aviation fuels and the burning oil — kerosene — which is often called "paraffin".

(3) *Middle distillates*, including diesel and other fuel oils, and

(4) a residue which can be used as a fuel oil or can be submitted to a further distillation under reduced pressure to give lubricating oils, paraffin wax and bitumen.

The proportions of the higher boiling constituents obtained by the first distillations are often in excess of market demand. These products are therefore submitted to further processes (cracking), which cause the larger molecules to break down into smaller molecules, some of which are of the branched chain type while others are of ethylenic or aromatic nature. Thermal cracking involves heating at about 500°C and a pressure of about 10 atm; catalytic cracking uses slightly lower temperatures and lower pressures in the presence of an alumina–silica catalyst.

Other processes are also used in the petroleum refineries to increase the yields of the more marketable products, i.e. improved motor and aviation fuels and a number of substances which form the basis of the petroleum chemical industry. They yield, by suitable chemical treatment, a wide range of substances including solvents such as acetone and esters, synthetic detergents, synthetic rubber, plastics and the synthetic resins used in paints.

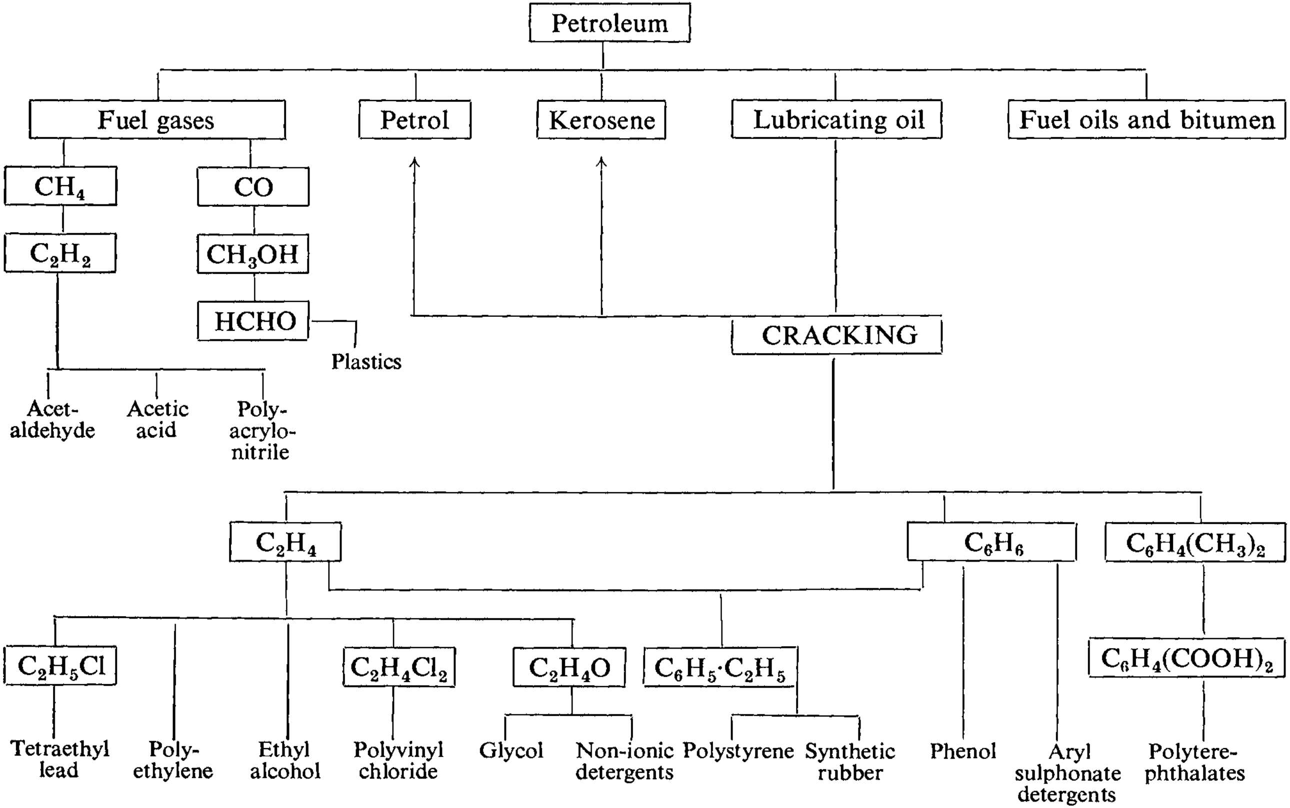
General Methods of Preparation of Paraffin Hydrocarbons

A pure sample of any particular hydrocarbon might be obtained by a very careful fractionation of petroleum oil, but the separation would be so costly that it is usually impracticable. The following reactions are available for the preparation of any member of the series.

(1) *Reduction of the halogen derivative of the hydrocarbon*, using concentrated hydriodic acid or the hydrogen liberated from sodium amalgam and water or from a zinc–copper couple (zinc coated with a thin layer of copper) and water or alcohol.

$$CH_3Br \xrightarrow{2H} CH_4 + HBr$$

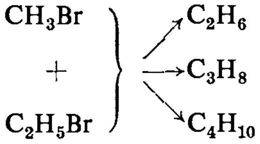
The Petroleum Chemical Industry



(2) *The action of sodium on a halogen derivative*, yielding a hydrocarbon containing twice the number of carbon atoms present in the original molecule.

$$CH_3\boxed{Br + 2Na + Br}CH_3 = C_2H_6 + 2NaBr$$

Hydrocarbons containing an odd number of carbon atoms in the molecule might be prepared by using a mixture of two halogen derivatives, but the reaction product contains three hydrocarbons which have to be separated.



(3) *The action of heat on a mixture of the sodium salt of a fatty acid and soda-lime.*

$$CH_3{\cdot}COONa + NaOH = CH_4 + Na_2CO_3$$

(4) *The hydrolysis of a Grignard reagent* (which is formed when magnesium is added to a solution of a halogen derivative in dry ether) yields a paraffin hydrocarbon.

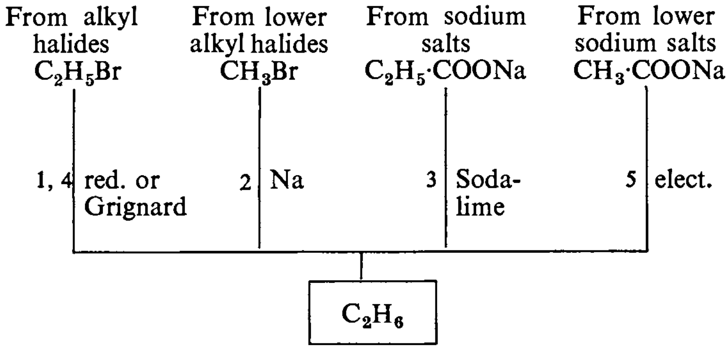
$$CH_3I + Mg = CH_3MgI$$

$$2CH_3MgI + 2H_2O = 2CH_4 + MgI_2 + Mg(OH)_2$$

(5) *The electrolysis of a salt of a fatty acid* yields, at the anode, a mixture of carbon dioxide and the paraffin hydrocarbon (*Kolbe's* synthesis).

$$2CH_3{\cdot}COO^- - 2e = CH_3{\cdot}CH_3 + 2CO_2$$

Preparation of Paraffin Hydrocarbons



The numbers refer to the reactions as set out in the preceding section.

Preparation of Methane

In addition to the general methods of preparation available for all the members of the series, *methane* may be prepared in small quantities by the following reactions:

(1) By the action of water on aluminium carbide (a convenient laboratory method).

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

(2) By reduction of carbon monoxide by hydrogen in the presence of reduced nickel as a catalyst. (Reduced nickel is very often used as a catalyst in organic chemistry for reactions involving combination with hydrogen.)

$$CO + 3H_2 = CH_4 + H_2O$$

Physical Properties of the Paraffin Hydrocarbons

The physical properties of the paraffin hydrocarbons vary gradually as the molecular weight increases. The *boiling point* and *melting point* rise. The lowest members (C_1–C_4) are gases at ordinary temperatures, then follow very volatile liquids, less volatile liquids, and finally (C_{18} upwards) waxy solids. The boiling points and melting points of the normal hydrocarbons are higher than those of the branched chain isomers, since the cohesive forces between molecules are greatest when the molecules can pack closest together, as happens in linear molecules arranged parallel-wise. The *specific gravity* increases as the number of carbon atoms in the molecule increases, although after about C_{11} the difference from compound to compound becomes small.

These variations in physical properties are similar to those shown by the members of most other homologous series.

The *solubilities* of the paraffin hydrocarbons resemble those of many other neutral organic substances. They are insoluble in water, but dissolve readily in, or are themselves good solvents for, many other non-ionic substances, e.g. chloroform, ether, essential oils.

Chemical Properties of the Paraffin Hydrocarbons

The chemical properties of the paraffin hydrocarbons are characterized by neutrality towards indicators and a general lack of chemical reactivity under ordinary laboratory conditions; hence the name paraffin (*parum affinis*). They do not react with the common reagents such as acids, alkalis, oxidizing or reducing agents. (Fuming nitric acid reacts slowly to oxidize them.) However, they take part in the following reactions:

(1) *Oxidation : Combustion.* The paraffin hydrocarbons combine directly with oxygen, burning or exploding in air. Controlled oxidation of the higher hydrocarbons produces shorter chain fatty acids, ketones, etc.

$$CH_4 + 2O_2 = CO_2 + 2H_2O$$

$$2C_2H_6 + 7O_2 = 4CO_2 + 6H_2O$$

$$CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CH_3 \rightarrow 2CH_3{\cdot}COOH$$

(2) *Cracking.* The higher paraffins are broken down at temperatures of 500–700°C into mixtures of compounds with smaller molecules. This pyrolytic decomposition forms the basis of the petroleum cracking process.

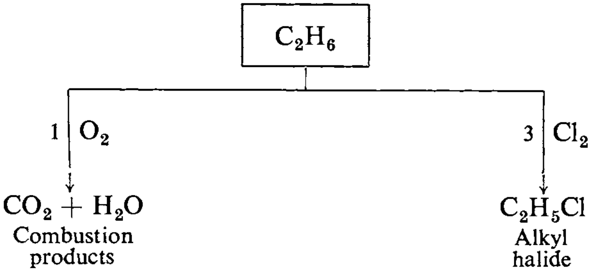
(3) *Halogen substitution.* The paraffin hydrocarbons react with chlorine and bromine (especially in strong light), hydrogen becoming replaced by the halogen, atom by atom (*substitution*).

$$\begin{aligned}
CH_4 + Cl_2 &= \underset{\substack{\text{Methyl}\\\text{chloride}}}{CH_3Cl} + HCl\\
CH_3Cl + Cl_2 &= \underset{\substack{\text{Methylene}\\\text{dichloride}}}{CH_2Cl_2} + HCl\\
CH_2Cl_2 + Cl_2 &= \underset{\text{Chloroform}}{CHCl_3} + HCl\\
CHCl_3 + Cl_2 &= \underset{\substack{\text{Carbon}\\\text{tetrachloride}}}{CCl_4} + HCl
\end{aligned}$$

The reaction sequence involves the formation of atoms of the halogen after absorption of light energy by the molecules followed by the transient formation of free alkyl radicals.

$$\begin{aligned}
Cl_2 &\rightarrow 2Cl\\
Cl + CH_4 &\rightarrow CH_3\text{—} + HCl\\
\text{—}CH_3 + Cl_2 &= CH_3Cl + Cl
\end{aligned}$$

Reactions of Paraffin Hydrocarbons



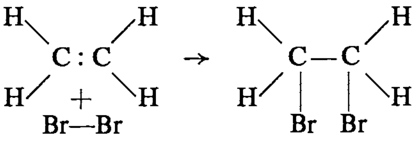
The numbers refer to the reactions as set out in the previous section.

Hydrocarbons of the Ethylene Series
(Functional Group $>C:C<$)

The gas ethylene is the simplest member of a homologous series (general formula C_nH_{2n}) whose members differ from the corresponding paraffins in having two atoms of hydrogen fewer in their molecules. They are sometimes referred to as the olefins. The names of the individual hydrocarbons are derived from the corresponding paraffins by replacing the terminal "-ane" by "-ylene", e.g. ethylene, propylene, butylene.

The molecular formula of ethylene is C_2H_4; the quadrivalency of carbon requires that the two carbon atoms are united by two valency bonds instead of one (i.e. $CH_2{:}CH_2$). Ethylene and its homologues possess a *double bond* in their molecules, and it is this feature which gives rise to the characteristic reactions of these compounds. Other substances containing carbon atoms united by double bonds react similarly and the double bond is an example of a functional group, the ending "ene" signifying its presence in the molecule. Correspondingly, the term "diene" indicates the presence of two such bonds, and so on.

The double bond is reactive and readily becomes converted by *addition reactions* into single bonds, e.g. by reaction with halogens, halogen hydrides and hydrogen.



Unsaturation (i.e. the ability to take part in addition reactions) is a characteristic property of the double bond between two carbon atoms. (The paraffin hydrocarbons which react only by replacement of their hydrogen, and do not form derivatives by addition, are said to be *saturated*.)

In complex substances, a double bond is often the weakest point of the molecule and the first point of chemical attack. This property is useful in the investigation of the molecular structure of unknown substances. Another characteristic feature of the double bond, in contrast to the single bond, is the restriction of free rotation in respect of the carbon to carbon linkage. This gives rise to geometrical isomerism in ethylenic compounds, as in maleic and fumaric acids (cf. p. 143).

Preparation of Ethylene and its Homologues

(1) *Breakdown of higher hydrocarbons.* The destructive distillation of wood, coal, or the higher fractions of petroleum oil (cracking) gives rise to ethylenic hydrocarbons. Ethylene is present only in small concentrations in the gaseous by-products of the standard cracking processes, but further quantities are obtained by the pyrolytic decomposition in the presence of steam of propane. It is separated from the other reaction products by liquefaction and fractional distillation.

(2) *Dehydration of alcohols.* Ethylenic compounds are prepared by the removal of the elements of water from alcohols. Ethylene is usually prepared in the laboratory by heating ethyl alcohol with excess concentrated sulphuric acid at 170°C.

$$C_2H_5OH + H_2SO_4 = C_2H_5HSO_4 + H_2O$$

$$C_2H_5HSO_4 = CH_2{:}CH_2 + H_2SO_4$$

(3) *Removal of halogen acid from alkyl halide.* Ethylenic compounds are prepared from alkyl halides by splitting off hydrogen halide from their molecules. This is usually carried out by treatment with concentrated alcoholic potash. The simplest reaction of this type (represented by the equation below) is much less effective (giving only a 1 per cent yield) than with more complex compounds, where bromination followed by the removal of hydrogen bromide can be used to introduce a double bond into the molecule.

$$CH_3{\cdot}CH_2Br + KOH = CH_2{:}CH_2 + KBr + H_2O$$

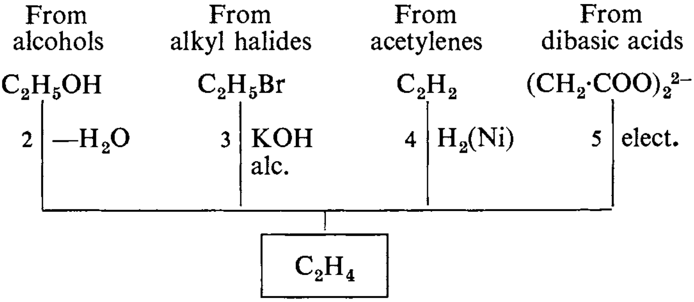
(4) *From acetylenic compounds.* The catalytic addition of hydrogen to acetylene derivatives in the presence of finely divided nickel may form the corresponding ethylene compound.

$$CH{:}CH + H_2 = CH_2{:}CH_2$$

(5) *Electrolysis of dibasic acids.* Ethylenic compounds are also obtained by electrolysis of the salts of dibasic acids.

$$(CH_2{\cdot}COO)_2^{2-} - 2e = CH_2{:}CH_2 + 2CO_2$$

Preparation of Ethylenic Hydrocarbons



Physical Properties of the Ethylenic Hydrocarbons

These vary in a similar manner to those of the paraffin hydrocarbons. Ethylene itself is slightly soluble in water but the higher members are insoluble.

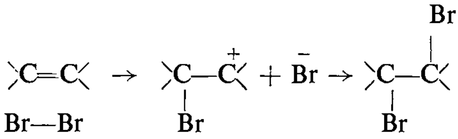
Chemical Properties of the Ethylenic Hydrocarbons

Chemically the ethylenic hydrocarbons are much more reactive than the paraffin hydrocarbons, and take part in the characteristic reactions of the double bond.

(1) *Addition of halogens.* Ethylenic compounds react rapidly with chlorine and bromine (chlorine reacts more vigorously than bromine).

$$\underset{\text{Ethylene}}{CH_2{:}CH_2} + Br_2 = \underset{\text{Ethylene dibromide}}{CH_2Br{\cdot}CH_2Br}$$

This reaction illustrates the fact that organic reactions may involve more complex changes than are revealed by a relatively simple equation correlating the initial reactants and the products. The addition of halogens to ethylenic compounds does not seem to proceed as a simple one-step process. It is suggested that the halogen atoms are affixed one at a time in a sequence which produces ions at the end of the first stage. During the next stage, the bromide ion adds on to the opposite side of the molecule to that occupied by the first bromine atom, owing to the repulsion between the negative ion and the slight negative charge on the bromine atom (due to the polarity of the C—Br linkage).



(2) *Addition of hydrogen halides.* Ethylenic compounds form addition products with hydrogen bromide and hydrogen iodide. Hydrogen iodide reacts more vigorously than hydrogen bromide.

$$CH_2{:}CH_2 + HI = CH_3{\cdot}CH_2I$$

With an unsymmetrical ethylenic hydrocarbon, the halogen becomes attached to the carbon atom joined to the least number of hydrogen atoms (*Markownikoff's rule*).

(3) *Addition of hydrogen.* Ethylenic compounds add on hydrogen and form the corresponding paraffin. This reduction of ethylenic derivatives is carried out by bringing them, in the vapour or liquid state, into contact with hydrogen in the presence of finely divided nickel as a catalyst at 200–300°C, or platinum at room temperature.

$$CH_2{:}CH_2 + H_2 = CH_3{\cdot}CH_3$$

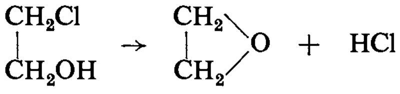
(4) *Addition of hypochlorous acid, etc.* Ethylenic compounds add on hypochlorous or hypobromous acid, when passed into

aqueous solutions of chlorine or bromine. The products are called chloro- or bromo-hydrins.

$$CH_2{:}CH_2 + HOCl = CH_2OH{\cdot}CH_2Cl$$

Ethylene chlorohydrin

The chlorohydrins are converted by alkalis into ethylene oxides.



Ethylene oxide

(5) *Absorption by permanganate solution.* Ethylenic compounds are easily oxidized and are readily absorbed in concentrated potassium permanganate solution. The first stage of the reaction is the addition of an oxygen atom.

$$CH_2{:}CH_2 + H_2O + O \rightarrow CH_2OH{\cdot}CH_2OH$$

Ethylene glycol

(6) *Absorption by sulphuric acid.* Ethylenic compounds are absorbed by cold concentrated or fuming sulphuric acid, by the reverse of the high temperature reaction which is involved in their preparation from alcohols. Hydrolysis of the products of absorption gives the corresponding alcohols.

$$C_2H_4 + H_2SO_4 = C_2H_5HSO_4$$

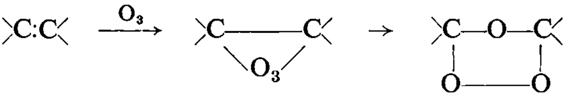
$$C_2H_5HSO_4 + NaOH = C_2H_5OH + NaHSO_4$$

(7) *Hydration.* Ethylene itself can be hydrated directly, as in the manufacturing process for ethyl alcohol. The catalysed reaction is carried out at 300°C and about 70 atm.

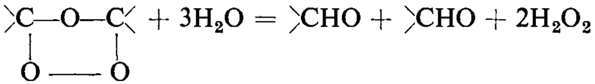
$$C_2H_4 + H_2O = C_2H_5OH$$

(8) *Ozonolysis.* Ethylenic compounds react readily with ozone; the first addition products undergoing molecular rearrangements

to form ozonides in which the carbon–carbon bond has been broken.

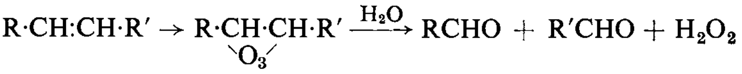


Ozonides are unstable substances which are not usually isolated in the pure state. They are easily hydrolysed to give mixtures of two carbonyl compounds.



$$\begin{array}{c}>C-O-C< \\ | \qquad | \\ O - O\end{array} + 3H_2O = \,>CHO + \,>CHO + 2H_2O_2$$

Ozone is an important reagent for the determination of the position of double bonds in unsaturated compounds from a study of the hydrolysis products.



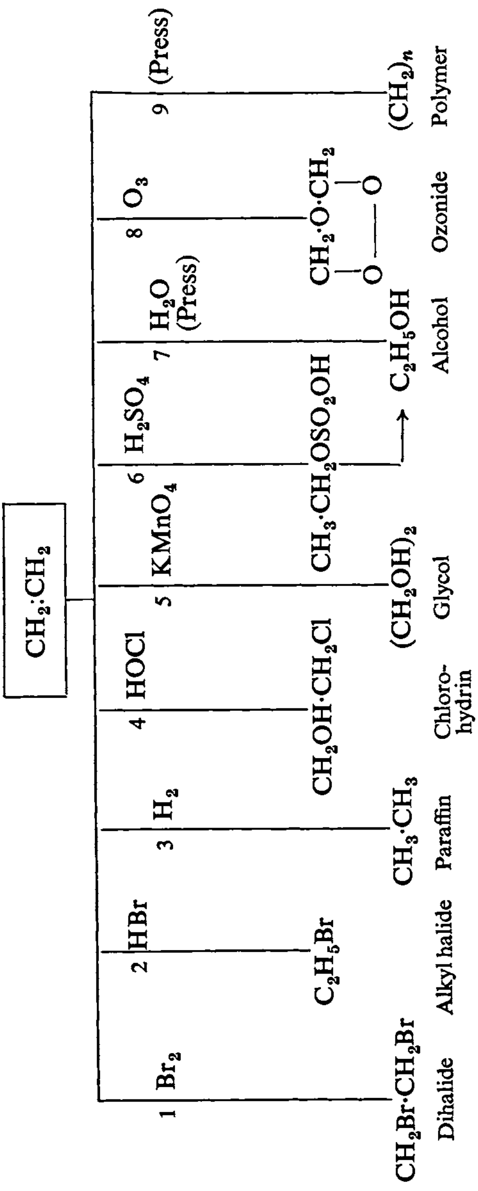
$$R{\cdot}CH{:}CH{\cdot}R' \rightarrow \underset{\diagdown O_3 \diagup}{R{\cdot}CH{\cdot}CH{\cdot}R'} \xrightarrow{H_2O} RCHO + R'CHO + H_2O_2$$

(9) *Polymerization.* Many ethylenic compounds may be caused to undergo polymerization reactions. *Polymerization occurs when several molecules of a simple substance combine together to form a single molecule of a substance with the same empirical formula but of greater molecular weight.*

Ethylene polymerizes to polyethylene by heating to about 200°C at very high pressures (about 1500 atm) or at 70°C and 10 atm in an inert solvent and in the presence of a catalyst containing titanium tetrachloride and an aluminium trialkyl (*Ziegler* process). Polyethylene is marketed as a well-known "plastic" but the physical properties of the materials obtained by the two processes differ, as the catalytic, low pressure process brings about less chain branching than the high pressure process.

Many other types of plastic are obtained from different substances containing double bonds, e.g. styrene $C_6H_5{\cdot}CH{:}CH_2$; vinyl chloride $CH_2{:}CHCl$; acrylonitrile $CH_2{:}CHCN$; methyl methacrylate $CH_2{:}C(CH_3){\cdot}COOCH_3$; butadiene $CH_2{:}CH{\cdot}CH{:}CH_2$.

Reactions of Ethylenic Hydrocarbons



The *addition polymerization* of ethylenic compounds involves the opening of the double bonds and the subsequent interlinkage of many molecules to give very large molecules, as in the example

$$CH_2{:}CH_2 \rightarrow \ldots\ldots CH_2{\cdot}CH_2 \ldots\ldots \rightarrow \ldots\ldots CH_2{\cdot}(CH_2)_n{\cdot}CH_2 \ldots\ldots$$

Monomer Polymer

The "plastics" industry has also developed materials of high molecular weight by other types of chemical reaction. These may involve the elimination of some other substance during the joining together of the simpler components and the products are therefore not actually "polymers" as defined above. However, the processes have become known as *condensation polymerizations* and typical examples are found in the manufacture of nylon (p. 128) and terylene (p. 232).

The shapes of large polymer molecules can be controlled to confer special properties on the polymers. Thus thermoplastics (which soften on heating and regain their rigidity on cooling) have long chain-like molecules with little branching, which do not link chemically with one another, although they may intertwine to give soft pliable materials. The thermosetting plastics have strongly branched molecules, chemically joined by cross-links to form a continuous network. These do not soften on heating, since the molecules, being joined together, have little freedom of movement.

HYDROCARBONS OF THE ACETYLENE SERIES
(FUNCTIONAL GROUP —C⋮C—)

The members of this series of hydrocarbons have the general formula C_nH_{2n-2} and their molecules contain a *triple bond* (e.g. the formula of acetylene itself is $CH{\vdots}CH$). The next member of the series is called allylene ($CH_3{\cdot}C{\vdots}CH$), while higher members are usually regarded as derivatives of acetylene and are named as such, e.g. ethyl acetylene ($C_2H_5{\cdot}C{\vdots}CH$).

Preparation of Acetylenic Compounds

Acetylene and its homologues can be prepared from dihalides, whether of the symmetrical type or the unsymmetrical type. By reacting with alcoholic potash, two molecules of hydrogen halide are removed.

$$C_2H_4Br_2 + 2KOH = C_2H_2 + 2KBr + 2H_2O$$

$$CH_2Br{\cdot}CH_2Br \rightarrow CH{:}CH$$

$$CH_3{\cdot}CHBr_2 \rightarrow CH{:}CH$$

Preparation of Acetylene

Acetylene is prepared on a large scale by the action of water on calcium carbide.

$$CaC_2 + 2H_2O = C_2H_2 + Ca(OH)_2$$

It is marketed in cylinders in the form of a solution in acetone. It is used for acetylene welding purposes, and for conversion into other important organic compounds, e.g. vinyl chloride and polyvinyl chloride (p. 41), tetrachloroethylene and trichloroethylene (p. 40), tetrachloroethane (p. 27), chloroprene and neoprene (p. 41), acetaldehyde (p. 74), acrylonitrile (p. 109).

Properties of the Acetylenic Hydrocarbons

The variations in the physical properties of the homologues of acetylene are similar to those of the other series of hydrocarbons.

The chemical properties are characterized by reactivity. The triple bond is readily converted by addition reactions either into a double bond or into a single bond, as illustrated by the following reactions.

(1) *Addition of halogens.* Acetylene adds on halogens readily. The reaction takes place in two stages.

$$\begin{array}{lcl} CH\vdots CH + Br_2 & = & CHBr{:}CHBr \\ \text{Acetylene} & & \text{Dibromoethylene} \end{array}$$

$$\begin{array}{lcl} CHBr{:}CHBr + Br_2 & = & CHBr_2{\cdot}CHBr_2 \\ \text{Dibromoethylene} & & \text{Tetrabromoethane} \end{array}$$

With chlorine, the reaction may become explosive and yield only carbon and hydrogen chloride. Tetrachloroethane is manufactured by carrying out the reaction in solution (in tetrachloroethane) and in the presence of ferric chloride or antimony pentachloride as a catalyst.

(2) *Addition of hydrogen halides.* Acetylenes add on hydrogen halides in two corresponding stages. As in the case of ethylenic compounds, hydrogen iodide reacts more vigorously than hydrogen bromide and this substance more vigorously than hydrogen chloride.

$$\begin{array}{lcl} CH\vdots CH + HBr & = & CH_2{:}CHBr \\ & & \text{Vinyl bromide} \end{array}$$

$$\begin{array}{lcl} CH_2{:}CHBr + HBr & = & CH_3{\cdot}CHBr_2 \\ & & \text{Ethylidene dibromide} \end{array}$$

The products formed by the addition to acetylene of halogens and halogen acids in the presence of catalysts are manufactured for use as solvents.

(3) *Addition of hydrogen.* Acetylenic compounds add on hydrogen in the presence of a catalyst.

$$CH\vdots CH + H_2 = CH_2{:}CH_2$$

$$CH_2{:}CH_2 + H_2 = CH_3{\cdot}CH_3$$

(4) *Conversion to aldehydes.* When acetylene is passed into warm, dilute sulphuric acid in the presence of a catalyst, a series of reactions occurs which leads to the formation of acetaldehyde. The first reaction involves addition

$$CH\vdots CH + H_2SO_4 = CH_2{:}CH(HSO_4)$$

Hydrolysis then occurs, possibly leading in the first place to the unstable vinyl alcohol which immediately isomerizes to acetaldehyde.

$$CH_2{:}CH(HSO_4) + H_2O = CH_2{:}CHOH + H_2SO_4$$

$$CH_2{:}CHOH \rightarrow CH_3{\cdot}CHO$$

(5) *Polymerization.* Acetylenic hydrocarbons polymerize on heating, e.g. acetylene forms small quantities of benzene when passed through a red-hot tube.

$$3C_2H_2 = C_6H_6$$

Acetylene dimerizes to form vinylacetylene when it is absorbed in a solution of ammonium and cuprous chlorides in concentrated hydrochloric acid.

$$CH{\vdots}CH + HC{\vdots}CH = CH_2{:}CH{\cdot}C{\vdots}CH$$

(6) *Metal derivatives.* Under certain circumstances, the hydrogen of acetylene and its homologues of the type $CH{\vdots}CR$, is replaceable by a metal. When acetylene is passed into an ammoniacal solution of cuprous chloride, a red deposit of copper acetylide is obtained. Similarly, white silver acetylide is obtained from an ammoniacal silver nitrate solution.

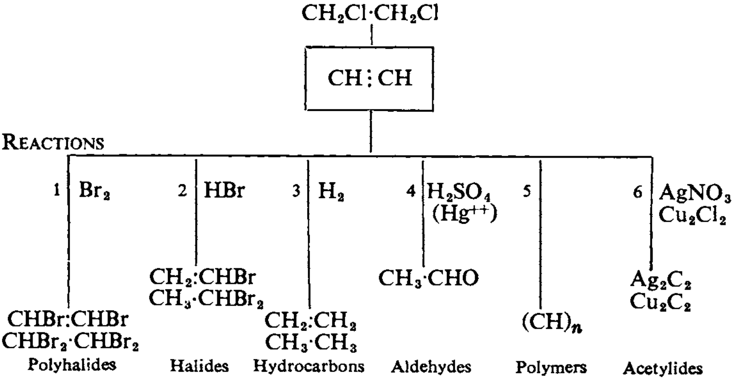
$$Cu_2Cl_2 + C_2H_2 + 2NH_4OH$$
$$= Cu_2C_2 + 2NH_4Cl + 2H_2O$$

$$2AgNO_3 + C_2H_2 + 2NH_4OH$$
$$= Ag_2C_2 + 2NH_4NO_3 + 2H_2O$$

The metallic derivatives of acetylene are unstable and liable to violent explosion. When treated with dilute acids they decompose, regenerating the hydrocarbon, and they can therefore be used as a means of separation and purification of acetylene hydrocarbons. Copper and silver acetylides have structures based on that of acetylene, e.g. $Cu{\cdot}C\vdots C{\cdot}Cu$ and in this respect they differ from calcium and similar carbides which have an ionic structure, $Ca^{++}[C\vdots C]^{--}$. The hydrogen atoms of paraffins or ethylenes are not replaceable by metals.

Triple-bonded Hydrocarbons

PREPARATION. From unsaturated dihalide



3

halogen derivatives of the paraffin hydrocarbons

HALOGEN DERIVATIVES

(FUNCTIONAL GROUPS $\mathord{-}\!\!\!\!\!\mathord{>}\mathrm{C}\cdot\mathrm{Cl}$; $\mathord{-}\!\!\!\!\!\mathord{>}\mathrm{C}\cdot\mathrm{Br}$ or $\mathord{-}\!\!\!\!\!\mathord{>}\mathrm{C}\cdot\mathrm{I}$)

The mono-halogen derivatives of the paraffin hydrocarbons (the alkyl halides) form a homologous series and resemble one another closely in their chemical reactions. There is a greater possibility of isomerism among the alkyl halides than among the corresponding hydrocarbons. For example, although propane exists in one form only, two propyl chlorides can be obtained by the replacement of a hydrogen atom, either of the central carbon atom (a), or of the terminal carbon atom (b).

$$\mathrm{CH_3{\cdot}\underset{(a)}{CH_2}{\cdot}\underset{(b)}{CH_3}} \rightarrow \mathrm{CH_3{\cdot}CHCl{\cdot}CH_3} \text{ or } \mathrm{CH_3{\cdot}CH_2{\cdot}CH_2Cl}$$

The number of isomers is even greater amongst di-halogen and higher derivatives, e.g. there are two substances having the formula $C_2H_4Cl_2$, viz.

$CH_3{\cdot}CHCl_2$	$CH_2Cl{\cdot}CH_2Cl$
Ethylidene dichloride	Ethylene dichloride

This type of isomerism can be described as *position isomerism*, as it is conditioned by the position at which the halogen atoms are introduced into the hydrocarbon molecule.

General Methods of Preparation of Halogen Derivatives

Halogen derivatives may be prepared:

(1) *From alcohols*, by replacement of the hydroxyl group by the halogen atom by reacting with a phosphorus halide. Ethyl chloride is prepared from ethyl alcohol and phosphorus pentachloride; ethyl bromide using phosphorus tribromide or a mixture of red phosphorus and bromine; ethyl iodide by adding iodine to red phosphorus in the presence of the alcohol.

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

$$3C_2H_5OH + PBr_3 = 3C_2H_5Br + H_3PO_3$$

(2) *From ethylenic or acetylenic hydrocarbons*, by addition of halogens or hydrogen halides.

$$C_2H_4 + HI = C_2H_5I \qquad \text{(ethyl iodide)}$$

$$C_2H_2 + 2Cl_2 = C_2H_2Cl_4 \qquad \text{(tetrachloroethane)}$$

(3) *From saturated hydrocarbons*, by substitution reactions with chlorine or bromine. The reaction is facilitated by the presence of a catalyst (e.g. iodine) and it also proceeds more rapidly in presence of bright light. By prolonged reaction, the hydrogen atoms may be replaced successively.

For example, from methane it is possible to prepare methyl chloride, methylene dichloride, chloroform, and carbon tetrachloride in successive stages. In practice, the reaction leads to the formation of a mixture of the derivatives. If used as a means of preparation, the theoretical weight of the halogen is added, to minimize the proportions of the unwanted derivatives.

$$CH_4 + Cl_2 = HCl + CH_3Cl \qquad \text{(methyl chloride)}$$

$$CH_3Cl + Cl_2 = HCl + CH_2Cl_2 \qquad \text{(methylene dichloride)}$$

$$CH_2Cl_2 + Cl_2 = HCl + CHCl_3 \qquad \text{(chloroform)}$$

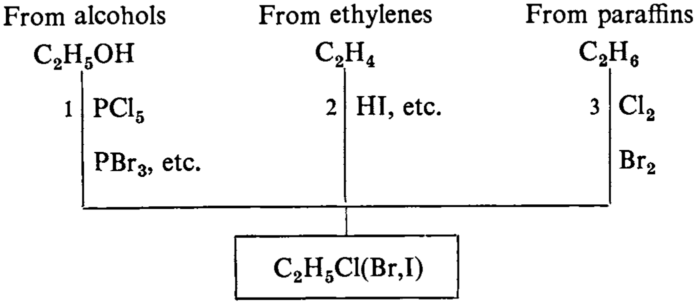
$$CHCl_3 + Cl_2 = HCl + CCl_4 \qquad \text{(carbon tetrachloride)}$$

Iodine derivatives cannot be prepared by direct substitution of a paraffin hydrocarbon.

(4) Certain di-halogen derivatives can be prepared from the corresponding aldehyde or ketone by reaction with phosphorus pentachloride.

$$(CH_3)_2CO + PCl_5 = (CH_3)_2CCl_2 + POCl_3$$

Preparation of Alkyl Halides



Physical Properties of the Halogen Derivatives of the Paraffin Hydrocarbons

The physical properties show the usual variations during the ascent of the homologous series. Melting and boiling points rise as the number of carbon atoms in the molecule increases. The melting and boiling points of the halogen derivatives are higher than those of the corresponding hydrocarbon, those of the iodine derivatives being the highest.

The specific gravities are greater than those of the corresponding hydrocarbons in the order iodide > bromide > chloride, but they decrease gradually as the number of carbon atoms in the molecule increases. Di-halogen and higher derivatives have higher melting and boiling points and specific gravities than the corresponding mono derivatives.

The halogen derivatives are insoluble in water, but dissolve readily in organic solvents.

Chemical Properties of the Halogen Derivatives of the Paraffin Hydrocarbons

The covalent aliphatic halides differ markedly in their reactions from the ionic metallic halides. In aqueous or alcoholic solution, an ionized halide will precipitate silver chloride quantitatively and instantaneously by the reaction

$$Ag^+ + Cl^- = Ag^+Cl^-$$

Some organic halides precipitate silver chloride from an alcoholic solution, slowly (because of the absence of chloride ions). Others do not act at all.

However, alkyl halides take part in a number of inter-molecular reactions, many of which result in the exchange of the halogen atom for organic groups following the breaking of the carbon–halogen bond. These groups become united to carbon by covalent linkages and therefore alkyl halides are important sources of many other compounds. The ease of reaction is usually greatest with the iodide.

In contrast to the relative ease of the exchange between the halogen atom and other groups, the presence of the halogen depresses the reactivity of the adjacent carbon and hydrogen atoms towards oxygen. Thus the halides are less inflammable than the hydrocarbons and carbon tetrachloride is used as a fire-extinguishing substance.

The chief reactions of the halogen derivatives are as follows:

(1) *Reduction.* The halogen derivatives may be reduced to hydrocarbons, e.g. by sodium amalgam and water or by a zinc–copper couple and water or alcohol.

$$C_2H_5I \xrightarrow{2H} = C_2H_6 + HI$$

(2) *Würtz reaction.* Alkyl halides are converted to hydrocarbons with double the number of carbon atoms in the molecule when heated in solution in dry ether with metallic sodium.

$$2CH_3I + 2Na = C_2H_6 + 2NaI$$

This reaction is often called the *Würtz* reaction, after its discoverer.

(3) *Hydrolysis.* Alkyl halides are converted to alcohols by treatment with an *aqueous* solution of potassium hydroxide (or moist silver oxide, which reacts as silver hydroxide).

$$C_2H_5Br + KOH = C_2H_5OH + KBr$$

(4) *Formation of double bond.* The higher alkyl halides react differently with an *alcoholic* solution of potassium hydroxide; for under these conditions a molecule of halogen acid may be removed from the alkyl halide molecule and an unsaturated compound produced.

$$C_4H_9Br + KOH = C_4H_8 + KBr + H_2O$$

This reaction can be used for the preparation of unsaturated compounds containing a double bond. By removing two molecules of halogen acid from a dihalogen derivative, triple bonded acetylenic compounds may be prepared.

$$C_2H_4Br_2 + 2KOH = C_2H_2 + 2KBr + 2H_2O$$

However, the ethyl halides react with alcoholic potash to yield mainly diethyl ether.

$$2C_2H_5Br + 2KOH = (C_2H_5)_2O + 2KBr + H_2O$$

Chloroform, iodoform, and carbon tetrachloride are hydrolysed either with alcoholic or with aqueous potash, on heating.

$$CHCl_3 + 4KOH = 3KCl + HCOOK + 2H_2O$$

$$CCl_4 + 6KOH = 4KCl + K_2CO_3 + 3H_2O$$

(5) *Formation of amines.* The alkyl halides are converted to amines by reaction with ammonia.

$$NH_3 + CH_3I = \underset{\text{Methylamine}}{CH_3NH_2} + HI\ (\rightarrow NH_4I)$$

$$CH_3NH_2 + CH_3I = \underset{\text{Dimethylamine}}{(CH_3)_2NH} + HI$$

$$(CH_3)_2NH + CH_3I = \underset{\text{Trimethylamine}}{(CH_3)_3N} + HI$$

$$CH_3I + (CH_3)_3N = \underset{\text{Tetramethylammonium iodide}}{(CH_3)_4NI}$$

(6) *Formation of nitriles.* The halogen atom of the alkyl halide may be replaced by the nitrile (or cyanide) radical by reaction with potassium cyanide.

$$CH_3I + KCN = \underset{\substack{\text{Methyl cyanide}\\ \text{or}\\ \text{acetonitrile}}}{CH_3CN} + KI$$

This reaction is important because the product may be converted into an organic acid by hydrolysis.

$$CH_3CN + 2H_2O = CH_3{\cdot}COONH_4$$

$$2CH_3{\cdot}COONH_4 + H_2SO_4 = 2CH_3{\cdot}COOH + (NH_4)_2SO_4$$

(7) *Formation of isonitriles.* The halogen atom may be replaced by an isonitrile group by reaction with silver cyanide.

$$CH_3I + AgCN = CH_3NC + AgI$$

(8) *Formation of ethers.* Alkyl halides react with the sodium derivatives of alcohols to form ethers.

$$C_2H_5I + C_2H_5ONa = \underset{\text{Diethyl ether}}{(C_2H_5)_2O} + NaI$$

(9) *Formation of nitro compounds.* The halogen atom in an alkyl halide may be replaced by a nitro group by reaction with silver nitrite.

$$\mathrm{CH_3I + AgNO_2 = \underset{\text{Nitromethane}}{CH_3NO_2} + AgI}$$

(10) *Formation of esters.* Alkyl halides react with the silver salts of organic acids forming esters.

$$\mathrm{CH_3{\cdot}COOAg + C_2H_5I = \underset{\text{Ethyl acetate}}{CH_3{\cdot}COOC_2H_5} + AgI}$$

(11) *Grignard reaction.* The alkyl halides, in dry ethereal solution, react with metallic magnesium to form *Grignard reagents.* These are reactive substances which have many applications in organic synthetic reactions (cf. p. 163).

$$\mathrm{C_2H_5I + Mg = \underset{\text{Magnesium ethyl iodide}}{C_2H_5MgI}}$$

(12) Alkyl halides react with the sodium derivatives of ethyl acetoacetate and ethyl malonate to give the alkyl derivatives of these esters, from which other compounds can be obtained on hydrolysis. These reactions are also of importance in organic synthesis (cf. p. 159 and p. 161).

Ethyl chloride

(Important commercially as an intermediate in the production of tetraethyl lead, which is added to most motor fuels as an "anti-knock") ethyl chloride is manufactured from ethylene and hydrogen chloride gas (in the presence of aluminium chloride as a catalyst) and is converted into tetraethyl lead by heating with a lead–sodium alloy.

$$\mathrm{CH_2{:}CH_2 + HCl = CH_3{\cdot}CH_2Cl}$$

$$\mathrm{4C_2H_5Cl + 4PbNa = Pb(C_2H_5)_4 + 4NaCl + 3Pb}$$

Reactions of Alkyl Halides

C_2H_5Cl

1	$Na\text{–}H_2O$	$CH_3{\cdot}CH_3$	Paraffin
2	Na	$C_2H_5{\cdot}C_2H_5$	Higher paraffin
3	KOH aq.	C_2H_5OH	Alcohol
4	KOH alc.	$CH_2{:}CH_2$	Ethylene (but see 4)
5	NH_3	$C_2H_5NH_2$	Amine
6	KCN	C_2H_5CN	Nitrile
7	AgCN	C_2H_5NC	Isonitrile
8	C_2H_5ONa	$C_2H_5OC_2H_5$	Ether
9	$AgNO_2$	$C_2H_5{\cdot}NO_2$	Nitro compound
10	$CH_3{\cdot}COOAg$	$CH_3{\cdot}COOC_2H_5$	Ester
11	Mg	C_2H_5MgCl	Grignard reagent

Chloroform ($CHCl_3$)

Chloroform is not conveniently prepared by the general methods for the aliphatic halides. It is usually prepared by the action of chlorine on ethyl alcohol or acetone in alkaline solution. The reactions take place in stages.

(a) Ethyl alcohol is first oxidized to acetaldehyde, which is then substituted by chlorine to form chloral. The chloral is then hydrolysed by the alkali to form chloroform.

$$C_2H_5OH + NaOCl = CH_3{\cdot}CHO + NaCl + H_2O$$

$$CH_3{\cdot}CHO + 3Cl_2 = CCl_3{\cdot}CHO + 3HCl$$

$$2CCl_3{\cdot}CHO + Ca(OH)_2 = 2CHCl_3 + (HCOO)_2Ca$$

(b) Acetone is substituted by chlorine to form trichloroacetone which is hydrolysed to chloroform by the alkali.

$$CH_3{\cdot}CO{\cdot}CH_3 + 3Cl_2 = CH_3{\cdot}CO{\cdot}CCl_3 + 3HCl$$

$$2CH_3{\cdot}CO{\cdot}CCl_3 + Ca(OH)_2 = 2CHCl_3 + (CH_3{\cdot}COO)_2Ca$$

In the laboratory and in the manufacturing process, chlorinated lime (bleaching powder) is used as a source of chlorine and alkali, the chloroform being distilled from the mixture of alcohol (or acetone) and chlorinated lime. As methyl alcohol does not give chloroform with chlorine and alkali, industrial methylated spirit can be used in the manufacturing process.

Chloroform is a heavy liquid with a characteristic odour. It is only slightly soluble in water, and is a good solvent for many organic substances. With alcoholic potash it is hydrolysed, and potassium formate is obtained, on heating.

$$CHCl_3 \rightarrow CH(OH)_3 \rightarrow HCOOH + H_2O$$

$$CHCl_3 + 4KOH = HCOOK + 3KCl + 2H_2O$$

Chloroform reacts with primary amines in alkaline alcoholic solution to form the characteristically evil smelling carbylamines or isocyanides.

$$CHCl_3 + CH_3NH_2 + 3KOH = CH_3NC + 3KCl + 3H_2O$$

Iodoform (CHI_3)

Iodoform is prepared by the action of iodine on ethyl alcohol or acetone in alkaline solution. The reaction proceeds in stages as in the preparation of chloroform. On a manufacturing scale a solution of potassium iodide containing alcohol or acetone and sodium carbonate is electrolysed. The alkali and iodine formed by the electrolysis react with the alcohol or acetone.

$$\begin{aligned} CH_3{\cdot}CH_2OH + I_2 + 2KOH &= CH_3{\cdot}CHO + 2KI + 2H_2O \\ CH_3{\cdot}CHO + 3I_2 + 3KOH &= CI_3{\cdot}CHO + 3KI + 3H_2O \\ CI_3{\cdot}CHO + KOH &= CHI_3 + HCOOK \end{aligned}$$

Iodoform is obtained, under similar conditions, from all compounds which contain an acetyl group attached to either carbon or hydrogen and also from other substances which can be converted into these compounds by the oxidizing action of iodine, e.g. ethyl alcohol, isopropyl alcohol and lactic acid.

$$\begin{aligned} CH_3{\cdot}CO{\cdot}R &\rightarrow CI_3{\cdot}CO{\cdot}R \rightarrow CHI_3 + HOCO{\cdot}R \\ C_2H_5OH &\rightarrow CH_3{\cdot}CHO \\ (CH_3)_2CHOH &\rightarrow CH_3{\cdot}CO{\cdot}CH_3 \\ CH_3{\cdot}CHOH{\cdot}COOH &\rightarrow CH_3{\cdot}CO{\cdot}COOH \end{aligned}$$

Carbon tetrachloride (CCl_4)

This is prepared commercially by the action of chlorine on carbon disulphide in the presence of a catalyst (e.g. ferric chloride).

$$CS_2 + 2Cl_2 = CCl_4 + 2S$$

It is non-inflammable (many fire extinguishers contain this substance) and not very reactive. With alcoholic caustic potash it is hydrolysed to form potassium carbonate, on heating.

$$CCl_4 + 6KOH = K_2CO_3 + 4KCl + 3H_2O$$

Dichlorodifluoromethane (CCl_2F_2)

This is prepared by the action of anhydrous hydrogen fluoride on carbon tetrachloride in the presence of a catalyst (antimony pentafluoride). It is used as a refrigerant and as the volatile dispersing agent of "aerosols".

$$CCl_4 + 2HF = CCl_2F_2 + 2HCl$$

THE UNSATURATED HALOGEN DERIVATIVES

These may be regarded as ethylenic hydrocarbons with hydrogen substituted by halogen, and thus they contain two functional groups (i.e. double bond and halogen atom) in their molecules. They are more reactive than the corresponding paraffin hydrocarbon halogen derivatives, e.g. they decolorize bromine as the result of addition at the double bond. Some are slowly decomposed by moisture, when exposed to light.

Trichloroethylene ($CHCl{:}CCl_2$)

This is prepared from acetylene by the addition of chlorine followed by the removal of hydrogen chloride, using barium chloride as a catalyst.

$$C_2H_2 + 2Cl_2 = C_2H_2Cl_4$$
$$C_2H_2Cl_4 = CHCl{:}CCl_2 + HCl$$

Tetrachloroethylene ($CCl_2{:}CCl_2$)

Obtained from trichloroethylene by addition of chlorine followed by removal of hydrogen chloride with milk of lime. These two chloroethylenes are used as dry-cleaning agents.

$$CHCl{:}CCl_2 + Cl_2 = CHCl_2{\cdot}CCl_3$$

$$CHCl_2{\cdot}CCl_3 = CCl_2{:}CCl_2 + HCl$$

Vinyl chloride ($CH_2{:}CHCl$)

Used to make its polymer (PVC), vinyl chloride is manufactured from acetylene by direct union with hydrogen chloride at temperatures between 100°C and 200°C and in the presence of a catalyst (e.g. mercuric and barium chlorides) or by the thermal decomposition of ethylene dichloride at 600°C.

$$CH\vdots CH + HCl = CH_2{:}CHCl$$

$$CH_2Cl{\cdot}CH_2Cl = CH_2{:}CHCl + HCl$$

Chloroprene ($CH_2{:}CH{\cdot}CCl{:}CH_2$)

Polymerized to form "neoprene" synthetic rubber, chloroprene is manufactured from vinylacetylene (cf. p. 28). This substance is converted to chloroprene by the addition of hydrogen chloride in the presence of a cuprous chloride catalyst.

$$CH_2{:}CH{\cdot}C\vdots CH + HCl = CH_2{:}CH{\cdot}CCl{:}CH_2$$

Tetrafluoroethylene

This is prepared by heating chlorodifluoromethane, which is obtained by the action of anhydrous hydrogen fluoride on chloroform. It is used to obtain its polymer which is an important "plastic". The polymerization is effected by pressure in the presence of a catalyst such as ammonium persulphate.

$$CHCl_3 + 2HF = CHF_2Cl + 2HCl$$

$$2CHF_2Cl = CF_2{:}CF_2 + 2HCl$$

4

the aliphatic alcohols and ethers

THE ALCOHOLS

(FUNCTIONAL GROUP $\gtrdot$C—OH)

The alcohols (alternatively known as carbinols) contain hydroxyl as their functional group. The monohydric alcohols possess one hydroxyl group in the molecule, while di-, tri-, etc., hydric alcohols possess two, three, or more hydroxyl groups. The simple mono-hydric alcohols, in which the hydroxyl group is attached to an alkyl radical, form a homologous series.

Constitution of the Alcohols

The constitutional formula of ethyl alcohol follows from its analysis and molecular weight (which indicate that the molecular formula is C_2H_6O), and its reaction with sodium which replaces one (and only one) hydrogen atom. The only way in which one of the hydrogen atoms can be differentiated from the others is by linkage through oxygen, as represented by the formula $CH_3{\cdot}CH_2OH$.

The presence of the hydroxyl group in alcohols is confirmed by their preparations from alkyl halides and potassium hydroxide, and by their reactions with phosphorus halides. The alcohols may be regarded as derivatives of water in which one hydrogen atom has been replaced by an alkyl group.

$$H—O—H \qquad C_2H_5—O—H$$

General Methods of Preparation of the Alcohols

The following methods are available for any alcohol:

(1) *Hydrolysis of halide.* From a halide by hydrolysis with aqueous caustic potash or moist silver oxide.

$$KOH + CH_3Br = CH_3OH + KBr$$

$$AgOH + C_2H_5I = AgI + C_2H_5OH$$

(2) *Hydrolysis of ester.* From an ester by hydrolysis.

$$CH_3{\cdot}COOC_2H_5 + H_2O = CH_3{\cdot}COOH + C_2H_5OH$$

(3) *Reduction of carbonyl group.* From an aldehyde or ketone by reduction by mild reducing agents such as sodium amalgam and water.

$$CH_3{\cdot}CHO \rightarrow C_2H_5OH$$

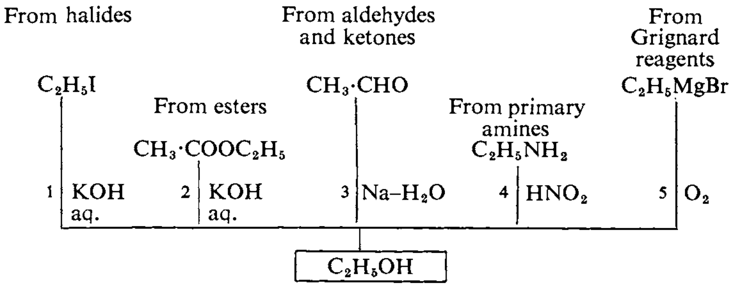
(4) *From primary amines.* From a primary amine by reaction with nitrous acid.

$$C_2H_5NH_2 + HNO_2 = C_2H_5OH + N_2 + H_2O$$

(5) *From Grignard reagent.* From a magnesium alkyl halide by the action of oxygen, followed by hydrolysis.

$$RMgBr \rightarrow ROMgBr \rightarrow ROH$$

Preparation of Alcohols



Physical Properties of the Alcohols

(a) Melting and Boiling Points.

The melting and boiling points of the monohydric alcohols rise with increase in molecular weight. The lowest alcohols are volatile liquids, the higher members are solids.

(b) Solubilities.

Methyl, ethyl and propyl alcohols are miscible with water in all proportions, but the solubility of alcohols in water rapidly diminishes as the number of carbon atoms in the molecule increases, and the higher members are practically insoluble. As solvents for other substances, the lower alcohols are intermediate between water and non-ionizing solvents such as the paraffin hydrocarbons.

Chemical Properties of the Alcohols

The following reactions are characteristic of the hydroxyl group and are given by all the aliphatic alcohols.

(1) *Formation of alkoxides.* Sodium and potassium react with alcohols, evolving hydrogen and forming compounds called the alkoxides (e.g. sodium methoxide, potassium ethoxide) in which the hydrogen of the hydroxyl group is replaced by the metal. Alkoxides react readily with water regenerating the alcohol.

$$2C_2H_5OH + 2Na = \underset{\text{Sodium ethoxide}}{2C_2H_5ONa} + H_2$$

$$C_2H_5ONa + H_2O = C_2H_5OH + NaOH$$

(2) *Conversion to halides.* Phosphorus halides (e.g. phosphorus trichloride, phosphorus pentachloride, or red phosphorus with either bromine or iodine) react with substances containing a hydroxyl group to replace that group by a halogen atom. The alcohols react to give the alkyl halides.

$$3C_2H_5OH + PCl_3 = 3C_2H_5Cl + H_3PO_3$$

(3) *Esterification.* Alcohols react with acids to form compounds which are called esters. This reaction, which is called *esterification,* is reversible; therefore a state of chemical equilibrium is eventually reached. Consequently, a large excess of one reactant favours the esterification reaction. Complete conversion of the alcohol into ester could be achieved by carrying out the reaction in the presence of a dehydrating agent, which removes the water formed by the reaction and so enables it to proceed to completion. In practice, the reaction is often carried out in the presence of sulphuric acid (or gaseous hydrogen chloride may be used). In these circumstances, the main function of the acid (i.e. the hydrogen ion) is a catalytic one.

The process of esterification between an alcohol and an acid is sometimes compared with that of salt formation between a base and an acid, but esterification is essentially a non-ionic reaction between the *hydroxyl group* of the acid and the *hydrogen atom* of the alcohol, while salt formation is ionic involving the *hydrogen ion* of the acid. The former reaction is therefore slow and reversible, the latter practically instantaneous. Further, esters are neutral, non-ionic substances, which are insoluble in water and do not resemble salts in their general characteristics.

$$CH_3{\cdot}CO\boxed{OH + H}OC_2H_5 = CH_3{\cdot}COOC_2H_5 + H_2O$$

Alcohols form esters with inorganic acids as well as with organic acids, e.g. ethyl alcohol and sulphuric acid form ethyl hydrogen sulphate.

$$C_2H_5OH + H_2SO_4 = C_2H_5HSO_4 + H_2O$$

The alkyl halides may be regarded as esters of the hydrogen–halide acids, but many of their reactions are not typical ester reactions.

(4) *Esterification with acid chlorides.* Esters are also obtained by the reaction of alcohols with acid chlorides (cf. acetylation, p. 94).

$$CH_3{\cdot}COCl + C_2H_5OH = CH_3{\cdot}COOC_2H_5 + HCl$$

(5) *Dehydration to ethers and ethylene.* Alcohols react with dehydrating agents to form either ethers or ethylenic compounds. With ethyl alcohol and concentrated sulphuric acid, the products are diethyl ether at 140°C with the alcohol in excess, or ethylene at 170°C with excess sulphuric acid.

$$C_2H_5O\boxed{H + HO}C_2H_5 = C_2H_5{-}O{-}C_2H_5 + H_2O$$

$$CH_3{\cdot}CH_2OH = CH_2{:}CH_2 + H_2O$$

These reactions are the basis of the laboratory preparations of ether and ethylene and the manufacturing process for ether. These products are obtained as the final results of a series of consecutive reactions:

(a) At 100°C ethyl alcohol and sulphuric acid react to form ethyl hydrogen sulphate (ethyl sulphuric acid).

$$C_2H_5OH + H_2SO_4 = C_2H_5HSO_4 + H_2O$$

(b) On further heating in presence of excess alcohol, this substance decomposes to form ether.

$$C_2H_5HSO_4 + C_2H_5OH = (C_2H_5)_2O + H_2SO_4$$

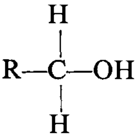
The sulphuric acid is regenerated and serves to convert further quantities of alcohol to ether.

(c) At a higher temperature, in the absence of further quantities of alcohol, the ethyl hydrogen sulphate decomposes to form ethylene and sulphuric acid.

$$C_2H_5HSO_4 = C_2H_4 + H_2SO_4$$

(6) *Oxidation.* There are three classes of alcohols distinguished by the number of hydrogen atoms united to the carbon atom to which the hydroxyl group is attached.

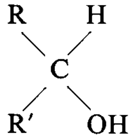
A *primary* alcohol (functional group $—CH_2OH$) has the hydroxyl group attached to a carbon atom which is attached to *two* hydrogen atoms and one alkyl group, thus:



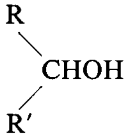
$$R-\overset{\displaystyle H}{\underset{\displaystyle H}{\overset{|}{\underset{|}{C}}}}-OH$$

or RCH_2OH

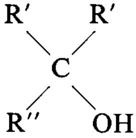
A *secondary* alcohol (functional group $>$CHOH) has *one* hydrogen atom attached to the carbon atom to which the hydroxyl group is attached.

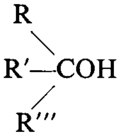


or

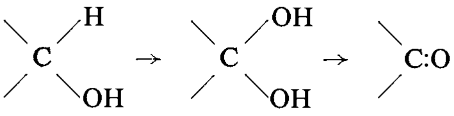


A *tertiary* alcohol (functional group $-\!\!>$COH) contains a carbon atom which is linked to three alkyl groups and to the hydroxyl group.



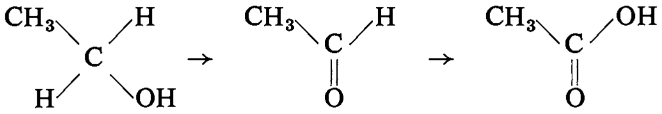


The oxidation of alcohols may be interpreted as proceeding by the conversion of a C—H linkage to a C—OH linkage. The initial product is unstable since it is a general rule that two hydroxyl groups attached to the same carbon atom do not form a stable system. Water is split off, and a compound is formed which contains a carbonyl group, i.e. a carbon atom linked to an oxygen atom by a double bond.



Further oxidation is possible if the carbon atom doubly linked to oxygen is also linked to hydrogen, for the C—H link can be converted to C·OH.

Primary alcohols are oxidized in two stages, first to aldehydes (as by potassium dichromate in the presence of dilute sulphuric acid) and then to acids (as by potassium permanganate and dilute sulphuric acid). No further oxidation is possible unless the acid molecule is completely broken up.



Ethyl alcohol Acetaldehyde Acetic acid

Secondary alcohols are oxidized to ketones, but cannot be oxidized further without breaking down.

$$(CH_3)_2CHOH \rightarrow (CH_3)_2CO$$

Isopropyl alcohol Acetone

The oxidation of a secondary alcohol to a ketone can be brought about by potassium dichromate in the presence of dilute sulphuric acid. Potassium permanganate causes a break down of the molecule.

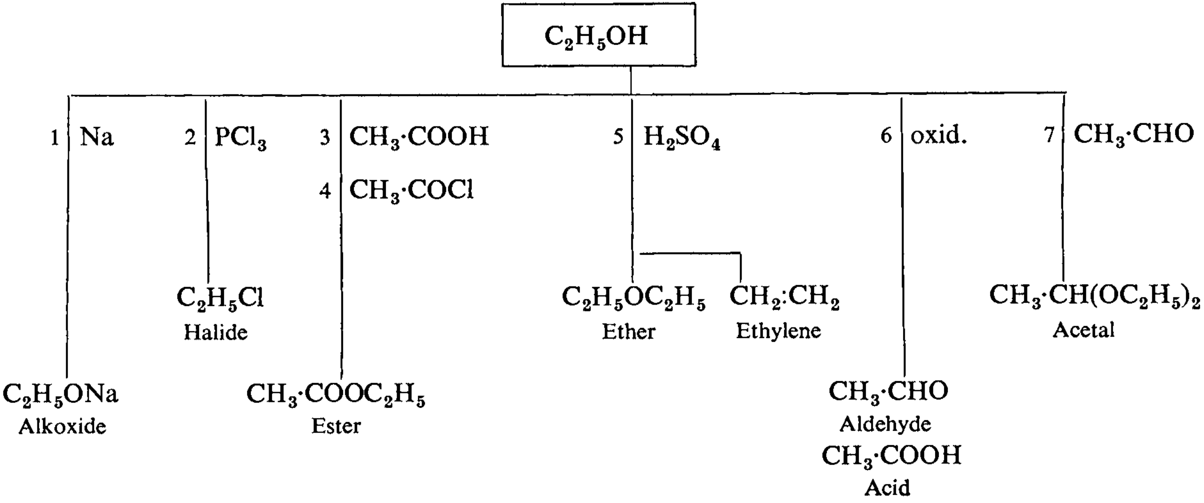
$$CH_3{\cdot}CO{\cdot}CH_3 \rightarrow CH_3{\cdot}COOH + H_2O + CO_2$$

The *tertiary alcohols* do not possess a hydrogen atom attached to the same carbon atom as the hydroxyl group and cannot be oxidized without the molecule being broken down into smaller fragments.

(7) *Formation of acetals.* Alcohols react with aldehydes, in the presence of a dehydrating agent, to form acetals.

$$CH_3{\cdot}CHO + 2C_2H_5OH = CH_3{\cdot}CH(OC_2H_5)_2 + H_2O$$

Reactions of Alcohols



Methyl alcohol (*methanol*)

The lowest member of the homologous series of alcohols is manufactured on a large scale by a synthetic reaction by passing a mixture of carbon monoxide and hydrogen over a catalyst (zinc oxide) at 300°C and at a pressure of 150–300 atm.

$$CO + 2H_2 = CH_3OH$$

(By the use of other catalysts and different conditions of temperature and pressure, higher alcohols may be obtained from these two gases.)

Methyl alcohol is used in the preparation of other important organic substances (e.g. dyes, plastics, etc.) and to "denature" ethyl alcohol to form methylated spirit. Industrial methylated spirit contains 1 vol of "wood spirit" to 19 vol of alcohol.

Methyl alcohol is a colourless liquid (b.p. 67°C) with a characteristic odour. It is completely miscible with water. Pure methyl alcohol may be distinguished from ethyl alcohol as it does not form iodoform by reaction with an alkaline solution of iodine.

Ethyl alcohol (*ethanol*)

For industrial purposes, ethanol is obtained from ethylene, which can be converted into the alcohol by absorption in concentrated sulphuric acid, followed by hydrolysis of the product. However, the chief manufacturing process involves direct hydration.

$$C_2H_4 + H_2O = C_2H_5OH$$

Ethylene and steam are passed over a phosphoric acid catalyst (absorbed on siliceous pellets) at 70 atm pressure and 300°C. A 5 per cent conversion into the alcohol is obtained and the uncombined gases are recirculated after condensing the alcohol. Anhydrous (or absolute) alcohol is obtained by taking advantage of the fact that a system containing alcohol, water, and benzene forms a constant boiling mixture containing all three substances and this boils at a lower temperature than any single constituent.

A mixture of petroleum ether (benzine) and benzene is added to the moist alcohol, and the mixture is distilled. The first fraction contains the whole of the water, a little alcohol and some of the petroleum ether–benzene mixture. After the water has been removed, the second runnings distil, consisting of the remainder of the petroleum ether–benzene mixture together with alcohol. Finally pure anhydrous alcohol distils.

Fermentation alcohol is obtained from molasses (the residues from the recovery of cane or beet sugar), and from the starch of potatoes and various grains, e.g. barley and maize. Sucrose and starch are not directly fermentable by yeast, but they can be fermented after hydrolysis into simpler sugars, such as glucose. The complex reactions taking place during the fermentation of monosaccharides may be summarized by the equation:

$$C_6H_{12}O_6 = 2C_2H_5OH + 2CO_2$$

The production of alcohol from barley is carried out in several stages. Firstly, the barley is allowed to germinate and the growing grain is killed by raising the temperature. The product is known as *malt*. During malting, an enzyme *diastase* is formed in greater proportion than it is present in the dormant seed and this enzyme is capable of hydrolysing starch into the disaccharide, maltose.

The dried and ground malt is mixed with water and seeded by yeast. (Fresh starchy material such as unmalted corn or potato paste may be added.) The enzymes present in yeast convert maltose into glucose (by maltase) and then glucose into ethyl alcohol (by zymase). The maximum concentration of alcohol obtainable by simple fermentation is about 18 per cent; above this concentration, the yeast cells are unable to live. Ninety-five per cent alcohol is obtainable by distillation.

Molasses is converted to alcohol directly by seeding with yeast.

Ethyl alcohol is a mobile liquid (b.p. 78°C), miscible in all proportions with water and chloroform. When dehydrated, it does not restore the blue colour to anhydrous copper sulphate. The formation of iodoform by the action of iodine in alkaline solution is a sensitive test for the presence of ethyl alcohol.

$$C_2H_5OH + I_2 + 2NaOH = CH_3{\cdot}CHO + 2NaI + H_2O$$

$$CH_3{\cdot}CHO + 3I_2 + 3NaOH = CI_3{\cdot}CHO + 3NaI + 3H_2O$$

$$CI_3{\cdot}CHO + NaOH = CHI_3 + HCOONa$$

Isopropyl alcohol is manufactured from propylene by reaction with sulphuric acid, followed by the hydrolysis of the product.

$$CH_3{\cdot}CH{:}CH_2 \rightarrow CH_3{\cdot}CH(HSO_4){\cdot}CH_3 \rightarrow CH_3{\cdot}CHOH{\cdot}CH_3$$

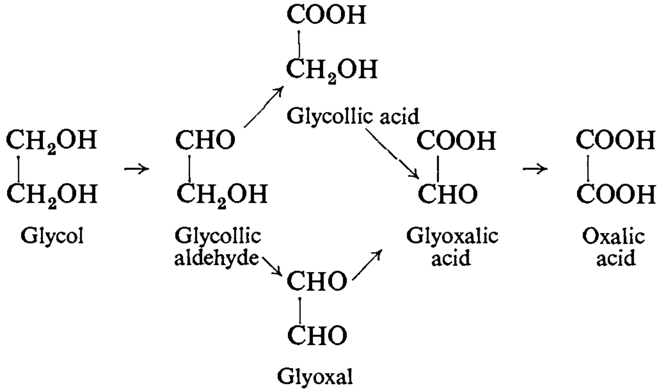
ALCOHOLS CONTAINING MORE THAN ONE HYDROXYL GROUP

Polyhydric alcohols contain more than one hydroxyl group; those with two hydroxyl groups are the *dihydric* alcohols (these are also called *glycols*), those with three hydroxyl groups are the *trihydric* alcohols, etc. The molecules of these alcohols contain more than one functional group and the compounds exhibit a series of reactions relating to each such group alone and further reactions which can only arise when more than one functional group is present in a molecule.

Polyhydric alcohols can be prepared by suitable modifications of the general methods of preparation for the monohydric alcohols. For example, the alkaline hydrolysis of ethylene dichloride, dibromide or di-iodide gives the simplest dihydric alcohol which is called glycol or ethylene glycol.

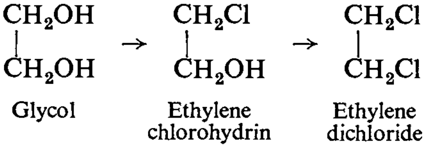
$$CH_2Br{\cdot}CH_2Br + 2KOH = CH_2OH{\cdot}CH_2OH + 2KBr$$

The properties of the polyhydric alcohols resemble those of the monohydric alcohols. However, a greater number of derivatives may be obtained from them, for the reactions can involve either one, or any number (or combination) of the hydroxyl groups. The oxidation of ethylene glycol (which contains two primary alcohol groupings) can be made to furnish the following products, some arising from the oxidation of one such group and the others arising from the oxidation of both groups.



$$\underset{\text{Glycol}}{\begin{array}{c}CH_2OH\\|\\CH_2OH\end{array}} \rightarrow \underset{\text{Glycollic aldehyde}}{\begin{array}{c}CHO\\|\\CH_2OH\end{array}} \begin{array}{c}\nearrow \underset{\text{Glycollic acid}}{\begin{array}{c}COOH\\|\\CH_2OH\end{array}} \searrow\\ \searrow \underset{\text{Glyoxal}}{\begin{array}{c}CHO\\|\\CHO\end{array}} \nearrow\end{array} \underset{\text{Glyoxalic acid}}{\begin{array}{c}COOH\\|\\CHO\end{array}} \rightarrow \underset{\text{Oxalic acid}}{\begin{array}{c}COOH\\|\\COOH\end{array}}$$

Correspondingly, glycol reacts with gaseous hydrogen chloride to yield ethylene chlorohydrin or ethylene dichloride.

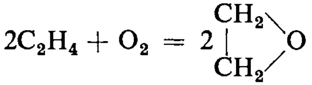


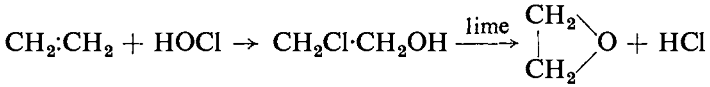
$$\underset{\text{Glycol}}{\begin{array}{c}CH_2OH\\|\\CH_2OH\end{array}} \rightarrow \underset{\text{Ethylene chlorohydrin}}{\begin{array}{c}CH_2Cl\\|\\CH_2OH\end{array}} \rightarrow \underset{\text{Ethylene dichloride}}{\begin{array}{c}CH_2Cl\\|\\CH_2Cl\end{array}}$$

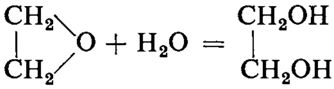
Due to the presence of two primary alcohol groupings in the same molecule, the glycols yield internal anhydrides by the elimination of water between the two hydroxyl groups. These anhydrides are chemically allied to ethers. The anhydride of glycol, which is called ethylene oxide, is an intermediate in the commercial production of glycol.

Glycol

This substance which is an important "anti-freeze" additive to water, is prepared from ethylene oxide which is made from ethylene, either by direct reaction with oxygen at 200–300°C in the presence of metallic silver as a catalyst or via the chlorohydrin prepared from ethylene, chlorine and water (hypochlorous acid). Ethylene oxide is converted into glycol by hot water under pressure.

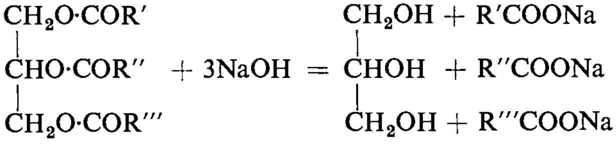






Glycerol (*or glycerin*, $CH_2OH{\cdot}CHOH{\cdot}CH_2OH$)

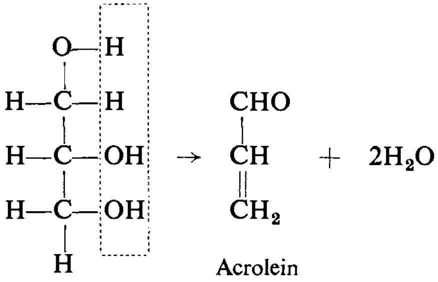
This is the most important representative of the class of trihydric alcohols. It can be prepared by suitable modifications of the general methods for monohydric alcohols, but it is obtained on a large scale from fats and fatty oils, which are the esters of glycerol and certain organic acids. They are converted into the acids and glycerol by hydrolysis, normally in alkaline solution, as in the manufacture of soap. After separation of the soap and any resinous matter, a watery liquid is obtained which contains glycerol and sodium chloride. The glycerol is extracted by distillation *in vacuo* after a preliminary concentration by evaporation *in vacuo*.



$$\begin{array}{l} CH_2O{\cdot}COR' \\ | \\ CHO{\cdot}COR'' \\ | \\ CH_2O{\cdot}COR''' \end{array} + 3NaOH = \begin{array}{l} CH_2OH + R'COONa \\ | \\ CHOH \;\; + R''COONa \\ | \\ CH_2OH + R'''COONa \end{array}$$

Glycerol is a hygroscopic, syrupy liquid which crystallizes on standing at low temperatures. Glycerol exhibits the general reactions of alcohols since its molecule contains two primary and one secondary alcohol grouping. It also undergoes reactions arising from the proximity of these particular groups.

(1) Dehydration. By the action of concentrated sulphuric acid or potassium bisulphate, two molecules of water are removed from the molecule of glycerol. Acrolein, an unsaturated aldehyde, which has a characteristic smell and lachrymatory action, is formed.

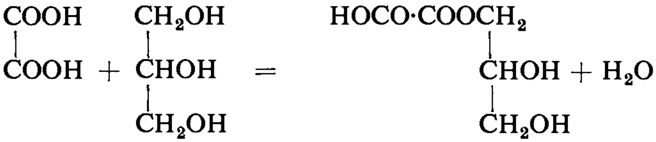


$$\begin{array}{l} \text{O—H} \\ \text{H—C—H} \\ \text{H—C—OH} \\ \text{H—C—OH} \\ \quad\text{H} \end{array} \rightarrow \begin{array}{c} CHO \\ | \\ CH \\ \| \\ CH_2 \end{array} + 2H_2O$$

Acrolein

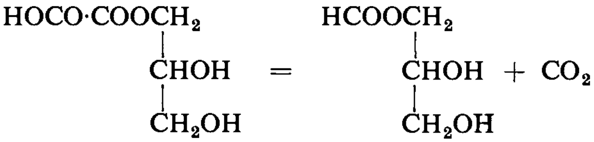
(2) Glycerol reacts with oxalic acid to yield either formic acid or allyl alcohol (the alcohol corresponding to the unsaturated aldehyde, acrolein).

The first product of the reaction between oxalic acid and glycerol is the mono-ester (glyceryl monoxalate).



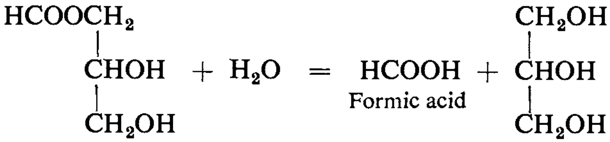
$$\begin{array}{l} COOH \\ | \\ COOH \end{array} + \begin{array}{l} CH_2OH \\ | \\ CHOH \\ | \\ CH_2OH \end{array} = \begin{array}{r} HOCO{\cdot}COOCH_2 \\ | \\ CHOH \\ | \\ CH_2OH \end{array} + H_2O$$

This substance loses carbon dioxide on heating, and is transformed into the monoglyceryl ester of formic acid (often called monoformin).



$$\begin{array}{r} HOCO{\cdot}COOCH_2 \\ | \\ CHOH \\ | \\ CH_2OH \end{array} = \begin{array}{r} HCOOCH_2 \\ | \\ CHOH \\ | \\ CH_2OH \end{array} + CO_2$$

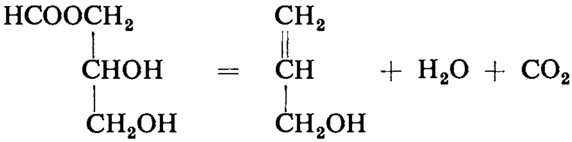
On gentle heating with excess oxalic acid (followed by steam distillation) formic acid is obtained by hydrolysis of the ester.



$$\begin{array}{r} HCOOCH_2 \\ | \\ CHOH \\ | \\ CH_2OH \end{array} + H_2O = HCOOH + \begin{array}{l} CH_2OH \\ | \\ CHOH \\ | \\ CH_2OH \end{array}$$

Formic acid

On heating to a higher temperature, and if excess glycerol is present, the ester breaks down and allyl alcohol is obtained.



$$\begin{array}{c}HCOOCH_2\\ |\\ CHOH\\ |\\ CH_2OH\end{array} = \begin{array}{c}CH_2\\ \|\\ CH\\ |\\ CH_2OH\end{array} + H_2O + CO_2$$

Allyl alcohol

(3) The nitric acid esters of glycerol are highly explosive (nitroglycerin).

THE ALIPHATIC ETHERS

(FUNCTIONAL GROUP $\rangle$C—O—C$\langle$)

Ethers may be regarded as derived from water by replacing both the hydrogen atoms with organic groups. The groups replacing the two hydrogen atoms need not be identical. Ethers formed from two dissimilar groups are known as *mixed ethers* in distinction to *simple ethers* where the two groups are the same.

C_2H_5—O—C_2H_5

Diethyl ether
(simple ether)

CH_3—O—C_2H_5

Methyl ethyl ether
(mixed ether)

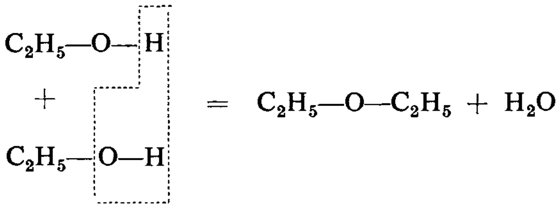
Isomerism of Ethers (Metamerism)

Diethyl ether (C_2H_5—O—C_2H_5) and methyl propyl ether (CH_3—O—C_3H_7) are isomeric. A similar type of isomerism, due to the difference in chain lengths of two alkyl groups, is found in many other classes of organic compounds (e.g. ketones, esters). It is sometimes called metamerism.

Preparation of Ethers

The two most important methods of preparation of ethers are:

(1) *By the dehydration of alcohols.* Alcohols react with concentrated sulphuric acid under appropriate conditions to give ethers (cf. p. 46).



$$\begin{matrix} C_2H_5\text{—}O\text{—}H \\ + \\ C_2H_5\text{—}O\text{—}H \end{matrix} = C_2H_5\text{—}O\text{—}C_2H_5 + H_2O$$

If sulphuric acid is made to react on a mixture of two different alcohols in equivalent proportions, the product contains some mixed ether as well as the two simple ethers formed from each alcohol.

$$C_2H_5O\boxed{H + HO}CH_3 = C_2H_5\text{—}O\text{—}CH_3 + H_2O$$

(2) *Williamson's synthesis.* From alkyl halides by reacting with the sodium derivatives of alcohols. This reaction can be used for the preparation of mixed ethers.

$$CH_3I + C_2H_5\text{—}O\text{—}Na = NaI + CH_3\text{—}O\text{—}C_2H_5$$

General Properties of Ethers

The commoner ethers are neutral liquids which are characterized by a general chemical inactivity. They are stable to dilute acids and alkalis. But some ethers absorb oxygen on standing, forming unstable ether peroxides whose composition has not been thoroughly established. (A possible representation of the composition of the peroxide of diethyl ether is

($CH_3{\cdot}CHOH{\cdot}O{\cdot}O{\cdot}CHOH{\cdot}CH_3{\cdot}$). Ether peroxides accumulate in the least volatile fractions during distillation and may lead to dangerous explosions.

(1) *Reaction with hydriodic acid.* Ethers are decomposed when heated with the constant boiling solution of hydriodic acid.

$$ROR' + HI = ROH + R'I$$

(2) *Reaction with phosphorus pentachloride.* Ethers are decomposed by heating with phosphorus pentachloride, but do not react with this substance in the cold.

$$C_2H_5{\cdot}O{\cdot}C_2H_5 + PCl_5 = 2C_2H_5Cl + POCl_3$$

Diethyl ether

The most important representative of the class is diethyl ether (often referred to as ether), which is a colourless, volatile, and inflammable liquid (b.p. 36°C) with a characteristic smell. It is prepared from ethyl alcohol and concentrated sulphuric acid. If industrial methylated spirit is used the product (*methylated ether*) contains methyl ethyl ether and acetone as well as diethyl ether.

THE ALIPHATIC SULPHUR COMPOUNDS

The sulphur compounds corresponding to the alcohols are the thio-alcohols or mercaptans; the compounds corresponding to the ethers are the thio-ethers.

The Thio-alcohols (Functional Group $-\!\!\!>\!C{—}SH$)

These may be prepared from the alkyl halides by reaction with potassium hydrogen sulphide.

$$C_2H_5Cl + KHS = C_2H_5SH + KCl$$

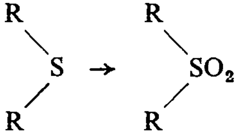
They are fairly reactive substances which possess characteristic smells.

The Thio-ethers (Functional Group $-\!\!>\!C-S-C\!<\!\!-$)

Thio-ethers are obtained by the reaction of alkyl halides with the sodium derivatives of thio-alcohols.

$$C_2H_5I + C_2H_5SNa = (C_2H_5)_2S + NaI$$

They are oxidized by concentrated nitric acid and by potassium permanganate to *sulphones.*



Thio-ether Sulphone

5

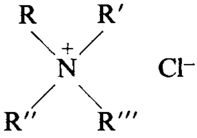
amino and nitro compounds

THE ALIPHATIC AMINES

(FUNCTIONAL GROUPS $—NH_2$; $>NH$; $\rightarrow N$)

The aliphatic amines are derivatives of ammonia obtained by the replacement of the hydrogen atoms by alkyl groups. One, two or three hydrogen atoms may be substituted forming compounds of the type $R—NH_2$ (primary amines), $\begin{matrix} R \\ R' \end{matrix}\!\!>\!NH$ (secondary amines), and $\begin{matrix} R \\ R'— \\ R'' \end{matrix}\!\!\!>\!N$ (tertiary amines).

It is also possible to obtain quaternary ammonium salts in which the four hydrogen atoms of ammonium chloride have been replaced by alkyl groups, e.g.



$$\left[R R' R'' R''' N \right]^+ Cl^-$$

(The alkyl groups need not necessarily be the same in these compounds.)

General Methods of Preparation of the Amines

(1) *From alkyl halides and ammonia.* Amines may be prepared by the direct substitution of ammonia by reaction with alkyl halides in alcoholic solution. Primary, secondary, tertiary, or quaternary compounds may be formed by successive substitution, and in many cases a mixture containing all four is obtained. Their separation may be troublesome. Firstly, sodium hydroxide is added and the primary, secondary and tertiary amines are distilled away from the unchanged quaternary salt. The primary, secondary and tertiary amines might be separated by fractional distillation, but alternative chemical methods are often preferred.

By reacting on the mixture with benzene (or *p*-tolyl) sulphonyl chloride and then making the solution alkaline, the primary amine is converted into a mono-alkylsulphonamide derivative, soluble in the alkali, the secondary amine into a dialkyl derivative, insoluble in the alkali, while the tertiary amine does not react and can be distilled unchanged. The sulphonamides can be hydrolysed back to the original amines.

$$C_6H_5{\cdot}SO_2Cl + RNH_2 = C_6H_5{\cdot}SO_2NHR + HCl$$

$$C_6H_5{\cdot}SO_2Cl + R_2NH = C_6H_5{\cdot}SO_2NR_2 + HCl$$

(2) *Hofmann reaction.* Primary amines are more conveniently prepared from acid amides by reaction with bromine in presence of potassium hydroxide (*Hofmann* reaction). The first reaction produces the bromine derivative of the acid amide.

$$\underset{\text{Acetamide}}{CH_3{\cdot}CONH_2} + Br_2 = \underset{\text{Monobromoacetamide}}{CH_3{\cdot}CONHBr} + HBr$$

This substance then loses a molecule of hydrogen bromide, and at the same time undergoes a molecular rearrangement.

$$CH_3{\cdot}CONHBr = \underset{\substack{\text{Methyl}\\ \text{isocyanate}}}{CH_3NCO} + HBr$$

The isocyanate thus formed yields the primary amine on hydrolysis.

$$CH_3NCO + 2KOH = CH_3NH_2 + K_2CO_3$$

The molecule of the amine formed contains one carbon atom less than the original acid amide and, to indicate this loss of a carbon atom, the reaction is sometimes referred to as the *Hofmann degradation.*

$$CH_3{\cdot}CONH_2 \rightarrow CH_3NH_2$$

(3) *Reduction of nitro compounds, etc.* Primary amines are also obtained when certain other compounds containing a nitrogen atom linked directly to a carbon atom are reduced, e.g. nitroparaffins, nitriles and oximes.

$$CH_3NO_2 \xrightarrow{6H} CH_3{\cdot}NH_2 + 2H_2O$$

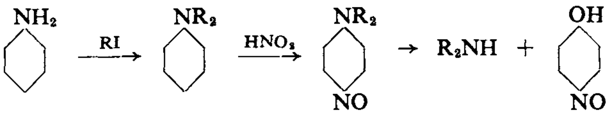
$$CH_3CN \xrightarrow{4H} CH_3{\cdot}CH_2NH_2$$

$$CH_3{\cdot}CH{:}NOH \xrightarrow{4H} CH_3{\cdot}CH_2NH_2 + H_2O$$

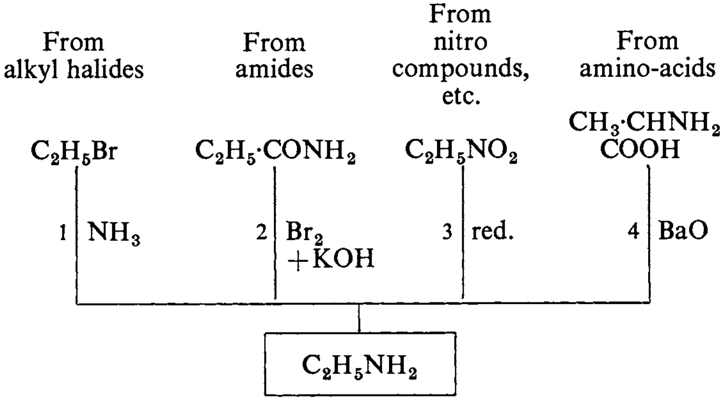
(4) *Decarboxylation of amino-acids.* Primary amines can be obtained by the decarboxylation of amino-acids by heating them with barium oxide (cf. conversion of carboxylic acid to hydrocarbon by heating with soda-lime).

$$CH_3{\cdot}CHNH_2{\cdot}COOH + BaO = CH_3{\cdot}CH_2NH_2 + BaCO_3$$

(5) *Secondary amines may be prepared* from alkyl halides by heating them with aniline and treating the resultant dialkylanilines with nitrous acid (cf. p. 203). The *p*-nitrosodialkylanilines, which are formed, are hydrolysed by boiling with sodium hydroxide solution to give the secondary amines and *p*-nitrosophenol.

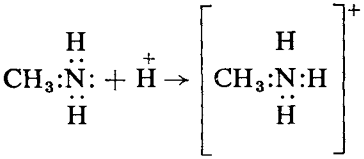


Preparation of Primary Amines



The Properties of Amines

(1) *Basic function.* The amines resemble ammonia in many ways. The lower members are gases, very soluble in water to give alkaline solutions. They possess characteristic odours. They are strongly basic substances and, like ammonia, form salts by reaction with hydrogen ions.



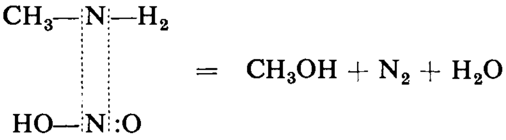
$$CH_3:\underset{H}{\overset{H}{\underset{\cdot\cdot}{\overset{\cdot\cdot}{N}}}}: + \overset{+}{H} \rightarrow \left[CH_3:\underset{H}{\overset{H}{\underset{\cdot\cdot}{\overset{\cdot\cdot}{N}}}}:H\right]^+$$

(Conventionally, salt formation is often written thus $CH_3NH_2{\cdot}HCl$.) The amines are stronger bases than ammonia and the strength of the base increases with increased substitution, i.e. the strengths in non-aqueous solvents are ammonia < primary amine < secondary amine < tertiary amine < quaternary base.

This order of strength indicates the increased ease of accessibility of a proton to the unshared electron pair of the nitrogen atom in the presence of the alkyl groups. This effect can be explained in terms of the unequal sharing of the electron pair involved in the C—N bond, so that the nitrogen atom is relatively more electronegative than the carbon atom. It will thus co-ordinate a proton more and more readily as the number of alkyl groups increases.

(2) *Reactions with nitrous acid.* Primary, secondary and tertiary amines react differently with nitrous acid.

(a) The primary amines give an immediate evolution of nitrogen; an alcohol is formed, which may react with excess nitrous acid to give a nitrous ester.



$$\begin{array}{l} CH_3\text{—}N\text{—}H_2 \\ \qquad \vdots \quad \vdots \\ HO\text{—}N:O \end{array} = CH_3OH + N_2 + H_2O$$

(b) The secondary amines form yellow, oily nitrosamines (functional group —N·N:O), which are neutral substances, insoluble in water but soluble in organic solvents.

$$(CH_3)_2N\boxed{H+HO}N:O = (CH_3)_2N\cdot NO + H_2O$$

Nitrosamines may be hydrolysed to re-form the original secondary amines.

(c) The tertiary amines do not react with nitrous acid.

(3) *Carbylamine reaction.* The primary amines may also be distinguished from the other amines by their reaction with chloroform and potassium hydroxide, whereby poisonous and unpleasantly smelling carbylamines or isocyanides are obtained.

$$CH_3NH_2 + 3KOH + CHCl_3 = CH_3NC + 3KCl + 3H_2O$$

(4) *Formation of acyl derivatives.* The primary and secondary amines react with acid chlorides and acid anhydrides to form derivatives in which a hydrogen atom of the amine is replaced by

an acyl group. (The products of these reactions may also be regarded as alkyl substituted acid amides.)

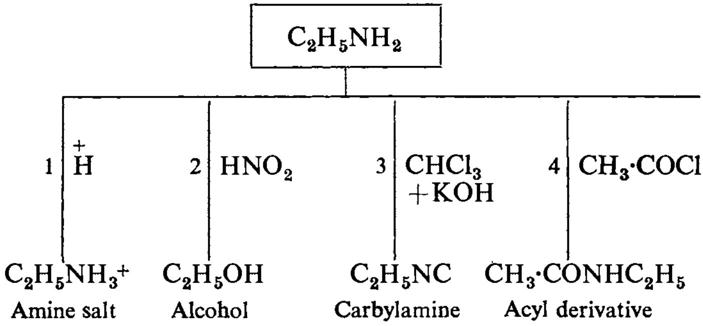
$$R{\cdot}COCl + R'NH_2 = R{\cdot}CONHR' + HCl$$

$$(R{\cdot}CO)_2O + R'NH_2 = 2R{\cdot}CONHR' + H_2O$$

(5) *Decomposition of quaternary compounds.* The quaternary ammonium compounds decompose to give tertiary amines on heating.

$$(CH_3)_4NI = N(CH_3)_3 + CH_3I$$

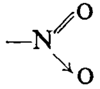
Reactions of Primary Amines



Comparison of Aliphatic Amines

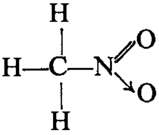
Reaction	*Primary amines*	*Secondary amines*	*Tertiary amines*
Alkyl halide	secondary amine	tertiary amine	quaternary compound
Nitrous acid	alcohol	nitrosamine	no action
Chloroform	carbylamine	no action	no action
Acid chloride or anhydride	substituted amide	substituted amide	no action

THE NITROPARAFFINS

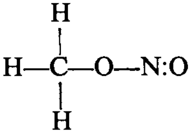
[FUNCTIONAL GROUP 
$—N(=O)\rightarrow O$ ($—NO_2$)]

The paraffin hydrocarbons cannot easily be nitrated directly, in contrast to the corresponding aromatic compounds, but in some cases nitration can be effected in the vapour phase, e.g. nitroethane is obtained when ethane is heated to 400°C with concentrated nitric acid (which is dissociated at this temperature into oxides of nitrogen).

The nitroparaffins are prepared in the laboratory by the reaction of silver nitrite on the alkyl halides. Reaction with sodium nitrite (or nitrous acid) yields the isomeric alkyl nitrites. Nitroparaffins differ from alkyl nitrites in that the nitrogen atom is linked directly to a carbon atom, and not through an oxygen atom.



Nitromethane



Methyl nitrite

The nitroparaffins are not affected by alkalis, and in this respect they differ from the nitrites which are readily hydrolysed.

$$C_2H_5ONO + NaOH = NaNO_2 + C_2H_5OH$$

On reduction, the nitroparaffins are converted to the primary amines while the alkyl nitrites give an alcohol, and either ammonia or hydroxylamine.

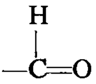
$$C_2H_5NO_2 \xrightarrow{6H} C_2H_5NH_2 + 2H_2O$$

$$C_2H_5ONO \xrightarrow{6H} C_2H_5OH + NH_3 + H_2O$$

6

the aliphatic aldehydes and ketones

The Aliphatic Aldehydes



[Functional Group $-\overset{\overset{\displaystyle H}{|}}{C}{=}O$ ($-CHO$)]

Aldehydes and ketones contain the functional group $>C{=}O$ (carbonyl) and give the reactions of this group. The presence of a hydrogen atom linked to the carbon of the carbonyl group confers properties on the aldehydes differing from those of the ketones which do not possess such a hydrogen atom.

General Methods of Preparation of Aldehydes

Aldehydes are prepared:

(1) *From primary alcohols by oxidation.* Methyl alcohol gives formaldehyde (cf. p. 74), and ethyl alcohol gives acetaldehyde (cf. p. 48).

$$CH_3OH \rightarrow CH_2(OH)_2 \rightarrow HCHO + H_2O$$

$$CH_3{\cdot}CH_2OH \rightarrow CH_3{\cdot}CH(OH)_2 \rightarrow CH_3{\cdot}CHO + H_2O$$

(2) *From acid chlorides* (cf. p. 94) *by reduction* (or in small yield by heating the calcium salt of the acid with calcium formate (cf. p. 77).

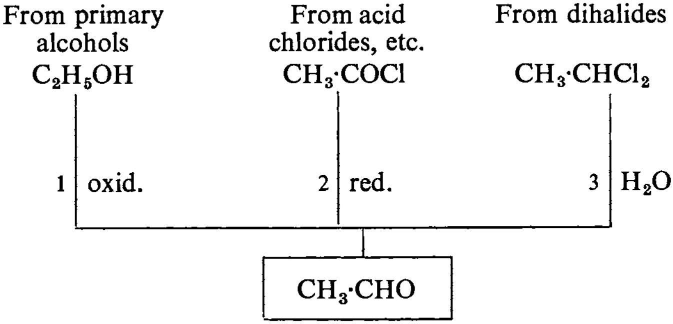
$$CH_3\cdot COCl \xrightarrow{2H} CH_3\cdot CHO + HCl$$

$$(CH_3\cdot COO)_2Ca + (HCOO)_2Ca = 2CH_3\cdot CHO + 2CaCO_3$$

(3) *From dihalides containing the* CHX_2 *group*, where X is Cl, Br or I, by hydrolysis with aqueous potassium hydroxide solution.

$$R\cdot CHX_2 \rightarrow RCH(OH)_2 \rightarrow RCHO$$

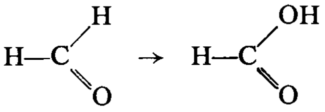
Preparation of Aldehydes



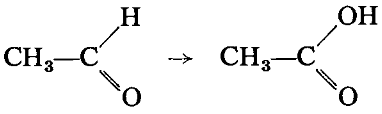
General Properties of Aldehydes

The aldehydes are reactive compounds.

(1) *Oxidation.* Aldehydes are easily oxidized to the corresponding acids, and behave as reducing agents.



Formaldehyde Formic acid



Acetaldehyde Acetic acid

The reductions of ammoniacal silver nitrate to silver, and Fehling's solution to red cuprous oxide, are commonly used as tests for aldehydes.

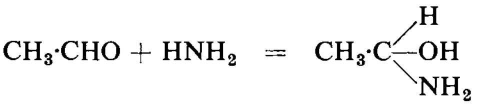
(2) *Reduction of carbonyl group.* Aldehydes are reduced to the corresponding primary alcohols. Sodium amalgam and water can be used as a reducing agent, or the vapour of the aldehyde may be passed mixed with hydrogen over a nickel catalyst.

$$CH_3{\cdot}CHO \xrightarrow{2H} CH_3{\cdot}CH_2OH$$

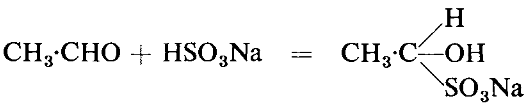
(3) *Replacement of carbonyl oxygen.* Phosphorus pentachloride reacts with aldehydes to replace the oxygen atom by two chlorine atoms.

$$CH_3{\cdot}CHO + PCl_5 = CH_3{\cdot}CHCl_2 + POCl_3$$

(4) *Addition to carbonyl group.* Aldehydes form addition compounds with ammonia, sodium bisulphite and hydrogen cyanide. The aldehyde–ammonia and bisulphite compounds are often crystalline substances, which are easily decomposed, reforming the aldehydes. They may be used in the purification of the aldehydes; in the case of acetaldehyde, the ammonia derivative is preferred as the bisulphite compound is appreciably soluble in water.

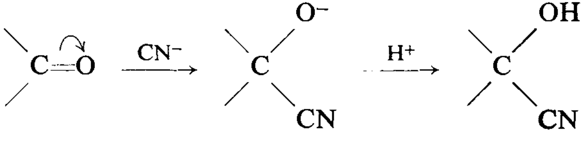


$$CH_3{\cdot}CHO + HNH_2 = CH_3{\cdot}C\begin{matrix}\diagup H\\ -OH\\ \diagdown NH_2\end{matrix}$$



$$CH_3{\cdot}CHO + HSO_3Na = CH_3{\cdot}C\begin{matrix}\diagup H\\ -OH\\ \diagdown SO_3Na\end{matrix}$$

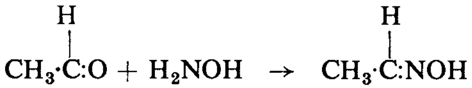
The first step in the addition of hydrogen cyanide to the carbonyl group involves the cyanide ion. The final reaction product is called a *cyanhydrin.*



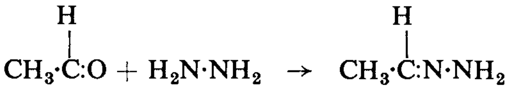
Cyanhydrins are important as a stage in the synthesis of hydroxy acids, since on hydrolysis the cyanide radical is converted to the carboxyl group.

$$\underset{\text{Acetaldehyde cyanhydrin}}{CH_3{\cdot}CHOH{\cdot}CN} \rightarrow \underset{\text{Lactic acid}}{CH_3{\cdot}CHOH{\cdot}COOH}$$

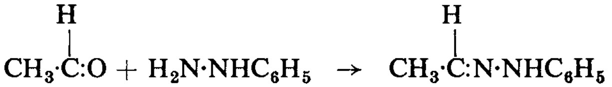
(5) *Condensation reactions of the carbonyl group.* Aldehydes take part in condensation reactions with hydroxylamine (NH_2OH) and with hydrazine ($NH_2{\cdot}NH_2$) or derivatives of hydrazine (especially phenylhydrazine or 2:4-dinitrophenylhydrazine). The carbonyl group is converted into the $\rangle C{:}N$— linkage, water being eliminated. A *condensation reaction* involves the union of two molecules accompanied by the elimination of a molecule of water (or in a few cases, other simple molecules such as hydrogen chloride).



$$CH_3{\cdot}\overset{\overset{H}{|}}{C}{:}O + H_2NOH \rightarrow CH_3{\cdot}\overset{\overset{H}{|}}{C}{:}NOH$$



$$CH_3{\cdot}\overset{\overset{H}{|}}{C}{:}O + H_2N{\cdot}NH_2 \rightarrow CH_3{\cdot}\overset{\overset{H}{|}}{C}{:}N{\cdot}NH_2$$



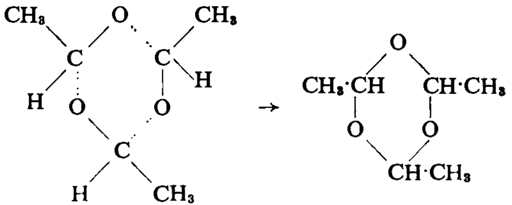
$$CH_3{\cdot}\overset{\overset{H}{|}}{C}{:}O + H_2N{\cdot}NHC_6H_5 \rightarrow CH_3{\cdot}\overset{\overset{H}{|}}{C}{:}N{\cdot}NHC_6H_5$$

The derivatives obtained by the reaction of hydroxylamine with aldehydes (or ketones) are called *oximes* (functional group $\rangle C{:}NOH$); the derivatives obtained from hydrazine are called *hydrazones* (functional group $\rangle C{:}N{\cdot}NH_2$). These compounds are commonly solid crystalline substances of definite melting point, which can be used for the identification of aldehydes (or ketones).

(6) *Polymerization.* Aldehydes undergo polymerization reactions easily. When acetaldehyde is mixed with concentrated

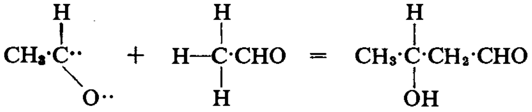
sulphuric or hydrochloric acid, it polymerizes to paraldehyde, which does not behave as an aldehyde since the polymerization takes place through the opening up of the carbonyl double bond of each acetaldehyde molecule.

$$3CH_3{\cdot}CHO = (C_2H_4O)_3$$



Paraldehyde

A different type of polymerization (the aldol condensation) occurs under the influence of small quantities of alkalis. In this case, the linkage of two molecules takes place by the migration of a hydrogen atom from the methyl group of one molecule to the oxygen atom of the other molecule.



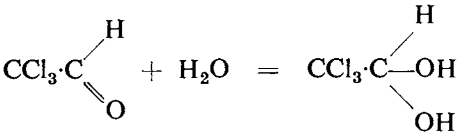
$$\mathrm{CH_3{\cdot}\overset{H}{\underset{O\cdot\cdot}{C}}\cdot\cdot \quad + \quad H{-}\overset{H}{\underset{H}{C}}{\cdot}CHO \quad = \quad CH_3{\cdot}\overset{H}{\underset{OH}{C}}{\cdot}CH_2{\cdot}CHO}$$

The product obtained is called *aldol,* since it is an *ald*ehyde and an alcoh*ol.* It loses water readily to form the unsaturated aldehyde, crotonic aldehyde, which, by this reaction, is prepared on a large scale for conversion into butyraldehyde ($CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CHO$) and thus into butyl alcohol ($CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2OH$).

$$\underset{\text{Aldol}}{CH_3{\cdot}CH(OH){\cdot}CH_2{\cdot}CHO} = \underset{\text{Crotonic aldehyde}}{CH_3{\cdot}CH{:}CH{\cdot}CHO} + H_2O$$

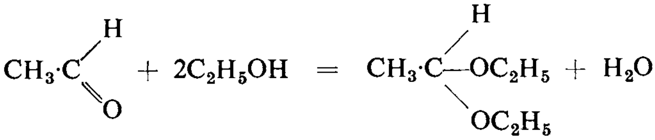
Under other conditions aldehydes form more complex polymerization products, e.g. acetaldehyde, when boiled with strong alkalis, polymerizes to a characteristically smelling resin of high molecular weight (aldehyde resin). Acetaldehyde with dilute acids at 0°C polymerizes to a white solid of composition $(C_2H_4O)_4$, to which the name metaldehyde is given. This substance is used as a solid fuel. Formaldehyde polymerizes into various sugar-like substances $(CH_2O)_6$, or to other polymeric derivatives called paraformaldehyde and metaformaldehyde.

(7) *Hydration and acetal formation.* The halogen substituted aldehydes, such as chloral ($CCl_3{\cdot}CHO$), form hydrates by the addition of water. These hydrates contain a carbon atom joined to two hydroxyl groups.



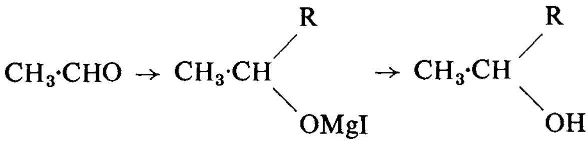
Chloral Chloral hydrate

Simple aldehydes do not form hydrates, but derivatives of such hydrates (called acetals) are formed by the interaction of aldehydes and alcohols in the presence of a dehydrating agent.



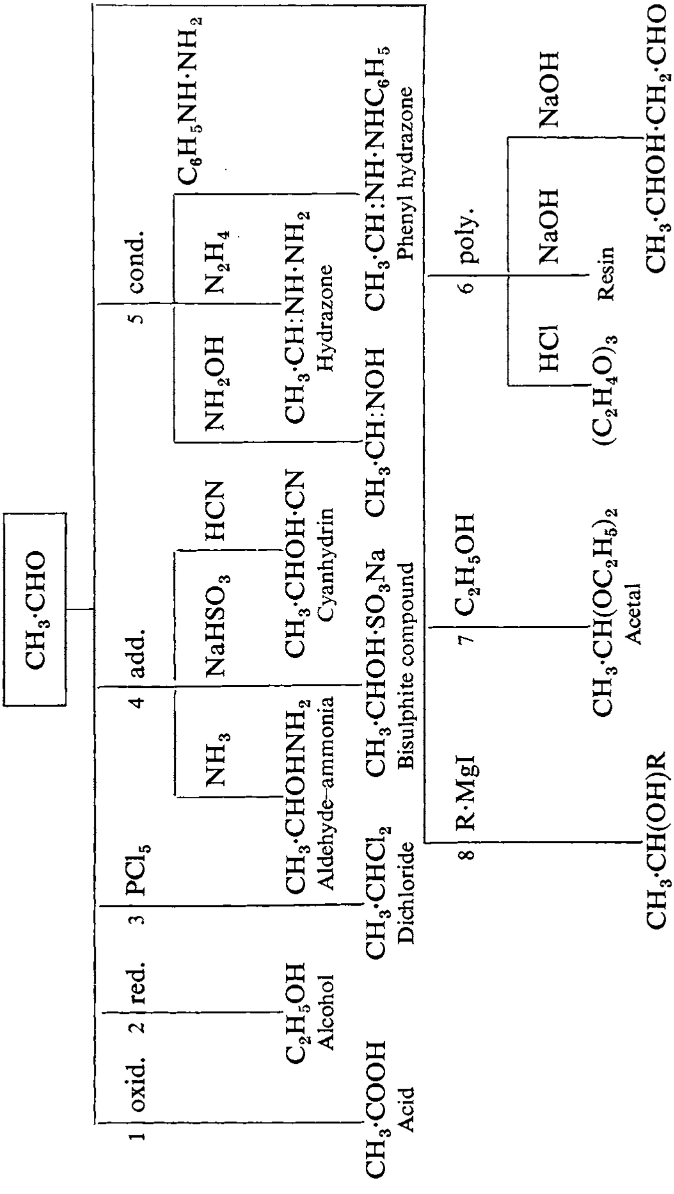
Acetal

(8) *Reaction of carbonyl group with Grignard reagent.* Aldehydes combine with magnesium alkyl halides to form compounds which give secondary alcohols by hydrolysis.



(9) *Schiff's test.* Aldehydes form a coloured complex compound with a solution of magenta decolorized by sulphur dioxide (*Schiff's* reagent). This reaction is used as a test for aldehydes.

Reactions of Aldehydes



Formaldehyde

The simplest aldehyde is a gas possessing a characteristic odour. It is soluble in water, and is normally handled in solution (formalin).

Formaldehyde is prepared commercially by the catalytic oxidation of methyl alcohol vapour by passing it mixed with air over a heated silver catalyst. The formaldehyde formed is absorbed in water.

$$2CH_3OH + O_2 = 2HCHO + 2H_2O$$

When a solution of formaldehyde is evaporated, some is converted into a white residue of its polymer (paraformaldehyde). Formaldehyde has many commercial applications. It is used as a soil sterilizing agent and is reacted with phenol, urea and other substances to obtain some important thermosetting "plastics".

In common with the first members of other homologous series, formaldehyde has some properties which differ from those characteristic of the higher members, e.g. it does not react with ammonia like the other aldehydes, but forms hexamethylenetetramine (hexamine).

$$6HCHO + 4NH_3 = \underset{\text{Hexamine}}{(CH_2)_6N_4} + 6H_2O$$

Formaldehyde undergoes a change with alkalis which is more characteristic of aromatic aldehydes (cf. *Cannizzaro* reaction, p. 223) than of the aldehydes which belong to the aliphatic series. It is converted into methyl alcohol and the salt of formic acid by simultaneous oxidation and reduction.

$$2HCHO + NaOH = CH_3OH + HCOONa$$

Acetaldehyde

Acetaldehyde is prepared on a large scale from acetylene by a process which forms the basis for the commercial preparation of acetic acid and other substances. Acetylene is passed into warm, sulphuric acid in the presence of a mercuric salt as a catalyst. A series of reactions takes place, the final result of which is the addition of a molecule of water to the acetylene molecule, and acetaldehyde is formed (cf. p. 27). The process is usually arranged to be continuous, the acetaldehyde vapour being removed and condensed as fast as it is formed.

$$CH\vdots CH + H_2O \rightarrow CH_3{\cdot}CHO$$

Acetaldehyde is also obtained from ethylene by passing this gas, mixed with air, into an aqueous solution of palladium and copper chlorides. The palladium salt oxidizes the ethylene and is then regenerated by catalytic oxidation in the presence of the copper salt.

$$C_2H_4 + PdCl_2 + H_2O = CH_3{\cdot}CHO + 2HCl + Pd$$

$$2CuCl_2 + Pd = PdCl_2 + Cu_2Cl_2$$

$$2Cu_2Cl_2 + 4HCl + O_2 = 4CuCl_2 + 2H_2O$$

In the laboratory, acetaldehyde is prepared by oxidizing ethyl alcohol, using sodium or potassium dichromate in acid solution.

Formaldehyde–Acetaldehyde: differences

Reactant	*Formaldehyde*	*Acetaldehyde*
Ammonia	hexamine	aldehyde–ammonia
Sodium hydroxide	methyl alcohol + sodium formate	aldehyde–resin
Phenol, urea, etc.	"plastics"	

Chloral [*trichloroacetaldehyde* ($CCl_3{\cdot}CHO$)]

Chloral is prepared by the action of chlorine on ethyl alcohol. The alcohol is first oxidized to acetaldehyde, which is then substituted.

$$C_2H_5OH \rightarrow CH_3{\cdot}CHO \rightarrow CCl_3{\cdot}CHO$$

Chloral combines with water to form chloral hydrate ($CCl_3 \cdot CH(OH)_2$). Chloral is decomposed by alkalis into chloroform and formic acid.

$$CCl_3 \cdot CHO + NaOH = CHCl_3 + HCOONa$$

Ketones (Functional Group $>$C:O)

General Methods of Preparation of Ketones

Ketones are prepared:

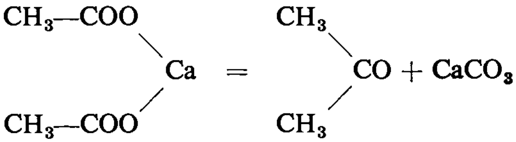
(1) *From secondary alcohols by oxidation*, e.g. isopropyl alcohol is oxidized to acetone using potassium dichromate and dilute sulphuric acid.

$$(CH_3)_2CHOH \xrightarrow{O} (CH_3)_2CO + H_2O$$

A commercial modification of this reaction is the dehydrogenation process in which the alcohol is passed over a catalyst at a suitable high temperature.

$$(CH_3)_2CHOH = (CH_3)_2CO + H_2$$

(2) *From the calcium salts of organic acids* by thermal decomposition.



Calcium acetate Acetone

In some cases the ketone may be obtained directly from the acid by heating it in contact with a suitable catalyst (thorium oxide).

$$2CH_3 \cdot COOH = (CH_3)_2CO + H_2O + CO_2$$

A ketone containing two different groups attached to the carbonyl group (mixed ketone) may be obtained, in poor yield, by heating together a mixture of calcium salts of two different acids.

$$\underset{\text{Calcium acetate}}{(CH_3{\cdot}COO)_2Ca} + \underset{\text{Calcium propionate}}{(C_2H_5{\cdot}COO)_2Ca}$$

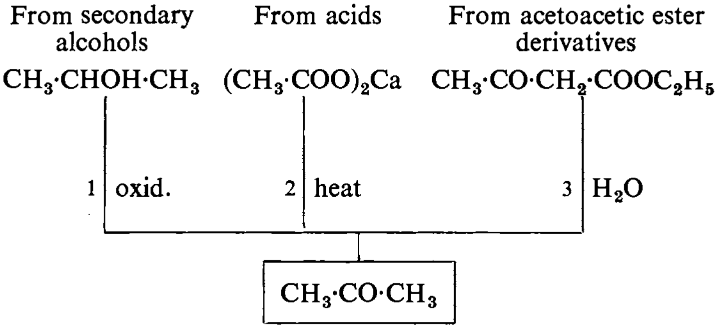
$$= \underset{\text{Methyl ethyl ketone}}{2CH_3{\cdot}CO{\cdot}C_2H_5} + 2CaCO_3$$

As a special case of this latter reaction, if the calcium salt of an acid is mixed with calcium formate and heated, an aldehyde may be obtained (cf. p. 67).

$$(CH_3{\cdot}COO)_2Ca + (HCOO)_2Ca = 2CH_3{\cdot}CHO + 2CaCO_3$$

(3) *From acetoacetic ester* and its derivatives (cf. p. 161) by hydrolysis.

Preparation of Ketones



General Properties of Ketones

(1) *Effect of oxidation.* Unlike aldehydes, ketones are not readily oxidized, and consequently do not reduce ammoniacal silver nitrate or Fehling's solutions. When they are oxidized, the

molecule is broken down into smaller fragments, e.g. acetone is oxidized to acetic acid. In a mixed ketone, the carbonyl group usually remains with the smaller alkyl radical.

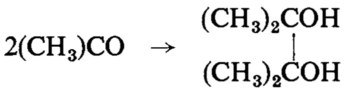
$$CH_3{\cdot}CO{\cdot}CH_3 \xrightarrow{4O} CH_3{\cdot}COOH + CO_2 + H_2O$$

$$CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_3 \xrightarrow{3O} CH_3{\cdot}COOH + CH_3{\cdot}COOH$$

(2) *Reduction of the carbonyl group.* Ketones usually give the corresponding secondary alcohol on reduction.

$$CH_3{\cdot}CO{\cdot}CH_3 + H_2 = CH_3{\cdot}CH(OH){\cdot}CH_3$$

However, by reduction with sodium amalgam, it is possible to obtain intermediate compounds called *pinacols*, in which only one atom of hydrogen is added to the ketone molecule and the group thus obtained is united to a similar group.



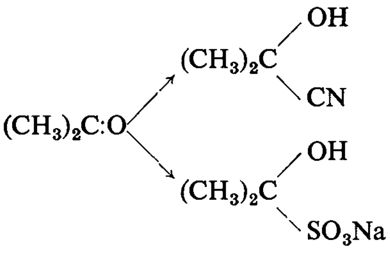
$$2(CH_3)CO \rightarrow \begin{array}{c}(CH_3)_2COH\\ |\\ (CH_3)_2COH\end{array}$$

Acetone Pinacol

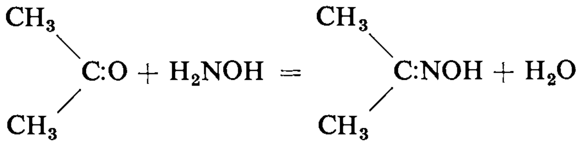
(3) *Replacement of carbonyl oxygen.* Phosphorus pentachloride reacts with ketones replacing the oxygen atom by two atoms of chlorine.

$$(CH_3)_2CO + PCl_5 = (CH_3)_2CCl_2 + POCl_3$$

(4) *Addition to the carbonyl group.* Ketones form addition compounds with sodium bisulphite and hydrogen cyanide, but not with ammonia.



(5) *Condensation reactions of the carbonyl group.* Ketones undergo condensation reactions with hydroxylamine, hydrazine and phenylhydrazine.



$$\begin{matrix} CH_3 \\ \end{matrix}\!\!\!\!>C{:}O + H_2NOH = \begin{matrix} CH_3 \\ CH_3 \end{matrix}\!>C{:}NOH + H_2O$$

$$(CH_3)_2C{:}O + H_2N{\cdot}NHC_6H_5 = (CH_3)_2C{:}N{\cdot}NHC_6H_5 + H_2O$$

(6) *No polymerization.* Unlike the aldehydes, ketones do not polymerize.

(7) *No acetal formation.* Ketones do not normally give acetals.

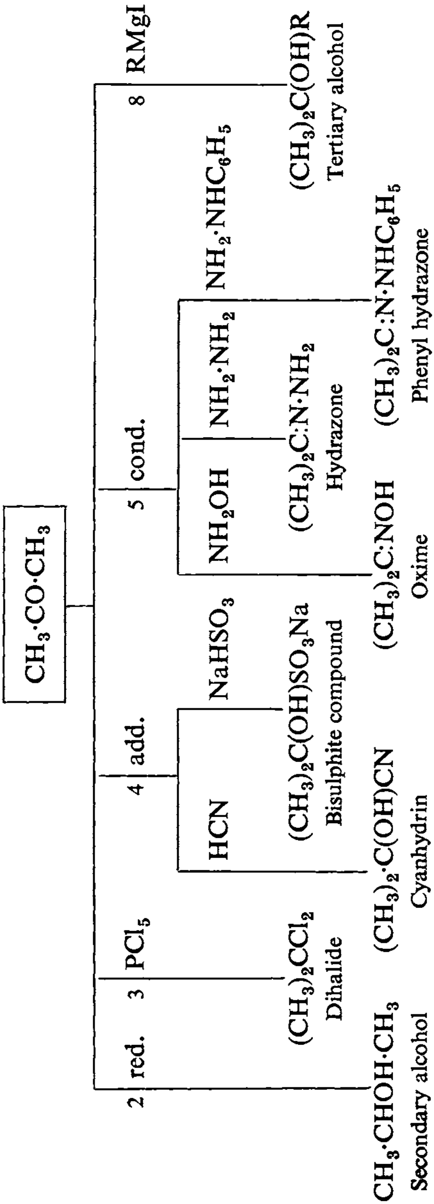
(8) *Reaction of the carbonyl group with Grignard reagents.* Ketones react with magnesium alkyl halides to give products which on hydrolysis yield tertiary alcohols.

$$(CH_3)_2CO + RMgI \rightarrow (CH_3)_2CR{\cdot}OMgI \rightarrow (CH_3)_2C(OH)R$$

Acetone

The most important ketone is dimethyl ketone or acetone. Acetone is manufactured from petroleum sources by the dehydrogenation of isopropyl alcohol at about 350°C in the presence of a catalyst (e.g. copper oxide). Higher ketones are also manufactured by the petroleum chemical industry for use as solvents or to convert into other substances.

Reactions of Ketones



Comparison of Aliphatic Aldehydes and Ketones

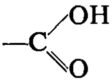
Reaction	*Aldehydes*	*Ketones*
Oxidation	one acid	mixture of acids
Silver nitrate	reduction	no action
Fehling's solution	reduction	no action
Reduction	primary alcohol	secondary alcohol or pinacol
Phosphorus pentachloride	dichloride	dichloride
Ammonia	addition	complex action
Sodium bisulphite or hydrogen cyanide	addition	addition
Hydroxylamine or hydrazine	condensation	condensation
Sodium hydroxide	resinous polymer	no action
Sulphuric acid	polymer	often no action*
Schiff's test	decolorization	no action

* Acetone yields mesitylene (cf. p. 176).

7

the aliphatic acids

ACIDS

[FUNCTIONAL GROUP 

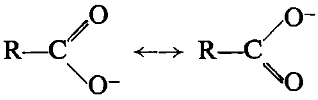
$-C\begin{matrix}\diagup OH\\ \diagdown\!\diagdown O\end{matrix}$

OR —COOH (CARBOXYL GROUP)]

The acids contain a functional group consisting of both carbonyl and hydroxyl. The presence of the latter group modifies the behaviour of the carbonyl group and does not allow it to enter into the addition reactions characteristic of aldehydes and ketones. Nor does acetic acid give the iodoform reaction, as acetaldehyde does.

$$CH_3{\cdot}CHO \rightarrow CI_3{\cdot}CHO \rightarrow CHI_3$$

The modifications in the carbonyl group properties may be explained by resonance (cf. p. 169) whereby the double and single bond lose their individual characteristics and partake of a hybrid nature, as for example in the ion:



The glyceryl esters of the higher members of the series of the simple aliphatic acids are the fats. The acids are therefore often called the fatty acids. The simplest members of the series are formic acid (HCOOH), acetic acid ($CH_3{\cdot}COOH$), propionic acid ($C_2H_5{\cdot}COOH$), butyric acid ($C_3H_7{\cdot}COOH$) and valeric acid ($C_4H_9{\cdot}COOH$). Other important members of the homologous series are palmitic acid ($C_{15}H_{31}{\cdot}COOH$) and stearic acid ($C_{17}H_{35}{\cdot}COOH$), which exist together with oleic acid (an unsaturated acid, $C_{17}H_{33}{\cdot}COOH$) as esters in the naturally occurring fats.

General Methods of Preparation of the Fatty Acids

Many acids are obtained directly from their naturally occurring salts, while others occur naturally in the form of their esters from which they are obtained by hydrolysis. The hydrolysis of fats is used to prepare the higher fatty acids.

Synthetically, acids may be prepared by the following methods:

(1) *By oxidation of primary alcohols or aldehydes*, e.g. using potassium permanganate in presence of dilute sulphuric acid.

(2) *By hydrolysis of the nitriles*. The hydrolysis may be carried out by heating with acid or alkali.

$$RCN + 2H_2O \rightarrow RCOOH + NH_3$$

(3) *By the hydrolysis of acetoacetic or malonic esters* or their derivatives (cf. pp. 161, 162).

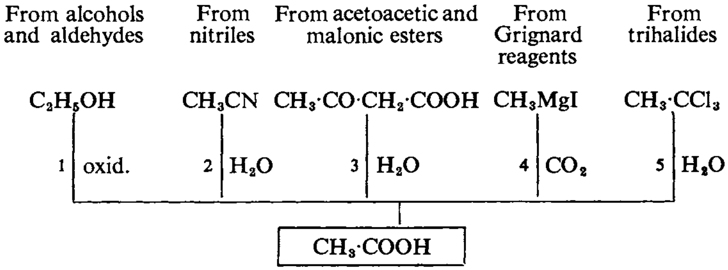
(4) *From the magnesium alkyl halides* by reaction with carbon dioxide followed by hydrolysis (cf. p. 163).

$$RMgBr + CO_2 \rightarrow RCOOMgBr \rightarrow RCOOH$$

(5) *By the hydrolysis of halides of the type* RCX_3.

$$RCX_3 \rightarrow RC(OH)_3 \rightarrow RCOOH$$

Preparation of Acids



Physical Properties of the Fatty Acids

The lower members of the series are corrosive liquids with characteristic smells. They dissolve readily in water, but the solubility decreases with increase in molecular weight and the higher solid members are practically insoluble in water. The melting points of the acids do not rise continuously, but show a series of alternations. The melting points of the acids containing an even number of carbon atoms in the alkyl group lie below those of the neighbouring acid containing an odd number. The alternations arise from different methods of arranging the molecular chains to form the crystals of the solids. The boiling points of the acids are considerably higher than those of other compounds of similar molecular weight, due to a tendency to form dimeric molecules, such as $(CH_3{\cdot}COOH)_2$.

Chemical Properties of the Fatty Acids

With the exception of formic acid, the fatty acids are resistant to oxidation. The following reactions are typical of these acids.

(1) *Ionization*. The hydrogen atom of the carboxyl group is acidic. The fatty acids possess the usual properties of weak acids.

$$CH_3{\cdot}COOH \rightleftharpoons CH_3{\cdot}COO^- + H^+$$

(2) *Esterification.* Acids react with alcohols to form esters, in which the hydrogen atom of the acid has been replaced by an alkyl group.

$$CH_3{\cdot}COOH + C_2H_5OH = CH_3{\cdot}COOC_2H_5 + H_2O$$

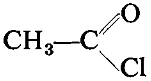
(3) *Formation of acid chlorides.* The hydroxyl group of the carboxyl radical can be replaced by a chlorine atom by reaction with phosphorus chlorides.

$$3CH_3{\cdot}COOH + PCl_3 = 3CH_3{\cdot}COCl + H_3PO_3$$

$$CH_3{\cdot}COOH + PCl_5 = CH_3{\cdot}COCl + POCl_3 + HCl$$

The substances formed by the replacement of the hydroxyl group by a chlorine atom are called the acid chlorides.

The radicals formed by the removal of the hydroxyl group from the fatty acids are called *acyl* groups. Their particular names are derived from those of the corresponding acid by altering the suffix *-ic* to *-yl*, thus acet*ic* acid $CH_3{\cdot}COOH$, acet*yl* group $(CH_3{\cdot}CO)$-, acet*yl* chloride $CH_3{\cdot}COCl$,



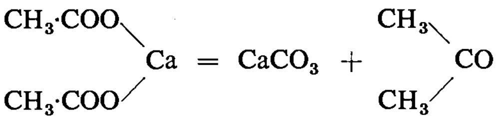
(4) *Formation of acid anhydride.* The acids yield anhydrides. Anhydrides are usually prepared by heating the sodium salts of the acids with the acid chloride.

$$CH_3{\cdot}COO\boxed{Na + Cl}CO{\cdot}CH_3 = \underset{\text{Acetic anhydride}}{CH_3{\cdot}CO{\cdot}O{\cdot}CO{\cdot}CH_3} + NaCl$$

(5) *Reduction.* Acids may be reduced using lithium aluminium hydride

$$CH_3{\cdot}COOH \xrightarrow{LiAlH_4} (CH_3{\cdot}CH_2O)_4AlLi \rightarrow CH_3{\cdot}CH_2OH$$

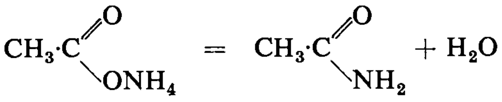
(6) *Conversion to ketones.* The calcium salts of the acids break down on heating to form ketones (cf. p. 76).



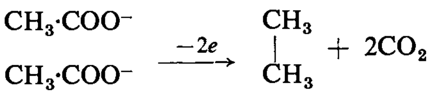
(7) *Conversion to paraffins.* The sodium salts, when mixed with soda-lime and heated, form hydrocarbons.

$$CH_3{\cdot}COONa + NaOH = CH_4 + Na_2CO_3$$

(8) *Conversion to amides.* The ammonium salts lose water on heating and are converted to acid amides in which the amino (NH_2) group replaces the hydroxyl group of the acid.

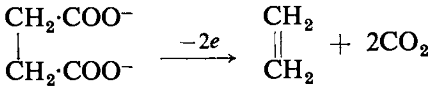


(9) *Electrolysis.* When a solution of an alkali metal salt of a fatty acid is electrolysed, a mixture of carbon dioxide and a paraffin hydrocarbon is obtained. This method of preparation of hydrocarbons is often called *Kolbe's* synthesis.

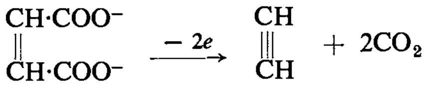


$$\begin{matrix} CH_3{\cdot}COO^- \\ CH_3{\cdot}COO^- \end{matrix} \xrightarrow{-2e} \begin{matrix} CH_3 \\ | \\ CH_3 \end{matrix} + 2CO_2$$

Under similar conditions, the salts of certain dibasic acids and unsaturated dibasic acids form ethylenic and acetylenic hydrocarbons respectively.

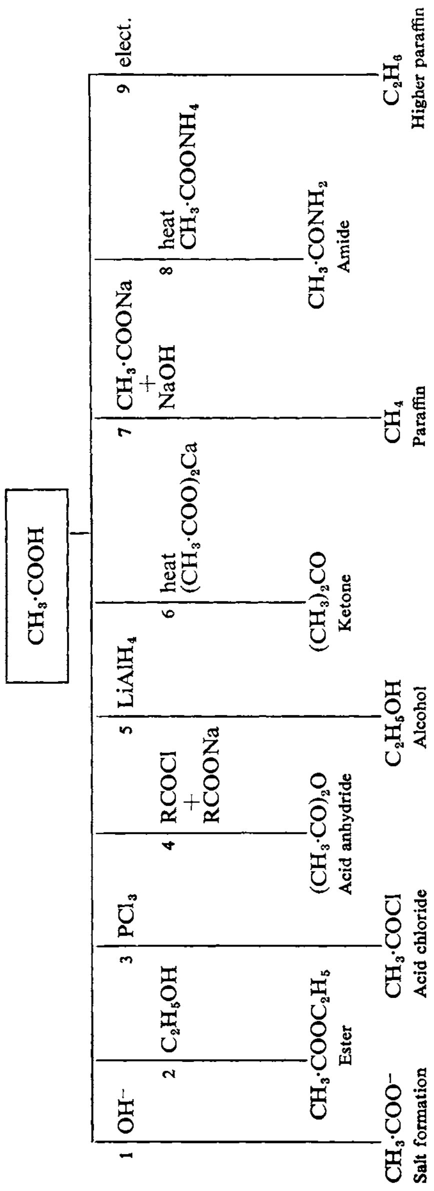


$$\begin{matrix} CH_2{\cdot}COO^- \\ | \\ CH_2{\cdot}COO^- \end{matrix} \xrightarrow{-2e} \begin{matrix} CH_2 \\ \| \\ CH_2 \end{matrix} + 2CO_2$$



$$\begin{matrix} CH{\cdot}COO^- \\ \| \\ CH{\cdot}COO^- \end{matrix} \xrightarrow{-2e} \begin{matrix} CH \\ ||| \\ CH \end{matrix} + 2CO_2$$

Reactions of Acids



Formic acid

This substance occurs naturally, e.g. in ants and stinging nettles. It is prepared in the laboratory by heating oxalic acid with glycerol (cf. p. 55). It is manufactured by heating sodium hydroxide with carbon monoxide under a pressure of about 10 atm. Combination occurs to form sodium formate, from which the acid may be obtained by distillation with sodium hydrogen sulphate.

$$NaOH + CO = HCOONa$$

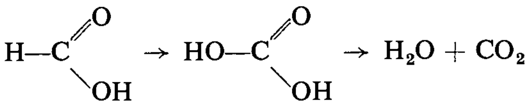
$$HCOONa + NaHSO_4 = HCOOH + Na_2SO_4$$

The pure acid may be obtained by forming the lead salt and, after drying, treating it with hydrogen sulphide.

$$PbO + 2HCOOH = (HCOO)_2Pb + H_2O$$

$$(HCOO)_2Pb + H_2S = 2HCOOH + PbS$$

Formic acid, like the lowest members of other homologous series, possesses certain abnormal properties. It is easily oxidized (for it can be regarded as an aldehyde) and is a reducing agent.



$$H{-}C\begin{smallmatrix}\nearrow O\\ \searrow OH\end{smallmatrix} \rightarrow HO{-}C\begin{smallmatrix}\nearrow O\\ \searrow OH\end{smallmatrix} \rightarrow H_2O + CO_2$$

Formic acid when treated with a dehydrating agent forms carbon monoxide, which is conveniently prepared in the laboratory by heating sodium formate and concentrated sulphuric acid.

$$HCOOH = CO + H_2O$$

Sodium formate decomposes on heating, evolving hydrogen and forming sodium oxalate.

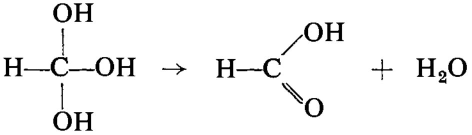
$$2HCOONa = (COONa)_2 + H_2$$

Orthoformic acid $HC(OH)_3$

This substance is very unstable and does not exist in the free state, but its ethyl ester can be obtained by reacting on chloroform with sodium ethoxide.

$$CHCl_3 + 3C_2H_5ONa = 3NaCl + CH(OC_2H_5)_3$$

Ethyl orthoformate



Acetic acid

Acetic acid is manufactured from acetaldehyde obtained from acetylene. The acetaldehyde may be directly oxidized by air in the presence of a suitable catalyst such as a manganese or a vanadium compound.

$$2CH_3{\cdot}CHO + O_2 = 2CH_3{\cdot}COOH$$

Acetic acid is also obtained by the controlled oxidation of butane with air, in the presence of a silver catalyst.

$$CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CH_3 \rightarrow 2CH_3{\cdot}COOH$$

The oxidation of alcohol by air under the influence of *Bacterium aceti* gives rise to a dilute solution of acetic acid (vinegar).

Acetic acid when anhydrous melts at 16·6°C and boils at 118°C. It mixes with water in all proportions. It forms well-defined salts (the acetates), most of which are soluble in water.

When chlorine is passed into hot acetic acid (especially in the presence of a catalyst, such as red phosphorus) the methyl group becomes substituted. The first product is chloro-acetic acid (monochloro-acetic acid), but on passing in the gas for a longer period, or by working at higher temperatures, dichloro-acetic and trichloro-acetic acids are obtained. (These substitutions prove the presence of three hydrogen atoms in the acetic acid molecule as well as the one hydroxyl hydrogen atom indicated by the reactions with sodium and with phosphorus chlorides. The formula $CH_3 \cdot COOH$ is thus established.)

$$CH_3 \cdot COOH + Cl_2 = \underset{\text{Monochloro-acetic acid}}{CH_2Cl \cdot COOH} + HCl$$

$$CH_2Cl \cdot COOH + Cl_2 = \underset{\text{Dichloro-acetic acid}}{CHCl_2 \cdot COOH} + HCl$$

$$CHCl_2 \cdot COOH + Cl_2 = \underset{\text{Trichloro-acetic acid}}{CCl_3 \cdot COOH} + H_2O$$

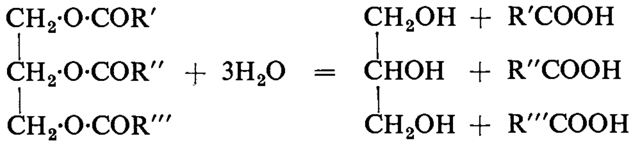
Formic Acid–Acetic acid : differences

Reactant	*Formic acid*	*Acetic acid*
Concentrated sulphuric acid	carbon monoxide	—
Ammoniacal silver nitrate	silver	—
Mercuric chloride	mercurous chloride	—
Heat on sodium salt	sodium oxalate	—

The Higher Fatty Acids and the Soaps

The most important of the higher members of the series of fatty acids are those which occur naturally in the form of their glyceryl esters in oils and fats of animal and vegetable origin. The waxes are esters of these acids with the higher monohydric alcohols, e.g. cetyl alcohol $C_{16}H_{33}OH$. The fatty acids can be obtained from fats by hydrolysis with steam or water under pressure.

Fat + water = glycerol + fatty acid



$$\begin{array}{llll} CH_2 \cdot O \cdot COR' & & & CH_2OH + R'COOH \\ | & & & | \\ CH_2 \cdot O \cdot COR'' & + 3H_2O & = & CHOH \;\; + R''COOH \\ | & & & | \\ CH_2 \cdot O \cdot COR''' & & & CH_2OH + R'''COOH \end{array}$$

The product obtained is a semi-solid mass, the important constituents of which are palmitic acid ($C_{15}H_{31}\cdot COOH$, m.p. 63°C), stearic acid ($C_{17}H_{35}\cdot COOH$, m.p. 69°C), and the liquid oleic acid ($C_{17}H_{33}\cdot COOH$, m.p. 14°C). The oleic acid can be separated from the solid acids by pressure. The latter substances are used in the manufacture of candles. Palmitic and stearic acids are saturated acids containing unbranched chains of carbon atoms,

$$CH_3\cdot CH_2\cdot CH_2 \ldots CH_2\cdot CH_2\cdot COOH$$

Oleic acid is an unsaturated acid which contains a double bond situated in the middle of the chain of carbon atoms.

$$CH_3\cdot(CH_2)_7\cdot CH{:}CH\cdot(CH_2)_7\cdot COOH$$

The sodium and potassium salts of these acids constitute the *soaps*. Soaps are manufactured by the action of hot caustic alkali on fats. The reaction is a particular example of the general action of caustic alkalis on esters.

$$\text{Fat} + \text{sodium hydroxide} = \text{soap} + \text{glycerol}$$

After heating together the fat and caustic soda for some time, the fat dissolves completely in the form of soap. The soap is separated from the solution by salting out. The addition of salt diminishes the solubility of the soap which rises to the surface, where it is scraped off, boiled with a little water, again separated, cut into shape and dried. The liquor remaining after the soap has been removed contains glycerol.

The *detergent action of soap.* Detergency is correlated with the nature of the soap molecule, which contains a long paraffin chain (insoluble in water, soluble in organic solvents and non-ionic in nature) united to an end-group which is the salt of an acid and therefore tends to dissolve in water.

The synthetic detergent substances also have molecules containing long paraffin chains and water-attracting groups. The latter may be anionic in nature (like soap) or cationic or neutral. The most important groups are anionic as, for example, those present in sodium dodecylbenzenesulphonate or the sodium secondary alkyl sulphates.

Insoluble soaps

The term soap is applied to the insoluble lead, zinc, calcium, and barium salts of the fatty acids as well as to their sodium and potassium salts. These insoluble salts can be made either by direct neutralization of the acid with the corresponding base, or by precipitation reactions. Such reactions take place when ordinary soap is added to a hard water containing dissolved calcium and magnesium salts. The soap is removed from solution as the insoluble calcium or magnesium salt.

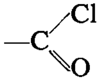
$$2NaX + CaCl_2 = 2NaCl + CaX_2$$

where X represents the organic anion.

8

derivatives of the aliphatic acids

THE ACID CHLORIDES

(FUNCTIONAL GROUP  $-C\begin{matrix}\diagup Cl \\ \diagdown\!\!\diagdown O\end{matrix}$ OR —COCl)

The acid chlorides are formed from acids or their sodium salts by interacting with phosphorus trichloride or thionyl chloride. (The latter is more advantageous in that the side products are easily removable as gases.)

$$PCl_3 + 3CH_3{\cdot}COOH = H_3PO_3 + \underset{\text{Acetyl chloride}}{3CH_3{\cdot}COCl}$$

$$SOCl_2 + 2CH_3{\cdot}COOH = H_2SO_3 + 2CH_3{\cdot}COCl$$

The lower members of the series of acid chlorides are fuming liquids with an irritating smell. The higher members are solids.

Reactions of Acid Chlorides

(1) *Hydrolysis.* Acid chlorides are easily hydrolysed by water to form the acids.

$$CH_3{\cdot}COCl + H_2O = CH_3{\cdot}COOH + HCl$$

(2) *Acetylation reaction.* Acid chlorides react with alcohols, replacing hydrogen by the acyl group to form esters (acetylation cf. p. 45).

$$CH_3{\cdot}COCl + C_2H_5OH = CH_3{\cdot}COOC_2H_5 + HCl$$

(3) *Conversion to anhydrides.* Acid chlorides react with sodium salts of acids to form the acid anhydrides.

$$CH_3{\cdot}COONa + CH_3{\cdot}COCl = CH_3{\cdot}CO{\cdot}O{\cdot}CO{\cdot}CH_3 + NaCl$$

(4) *Conversion to amides.* Acid chlorides react with ammonia and with primary and secondary amines replacing a hydrogen atom by the acyl group to form amides and substituted amides.

$$CH_3{\cdot}COCl + NH_3 = CH_3{\cdot}CONH_2 + HCl\ (\rightarrow NH_4Cl)$$

(5) *Reduction.* Acid chlorides can be reduced to aldehydes by hydrogen in presence of metallic palladium.

$$CH_3{\cdot}COCl + H_2 = CH_3{\cdot}CHO + HCl$$

Acetyl chloride

This is the most important member of the series. It is obtained from acetic acid by reaction with phosphorus trichloride, sulphur monochloride, thionyl chloride or carbonyl chloride. It is used for acetylating various alcohols and amines, e.g. cellulose and aniline.

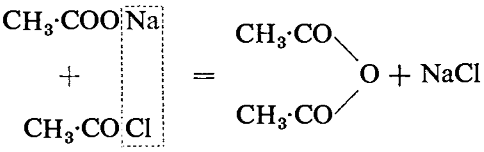
Acetyl chloride is also used to determine the number of hydroxyl groups and amino groups present in a compound, as each such group reacts with one molecule of acetyl chloride.

$$R{\cdot}OH + CH_3{\cdot}COCl = HCl + CH_3{\cdot}COOR$$

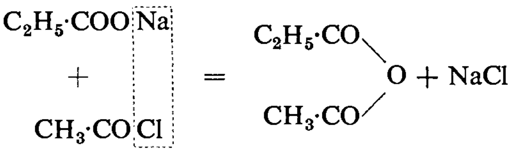
$$R{\cdot}NH_2 + CH_3{\cdot}COCl = HCl + RNH{\cdot}CO{\cdot}CH_3$$

THE ACID ANHYDRIDES

Acid anhydrides are prepared by the interaction of the sodium salts of acids with the acid chlorides.



By reacting an acid chloride with the sodium salt of a different acid, a mixed anhydride can be obtained. On distillation, mixed anhydrides break down to give a mixture of two simple anhydrides.



$$2CH_3{\cdot}CO{\cdot}O{\cdot}CO{\cdot}C_2H_5 = (CH_3{\cdot}CO)_2O + (C_2H_5{\cdot}CO)_2O$$

Acid anhydrides are hydrolysed by water to form the acids. They react with alcohols and amines to form esters and acetyl derivatives respectively. They react less vigorously than the acid chlorides but more vigorously than the acids. Acetic anhydride is often used alone or mixed with acetyl chloride in the manufacture of the acetates of cellulose and other higher hydroxylic derivatives.

$$(CH_3{\cdot}CO)_2O + H_2O = 2CH_3{\cdot}COOH$$

$$(CH_3{\cdot}CO)_2O + C_2H_5OH = CH_3{\cdot}COOC_2H_5 + CH_3{\cdot}COOH$$

$$(CH_3{\cdot}CO)_2O + C_6H_5NH_2 = CH_3{\cdot}CO{\cdot}NH{\cdot}C_6H_5 + \\ + CH_3{\cdot}COOH$$

Acid anhydrides may be reduced to aldehydes, using sodium amalgam and water, or to primary alcohols using the more powerful reducing agent lithium aluminium hydride.

THE ACID AMIDES

(FUNCTIONAL GROUP —$CONH_2$)

Acid amides can be regarded as derivatives of ammonia in which a hydrogen atom has been replaced by an acyl group, or as acids in which the hydroxyl group has been replaced by the NH_2 group. Thus, acetamide can be regarded as the acetyl derivative of ammonia $CH_3{\cdot}CO{-}NH_2$, or as a derivative of acetic acid $CH_3{\cdot}COOH \rightarrow CH_3{\cdot}CONH_2$.

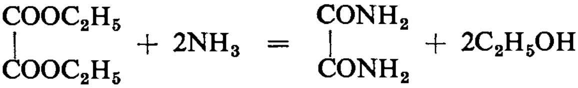
Preparation of Acid Amides

Acid amides are prepared:

(1) *From ammonia by the action of acid chlorides or anhydrides.*

$$CH_3{\cdot}COCl + NH_3 = CH_3{\cdot}CONH_2 + HCl$$

In some cases the ester can be used, e.g. the addition of ammonia to ethyl oxalate causes a precipitate of oxamide to be formed.



$$\begin{array}{l}COOC_2H_5\\ |\\ COOC_2H_5\end{array} + 2NH_3 = \begin{array}{l}CONH_2\\ |\\ CONH_2\end{array} + 2C_2H_5OH$$

(2) *From ammonium salts by dehydration reactions* (often by heating).

$$CH_3{\cdot}COONH_4 = CH_3{\cdot}CONH_2 + H_2O$$

(3) *From nitriles by partial hydrolysis.*

$$RCN + H_2O = R{\cdot}CONH_2$$

Physical Properties of Amides

The lowest member of the series (formamide $HCONH_2$) is liquid at ordinary temperatures, but the higher members are crystalline solids, many being soluble in water. Acetamide ($CH_3{\cdot}CONH_2$), when pure, forms odourless crystals, but ordinary specimens have a strong characteristic odour.

Chemical Properties of the Amides

(1) *Amides show few basic properties* and do not form stable salts with acids.

(2) *Amides react with nitrous acid* in a manner resembling the primary amines. Nitrogen is evolved and the amino group is replaced by the hydroxyl group to form the acid.

$$CH_3{\cdot}CONH_2 + HNO_2 = CH_3{\cdot}COOH + N_2 + H_2O$$

(3) *Hydrolysis.* Amides are easily hydrolysed to form the ammonium salts of acids. The evolution of ammonia when amides are heated with alkalis is often used as a test for their identification.

$$CH_3{\cdot}CONH_2 + H_2O = CH_3{\cdot}COONH_4$$

$$CH_3{\cdot}COONH_4 + NaOH = CH_3{\cdot}COONa + NH_3 + H_2O$$

(4) *Dehydration.* Amides are dehydrated, by heating with phosphorus pentoxide, to form nitriles.

$$R{\cdot}CONH_2 + P_2O_5 = RCN + 2HPO_3$$

In these hydrolytic and dehydration reactions the amides are intermediate between ammonium salts and nitriles.

$$\text{Nitriles} \qquad \underset{\xleftarrow[\text{Dehydration}]{\hspace{5em}}}{\overset{\xrightarrow{\text{Hydrolysis}}}{\text{Amides}}} \qquad \text{Ammonium salts}$$

(5) *Hofmann reaction.* Amides react with bromine and potassium hydroxide to form the primary amines (*Hofmann* reaction, cf. p. 61).

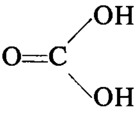
$$R{\cdot}CONH_2 \rightarrow R{\cdot}CONHBr \rightarrow RNCO \rightarrow RNH_2$$

(6) *Reduction.* Amides are reduced to primary amines by sodium and alcohol or by lithium aluminium hydride.

$$CH_3{\cdot}CONH_2 \rightarrow CH_3{\cdot}CH_2NH_2$$

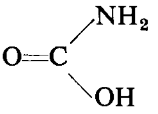
Amides of Carbonic Acid

Carbonic acid is a dibasic acid, and thus it can form a mono-amide when one hydroxyl group is replaced by the NH_2 group, and a di-amide when both hydroxyl groups are replaced.



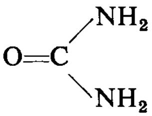
$$\mathrm{O{=}C}\begin{matrix}\diagup \mathrm{OH}\\ \diagdown \mathrm{OH}\end{matrix}$$

Carbonic acid



$$\mathrm{O{=}C}\begin{matrix}\diagup \mathrm{NH_2}\\ \diagdown \mathrm{OH}\end{matrix}$$

Carbamic acid



$$\mathrm{O{=}C}\begin{matrix}\diagup \mathrm{NH_2}\\ \diagdown \mathrm{NH_2}\end{matrix}$$

Urea

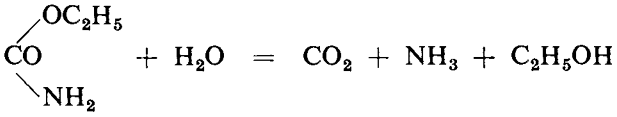
The mono-amide possesses acid properties, and is called carbamic acid. It is not known in the free state, but its salts and esters are important, ammonium carbamate being one of the constituents of commercial ammonium carbonate, while the esters are the *urethanes.* (The name urethane is given to ethyl carbamate.) The di-amide of carbonic acid is *urea.*

Urethane is prepared from ethyl carbonate or ethyl chloroformate and ammonia, in accordance with the general methods for the preparation of acid amides.

$$C_2H_5OCOOC_2H_5 + NH_3 = NH_2{\cdot}COOC_2H_5 + C_2H_5OH$$

$$ClCOOC_2H_5 + 2NH_3 = NH_2{\cdot}COOC_2H_5 + NH_4Cl$$

The urethanes are crystalline solids. They can be regarded as both amides and esters, and on hydrolysis yield carbon dioxide, ammonia and the corresponding alcohol.



$$CO\begin{matrix}\diagup OC_2H_5\\ \\ \diagdown NH_2\end{matrix} + H_2O = CO_2 + NH_3 + C_2H_5OH$$

Urea

This was the first substance of organic origin to be synthesized in the laboratory from inorganic sources. It occurs in the urine of man and other mammals, from whence it may be obtained by evaporation and extraction as the nitric acid salt. The following synthetic methods can be used for the preparation of urea.

(1) Urea is prepared in the laboratory by the synthetic process, first used by *Wöhler* in 1828. A solution containing ammonium sulphate and potassium cyanate is evaporated. Ammonium cyanate is formed and is then converted into urea by an intramolecular change. The urea is separated by extracting in alcohol.

$$2KCNO + (NH_4)_2SO_4 = 2NH_4CNO + K_2SO_4$$

$$NH_4CNO = CO(NH_2)_2$$

Alkyl derivatives of urea can be obtained by similar reactions from amine salts of cyanic acid.

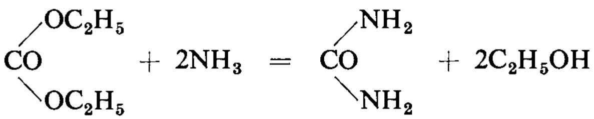
$$\underset{\text{Methylammonium cyanate}}{CH_3NH_3CNO} = \underset{\text{Methyl urea}}{NH_2{\cdot}CO{\cdot}NH{\cdot}CH_3}$$

(2) Urea is manufactured by the direct reaction of carbon dioxide and ammonia at 200°C under a pressure of about 200 atm.

$$2NH_3 + CO_2 = CO(NH_2)_2 + H_2O$$

It is used in the manufacture of urea–formaldehyde resins and plastics and as a source of various drugs, etc.

(3) In accordance with the general methods for the preparation of the acid amides, urea can also be obtained by the action of ammonia on ethyl carbonate or carbonyl chloride.



$$\mathrm{CO}\begin{smallmatrix}\diagup \mathrm{OC_2H_5}\\ \diagdown \mathrm{OC_2H_5}\end{smallmatrix} + 2\mathrm{NH_3} = \mathrm{CO}\begin{smallmatrix}\diagup \mathrm{NH_2}\\ \diagdown \mathrm{NH_2}\end{smallmatrix} + 2\mathrm{C_2H_5OH}$$

$$\mathrm{COCl_2} + 2\mathrm{NH_3} = \mathrm{CO(NH_2)_2} + 2\mathrm{HCl}$$

Alkyl derivatives of urea can be obtained by similar reactions using amines instead of ammonia.

$$\mathrm{COCl_2} + \underset{\text{Methylamine}}{2\mathrm{NH_2CH_3}} = \underset{\text{Dimethyl urea}}{\mathrm{CH_3{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}CH_3}} + 2\mathrm{HCl}$$

Properties of urea. Urea crystallizes in colourless prisms melting at 132°C, above which temperature it decomposes, and ammonia is evolved. The molten mass re-solidifies owing to the formation of *biuret* (m.p. 190°C), which gives a violet colour on addition of copper sulphate and alkali.

$$\mathrm{NH_2{\cdot}CO{\cdot}NH_2} + \mathrm{NH_2{\cdot}CO{\cdot}NH_2}$$
$$= \mathrm{NH_3} + \underset{\text{Biuret}}{\mathrm{NH_2{\cdot}CO{\cdot}NH{\cdot}CO{\cdot}NH_2}}$$

On dry distillation, urea gives cyanuric acid.

$$3\mathrm{CO(NH_2)_2} = \mathrm{H_3O_3C_3N_3} + 3\mathrm{NH_3}$$

Urea gives the characteristic reactions of acid amides, e.g. it is hydrolysed to ammonia and a carbonate by alkalis, and it reacts with nitrous acid evolving nitrogen and carbon dioxide.

$$\mathrm{CO(NH_2)_2} + 2\mathrm{NaOH} = \mathrm{Na_2CO_3} + 2\mathrm{NH_3}$$

$$\mathrm{CO(NH_2)_2} + 2\mathrm{HNO_2} = 2\mathrm{N_2} + \mathrm{CO_2} + 3\mathrm{H_2O}$$

Urea behaves as a mono-acid base and forms salts with acids (the formula indicates the presence of an amino group and an amido group). Of these salts, the nitrate [$CO(NH_2)_2,HNO_3$] and oxalate [$2CO(NH_2)_2,H_2C_2O_4,H_2O$] are not very soluble in water, and are precipitated from fairly concentrated aqueous solutions of urea on the addition of the corresponding acids.

Determination of urea. The determination of urea in urine and other biological fluids is of importance. The following methods are used:

(1) By oxidation with an alkaline solution of sodium hypobromite, prepared by the addition of bromine to sodium hydroxide solution. Nitrogen is set free as a gas, the volume of which is measured. The experiment is carried out in a nitrometer.

$$CO(NH_2)_2 \xrightarrow{3O} N_2 + CO_2 + 2H_2O$$

(2) By hydrolysis to ammonia. An enzyme (urease), present in the soya bean, hydrolyses urea (in neutral solution) to ammonia.

$$CO(NH_2)_2 + 2H_2O = (NH_4)_2CO_3 \rightarrow 2NH_3$$

The hydrolysis is carried out by mixing the solution to be determined with the ground beans and allowing to stand at 40°C. A current of ammonia-free air is drawn continuously through the mixture to remove the ammonia as it is formed. This is then absorbed in an excess of standard acid and the excess acid is determined by titration.

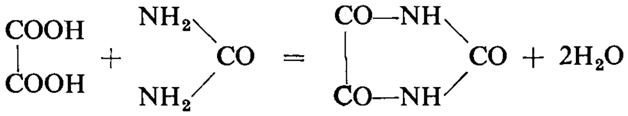
Derivatives of Urea

Urea reacts with acid chlorides (less readily with the corresponding acids) to form the acyl derivatives of urea, e.g. with acetyl chloride, acetylurea is obtained.

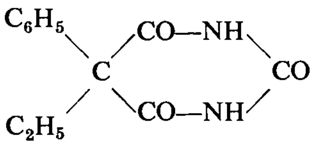
$$CH_3{\cdot}COCl + NH_2CONH_2 = HCl + \underset{\text{Acetylurea}}{CH_3{\cdot}CO{\cdot}NH{\cdot}CO{\cdot}NH_2}$$

With the dibasic acids, urea derivatives can be obtained by reaction with either one or both of the carboxyl groups, e.g. two derivatives are possible with oxalic acid.

$$\begin{array}{l}\mathrm{COOH}\\ |\\ \mathrm{COOH}\end{array} + \mathrm{NH_2CONH_2} = \mathrm{HOCO{\cdot}CO{\cdot}NH{\cdot}CO{\cdot}NH_2} + \mathrm{H_2O}$$



The closed ring compounds obtained by union with both carboxyl groups are the more important of these two classes of compounds. They are the ureides, the most important being phenobarbitone, which is derived from urea and phenyl ethyl malonic acid.



The ureides are crystalline substances, which have acidic properties. The sodium salts are soluble in water; the acids are only sparingly soluble in water, but more soluble in ether.

The ureides are related to purine and its derivatives, the most important of which are xanthine, caffeine, theobromine, theophylline and uric acid.

Thiourea

This is obtained by the action of heat on ammonium thiocyanate.

$$NH_4CNS = (NH_2)_2CS$$

THE ESTERS

(FUNCTIONAL GROUP —COOR)

The esters are derived from the acids (organic or inorganic) by the replacement of the acidic hydrogen by an alkyl group or substituted alkyl group. Esters may be prepared:

(1) *By the interaction of an acid and an alcohol.* This reversible reaction is catalysed by mineral acids, and the presence of concentrated sulphuric acid increases the rate (cf. p. 45). An alternative method (which is more effective than the sulphuric acid method with secondary and tertiary alcohols) is to pass gaseous hydrogen chloride into a mixture of the alcohol and acid until a 3 per cent increase in weight has been obtained (*Fischer–Speier* method).

$$\mathrm{RCO}\boxed{\mathrm{OH + H}}\mathrm{OR'} \rightleftarrows \mathrm{RCOOR'} + \mathrm{H_2O}$$

(2) *By the interaction of an acid chloride or anhydride and an alcohol.*

$$\mathrm{RCOCl} + \mathrm{R'OH} = \mathrm{RCOOR'} + \mathrm{HCl}$$

$$\mathrm{(RCO)_2O} + \mathrm{R'OH} = \mathrm{RCOOR'} + \mathrm{RCOOH}$$

(3) *By the interaction of a silver salt of the acid and an alkyl halide.*

$$\mathrm{CH_3{\cdot}COOAg} + \mathrm{C_2H_5I} = \mathrm{AgI} + \underset{\text{Ethyl acetate}}{\mathrm{CH_3{\cdot}COOC_2H_5}}$$

Properties of Esters

Many esters are volatile liquids, insoluble in water but soluble in organic solvents. Esters usually have characteristic pleasant odours, and the smell of many volatile oils is due to their ester content. Many esters are manufactured for use as artificial essences, and others are manufactured for use as solvents of the esters of cellulose and other substances used in the "plastics" industry.

The esters are not very reactive and their properties differ from those of the salts of the acids. They take part in the following reactions:

(1) *Hydrolysis and saponification.* The esters are partially hydrolysed by water; acids and certain enzymes (e.g. lipase) catalyse this reaction.

$$CH_3{\cdot}COOC_2H_5 + H_2O \rightleftarrows CH_3{\cdot}COOH + C_2H_5OH$$

Alkalis cause a complete conversion of the ester into the salt of the acid.

$$CH_3{\cdot}COOC_2H_5 + NaOH = CH_3{\cdot}COONa + C_2H_5OH$$

This reaction is called the *saponification* of the ester, and it may be compared with the conversion of fats (esters of glycerol) to soaps by heating with caustic alkali.

(2) *Conversion to amides.* Some esters react with ammonia to form amides.

$$CH_3{\cdot}COOC_2H_5 + NH_3 = CH_3{\cdot}CONH_2 + C_2H_5OH$$

(3) *Reduction.* Esters are reduced to a mixture of two alcohols by powerful reducing agents such as lithium aluminium hydride ($LiAlH_4$).

$$\begin{aligned} C_2H_5{\cdot}COOC_2H_5 &\rightarrow C_2H_5{\cdot}COOH + \\ &+ C_2H_5OH \rightarrow C_3H_7OH + C_2H_5OH \end{aligned}$$

The Esters of Inorganic Acids

Esters of sulphuric acid

When ethyl alcohol and sulphuric acid react together only one atom of hydrogen is initially replaced by an alkyl group and *ethyl hydrogen sulphate* is obtained. It is possible to prepare *diethyl sulphate* by further reaction.

Dimethyl sulphate is prepared from the corresponding methyl hydrogen sulphate by the action of heat.

$$2CH_3HSO_4 = (CH_3)_2SO_4 + H_2SO_4$$

Dimethyl sulphate is a poisonous substance which has an extensive use as a reagent in the laboratory and in industry. It reacts readily with alcohols replacing the hydrogen atom of the hydroxyl group by a methyl group (*methylation*).

$$C_2H_5OH + (CH_3)_2SO_4 = C_2H_5{\cdot}O{\cdot}CH_3 + CH_3HSO_4$$

The esters of nitric acid

Ethyl nitrate. Concentrated nitric acid reacts violently with ethyl alcohol and, owing to the oxidizing action of the acid, clouds of brown fumes are evolved. When the rate of reaction is controlled, a mixture of ethyl nitrate and ethyl nitrite is formed, owing to the reduction of part of the nitric acid by some of the alcohol, which is oxidized to acetaldehyde.

$$HNO_3 + C_2H_5OH = HNO_2 + CH_3{\cdot}CHO + H_2O$$

Pure ethyl nitrate can be obtained by reaction in the presence of urea, which removes the nitrous acid as soon as it is formed.

Glyceryl trinitrate. Glycerol contains three hydroxyl groups and therefore forms a tri-nitric ester with three molecules of nitric acid. This ester is also called nitroglycerin, although it is not a true nitro-derivative.

Glyceryl trinitrate is manufactured by adding pure anhydrous glycerol with continuous stirring to a well-cooled mixture of sulphuric and nitric acids. (Care is required in the design and manipulation of the apparatus, to avoid frictional contacts likely to cause explosion.) After the reaction is complete, the liquids are run into vessels where the nitroglycerin rises to the surface and is skimmed off, washed free from acid and dried.

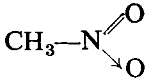
In the pure state nitroglycerin is too sensitive to be a reliable explosive. It is rendered safer to handle by mixing with an inert substance such as kieselguhr (a siliceous earth) in the manufacture of dynamite, or by mixing with nitrocellulose in the manufacture of cordite and blasting gelatin.

The esters of nitrous acid

The nitrous acid esters are isomeric with the nitroparaffins, but they have a different molecular structure and different properties (cf. p. 66).

$CH_3—O—N:O$

Methyl nitrite



$CH_3—N{\nearrow\!\!\!\!\!\!\nearrow O \atop \searrow O}$

Nitromethane

Ethyl nitrite is formed by the reaction of nitrous acid and ethyl alcohol. It is prepared either (1) by adding sodium nitrite to a cold acidified solution of ethyl alcohol, or (2) by distilling a mixture of sulphuric and nitric acids with alcohol and copper, when an alcoholic solution of ethyl nitrite is obtained.

$$NaNO_2 + HCl + C_2H_5OH = C_2H_5NO_2 + NaCl + H_2O$$

$$\begin{aligned} Cu + HNO_3 + C_2H_5OH + H_2SO_4 \\ = C_2H_5NO_2 + CuSO_4 + 2H_2O \end{aligned}$$

Amyl nitrite is prepared by acting with sulphuric acid on a solution of sodium nitrite and amyl alcohol.

The esters of carbonic acid

These substances are prepared by the following reactions.

(1) By the action of the corresponding alcohol on carbonyl chloride.

$$COCl_2 + 2C_2H_5OH = CO(OC_2H_5)_2 + 2HCl$$

(2) By the action of alkyl halides on silver carbonate.

$$2C_2H_5I + AgCO_3 = 2AgI + (C_2H_5)_2CO_3$$

The carbonate esters are soluble in water, by which they are slowly hydrolysed. Orthocarbonate esters can also be prepared although the corresponding acid [i.e. $C(OH)_4$] is not known in the free state.

The Esters of Organic Acids

Ethyl acetate

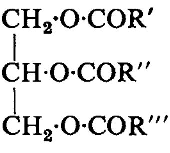
This ester is prepared on an industrial scale from ethyl alcohol and acetic acid for use as a solvent and in the manufacture of perfumes. It is also obtained from acetaldehyde by a catalytic reaction, in the presence of aluminium ethoxide $Al(OC_2H_5)_3$.

$$2CH_3{\cdot}CHO = CH_3{\cdot}COOC_2H_5$$

Many other esters are prepared commercially for use as solvents and in the perfume industry, e.g. amyl acetate, butyl acetate, ethyl butyrate.

The Oils, Fats and Waxes

The fats of animal and vegetable origin are mixtures containing various proportions of the esters of glycerol with palmitic, stearic, and oleic acids. The pure esters are called *tripalmitin*, *tristearin* and *triolein* respectively, the prefix indicating that all three of the hydroxyl groups of the glycerol have taken part in ester formation. A similar nomenclature is sometimes used for the glyceryl esters of other acids, e.g. triacetin (glyceryl triacetate), trinitrin (glyceryl trinitrate), monoformin (glyceryl monoformate). Glycerides of the type in which all three hydroxyl groups are united to similar acid radicals are called *simple glycerides*. Many natural fats contain large quantities of *mixed glycerides* which contain different acid radicals, e.g.



$$\begin{array}{l}CH_2{\cdot}O{\cdot}COR' \\ | \\ CH{\cdot}O{\cdot}COR'' \\ | \\ CH_2{\cdot}O{\cdot}COR'''\end{array}$$

The melting points of the pure fatty esters are tripalmitin 63°C, tristearin 66°C, triolein −6°C. The consistency of any particular oil or fat depends on the relative proportion of triolein it contains; the more liquid oils containing a high proportion.

The fats and fatty oils are extracted from the raw material by melting out, or by the influence of pressure. They may also be obtained by extraction with a suitable organic solvent. (The fats are insoluble in water, more soluble in alcohol, but readily soluble in such solvents as chloroform or benzene.)

The oils and fats behave in accordance with the reactions of esters. (1) They are hydrolysed by treatment with steam or acids to give glycerol and the fat acids, which are often prepared by this reaction. (2) They react with alkalis to form glycerol and salts of the acids (the soaps).

The waxes are esters, not of glycerol, but of simple monohydric alcohols containing a long carbon chain. Beeswax contains the palmitic esters of myricyl alcohol ($C_{30}H_{61}OH$) together with other alcohols and acids in the uncombined state.

THE NITRILES

(FUNCTIONAL GROUP $—C{:}N$)

The nitriles are named according to the acid they yield on hydrolysis. They may also be called cyanides, and acetonitrile and methyl cyanide are alternative names for the same substance $CH_3{\cdot}CN$. The nitriles may be prepared by the following methods:

(1) By the dehydration of amides, usually by heating with phosphorus pentoxide.

$$CH_3{\cdot}CONH_2 + P_2O_5 = CH_3CN + 2HPO_3$$

(2) By the action of potassium cyanide on an alkyl halide.

$$CH_3I + KCN = CH_3CN + KI$$

Properties of the Nitriles

(1) *Hydrolysis.* The most important reaction of the nitriles is their conversion into acids by hydrolysis. When warmed either with acids or alkalis, two molecules of water are taken up and the ammonium salt of the acid is formed, the free acid being obtained from this salt. This reaction affords an important method of synthesis of acids.

$$CH_3CN + 2H_2O = CH_3{\cdot}COONH_4$$
$$2CH_3{\cdot}COONH_4 + H_2SO_4 = 2CH_3{\cdot}COOH + (NH_4)_2SO_4$$

By more gentle hydrolysis (e.g. using hydrogen peroxide) only one molecule of water is taken up by the nitrile and the acid amide is obtained.

$$CH_3CN + H_2O = CH_3{\cdot}CONH_2$$

(2) *Reduction.* On reduction, using sodium and alcohol, the nitriles yield primary amines.

$$CH_3CN \xrightarrow{4H} CH_3{\cdot}CH_2NH_2$$

Acrylonitrile

This is obtained by the action of hydrogen cyanide on acetylene, by passing the gases at 90°C through a solution containing ammonium chloride and cuprous chloride as a catalyst. Another process involves the controlled oxidation of propylene by air, in the presence of ammonia and steam at 450°C.

$$CH{\vdots}CH + HCN = CH_2{:}CHCN$$
$$CH_2{:}CH{\cdot}CH_3 + NH_3 \xrightarrow{O_2} CH_2{:}CH{\cdot}CN$$

Acrylonitrile is polymerized to its commercial "plastic" polymer by heating in the presence of water and a peroxy catalyst.

THE ISONITRILES

(FUNCTIONAL GROUP —NC)

The isonitriles (or carbylamines or isocyanides) differ from the nitriles in having the nitrogen atom attached to the alkyl group.

$\mathrm{CH_3{-}C{:}N}$	$\mathrm{CH_3{-}N\overset{\rightarrow}{=}C}$
Nitrile or cyanide	Isonitrile, isocyanide or carbylamine

They may be prepared from the alkyl halides by reacting with silver cyanide instead of potassium cyanide.

$$\mathrm{AgNC + CH_3I = CH_3NC + AgI}$$

They are also prepared by the carbylamine reaction from chloroform and primary amines.

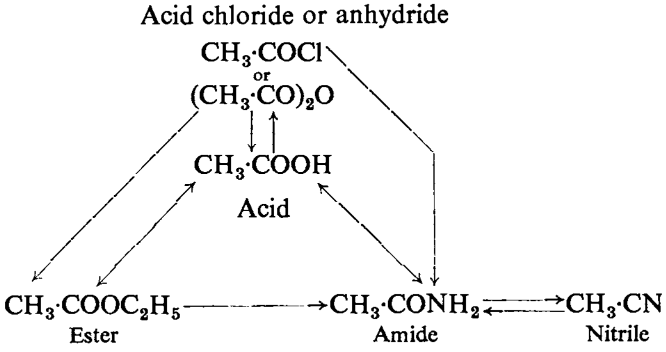
$$\mathrm{CH_3NH_2 + 3KOH + CHCl_3 = CH_3NC + 3KCl + 3H_2O}$$

The properties of the isonitriles differ from those of the nitriles. They are more toxic and have characteristic unpleasant smells. They are hydrolysed by acids, but not alkalis, to form amines and they yield secondary amines on reduction.

$$\mathrm{CH_3NC + 2H_2O = CH_3NH_2 + HCOOH}$$

$$\mathrm{CH_3NC \xrightarrow{4H} (CH_3)_2NH}$$

Interconversion of Derivatives of Acids

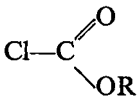


9

halogen, hydroxy, aldehydic, ketonic and amino-acids

The Halogen Substituted Acids

The halogen substituted acids possess two functional groups (i.e. the halogen atom and the carboxyl group) and are prepared and react accordingly, e.g. the chloroacetic acids are prepared by introducing chlorine (by direct reaction) into the molecule of acetic acid. They give the reactions of halides as well as of acids. The simplest halogen substituted acid (chloroformic acid $Cl{\cdot}COOH$), cannot be prepared except as esters. These are obtained by the action of carbonyl chloride on alcohols and possess properties associated with acid chlorides



$$Cl{-}C(=O){-}OR$$

$$ClCOCl + HOC_2H_5 = \underset{\text{Ethyl chloroformate}}{ClCOOC_2H_5} + HCl$$

The higher halogen substituted acids are stable.

The chloroacetic acids

When the direct halogenation of acetic acid is used as a source of the substituted acetic acids, the passage of chlorine is continued until the theoretical gain in weight has been obtained.

$$CH_3\cdot COOH + Cl_2 = CH_2Cl\cdot COOH + HCl$$

$$CH_2Cl\cdot COOH + Cl_2 = CHCl_2\cdot COOH + HCl$$

$$CHCl_2\cdot COOH + Cl_2 = CCl_3\cdot COOH + HCl$$

Dichloroacetic acid is more conveniently prepared from chloral hydrate by the action of calcium carbonate and sodium cyanide. The reaction mechanism and the function of the latter reagent is not yet understood.

$$CCl_3\cdot CH(OH)_2 \rightarrow CHCl_2\cdot COOH + HCl$$

Trichloroacetic acid is best made by the oxidation of the corresponding aldehyde (chloral) with nitrous acid.

$$CCl_3\cdot CHO \xrightarrow{O} CCl_3\cdot COOH$$

The strengths of these three acids increase with the number of chlorine atoms introduced into the molecule, since the unequal sharing of the electron pair involved in the carbon–chlorine bond (induced by the electronegativity of the chlorine atom) renders the carbon atom slightly electron deficient. This leads to shifts in the electron distribution away from the carboxyl oxygen, and thus favours the separation, by ionization, of a proton.

$$Cl \leftarrow CH_2 \leftarrow \overset{\overset{O}{\|}}{C} \leftarrow OH \rightarrow ClCH_2\cdot COO^- + H^+$$

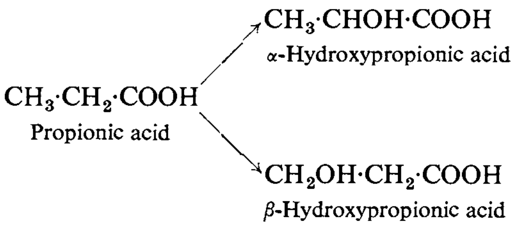
The chlorine atoms possess the usual properties of halogen atoms substituted in organic compounds, e.g. they may be replaced by hydroxyl and amino groups. In consequence of the reactivity of these halogen atoms, the substituted acids are important in the synthesis of many other compounds, e.g. glycollic acid and glycine are obtained in the form of their salts by reaction with aqueous caustic potash (cf. reaction 3, p. 34) or ammonia (reaction 5, p. 35).

$$CH_2Cl\cdot COOH + KOH = CH_2OH\cdot COOH + KCl$$

$$CH_2Cl\cdot COOH + 2NH_3 = CH_2NH_2\cdot COOH + NH_4Cl$$

The Hydroxy Acids

The hydroxy acids possess two functional groups (i.e. the alcohol and the carboxyl groups) and are prepared and react accordingly, e.g. glycollic acid is prepared from a halogen acid by hydrolysis and it gives the reactions of primary alcohols as well as those of acids. The simplest member of the series of hydroxy acids is glycollic acid ($CH_2OH\cdot COOH$) (hydroxyacetic acid). The next members of the series are derived from propionic acid. Two isomeric acids exist since it is possible to substitute a hydroxyl group in the propionic acid molecule in two different positions thus:



$$\begin{tikzcd} & CH_3\cdot CHOH\cdot COOH \\ CH_3\cdot CH_2\cdot COOH \arrow[ur] \arrow[dr] & \\ & CH_2OH\cdot CH_2\cdot COOH \end{tikzcd}$$

α-Hydroxypropionic acid

Propionic acid

β-Hydroxypropionic acid

In these and similar cases, the derivatives obtained are distinguished from one another by the use of the letters α, β, γ, etc., to indicate the position of the hydroxyl, or other substituted group, starting with the carbon atom next to the carboxyl group, e.g.

$CH_3{\cdot}CHOH{\cdot}COOH$ — α-Hydroxypropionic acid

$CH_2OH{\cdot}CH_2{\cdot}COOH$ — β-Hydroxypropionic acid

$CH_2OH{\cdot}CH_2{\cdot}CH_2{\cdot}COOH$ — γ-Hydroxybutyric acid

α- and β-hydroxypropionic acids are more commonly known as lactic and hydracrylic acids respectively.

The General Methods of Preparation of Hydroxy Acids

These are:

(1) By introducing the hydroxyl group into an acid molecule:

(a) From the halogen substituted acids, by hydrolysis, e.g. with moist silver oxide (cf. reaction 1, p. 43).

$$CH_2Cl{\cdot}COOH + H_2O = CH_2OH{\cdot}COOH + HCl$$

(b) From the amino-acids, by reaction with nitrous acid (cf. reaction 4, p. 43).

$$CH_2NH_2{\cdot}COOH + HNO_2 = CH_2OH{\cdot}COOH + N_2 + H_2O$$

(2) By introducing a carboxyl group into an alcohol.

(a) From aldehyde cyanhydrins, by hydrolysis.

$$CH_3{\cdot}CH(OH)CN + 2H_2O = CH_3{\cdot}CHOH{\cdot}COONH_4$$

(b) From glycols, by partial oxidation.

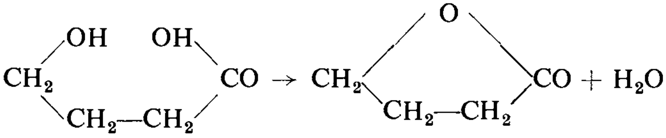
$$CH_2OH{\cdot}CH_2OH \rightarrow CH_2OH{\cdot}COOH$$

The Properties of Hydroxy Acids

The hydroxy acids contain both a hydroxyl group and a carboxyl group in their molecules, and in general exhibit the properties of alcohols as well as those of acids, e.g. lactic acid, which contains a secondary alcohol grouping, is oxidized to pyruvic acid.

$$CH_3{\cdot}CHOH{\cdot}COOH \rightarrow CH_3{\cdot}CO{\cdot}COOH$$

The alcoholic hydroxyl groups and the acidic carboxyl group tend to react with one another to form ester-like compounds whose molecules contain ring structures. The properties of a particular hydroxy acid depend on the relative position of these two groups in its molecule. For example, with γ- and δ-hydroxy acids, the interaction of the alcoholic and acidic groups takes place on heating, and the resulting compound is called a *lactone* (or internal anhydride).



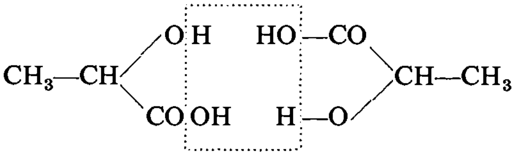
Hydroxybutyric acid Butyrolactone

With the β-hydroxy acids, the strain involved in ring formation prevents ring closure and these acids do not form β-lactones (anhydrides). On heating these acids, they break down to form unsaturated acids.

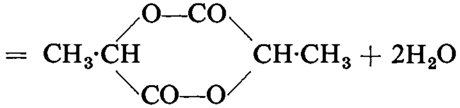
$$CH_2OH{\cdot}CH_2{\cdot}COOH = CH_2{:}CH{\cdot}COOH + H_2O$$

β-Hydroxypropionic acid (Hydracrylic acid) Acrylic acid

No lactones can be formed when the hydroxyl group and the carboxyl groups are immediate neighbours, but instead, esters can be formed between two molecules of the α-hydroxy acids when the hydroxyl group of the one acid reacts with the carboxyl group of the other. Such cyclic esters are called *lactides*.

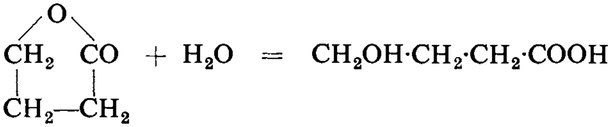


α-Hydroxypropionic acid (lactic acid)

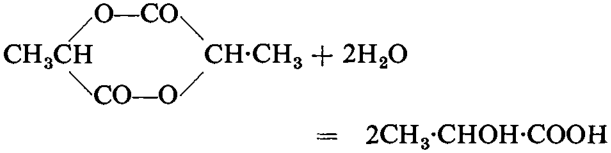


Lactide

Lactones and lactides can be hydrolysed to reform the original hydroxy acids.



$+ H_2O = CH_2OH\cdot CH_2\cdot CH_2\cdot COOH$



$= 2CH_3\cdot CHOH\cdot COOH$

Glycollic acid (hydroxyacetic acid)

This may be prepared by any of these general methods:

(a) $CH_2Cl\cdot COOH + AgOH = AgCl + CH_2OH\cdot COOH$

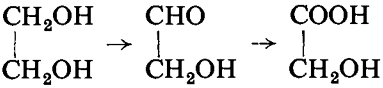
(b) $CH_2NH_2\cdot COOH + HNO_2$

$= CH_2OH\cdot COOH + N_2 + H_2O$

(c) $CH_2OH\cdot CN + H_2O = CH_2OH\cdot CONH_2$

$CH_2OH\cdot CONH_2 + H_2O = CH_2OH\cdot COONH_4$

(d)



$$\begin{array}{c}CH_2OH\\|\\CH_2OH\end{array} \rightarrow \begin{array}{c}CHO\\|\\CH_2OH\end{array} \rightarrow \begin{array}{c}COOH\\|\\CH_2OH\end{array}$$

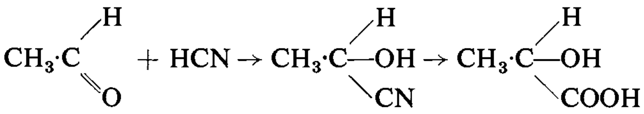
Lactic acid

Lactic acid is α-hydroxypropionic acid ($CH_3{\cdot}CHOH{\cdot}COOH$) and contains a carbon atom united to four different groups and, therefore, stereoisomerism (cf. p. 136) is possible. Ordinary lactic acid is the inactive (or racemic) form. The *dextro*-rotatory acid (sarcolactic acid) occurs in meat juices and is obtainable from meat extract. The *laevo*-form does not occur naturally but may be obtained by removing the *dextro*-rotatory fraction of the inactive mixture.

Ordinary or fermentation lactic acid is formed during the souring of milk, as the result of the "lactic fermentation" of lactose by the lactic bacillus. It is manufactured from sour milk or by the lactic fermentation of sugars other than lactose (e.g. sucrose in sugar molasses or the sugars formed by the hydrolysis of wood shavings).

$$C_{12}H_{22}O_{11} + H_2O = 4CH_3{\cdot}CHOH{\cdot}COOH$$

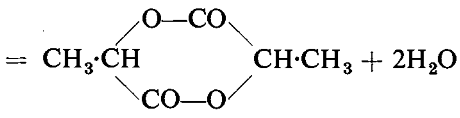
Lactic acid can also be prepared by the general methods for hydroxy acids, e.g. acetaldehyde adds on hydrogen cyanide to form acetaldehyde cyanhydrin, which on hydrolysis yields lactic acid. (This series of reactions establishes the constitutional formula of lactic acid.)



$$CH_3{\cdot}\overset{\diagup H}{\underset{\diagdown O}{C}} + HCN \rightarrow CH_3{\cdot}\overset{\diagup H}{\underset{\diagdown CN}{C}}\text{—}OH \rightarrow CH_3{\cdot}\overset{\diagup H}{\underset{\diagdown COOH}{C}}\text{—}OH$$

Lactic acid, when free from water, is a crystalline solid (m.p. 18°C) but, as it is very hygroscopic, it is usually marketed as a syrupy, viscous liquid containing 10 per cent or more of water. Commercial lactic acid contains lactide formed during concentration by evaporation *in vacuo*.

$$2CH_3{\cdot}CHOH{\cdot}COOH$$



Lactic acid yields acetaldehyde on oxidation with potassium permanganate. Milder oxidation gives pyruvic acid.

$$CH_3{\cdot}CHOH{\cdot}COOH \xrightarrow{O} CH_3{\cdot}CHO + CO_2 + H_2O$$

$$CH_3{\cdot}CHOH{\cdot}COOH \xrightarrow{O} CH_3{\cdot}CO{\cdot}COOH + H_2O$$

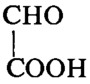
Hydracrylic acid

This substance is obtained by the hydrolysis of its cyanhydrin, which is prepared by the action of potassium cyanide on ethylene chlorohydrin.

$$CH_2OH{\cdot}CH_2Cl \rightarrow CH_2OH{\cdot}CH_2CN \rightarrow CH_2OH{\cdot}CH_2{\cdot}COOH$$

On oxidation hydracrylic acid yields malonic acid [$CH_2(COOH)_2$]. Unlike lactic acid, hydracrylic acid does not exist in optically isomeric forms.

ALDEHYDIC AND KETONIC ACIDS

The most important aldehydic acid is glyoxalic acid  $\begin{array}{l}CHO\\ |\\ COOH\end{array}$ (a product of the oxidation of glycol), and the chief ketonic acids are pyruvic acid ($CH_3{\cdot}CO{\cdot}COOH$ — an intermediate product in the fermentation of sugar) and acetoacetic acid the ethyl ester of which is an important synthetic reagent (cf. p. 159). Acetoacetic acid may be regarded as acetic acid with one of the hydrogen atoms replaced by the acetyl group. The free acid is not known.

Ethyl acetoacetate is prepared by the action of sodium on dry ethyl acetate. The reaction is complex. It starts slowly and gradually builds up to a vigorous reaction. The final result of the reaction may be represented by the equation:

$$2CH_3{\cdot}COOC_2H_5 + 2HCH_2{\cdot}COOC_2H_5 + 2Na$$
$$= 2CH_3{\cdot}CO{\cdot}CH_2{\cdot}COOC_2H_5 + 2C_2H_5ONa + H_2$$

Tautomerism of acetoacetic ester. Ethyl acetoacetate is a sweet-smelling liquid which is very reactive. For many years its reactions were difficult to explain, as it seemed to behave as if it possessed two distinct constitutions, i.e. a saturated ketonic acid and an unsaturated hydroxy acid. In accordance with the first formula (given opposite) it behaves as a ketone and forms a phenylhydrazone. The ketonic formula also explains the products obtained when ethyl acetoacetate is hydrolysed. But ethyl acetoacetate also gives a colour with ferric chloride (normally indicative of the presence of a hydroxyl group in the molecule), and it reacts with sodium evolving hydrogen. These reactions can be interpreted by the enolic formula (en = ethylenic linkage; ol = hydroxyl group).

$$CH_3\cdot\underset{\underset{\displaystyle OH}{|}}{C}{:}CH\cdot COOC_2H_5$$

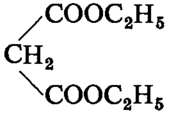
It was found that acetoacetic ester consists of a mixture of two distinct substances, which are so easily interconverted by the migration of a hydrogen atom that a state of chemical equilibrium is attained. In keeping with the usual properties of equilibrium mixtures, when one form is removed as a derivative, the equilibrium is adjusted until the whole of the ethyl acetoacetate is converted into the derivative of that one form.

$$\underset{\text{Ketonic form}}{CH_3\cdot CO\cdot CH_2\cdot COOC_2H_5} \rightleftarrows \underset{\text{Enolic form}}{CH_3\cdot C(OH){:}CH\cdot COOC_2H_5}$$

The two forms of acetoacetic ester may be separated, provided care is taken to avoid contamination with substances which catalyse the interconversion. If the ester (in alcoholic solution) is cooled to −78°C the pure ketonic form (m.p. 39°C) separates and the enolic form remains in the mother liquor. Alternatively, the ester may be distilled with phthalic acid in a hard glass apparatus and at reduced pressure, using a silica receiver. The enolic form, 88 per cent pure, collects. If this is re-distilled in a silica apparatus, the pure enolic form is obtained. But as soon as traces of catalysts (e.g. dust particles) are introduced, interconversion proceeds rapidly, and either the pure ketonic or the pure enolic form quickly reverts to the ordinary equilibrium mixture.

When two distinct isomers are so easily interconverted that only one substance is ordinarily obtained (which is an equilibrium mixture containing both forms), the type of isomerism is called *dynamic isomerism*, or *tautomerism*. The two forms are called dynamic isomers or tautomers.

Dynamic isomerism is found among more than one class of substance. The class (as in acetoacetic ester) where dynamic isomerism takes place between a ketone and an unsaturated alcohol is commonly called keto-enol isomerism. Keto-enol isomerism is found in those compounds which contain a carbon atom (united to one or two hydrogen atoms) placed between a carbonyl group and an ester group (as in acetoacetic ester), or between two carbonyl groups (as in acetylacetone $CH_3{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}CH_3$) or two ester groups as in malonic ester



$$CH_2\begin{cases} COOC_2H_5 \\ COOC_2H_5 \end{cases}$$

The Amino-acids and the Proteins

The amino-acids possess two functional groups in their molecules (i.e. the amino and the carboxyl groups) and are prepared and react accordingly. The simplest amino-acid is glycine (aminoacetic acid, $NH_2CH_2{\cdot}COOH$). The properties of the higher amino-acids vary according to the relative positions of the amino and the carbonyl groups, and α-, β- and γ-amino-acids are distinguished.

$CH_3{\cdot}CH(NH_2){\cdot}COOH$	$NH_2CH_2{\cdot}CH_2{\cdot}COOH$
α-Aminopropionic acid	β-Aminopropionic acid

$NH_2CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}COOH$
γ-Aminobutyric acid

The α-amino-acids are the most important, for proteins are hydrolysed into a mixture of α-amino-acids, e.g. by the enzymes present in the digestive juices in the animal body.

Preparation of Amino-acids

Most of the commoner amino-acids are prepared by the hydrolysis of proteins in acid or alkaline solution, but they may be obtained synthetically by modifications of the general methods for the formation of amino and acidic compounds, e.g.

$$CH_2Cl\cdot COOH + 2NH_3 = CH_2NH_2COOH + NH_4Cl$$

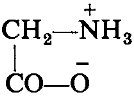
Properties of Amino-acids

Amino-acids contain an amino group and a carboxyl group. Consequently their properties are a combination of those of acids and bases, and they form two classes of salts.

(a) With bases, e.g. $NH_2\cdot CH_2\cdot CO\overset{-}{O}\ \overset{+}{Na}$

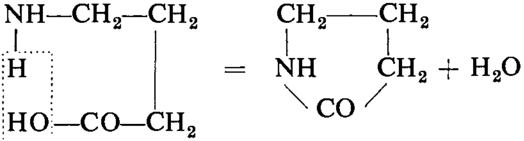
(b) With acids, e.g. $\overset{+}{N}H_3\cdot CH_2\cdot COOH\ \ \overset{-}{Cl}$

The free amino-acids are crystalline compounds, soluble in water and insoluble in organic solvents. These characteristics are those of salt-like bodies, and it is suggested that crystallization occurs in the form of internal salts, e.g.



$$\begin{array}{l} CH_2\text{—}\overset{+}{N}H_3 \\ | \\ CO\text{—}\overset{-}{O} \end{array}$$

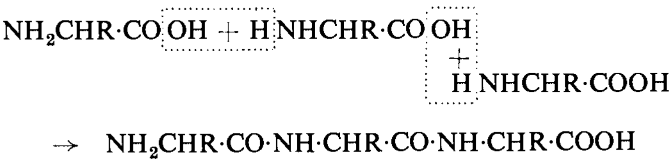
In the case of γ- and δ-amino-acids, the union between the amino and acidic radicals takes place with loss of water and *lactams* are formed. These compounds, which correspond to the lactones of the hydroxy acids, indicate the ease of formation of closed ring compounds if the reacting groups are separated by a suitable distance.



Lactam

Proteins and Polypeptides

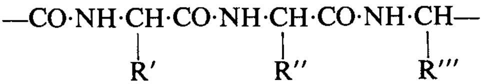
The proteins are biological products, of very high molecular weight and consequently of colloidal nature. Some have been obtained in a crystalline state. On hydrolysis, proteins yield a mixture of various simpler substances, the final products being α-amino-acids. Proteins are formed by the combination of amino-acid residues as in the example



$$\begin{array}{l} NH_2CHR{\cdot}CO\,OH + H\,NHCHR{\cdot}CO\,OH \\ \qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad + \\ \qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad H\,NHCHR{\cdot}COOH \end{array}$$

$$\rightarrow NH_2CHR{\cdot}CO{\cdot}NH{\cdot}CHR{\cdot}CO{\cdot}NH{\cdot}CHR{\cdot}COOH$$

The formulae of proteins can therefore be represented as containing a chain of nitrogen and carbon atoms united as follows:



$$—CO{\cdot}NH{\cdot}\underset{\displaystyle R'}{\underset{|}{CH}}{\cdot}CO{\cdot}NH{\cdot}\underset{\displaystyle R''}{\underset{|}{CH}}{\cdot}CO{\cdot}NH{\cdot}\underset{\displaystyle R'''}{\underset{|}{CH}}—$$

At one end of the protein chain there is an uncombined amino group while at the other end there is an uncombined carboxyl group. Consequently, proteins have both acidic and basic properties, and form salts with either acids or alkalis. They are *amphoteric electrolytes.*

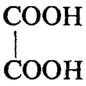
The properties of amphoteric electrolytes vary considerably with the pH of the solution, since in acid solutions the protein exists as the salt of the acid while in alkaline solutions it exists as the salt of the alkali. At a certain intermediate pH (known as the *iso-electric point*) (in the case of gelatin at pH 4·7), the acidic and basic ionizations balance and the protein exists mainly as the neutral ion which carries both types of charge.

Proteins are often coagulated and rendered insoluble by heating (e.g. egg albumin). The coagulation is irreversible, for the precipitated protein is not re-dispersed on cooling.

10

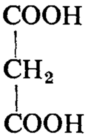
the dibasic acids

DIBASIC organic acids contain two identical functional groups, i.e. two carboxyl groups. They form a homologous series. Oxalic acid is the simplest member. Other important members of the series are malonic acid and succinic acid.



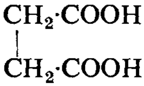
$$\begin{array}{l} \mathrm{COOH} \\ | \\ \mathrm{COOH} \end{array}$$

Oxalic acid



$$\begin{array}{l} \mathrm{COOH} \\ | \\ \mathrm{CH_2} \\ | \\ \mathrm{COOH} \end{array}$$

Malonic acid



$$\begin{array}{l} \mathrm{CH_2{\cdot}COOH} \\ | \\ \mathrm{CH_2{\cdot}COOH} \end{array}$$

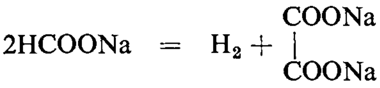
Succinic acid

The dibasic acids occur in nature in the free state and in the form of their salts. They may be prepared synthetically by general methods, and these synthetic methods are often of importance in proving the constitutions of the particular acids.

The dibasic acids are usually crystalline solids, soluble in water. They possess the usual acid properties and, being dibasic, normal and acid salts may be obtained.

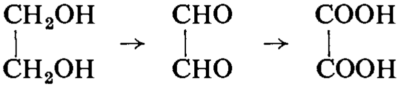
Oxalic acid

Some plants contain the acid potassium salt (KHC_2O_4) in considerable quantity, some contain the calcium salt, while others contain the free acid. Oxalic acid is obtained as a product of the oxidation of many organic compounds, and in the laboratory it is often prepared by the oxidation of cane sugar with nitric acid. Oxalic acid is manufactured from sodium formate (prepared from carbon monoxide and sodium hydroxide). On heating, the formate decomposes and sodium oxalate is obtained.

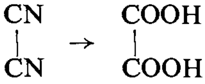


$$2HCOONa = H_2 + \begin{array}{c}COONa\\|\\COONa\end{array}$$

The constitution of oxalic acid may be established by its formation from glycol by oxidation, and from cyanogen by hydrolysis, thus indicating the presence of two carboxyl groups in the molecule.



$$\begin{array}{c}CH_2OH\\|\\CH_2OH\end{array} \rightarrow \begin{array}{c}CHO\\|\\CHO\end{array} \rightarrow \begin{array}{c}COOH\\|\\COOH\end{array}$$



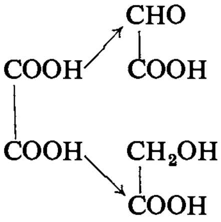
$$\begin{array}{c}CN\\|\\CN\end{array} \rightarrow \begin{array}{c}COOH\\|\\COOH\end{array}$$

Oxalic acid crystallizes with two molecules of water of crystallization. It is a dibasic acid, and forms acid salts such as potassium binoxalate KHC_2O_4, and neutral salts such as potassium oxalate $K_2C_2O_4.2H_2O$. The salts of the alkali metals are soluble in water, but the oxalates of other metals are insoluble in water. In addition to the acid and neutral salts, quadroxalates are known, which are formed by the combination of a molecule of oxalic acid with a molecule of the acid salt, e.g. potassium quadroxalate $KHC_2O_4.H_2C_2O_4.2H_2O$. Oxalic acid and its soluble salts are poisonous.

Oxalic acid is oxidized to carbon dioxide and water by a warm acidified solution of potassium permanganate.

$$H_2C_2O_4 \xrightarrow{O} H_2O + 2CO_2$$

Reduction of oxalic acid converts only one of the two carboxyl groups. Thus, with magnesium and sulphuric acid, glyoxalic acid (containing an aldehyde group) is obtained while with zinc and sulphuric acid, glycollic acid (containing a primary alcohol group) is obtained.



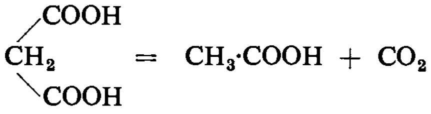
When subjected to the action of dehydrating agents (for example, when heated with concentrated sulphuric acid) oxalic acid yields a mixture of carbon monoxide and carbon dioxide. It is used for the laboratory preparation of carbon monoxide.

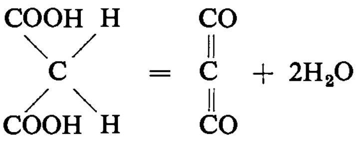
$$H_2C_2O_4 = H_2O + CO + CO_2$$

When heated with glycerol, oxalic acid breaks down into formic acid (cf. p. 55).

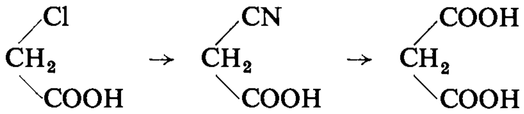
Malonic acid

This acid occurs in beetroot as the calcium salt. Malonic acid, when heated alone, loses carbon dioxide and acetic acid is formed, but in the presence of a dehydrating agent malonic anhydride (carbon suboxide C_3O_2) is obtained.



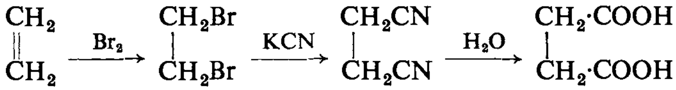


Diethyl malonate is used as a synthetic reagent for the preparation of organic acids. It is prepared from monochloroacetic acid by heating its potassium salt with potassium cyanide. This gives a cyanacetate which is hydrolysed and then esterified by refluxing with ethyl alcohol and concentrated sulphuric acid. The ester is finally separated by pouring into water and is then dried and distilled. This sequence of reactions confirms the constitution of malonic acid.



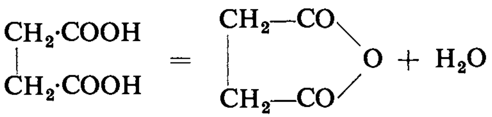
Succinic acid

This acid occurs in many plants and animal products. Its constitution is confirmed by its synthesis by the following series of reactions:



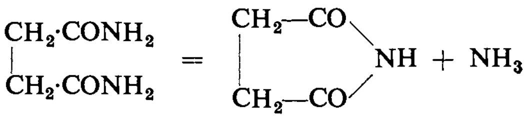
$$\begin{array}{c}CH_2\\ \|\\ CH_2\end{array} \xrightarrow{Br_2} \begin{array}{c}CH_2Br\\ |\\ CH_2Br\end{array} \xrightarrow{KCN} \begin{array}{c}CH_2CN\\ |\\ CH_2CN\end{array} \xrightarrow{H_2O} \begin{array}{c}CH_2{\cdot}COOH\\ |\\ CH_2{\cdot}COOH\end{array}$$

Succinic acid differs from the lower members of the series of dibasic acids as it forms an internal anhydride when heated.



Succinic anhydride

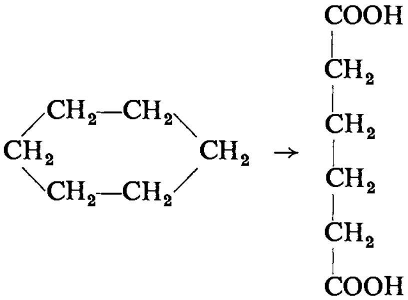
In a similar manner succinamide forms succinimide with loss of ammonia.



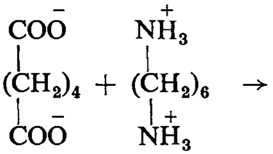
Succinamide Succinimide

Adipic acid

This acid is prepared by the oxidation of cyclohexane and is important as the starting point of the substance "nylon".



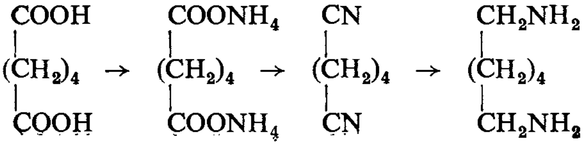
Adipic acid is reacted with hexamethylenediamine in methyl alcoholic solution to give "nylon salt", which is then polymerized at 280°C in the presence of acetic acid and in a nitrogen atmosphere. The polymerization proceeds by a series of elimination reactions involving amide formation.



$$\begin{array}{l} \overset{-}{\mathrm{COO}} \\ | \\ (\mathrm{CH_2})_4 \\ | \\ \overset{-}{\mathrm{COO}} \end{array} + \begin{array}{l} \overset{+}{\mathrm{NH_3}} \\ | \\ (\mathrm{CH_2})_6 \\ | \\ \overset{+}{\mathrm{NH_3}} \end{array} \rightarrow$$

$$\overset{-}{\mathrm{COO}}\cdot(\mathrm{CH_2})_4[\mathrm{CO}\cdot\mathrm{NH}\cdot(\mathrm{CH_2})_6\mathrm{NH}\cdot\mathrm{CO}\cdot(\mathrm{CH_2})_4\cdot\mathrm{CO}]_n\mathrm{NH}\cdot(\mathrm{CH_2})_6\overset{+}{\mathrm{NH_3}}$$

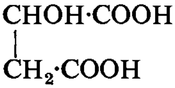
The hexamethylenediamine is itself obtained from adipic acid by interaction with ammonia at 400°C in the presence of a catalyst. This gives adipic nitrile, which is catalytically hydrogenated.



$$\begin{array}{l} \mathrm{COOH} \\ | \\ (\mathrm{CH_2})_4 \\ | \\ \mathrm{COOH} \end{array} \rightarrow \begin{array}{l} \mathrm{COONH_4} \\ | \\ (\mathrm{CH_2})_4 \\ | \\ \mathrm{COONH_4} \end{array} \rightarrow \begin{array}{l} \mathrm{CN} \\ | \\ (\mathrm{CH_2})_4 \\ | \\ \mathrm{CN} \end{array} \rightarrow \begin{array}{l} \mathrm{CH_2NH_2} \\ | \\ (\mathrm{CH_2})_4 \\ | \\ \mathrm{CH_2NH_2} \end{array}$$

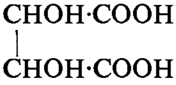
THE HYDROXYDIBASIC AND POLYBASIC ACIDS

The most important hydroxydibasic acids are derivatives of succinic acid. The monohydroxy derivative is malic acid. The dihydroxy derivative is tartaric acid.



$$\begin{array}{l} \mathrm{CHOH{\cdot}COOH} \\ | \\ \mathrm{CH_2{\cdot}COOH} \end{array}$$

Malic acid



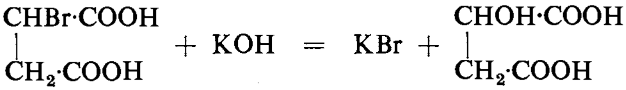
$$\begin{array}{l} \mathrm{CHOH{\cdot}COOH} \\ | \\ \mathrm{CHOH{\cdot}COOH} \end{array}$$

Tartaric acid

Malic acid

This acid is found in many fruits (sour grapes, apples and mountain ash berries). The molecule of malic acid contains a carbon atom united to four different radicals and has no plane of symmetry. It therefore exists in optically active forms (cf. p. 133). The naturally occurring form is *laevo*-rotatory; the *dextro*-rotatory form may be obtained by separation of the inactive racemic mixture.

The constitution of malic acid may be established by its formation by the hydrolysis of monobromosuccinic acid.



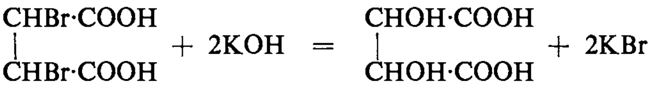
$$\begin{array}{l} \mathrm{CHBr{\cdot}COOH} \\ | \\ \mathrm{CH_2{\cdot}COOH} \end{array} + \mathrm{KOH} = \mathrm{KBr} + \begin{array}{l} \mathrm{CHOH{\cdot}COOH} \\ | \\ \mathrm{CH_2{\cdot}COOH} \end{array}$$

Tartaric acid

Tartaric acid contains two asymmetric carbon atoms. Two optically active forms (*dextro*- and *laevo*-rotatory) and two optically inactive forms of tartaric acid are obtainable; all are represented by the above formula (cf. p. 136).

The naturally occurring form of tartaric acid is *dextro*-rotatory. This is found in many fruits, and the sparingly soluble potassium acid tartrate separates out during the fermentation of grape-juice and is deposited at the bottom of the vats. *Dextro*-rotatory tartaric acid may be converted into either of the two inactive forms by heating its aqueous solution. The *laevo*-rotatory form is obtained by removing the *dextro*-rotatory fraction from the racemic mixture.

The constitution of tartaric acid is established by its synthesis from dibromosuccinic acid.



$$\begin{array}{l}\text{CHBr·COOH}\\ \mid\\ \text{CHBr·COOH}\end{array} + 2\text{KOH} = \begin{array}{l}\text{CHOH·COOH}\\ \mid\\ \text{CHOH·COOH}\end{array} + 2\text{KBr}$$

Dibromosuccinic acid

Tartaric acid

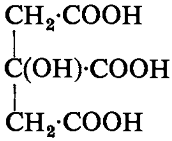
On heating, tartaric acid chars readily, and it darkens fairly rapidly when heated with concentrated sulphuric acid.

Tartaric acid is a reducing agent. It reduces ammoniacal silver nitrate solution forming a silver mirror.

Tartrates form complex compounds with many metals, which do not then give their ordinary ionic reactions. For example, copper is not precipitated from an alkaline solution containing tartrates. The resulting solution (*Fehling's* solution) gives a precipitate of cuprous oxide on reduction.

Citric acid

This acid is a tribasic monohydroxy acid of the constitution

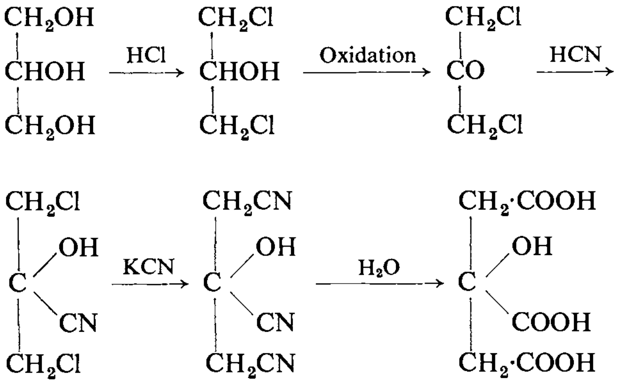


$$\begin{array}{l}\text{CH}_2\text{·COOH}\\ \mid\\ \text{C(OH)·COOH}\\ \mid\\ \text{CH}_2\text{·COOH}\end{array}$$

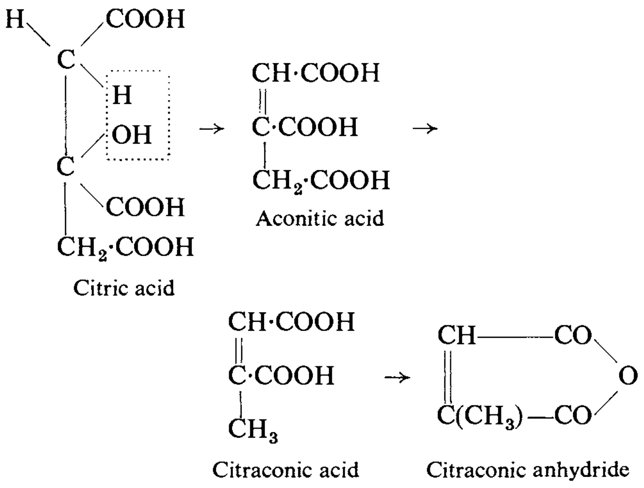
It is present in the juices of citrus fruits, and is prepared from lemon juice by neutralization with milk of lime. Citric acid is also obtained by the fermentation of sugars by *Aspergillus niger*.

$$C_{12}H_{22}O_{11} \xrightarrow{6O} 2C_6H_8O_7 + 3H_2O$$

The constitution of citric acid follows from its synthesis by means of the following series of reactions. By the addition of hydrogen cyanide to symmetrical dichloro-acetone (which is obtained from glycerol), followed by reaction with potassium cyanide, a substance is obtained which on hydrolysis yields citric acid.



If citric acid is heated carefully, it breaks down into simpler substances according to the scheme:



Citrates resemble tartrates in forming complex compounds with metal ions. They may be distinguished by their reactions with calcium chloride. A crystalline precipitate of calcium tartrate is obtained when calcium chloride is added to a neutral solution of a tartrate. Under similar conditions, citrates give a precipitate of calcium citrate only if the solution is boiled. (Calcium citrate is appreciably soluble in cold water, although less soluble in hot water.)

11

stereochemistry — optical isomerism

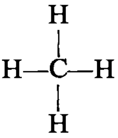
PLANE polarized light is unaffected during transmission through most substances, but certain crystals and liquids cause a rotation of the plane of polarization, either to the right or to the left. It has been established that the cause of the rotation is connected with asymmetry either in the crystal structure of the solid or in the individual molecules present in the liquid or solution states. The particular form of asymmetry involves the absence of a plane of symmetry; under these conditions object and mirror image forms are permissible which cannot occupy exactly the same position and arrangement in space. Only three-dimensional (not one- or two-dimensional) objects can exhibit this type of asymmetry and the two permissible forms are related to one another as the right hand is related to the left.

Organic substances which rotate the plane of polarization are said to be *optically active* and exhibit the effect either in solution or in the fused condition. Their molecules are three dimensional and have no plane of symmetry. When optical activity exists, two separate substances are found, one rotating the plane of polarization to the right and the other to the left, by an equal amount, under similar conditions. These two substances correspond to the right- and left-hand forms of the molecular models and their physical properties are identical, except in respect to polarized light, owing to the close resemblance between object and mirror image. Their chemical properties are also identical, except in reactions with other optically active substances, but their physiological behaviour often differs because many reactions in the living organism involve such optically active substances. Most (but not all) of the organic compounds whose molecules have no plane of symmetry contain an asymmetric carbon atom.

Isomerism arising from the spatial arrangement of the atoms within the molecule is called *stereoisomerism* (the isomers being known as stereoisomers).

The Asymmetric Carbon Atom

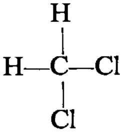
The four radicals which are attached to a carbon atom have been represented as lying in a plane (the plane of the paper); e.g the formula of methane has been written thus:



$$\begin{array}{ccc} & \mathrm{H} & \\ & | & \\ \mathrm{H}- & \mathrm{C} & -\mathrm{H} \\ & | & \\ & \mathrm{H} & \end{array}$$

This method of writing the formula has been adopted for convenience, but it does not represent the true arrangement in which the four radicals are grouped around the carbon atom.

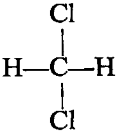
If the co-planar arrangement existed it would be possible to obtain two isomeric dichloromethanes, which are not actually obtainable, thus —



$$\begin{array}{ccc} & \mathrm{H} & \\ & | & \\ \mathrm{H}- & \mathrm{C} & -\mathrm{Cl} \\ & | & \\ & \mathrm{Cl} & \end{array}$$

Cis form

(Similar radicals adjacent)



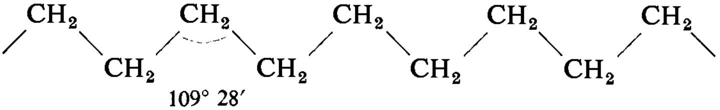
$$\begin{array}{ccc} & \mathrm{Cl} & \\ & | & \\ \mathrm{H}- & \mathrm{C} & -\mathrm{H} \\ & | & \\ & \mathrm{Cl} & \end{array}$$

Trans form

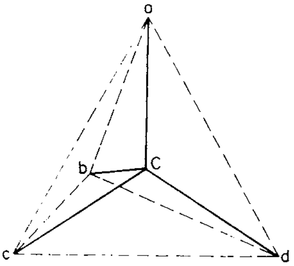
(Similar radicals not adjacent)

In reality, the four radicals are arranged spatially (i.e. in three dimensions) about the carbon atom, so that the resulting molecule is solid rather than flat. With this arrangement, only one dichloromethane can exist.

The observed equivalence of the four hydrogen atoms in the methane molecule indicates that they are symmetrically disposed with reference to the carbon atom. This symmetrical arrangement is obtained when the carbon atom is placed at the centre of a regular tetrahedron, and a hydrogen atom at each of the four corners. It was first suggested in 1874 by *Van't Hoff* that the four valencies of carbon were directed towards the corners of a regular tetrahedron. Almost simultaneously *Le Bel* suggested that the carbon valencies were arranged spatially, and Van't Hoff and Le Bel were able to explain the optical activity of carbon compounds on these assumptions. In accordance with this hypothesis, the valency angles of carbon are at 109° 28′ (the tetrahedral angle). It follows that in a chain the carbon atoms do not lie in the same straight line but form a zig-zag arrangement as in the diagram.



The shape of the molecule of the compound C *abcd* can be represented by an arrangement as in the diagram, where the radicals are indicated by the letters *a*, *b*, *c* and *d*.



If *a*, *b*, *c* and *d* are different, it is not possible to divide this molecular arrangement by any plane in such a way that the portions of the molecule on either side of the plane correspond exactly. The molecule is without a plane of symmetry. A carbon atom which is attached to four different radicals, and which forms an arrangement possessing no plane of symmetry, is called an *asymmetric carbon atom.*

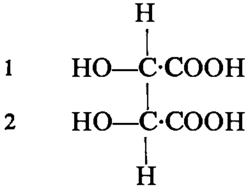
Optical Isomerism of Lactic Acid

A compound containing one asymmetric carbon atom (such as lactic acid) is found to exist in three isomeric forms, two optically active, and one optically inactive. The two optically active forms have similar physical and chemical properties and differ only in their behaviour to polarized light. One form rotates the plane of polarization to the right, the other rotates the plane of polarization to the left. Under equivalent conditions, the *dextro-* and *laevo-*rotations of the two forms are exactly equal but of opposite sign. These two forms correspond to the object and mirror image molecular arrangements. They are called *enantiomorphous* forms (cf. *enantios*, opposite; *morphos*, form).

The third isomeric form is found to be a mixture in equal proportions of the two optically active forms. Its optical inactivity is due to the mutual neutralization of the *dextro-* and *laevo-*rotations. It is said to be inactive by *external compensation.* (It is sometimes called the *racemic* or *dl* form or racemic mixture.) The physical properties of the racemic form differ slightly from those of its optically active constituents.

Stereoisomerism of Tartaric Acid

Tartaric acid exists in four modifications, two of which are optically active and two inactive. Ordinary tartaric acid is the *dextro*-rotatory isomer. The corresponding *laevo* form can be obtained by removing the *dextro* component from the inactive racemic mixture. The other inactive form (mesotartaric acid) is not capable of being split into two optically active forms, Tartaric acid contains two asymmetric carbon atoms



$$\begin{array}{cl} & \qquad\ \ \text{H} \\ & \qquad\ \ | \\ 1 & \text{HO—C·COOH} \\ & \qquad\ \ | \\ 2 & \text{HO—C·COOH} \\ & \qquad\ \ | \\ & \qquad\ \ \text{H} \end{array}$$

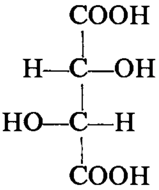
If the asymmetric groupings 1 and 2 around the two carbon atoms are considered independently of one another, the following combinations are possible.

(a) *Dextro* (1) + *Dextro* (2)
(b) *Dextro* (1) + *Laevo* (2)
(c) *Laevo* (1) + *Dextro* (2)
(d) *Laevo* (1) + *Laevo* (2)

The groupings attached to the two asymmetric carbon atoms in 1 and 2 are identical, so that the compound represented by arrangements (b) and (c) is optically inactive.

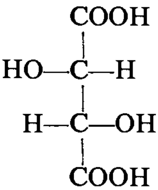
This inactive form differs from the inactive racemic form (obtained by mixing the *dextro* and *laevo* forms (a) and (d) in equal proportions), for it is inactive through mutual neutralization of two active groupings inside the same molecule. It is said to be *inactive by internal compensation,* in contrast to the racemic form which is *inactive by external compensation.*

The molecules of *dextro*-rotatory, *laevo*-rotatory and internally compensated inactive mesotartaric acid may be conventionally represented as shown below. In the latter form, the opposing configurations form an arrangement containing a plane of symmetry, illustrating the optical inactivity of the compound.



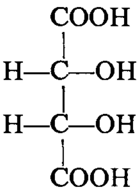
$$\begin{array}{c} \text{COOH} \\ | \\ \text{H—C—OH} \\ | \\ \text{HO—C—H} \\ | \\ \text{COOH} \end{array}$$

$d + d =$ D tartaric acid



$$\begin{array}{c} \text{COOH} \\ | \\ \text{HO—C—H} \\ | \\ \text{H—C—OH} \\ | \\ \text{COOH} \end{array}$$

$l + l =$ L tartaric acid



$$\begin{array}{c} \text{COOH} \\ | \\ \text{H—C—OH} \\ | \\ \text{H—C—OH} \\ | \\ \text{COOH} \end{array}$$

$l + d =$ mesotartaric acid

In compounds containing more than two asymmetric carbon atoms, it is possible to predict the number of isomeric forms obtainable, by considering the effects of each asymmetric grouping independently, as in the case of tartaric acid. For example, there are sixteen stereoisomeric aldose sugars.

Resolution of Racemic Compounds

Substances which are capable of exhibiting optical activity usually occur naturally in an optically active form. When these substances are synthesized in the laboratory from inactive sources the racemic mixture is obtained. In order to obtain a product which is identical with the natural form the synthetic mixture must be *resolved*, i.e. separated into its active components. Owing to the similarity in the physical and chemical properties of the *dextro*- and *laevo*-rotatory forms no simple separation is possible. The resolution can be carried out by three methods.

(1) The first separation of a racemic form into its active constituents was carried out by *Pasteur* in 1848. He found that when the sodium ammonium salt of racemic tartaric acid was allowed to crystallize at a fairly low temperature, the crystals which separated could be sorted out under the microscope into two groups, one of which was composed of crystals which were the mirror images of those in the other group.

Pasteur found that one group of crystals consisted of the salt of naturally occurring *dextro*-rotatory tartaric acid, while the other group of crystals consisted of the corresponding *laevo*-tartaric acid salt.

This method of resolution by sorting out mirror image crystals is not of very general application.

(2) Pasteur found a second method of separation. A mould or fungus may be found which grows on one optically active form only, so that in a racemic mixture one form is destroyed and the other remains, e.g. *Pencillium glaucum* when grown in a solution of racemic tartaric acid destroys the *dextro* form and leaves the *laevo* form unchanged.

This method of resolution suffers from the disadvantage that one optically active isomer is lost in order to obtain the other.

(3) The most important method for the resolution of racemic forms is the crystallization of a suitable salt of the substance with another optically active substance. If the substance to be resolved is an acid it is converted into its salt with an optically active base (e.g. *l*-brucine) if the substance to be resolved is a base it is converted into its salt with an optically active acid (e.g. *d*-tartaric acid).

For example, suppose the resolution of an inactive acid is being carried out by means of *l*-brucine. The inactive acid (*d*-acid + *l*-acid) is converted into its *l*-brucine salt, so that there is present *d*-acid + *l*-brucine salt, and *l*-acid + *l*-brucine salt. These two compounds are not optical antipodes (for the corresponding compound to *d*-acid + *l*-brucine would be *l*-acid + *d*-brucine). Therefore their physical properties are no longer identical. One form is more soluble than the other, and the two forms can be separated by fractional crystallization. The two optically active forms of the acid can then be liberated from their alkaloidal salts.

12

unsaturated acids—geometrical isomerism

THE UNSATURATED ACIDS

Unsaturated acids contain a double bond and a carboxyl group. The simplest acid is acrylic acid ($CH_2{:}CH{\cdot}COOH$), which corresponds to allyl alcohol ($CH_2{:}CH{\cdot}CH_2{\cdot}OH$, and acrolein $CH_2{:}CH{\cdot}CHO$).

Crotonic acid ($CH_3{\cdot}CH{:}CH{\cdot}COOH$) is the next member of the series (the corresponding aldehyde being obtained from acetaldehyde by the aldol condensation). The most important member of the series is oleic acid [$CH_3{\cdot}(CH_2)_7{\cdot}CH{:}CH{\cdot}(CH_2)_7{\cdot}COOH$]. Ricinoleic acid is a hydroxy unsaturated acid related to oleic acid [$CH_3{\cdot}(CH_2)_5{\cdot}CHOH{\cdot}CH_2{\cdot}CH{:}CH(CH_2)_7COOH$]. Its glyceride is the chief constituent of castor oil. Linseed and other drying oils contain the glycerides of other long chain unsaturated acids.

The unsaturated acids possess properties characteristic of ethylenic derivatives as well as the acidic properties due to the carboxyl group. They are readily oxidized, splitting at the double bond which can thus be located. They combine readily with halogens, hydrogen halides and hydrogen (in the presence of a catalyst) to form addition compounds. The proportion of olein in a fat can be determined by measurement of the quantity of iodine absorbed, for the other constituents (palmitin and stearin) being saturated, do not react with iodine.

The Hardening of Fats

Fat hardening is an industrial process by which unsaturated fats and oils can be converted into clean and edible fats derived from saturated acids. The conversion is carried out by reacting, in the presence of a nickel catalyst, with hydrogen which adds on to the double bond. The liquid fat is allowed to trickle down over the surface of the nickel catalyst in an atmosphere of hydrogen, the saturated fat being collected as it is formed.

$$CH_3{\cdot}(CH_2)_7{\cdot}CH{:}CH{\cdot}(CH_2)_7{\cdot}COOH + H_2 = CH_3{\cdot}(CH_2)_{16}{\cdot}COOH$$

Oleic acid

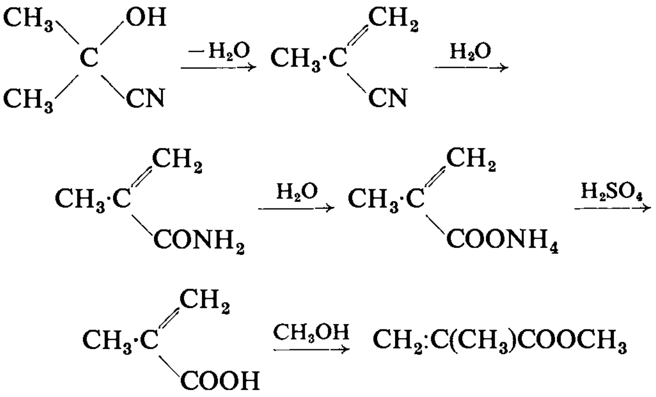
Oleic acid is obtained by the hydrolysis of suitable fats, by dilute acids or steam. The position of the double bond in oleic acid is shown by the fact that on oxidation it gives a mixture of two acids each containing nine carbon atoms.

$$CH_3{\cdot}(CH_2)_7{\cdot}CH{:}CH{\cdot}(CH_2)_7{\cdot}COOH \xrightarrow{4O} CH_3{\cdot}(CH_2)_7{\cdot}COOH + COOH{\cdot}(CH_2)_7{\cdot}COOH$$

Elaidic acid is represented by the same formula as oleic acid and the two substances are geometrical isomers (cf. p. 143).

Methylacrylic acid

This acid is important commercially since its methyl ester is polymerized to give the substance known as "Perspex". Methyl methacrylate is manufactured from acetone cyanhydrin and methyl alcohol in the presence of concentrated sulphuric acid,

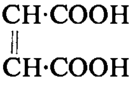


The polymerization of the unsaturated ester is carried out in the presence of benzoyl peroxide as a catalyst.

Unsaturated Dibasic Acids

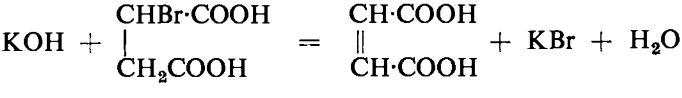
Maleic and fumaric acids

The simplest acids of this class are the geometrical isomers (cf. p. 144), maleic and fumaric acids, both of which are represented by the formula:



$$\begin{array}{l} CH{\cdot}COOH \\ \| \\ CH{\cdot}COOH \end{array}$$

A mixture of the two is obtained by the action of alkali on bromosuccinic acid.



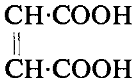
$$KOH + \begin{array}{l} CHBr{\cdot}COOH \\ | \\ CH_2COOH \end{array} = \begin{array}{l} CH{\cdot}COOH \\ \| \\ CH{\cdot}COOH \end{array} + KBr + H_2O$$

Both acids are reduced to succinic acid and oxidized to forms of tartaric acid (maleic → mesotartaric; fumaric → the racemic acid). Fumaric acid is converted into maleic acid by boiling in acid or alkaline solution. Maleic acid on heating forms an anhydride.

Fumaric acid gives no anhydride of its own, but on heating it yields maleic anhydride.

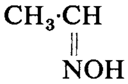
GEOMETRICAL ISOMERISM

The concept of the spatial arrangement of the four valencies of carbon explains the existence of geometrical isomerism, which occurs in compounds containing a double bond between two carbon atoms or between a carbon and a nitrogen atom, e.g.



$$\begin{array}{c}\mathrm{CH{\cdot}COOH}\\ \| \\ \mathrm{CH{\cdot}COOH}\end{array}$$

(1)

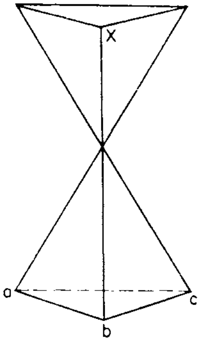


$$\begin{array}{r}\mathrm{CH_3{\cdot}CH}\\ \| \\ \mathrm{NOH}\end{array}$$

(2)

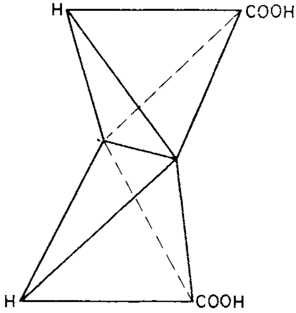
It occurs in ethylenic derivatives when the two radicals attached to each double-bonded carbon atom are different. The two compounds (maleic and fumaric acid) represented by the formula (1) form an example of this type of isomerism.

In accordance with the tetrahedral model of the carbon atom the single bond (C—C) is represented by two tetrahedra joined at the corners, e.g. ethane is represented as in the diagram.

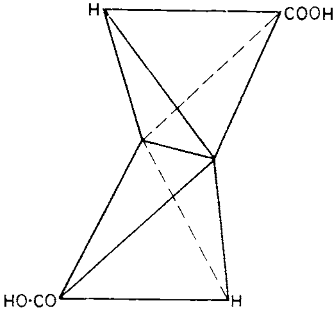


In order to explain the non-existence of a large number of isomeric ethane derivatives depending on the relative position of the two tetrahedra (e.g. atom X opposite either *a*, *b* or *c*), it is necessary to assume that the two tetrahedra are free to rotate about their common axis. The existence of geometrical isomers arises from the restriction of this free rotation on the formation of a double bond.

Two carbon atoms united by a double bond are represented by two tetrahedra joined edge to edge. Under these conditions, the only motion of the tetrahedra is an oscillation about the line of contact, and it is possible to have two arrangements, which cannot be inter-converted without disruption of the double bond. In arrangement (1) the two like groups are near to one another (the *cis* position); in arrangement (2) the two like groups are separated from one another (the *trans* position).

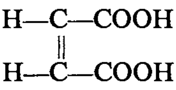


Maleic acid



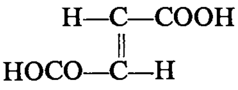
Fumaric acid

The two isomers differ in their chemical behaviours; the differences enable the configuration to be allocated to each substance. For example, maleic acid forms an anhydride; therefore the two carboxyl groups must be close together with this acid, which is therefore the *cis* isomer. Fumaric acid (which does not form an anhydride) is the *trans* isomer. Correspondingly, oleic acid is the *cis* and elaidic acid the *trans* isomer.



$$\begin{array}{l} \mathrm{H{-}C{-}COOH} \\ \quad\ \| \\ \mathrm{H{-}C{-}COOH} \end{array}$$

Maleic acid



$$\begin{array}{r} \mathrm{H{-}C{-}COOH} \\ \|\qquad\quad \\ \mathrm{HOCO{-}C{-}H} \end{array}$$

Fumaric acid

13

carbohydrates

THE NAME "carbohydrates" was given to substances such as the sugars, starch and cellulose when it was found that these compounds have the empirical composition $C_x(H_2O)_y$. Other related substances are now often included under this heading. The carbohydrates are divided into three main classes of substances: (1) Monosaccharides — not hydrolysable to smaller components, e.g. glucose, fructose. (2) Polysaccharides — hydrolysable to monosaccharides. A large proportion of this class are disaccharides, e.g. sucrose, lactose. Starch and cellulose are also included. (3) Glycosides — hydrolysable to monosaccharides together with other substances.

THE MONOSACCHARIDES

The commoner monosaccharides are crystalline, water soluble and sweet-tasting substances of formula $C_6H_{12}O_6$. They are reducing agents, and reduce ammoniacal silver nitrate and Fehling's solution. Certain monosaccharide sugars, e.g. glucose and fructose, are fermented by yeast.

Monosaccharides give the reactions of alcohols. Some of them (the aldose sugars) also give the reactions of aldehydes. Others (the ketose sugars) give the reactions of ketones.

Glucose (*grape sugar*, *dextrose*)

Glucose is found in grapes, honey and other fruits. Commercially it is obtained from starch by hydrolysis with dilute hydrochloric acid.

Fructose (*laevulose*)

Fructose is found in honey and some fruits, and occurs combined with glucose in the disaccharide, sucrose. Hydrolysis of sucrose gives a mixture of glucose and fructose, and the two simple sugars can be separated by fractional crystallization. Commercially, fructose is obtained by the hydrolysis of inulin (a starch-like polysaccharide occurring in some plant tubers).

Constitutional Formulae of Monosaccharides

The aldoses

The most widely occurring member of this group is glucose, and its structure may be derived from the following experimental facts:

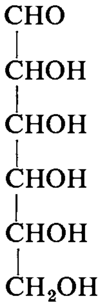
(1) The six carbon atoms form a straight chain, since reduction with hydriodic acid yields a derivative of normal hexane.

(2) Glucose contains five hydroxyl groups, since it forms a penta-acetate.

(3) The presence of an aldehyde group is shown by the formation of a cyanhydrin yielding heptoic acid, $CH_3(CH_2)_5COOH$, on hydrolysis, and also by the formation of a primary alcohol on reduction.

(4) Oxidation with bromine water yields gluconic acid $CH_2{\cdot}OH{\cdot}(CHOH)_4{\cdot}COOH$, and further oxidation yields saccharic acid, $COOH{\cdot}(CHOH)_4COOH$. These reactions show the presence of a terminal $—CH_2OH$ group.

These facts are consistent with the following formula for glucose.

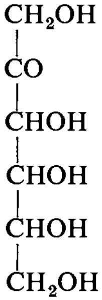


$$\begin{array}{l} CHO \\ | \\ CHOH \\ | \\ CHOH \\ | \\ CHOH \\ | \\ CHOH \\ | \\ CH_2OH \end{array}$$

This formula indicates the presence of four asymmetric carbon atoms, and therefore glucose is one of sixteen compounds which differ only in their stereochemical configurations. Each of these has a terminal aldehyde grouping and they are referred to as the *aldohexoses.*

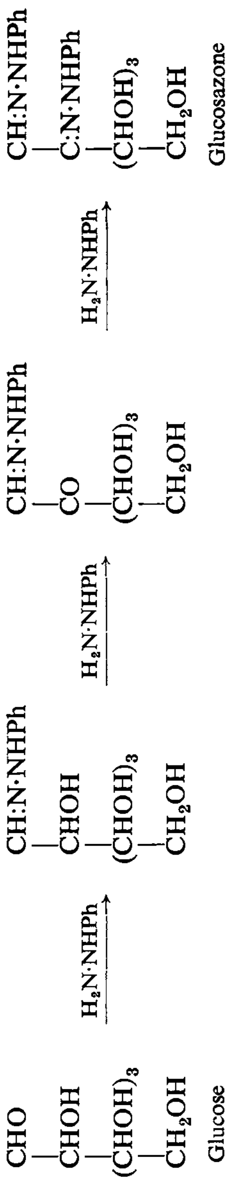
The ketoses

Fructose is the most important monosaccharide of this group and, as a result of the study of reactions similar to those already described for glucose, it has been shown to be a ketone with the ketonic grouping situated at the penultimate carbon atom as shown below.

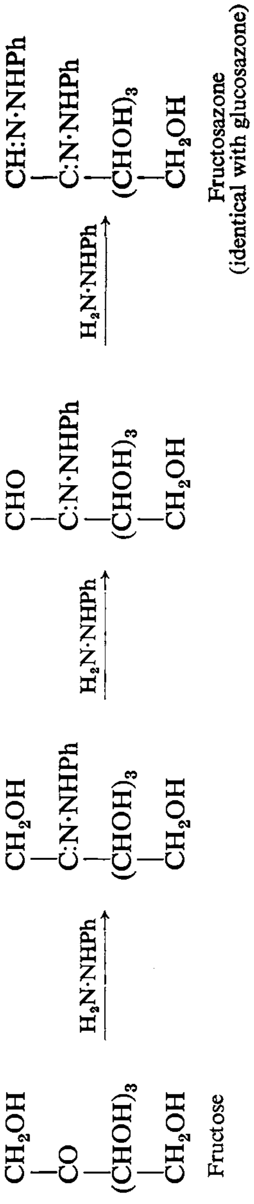


$$\begin{array}{l} CH_2OH \\ | \\ CO \\ | \\ CHOH \\ | \\ CHOH \\ | \\ CHOH \\ | \\ CH_2OH \end{array}$$

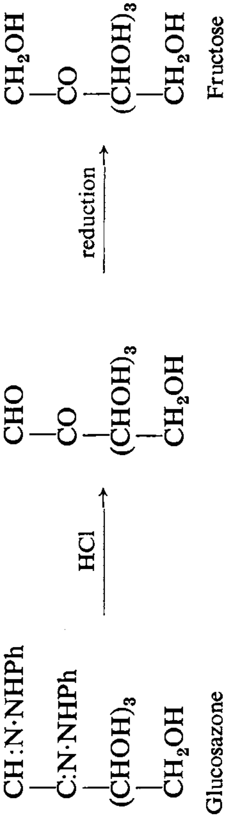
This formula indicates the presence of three asymmetric carbon atoms and fructose is one of eight compounds which differ only in their stereochemical configurations. These are referred to as *ketohexoses.*



$$\begin{array}{l}\mathrm{CHO}\\|\\\mathrm{CHOH}\\|\\\mathrm{(CHOH)_3}\\|\\\mathrm{CH_2OH}\end{array}\xrightarrow{\mathrm{H_2N{\cdot}NHPh}}\begin{array}{l}\mathrm{CH{:}N{\cdot}NHPh}\\|\\\mathrm{CHOH}\\|\\\mathrm{(CHOH)_3}\\|\\\mathrm{CH_2OH}\end{array}\xrightarrow{\mathrm{H_2N{\cdot}NHPh}}\begin{array}{l}\mathrm{CH{:}N{\cdot}NHPh}\\|\\\mathrm{CO}\\|\\\mathrm{(CHOH)_3}\\|\\\mathrm{CH_2OH}\end{array}\xrightarrow{\mathrm{H_2N{\cdot}NHPh}}\begin{array}{l}\mathrm{CH{:}N{\cdot}NHPh}\\|\\\mathrm{C{:}N{\cdot}NHPh}\\|\\\mathrm{(CHOH)_3}\\|\\\mathrm{CH_2OH}\end{array}$$



$$\begin{array}{l}\mathrm{CH_2OH}\\|\\\mathrm{CO}\\|\\\mathrm{(CHOH)_3}\\|\\\mathrm{CH_2OH}\end{array}\xrightarrow{\mathrm{H_2N{\cdot}NHPh}}\begin{array}{l}\mathrm{CH_2OH}\\|\\\mathrm{C{:}N{\cdot}NHPh}\\|\\\mathrm{(CHOH)_3}\\|\\\mathrm{CH_2OH}\end{array}\xrightarrow{\mathrm{H_2N{\cdot}NHPh}}\begin{array}{l}\mathrm{CHO}\\|\\\mathrm{C{:}N{\cdot}NHPh}\\|\\\mathrm{(CHOH)_3}\\|\\\mathrm{CH_2OH}\end{array}\xrightarrow{\mathrm{H_2N{\cdot}NHPh}}\begin{array}{l}\mathrm{CH{:}N{\cdot}NHPh}\\|\\\mathrm{C{:}N{\cdot}NHPh}\\|\\\mathrm{(CHOH)_3}\\|\\\mathrm{CH_2OH}\end{array}$$



$$\begin{array}{l}\mathrm{CH{:}N{\cdot}NHPh}\\|\\\mathrm{C{:}N{\cdot}NHPh}\\|\\\mathrm{(CHOH)_3}\\|\\\mathrm{CH_2OH}\end{array}\xrightarrow{\mathrm{HCl}}\begin{array}{l}\mathrm{CHO}\\|\\\mathrm{CO}\\|\\\mathrm{(CHOH)_3}\\|\\\mathrm{CH_2OH}\end{array}\xrightarrow{\text{reduction}}\begin{array}{l}\mathrm{CH_2OH}\\|\\\mathrm{CO}\\|\\\mathrm{(CHOH)_3}\\|\\\mathrm{CH_2OH}\end{array}$$

Osazones

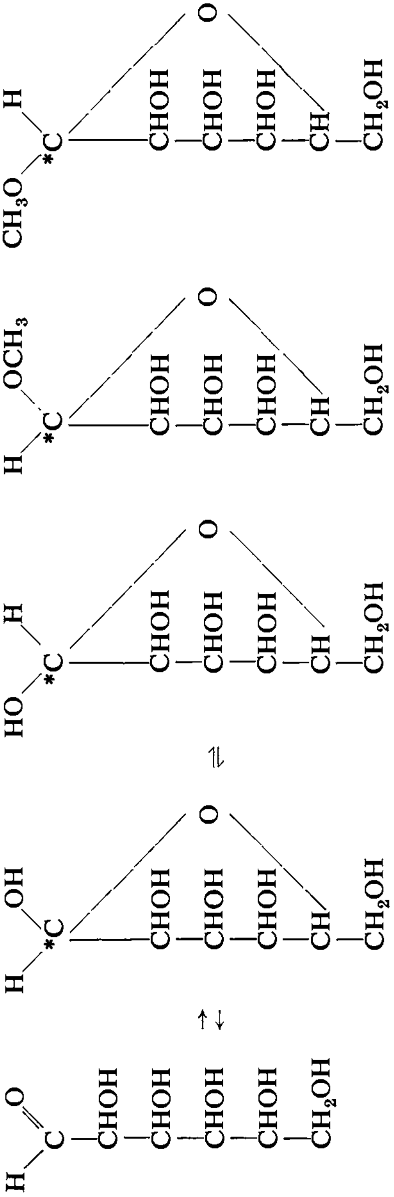
Phenylhydrazine has been proved to be a most useful reagent in the study of sugar chemistry. Glucose and fructose react readily (as typical aldehydic and ketonic compounds) to form phenylhydrazones. With excess of the reagent, these sugar derivatives react further (including oxidation) to form osazones. The osazones obtained from glucose and fructose are identical. The relationship between these two sugars is shown further by the fact that hydrolysis of their osazones with hydrochloric acid, followed by reduction, yields fructose. These reactions show that glucose and fructose have the same stereochemical configurations after the first two carbon atoms.

The open chain formulae for aldo- and keto-hexoses have been found inadequate to account for all the properties of these substances. For example, anhydrous glucose exists in two forms with different melting points, different solubilities and different specific rotations. The two forms are called α-glucose and β-glucose. The optical rotation of a freshly prepared aqueous solution of either form of glucose changes rapidly until it reaches a constant value. This phenomenon is known as *mutarotation.* α-Glucose has an initial specific rotation of +113°, falling off to +52·5°. For β-glucose the initial specific rotation is +19°, rising to +52·5°. The existence of these two isomers cannot be explained by an open chain formula.

$$\alpha\text{-glucose} \rightleftharpoons \beta\text{-glucose}$$

Also, glucose reacts with methyl alcohol to give a mixture of two isomeric (α and β)-methyl glucosides. (Other sugars form similar compounds, the general name for such derivatives being *glycoside.*)

The methyl glucosides are non-reducing, i.e. they do not possess aldehydic groups. Although stable to alkalis, they are easily hydrolysed by dilute acids and by enzymes. Maltose hydrolyses the α-isomer but does not affect the β-form, while emulsin (an enzyme from bitter almonds) hydrolyses the β-form but not the α-form. This difference in enzyme behaviour suggests



Glucose (straight-chain)

α-Glucose

β-Glucose

α- Methyl glucosides β-that these two glucosides differ stereochemically and the existence and properties of these two isomers can be explained by assigning to them (and correspondingly to α- and β-glucose) cyclic or ring structures (as shown opposite) with an additional asymmetric carbon atom indicated by an asterisk.

THE DISACCHARIDES

The disaccharides are crystalline solids, soluble in water. They are derived from two molecules of monosaccharides, and are easily hydrolysed to form the monosaccharide units. They have the general formula $C_{12}H_{22}O_{11}$.

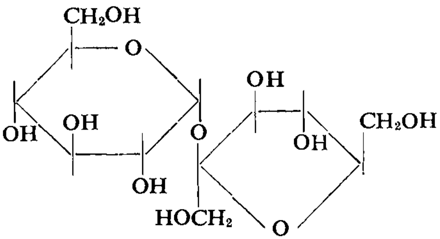
$$C_{12}H_{22}O_{11} + H_2O = C_6H_{12}O_6 + C_6H_{12}O_6$$

sucrose	→	glucose	+	fructose
maltose	→	glucose	+	glucose
lactose	→	glucose	+	galactose

The linkage between the two monosaccharides is formed by the elimination of water between two hydroxyl groups, creating a linkage through an oxygen atom as in ethers, acetals and glycosides.

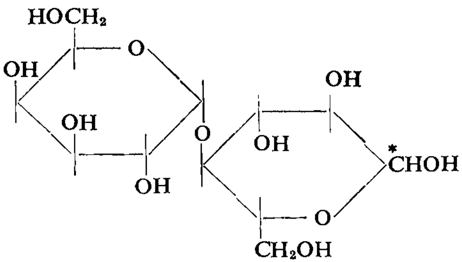
Disaccharides can be divided into two main types, (a) reducing and (b) non-reducing. This classification is illustrated by considering some well-known sugars of each type. The diagrammatical formulae overleaf indicate their constitutions and stereochemical configurations. (Note that the hydrogen atoms have been omitted for simplicity of representation.)

Sucrose occurs in the juices of the sugar cane, sugar beet and other plants. It is obtained commercially from sugar cane and sugar beet. The juice is heated with milk of lime to remove acids and coagulate proteins. The syrup is concentrated by evaporation under reduced pressure. On cooling, crystals of sucrose settle out and are collected by centrifuging.



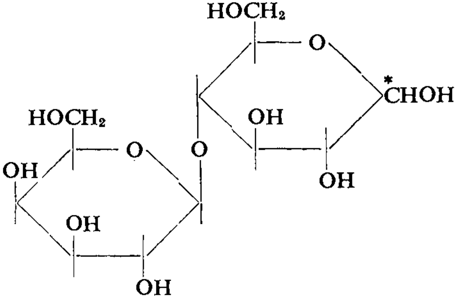
← glucose → ← fructose →

Sucrose (non-reducing)



← glucose → ← glucose →

Maltose (reducing group*)



← galactose → ← glucose →

Lactose (reducing group*)

On hydrolysis, sucrose yields glucose and fructose. The above structure indicates the glucose unit A and the fructose unit B. Sucrose is a non-reducing sugar and this is explained by the fact that the two units are joined at the reducing groups of the monosaccharides so that the reducing properties are lost. It should be observed that the fructose unit in sucrose contains a five-membered and not a six-membered ring as in fructose itself.

Inversion of cane sugar

Cane sugar has a specific rotation of +66·5°. The specific rotations of glucose and fructose are respectively +52° and −81°. Accordingly, on hydrolysis, the specific rotation changes from +66·5° to −29° (i.e. an inversion of rotation). The product is sometimes called "Invert Sugar".

Maltose and lactose

Maltose is produced by the hydrolysis of starch with malt (which contains the enzyme, diastase). Lactose is found in the milk of mammals. It is prepared from whey, which is a by-product of the manufacture of cheese. The sugar is recovered from the whey after precipitation of the albuminoids with dilute acetic acid and filtering. The lactose is obtained by evaporation *in vacuo.*

Maltose, on hydrolysis, yields glucose while lactose yields a mixture of glucose and galactose (a stereoisomer of glucose). Both disaccharides are reducing sugars and the cross-linkages between the monosaccharide units involve the reducing group of one unit only. Lactose undergoes the lactic fermentation, which reaction takes place during the souring of milk.

$$C_{12}H_{22}O_{11} + H_2O = 4CH_3{\cdot}CHOH{\cdot}COOH$$

THE POLYSACCHARIDES

The complex higher carbohydrates are derived from the monosaccharides by condensation. The most important are starch and cellulose which are usually represented by the formula $(C_6H_{10}O_5)_n$

where *n* is a large number. Polysaccharides are insoluble amorphous substances which are hydrolysed by acids or by enzyme action into simpler monosaccharides.

$$(C_6H_{10}O_5)_n + nH_2O = nC_6H_{12}O_6$$

Starch

Starch is a substance which occurs widely in the vegetable kingdom, where it serves as a store of carbohydrate food in seeds (e.g. the grain of wheat, maize and rice), and in tubers (e.g. potatoes). The starch is stored in granules which, when seen under the microscope, have characteristic appearances from which the sources of the starch may be identified. Starch is obtained commercially from maize, rice or other cereals and from potatoes.

Starch is a white amorphous powder which is insoluble in water. On heating with water the starch granules burst and starch paste is formed. Starch paste when cold forms an intense blue-coloured compound with iodine, which decomposes on heating. The formation of the blue colour with starch paste enables small quantities of iodine to be detected.

When starch is hydrolysed by acids, or the enzyme diastase, simpler products are formed. The first product is a gummy substance, known as dextrin or British gum. A second stage (as by the action of the enzyme diastase) yields maltose. The final product of hydrolysis is glucose.

$$2(C_6H_{10}O_5)_n + nH_2O = \underset{\text{Maltose}}{nC_{12}H_{22}O_{11}}$$

$$(C_6H_{10}O_5)_n + nH_2O = \underset{\text{Glucose}}{nC_6H_{12}O_6}$$

Starch is non-reducing, so that each of the glucose residues is linked in the starch molecule through its reducing carbon atom (probably by an α-glucosidic linkage). Starch grains contain two types of substances — amylose in which 50–250 glucose residues are linked more or less in a line, and amylopectin, which contains a much greater number of glucose residues not wholly arranged in a straight line. The two constituents are not in the same proportion throughout the starch grain, and there is a greater concentration of amylose in the interior.

Cellulose

Cellulose is the complex polysaccharide which forms the cell walls of plants. The formula of cellulose is $(C_6H_{10}O_5)_n$, where n lies between 100 and 200, and the molecule is derived from a series of glucose molecule units. The monosaccharide units are joined by β-glucoside linkages. Under these circumstances, the glucose residues form a linear chain, and the cellulose molecule takes on a thread-like structure. The cellulose fibre consists of bundles of cellulose molecules arranged roughly parallel to one another with their long axes pointing along the length of the fibre.

Cellulose is obtained from many plant products (e.g. wood, cotton, flax, hemp, etc.). To obtain pure cellulose the other substances present in the plant material (e.g. cotton wool) are removed by treatment with various solvents, e.g. water, acids and alkalis, alcohol and ether. Cellulose remains in the form of a white amorphous mass. The finest filter-papers consist of almost pure cellulose, while ordinary paper, cotton and linen fabrics consist mainly of cellulose.

Cellulose is not soluble in the commoner reagents, but it can be dissolved by reacting with carbon disulphide in alkaline solution. Viscose rayon is obtained by treating cellulose with sodium hydroxide solution and then with carbon disulphide to yield a "xanthate". When the xanthate solution is forced through fine apertures into dilute sulphuric acid, cellulose is regenerated in the form of the rayon fibre.

Cellulose breaks down on hydrolysis into simpler products. The most important of these is a disaccharide sugar $(C_{12}H_{22}O_{11})$, called cellobiose, and the product of the further hydrolysis of this disaccharide is glucose.

$$\underset{\text{Cellulose}}{2(C_6H_{10}O_5)_n} + nH_2O = \underset{\text{Cellobiose}}{nC_{12}H_{22}O_{11}}$$

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

Esters of cellulose

The formula of cellulose can be represented by $[C_6H_7O_2(OH)_3]_n$. The hydroxyl groups give rise to esters by interaction with acids. These esters are of considerable commercial importance.

The *cellulose nitrates* (or nitrocelluloses, as they are less accurately called) are obtained by the reaction of nitric and sulphuric acids on cellulose. The number of hydroxyl groups which are esterified depends on the length of time treated and the concentration of the acids, and the products vary from the mononitrate $[C_6H_7O_2NO_3(OH)_2]_n$ to the fully nitrated trinitrate $[C_6H_7O_2(NO_3)_3]_n$, obtained by using the strongest acids. It is not practicable to isolate any one of these products; a mixture is always obtained.

The medium nitrate esters of cellulose are inflammable substances which dissolve more readily than cellulose. When brought into contact with solvents such as acetone or ethyl acetate, they swell up and pass into solution. A solution in alcohol–ether is known as collodion. These esters are used in the manufacture of varnishes.

The medium nitrates of cellulose when mixed with camphor and heated form celluloid.

The fully nitrated ester of cellulose is explosive (gun-cotton). It is used either alone or mixed with nitroglycerin in the form of blasting gelatine and smokeless powders. Gun-cotton is insoluble in alcohol–ether.

Cellulose acetates

The acetic acid esters of cellulose can be obtained by the treatment of cellulose with acetic acid, acetyl chloride, or acetic anhydride. Mono-, di-, or tri-acetates of cellulose can be obtained. They are used for the manufacture of non-inflammable films and varnishes and for the production of "acetate-rayon".

14

synthetic processes in organic chemistry

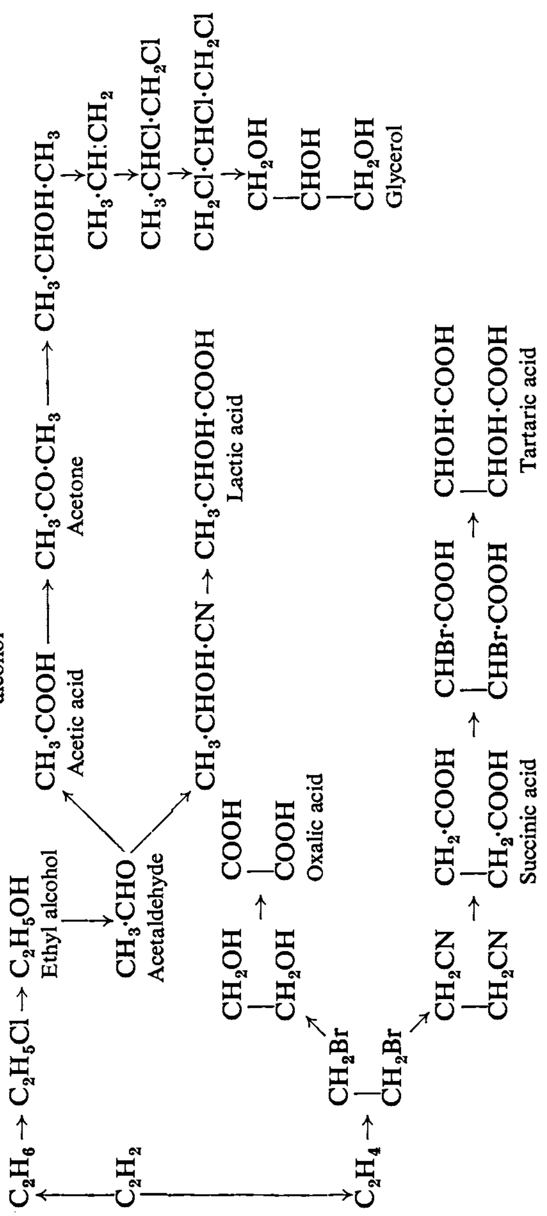
After the molecular formula of any organic substance has been determined, its constitution is deduced from its reactions and from the nature of the simpler substances obtained when the compound is broken down.

Having arrived at a possible composition of the compound by breaking it down (*analysis*), the composition is confirmed by preparing synthetically the compound which possesses this composition. Comparison is then made with the original substance. *Synthesis* is the process of building up a compound from its constituent elements, or from simpler compounds which in their turn can be built up from their elements.

There are several standard methods and reagents which are suitable for synthesizing the more complex organic compounds, but any of the reactions mentioned previously for the preparation of the different classes of organic compounds may be adapted for synthetic purposes.

In practice, the route selected for any synthesis is decided by choosing reactions which give good yields of the desired products. This is particularly important when a series of reactions has to be carried out before the final end-product is obtained, otherwise the inadequate supply of some intermediate material may prevent the objective being obtained.

Typical syntheses of some of the simpler aliphatic organic compounds are shown in the following scheme.


C + 2H₂ = CH₄
2C + H₂ = C₂H₂
CO + 2H₂ = CH₃OH
CO + NaOH = HCOONa
CH₄ → CH₃Cl → CH₃OH → HCHO → HCOOH
Methyl alcohol
Formaldehyde
Formic acid
C₂H₆ → C₂H₅Cl → C₂H₅OH
Ethyl alcohol
C₂H₂
C₂H₄
CH₃·CHO
Acetaldehyde
CH₃·COOH
Acetic acid
CH₃·CO·CH₃
Acetone
CH₃·CHOH·CH₃
CH₃·CH:CH₂
CH₃·CHCl·CH₂Cl
CH₂Cl·CHCl·CH₂Cl
CH₂OH·CHOH·CH₂OH
Glycerol
CH₃·CHOH·CN → CH₃·CHOH·COOH
Lactic acid
CH₂Br·CH₂Br
CH₂OH·CH₂OH → COOH·COOH
Oxalic acid
CH₂CN·CH₂CN → CH₂·COOH·CH₂·COOH
Succinic acid
CHBr·COOH·CHBr·COOH → CHOH·COOH·CHOH·COOH
Tartaric acid

Ascent of a Homologous Series

The formation of a nitrile and its subsequent hydrolysis gives a compound containing an additional carbon atom in the molecule. A complete series of reactions for the ascent of a homologous series based on this reaction is represented as follows:

$$CH_3OH \rightarrow CH_3I \rightarrow CH_3CN \rightarrow CH_3{\cdot}COOH \rightarrow CH_3{\cdot}CHO \rightarrow C_2H_5OH$$

Descent of a Homologous Series

The reaction by which acid amides are converted into amines with one atom of carbon less in their molecules is the basis of a useful method of descending a homologous series. A complete series of reactions may be represented as follows:

$$CH_3{\cdot}COOH \rightarrow CH_3{\cdot}COONH_4 \rightarrow CH_3{\cdot}CONH_2 \rightarrow CH_3{\cdot}NH_2 \rightarrow CH_3OH \rightarrow HCOOH$$

Another reaction which may be utilized for the descent of a homologous series is the conversion, by heating with soda-lime, of a sodium salt of a fatty acid into a hydrocarbon with one fewer carbon atom in its molecule. A complete series of reactions may be represented as follows:

$$C_2H_6 \rightarrow C_2H_5Cl \rightarrow C_2H_5OH \rightarrow CH_3{\cdot}CHO \rightarrow CH_3{\cdot}COOH \rightarrow CH_4$$

Synthesis of Acids and Ketones by means of Acetoacetic Ester

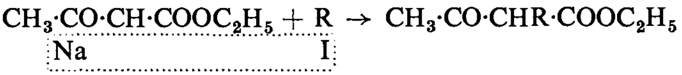
Ethyl acetoacetate is used for the synthesis of methyl ketones of the formulae (cf. p. 77)

$RCH_2{\cdot}CO{\cdot}CH_3$ and $RR'CH{\cdot}CO{\cdot}CH_3$ (or $R_2CH{\cdot}CO{\cdot}CH_3$), and of acids of the formulae (cf. p. 83)

$$RCH_2{\cdot}COOH \text{ and } RR'CH{\cdot}COOH \text{ (or } R_2CH{\cdot}COOH)$$

(Ethyl malonate is often a more convenient reagent for the synthesis of acids, as on hydrolysis it yields acids only. In the case of ethyl acetoacetate, some loss always occurs owing to the alternative hydrolysis to form a ketone.)

The importance of acetoacetic ester in synthetic organic chemistry is closely connected with its tautomeric properties. When it reacts with sodium, a derivative is obtained which reacts with alkyl halides to form an alkyl derivative, in which one of the central hydrogen atoms of the acetoacetic ester is replaced by an alkyl group.



$$\underset{\boxed{\text{Na} \qquad\qquad\qquad\qquad \text{I}}}{CH_3{\cdot}CO{\cdot}CH{\cdot}COOC_2H_5 + R} \rightarrow CH_3{\cdot}CO{\cdot}CHR{\cdot}COOC_2H_5$$

The mono-alkyl derivatives of acetoacetic ester are tautomeric.

$$CH_3{\cdot}CO{\cdot}CHR{\cdot}COOC_2H_5 \rightleftharpoons CH_3{\cdot}C(OH){:}CR{\cdot}COOC_2H_5$$

By forming the sodium derivative and reacting with an alkyl halide, a di-alkyl derivative of acetoacetic ester is obtained. The di-alkyl derivatives are not tautomeric, since the central carbon atom is no longer united to hydrogen atoms.

$$CH_2{\cdot}CO\overset{\curvearrowleft}{\cdot}CH_2{\cdot}COOC_2H_5 \qquad CH_3{\cdot}CO\overset{\curvearrowleft}{\cdot}CHR{\cdot}COOC_2H_5$$

Ethyl acetoacetate (tautomeric) — Mono-alkyl derivative (tautomeric)

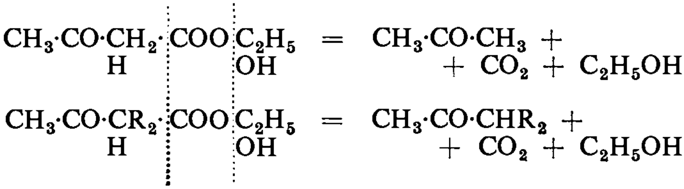
$$CH_3{\cdot}CO{\cdot}CRR{\cdot}COOC_2H_5$$

Di-alkyl derivative
(not tautomeric)

It must be noted that in order to introduce two alkyl groups, the substitution reactions must be performed twice. It is not possible to achieve the di-substitution in one process by using excess of the alkyl halide.

Synthesis of ketones

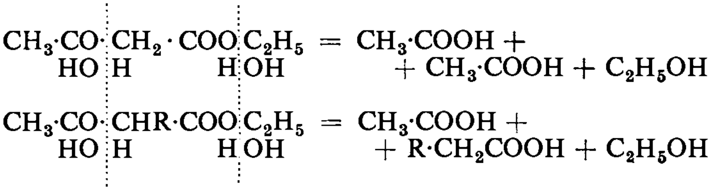
When heated in acid, neutral, or weakly alkaline solutions, acetoacetic ester and its derivatives are hydrolysed to form ketones.



$$\begin{array}{lcl} CH_3\cdot CO\cdot CH_2\cdot \vdots COO \vdots C_2H_5 & = & CH_3\cdot CO\cdot CH_3 + \\ \qquad\qquad H \quad \vdots \qquad\quad \vdots OH & & \qquad + CO_2 + C_2H_5OH \\ CH_3\cdot CO\cdot CR_2\cdot \vdots COO \vdots C_2H_5 & = & CH_3\cdot CO\cdot CHR_2 + \\ \qquad\qquad H \quad \vdots \qquad\quad \vdots OH & & \qquad + CO_2 + C_2H_5OH \end{array}$$

Synthesis of acids

When heated with strong alkalis, acetoacetic ester and its derivatives hydrolyse to form acids.



$$\begin{array}{lcl} CH_3\cdot CO\cdot \vdots CH_2\cdot COO \vdots C_2H_5 & = & CH_3\cdot COOH + \\ \qquad\; HO \vdots H \qquad\quad H \vdots OH & & \qquad + CH_3\cdot COOH + C_2H_5OH \\ CH_3\cdot CO\cdot \vdots CHR\cdot COO \vdots C_2H_5 & = & CH_3\cdot COOH + \\ \qquad\; HO \vdots H \qquad\quad H \vdots OH & & \qquad + R\cdot CH_2COOH + C_2H_5OH \end{array}$$

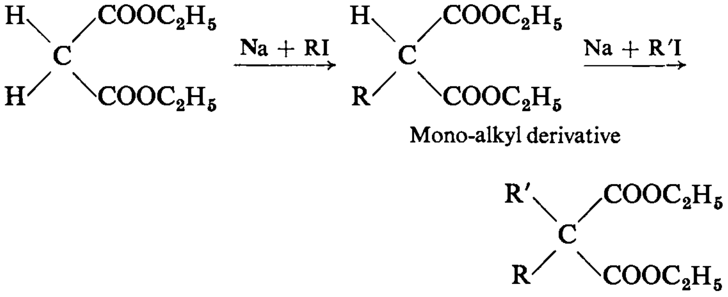
Synthesis of Acids by means of Ethyl Malonate

Malonic ester is used for the synthesis of acids represented by the formulae (cf. p. 83)

$$RCH_2\cdot COOH \text{ and } RR'CH\cdot COOH \text{ (or } R_2CH\cdot COOH)$$

Ethyl malonate exists in tautomeric forms and forms a sodium derivative, which reacts with an alkyl halide to form a mono-alkyl derivative. The mono-alkyl derivatives are also tautomeric, and by further reaction with sodium and alkyl halides, di-alkyl derivatives of malonic ester are obtained.

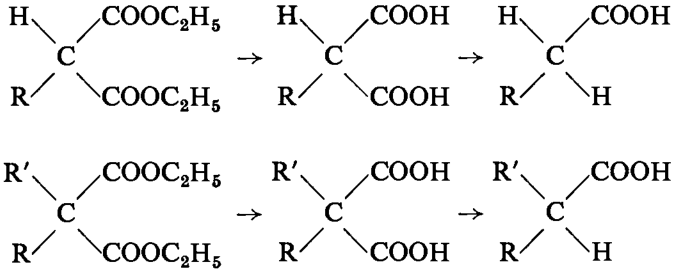
$$CH(Na)(COOC_2H_5)_2 + RI = CHR(COOC_2H_5)_2$$



Mono-alkyl derivative

Di-alkyl derivative

When the substituted malonic esters are hydrolysed, they form the corresponding substituted malonic acids, which on heating lose carbon dioxide and the corresponding monobasic acid is obtained.

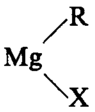


The Organo-metallic Compounds

Some metals form reactive metal-alkyls in which the metal atom is united directly to an alkyl group, e.g. lead tetraethyl $Pb(C_2H_5)_4$, which is used as an "anti-knock" in internal combustion engines, and the zinc alkyls which are prepared by the direct action of the metal on the corresponding halide.

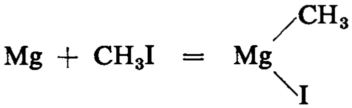
$$2CH_3I + 2Zn = Zn(CH_3)_2 + ZnI_2$$

The related magnesium compounds, discovered in 1901 by *Grignard*, have been used extensively in organic synthesis. When magnesium is added to a solution of an alkyl halide in dry ether, a reaction takes place to form a compound of the formula



$$\mathrm{Mg}\begin{array}{l}\diagup\mathrm{R}\\ \diagdown\mathrm{X}\end{array}$$

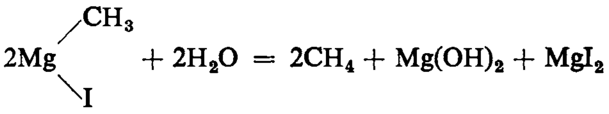
where X represents a halogen atom,



$$\mathrm{Mg} + \mathrm{CH_3I} = \mathrm{Mg}\begin{array}{l}\diagup\mathrm{CH_3}\\ \diagdown\mathrm{I}\end{array}$$

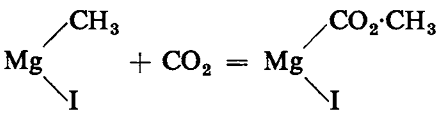
These substances (which are called "*Grignard* reagents") are very reactive as shown by the following examples.

(1) *Synthesis of hydrocarbons.* The *Grignard* reagents are hydrolysed to give hydrocarbons.

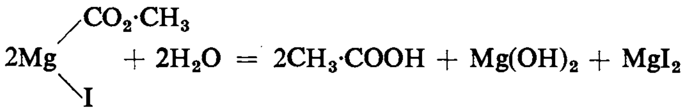


$$2\mathrm{Mg}\begin{array}{l}\diagup\mathrm{CH_3}\\ \diagdown\mathrm{I}\end{array} + 2\mathrm{H_2O} = 2\mathrm{CH_4} + \mathrm{Mg(OH)_2} + \mathrm{MgI_2}$$

(2) *Synthesis of acids.* The *Grignard* reagents absorb carbon dioxide, and the products on hydrolysis form acids.



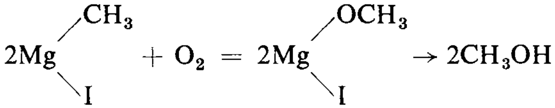
$$\mathrm{Mg}\begin{array}{l}\diagup\mathrm{CH_3}\\ \diagdown\mathrm{I}\end{array} + \mathrm{CO_2} = \mathrm{Mg}\begin{array}{l}\diagup\mathrm{CO_2{\cdot}CH_3}\\ \diagdown\mathrm{I}\end{array}$$



$$2\mathrm{Mg}\begin{array}{l}\diagup\mathrm{CO_2{\cdot}CH_3}\\ \diagdown\mathrm{I}\end{array} + 2\mathrm{H_2O} = 2\mathrm{CH_3{\cdot}COOH} + \mathrm{Mg(OH)_2} + \mathrm{MgI_2}$$

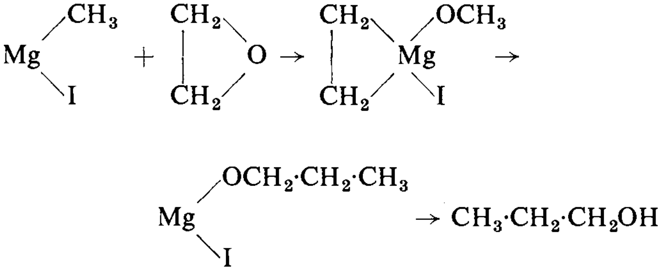
(3) *Synthesis of alcohols.*

(a) The *Grignard* reagents absorb oxygen and on hydrolysis the products form alcohols.



$$2\mathrm{Mg}\genfrac{}{}{0pt}{}{\diagup CH_3}{\diagdown I} + O_2 = 2\mathrm{Mg}\genfrac{}{}{0pt}{}{\diagup OCH_3}{\diagdown I} \rightarrow 2CH_3OH$$

(b) The *Grignard* reagents react with ethylene oxide and the products, on hydrolysis, yield alcohols containing two more carbon atoms than were present in the alkyl group of the reagent.

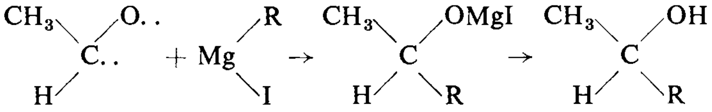


$$\mathrm{Mg}\genfrac{}{}{0pt}{}{\diagup CH_3}{\diagdown I} + \genfrac{}{}{0pt}{}{CH_2\diagdown}{CH_2\diagup}O \rightarrow \genfrac{}{}{0pt}{}{CH_2\diagdown}{CH_2\diagup}\mathrm{Mg}\genfrac{}{}{0pt}{}{\diagup OCH_3}{\diagdown I} \rightarrow$$

$$\mathrm{Mg}\genfrac{}{}{0pt}{}{\diagup OCH_2{\cdot}CH_2{\cdot}CH_3}{\diagdown I} \rightarrow CH_3{\cdot}CH_2{\cdot}CH_2OH$$

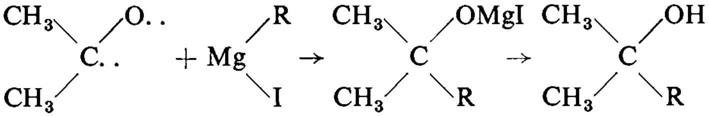
(c) The commonest application of *Grignard* reagents depends on their reactions with aldehydes, ketones and esters. These substances combine with *Grignard* reagents to form substances which hydrolyse to form alcohols. Secondary alcohols are obtained from aldehydes, while ketones and esters yield tertiary alcohols.

The first reaction proceeds by the opening up of the carbonyl double bond and the addition of the *Grignard* reagent. After the hydrolysis of the addition product, a substance is obtained corresponding to the addition of RH to the carbonyl double bond. In the case of the ester, a further reaction takes place, and another alkyl group is introduced.



$$\genfrac{}{}{0pt}{}{CH_3\diagdown}{H\diagup}C{:}\diagup O{:} + \mathrm{Mg}\genfrac{}{}{0pt}{}{\diagup R}{\diagdown I} \rightarrow \genfrac{}{}{0pt}{}{CH_3\diagdown}{H\diagup}C\genfrac{}{}{0pt}{}{\diagup OMgI}{\diagdown R} \rightarrow \genfrac{}{}{0pt}{}{CH_3\diagdown}{H\diagup}C\genfrac{}{}{0pt}{}{\diagup OH}{\diagdown R}$$

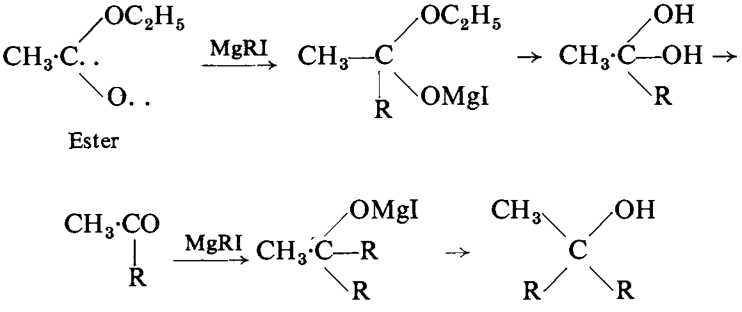
Aldehyde Secondary alcohol



$$(CH_3)_2C{:}O + Mg\begin{smallmatrix}R\\I\end{smallmatrix} \rightarrow (CH_3)_2C\begin{smallmatrix}OMgI\\R\end{smallmatrix} \rightarrow (CH_3)_2C\begin{smallmatrix}OH\\R\end{smallmatrix}$$

Ketone

Tertiary alcohol



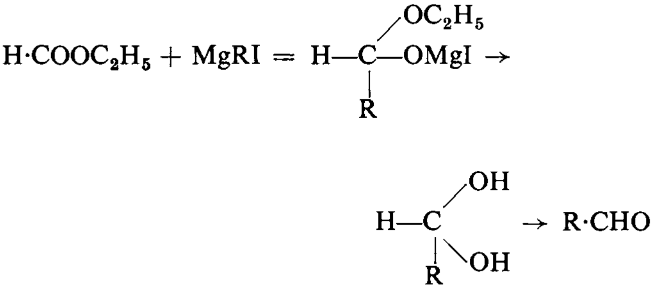
$$CH_3{\cdot}C\begin{smallmatrix}OC_2H_5\\O\end{smallmatrix} \xrightarrow{MgRI} CH_3{-}C(R)\begin{smallmatrix}OC_2H_5\\OMgI\end{smallmatrix} \rightarrow CH_3{\cdot}C\begin{smallmatrix}OH\\OH\\R\end{smallmatrix} \rightarrow$$

Ester

$$CH_3{\cdot}CO{-}R \xrightarrow{MgRI} CH_3{\cdot}C\begin{smallmatrix}OMgI\\R\\R\end{smallmatrix} \rightarrow CH_3{\cdot}C\begin{smallmatrix}OH\\R\\R\end{smallmatrix}$$

Tertiary alcohol

(4) *Synthesis of aldehydes.* Aldehydes may be synthesized by a modification of the above reaction using formate esters.



$$H{\cdot}COOC_2H_5 + MgRI = H{-}C(R)\begin{smallmatrix}OC_2H_5\\OMgI\end{smallmatrix} \rightarrow H{-}C(R)\begin{smallmatrix}OH\\OH\end{smallmatrix} \rightarrow R{\cdot}CHO$$

15

the aromatic series of organic compounds

The compounds derived from the hydrocarbon benzene have been named *aromatic compounds* in contradistinction to the aliphatic compounds derived from methane. Their properties differ in many respects from those of the corresponding aliphatic compounds and as they are often more readily crystallized, experimental work with them is facilitated.

Aromatic compounds can be derived from, and converted into, compounds containing six carbon atoms. It is not possible to break them up into fragments containing less than six carbon atoms without losing the characteristic aromatic properties. The six carbon atom unit, which constitutes the essential *nucleus* of aromatic compounds, is very stable. It is not easily destroyed and it remains unchanged during most of the reactions undergone by aromatic compounds. The simplest substance which possesses aromatic qualities is the hydrocarbon benzene (C_6H_6), and from this hydrocarbon all the other compounds are obtainable. The structure of the benzene molecule is the foundation of the chemistry of aromatic compounds.

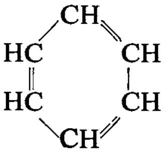
The molecular formula of benzene, when determined by the usual methods, is C_6H_6. The corresponding paraffin is hexane, C_6H_{14}. Since the proportion of hydrogen in benzene is so much less, it would be expected that benzene would exhibit strong unsaturated properties and be more reactive than it actually is.

Benzene can be made to add on six atoms of hydrogen or a halogen, and treatment with ozone yields a triozonide. These facts indicate the presence of three double bonds in the molecule. However, these double bonds behave in a different manner from the double bonds of aliphatic compounds, and benzene behaves in most respects as a relatively inactive and saturated compound. Alkaline permanganate has no action in the cold; halogen acids do not add on to benzene; and in the absence of sunlight, benzene undergoes substitution (instead of addition) reactions with halogens.

This degree of saturation together with the stability and the characteristic substitution reactions of benzene constitute the "aromatic" properties of benzene and its derivatives.

The Structure of Benzene

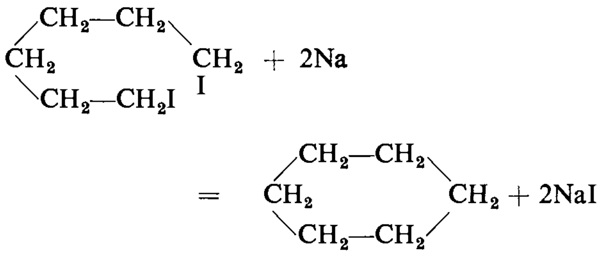
Kekulé was the first to suggest a ring structure for the benzene molecule, each carbon atom being attached to a hydrogen atom in the form of a regular hexagon. Accepting the quadrivalency of carbon, *Kekulé* accounted for the remaining valency of each carbon atom by three double and three single bonds placed alternately around the ring.



The following evidence favoured the *Kekulé* structure:

(1) The six hydrogen atoms in benzene are found to be equivalent.

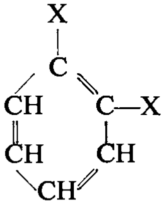
(2) By the addition of hydrogen, benzene forms a compound of the formula C_6H_{12}, whose molecule can be shown to have a ring structure of six carbon atoms by the following synthesis. The open chain compound, 1:6-di-iodohexane, when heated with sodium undergoes ring closure after removal of the terminal iodine atoms. The product is cyclohexane (C_6H_{12}).

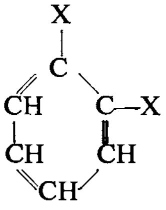


(3) X-ray analysis of benzene and its derivatives confirms the presence in their molecules of six carbon atoms arranged in the form of a flat, regular hexagonal ring.

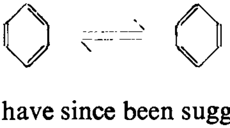
(4) Only one substitution product of the formula C_6H_5X exists.

The main objection to the formula suggested by *Kekulé* was directed towards the number of possible disubstituted products. If the double bonds are in fixed positions, two disubstituted products, corresponding to the following formulae, should exist.





At first, the difficulty was overcome by suggesting a "dynamic formula" in which the double bonds of the ring were in a state of constant oscillation. In other words, each C—C pair was to have a single bond half of the time and a double bond the other half.

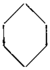


Several other formulae have since been suggested for benzene and it is now accepted that no one formula represents the structure, which is actually a "resonance hybrid" of all of them.

The concept of resonance has arisen from the recognition of the part played by electrons in the bonding of atoms. Cases arise where more than one electronic arrangement is possible in a molecule, while the atomic nuclei occupy practically the same positions. It is then found that the actual formula does not correspond with any of the electronic arrangements but partakes of the nature of them all. It is not the result of equilibrium between the possible forms, neither is it a mixture of rapidly interconverting molecules. It is a completely new formula, intermediate between all those which are theoretically possible. The resonance hybrid has greater stability than would correspond with any one of the theoretical structures.

In the case of benzene, the two *Kekulé* molecules, shown opposite, differ only in their electronic dispositions and the conditions for resonance apply. Other formulae are theoretically possible which differ only in their electronic arrangements, but the *Kekulé* structures are the most stable of them all and contribute most to the resonance hybrid. However, the existence of resonance makes benzene more stable than would be expected by comparison with simple aliphatic unsaturated compounds and confers the characteristic "aromatic" properties on the substance and its derivatives.

For most purposes, the details of the benzene structure can be disregarded and for convenience the molecule is usually written as a hexagon, omitting both the carbon and the hydrogen atoms.

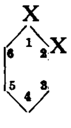


Substitution of hydrogen is indicated by marking outside the ring the place occupied by the substituent.

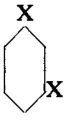
Isomerism of Benzene Derivatives

Since all the hydrogen atoms in benzene are equivalent, replacement of a hydrogen atom by a univalent group (X) yields only one product (C_6H_5X).

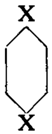
When two hydrogen atoms are replaced by X, three isomeric derivatives of the formula $C_6H_4X_2$ may be obtained.



ortho (*o*)

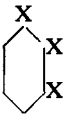


meta (*m*)

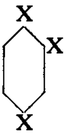


para (*p*)

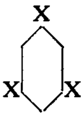
When three hydrogen atoms are replaced by X, there are three isomeric derivatives of the formula $C_6H_3X_3$. (When the substituent groups are different the number of isomers in trisubstitution increases.)



1:2:3



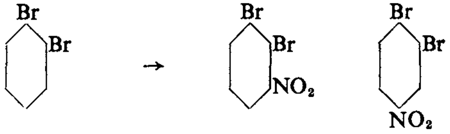
1:2:4



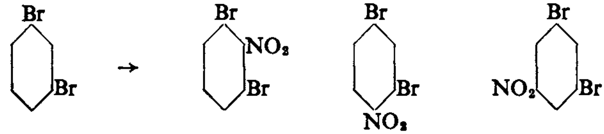
1:3:5

Orientation

The orientation of benzene substitution products is the assignment of the configuration to each experimentally prepared benzene derivative. Once a series of compounds of known orientation had been developed, it was found to be easy to determine the orientation of other substances by interconversion into or from these reference compounds. Several methods are available. The *Körner* method is based on the nitration of the three isomeric dibromobenzenes.

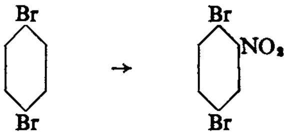


ortho two derivatives



meta

three derivatives



para

one derivative

The Benzene Series of Hydrocarbons

Benzene (C_6H_6) is the simplest member of a homologous series, all members of which have similar chemical properties. As with the homologous series of the aliphatic compounds, each member differs from the next by a —CH_2— group, but the possibilities of isomerism are rather different from the aliphatic series.

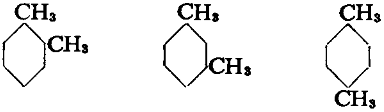
The next member of the series after benzene is *toluene* (C_7H_8) and there is only one substance of this formula, i.e.

or $C_6H_5{\cdot}CH_3$

The benzene residue C_6H_5 is called the *phenyl* group and is sometimes represented by the symbol Ph. The general name for a group derived from an aromatic hydrocarbon is *aryl* (symbol Ar).

The next members of the homologous series have the formula C_8H_{10}, and there are four isomeric hydrocarbons of this formula, e.g. ethylbenzene, and the three dimethylbenzenes — *ortho*, *meta* and *para*. The latter three substances are called the *xylenes*.

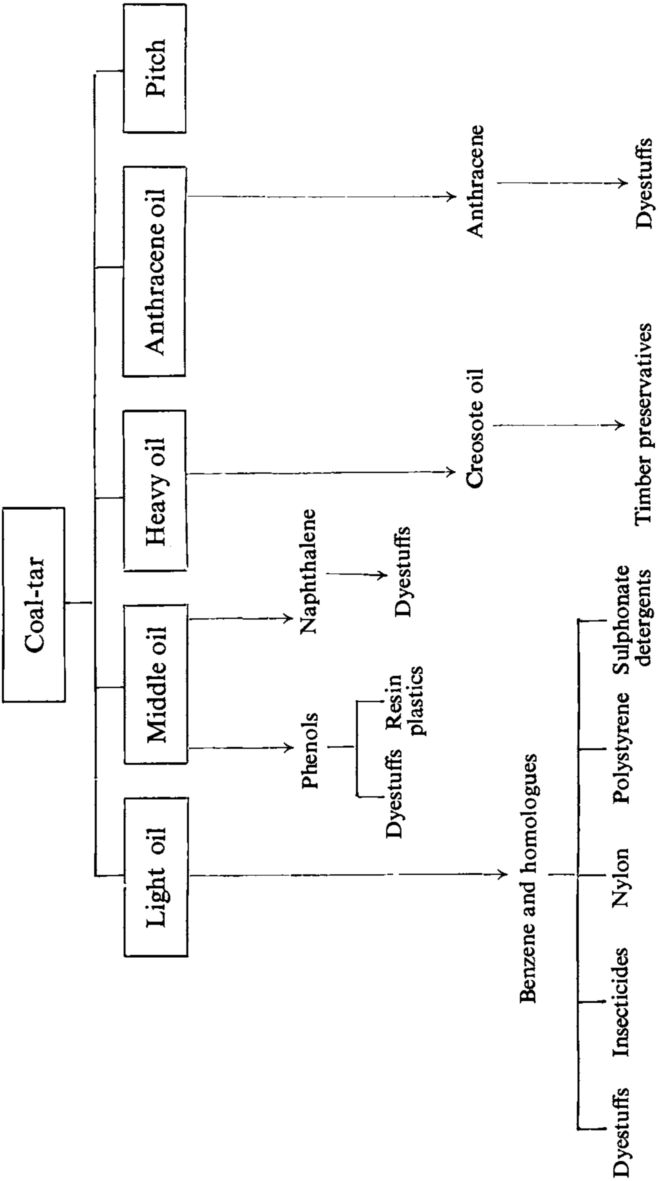
Ethylbenzene



ortho *meta* *para*

Dimethylbenzenes or xylenes

Coal-tar Products



Preparation of the Benzene Hydrocarbons

On a commercial scale benzene, toluene, and the xylenes are obtained from coal-tar and from petroleum sources.

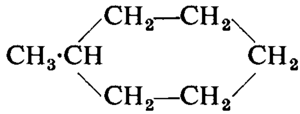
The destructive distillation of coal yields coal-gas, a watery ammoniacal liquid, coal-tar, and coke. Coal-tar is a black, viscous liquid containing (a) acid substances, chiefly phenols, (b) basic substances (chiefly pyridine derivatives), and (c) neutral hydrocarbons of the aromatic series, including not only benzene and its derivatives but also derivatives of naphthalene and anthracene.

The various constituents of coal-tar are separated by fractional distillation, the most volatile fraction containing benzene and its homologues. Commercially the first distillate (the light oil) is collected between the ranges 80–170°C, while succeeding fractions (middle or carbolic oil 170–240°C, containing chiefly phenols and naphthalene; heavy oil 240–270°C; anthracene oil 270–400°C, containing chiefly anthracene) are collected at higher temperatures. Finally, a residue of pitch remains in the retort.

The light oil is treated first with dilute alkali to remove phenolic impurities, then with concentrated sulphuric acid to remove basic impurities, and finally it is refractionated, thus obtaining commercial benzene (benzol), toluene (toluol), and xylene (xylol). A complete separation to prepare the pure hydrocarbons is obtained by partial freezing and recrystallization.

Benzene hydrocarbons are present in many petroleum oils and tend to diminish "knocking" when present in motor fuels. Their proportion is increased by cracking and other processes. The aromatic hydrocarbons arise from the paraffin and cycloparaffins in the crude petroleum by reactions involving (a) dehydrogenation, (b) isomerization and (c) cyclization, as in the following examples.

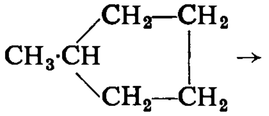
(a)



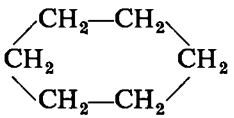
$= CH_3{\cdot}C_6H_5 + 3H_2$

Methyl cyclohexane Toluene

(b)



Methyl cyclopentane

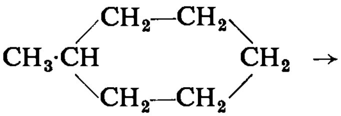


$\rightarrow C_6H_6 + 3H_2$

Cyclohexane Benzene

(c) $CH_3\cdot(CH_2)_5\cdot CH_3 \rightarrow$

n-heptane



$CH_3\cdot C_6H_5 + 3H_2$

It is not possible to separate the individual hydrocarbons from the cracking reaction products by direct fractional distillation owing to the formation of azeotropes; the commercial separation is carried out by solvent extraction processes. On a small scale, benzene hydrocarbons may be prepared:

(1) By the action of heat on a mixture of soda-lime and the sodium salt of the corresponding aromatic acid. This reaction is analogous to that used for the preparation of aliphatic hydrocarbons.

$$C_6H_5\cdot COONa + NaOH = C_6H_6 + Na_2CO_3$$

Sodium benzoate Benzene

(2) By the reaction of sodium on a mixture of an alkyl halide and a halogen derivative of a benzene hydrocarbon. This reaction is analogous to the *Würtz* reaction in which sodium reacts with a

mixture of two alkyl halides. It is usually known as *Fittig's* reaction, as *Fittig* first extended the reaction to the aromatic series.

$$C_6H_5Br + CH_3Br + 2Na = C_6H_5{\cdot}CH_3 + 2NaBr$$

Bromobenzene or phenyl bromide — Toluene

(3) The homologues of benzene may be prepared from benzene by the *Friedel–Craft's* reaction using anhydrous aluminium chloride as the catalyst, and either an aryl or an acyl halide. In the latter case, the first product is a ketone which is converted to the hydrocarbon by reduction using the *Clemmensen* reaction (cf. p. 225).

$$C_6H_6 + CH_3Br = C_6H_5{\cdot}CH_3 + HBr$$

$$C_6H_6 + CH_3{\cdot}COCl = C_6H_5{\cdot}CO{\cdot}CH_3 + HCl$$

$$C_6H_5{\cdot}CO{\cdot}CH_3 \xrightarrow{4H} C_6H_5{\cdot}CH_2{\cdot}CH_3 + H_2O$$

(4) Aromatic hydrocarbons may be obtained from the diazo compounds by reduction.

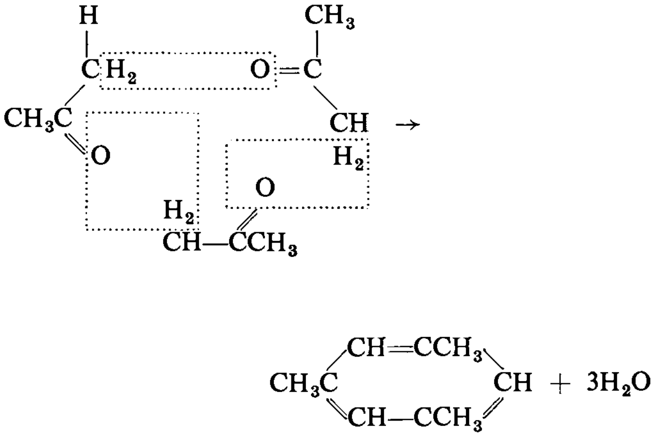
$$C_6H_5N_2HSO_4 \xrightarrow{2H} C_6H_6 + N_2 + H_2SO_4$$

(5) Some benzene is obtained when acetylene is caused to polymerize by passing through a red-hot tube.

$$3C_2H_2 = C_6H_6$$

This reaction enables a complete synthesis from the constituent elements to be developed for the aromatic compounds.

(6) 1:3:5-Trimethylbenzene or mesitylene is obtained from acetone by a condensation reaction, in the presence of concentrated sulphuric acid.



Physical Properties of the Benzene Hydrocarbons

Benzene and its lower homologues are colourless, inflammable liquids, with characteristic smell and taste. They are insoluble in water, but dissolve in, and are good solvents for, most organic substances. They burn with a smoky flame.

Chemical Properties of the Benzene Hydrocarbons

Benzene is inert to ordinary reagents (dilute acids, alkalis, oxidizing and reducing agents), but it reacts characteristically with halogens, concentrated sulphuric acid and concentrated nitric acid. The reactions with these reagents proceed more readily with the homologues, such as toluene, and in addition these hydrocarbons react with oxidizing agents.

Substitution reactions of benzene and its homologues

These substitution reactions are often of considerable practical importance. They are characteristic of aromatic compounds generally, and except for the first reaction below, aliphatic compounds do not undergo the corresponding reactions.

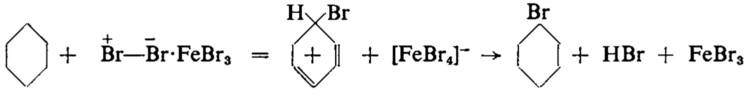
(1) *Halogenation.* Chlorine reacts slowly with benzene to form the substitution product chlorobenzene. This reaction takes place in the cold, in the dark, and in the presence of a catalyst, e.g. iodine, pyridine or iron wire. (In contrast, addition is favoured by carrying out the reaction in the light and without a catalyst.) By more prolonged attack, further substitution may be effected to give a di-derivative.

$$C_6H_6 + Cl_2 = C_6H_5Cl + HCl$$

$$C_6H_5Cl + Cl_2 = C_6H_4Cl_2 + HCl$$

Bromine also substitutes slowly in a similar manner, but the iodine substitution product is only obtained by carrying out the reaction in the presence of nitric acid or other strong oxidizing agent. (The iodo derivative is more easily obtained from the diazo compound.) Although these substitutions are analogous to those of the paraffin hydrocarbons, the reactions involve different mechanisms. Aromatic halogenation involves a catalyst whose function is to lead to the formation of a molecule in which one bromine atom is electron deficient and is therefore attracted towards the aromatic nucleus.

$$Br_2 + FeBr_3 \rightarrow \overset{+}{Br}—\overset{-}{Br}\cdot FeBr_3$$



(2) *Sulphonation.* Concentrated sulphuric acid reacts with benzene with the elimination of water, to form a substitution product called a sulphonic acid. The detailed mechanism of the reaction has not been fully elucidated.

$$C_6H_6 + HOSO_2OH = C_6H_5SO_2OH + H_2O$$

(3) *Nitration.* Concentrated nitric acid reacts with benzene with elimination of water. The product contains the nitro grouping.

$$C_6H_5\cdot\boxed{H + HO}NO_2 \quad = \quad C_6H_5NO_2 + H_2O$$

The reaction is considerably accelerated by the presence of concentrated sulphuric acid. The nitration reaction is not reversible and the effect of the sulphuric acid differs from its behaviour in esterification. In nitration, the sulphuric acid reacts with the nitric acid to form the nitronium ion.

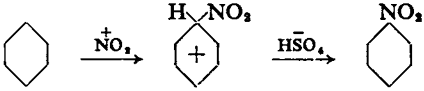
$$H_2SO_4 \rightarrow H^+ + HSO_4^-$$

$$HNO_3 + H^+ \rightleftarrows (H_2NO_3)^+$$

$$(H_2NO_3)^+ \rightleftarrows NO_2^+ + H_2O$$

$$H^+ + H_2O \rightleftarrows (H_3O)^+$$

The nitronium ion is the actual nitrating agent.



More concentrated acids and further length of time of reaction enable more than one hydrogen atom of benzene to be substituted, e.g. a mixture of fuming sulphuric and nitric acids forms dinitro- and, at higher temperatures, trinitro-benzene.

$$C_6H_5NO_2 + HNO_3 \quad = \quad C_6H_4(NO_2)_2 + H_2O$$

Dinitrobenzene

$$C_6H_4(NO_2)_2 + HNO_3 \quad = \quad C_6H_3(NO_2)_3 + H_2O$$

Trinitrobenzene

(4) *Friedel–Craft's reaction.* The benzene hydrocarbons react with alkyl halides in the presence of anhydrous aluminium chloride as a catalyst. Gaseous hydrogen halide is evolved, and a homologue of the hydrocarbon is obtained. Additional hydrogen atoms may be replaced by alkyl groups by further reaction.

$$C_6H_6 + CH_3Cl = C_6H_5{\cdot}CH_3 + HCl$$

Acid chlorides also react with benzene hydrocarbons under the same conditions, when ketones are obtained.

$$C_6H_6 + CH_3{\cdot}COCl = \underset{\text{Acetophenone}}{C_6H_5{\cdot}CO{\cdot}CH_3} + HCl$$

The catalyst acts by combining with the alkyl halide, thus providing a cation which carries out the substitution.

$$CH_3Cl + AlCl_3 = [CH_3]^+[AlCl_4]^-$$

THE NUCLEAR SUBSTITUTION OF BENZENE DERIVATIVES

Aromatic compounds vary widely in the ease with which they undergo nuclear substitution by halogenating, alkylating, nitrating or sulphonating agents. The factors which cause these variations also influence the positions at which substitution takes place.

Only one mono-substitution product is possible from benzene itself, but the introduction of a second group (Y) into a mono derivative (C_6H_5X) could lead, theoretically, to three possible compounds (*ortho-*, *meta-* and *para*-C_6H_4XY). Experimentally it is found that, in most cases, the product is either a mixture of the *ortho-* and *para*-compounds or only the *meta*-derivative, and which of these two alternatives result is largely determined by the nature of the group (X) already present on the nucleus.

o- and *p*-substitution when X is $—OH$, $—NH_2$, $—Cl$, $—CH_3$, $—OCH_3$

m-substitution when X is $—NO_2$, $—CN$, $—COOH$, $—SO_2OH$

The theoretical explanation of these facts involves the electronic mechanism of the substitution reaction (a) in respect of the substituting reagent, (b) in respect of the influence of the group X.

The Types of Substitution Reagent

Three types of reagent can be recognized, from the electronic point of view, but the first type is the more important in aromatic substitution, and only this type is dealt with here.

(a) *Electrophilic* (electron-loving) reagents, which provide groups deficient in electrons (e.g. cations, such as NO_2^+) and thus can react in a way which leads to the elimination of a nuclear hydrogen atom as a proton.

$$C_6H_5 - H + \overset{+}{N}O_2 \rightarrow C_6H_5{\cdot}NO_2 + \overset{+}{H}$$

Because of their positive charge, electrophilic groups are attracted towards and interact with the ring at points of high electron density (electrophilic substitution).

Halogenating, alkylating, nitrating and sulphonating reagents are of the electrophilic type.

(b) *Nucleophilic* (nucleus-loving) reagents contain an electron pair which can be used to bond to the ring (nucleophilic substitution).

(c) *Free radicals*, which contain unpaired electrons which can be shared with other electrons from the ring to give the final bonds.

The Effect of the Group Already Substituted (X)

The group already substituted has an influence on the nuclear electronic system which leads to the creation of points within the ring with high (and other points with low) electron densities.

In addition it also has some influence on the total electronic charge for the whole ring. The first effect determines where electrophilic substitution takes place and the second the ease of attack.

The inductive effect

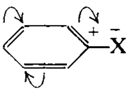
The inductive effect represents the influence on the ring system of the unequal sharing of the pair of electrons bonding a nuclear carbon atom to a substituent group. This leads to the carbon atom acquiring a slight negative or positive charge, according to the nature of the attached group, e.g.

$$\overset{+}{C} - \overset{-}{Cl} \qquad\qquad \overset{-}{C} - \overset{+}{C}H_3$$

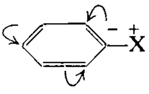
The effect on the carbon atom spreads throughout the ring and so groups as in the left-hand example (Cl, NO_2, etc.) tend to withdraw electrons from the ring, and those as in the right-hand example tend to increase the available electrons within the ring. These changes either hinder or facilitate attack by an electrophilic (i.e. electropositive) agent and the groups are therefore said to be either deactivating or activating respectively.

In addition to this general control of the ease of attack, the inductive effect also causes some positions in the ring to be relatively deficient in electrons as opposed to other positions. The electropositive reactant is attracted towards the negative centres.

Deactiving: *meta*-substitution favoured



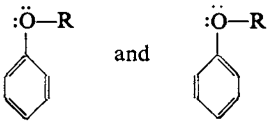
Activating: *ortho-*, *para*-substitutions favoured



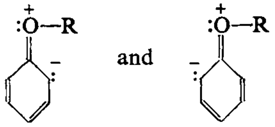
The mesomeric (or resonance) effect

The mesomeric effect is obtained when the atom of the substituted group X which is nearest to the ring contains a lone pair of electrons, e.g. O in OH or OR; N in NH_2, etc. This lone pair can then take part in the resonance of the electronic ring system and can move into the ring to contribute new structures to the final resonance hybrids (in which certain atoms in the ring are slightly charged). For example, the following resonating structures for the compound C_6H_5OR show that the hybrid molecule has small negative charges on the *o*- and *p*-carbon atoms.

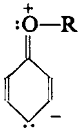
(a) normal



(b) *o*-quinonoid



(c) *p*-quinonoid



The electromeric effect

This effect differs from the inductive and mesomeric effects in being temporary. It occurs only on the approach of the substituting cation towards the seat of the fractional negative charges and enhances the mesomeric effect.

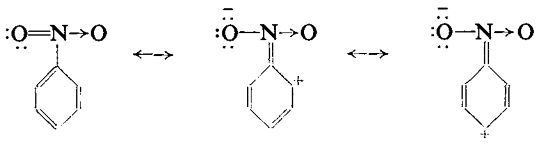
The nature of the product in electrophilic substitution

The nature of the substitution product in electrophilic substitution depends on the interaction of the inductive, mesomeric and electromeric effects as may be shown by considering three examples. The mesomeric effect can supplement or oppose the inductive effect; in the latter case, the mesomeric effect has the stronger influence and determines the position of entry of the substituent.

(a) *Nitration of toluene*. The methyl group has no lone pair of electrons or double bonds and mesomeric and electromeric effects cannot operate. Thus the only controlling factor is the inductive effect of the methyl group, which is activating and leads to *ortho*- and *para*-substitution. The rate of reaction is fast.

(b) *Nitration of nitrobenzene*. The inductive effect of the nitro group is deactivating and the reaction is therefore slow and *meta*-substitution is favoured.

Mesomeric effects arise from the existence of lone pairs of electrons on the oxygen atoms of the nitro groups. The various resonating structures lead to points of relatively low electron density at the *ortho*- and *para*-positions, and favour *meta*-substitution. The inductive effect is therefore enhanced.



(c) *Nitration of chlorobenzene* (*ortho-/para*-product — slow reaction). The inductive effect of the chlorine atom is de-activating; hence the reaction proceeds slowly. Mesomeric effects are possible owing to the lone pairs of electrons on the chlorine atom and these give rise to small negative charges on the *o*- and *p*-atoms and therefore substitution occurs in these two positions (since the mesomeric effect predominates over the *m*-orientating inductive effect). This is an example of *o*- and *p*-substitution proceeding in a de-activated ring.

Addition reaction of benzene and its homologues

(1) *Halogen addition.* When chlorine or bromine is allowed to react with benzene in bright sunlight, three molecules of the halogen are added to the benzene molecule. The product is a derivative of cyclohexane. Benzene hexachloride is manufactured commercially for use as an insecticide.

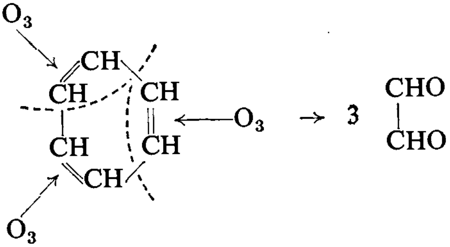
$$C_6H_6 + 3Cl_2 = C_6H_6Cl_6$$

$$C_6H_6 + 3Br_2 = C_6H_6Br_6$$

(2) *Hydrogenation.* When benzene vapour is led, mixed with hydrogen, over a suitable catalyst (e.g. freshly reduced nickel) at about 200°C, addition takes place to form cyclohexane.

$$C_6H_6 + 3H_2 = C_6H_{12}$$

(3) The addition of ozone to benzene, followed by hydrolysis, leads to the formation of glyoxal by rupture of the ring.



The reactions of the homologues of benzene

The homologues of benzene differ from benzene in that they possess an aliphatic residue (which is called the *side chain*) in addition to the aromatic *nucleus*. Thus toluene $C_6H_5{\cdot}CH_3$ contains the phenyl nucleus (C_6H_5) united to the methyl side chain.

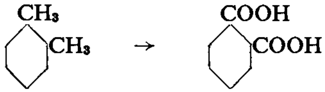
Consequently, in addition to the reactions characteristic of the aromatic benzene nucleus, the homologues of benzene have properties due to the presence of this aliphatic side chain.

The most important of these other properties are:

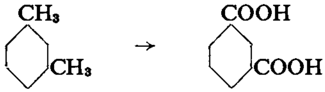
(1) *Behaviour on oxidation.* All benzene derivatives which contain an aliphatic or substituted aliphatic side chain are easily oxidized. The side chain is completely oxidized to a carboxyl group, e.g. toluene is oxidized to benzoic acid, and this product is also obtained by the oxidation of ethyl, propyl or any similar hydrocarbon with one side chain.

$$C_6H_5{\cdot}CH_3 \rightarrow C_6H_5{\cdot}COOH$$

By this reaction the position of the side chain in any substance can be determined from the nature of the carboxylic acid formed, e.g. *ortho-*, *meta-* and *para-*xylenes form the corresponding benzene-dicarboxylic acids:



Ortho Phthalic acid



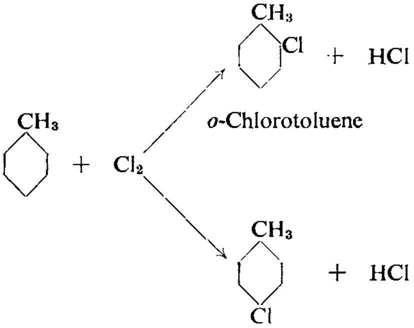
Meta Isophthalic acid

Para Terephthalic acid

The oxidation of *p*-xylene to terephthalic acid is of commercial importance as an early stage in the making of polyethylene terephthalate.

(2) *Reaction with chlorine.* Unlike nitric and sulphuric acids which can only bring about nuclear substitution, chlorine reacts in two ways. Substitution may take place either in the aromatic nucleus or in the aliphatic side chain depending on the conditions.

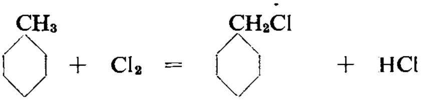
(a) *Substitution in the nucleus.* When chlorine is passed into cold toluene in the dark and in the presence of a catalyst (e.g. iodine), the chlorine substitutes in the nucleus to form chlorotoluenes.



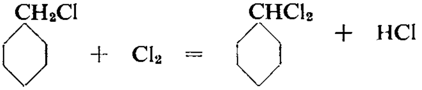
o-Chlorotoluene

p-Chlorotoluene

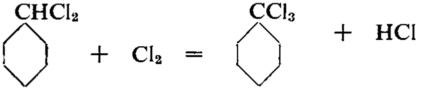
(b) *Substitution in the side chain.* When chlorine is passed into boiling toluene, the substitution takes place in the side chain. Sunlight also favours side-chain substitution.



Benzylchloride

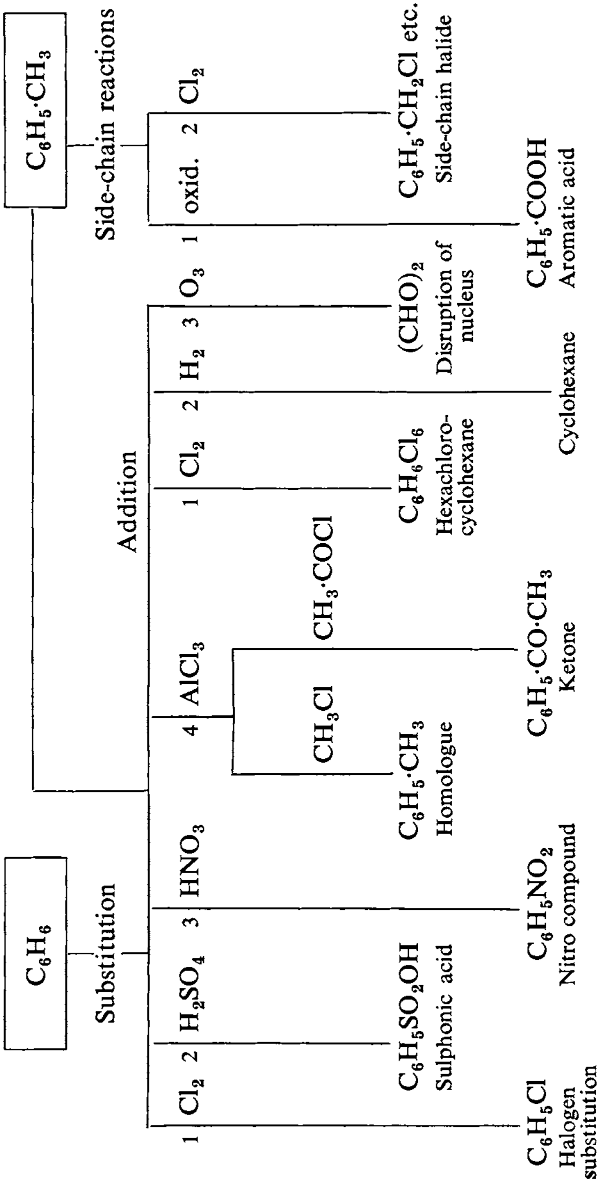


Benzalchloride



Benzotrichloride

Reactions of Benzene Hydrocarbons



Comparison of Reactions of Hydrocarbons

Reactant	*Aliphatic*			*Aromatic*	
	Paraffins	*Ethylenes*	*Acetylenes*	*Benzene*	*Homologues*
Hydrogen	no action	addition	addition	addition	addition
Chlorine; bromine	substitution	addition	addition	addition or substitution	nuclear or side-chain substitution
Iodine	no action	addition	addition	no action	no action
Hydrogen halide	no action	addition	addition	no action	no action
Permanganate	no action	decolorization	decolorization	no action	acid formed
Ozone	no action	addition	addition	addition	addition
Sulphuric acid	no action	addition	addition	sulphonation	sulphonation
Nitric acid	no action	no action	complex action	nitration	nitration

Unsaturated Aromatic Hydrocarbons

These compounds contain a double bond in their side chains. The most important is styrene ($C_6H_5{\cdot}CH{:}CH_2$) which is prepared commercially (for conversion into its polymer) from ethylbenzene, which is obtained by reacting together ethylene and benzene in the presence of anhydrous aluminium chloride as a catalyst.

$$C_6H_6 + C_2H_4 = C_6H_5{\cdot}C_2H_5$$

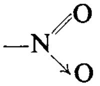
Ethylbenzene may be dehydrogenated by heating *in vacuo* with a suitable catalyst.

$$C_6H_5{\cdot}CH_2{\cdot}CH_3 = C_6H_5{\cdot}CH{:}CH_2 + H_2$$

16

the aromatic nitro, amino and diazo compounds

THE NITRO-DERIVATIVES

(FUNCTIONAL GROUP  $-N\overset{\nearrow O}{\underset{\searrow O}{}}$ OR NO_2)

The nitro-derivatives of the aromatic hydrocarbons are of practical importance, being a first stage in the conversion of the hydrocarbons into many other derivatives. They are prepared by the action of a mixture of concentrated nitric acid and sulphuric acid on the aromatic hydrocarbons (cf. p. 178).

$$C_6H_6 + HNO_3 = \underset{\text{Nitrobenzene}}{C_6H_5NO_2} + H_2O$$

Properties of the Nitro-derivatives

The aromatic nitro-derivatives are yellow liquids or solids. They are not very reactive, the nitro group being bound strongly to the nucleus. Their importance lies mainly in their reduction products. When reduced completely, they are converted into the corresponding primary amines.

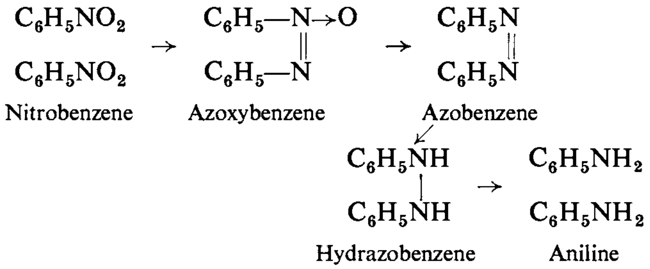
$$\underset{\text{Nitrobenzene}}{C_6H_5NO_2} \xrightarrow{6H} \underset{\text{Aniline}}{C_6H_5NH_2} + 2H_2O$$

The reduction can be modified to obtain intermediate products, e.g. by using electrolytic reduction methods and adjusting the acidity or alkalinity of the solution. The intermediate stages may be represented as follows:

(a) Acid solution

$$\underset{\text{Nitrobenzene}}{C_6H_5NO_2} \rightarrow \underset{\text{Nitrosobenzene}}{C_6H_5NO} \rightarrow \underset{\substack{\text{Phenyl}\\\text{hydroxylamine}}}{C_6H_5NHOH} \rightarrow \underset{\text{Aniline}}{C_6H_5NH_2}$$

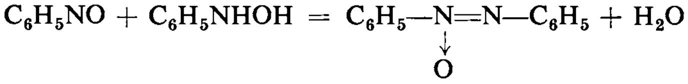
(b) Alkaline solution



$$\begin{matrix} C_6H_5NO_2 & & C_6H_5{-}N{\rightarrow}O & & C_6H_5N \\ & \rightarrow & \| & \rightarrow & \| \\ C_6H_5NO_2 & & C_6H_5{-}N & & C_6H_5N \end{matrix}$$

$$\begin{matrix} C_6H_5NH & & C_6H_5NH_2 \\ | & \rightarrow & \\ C_6H_5NH & & C_6H_5NH_2 \end{matrix}$$

Azoxybenzene and azobenzene are probably formed from nitrosobenzene and phenyl hydroxylamine.



$$C_6H_5NO + C_6H_5NHOH = C_6H_5{-}\underset{\underset{O}{\downarrow}}{N}{=}N{-}C_6H_5 + H_2O$$

$$2C_6H_5NHOH = C_6H_5N{:}NC_6H_5 + 2H_2O$$

Selective reduction of one nitro group only in a polynitro compound can be achieved by controlled reduction with a mild reducing agent such as ammonium sulphide; *m*-dinitrobenzene is reduced in this way to *m*-nitroaniline.

Nitrobenzene

A pale yellow liquid (b.p. 208°C). By virtue of its characteristic smell, it is used as a cheap substitute for oil of bitter almonds in the manufacture of perfumes and scented soaps.

m-*Dinitrobenzene*

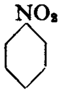
A solid (m.p. 90°C). It is prepared by further nitration of nitrobenzene by heating with fuming nitric acid.

Picric acid (*symmetrical 2:4:6-trinitrophenol*)

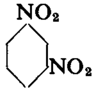
Picric acid is obtained by treating phenol with concentrated sulphuric acid and adding the cold mixture to concentrated nitric acid. After warming to complete the reaction, picric acid crystallizes on cooling. It is an intensely yellow solid which has been used as a dye for wool and silk and as a high explosive. Some picrates are very sensitive to shock, and care is necessary to prevent picric acid coming into contact with metals during storage.

Trinitrotoluene (*TNT*)

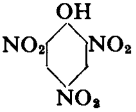
This is prepared, for use as a high explosive, by the action of a mixture of concentrated nitric and sulphuric acids on toluene.



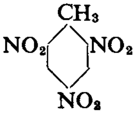
Nitrobenzene



m-Dinitrobenzene



Picric acid

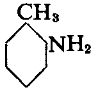


Trinitrotoluene

The Aromatic Amines (Functional Group —NH_2)

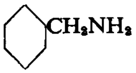
The aromatic amines (in which the amino group is united directly to the nucleus) differ to some extent from the aliphatic amines. Compounds containing an amino group in their side chain resemble the aliphatic amines.

Aminobenzene
or aniline



o-Aminotoluene
or *o*-toluidine

Aromatic type amines



Benzylamine

Aliphatic type amine

Primary, secondary, and tertiary aromatic amines and mixed aliphatic–aromatic amines may be prepared, e.g. monophenylamine (aniline) $C_6H_5NH_2$, diphenylamine $(C_6H_5)_2NH$, dimethylphenylamine (dimethylaniline) $C_6H_5N(CH_3)_2$.

The primary amines are the most important, more especially aniline.

Preparation of Aromatic Amines with the —NH_2 *Group in the Nucleus*

Primary aromatic amines are generally prepared by the reduction of the corresponding nitro compound.

$$RNO_2 \xrightarrow{6H} RNH_2 + 2H_2O$$

The reduction can be carried out in various ways. In the laboratory the hydrogen evolved when tin dissolves in hydrochloric acid is used as the reducing agent. On a commercial scale the reduction is effected by iron and acid. Nitrobenzene is mixed with water and heated. Iron filings and a little hydrochloric acid or solution of ferrous chloride are added, and the reaction allowed to proceed. Ferrous chloride solution is sufficiently acid to cause the iron to react. After the reduction is complete, the mixture is poured into water and allowed to settle. The lower aniline layer is drawn off and purified by distillation.

$$9Fe + 4H_2O + 4C_6H_5NO_2 = 4C_6H_5NH_2 + 3Fe_3O_4$$

Aniline may also be prepared by the reaction of chlorobenzene on ammonia under 50 atm in the presence of a suitable catalyst (e.g. cuprous chloride).

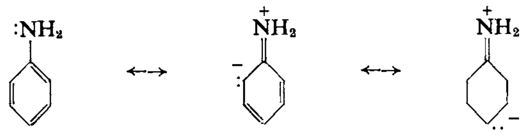
$$C_6H_5Cl + 2NH_3 = C_6H_5NH_2 + NH_4Cl$$

Physical Properties of the Primary Aromatic Amines with the —NH_2 *Group in the Nucleus*

Aniline is a colourless liquid (b.p. 189°C), volatile in steam and with a characteristic smell. It rapidly darkens in colour on standing exposed to light. It is not very soluble in water. The toluidines (*o*-, *m*-, and *p*-amino derivatives of toluene) generally resemble aniline in their physical properties, but the *p*-isomer is a solid. The di- and higher aromatic amines are usually solids.

General Reactions of the Aromatic Amines with the —NH_2 *Group in the Nucleus*

(1) *Basicity.* The primary aromatic amines, being derivatives of ammonia, exhibit basic properties. Their basicity is, however, weak and they do not give an alkaline reaction in solution. In this respect they differ from the aliphatic amines which are strong bases. The basicity of ammonia is increased by the substitution of an alkyl group for a hydrogen atom, but is weakened by the substitution of the aromatic nucleus. Accordingly, methylaniline ($C_6H_5NHCH_3$), and dimethylaniline [$C_6H_5N(CH_3)_2$] are stronger bases than aniline, while diphenylamine [$(C_6H_5)_2NH$] is a very weak base and triphenylamine [$(C_6H_5)_3N$] has no basic properties. The lower strength of the aromatic amines, as bases, indicates that the presence of the aromatic nucleus tends to withdraw electrons from the nitrogen atom (in contrast to aliphatic groups which tend to increase its electronegativity — cf. p. 181). The electron withdrawal arises from the participation of new structures in the nuclear resonance system.



The positive charge on the nitrogen atom tends to prevent the addition of a proton.

The salts of the aromatic amines are soluble in water. Being easily hydrolysed, they form acid solutions. They are easily decomposed by sodium hydroxide and other strong bases with the formation of the free amine.

$$C_6H_5NH_2{\cdot}HCl + NaOH = C_6H_5NH_2 + NaCl + H_2O$$

(2) *Formation of acyl derivatives.* The aromatic amines resemble the aliphatic amines in their reactions with acetic anhydride and acetyl chloride. They readily form the acetyl derivatives of the amine. These derivatives are often valuable as aids in the identification of the amines themselves.

$$C_6H_5NH_2 + ClCO{\cdot}CH_3 = C_6H_5NH{\cdot}CO{\cdot}CH_3 + HCl$$

Acetyl derivative of aniline,
i.e. acetanilide

Preparation of acetanilide. Acetanilide may be prepared by the reaction of aniline with acetic acid, acetic anhydride, or acetyl chloride. With the two latter substances the reaction proceeds rapidly in the cold; but with acetic acid in the cold, aniline forms aniline acetate. On heating, this substance loses water and acetanilide is formed.

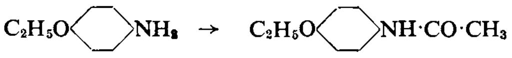
$$\underset{\text{Aniline acetate}}{C_6H_5NH_3OCO{\cdot}CH_3} = \underset{\text{Acetanilide}}{C_6H_5NH{\cdot}CO{\cdot}CH_3} + H_2O$$

Acetanilide crystallizes from water or dilute alcohol in white plates (m.p. 112°C).

Acetanilide, like other acetyl derivatives of amines, is hydrolysed to reform the amine and acid.

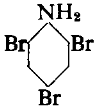
$$C_6H_5NH{\cdot}CO{\cdot}CH_3 + H_2O = C_6H_5NH_2 + CH_3{\cdot}COOH$$

For medicinal purposes acetanilide is now largely replaced by phenacetin, which is the *p*-ethoxy derivative of acetanilide and is prepared by acetylation of the corresponding base *p*-phenetidine.

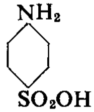


(3) *Nuclear substitution.* Nuclear substitution of the aromatic amines by halogens proceeds very readily, e.g. bromine water reacts with aniline to form an immediate precipitate of 2:4:6-tribromoaniline. (If the mono-bromo derivative is required, it is necessary to lower the reactivity by prior acetylation.)

At ordinary temperatures, aniline reacts with dilute sulphuric acid to form aniline hydrogen sulphate, but on heating with the concentrated acid, nuclear substitution takes place and *p*-aminobenzenesulphonic acid (sulphanilic acid) is formed.

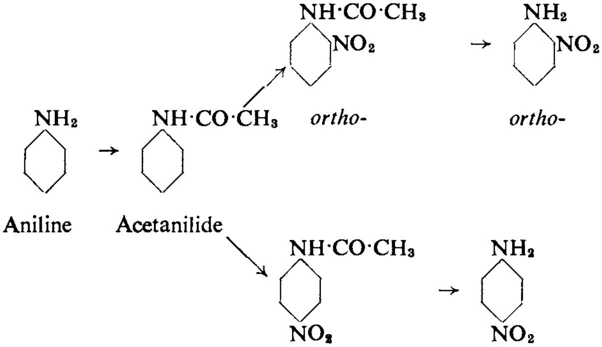


2:4:6-Tribromoaniline



Sulphanilic acid

The aromatic amines are not easily nitrated directly, because they are oxidized by nitric acid. But nitration can be effected if the amino group is protected by conversion into the acetyl derivative. For the preparation of *p*-nitroaniline, aniline is converted into acetanilide, which on nitration yields *p*-nitroacetanilide, together with a small proportion of *o*-nitroacetanilide. These substances on hydrolysis form the corresponding nitroanilines.



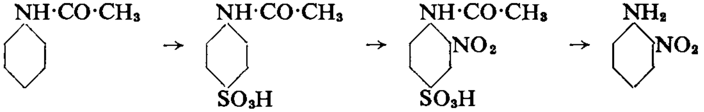
Aniline Acetanilide

ortho- *ortho-*

para- *para-*

Nitroacetanilides Nitroanilines

A good yield of *o*-nitroaniline may be obtained by first sulphonating acetanilide and then nitrating the sulphonic acid derivative and hydrolysing the product.



m-Nitroaniline cannot be obtained by direct nitration and is prepared by the partial reduction of *m*-dinitrobenzene.

(4) *Oxidation.* Some aromatic amines, e.g. aniline, are readily oxidized to a number of products. The formation of a deep violet colour on the addition of bleaching powder, and a deep blue or black colour with potassium dichromate are used as tests for aniline. The oxidation of aniline with potassium dichromate and sulphuric acid is of technical importance as a source of quinone. The reaction proceeds through several intermediate stages. Diphenylamine is readily oxidized to form a dark-coloured derivative and it is sometimes used as an indicator in oxidation–reduction reactions.

(5) *Carbylamine reaction.* The primary aromatic amines react like the aliphatic amines with chloroform and caustic potash to form isocyanides.

$$C_6H_5NH_2 + CHCl_3 + 3KOH = C_6H_5NC + 3KCl + 3H_2O$$

(6) *Conversion to secondary and tertiary amines.* Primary aromatic amines are converted into mixed aromatic–aliphatic secondary or tertiary amines by heating with alkyl halides.

$$C_6H_5NH_2 + CH_3I = \underset{\text{Methylaniline}}{C_6H_5NHCH_3} + HI$$

$$C_6H_5NHCH_3 + CH_3I = \underset{\text{Dimethylaniline}}{C_6H_5N(CH_3)_2} + HI$$

(7) *Diazo reaction.* The diazo reaction is given by primary aromatic amines but not by primary aliphatic amines.

The Diazo Compounds

Primary aromatic amines with the $—NH_2$ group in the nucleus react with nitrous acid under acid conditions and at temperatures in the region of 0°C, without any evolution of nitrogen. The resulting solutions contain the diazo compounds. An excess of mineral acid is required for satisfactory diazotization to ensure that the amine is available in the salt form. In practice, sodium nitrite solution is added to an ice-cold solution of the amine in dilute hydrochloric acid.

$$[C_6H_5NH_3]^+ Cl^- + HNO_2 = [C_6H_5N_2]^+ Cl^- + 2H_2O$$

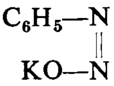
The constitution of the diazo compounds. The diazo compounds have properties suggestive of more than one formula. On the one hand, they form diazonium salts, which are analogous to ammonium salts and form electrically conducting solutions.

$$[C_6H_5—\overset{+}{N}{\equiv}N]\, Cl^- \rightarrow [C_6H_5—\overset{+}{N}{\equiv}N] + Cl^-$$

On the other hand, when a diazonium salt solution is made alkaline, diazonium hydroxide is liberated but it rapidly rearranges to form a diazotate.

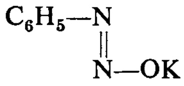
$$C_6H_5{\cdot}\overset{+}{N}{\equiv}N\overset{-}{O}H \rightarrow C_6H_5{\cdot}N{=}NOH \xrightarrow{KOH} C_6H_5{\cdot}N{=}NOK$$

Diazotates exist in two geometrical isomeric forms and are represented by the following structures



$$\begin{array}{r} C_6H_5—N \\ \| \\ KO—N \end{array}$$

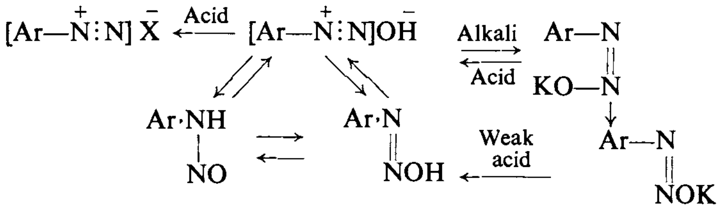
Potassium *n*-diazotate
(*syn-*)



$$\begin{array}{l} C_6H_5—N \\ \qquad\;\; \| \\ \qquad\;\; N—OK \end{array}$$

Potassium isodiazotate
(*anti-*)

Another possible isomeric structure for the diazonium hydroxide is the nitrosamine $C_6H_5NH(NO)$ and the interconversions of these isomers can be represented diagrammatically:



Reactions of the diazo compounds

The diazo compounds are unstable and tend to explode when isolated from solution. They are usually prepared in aqueous solution and converted directly into other substances.

The diazo group is readily replaced by other groups, nitrogen being eliminated. The new group occupies the same position in the benzene nucleus as the amino group of the primary amine from which the diazo compound was prepared. By means of the sequence — hydrocarbon → nitro compound → amine → diazo compound, a large number of derivatives of the hydrocarbon can be obtained.

(1) *Conversion to phenols.* When an acid solution of a diazo compound is warmed, nitrogen is evolved and the diazo group is replaced by the hydroxyl group. Thus phenol is obtained from aniline. (This replacement of a primary amino by a hydroxy group by the action of nitrous acid with the evolution of nitrogen may be compared with the similar replacement in the aliphatic series. In the latter case, no intermediate compound is obtained.)

$$C_6H_5NH_2 + HNO_2 = C_6H_5N_2OH + H_2O$$

$$C_6H_5N_2OH = C_6H_5OH + N_2$$

(2) *Conversion to hydrocarbons.* When a solution of a diazo compound is warmed after the addition of a suitable reducing

agent (e.g. alcohol), the diazonium group is replaced by hydrogen, and a hydrocarbon is obtained.

$$C_6H_5N_2{\cdot}HSO_4 + C_2H_5OH = C_6H_6 + N_2 + CH_3{\cdot}CHO + H_2SO_4$$

(3) *Conversion to iodo derivatives.* Replacement of the diazonium group by iodine is carried out by boiling the solution of the diazo compound after the addition of potassium iodide.

$$C_6H_5N_2Cl + KI = \underset{\text{Iodobenzene}}{C_6H_5I} + N_2 + KCl$$

(4) *Conversion to halogeno and cyano derivatives.* Replacement of the diazonium group by chlorine, bromine or cyanogen cannot be effected by the addition of the corresponding potassium salts, as in the case of the iodide. But the corresponding replacement occurs by warming in the presence of cuprous chloride, cuprous bromide or potassium cupro-cyanide. This reaction, which is known as *Sandmeyer's* reaction, is an important stage in the conversion of aromatic hydrocarbons into their halogen, cyanogen, and (by hydrolysis) carboxyl derivatives.

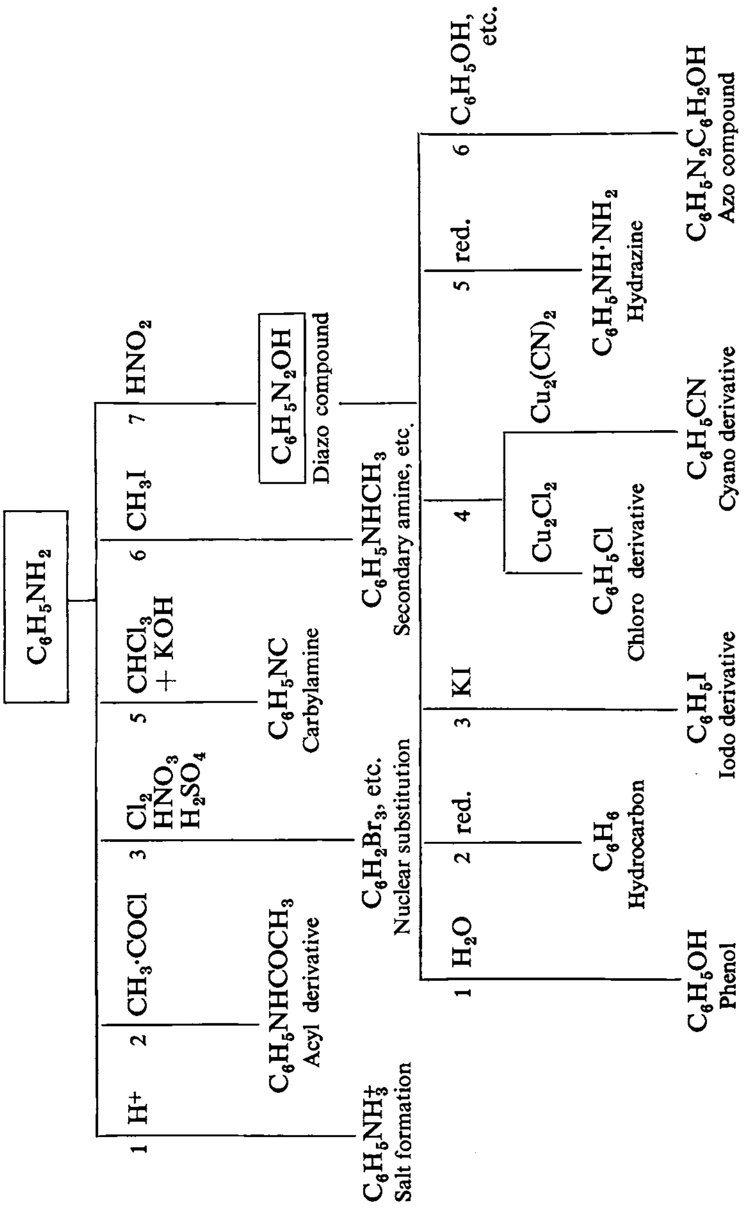
$$C_6H_5N_2Cl = C_6H_5Cl + N_2$$
$$C_6H_5N_2Br = C_6H_5Br + N_2$$
$$C_6H_5N_2CN = C_6H_5CN + N_2$$
$$C_6H_5CN \xrightarrow{\text{hydrolysis}} C_6H_5COOH$$

(5) *Reduction.* Diazo compounds take part in reduction and coupling reactions which proceed without elimination of nitrogen. The diazo compounds may be reduced with stannous chloride or sulphur dioxide to form derivatives of hydrazine. Phenylhydrazine (which is an important reagent for the detection of aldehydes, ketones and sugars) is obtained from aniline by diazotization and reduction.

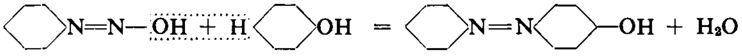
$$C_6H_5\text{—N:N—OH} \xrightarrow{4H} \underset{\text{Phenylhydrazine}}{C_6H_5\text{NH—NH}_2} + H_2O$$

With strong reducing agents, aniline is formed.

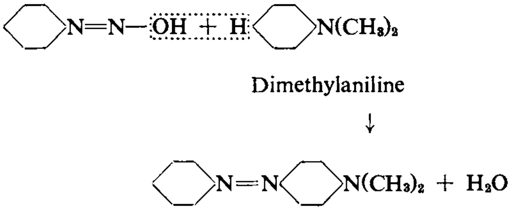
Reactions of Amines and Diazo Compounds



(6) *Coupling*. The diazo compounds are of technical importance by reason of their coupling reactions. These reactions take place between the diazo compounds and aromatic amines or phenols in alkaline solution.



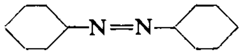
Phenol Hydroxyazobenzene



Dimethylaniline

Dimethylaminoazobenzene

The resultant compounds (the azo dyes) contain a skeleton consisting of two benzene nuclei united by an *azo* (—N:N—) group.



They are stable non-reactive substances, whose colour can be varied by the presence of different groups substituted in the two benzene nuclei. The presence of the hydroxyl or amino group, from the original phenol or amine, confers acidic or basic properties which help to fix the dye in the fibres of the fabric.

SECONDARY AND TERTIARY AROMATIC AMINES

(FUNCTIONAL GROUPS $>$NH AND $-\!\!>$N)

Secondary and tertiary aromatic amines can be prepared from primary amines by reaction with alkyl halides. The large scale process to form methylaniline involves the reaction of aniline with methyl alcohol and hydrochloric acid under pressure at 180°C.

Higher pressures and temperatures and using sulphuric acid gives dimethylaniline.

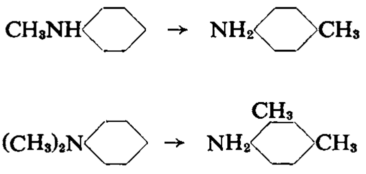
$$C_6H_5NH_2 + CH_3OH = C_6H_5NHCH_3 + H_2O$$

Methylaniline may also be prepared by the reduction of the product of interaction of aniline and formaldehyde

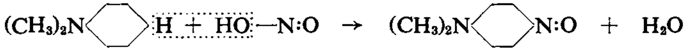
$$C_6H_5NH_2 + HCHO = C_6H_5N{:}CH_2 + H_2O$$

$$C_6H_5N{:}CH_2 \xrightarrow{2H} C_6H_5NHCH_3$$

The reactions of the secondary and tertiary amines resemble those of the aliphatic secondary and tertiary amines. In addition, they undergo an intramolecular transformation on heating, the methyl groups being transferred to the nucleus.



The *para* hydrogen atom of dimethylaniline is reactive and takes part in coupling reactions. It also reacts with nitrous acid to give *p*-nitrosodimethylaniline (cf. p. 62).



p-Nitrosodimethylaniline

The Aromatic Side-chain Amines

Aromatic side-chain amines have properties resembling the aliphatic amines (e.g. they are bases). They are prepared in corresponding ways.

Comparison of Amines

Reactant	*Aliphatic*			*Aromatic (nuclear —NH_2)*		
	Primary	*Secondary*	*Tertiary*	*Primary*	*Secondary*	*Tertiary*
Alkyl halide	secondary amine	tertiary amine	quaternary compound	secondary amine	tertiary amine	quaternary compound
Nitrous acid	alcohol	nitrosamine	no action	phenol or diazo	nitrosamine	*p*-nitroso derivative
Chloroform	carbylamine	no action	no action	carbylamine	no action	no action
Acid chloride or anhydride	substituted amide	substituted amide	no action	substituted amide	substituted amide	no action

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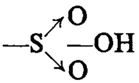
the aromatic sulphonic acids, phenols and ethers

THE SULPHONIC ACIDS



(FUNCTIONAL GROUP $-S\begin{smallmatrix}\nearrow O\\ \searrow O\end{smallmatrix}-OH$ OR $-SO_2OH$)

Aromatic hydrocarbons may be converted into derivatives (as an alternative to the route through the nitro compounds and the amines) by first forming sulphonic acids by treatment with concentrated or fuming sulphuric acid (cf. p. 177)

$$\underset{\text{Benzene}}{C_6H_5H} + \underset{\text{Sulphuric acid}}{HOSO_2OH} = \underset{\text{Benzenesulphonic acid}}{C_6H_5{\cdot}SO_2OH} + H_2O$$

Reactions of Sulphonic Acids

The sulphonic acids are soluble, strong, monobasic acids, which are easily converted into their salts.

$$C_6H_5{\cdot}SO_2OH \rightarrow C_6H_5{\cdot}SO_2O^- + [H]^+$$

When the alkali metal salts of sulphonic acids are fused with potassium hydroxide or potassium cyanide, reactions take place by which the sulphonic acid group is replaced by a hydroxyl or cyanide radical. Thus through the intermediate formation of a sulphonic acid, an aromatic hydrocarbon may be converted to its hydroxyl or cyanide and, thence, carboxyl derivative.

$$C_6H_5{\cdot}SO_3K + KOH = C_6H_5OK + KHSO_3$$

$$C_6H_5{\cdot}SO_3K + KCN = C_6H_5CN + K_2SO_3$$

The hydroxyl groups of the aromatic sulphonic acids react with phosphorus pentachloride and ammonia similarly to the hydroxyl groups of the carboxylic acids. The products (sulphonyl chloride and sulphonamides) resemble the corresponding acid chlorides and acid amides.

$$C_6H_5{\cdot}SO_2OH + PCl_5 = \underset{\text{Benzenesulphonyl chloride}}{C_6H_5{\cdot}SO_2Cl} + POCl_3 + HCl$$

$$C_6H_5{\cdot}SO_2OH + NH_3 = \underset{\text{Benzenesulphonamide}}{C_6H_5{\cdot}SO_2NH_2} + H_2O$$

Reactions of Sulphonyl Chlorides

The sulphonyl chlorides are fairly reactive liquids which are hydrolysed slowly by water but quite rapidly by alkali. However, they react with alcohols in the presence of alkali to give the sulphonic acid esters (cf. *Schotten–Baumann* reaction, p. 230). (These esters cannot be obtained by the direct action of the sulphonic acid on alcohols.)

$$C_6H_5{\cdot}SO_2Cl + H_2O = C_6H_5{\cdot}SO_2OH + HCl$$

$$C_6H_5{\cdot}SO_2Cl + C_2H_5OH = C_6H_5{\cdot}SO_2OC_2H_5 + HCl$$

The sulphonyl chlorides react with ammonia to give sulphonamides. The corresponding reactions with primary and secondary (but not tertiary) aliphatic amines are utilized in the identification and separation of these amines (cf. p. 61).

$$C_6H_5{\cdot}SO_2Cl + NH_3 = C_6H_5{\cdot}SO_2NH_2 + HCl$$

$$C_6H_5{\cdot}SO_2Cl + NH_2R = C_6H_5{\cdot}SO_2NHR + HCl$$

$$C_6H_5{\cdot}SO_2Cl + NHR_2 = C_6H_5{\cdot}SO_2NR_2 + HCl$$

Sulphonyl chlorides are converted into nuclear substituted halogen derivatives by reaction with phosphorus pentachloride.

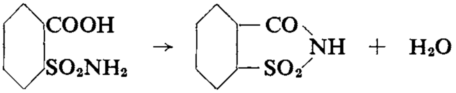
$$C_6H_5{\cdot}SO_2Cl + PCl_5 = C_6H_5Cl + POCl_3 + SOCl_2$$

Reactions of Sulphonamides

The sulphonamides are neutral crystalline solids. Those derived from sulphanilic acid have important therapeutic actions; the simplest of these is sulphanilamide (p-$NH_2{\cdot}C_6H_4{\cdot}SO_2NH_2$). The sulphonamide of *o*-toluene sulphonic acid, after oxidation of the methyl group to the carboxyl group, yields an internal anhydride (saccharin) which is of importance as a sugar substitute, by reason of its intense sweet taste.

$$CH_3{\cdot}C_6H_4{\cdot}SO_2OH \rightarrow CH_3{\cdot}C_6H_4{\cdot}SO_2Cl \rightarrow$$

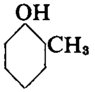
$$CH_3{\cdot}C_6H_4{\cdot}SO_2NH_2 \rightarrow COOH{\cdot}C_6H_4{\cdot}SO_2NH_2$$



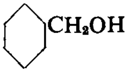
THE PHENOLS (FUNCTIONAL GROUP —OH)

The phenols are hydroxy derivatives of the aromatic hydrocarbons, in which the hydroxyl group has been substituted in the nucleus. The aromatic alcohols are hydroxy derivatives containing the hydroxyl group in the side chain. The lowest member of the series of phenols is itself called phenol.

Phenol



Cresol (phenolic)

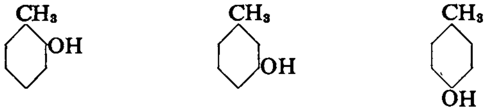


Benzyl alcohol

General Methods of Preparation of Phenols

(1) *The separation of phenols from coal-tar.* Coal-tar is the most important source of phenol (C_6H_5OH) and its simpler homologues. When it is distilled, the phenol is contained in the middle or carbolic oil. On cooling, the naphthalene in this oil crystallizes, while the phenols remain in the liquid fraction. This is treated with caustic soda solution (in which the phenol dissolves). The non-acidic impurities are separated. The phenol solution is then acidified (often by passing in carbon dioxide), when the phenol separates. It is purified further by distillation. Phenol occurs as colourless crystals, which become pink on keeping. It possesses a characteristic odour.

The cresols (the next members of the homologous series of phenols), are also obtained from coal-tar. The separation of the isomers is not easy, and is not carried out for ordinary commercial purposes.



ortho *meta* *para*

Cresol

(2) Phenols may be prepared by fusing the sodium salt of a sulphonic acid with sodium hydroxide. This method of preparation can be applied on a large scale.

$$C_6H_5\cdot SO_2ONa + NaOH = C_6H_5ONa + NaHSO_3$$

(3) Phenols may be prepared from the amines by the diazo reaction (cf. p. 198).

(4) Phenol can be obtained from chlorobenzene by reacting with alkali at high temperature under pressure.

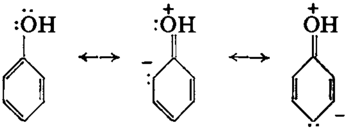
$$C_6H_5Cl + KOH = C_6H_5OH + KCl$$

General Reactions of the Phenols

(1) *Acid function.* The most important difference between phenols and alcohols lies in the acidity of the former. The alcohols do not exhibit acidic properties.

$$C_6H_5OH \rightleftarrows C_6H_5O^- + H^+$$

Phenol is not very soluble in water but dissolves readily, as its salt, on the addition of alkali. Phenol is a very weak acid, and its salts are easily decomposed by the addition of stronger acids. The passage of carbon dioxide into a solution of sodium phenate is sufficient to cause the phenol to be displaced from solution. The introduction of other groups into the benzene nucleus may increase the acid strength of the phenolic group and trinitrophenol forms well-defined picrate salts. The acidity of the phenolic hydroxylic group (in contrast with the alcoholic hydroxylic group) arises from the participation of new structures in the nuclear resonance system leading to a positive charge on the oxygen atom (cf. aromatic amines p. 193).



The positive charge attracts the electron pairs of the —OH bond and facilitates ionization.

(2) *Phenol esters.* Phenols resemble alcohols in their capacity for forming esters. They do not react directly with acids, but the

esters are obtained when acid chlorides or acid anhydrides react with phenols in alkaline solution.

$$\underset{\text{Phenol}}{C_6H_5OH} + \underset{\text{Benzoyl chloride}}{C_6H_5{\cdot}COCl} = \underset{\text{Phenyl benzoate}}{C_6H_5{\cdot}COOC_6H_5} + HCl$$

(3) *Phenol ethers.* Phenols resemble alcohols in their capacity for forming ethers, which are prepared from phenols by reacting with alkyl halides on their sodium salts. In this way mixed aliphatic aromatic ethers are obtained. Purely aromatic ethers can also be prepared (e.g. C_6H_5—O—C_6H_5 diphenyl ether).

$$C_6H_5ONa + CH_3I = \underset{\substack{\text{Phenyl methyl ether}\\ \text{(anisole)}}}{C_6H_5OCH_3} + NaI$$

$$C_6H_5ONa + C_2H_5I = \underset{\substack{\text{Phenyl ethyl ether}\\ \text{(phenetole)}}}{C_6H_5OC_2H_5} + NaI$$

(4) *Replacement of hydroxyl group.* Phenols resemble alcohols in their reaction with phosphorus pentachloride, whereby the hydroxyl group is replaced by chlorine.

$$C_6H_5OH + PCl_5 = C_6H_5Cl + POCl_3 + HCl$$

(5) *Nuclear substitution.* The aromatic nucleus present in the phenol molecule is readily substituted by the ordinary aromatic substituting reagents; e.g. dilute nitric acid converts phenol into a mixture of *o*- and *p*-mononitrophenol, while a mixture of concentrated sulphuric and nitric acids forms the trinitro derivative. Bromine water added to a dilute solution of phenol produces an immediate precipitate of tribromophenol.

$$C_6H_5OH + HNO_3 = C_6H_4(OH)NO_2 + H_2O$$

$$C_6H_5OH + 3Br_2 = C_6H_2Br_3OH + 3HBr$$

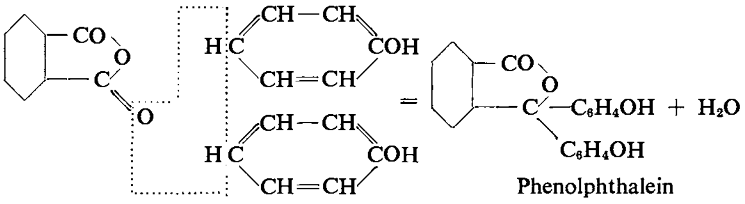
(6) *Reduction.* Phenols can be reduced to the corresponding hydrocarbon by heating with zinc dust.

$$C_6H_5OH + Zn = C_6H_6 + ZnO$$

(7) *Coupling.* Phenols, in alkaline solution, combine with diazotized aromatic amines to form the azo dyes.

$$C_6H_5N{:}NOH + C_6H_5ONa = C_6H_5{\cdot}N{:}N{\cdot}C_6H_4ONa + H_2O$$

(8) *Conversion to phthaleins.* Phenols condense with phthalic anhydride in the presence of dehydrating agents to form substances called *phthaleins.* An oxygen atom of the phthalic anhydride combines with one nuclear hydrogen atom from each of two phenol molecules. The resulting compound is a derivative of phthalic anhydride with two phenol residues replacing an oxygen atom. The simplest member of this class of substance (many of which are of industrial importance as dyes) is phenolphthalein.

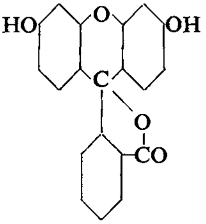


Phenolphthalein

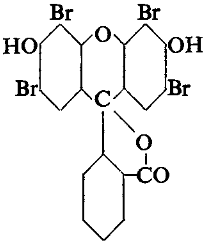
This is obtained by heating phenol and phthalic anhydride to about 120°C with concentrated sulphuric acid (which acts as a dehydrating agent). It is a white crystalline substance, almost insoluble in water but soluble in alkalis forming a red solution. (The colour change is due to an intramolecular rearrangement which accompanies ionization.)

Fluorescein

This is obtained when resorcinol is condensed with phthalic anhydride. It is characterized by the brilliant greenish yellow fluorescence of its solutions. Many of its derivatives are also fluorescent. When fluorescein is treated with bromine, the resorcinol residues become substituted and tetrabromofluorescein is obtained, the sodium salt of which is *eosin.*

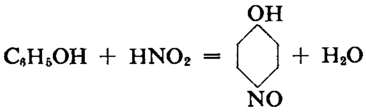


Fluorescein

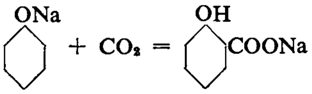


Eosin

(9) *Conversion to nitrosophenols.* Many phenols react with sodium nitrite in presence of concentrated sulphuric acid to form nitrosophenols. The colour is first green, but becomes red on adding water and then bluish green on pouring into excess alkali (*Liebermann's* test).

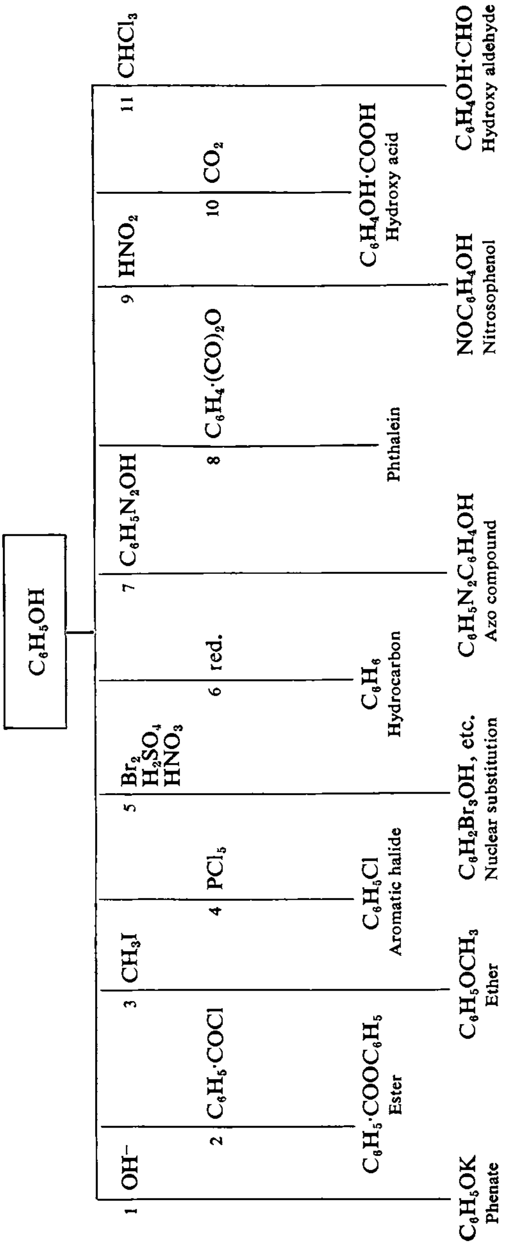


(10) *Conversion to hydroxy acids.* The sodium salts of phenols react with carbon dioxide under pressure to give salts of carboxylic acids, the complex reaction accomplishing the effect of a nuclear substitution (*Kolbe–Schmitt* reaction).

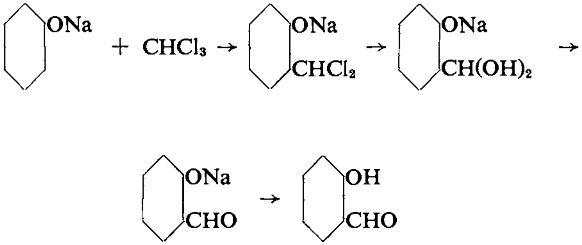


Sodium phenate Sodium salicylate

Reactions of Phenols



(11) *Conversion to hydroxy aldehydes.* Phenols in alkaline solution react with chloroform at 60°C to give phenolic aldehydes, as a result of a complex reaction giving the effect of nuclear substitution (*Reimer–Tiemann* reaction).



Salicylaldehyde

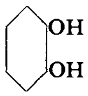
(12) *Ferric chloride colours.* Many phenols give characteristic colour reactions with ferric chloride. Phenol itself gives a violet colour.

The Dihydric and Trihydric Phenols

In addition to the characteristic phenolic properties, many of the di- and tri-hydric phenols possess reducing properties in alkaline solution. Some are used as photographic developers.

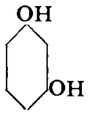
Dihydroxybenzenes

The three isomeric dihydroxybenzenes are known as catechol, resorcinol and hydroquinone (quinol).



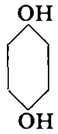
ortho-

Catechol



meta-

Resorcinol

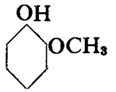


para-

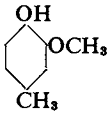
Hydroquinone or quinol

Catechol

This is obtained from various plant sources and from wood-tar. The corresponding mono-ether *guaiacol* is an important constituent of wood-tar from which it is obtainable by fractional distillation. It can also be prepared synthetically. *Creosol*, another constituent of wood-tar, is a homologue of guaiacol.



Guaiacol



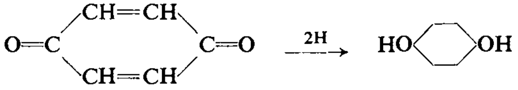
Creosol

Resorcinol

This is prepared synthetically on the technical scale. Benzene when sulphonated with fuming sulphuric acid forms the *m*-disulphonic acid, from which *m*-dihydroxybenzene is obtained by fusion with alkali.

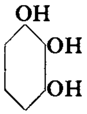
Hydroquinone (or quinol)

This is prepared by reduction of quinone. It is a valuable photographic developer.

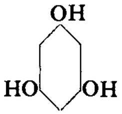


Trihydroxybenzenes

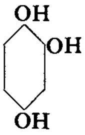
The three possible isomerides are



Pyrogallol
1:2:3



Phloroglucinol
1:3:5



Trihydroxybenzene
1:2:4

Pyrogallol

This is prepared by the action of heat on gallic acid. It is easily oxidized in alkaline solution and is used as a photographic developer and to absorb oxygen in gas analysis.

Comparison of Alcohols and Phenols

Chief reactant	*Primary alcohols*	*Phenols*
Sodium	alkoxide	phenoxide
Sodium hydroxide	no action	phenoxide
Phosphorus pentachloride	halide	halide
Carboxylic acid	ester	no action
Acid chloride	ester	ester
Sulphuric acid	ester, ether or olefine	sulphonation
Oxidation	aldehyde or acid	no action
Chlorine; bromine	halogeno-aldehyde or derivative	substitution
Diazo compound	no action	azo dye
Ferric chloride	no action	colour
Liebermann's test	no action	colour

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the aromatic halogen derivatives, alcohols, aldehydes and ketones

THE HALOGEN DERIVATIVES

The nuclear-substituted halogen derivatives of benzene and its homologues differ in many ways from the aliphatic halides. The compounds obtained by introducing halogens into the side chain of a benzene homologue possess properties characteristic of the alkyl halides as well as the aromatic properties due to the presence of the nucleus.

Preparation of Nuclear Substituted Aromatic Halides

(1) *Direct substitution.* Nuclear substituted halogen derivatives may be obtained by direct substitution of the hydrocarbons. The reaction is carried out in the cold and in the absence of light. The presence of a halogen carrier (e.g. iron wire or pyridine) facilitates the reaction.

$$C_6H_6 + Cl_2 = C_6H_5Cl + HCl$$

(2) *By diazo reaction.* Nuclear substituted halogen derivatives are conveniently prepared from the diazo compounds by warming after the addition of the cuprous halide, or potassium iodide for the iodo derivative.

$$C_6H_5N_2Cl = C_6H_5Cl + N_2$$

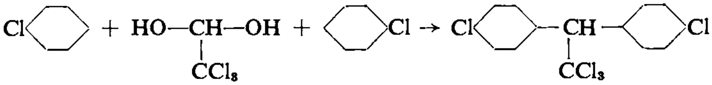
Properties of the Nuclear Substituted Aromatic Halides

The nuclear substituted halogen derivatives are pleasant-smelling liquids, insoluble in water. The halogen atom is bound strongly to the nucleus, and is comparatively unreactive. Thus the aryl halides differ from the alkyl halides in that they do not react readily with caustic potash and ammonia under ordinary conditions of temperature and pressure.

The reactions with sodium and magnesium are common to both classes of halides.

Chlorobenzene

This is prepared on a commercial scale for conversion (by reaction with chloral hydrate in the presence of sulphuric acid) into the insecticide DDT (dichloro-diphenyl-trichloroethane).



Preparation of Side-chain Substituted Aromatic Halides

Benzyl chloride, benzal chloride and benzotrichloride are obtained successively by the side-chain chlorination of toluene. This reaction is stimulated by strong sunlight and occurs preferentially to substitution at the boiling point of toluene and in the absence of a halogen carrier.

Properties of Side-chain Substituted Aromatic Halides

The side-chain substituted halides possess irritating and unpleasant smells. They react with caustic potash and with ammonia like alkyl halides, the halogen atom becoming replaced by a hydroxyl or an amino group. Thus the hydrolysis products of the mono-, di- and tri-halogeno derivatives of toluene are benzyl alcohol, benzaldehyde and benzoic acid respectively.

$$\begin{aligned} &C_6H_5{\cdot}CH_2Cl \rightarrow C_6H_5{\cdot}CH_2OH \\ &C_6H_5{\cdot}CHCl_2 \rightarrow C_6H_5{\cdot}CH(OH)_2 \rightarrow C_6H_5{\cdot}CHO \\ &C_6H_5{\cdot}CCl_3 \rightarrow C_6H_5{\cdot}C(OH)_3 \rightarrow C_6H_5{\cdot}COOH \end{aligned}$$

THE AROMATIC ALCOHOLS

The aromatic alcohols contain a hydroxyl group in the side chain.

Preparation of Aromatic Alcohols

(1) *From side-chain halides.* The aromatic alcohols are prepared by the hydrolysis of the corresponding halogen derivatives. *Benzyl alcohol* ($C_6H_5{\cdot}CH_2OH$) is prepared by hydrolysis of benzyl chloride, which is the monochloro side-chain substitution product of toluene.

$$C_6H_5{\cdot}CH_2Cl + KOH = C_6H_5{\cdot}CH_2OH + KCl$$

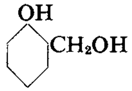
(2) *From aldehydes.* The aromatic alcohols can be obtained by the reduction of the corresponding aldehyde, using sodium amalgam and water.

$$C_6H_5{\cdot}CHO + H_2 = C_6H_5{\cdot}CH_2OH$$

(3) *By the Cannizzaro reaction.* The aromatic aldehydes can be partially converted into the corresponding alcohols by means of the *Cannizzaro* reaction, i.e. the action of alkali. The two products (the alcohol and the salt of the acid) can be separated by distilling off the volatile alcohol.

$$2C_6H_5{\cdot}CHO + KOH = C_6H_5{\cdot}CH_2OH + C_6H_5{\cdot}COOK$$

(4) *Salicyl alcohol* is usually obtained from the glucoside, salicin, by hydrolysis. It is an example of a phenolic alcohol.



Salicyl alcohol

Comparison of Aliphatic and Aromatic Halogen Compounds

Reagent	*Alkyl halide*	*Side-chain aromatic halide*	*Nuclear aromatic halide*
Reduction: zinc–copper + alcohol	hydrocarbon	hydrocarbon	no action
Sodium	hydrocarbon	hydrocarbon	hydrocarbon
Aqueous potassium hydroxide	alcohol	alcohol	no action
Alcoholic potassium hydroxide	olefin	olefin	no action
Sodium + alkyl halide	higher hydrocarbon	higher hydrocarbon	higher hydrocarbon
Sodium alkoxide	ether	ether	no action
Ammonia	amine (aliphatic type)	side-chain amine (aliphatic type)	no action
Potassium cyanide	nitrile	nitrile	no action
Silver cyanide	isonitrile	isonitrile	no action
Silver salt of organic acid	ester	ester	no action
Silver nitrite	nitro compound (aliphatic type)	side-chain nitro compound (aliphatic type)	no action
Magnesium	*Grignard* reagent	*Grignard* reagent	*Grignard* reagent

Properties of Aromatic Alcohols

The aromatic alcohols resemble the aliphatic alcohols, e.g. benzyl alcohol is oxidized to the corresponding aldehyde and then to the acid.

$$C_6H_5{\cdot}CH_2OH \rightarrow C_6H_5{\cdot}CHO \rightarrow C_6H_5{\cdot}COOH$$

Salicyl alcohol on oxidation usually gives salicylic acid as the first product capable of isolation.

$$C_6H_4OH{\cdot}CH_2OH \rightarrow C_6H_4OH{\cdot}CHO \rightarrow C_6H_4OH{\cdot}COOH$$

The aromatic alcohols also react similarly to the aliphatic alcohols with sodium and with phosphorus pentachloride. They give esters with acetic anhydride, etc.

$$\begin{aligned} 2C_6H_5{\cdot}CH_2OH &+ (CH_3{\cdot}CO)_2O \\ &= 2CH_3{\cdot}COO{\cdot}CH_2{\cdot}C_6H_5 + H_2O \end{aligned}$$

THE AROMATIC ETHERS

There are two classes of aromatic ethers. In one (phenolic ethers), only one group attached to the oxygen atom is of the aromatic type. In the other class, both radicals are aromatic.

(1) Phenolic ethers are prepared by the action of alkyl halides on phenol in alkaline solution.

$$C_6H_5ONa + CH_3I = \underset{\text{Anisole}}{C_6H_5OCH_3} + NaI$$

(2) Di-aryl ethers are prepared by the action of aryl halides on alkali metal derivatives of phenols in the presence of metallic copper.

$$C_6H_5ONa + C_6H_5Br = \underset{\text{Phenetole}}{C_6H_5{-}O{-}C_6H_5} + NaBr$$

The two classes of aromatic ethers differ in their behaviour towards hydrogen iodide, for the di-aryl ethers are not attacked by this reagent.

$$C_6H_5OCH_3 + HI = C_6H_5OH + CH_3I$$

THE AROMATIC ALDEHYDES

The side-chain substituted aldehydes have similar methods of preparation and properties to the aliphatic aldehydes. The aromatic aldehydes with the —CHO group attached directly to the nucleus have many points of resemblance to the aliphatic aldehydes, but also some differences.

Preparation of Aromatic Aldehydes (nuclear —CHO)

Aromatic aldehydes may be prepared by suitable modifications of the general methods for the preparation of aliphatic aldehydes. Benzaldehyde can be prepared by the oxidation of benzyl alcohol, or from benzyl chloride or bromide by simultaneous hydrolysis and oxidation by heating with a solution of lead, copper, or sodium nitrate. It can also be prepared by hydrolysis of benzal chloride. The last two reactions are applied in the preparation of benzaldehyde from toluene on a commercial scale.

$$C_6H_5{\cdot}CH_3 \rightarrow C_6H_5{\cdot}CH_2Cl \rightarrow C_6H_5{\cdot}CH_2OH \rightarrow C_6H_5{\cdot}CHO$$

$$C_6H_5{\cdot}CH_3 \rightarrow C_6H_5{\cdot}CHCl_2 \rightarrow C_6H_5{\cdot}CH(OH)_2 \rightarrow C_6H_5{\cdot}CHO$$

A small scale preparation by the action of heat on a mixture of calcium benzoate and calcium formate resembles a method of preparation of aliphatic aldehydes.

$$(C_6H_5{\cdot}COO)_2Ca + (HCOO)_2Ca = 2C_6H_5{\cdot}CHO + 2CaCO_3$$

Benzaldehyde is also obtained from the glucoside amygdalin, which occurs in bitter almonds. On hydrolysis, amygdalin forms glucose, hydrogen cyanide and benzaldehyde.

$$C_{20}H_{27}NO_{11} + 2H_2O = C_6H_5{\cdot}CHO + 2C_6H_{12}O_6 + HCN$$

Benzaldehyde is a liquid with an almond-like smell (oil of bitter almonds).

Properties of the Aromatic Aldehydes

The aromatic aldehydes, like the aliphatic aldehydes, can be reduced to the corresponding alcohols and are easily oxidized to the corresponding acids. Benzaldehyde, unless very pure, absorbs oxygen readily from the air and reduces ammoniacal silver nitrate solution; but it does not reduce Fehling's solution.

The aromatic aldehydes resemble aliphatic aldehydes in their reactions with phosphorus pentachloride. They form condensation products with hydroxylamine and phenylhydrazine and addition products with sodium bisulphite and hydrogen cyanide. But they do not undergo polymerization in the presence of concentrated sulphuric acid. (Substitution reactions may occur giving sulphonic acid derivatives.)

Nuclear aromatic aldehydes (e.g. benzaldehyde) are more reactive than the aliphatic aldehydes, and take part in the following additional reactions.

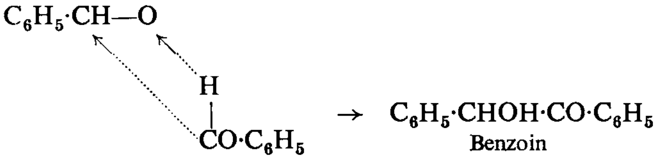
(1) *With ammonia.* An addition product is not formed with ammonia, but a more complex condensation reaction takes place.

$$3C_6H_5{\cdot}CHO + 2NH_3 = \underset{\text{Hydrobenzamide}}{(C_6H_5{\cdot}CH)_3N_2} + 3H_2O$$

(2) *Cannizzaro reaction.* In the presence of alkalis, simultaneous oxidation and reduction take place, and a mixture of the corresponding acid and alcohol is formed (cf. formaldehyde p. 74).

$$2C_6H_5{\cdot}CHO + NaOH = C_6H_5{\cdot}COONa + C_6H_5{\cdot}CH_2OH$$

(3) *Benzoin condensation.* In the presence of potassium cyanide, benzaldehyde is converted into a ketonic alcohol, obtained by the union of two molecules of the aldehyde.



$$\begin{array}{l} C_6H_5{\cdot}CH{-}O \\ \quad H \\ \quad | \\ \quad CO{\cdot}C_6H_5 \end{array} \rightarrow \underset{\text{Benzoin}}{C_6H_5{\cdot}CHOH{\cdot}CO{\cdot}C_6H_5}$$

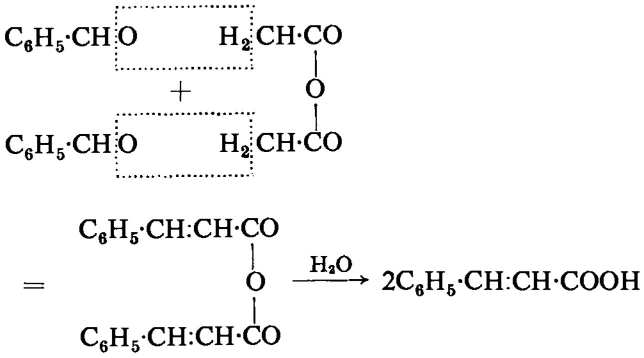
(4) *Condensation reactions.* The oxygen of the carbonyl group of the aromatic aldehydes is capable of removing hydrogen (as water) from the molecules of many other substances.

(a) *Claisen reaction.* Benzaldehyde condenses with aliphatic aldehydes or ketones to form unsaturated aldehydes or ketones.

$$C_6H_5{\cdot}CHO + CH_3{\cdot}CHO = \underset{\text{Cinnamic aldehyde}}{C_6H_5{\cdot}CH{:}CH{\cdot}CHO} + H_2O$$

$$C_6H_5{\cdot}CHO + CH_3{\cdot}CO{\cdot}CH_3 = \underset{\text{Benzylidene acetone}}{C_6H_5{\cdot}CH{:}CH{\cdot}CO{\cdot}CH_3} + H_2O$$

(b) *Perkin reaction.* When benzaldehyde reacts with a mixture of an acid anhydride and the sodium salt of the corresponding acid, an unsaturated acid is obtained. (A similar reaction is given by some aliphatic aldehydes.)



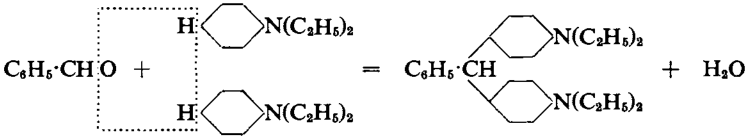
$$\begin{array}{llr} C_6H_5{\cdot}CH & \boxed{O \qquad H_2} & CH{\cdot}CO \\ & \quad + & | \\ & & O \\ & & | \\ C_6H_5{\cdot}CH & \boxed{O \qquad H_2} & CH{\cdot}CO \end{array}$$

$$= \begin{array}{r} C_6H_5{\cdot}CH{:}CH{\cdot}CO \\ | \\ O \\ | \\ C_6H_5{\cdot}CH{:}CH{\cdot}CO \end{array} \xrightarrow{H_2O} 2C_6H_5{\cdot}CH{:}CH{\cdot}COOH$$

(c) Benzaldehyde undergoes a condensation reaction with primary aromatic amines.

$$C_6H_5{\cdot}CHO + H_2N{\cdot}C_6H_5 = \underset{\text{Benzylidene aniline}}{C_6H_5{\cdot}CH{:}N{\cdot}C_6H_5} + H_2O$$

The condensation products obtained from the alkyl anilines are important dyes (triphenylmethane derivatives).



Diethylaniline Brilliant Green

THE AROMATIC KETONES

These compounds resemble the ketones of the aliphatic series in their method of preparation and in their properties. For example, acetophenone is obtained when calcium acetate and calcium benzoate are heated together.

$$(C_6H_5{\cdot}COO)_2Ca + (CH_3{\cdot}COO)_2Ca$$
$$= 2C_6H_5{\cdot}CO{\cdot}CH_3 + 2CaCO_3$$

However, a more convenient method of preparation is the use of the *Friedel–Craft's* reaction using benzene and acetyl chloride in the presence of anhydrous aluminium chloride.

$$CH_3COCl + C_6H_6 = CH_3{\cdot}CO{\cdot}C_6H_5 + HCl$$

Aromatic ketones are reduced to hydrocarbons using amalgamated zinc and hydrochloric acid (*Clemmensen* reaction).

$$C_6H_5{\cdot}CO{\cdot}CH_3 \rightarrow C_6H_5{\cdot}CH_2{\cdot}CH_3$$

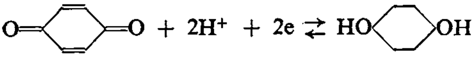
Acetophenone does not form a sodium bisulphite addition compound.

The Quinones

Quinones are diketones possessing a non-aromatic, two double-bonded, six-membered ring of carbon atoms. They are analogous to unsaturated aliphatic ketones. Benzene forms two quinones (*ortho-* and *para-*) but the latter compound is the commoner and is often called "Quinone". It is a reactive substance which is easily reduced to hydroquinone. The reaction is reversible and is the basis for the use of the quinhydrone electrode potential method for the determination of hydrogen ion concentration. Quinhydrone is a compound of quinone and hydroquinone in equimolecular proportions.

ortho- *para-*

Benzoquinones



Quinone Hydroquinone

Comparison of Aliphatic and Aromatic Aldehydes and Ketones

Reactant	*Aldehydes*	*Ketones (aliphatic or aromatic)*	*Aromatic aldehydes*
Oxidation	one acid	mixture of acids	one acid
Ammoniacal silver nitrate	reduction	no action	slow reduction
Fehling's solution	reduction	no action	no action
Reduction	primary alcohol	secondary alcohol or pinacol	primary alcohol
Phosphorus pentachloride	dichloride	dichloride	dichloride
Ammonia	addition	complex action	complex action
Sodium bisulphite or hydrogen cyanide	addition	addition	addition
Hydroxylamine or hydrazine	condensation	condensation	condensation
Sodium hydroxide	resinous polymer	no action	Cannizzaro reaction
Sulphuric acid	polymer	often no action	sulphonation
Schiff's test	decolorization	no action	no action
Alcohol + dehydrating agent	acetal	no action	acetal
Grignard reagent + hydrolysis	secondary alcohol	tertiary alcohol	secondary alcohol

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the aromatic acids and hydroxy acids

THE AROMATIC ACIDS

Aromatic acids in which the carboxyl group is present in the side chain resemble aliphatic acids. Those with the carboxyl group attached directly to the nucleus show some differences.

Preparation of Nuclear-substituted Aromatic Acids

Many of these acids occur naturally in the free and combined states. They may be prepared from their naturally occurring derivatives, and synthetically by the following general methods.

(1) By oxidation of aromatic compounds which contain an aliphatic side chain. On oxidation, the side chain is converted into a carboxyl group.

$$\underset{\text{Toluene}}{C_6H_5\cdot CH_3} \rightarrow \underset{\text{Benzoic acid}}{C_6H_5\cdot COOH}$$

(2) By oxidation of the corresponding alcohols and aldehydes.

$$C_6H_5\cdot CH_2OH \rightarrow C_6H_5\cdot CHO \rightarrow C_6H_5\cdot COOH$$

(3) By hydrolysis of the corresponding cyanides.

$$C_6H_5CN \rightarrow C_6H_5\cdot COOH$$

(4) From the corresponding *Grignard* reagent by reaction with carbon dioxide, followed by hydrolysis with dilute acid.

$$2C_6H_5MgBr + 2CO_2 + 2H_2O \rightarrow 2C_6H_5{\cdot}COOH + MgBr_2 + Mg(OH)_2$$

(5) From the corresponding aldehyde by the *Cannizzaro* reaction. The alcohol, which is also formed, may be removed by distillation and the acid is then obtained by acidification.

$$2C_6H_5{\cdot}CHO + KOH = C_6H_5{\cdot}COOK + C_6H_5{\cdot}CH_2OH$$

Properties of Aromatic Acids (nuclear —COOH)

The aromatic acids are generally crystalline solids, soluble in hot water but sparingly soluble in cold water. The addition of dilute hydrochloric acid to cold solutions of their salts causes the acids to be precipitated. Aromatic acids, while stronger than aliphatic acids, resemble them in forming salts, esters and other derivatives. The decarboxylation reaction involving heating the sodium salt with soda-lime (cf. p. 174) is also analogous to the conversion of aliphatic acids into hydrocarbons.

$$C_6H_5{\cdot}COONa + NaOH = C_6H_6 + Na_2CO_3$$

Benzoic acid

Benzoic acid ($C_6H_5{\cdot}COOH$) occurs in gum benzoin, and in various balsams. When gum benzoin is heated, benzoic acid sublimes. It is also prepared synthetically from toluene. By passing chlorine into boiling toluene, benzotrichloride is prepared. This is then hydrolysed with milk of lime, and calcium benzoate is formed. Benzaldehyde (formed by hydrolysis of benzal chloride present, due to incomplete chlorination) is removed by distillation in steam, and the calcium benzoate is decomposed with dilute hydrochloric acid. (Some benzoic acid is also obtained as a side product during the manufacture of benzaldehyde.)

$$C_6H_5{\cdot}CCl_3 \rightarrow C_6H_5{\cdot}C(OH)_3 \rightarrow C_6H_5{\cdot}COOH$$

Benzoic acid is not very soluble in cold water, but dissolves more readily in hot water and in organic solvents. In solvents such as benzene or carbon tetrachloride, the acid is present in the associated double molecule form.

$$(C_6H_5\cdot COOH)_2$$

Derivatives of Benzoic Acid

Benzoyl chloride

The acid chloride of benzoic acid is prepared by the action of phosphorus pentachloride or thionyl chloride on benzoic acid.

$$C_6H_5\cdot COOH + SOCl_2 = C_6H_5\cdot COCl + SO_2 + HCl$$

Benzoyl chloride is hydrolysed slowly by water and by dilute alkalis. This slow rate of hydrolysis enables benzoyl chloride to be used as an important reagent for "benzoylation", as in the preparation of the esters of benzoic acid, especially using the *Schotten–Baumann* reaction which involves acting on alcohols with benzoyl chloride in the presence of dilute aqueous sodium hydroxide solution. *p*-Nitro and 3:5-dinitrobenzoyl chlorides are used in the recognition of alcohols by ester formation.

Benzoic acid esters

These are obtained from the alcohols by reaction with benzoyl chloride or by the action of benzoic acid after saturation with hydrogen chloride gas.

$$C_6H_5\cdot COCl + ROH = C_6H_5\cdot COOR + HCl$$

$$C_6H_5\cdot COOH + ROH = C_6H_5\cdot COOR + H_2O$$

Benzoic anhydride

This is prepared by the action of benzoyl chloride on sodium benzoate.

$$C_6H_5\cdot COCl + C_6H_5\cdot COONa = (C_6H_5\cdot CO)_2O + NaCl$$

Benzamide

This is prepared by the action of ammonia on benzoate esters or from benzoyl chloride by reaction with ammonium carbonate.

$$C_6H_5{\cdot}COOC_2H_5 + NH_3 = C_6H_5{\cdot}CONH_2 + C_2H_5OH$$

$$C_6H_5{\cdot}COCl + (NH_4)_2CO_3 = C_6H_5{\cdot}CONH_2 + NH_4Cl + CO_2 + H_2O$$

Benzonitrile

This is prepared by the dehydration of benzamide with phosphorus pentoxide. It cannot be prepared from chlorobenzene and potassium cyanide owing to the low reactivity of the nuclear substituted halogen atom.

$$C_6H_5{\cdot}CONH_2 + P_2O_5 = C_6H_5CN + 2HPO_3$$

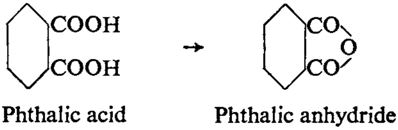
Benzonitrile is most easily prepared by treating a diazotized aniline solution with potassium cuprocyanide [$K_3Cu(CN)_4$].

$$C_6H_5N_2OH \rightarrow C_6H_5N_2CN \rightarrow C_6H_5CN + N_2$$

Dibasic Aromatic Acids

Phthalic acid (o-*benzenedicarboxylic acid*)

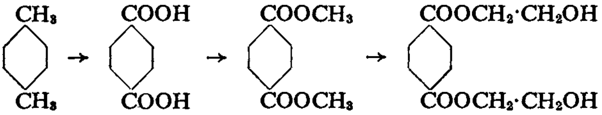
Obtained by oxidation of naphthalene, e.g. by passing naphthalene vapour mixed with air over a heated catalyst (e.g. vanadium pentoxide). Phthalic acid is a dibasic acid. Owing to the proximity of the carboxyl groups of phthalic acid, anhydride formation takes place readily.



The anhydride is now manufactured by direct oxidation of *o*-xylene.

Terephthalic acid (p-*benzene dicarboxylic acid*)

It is important as a source of polyethylene terephthalate (trade name "Terylene"). The dimethyl ester of terephthalic acid is obtained by the oxidation of *p*-xylene in the presence of methyl alcohol. The ester is caused to react with ethylene glycol and the product is polymerized by heating under reduced pressure.



The polymerization proceeds by a series of reactions involving the elimination of ethylene glycol molecules, as in the example

$$\supset COOCH_2\boxed{CH_2OH + HOCH_2}CH_2OCO \subset \rightarrow$$

$$\supset COOCH_2{\cdot}CH_2OCO \subset +$$

$$+ (CH_2OH)_2$$

$$n(HOCH_2{\cdot}CH_2OCO{\cdot}C_6H_4{\cdot}COOCH_2{\cdot}CH_2OH) \rightarrow$$

$$HOCH_2(CH_2OCO{\cdot}C_6H_4COOCH_2)_n{\cdot}CH_2OH +$$

$$+ (n - 1)(CH_2OH)_2$$

Aromatic Acids with the Carboxyl Group in the Side Chain

These acids may be prepared by the general methods used for aliphatic acids, provided a suitable compound is available as a starting material. It is often more convenient to obtain the saturated acids by the reduction of unsaturated acids, which are obtained by the condensation of aromatic aldehydes with aliphatic acid anhydrides (*Perkin* reaction).

$$2C_6H_5{\cdot}CHO + (CH_3{\cdot}CO)_2O = 2C_6H_5{\cdot}CH{:}CH{\cdot}COOH + H_2O$$

$$C_6H_5{\cdot}CH{:}CH{\cdot}COOH \xrightarrow{2H} C_6H_5CH_2{\cdot}CH_2COOH$$

The saturated side-chain acids have the properties of aliphatic acids, together with the reactions characteristic of the aromatic nucleus, such as nitration, sulphonation and halogenation.

Unsaturated Aromatic Acids

The most important unsaturated aromatic acid is cinnamic acid, which occurs free or combined in various balsams. It may be prepared from benzaldehyde by condensation with acetic anhydride in the presence of sodium acetate, or from benzal chloride by reaction with sodium acetate.

$$2C_6H_5{\cdot}CHO + (CH_3{\cdot}CO)_2O$$
$$= (C_6H_5{\cdot}CH{:}CH{\cdot}CO)_2O \rightarrow 2C_6H_5{\cdot}CH{:}CH{\cdot}COOH$$

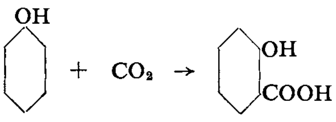
$$C_6H_5{\cdot}CHCl_2 + CH_3{\cdot}COONa$$
$$= C_6H_5{\cdot}CH{:}CH{\cdot}COONa + 2HCl$$

HYDROXY AROMATIC ACIDS

Salicylic acid

The most important of the three monohydroxy benzoic acids is the *ortho*-derivative (salicylic acid) which occurs naturally as its methyl ester, which is the chief constituent of oil of wintergreen. Salicylic acid may be prepared by the general methods, but it is usually obtained from phenol using the *Kolbe–Schmitt* reaction.

When sodium phenoxide is heated under pressure with carbon dioxide, sodium salicylate is formed. Salicylic acid is precipitated when the solution of the sodium salt is acidified. It forms colourless crystals (m.p. 159°C).



Derivatives of Salicylic Acid

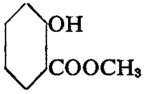
Salicylic acid forms esters derived from the carboxyl group, which are prepared by the general methods. Derivatives can also be obtained by reactions involving the phenolic hydroxyl group.

Methyl salicylate

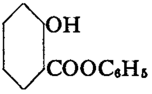
This is prepared by the action of methyl alcohol on salicylic acid in the presence of sulphuric acid.

Phenyl salicylate (salol)

This is prepared by the reaction of phenol on salicylic acid in the presence of phosphorus oxychloride or carbonyl chloride, which assists in the removal of water.



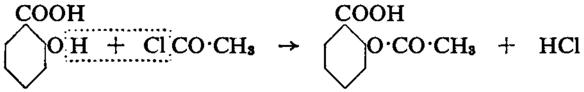
Methyl salicylate



Phenyl salicylate

Acetylsalicylic acid (aspirin)

This is prepared by the action of acetic anhydride or acetyl chloride on salicylic acid. It is purified by recrystallization.



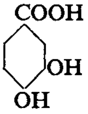
Like other phenol esters, aspirin can be hydrolysed to form acetic acid and salicylic acid.

$$CH_3{\cdot}CO{\cdot}OC_6H_4{\cdot}COOH + H_2O$$

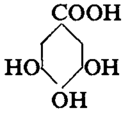
$$= CH_3{\cdot}COOH + C_6H_4OH{\cdot}COOH$$

Di- and tri-hydroxy acids

The most important di- and tri-hydroxy aromatic acids are 2:3-dihydroxybenzoic acid (protocatechuic acid) and 3:4:5-trihydroxybenzoic acid (gallic acid). Gallic acid occurs in oak galls, tea and other plant products. It is usually obtained from tannin by hydrolysis with dilute acid.



Protocatechuic acid



Gallic acid

Aromatic Side-chain Hydroxy Acids

Mandelic acid ($C_6H_5 \cdot CHOH \cdot COOH$)

This is an example of an aromatic acid containing an alcoholic hydroxyl group. The corresponding nitrile can be obtained by the regulated hydrolysis of amygdalin or synthetically from benzaldehyde.

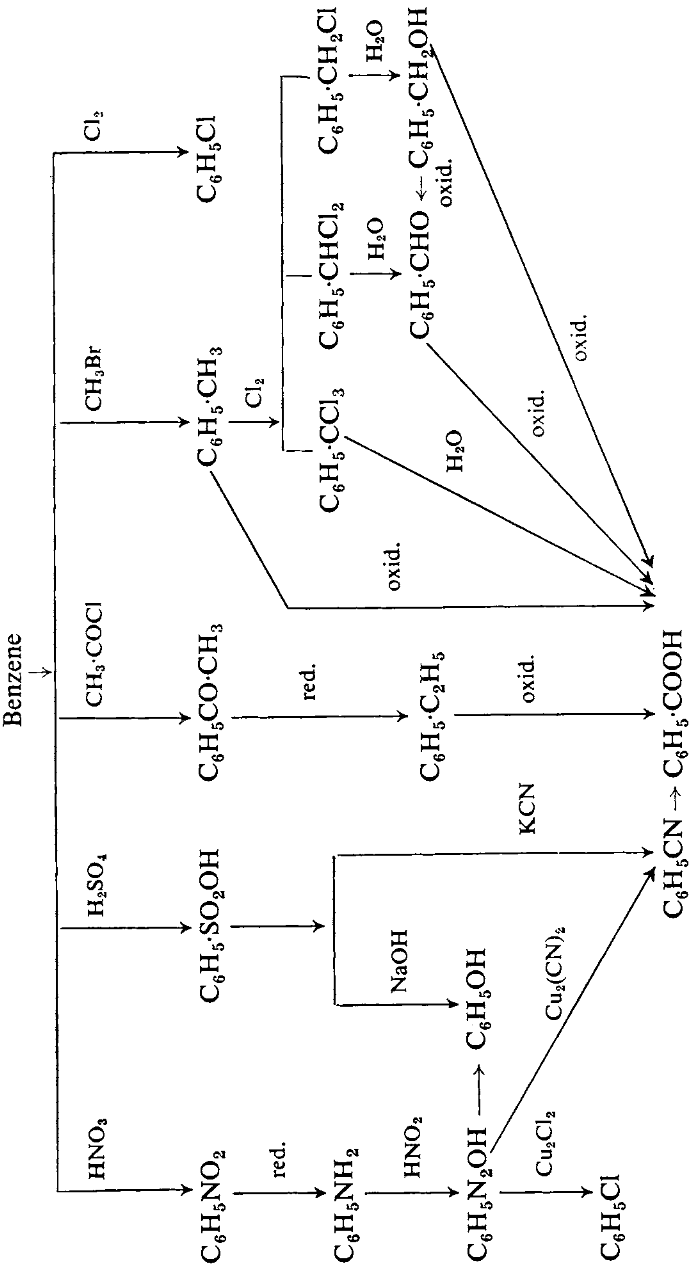
$$\underset{\text{Amygdalin}}{C_6H_5 \cdot CH \cdot (CN) - O - C_{12}H_{21}O_{10}} + 2H_2O$$

$$= \underset{\text{Mandelonitrile}}{C_6H_5 \cdot CHOH \cdot CN} + 2C_6H_{12}O_6$$

$$C_6H_5 \cdot CHO + HCN \rightarrow C_6H_5 \cdot CHOH \cdot CN$$

$$C_6H_5 \cdot CHOH \cdot CN \rightarrow C_6H_5 \cdot CHOH \cdot COOH$$

Interconversion of Aromatic Compounds



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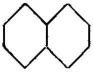
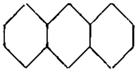
other ring systems

FUSED CARBON RING SYSTEMS

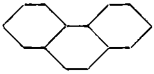
A large number of aromatic-type compounds are known whose molecules are formed by the fusion of two or more benzene rings. Naphthalene ($C_{10}H_8$), containing two benzene rings, and anthracene and phenanthrene ($C_{14}H_{10}$), containing three benzene rings, are important compounds in this group of polynuclear compounds.



Naphthalene



Anthracene

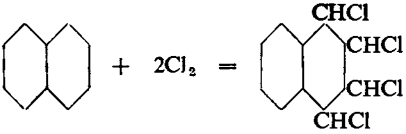


Phenanthrene

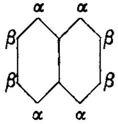
These hydrocarbons occur in coal-tar, from which naphthalene is obtained by cooling the middle and heavy oil fractions. Anthracene and phenanthrene are obtained from the anthracene oil fraction. The molecules of these two isomeric substances differ in that the fusion of the three rings is co-linearly in anthracene but not in phenanthrene.

Properties of naphthalenic compounds

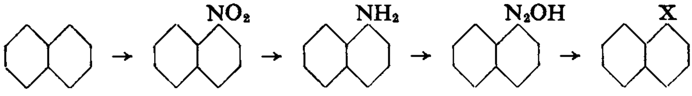
The properties of naphthalene and its derivatives are essentially those of aromatic compounds. Naphthalene reacts with nitric and sulphuric acids to form nitro and sulphonic acid derivatives; the hydroxy compounds are phenolic in character and the amines give the diazo reaction. However, naphthalene is more reactive than benzene, e.g. it combines with chlorine, without photochemical stimulus, to give the tetrachloride.



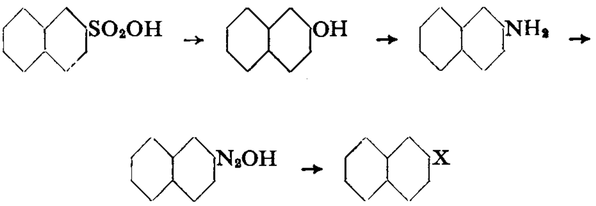
Nuclear substitution also takes place readily. Naphthalene derivatives have greater possibility of isomerism than benzene derivatives, e.g. there are two mono-substitution products of naphthalene which are called α and β.



The α-positions are much more readily attacked than the β-positions, e.g. mono-nitration is easily accomplished to give α-nitronaphthalene. This compound is readily reduced to α-naphthylamine, and other α-substitution derivatives may be prepared through the diazo reaction, following the scheme (where X may be Cl, Br, I, CN, OH).



The β-derivatives are obtained through the sulphonic acid route. The sulphonation of naphthalene at temperatures up to 50°C produces the α-sulphonic acid, but at 160°C the β-acid is the main product. The fusion of the salts of these sulphonic acids with alkali gives the α- and β-naphthols, and (unlike phenols of the benzene series) these naphthols are readily converted to the primary amines by heating under pressure with ammonium bisulphite (*Bücherer* reaction). Other substitution derivatives are prepared through the diazo reaction.



ALICYCLIC RING COMPOUNDS

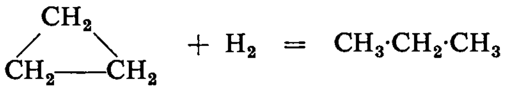
Carbon ring compounds are known which are equivalent to an aliphatic chain of carbon atoms with the two ends joined together, i.e. all the carbon–carbon bonds are single, unlike those in the benzene ring which is based on a resonating system of alternate double and single bonds. Hydrocarbon compounds of this type are called the *cycloparaffins*, and they are the parent substances of the alicyclic (aliphatic–cyclic) compounds.

Relative stability of alicyclic ring systems

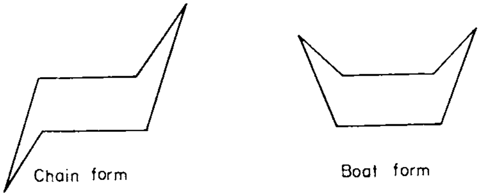
It has been shown that the natural angles between the four valencies of a carbon atom is 109° 28′. If a co-planar symmetrical ring is formed, there must be some alteration in these angles. The angles of the rings and the bending from the natural valency angles are given below.

Number of atoms in ring	*Angle*	*Deviation of valency angle from normal*	
3	60°	24° 44′	
4	90°	9° 44′	
5	108°	0° 44′	
6	120°	5° 16′	deviation in opposite direction
7	129° 26′	9° 59′	
>7	$>$ 129° 26′	$>$ 9° 59′	

It is clear that ring formation involves strain on the carbon atom corresponding to the bending of its valency directions, and this strain is reflected in the relative stabilities of the various ring systems. The five- and six-ring systems are stable, but the lower ones are less stable and the compounds with these rings are more reactive. Cyclopropane, for example, undergoes addition reactions nearly as readily as ethylene.



It would appear that compounds with large rings should be heavily strained and therefore unstable. But, in fact, large cycloparaffin rings (e.g. $C_{20}H_{40}$) are known and are quite stable, because the carbon atoms are not arranged in a plane, but form a zig-zag pattern as in the open chain compounds. Even the cyclohexane ring can exist in bent forms (i.e. strainless forms) and the existence of such forms gives rise to additional possibilities of isomerism as compared with the benzene ring system, which is invariably co-planar. The smaller cycloparaffin rings are also co-planar.



Chain form

Boat form

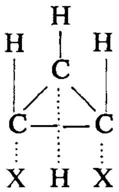
The strainless forms of the cyclohexane ring

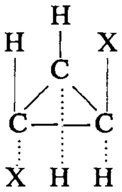
Isomerism in alicyclic compounds

Apart from the question of non-planar configurations of the alicyclic rings, geometrical isomerism and optical isomerism occur in these compounds, often giving rise to quite large numbers of isomerides.

The isomerism arises from the fact that the groups attached to the ring-forming carbon atoms are not co-planar with the ring, as in the case of benzene, but are above and below it as a consequence of the tetrahedral distribution of the carbon valencies.

The simplest case occurs with the cyclopropane derivatives of the type





where the diagram shows that there are two compounds of the same formula, differing in that the X groups are on the same side of the ring in one case and on opposite sides in the other. If X = COOH, the two compounds can be readily distinguished, for the *cis* compound forms an anhydride while the *trans* compound does not (cf. fumaric and maleic acids).

It will be noticed that while the *cis* molecule has a plane of symmetry, the *trans* molecule has no such plane, i.e. it is not superimposable on its mirror image and therefore is capable of optical resolution.

General properties of cycloparaffins

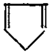
These compounds generally resemble the aliphatic rather than the aromatic compounds, e.g. nitric and sulphuric acids oxidize them and do not substitute. The various derivatives resemble the corresponding aliphatic compounds; the hydroxy compounds are alcoholic in type rather than phenolic and the amines resemble the aliphatic amines.

HETEROCYCLIC COMPOUNDS

Heterocyclic compounds are cyclic compounds which contain atoms of other elements (notably nitrogen, oxygen and sulphur) in place of carbon atoms. Compounds such as ethylene oxide and succinic anhydride contain heterocyclic rings, but the term heterocyclic is usually reserved for stable ring systems which exhibit aromatic character and contain at least one hetero atom. The most important compounds of this type possess either five- or six-membered rings. These ring systems owe their aromatic character to resonating systems based on alternate double and single bonds, as in benzene itself, but the presence of the hetero atom modifies the conditions of resonance so that the compounds show some differences in reactivities and properties from one another and from benzene.

The most important heterocyclic ring systems are:

(a) Those with five-membered rings, i.e. derived from cyclopentadiene, by the replacement of CH_2 by O, S or NH.


Cyclopentadiene

Furan

Thiophene

Pyrrole

(b) The six-membered pyridine ring is derived from benzene by the replacement of CH by N.

Pyridine

appendix 1

types of isomerism

Structural isomerism (Different structural formulae)

(a) *Distinct chemical type,* e.g. C_2H_5OH and CH_3OCH_3; $C_2H_5{\cdot}CHO$ and $CH_3{\cdot}CO{\cdot}CH_3$.
Special case: Dynamic isomerism (tautomerism), e.g. $CH_3{\cdot}CO{\cdot}CH_2{\cdot}COOC_2H_5 \rightleftarrows CH_3{\cdot}C(OH){:}CH{\cdot}COOC_2H_5$.

(b) *Same chemical type*

(1) Position isomerism, e.g. $CH_3{\cdot}CHCl{\cdot}CH_3$ and $CH_2Cl{\cdot}CH_2{\cdot}CH_3$.
(2) Chain isomerism, e.g. $CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CH_3$ and $(CH_3)_2CH{\cdot}CH_3$.
(3) Metamerism, e.g. $CH_3OC_3H_7$ and $C_2H_5OC_2H_5$; $CH_3{\cdot}COOC_2H_5$ and $C_2H_5{\cdot}COOCH_3$.
(4) Aromatic substitution isomerism, e.g. *ortho, meta, para.*

Stereoisomerism (Same structural formulae)

(1) Optical isomerism, e.g. lactic acid.
(2) Geometrical isomerism, e.g. maleic and fumaric acids.

appendix 2

the commoner named reactions

Name	*Chief reactant(s)*	*Products*	*Page*
Bücherer	Naphthol + ammonium bisulphite	Naphthylamine	239
Cannizzaro	Aromatic aldehyde	Alcohol + acid	223
Claisen	Aromatic + aliphatic aldehyde	Unsaturated aldehyde	224
Clemmensen	Aromatic ketone	Aromatic hydrocarbon	225
Fischer–Speier	Acid + alcohol	Ester	103
Fittig	Aromatic halide + sodium	Aromatic hydrocarbon	175
Friedel–Craft	Halide + aromatic hydrocarbon	Aromatic hydrocarbon	175
Hofmann	Amide + bromine	Amine	61
Kolbe	Salt of acid (electrolysis)	Hydrocarbon	14
Kolbe–Schmitt	Phenol + carbon dioxide	Phenolic acid	212
Liebermann	Phenol + nitrous acid	Nitrosophenol	212
Perkin	Aromatic aldehyde + acid anhydride	Unsaturated acid	224
Reimer–Tiemann	Phenol + chloroform	Phenolic aldehyde	214
Sandmeyer	Diazo compound + cuprous halide	Aromatic halide	200
Schotten–Baumann	Aromatic acid chloride + alcohol	Ester	230
Williamson	Alkoxide + halide	Ether	57
Würtz	Halide + sodium	Aliphatic hydrocarbon	33

appendix 3

recognition of some common functional groups

GROUP	*Reagent*	*Result*
Aliphatic		
$C{:}C$ or $C\vdots C$	Bromine water or pot. permanganate	Decolorized
C—Cl (Br, I)	Hydrolysis with pot. hydroxide	Alcohol
CH_2OH	Oxidation by dichromate + dil. sulphuric acid	Aldehyde
CHOH	Oxidation by dichromate + dil. sulphuric acid	Ketone
C_2H_5OH or $(CH_3)_2CHOH$	Iodine + sodium hydroxide	Iodoform
C—O—C	Hydrogen iodide	Alkyl halide
$—NH_2$	Chloroform + pot. hydroxide Nitrous acid Acetyl chloride	Carbylamine Nitrogen + alcohol Substituted amide
$>$NH	Nitrous acid Acetyl chloride	Nitrosamine (yellow oil) Substituted amide
CO or CHO	Hydroxylamine	Oxime
CO or CHO	Phenyl hydrazine	Phenyl hydrazone
CHO	Silver salt; Fehling's solution	Reduction
COOH	Phosphorus pentachloride	Acid chloride
COCl or $(CO)_2O$	Primary amine	Substituted amide
Ester	Potassium hydroxide	Alcohol + salt of acid
Aromatic		
Primary amine	Nitrous acid then phenol and alkali	Diazo compound Azo compound
Phenol	Diazo compound + alkali	Azo compound

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