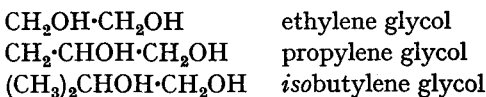


## POLYHYDRIC ALCOHOLS

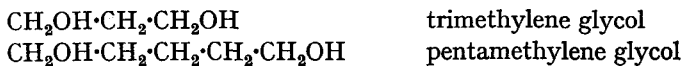
## DIHYDRIC ALCOHOLS OR GLYCOLS

DIHYDRIC alcohols are compounds containing two hydroxyl groups. They are classified as  $\alpha$ ,  $\beta$ ,  $\gamma$  . . . glycols, according to the relative positions of the two hydroxyl groups:  $\alpha$  is the 1:2 glycol;  $\beta$ , 1:3;  $\gamma$ , 1:4 . . . Although it is unusual to find a compound with two hydroxyl groups attached to the same carbon atom, ether derivatives of these 1:1 glycols are stable, *e.g.*, acetals (p. 161). The commonest glycols are the  $\alpha$ -glycols.

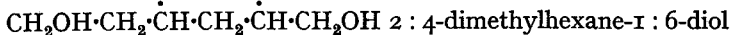
**Nomenclature.** The common names of the  $\alpha$ -glycols are derived from the corresponding olefin from which they may be prepared by direct hydroxylation, *e.g.*,



$\beta$ -,  $\gamma$ - . . . Glycols are named as the corresponding *polymethylene glycols*, *e.g.*,

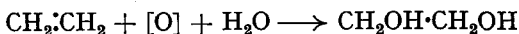


According to the I.U.P.A.C. system of nomenclature, the class suffix is *-diol*, and numbers are used to indicate the positions of side-chains and the two hydroxyl groups, *e.g.*,

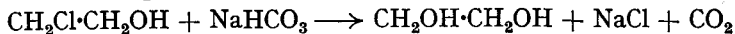
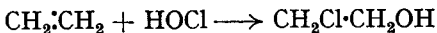


**Ethylene glycol, glycol, (ethane-1:2-diol)**,  $\text{CH}_2\text{OH}\cdot\text{CH}_2\text{OH}$ , is the simplest glycol, and may be prepared as follows:

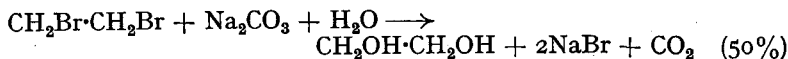
(i) By passing ethylene into cold dilute alkaline permanganate solution:



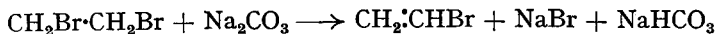
(ii) By passing ethylene into hypochlorous acid, and then hydrolysing the ethylene chlorohydrin by boiling with aqueous sodium hydrogen carbonate:



(iii) By boiling ethylene bromide with aqueous sodium carbonate:

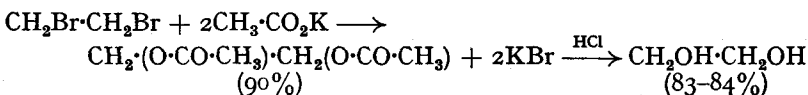


The low yield in this reaction is due to the conversion of some ethylene bromide into vinyl bromide:

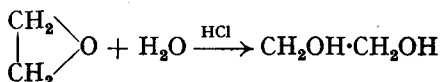


If aqueous sodium hydroxide is used instead of sodium carbonate, vinyl bromide is again obtained as a by-product. The best yield of glycol from ethylene bromide is obtained by heating ethylene bromide with potassium

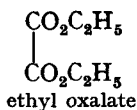
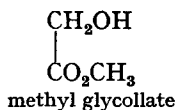
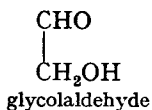
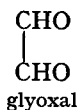
acetate in glacial acetic acid, and subsequently hydrolysing the glycol diacetate with hydrogen chloride in methanolic solution:



(iv) By treating ethylene oxide with dilute hydrochloric acid:



(v) By the reduction of any of the following compounds:

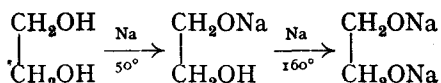


Glycol is prepared industrially by methods (ii) and (iv), and by the catalytic reduction of methyl glycolate which is produced synthetically (see p. 397).

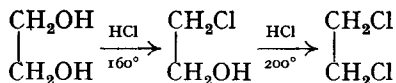
Glycol is a colourless viscous liquid, b.p.  $197^\circ$ , and has a sweet taste (the prefix *glyc-* indicates that the compound has a sweet taste: Greek *glukus*, sweet). It is miscible in all proportions with water and ethanol, but is insoluble in ether. It is widely used as a solvent and as an antifreeze agent.

The chemical reactions of glycol are those which might have been expected of a monohydric primary alcohol. One hydroxyl group, however, is almost always completely attacked before the other reacts. This is probably due to the fact that the primary alcoholic group is more reactive in glycol itself than in a compound of structure, *e.g.*,  $\text{R}\cdot\text{O}\cdot\text{CH}_2\cdot\text{CH}_2\text{OH}$ . Thus one group can be made to undergo one type of reaction and the other group another type of reaction, to give complex products.

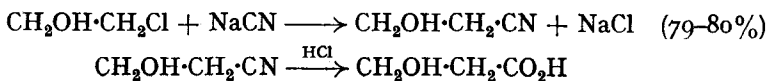
(i) When glycol is treated with sodium at  $50^\circ$ , only one alcoholic group is attacked. To obtain the disodium derivative the temperature must be raised to  $160^\circ$ :



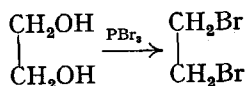
(ii) Hydrogen chloride converts glycol into ethylene chlorohydrin at  $160^\circ$ . To obtain ethylene chloride it is necessary to raise the temperature to  $200^\circ$ :



**Ethylene chlorohydrin** ( *$\beta$ -chloroethyl alcohol*, *2-chloroethanol*) is a colourless liquid, b.p.  $128.8^\circ$ . It is very useful in organic syntheses since it contains two different reactive groups; *e.g.*, by heating with aqueous sodium cyanide it may be converted into ethylene cyanohydrin, which, on hydrolysis, gives  $\beta$ -hydroxypropionic acid (p. 407):



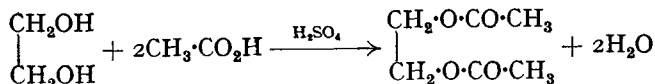
(iii) When glycol is treated with phosphorus trichloride or phosphorus tribromide, the corresponding ethylene halide is obtained:



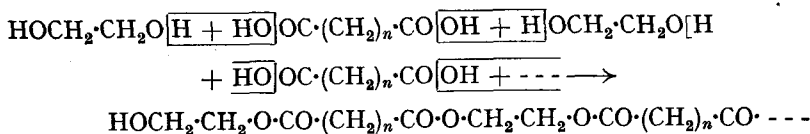
Phosphorus tri-iodide, however, produces ethylene. Ethylene iodide is formed as an intermediate, but readily eliminates iodine to form the corresponding olefin (see p. 116):



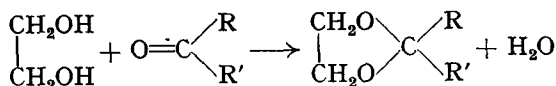
(iv) When glycol is treated with organic acids or inorganic oxygen acids, the mono- or di-esters are obtained, depending on the relative amounts of glycol and acid; e.g., glycol diacetate is obtained by heating glycol with acetic acid in the presence of a small amount of sulphuric acid as catalyst:



When glycol is heated with dibasic acids, condensation polymers are obtained:

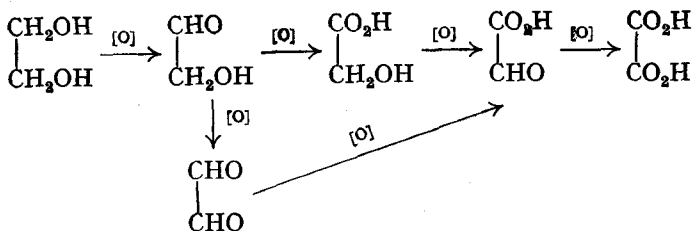


(v) Glycol condenses with aldehydes or ketones in the presence of acid to yield respectively cyclic acetals or cyclic ketals (1: 3-dioxolanes):



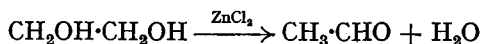
Compounds of this type are useful in sugar chemistry (see p. 440).

(vi) When glycol is oxidised with nitric acid, glycollic and oxalic acids may be readily isolated. All theoretically possible oxidation products have been isolated, but since, except for glycollic and oxalic acids, they are more readily oxidised than glycol itself, they have only been obtained in very poor yields.

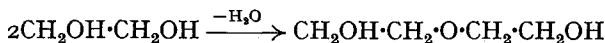


Oxidation of glycol with acid permanganate, acid dichromate, lead tetraacetate or periodic acid results in fission of the carbon-carbon bond (see p. 72).

(vii) Glycol is converted in acetaldehyde when heated with dehydrating agents, *e.g.*,

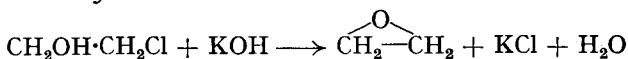


On the other hand, when glycol is heated with a dehydrating agent such as phosphoric acid, *polyethylene glycols* are obtained, *e.g.*, diethylene glycol:

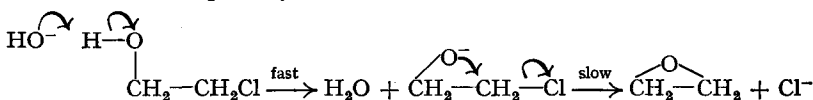


By varying the amount of phosphoric acid and the temperature, the polyethylene glycols up to decaethylene glycol can be obtained. These condensation polymers contain both the alcohol and ether functional groups: they are soluble in water (alcohol function) and are very good solvents (ether function). They are widely used as solvents for gums, resins, cellulose esters, etc.

**Ethylene oxide**,  $\begin{array}{c} \text{O} \\ \diagup \quad \diagdown \\ \text{CH}_2-\text{CH}_2 \end{array}$ . According to the I.U.P.A.C. system of nomenclature, an oxygen atom linked to two of the carbon atoms in a carbon chain is denoted by the prefix *epoxy* in all cases other than those in which a substance is named as a cyclic compound; thus ethylene oxide is *epoxyethane*. Epoxy-compounds contain the *oxiran* (*oxirane*) ring, and ethylene oxide is also known as *oxiran* (*oxirane*). Oxiran compounds are also referred to as *cyclic ethers* or *alkylene oxides*.

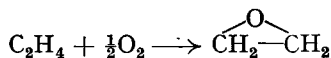


The mechanism is possibly:



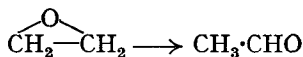
This is an example of neighbouring group participation.

This method is used industrially, but the potassium hydroxide is replaced by calcium hydroxide. A recent industrial preparation of ethylene oxide is to pass ethylene and air under pressure over a silver catalyst at 200–400°:



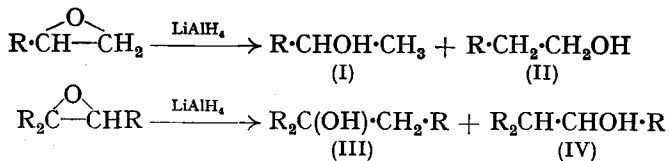
Ethylene oxide is a colourless gas, b.p. 10·7°, soluble in water, ethanol and ether.

Ethylene oxide undergoes molecular rearrangement on heating to form acetaldehyde:



It reduces ammoniacal silver nitrate solution, and is reduced to ethanol by sodium amalgam.

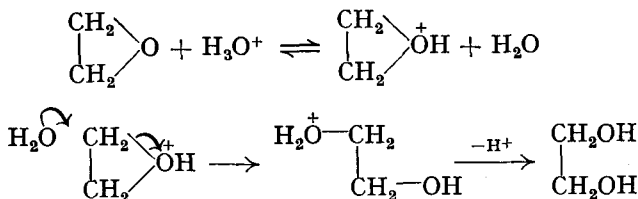
Epoxydes are reduced by lithium aluminium hydride to alcohols, unsymmetrical epoxydes giving as main product the more highly substituted alcohol; thus I and III are the main products:



Eliel *et al.* (1956), however, have shown that the reverse takes place if the reduction with lithium aluminium hydride is carried out in the presence of aluminium chloride or bromide, *i.e.*, II and IV are now the main products.

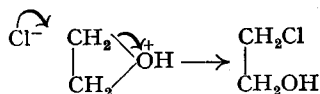
Ethylene oxide is used as an insecticide and in many laboratory syntheses.

Ethylene oxide is converted into ethylene glycol in *dilute* acid solution and into ethylene halogenohydrins with *concentrated* halogen acid solutions. Ethylene oxide also forms mono-ethers with alcohols in the presence of a small amount of acid as catalyst. The mechanisms of these reactions in acid media probably follow the same pattern, *e.g.*, with *dilute* acid (with alcohols, replace  $\text{H}_2\text{O}$  by  $\text{ROH}$ ):

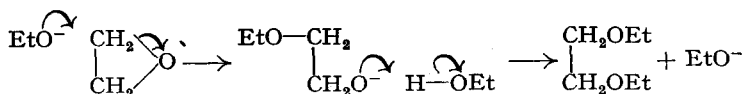


Evidence from kinetic studies on solutions of epoxides under high pressure strongly suggests that acid-catalysed hydrolysis is a bimolecular substitution of the conjugate acid (Whalley *et al.*, 1959).

With *concentrated* halogen acid:



Ethylene oxide also reacts with alcohols under the influence of *basic* catalysts. A possible mechanism is:



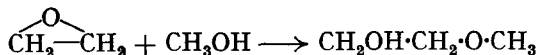
Of particular interest is the addition of hydrogen cyanide to form ethylene cyanohydrin:



Sekino (1950) has obtained ethylene cyanohydrin (yield: 95–96 per cent.) by reaction between liquefied ethylene oxide and liquefied hydrogen cyanide in the presence of a catalyst such as an alkali-earth oxide.

The structure of ethylene oxide is uncertain; it may contain "bent" bonds (see cyclopropane, p. 488).

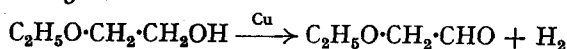
When ethylene oxide is heated with methanol under pressure, the mono-methyl ether of glycol is formed:



This is known as *methyl cellosolve*; the corresponding ethyl ether is known as *ethyl cellosolve*. Cellosolves are very useful as solvents since they contain both the alcohol and ether functional groups (*cf.* polyethylene glycols, above).

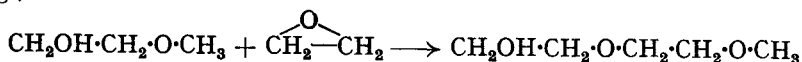
Ethyl cellosolve may be used to prepare the ethyl ether of glycolaldehyde.

The vapour of ethyl cellosolve is dehydrogenated by passing it over copper heated at about 250°:

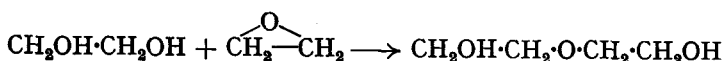


This ethyl ether derivative does not polymerise so readily as glycolaldehyde, and so may be used instead of the latter in certain syntheses. The ethyl group is finally removed by means of concentrated hydrogen bromide.

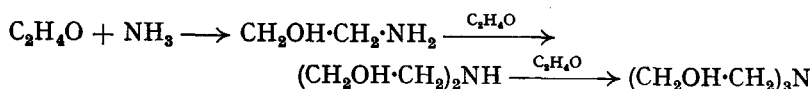
The further action of ethylene oxide on cellosolves produces *carbitols*, e.g.,



When glycol is treated with ethylene oxide, diethylene glycol is formed:

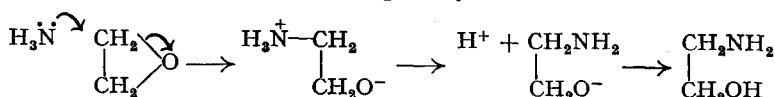


Ethylene oxide reacts with ammonia to form a mixture of three amino-alcohols which are usually referred to as the *ethanolamines*:



The ethanolamines are widely used as emulsifying agents.

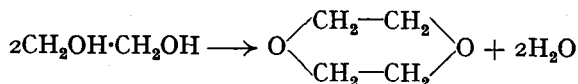
The mechanism of these reactions is possibly:



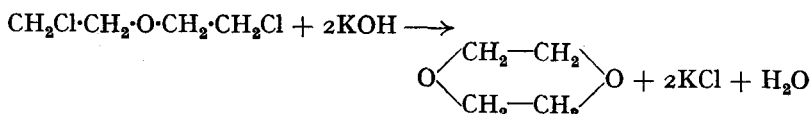
In the presence of excess of ethylene oxide, the reaction proceeds with the ethanolamine now being the amino reagent, etc.

**Dioxan** (1 : 4-*dioxan*, *diethylene dioxide*) may be prepared:

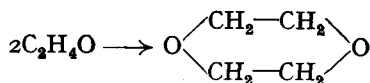
(i) By distilling glycol with a little sulphuric acid or concentrated phosphoric acid:



(ii) By heating 2 : 2'-dichlorodiethyl ether with aqueous potassium hydroxide:



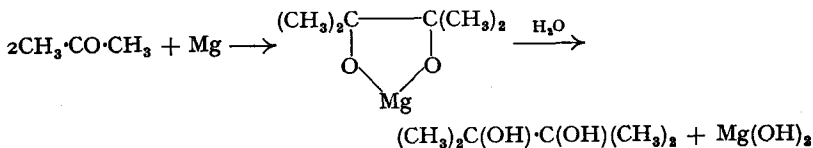
(iii) Dioxan is prepared industrially by distilling glycol with phosphoric acid (method i), and by dimerising ethylene oxide with 4 per cent. sulphuric acid:



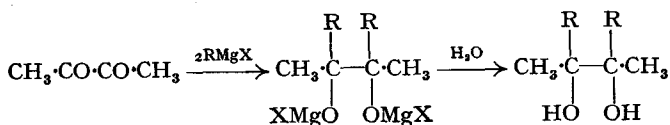
Dioxan is a colourless liquid, b.p. 101.5°, miscible in all proportions with water and most organic solvents. It is a useful solvent for cryoscopic and ebullioscopic work.

**General Methods of Preparation of 1 : 2 Glycols Other than Glycol itself**

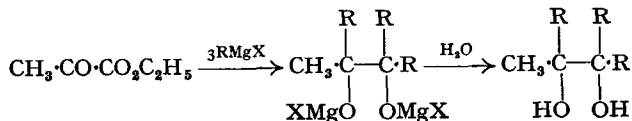
1. By the reduction of ketones with magnesium amalgam, *e.g.*, pinacol may be prepared by adding mercuric chloride in acetone to a mixture of magnesium and benzene, refluxing the mixture, and then adding water to decompose the magnesium "pinacolate" (the yield is 43-50 per cent. based on the magnesium):



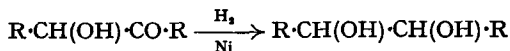
2. By the action of a Grignard reagent on  $\alpha$ -diketones, *e.g.*,



3. By the action of a Grignard reagent on  $\alpha$ -ketoic esters, *e.g.*,

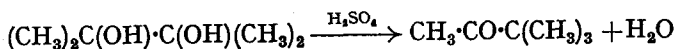


4. By the catalytic reduction of acyloins:



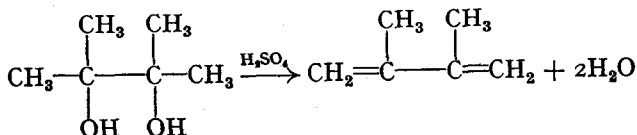
5. By hydroxylation of unsaturated compounds (see p. 72).

**Pinacol** (*tetramethylethylene glycol*, 2 : 3-*dimethylbutane-2 : 3-diol*),  $(\text{CH}_3)_2\text{C}(\text{OH})\cdot\text{C}(\text{OH})(\text{CH}_3)_2$ , is most conveniently prepared by reducing acetone with magnesium amalgam (see above). It crystallises out of solution as the hexahydrate. The most important reaction of pinacol is the rearrangement it undergoes when distilled with dilute sulphuric acid:



The *pinacol-pinacolone rearrangement* (p. 171) is general for pinacols (di-tertiary alcohols).

When sulphuric acid is used as the catalyst, some diene is formed as by-product:

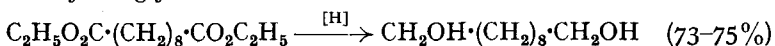


If pinacol is heated with 48 per cent. hydrobromic acid, 22-25 per cent. of pinacolone and 55-60 per cent. of diene are obtained. The yield of diene is further increased (79-86 per cent.) by passing pinacol over alumina at 420-470°.

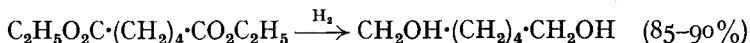
**Polymethylene Glycols**

A general method of preparing polymethylene glycols is to reduce  $\alpha\omega$ -dicarboxylic esters with sodium and ethanol or lithium aluminium hydride, or

catalytically, *e.g.*, (i) ethyl sebacate refluxed with sodium in ethanol gives decamethylene glycol:



(ii) Ethyl adipate heated with hydrogen under pressure in the presence of copper chromite as catalyst gives hexamethylene glycol:



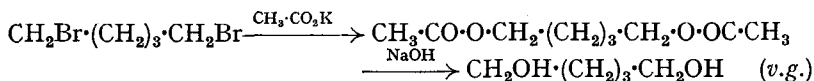
Individual polymethylene glycols are usually prepared by special methods.

**Trimethylene glycol (propane-1:3-diol)**,  $CH_2OH \cdot CH_2 \cdot CH_2OH$ , b.p.  $214^\circ$  (with decomposition), may be prepared by the hydrolysis of trimethylene bromide, or by fermentation of glycerol by *Schizomycetes* (together with *n*-butanol).

**Tetramethylene glycol (butane-1:4-diol)**,  $CH_2OH \cdot (CH_2)_2 \cdot CH_2OH$ , b.p.  $230^\circ$ , and **hexamethylene glycol (hexane-1:6-diol)**,  $CH_2OH \cdot (CH_2)_4 \cdot CH_2OH$ , m.p.  $42^\circ$ , are most conveniently prepared by reducing the corresponding  $\alpha\omega$ -dicarboxylic esters (succinic and adipic, respectively). Tetramethylene glycol is prepared industrially by hydrogenating butynediol. It is used for preparing butadiene,  $\gamma$ -butyrolactone and tetrahydrofuran.

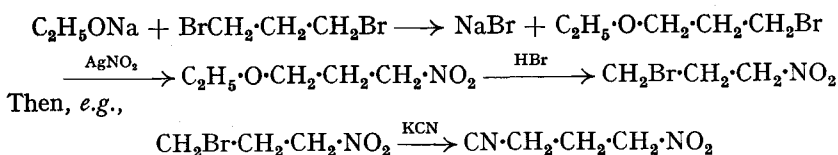
**Pentamethylene glycol (pentane-1:5-diol)**,  $CH_2OH \cdot (CH_2)_3 \cdot CH_2OH$ , b.p.  $239^\circ$ , can be obtained from pentamethylene bromide, which is obtained from piperidine by the *von Braun reaction* (p. 762).

The pentamethylene bromide is converted into the corresponding glycol by heating with potassium acetate in glacial acetic acid, and subsequently hydrolysing the diacetate with alkali (*cf.* glycol):



The four  $\alpha : \omega$ -diols  $C_{22}$ ,  $C_{24}$ ,  $C_{26}$ , and  $C_{28}$  have been isolated from carnauba wax (Murray *et al.*, 1955). These authors have also isolated seven  $\omega$ -hydroxyacids from the same source:  $C_{18}$ ,  $C_{20}$ ,  $C_{22}$ ,  $C_{24}$ ,  $C_{26}$ ,  $C_{28}$ ,  $C_{30}$ .

The polymethylene glycols are readily converted into the corresponding mono- or di-halogen derivative by halogen acid, according to the amount of halogen acid used. These polymethylene halides are useful reagents in organic syntheses since they contain two reactive halogen atoms, one or both of which may be made to undergo reaction. If the synthesis requires reaction with one halogen atom only, the most satisfactory procedure is to "protect" the other halogen atom by ether formation and subsequently decompose the ether with concentrated hydrobromic acid, *e.g.*,



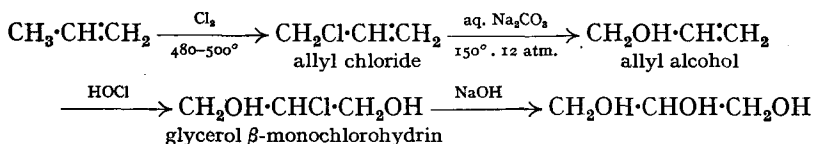
#### TRIHYDRIC ALCOHOLS

The only important trihydric alcohol is **glycerol (propane-1:2:3-triol)**,  $CH_2OH \cdot CHOH \cdot CH_2OH$ . It occurs in almost all animal and vegetable oils and fats as the glyceryl esters of mainly palmitic, stearic and oleic acids (see below).

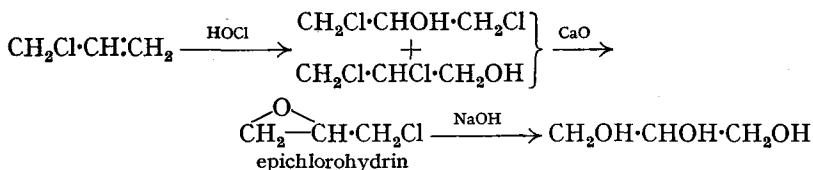
Glycerol is obtained in large quantities as a by-product in the manufacture



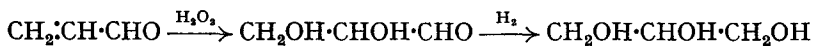
of soap, and this is still a commercial source of glycerol (see below). Another method of preparing glycerol is the fermentation of glucose to which sodium sulphite has been added (the yield is 20–25 per cent.). Glycerol is now also prepared synthetically as follows:



An alternative route that is used is:



A new process is to add osmium tetroxide and hydrogen peroxide to acraldehyde; this produces glycerinaldehyde which is then catalytically hydrogenated to glycerol.

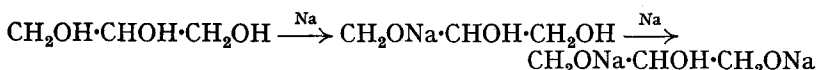


Glycerol is a colourless, syrupy liquid, b.p.  $290^\circ$  (with some decomposition). It is miscible with water and ethanol in all proportions, but is almost insoluble in ether. It is used as an antifreeze, for making explosives, and, because of its hygroscopic properties, as a moistening agent for tobacco, shaving soaps, etc.

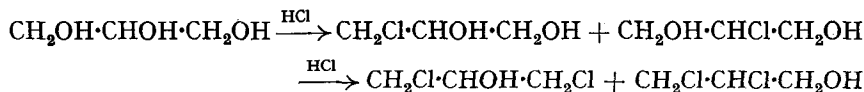
Glycerol contains one secondary and two primary alcoholic groups, and it undergoes many of the reactions to be expected of these types of alcohols.

The carbon atoms in glycerol are indicated as shown:  $\overset{\alpha}{\text{C}}\text{H}_2\text{OH} \cdot \overset{\beta}{\text{C}}\text{HOH} \cdot \overset{\alpha \text{ or } \gamma}{\text{C}}\text{H}_2\text{OH}$ .

(i) When glycerol is treated with sodium, one  $\alpha$ -hydroxyl group is readily attacked, and the other  $\alpha$ -group less readily; the  $\beta$ -hydroxyl group is not attacked at all:



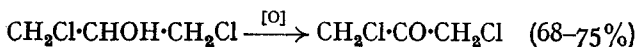
(ii) On passing hydrogen chloride into glycerol at  $110^\circ$  until there is the theoretical increase in weight corresponding to the esterification of one hydroxyl group, both  $\alpha$ - and  $\beta$ -glycerol monochlorohydrin are formed, the former predominating (66 per cent.). Continued action of hydrogen chloride at  $110^\circ$ , using 25 per cent. of acid in excess required by theory for the esterification of two hydroxyl groups, produces glycerol  $\alpha$ :  $\alpha'$ -dichlorohydrin ( $\alpha$ -dichlorohydrin) and glycerol  $\alpha$ :  $\beta$ -dichlorohydrin ( $\beta$ -dichlorohydrin), the former predominating (55–57 per cent.); some other products are also formed:



When either of these dichlorohydrins or glycerol itself is treated with phosphorus pentachloride, glycerol trichlorohydrin (1:2:3-trichloro-

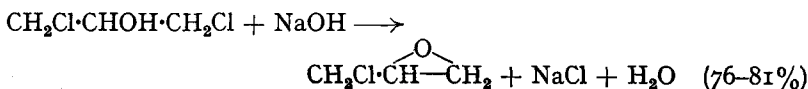
propane) is obtained. This is a liquid, b.p. 156–158°, which smells like chloroform.

When glycerol  $\alpha$  :  $\alpha'$ -dichlorohydrin is oxidised with sodium dichromate-sulphuric acid mixture, *s*-dichloroacetone (1 : 3-dichloropropan-2-one) is obtained:



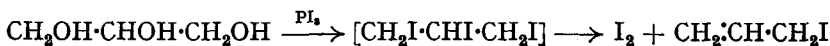
It is a solid, m.p. 45°, and is a useful starting material in many syntheses.

When glycerol  $\alpha$  :  $\alpha'$ -dichlorohydrin is treated with powdered sodium hydroxide in ether solution, **epichlorohydrin** (3-chloro-1 : 2-epoxypropane) is obtained (see p. 250 for the mechanism):

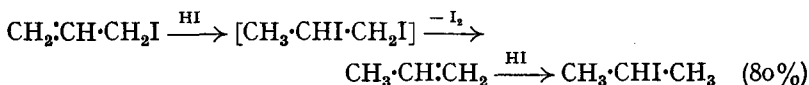


Epichlorohydrin is also obtained by distilling an alkaline solution of the  $\alpha$ -dichlorohydrin under reduced pressure (yield: 90 per cent.). It is a liquid, b.p. 117°, and smells like chloroform.

Hydrogen bromide and the phosphorus bromides react with glycerol in the same way as the corresponding chlorine compounds, but the analogous iodine compounds behave differently, the products depending on the amount of reagent used. When glycerol is heated with a *small* amount of hydrogen iodide or phosphorus tri-iodide, *allyl iodide* is the main product:

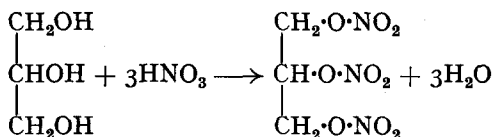


When a *large* amount of phosphorus tri-iodide is used, the main product is *isopropyl iodide*, which is formed by the following sequence of reactions from the allyl iodide first formed:



(iii) When glycerol is treated with monocarboxylic acids, esters are obtained which may be mono-, di- or tri-esters, according to the amount of acid used; high temperature and an excess of acid favour the formation of the tri-ester (see the glycerides, below).

**Nitroglycerine** is manufactured by adding glycerol in a thin stream to a cold mixture of concentrated nitric and sulphuric acids:



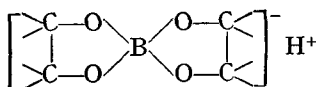
Nitroglycerine is an ester, not a nitro-compound; it is *glyceryl trinitrate*. The incorrect name appears to have been introduced due to the use of "mixed acid" which is normally used for nitration (see p. 553).

Nitroglycerine is a poisonous, colourless, oily liquid, insoluble in water. It usually burns quietly when ignited, but when heated, rapidly struck or detonated, it explodes violently. Nobel (1867) found that nitroglycerine could be stabilised by absorbing it in kieselguhr. This was *dynamite*, which is now, however, usually manufactured by using sawdust as the absorbent, and adding solid ammonium nitrate. *Blasting gelatin* or *gelignite* is made by mixing nitroglycerine with gun-cotton (cellulose nitrate).

The smokeless powder, *cordite*, is a mixture of nitroglycerine, gun-cotton and vaseline.

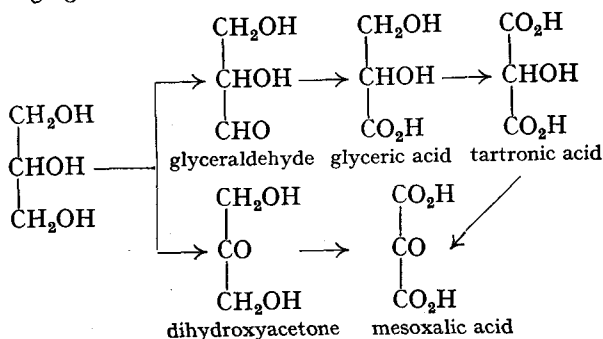
When heated with formic acid or oxalic acid at  $260^\circ$ , glycerol is converted into allyl alcohol (p. 267). With dibasic acids, glycerol forms condensation polymers known as *alkyd resins*, the commonest of which is glyptal, formed by heating glycerol with phthalic anhydride.

When boric acid is added to an aqueous solution of glycerol, a complex is produced which has a higher electrical conductivity than boric acid itself, *i.e.*, is a stronger acid. This complex is believed to be a borospiranic acid in which the two rings attached to the boron atom are perpendicular to each other (hence name spiran):

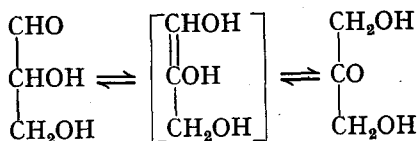


Glycol does not increase the conductivity of boric acid. It is therefore believed that the two hydroxyl groups in glycol are in the *trans*-position, whereas the hydroxyl groups in glycerol are in the *cis*-position.

(iv) Glycerol can theoretically give rise to a large variety of oxidation products. The actual product obtained in practice depends on the nature of the oxidising agent used:



Dilute nitric acid converts glycerol into glyceric and tartronic acids; concentrated nitric acid oxidises it to mainly glyceric acid (80 per cent.); bismuth nitrate produces mainly mesoxalic acid. Bromine water, sodium hypobromite and Fenton's reagent (hydrogen peroxide and ferrous sulphate) oxidise glycerol to a mixture of glyceraldehyde (predominantly) and dihydroxyacetone; this mixture is known as *glycerose*. These two compounds are interconvertible in the presence of anhydrous pyridine, this being known as the *Lobry de Bruyn-van Ekenstein rearrangement* (see also p. 450):

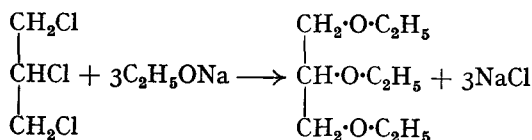


(v) When heated with potassium hydrogen sulphate, glycerol is dehydrated to acraldehyde:

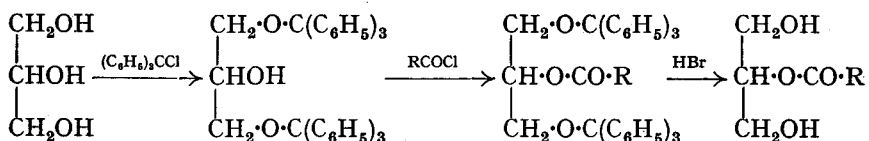


(vi) The mixed ethers of glycerol may be conveniently prepared by the action of sodium alkoxide on a glycerol chlorohydrin, *e.g.*, *triethylin*, the

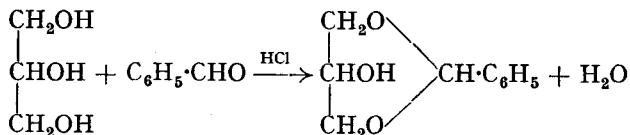
triethyl ether of glycerol, is prepared by heating 1 : 2 : 3-trichloropropane with sodium ethoxide:



Helferich and co-workers (1923) found that triphenylmethyl chloride (trityl chloride),  $(\text{C}_6\text{H}_5)_3\text{CCl}$ , usually formed ethers only with primary alcoholic groups. Thus the  $\alpha$ -mono- and the  $\alpha$ : $\alpha'$ -di-triphenylmethyl (trityl) ethers of glycerol can be prepared, the latter offering a means of preparing  $\beta$ -esters of glycerol, *e.g.*,



A better means of obtaining the  $\beta$ -ester is to protect the  $\alpha\alpha'$ -hydroxyl groups by cyclic ether formation with benzaldehyde (Bergmann and Carter 1930). This acetal-like compound is formed when glycerol and benzaldehyde are heated together, or the cool mixture treated with hydrogen chloride:

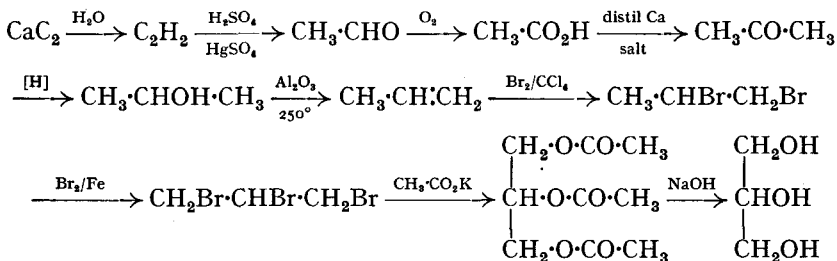


(vii) Glycerol can be fermented to produce a variety of compounds, *e.g.*, propionic acid, succinic acid, acetic acid, *n*-butanol, trimethylene glycol, lactic acid, *n*-butyric acid, etc. Fermentation by means of a particular micro-organism usually produces more than one compound, *e.g.*, propionic acid bacteria produce propionic acid, succinic acid and acetic acid.

**Structure of glycerol.** All the chemical reactions of glycerol indicate that its structure is  $\text{CH}_2\text{OH}\cdot\text{CHOH}\cdot\text{CH}_2\text{OH}$ , and this is supported by many syntheses, *e.g.*,

(i) From propylene (see above).

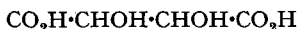
(ii) The following absolute synthesis:



### Polyhydric Alcohols

**Tetrahydric alcohols.** Erythritol,  $\text{CH}_2\text{OH}\cdot\text{CHOH}\cdot\text{CHOH}\cdot\text{CH}_2\text{OH}$ , exists in three forms: dextrorotatory erythritol, m.p.  $88^\circ$ ; laevorotatory erythritol, m.p.

88°; *meso*-erythritol, m.p. 121.5°. The *meso*-form occurs in certain lichens and seaweeds. All three forms may be oxidised to tartaric acid,



**Pentaerythritol**,  $\text{C}(\text{CH}_2\text{OH})_4$ , is prepared by the condensation of formaldehyde with acetaldehyde (see p. 166).

**Pentahydric alcohols** (*pentitols*). There are four pentitols with the structure  $\text{CH}_2\text{OH}\cdot(\text{CHOH})_3\cdot\text{CH}_2\text{OH}$ , which may be prepared by reducing the corresponding aldopentoses (see p. 437). Two are optically active, forming a pair of enantiomorphs—*D*- and *L*-arabitol—and the other two are optically inactive, existing as *meso* forms—adonitol and xylitol.

<i>Aldopentose</i>	<i>Pentitol</i>
<i>D</i> - and <i>L</i> -ribose	adonitol (ribitol)
<i>D</i> - and <i>L</i> -xylose	xylitol
<i>D</i> -arabinose } <i>D</i> -lyxose }	<i>D</i> -arabitol ( <i>D</i> -lyxitol)
<i>L</i> -arabinose } <i>L</i> -lyxose }	<i>L</i> -arabitol ( <i>L</i> -lyxitol)

Adonitol and *D*-arabitol occur naturally.

*D*-Rhamnitol,  $\text{CH}_3\cdot(\text{CHOH})_4\cdot\text{CH}_2\text{OH}$ , may be prepared by reducing the corresponding deoxyhexose, *D*-rhamnose.

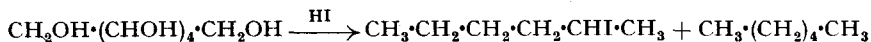
**Hexahydric Alcohols** (*hexitols*). There are ten hexitols with the structure  $\text{CH}_2\text{OH}\cdot(\text{CHOH})_4\cdot\text{CH}_2\text{OH}$ , which may be prepared by reducing the corresponding aldohexoses (see p. 438). Eight exist as four pairs of enantiomorphs, and the remaining two as *meso* forms.

<i>Aldohexose</i>	<i>Hexitol</i>
<i>D</i> -glucose and <i>L</i> -gulose	<i>D</i> -sorbitol ( <i>D</i> -glucitol)
<i>L</i> -glucose and <i>D</i> -gulose	<i>L</i> -sorbitol ( <i>L</i> -glucitol)
<i>D</i> -mannose	<i>D</i> -mannitol
<i>L</i> -mannose	<i>L</i> -mannitol
<i>D</i> -idose	<i>D</i> -iditol
<i>L</i> -idose	<i>L</i> -iditol
<i>D</i> -talose and <i>D</i> -altrose	<i>D</i> -talitol
<i>L</i> -talose and <i>L</i> -altrose	<i>L</i> -talitol
<i>D</i> - and <i>L</i> -galactose	dulcitol
<i>D</i> - and <i>L</i> -allose	allodulcitol (allitol)

*D*-Sorbitol, *D*-mannitol and dulcitol occur naturally.

**Rhamnohexitol**,  $\text{CH}_3\cdot(\text{CHOH})_5\cdot\text{CH}_2\text{OH}$ , is prepared by reducing the corresponding aldose, rhamnohexose.

The polyhydric alcohols chemically resemble glycerol in many ways. When heated with concentrated hydriodic acid or with a mixture of red phosphorus, iodine and water, they are converted into the corresponding 2-iodoparaffin and paraffin; *e.g.*, any hexitol gives a mixture of 2-iodohexane and *n*-hexane when heated with hydriodic acid (see also the sugars, p. 438):

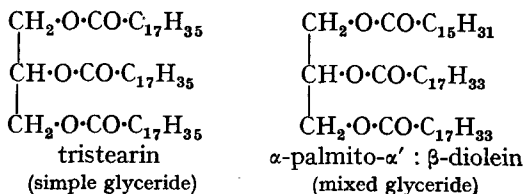


#### OILS, FATS AND WAXES

Oils and fats are compounds of glycerol and various organic acids, *i.e.*, they are glyceryl esters or *glycerides*. Oils, which are liquids at ordinary temperatures, contain a larger proportion of unsaturated acids than do the fats, which are solids at ordinary temperatures. The acids present in the glycerides are almost exclusively straight-chain acids, and almost always contain an even number of carbon atoms. The chief saturated acids are lauric, myristic, palmitic and stearic (see p. 186). The chief unsaturated acids are oleic, linoleic and linolenic (see p. 285). Palmitic acid is the most abundant of the saturated acids, and acids containing less than eighteen carbon atoms are usually present only as minor constituents, but

sometimes they are present in appreciable amounts in insect waxes and marine fats.

Glycerides are named according to the nature of the acids present, the suffix *-ic* of the common name of the acid being changed into *-in*. Glycerides are said to be "simple" when all the acids are the same, and "mixed" when the acids are different:



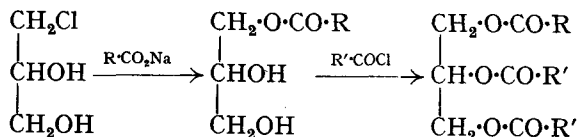
It is still not certain whether simple glycerides occur naturally; if they do, they are definitely not as common as the mixed glycerides.

According to Desnuelle *et al.* (1959), the structure of natural glycerides is not random; the position of the acid residue depends on the chain-length of the unsaturated acids and on the degree of their unsaturation. In vegetable oils the saturated acids occur mainly at the 1- and 3-positions and unsaturated acids at the 2-position. In animal fats the distribution is not so rigid.

**Synthesis of glycerides.** Simple triglycerides are readily prepared from glycerol and an excess of acyl chloride, or from 1:2:3-tribromopropane and the silver or potassium salts of the fatty acids.

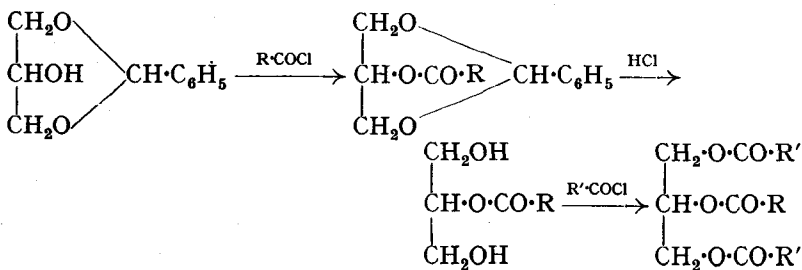
Mixed triglycerides are far more difficult to prepare. A number of methods have been developed, *e.g.*,

- (i) The sodium salt of an acid is heated with glycerol monochlorohydrin, and the monoester so formed is acylated:

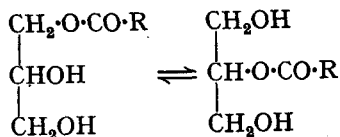


The preparation of 1-monoglycerides has been improved by Hartman (1960). The 2- and 3-positions in glycerol are protected by the formation of the isopropylidene derivative (*cf.* (ii) below; see also p. 440), and the protecting group is removed by boric acid in hot 2-methoxyethanol.

- (ii) 1:3-Benzylidene-glycerol is treated with an acid chloride, the benzaldehyde residue is removed by hydrolysis, and the monoester so formed is then further acylated:



In both methods (i) and (ii) there is, however, still difficulty in knowing with certainty the position of the acyl group introduced first, since the acyl group tends to migrate in the monoester, producing the following equilibrium:



This isomerisation has been shown to be intramolecular. When 2-palmitin was isomerised to the 1-isomer in alcohol containing glycerol labelled with  $^{14}\text{C}$ , no  $^{14}\text{C}$  was found in the ester (Doerschuk, 1952). Martin (1953) has shown that perchloric acid rapidly catalyses the change of 1- or 2-monoglycerides to the equilibrium mixture containing 90–92 per cent. of the 1-isomer. Isomerisation of aliphatic 2-monoglycerides to the corresponding 1-isomer may even occur slowly in the solid state (Brokaw *et al.*, 1955).

An interesting difference between the 1- and 2-isomers is that the former form urea inclusion compounds (p. 387) whereas the latter do not (Aylward *et al.*, 1956).

**Analysis of oils and fats.** Oils and fats are characterised by means of physical as well as chemical tests. The usual physical constants that are determined are melting point, solidifying point, specific gravity and refractive index.

The chemical tests give an indication of the type of fatty acids present in the oil or fat.

The **acid value**, which is the number of milligrams of potassium hydroxide required to neutralise 1 gram of the oil or fat, indicates the amount of free acid present.

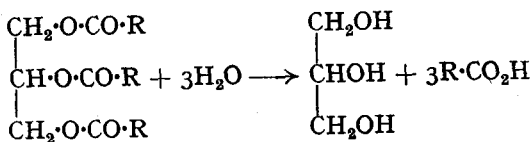
The **saponification value** is the number of milligrams of potassium hydroxide required to neutralise the fatty acids resulting from the complete hydrolysis of 1 gram of the oil or fat.

The **iodine value**, which is the number of grams of iodine that combine with 100 grams of oil or fat, gives the degree of unsaturation of the acids in the substance. Several methods are used for determining the iodine value. In *Hubl's method*, a carbon tetrachloride solution of the substance is treated with a solution of iodine and mercuric chloride in ethanol; in *Wijs' method*, iodine monochloride in glacial acetic acid is used. Another method is to use a solution of glacial acetic acid containing pyridine, bromine and concentrated sulphuric acid (*Dam's solution*).

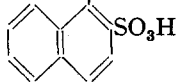
The **Reichert-Meissl value**, which is the number of ml. of 0.1N-potassium hydroxide required to neutralise the distillate of 5 grams of hydrolysed fat, indicates the amount of steam-volatile fatty acids (*i.e.*, acids up to lauric) present in the substance.

The **acetyl value**, which is the number of milligrams of potassium hydroxide required to neutralise the acetic acid obtained when 1 gram of an acetylated oil or fat is hydrolysed, indicates the number of free hydroxyl groups present in the substance.

**Preparation of glycerol from oils and fats.** When an oil or fat is hydrolysed by superheated steam, glycerol and the free fatty acids are obtained:



Alternatively, the hydrolysis may be carried out by means of very dilute sulphuric acid in the presence of a catalyst, *e.g.*, 2-( $\beta$ -sulphonaphthyl)-stearic acid. This method is rapidly gaining industrial importance. The free fatty acids are used in the manufacture of candles.



If an oil or fat is saponified, *i.e.*, hydrolysed with alkali, soaps are obtained. Any metallic salt of a fatty acid is a soap, but the term soap is usually applied to the water-soluble salts since only these have detergent properties. The saturated fats give hard soaps whereas the unsaturated fats, *i.e.*, the oils, give soft soaps. Ordinary soap is a mixture of the sodium salts of the even fatty acids from octoic to stearic. The sodium salts of a given oil or fat are harder and less soluble than the corresponding potassium salts. Thus soft soaps are usually the potassium salts, particularly when they are derived from oils.

The preparation of soaps and glycerol is carried out by saponifying the oil or fat with sodium hydroxide solution, and then adding sodium chloride to "salt out" the soap, *i.e.*, help the soap to separate out by causing it to rise to the top of the liquid. The lower aqueous layer is run off and glycerol is obtained from it. The soap is again heated with sodium hydroxide solution to ensure complete saponification, and allowed to separate out to the top. The lower layer is run off, and the soap is then boiled with water and allowed to set.

Glycerol is obtained from the aqueous layer by neutralising the excess of sodium hydroxide with sulphuric acid, and evaporating *in vacuo* until the liquid contains about 50 per cent. glycerol. Sodium chloride (which was added for salting out the soap) is precipitated. The liquid is filtered and the sodium chloride is used again. The filtrate is concentrated further by evaporation *in vacuo* until the glycerol content is about 85 per cent. Glycerol is then obtained in over 99 per cent. purity by steam distillation *in vacuo*. A more recent method of purification of crude glycerol is by means of ion-exchange resins.

**Hardening of oils.** Glycerides of the unsaturated acids are liquid at room temperature and so are unsuitable for edible fats. By converting the unsaturated acids into saturated acids, oils are changed into fats. This introduction of hydrogen is known as the hydrogenation or *hardening of oils*, and is carried out by the Sabatier-Senderens reduction (p. 38). The oil is heated to 150–200° and hydrogen is passed in, under pressure, in the presence of a finely divided nickel catalyst. The nickel is recovered by filtration. In the hydrogenation process only a proportion of the unsaturated acids are converted into the saturated acids, otherwise a fat as hard as tallow would be obtained; the hydrogenation is carried out until a fat of the desired consistency is obtained.

**Synthetic fats.** Truly synthetic fats would be those prepared from synthetic glycerol and synthetic fatty acids. The cost of synthetic glycerol is so high that synthetic fats are not, so far, prepared industrially since they cannot compete, in price, with natural fats. During the war (1939–1945), however, synthetic fats were prepared in Germany by three methods:

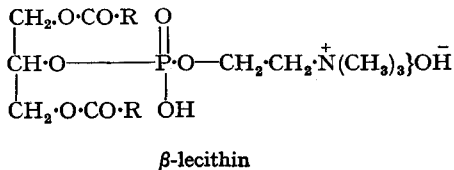
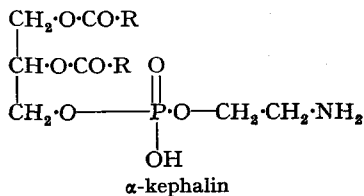
(i) Glycerol and fatty acids, both of which are obtained as by-products from natural fats, were recombined.

(ii) Fatty acids were esterified with alcohols other than glycerol, *e.g.*, ethanol. These ethyl esters hydrolyse fairly easily, giving rise to an unpleasant taste.

(iii) Acids, obtained by the oxidation of hydrocarbons (p. 175), were esterified with glycerol in the presence of tin or zinc, and under reduced pressure; under these conditions the excess glycerol and the water formed during the reaction were removed.



**Phosphatides (phospholipids).** These occur in all animal and vegetable cells, and are glycerides in which one organic acid residue, the  $\alpha$ - or  $\beta$ -, is replaced by a group containing phosphoric acid and a base. When the base is **cholamine**,  $\text{CH}_2\cdot\text{OH}\cdot\text{CH}_2\cdot\text{NH}_2$ , the phosphatide is known as a **kephalin**; when the base is **choline**,  $\text{CH}_2\text{OH}\cdot\text{CH}_2\cdot\overset{+}{\text{N}}(\text{CH}_3)_3\text{OH}^-$ , the phosphatide is known as a **lecithin**, *e.g.*,



It is quite likely that both kephalins and lecithins have a betaine structure (see p. 325).

Only a few monocarboxylic acids have been isolated from phosphatides: stearic, oleic, linoleic and arachidonic from kephalins, and palmitic, stearic, oleic, linoleic, linolenic and arachidonic from lecithins. Enzymic studies of phospholipids have shown that saturated acids predominate at the 1-position and unsaturated acids at the 2-position (Hanahan *et al.*, 1960).

**Drying oils.** These are oils which, on exposure to air, change into hard solids, *e.g.*, linseed oil. All drying oils contain a large proportion of the unsaturated acids linoleic and linolenic, and it is this "drying" property which makes these oils valuable in the paint industry. The mechanism of drying is not known. It appears to be a complicated process involving oxidation, polymerisation and colloidal gel formation, and it has been found to be catalysed by various metallic oxides, particularly lead monoxide.

**Waxes.** These are esters of the higher homologues of both the fatty acids and monohydric alcohols, *e.g.*,

beeswax	myricyl palmitate	$\text{C}_{15}\text{H}_{31}\cdot\text{CO}_2\text{C}_{30}\text{H}_{61}$
spermaceti	cetyl palmitate	$\text{C}_{15}\text{H}_{31}\cdot\text{CO}_2\text{C}_{16}\text{H}_{33}$
carnauba wax	myricyl cerotate	$\text{C}_{25}\text{H}_{51}\cdot\text{CO}_2\text{C}_{30}\text{H}_{61}$

Some waxes are also esters of cholesterol, *e.g.*, cholesteryl esters occur in wool-wax.

### QUESTIONS

- Name the compounds and state the conditions under which they are formed when glycol is treated with:—(a) Na, (b) HBr, (c)  $\text{PCl}_5$ , (d)  $\text{PI}_3$ , (e)  $\text{AcCl}$ , (f)  $\text{CH}_3\cdot\text{CHO}$ , (g)  $\text{CH}_3\cdot\text{CO}\cdot\text{CH}_3$ , (h)  $\text{H}_3\text{PO}_4$ , (i)  $\text{HNO}_3$ , (j)  $\text{KMnO}_4$ , (k)  $\text{ZnCl}_2$ , (l)  $\text{C}_6\text{H}_5\cdot\text{NCO}$ .
- Name the compounds and state the conditions under which they are formed when glycerol is treated with:—(a) Na, (b) HCl, (c)  $\text{PCl}_5$ , (d)  $\text{PI}_3$ , (e)  $\text{Ac}_2\text{O}$ , (f)  $\text{HNO}_3$ , (g)  $\text{H}\cdot\text{CO}_2\text{H}$ , (h)  $(\text{CO}_2\text{H})_2$ , (i)  $\text{H}_3\text{BO}_3$ , (j)  $\text{Br}_2$ , (k)  $\text{KHSO}_4$ , (l)  $\text{C}_6\text{H}_5\cdot\text{CHO}$ .
- How are glycol and glycerol prepared (i) in the laboratory; (ii) industrially?
- By means of equations show how you would convert glycerol into:—(a) *n*-PrOH, (b) dihydroxyacetone, (c) diallyl ether, (d) epichlorohydrin, (e)  $\beta$ -ketoglutaric acid.
- Show by means of equations how you would prepare:—(a)  $\text{CH}_2\text{OH}\cdot\text{CH}_2\cdot\text{OMe}$ , (b)  $\text{CH}_2(\text{OEt})\cdot\text{CH}_2\cdot\text{OEt}$ , (c)  $\text{CH}_2(\text{OAc})\cdot\text{CH}_2\cdot\text{O}\cdot\text{CO}\cdot\text{C}_2\text{H}_5$ , (d)  $\text{C}_2\text{H}_4\text{O}$ , (e)  $\text{MeO}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{O}\cdot\text{CH}_2\cdot\text{CH}_2\text{OH}$ , (f)  $\text{O} \begin{array}{c} \text{CH}_2\text{---CH}_2 \\ \diagdown \quad \diagup \\ \text{CH}_2\text{---CH}_2 \end{array} \text{O}$ , (g)  $\text{Et}_2\text{C}(\text{OH})\cdot\text{C}(\text{OH})\text{Et}_2$ , (h)  $\text{CH}_2\text{OH}\cdot(\text{CH}_2)_n\cdot\text{CH}_2\text{OH}$ , where *n* = 1, 2, 3 and 4, respectively, (i)  $\text{CH}_2\text{OH}\cdot(\text{CH}_2)_6\cdot\text{CH}_2\cdot\text{CO}_2\text{H}$ , (j)  $\text{CH}_2\text{OMe}\cdot\text{CHOMe}\cdot\text{CH}_2\text{OMe}$ , (k)  $\text{CH}_2\text{OH}\cdot\text{CHOAc}\cdot\text{CH}_2\text{OH}$ .
- Define and give examples of:—(a) oils, fats and waxes, (b) acid value, (c) saponification value, (d) iodine value, (e) Reichert-Meissl value, (f) acetyl value, (g) soap, (h) hardening of oils, (i) kephalins, (j) lecithins, (k) drying oils.
- Show how you would distinguish between:
  - a mineral oil and a vegetable oil;
  - triolein and tristearin.

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CHAPTER XII

UNSATURATED ALCOHOLS, ETHERS, CARBONYL  
COMPOUNDS AND ACIDS

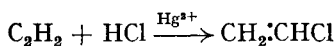
UNSATURATED ALCOHOLS

THE simplest unsaturated alcohol is **vinyl alcohol**,  $\text{CH}_2\text{:CHOH}$ . This is, however, unknown; all attempts to prepare it result in the formation of acetaldehyde (together with a small amount of ethylene oxide), *e.g.*, vinyl bromide on treatment with silver oxide in boiling water gives acetaldehyde:

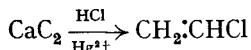


It thus appears that the group  $-\text{CH}\text{:CHOH}$  is unstable. It should, however, be noted that this group is unstable only when the  $\text{CHOH}$  group is at the end of a chain; when it occurs in the chain, *i.e.*, as  $-\text{CH}\text{:C}(\text{OH})-$ , it is stable (*cf.* keto-enol tautomerism, p. 220).

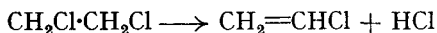
Although vinyl alcohol itself is unknown, many of its derivatives have been prepared, and are quite stable. These derivatives may be prepared by the interaction between acetylene and the other reactant in the presence of a suitable catalyst (see also p. 93); *e.g.*, *vinyl chloride*:



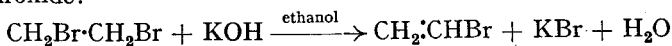
Vinyl chloride may also be prepared directly by the action of concentrated hydrochloric acid on calcium carbide in the presence of mercuric ions as catalyst:



Vinyl chloride is manufactured by the thermal decomposition of ethylene chloride at 600–650°:

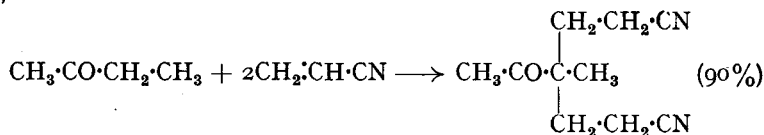


*Vinyl chloride* and *bromide* are conveniently prepared in the laboratory by heating ethylene chloride and bromide, respectively, with ethanolic potassium hydroxide:



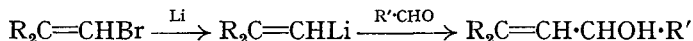
Many of the vinyl compounds are used to make plastics. *Vinyon*, which is a thermoplastic, is a copolymer of vinyl chloride and vinyl acetate. Its main use at the moment is the manufacture of industrial filter cloth which is very resistant to the action of acids and alkalis, and which has great strength both wet and dry.

**Vinyl cyanide** (*acrylonitrile*) is very useful for introducing the cyanoethyl group,  $\text{CH}_2\text{:CH}_2\text{:CN}$ , by reaction with compounds containing an active methylene group. The best catalyst for **cyanoethylation** is benzyltrimethylammonium hydroxide,  $\text{C}_6\text{H}_5\text{:CH}_2\text{:N}^+(\text{CH}_3)_3\text{OH}^-$ , but in many cases an aqueous or ethanolic solution of alkalis is effective (Bruson, 1942, 1943), *e.g.*,

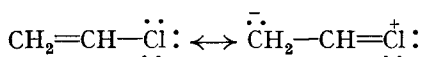


This type of reaction offers a means of preparing a variety of compounds. Vinyl cyanide normally causes di- or tri-cyanoethylation of compounds which have an active methylene or methyl group respectively, but Campbell *et. al.* (1956) have described conditions for monocyanoethylation. In addition to active methylene and methyl groups, compounds such as primary and secondary amines, alcohols, phenols, etc., can also undergo cyanoethylation.

The halogen atom in vinyl halides is not reactive; vinyl halides do not undergo the usual double decomposition reactions of the alkyl halides. Vinyl chlorides and bromides readily form Grignard reagents in *tetrahydrofuran* as solvent (Normant, 1954, 1957), and they react with lithium to form lithium compounds which undergo the usual reactions (Braude, 1950-1952; see p. 362), *e.g.*,



The reason for the unreactivity of the halogen atom is not clear. Some believe it to be due to resonance through which the halogen atom acquires some double-bond character, and is thereby more strongly bound to the carbon atom due to the shortening of the C—Cl bond (p. 19):



At the same time, resonance also stabilises the compound, and so the chlorine atom will not be so reactive.

An alternative explanation is that due to Walsh (1947). As we have seen (p. 96), an  $sp^2$  hybridised carbon atom attracts electrons more than does an  $sp^3$  hybridised carbon atom. Thus the Cl atom in the C—Cl group is more tightly bound in C=C—Cl than in C—C—Cl.

The non-reactivity of the chlorine atom in vinyl chloride may be explained from the M.O. point of view as follows. If the chlorine atom has  $sp^3$  hybridisation, the C—Cl bond will be a  $\sigma$ -bond and the two lone pairs of electrons would occupy the other two  $sp^3$  orbitals. This would leave a  $p$  orbital containing a lone pair, and this orbital could now conjugate with the  $\pi$ -bond of the ethylenic link (Fig. 1). Thus two M.O.s will be required to accommodate these four  $\pi$ -electrons (*cf.* the carboxyl group, p. 184). Furthermore, since chlorine is far more electron-attracting than carbon, the electrons will tend to be found in the vicinity of the chlorine atom. Nevertheless, the chlorine atom has now lost "full control" of the lone pair, and so acquires a small positive charge (or alternatively, it is less negative than it would have been had there been no conjugation). Since two carbon atoms have acquired a share in the lone pair, each carbon atom acquires a small negative charge. Hence, owing to delocalisation of bonds (through conjugation), the vinyl chloride molecule has an increased stability. Before the chlorine atom can be displaced by some other group, the lone pair must be localised again on the chlorine atom. This requires energy, and so the chlorine is more "firmly bound" than had no conjugation occurred.

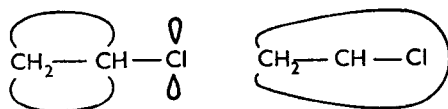
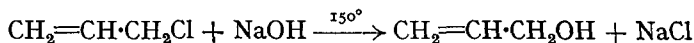


FIG. 12.1.

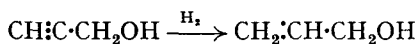
**Allyl alcohol** (*prop-2-en-1-ol*),  $\text{CH}_2\text{:CH}\cdot\text{CH}_2\text{OH}$ , may be prepared as follows:

(i) By boiling allyl chloride with dilute sodium hydroxide solution under pressure (this is a commercial method).

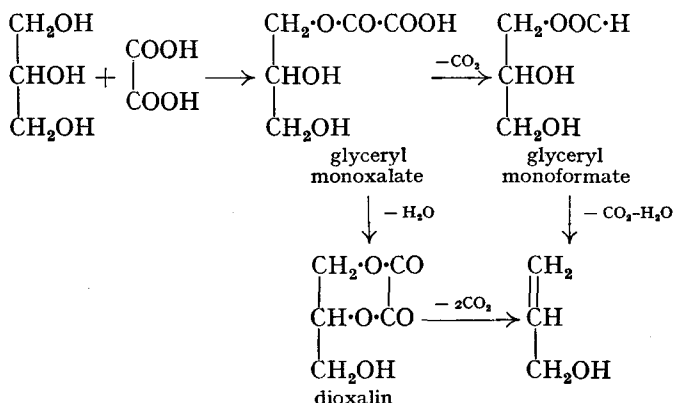


Another commercial method is the isomerisation of propylene oxide in the presence of lithium phosphate as catalyst (*cf.* p. 169).

(ii) By the controlled catalytic reduction of propargyl alcohol:



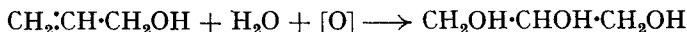
(iii) By heating glycerol with formic acid or oxalic acid at 260°:



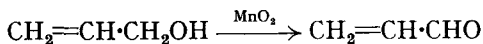
In practice it is better to use formic acid since this gives a higher yield (45–47 per cent.).

Allyl alcohol is a colourless, pungent-smelling liquid, b.p. 97°, miscible with water in all proportions. The presence of the allyl group produces a pungent smell in compounds containing it, *e.g.*, mustard oils contain allyl isothiocyanate; onions and garlic, allyl sulphide.

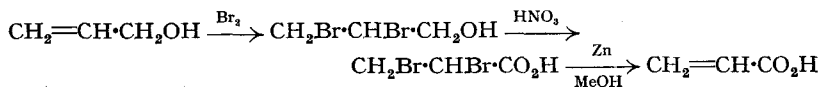
Allyl alcohol has the properties of an unsaturated compound and a primary alcohol. It is oxidised to glycerol by dilute alkaline permanganate:



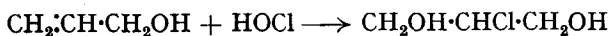
Allyl alcohol (and other  $\alpha,\beta$ -unsaturated primary and secondary alcohols) may be conveniently oxidised to the corresponding oxo compound with manganese dioxide at room temperature (Morton *et al.*, 1948):



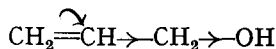
In general, oxidising agents attack the double bond in allyl alcohol as well as the alcoholic group. Oxidation, however, may be carried out by "protecting" the double bond by bromination and then oxidising and debrominating with zinc dust in methanolic solution, *e.g.*,



Allyl alcohol adds on chlorine or bromine to form the corresponding 2 : 3-dihalogeno-propan-1-ol. Allyl alcohol also adds on halogen acids and hypohalous acids, but the addition takes place *contrary* to Markownikoff's rule, *e.g.*, glycerol  $\beta$ -monochlorohydrin is formed with hypochlorous acid:



This may be due to the presence of the oxygen atom which exerts a strong inductive effect causing the electromeric effect to take place *towards* the oxygen atom, *i.e.*,



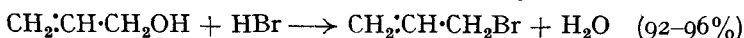
The allyl halides form an interesting group of compounds because of the high reactivity of the halogen atom.

**Allyl chloride** (*3-chloropropene*), b.p. 45°, is prepared industrially by the chlorination of propylene at high temperature. It may be conveniently prepared in the laboratory by warming allyl alcohol with hydrochloric acid:



It is now important as a chemical raw material for the production of drugs, plastics, etc.

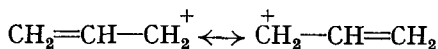
**Allyl bromide** (*3-bromopropene*), b.p. 70°, is best prepared in the laboratory by distilling aqueous allyl alcohol with 48 per cent. hydrobromic acid in the presence of sulphuric acid:



**Allyl iodide** (*3-iodopropene*), b.p. 103.1°, may be prepared by heating glycerol with a small amount of hydriodic acid (p. 256).

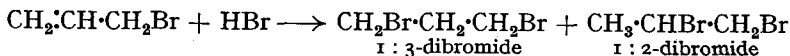
The halogen atom in the allyl halides is very reactive, and it has been found experimentally that the position of the double bond with respect to the halogen atom determines the reactivity of the halogen atom. In compounds of the type C:C-X, the halogen atom X is unreactive (see vinyl halides, above). In C:C-C-X, X is more reactive than in the alkyl halides. When the halogen atom in an unsaturated compound is further removed from the double bond than in the allyl position, it behaves similarly to the halogen atom in alkyl halides; *e.g.*, 4-chlorobut-1-ene, CH<sub>2</sub>:CH·CH<sub>2</sub>·CH<sub>2</sub>Cl, undergoes the usual reactions of the alkyl halides with reagents that do not affect the double bond.

The high reactivity of the allyl halides may be explained by the fact that when the halogen atom ionises, the allyl carbonium ion produced is a resonance hybrid, and consequently it is stabilised (see also p. 271):



The more stable the ion produced, the more easily it is formed. Alkyl carbonium ions cannot be stabilised by resonance, and hence the alkyl halides are not so reactive as the allyl halides.

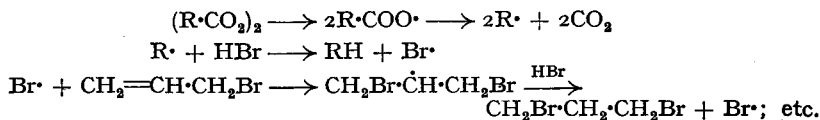
The allyl halides add on the halogen acids to form a mixture of the 1:2- and 1:3-dihalides. The addition of hydrogen bromide to allyl bromide has been studied in great detail (Kharasch, 1933):



In the presence of peroxides, the 1:3-dibromide is obtained in 90 per cent. yield. In the absence of peroxides, the 1:2-dibromide is obtained in 90 per cent. yield. When allyl bromide, which has not been carefully purified, is treated with hydrogen bromide, without special precautions being taken to exclude all traces of air, a mixture of the 1:2- and 1:3-dibromides is obtained.

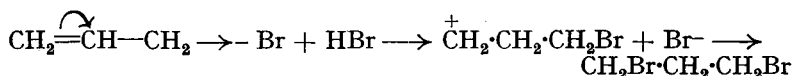
The explanation for these results is as follows. The 1:3-dibromide is formed by a free-radical mechanism, the peroxides producing atomic

bromine from the hydrogen bromide, thereby setting up a free-radical chain reaction (*cf.* p. 68):

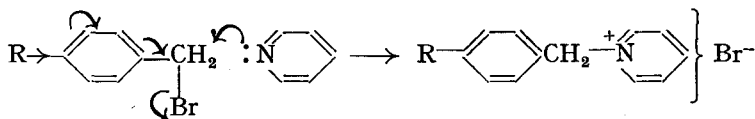


Mayo (1940) has suggested that the bromine atom adds to the terminal carbon to give a secondary free radical which is more stable than a primary free radical. Evidence for this free-radical mechanism is that it takes place in the presence of peroxides; the formation of the 1 : 3-dibromo compound is very largely suppressed in the presence of antioxidants (which destroy peroxides); and its formation is catalysed by light (which is known to produce free radicals).

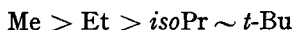
The mechanism for the formation of the 1 : 2-dibromide is *polar* (which gives "normal" addition; see p. 68). At first sight, however, the polar mechanism would be expected to produce the 1 : 3-dibromide because of the inductive effect of the bromine atom, *i.e.*



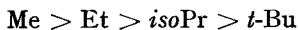
Baker and Nathan (1953), however, have explained the 1 : 2-addition by what is often referred to as the *Baker-Nathan effect*. As we have seen, the general inductive effect of alkyl groups is  $Me_3C > Me_2CH > MeCH_2 > Me$ . This inductive order has been used satisfactorily to explain various physical data, etc. In some reactions, however, the inductive order is reversed, *e.g.*, Baker and Nathan (1935) examined kinetically the reaction between *p*-substituted benzyl bromides and pyridine. The reaction was carried out in acetone, and was shown to be entirely  $S_N2$ . Thus the reaction may be formulated:



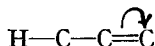
The greater the +I effect of the R group, the faster should be the reaction, but it was found that the rate order for the R groups was



Thus the order of electron release is almost exactly the *reverse* of that given above. Therefore alkyl groups must possess some mechanism of electron-release in which the order is

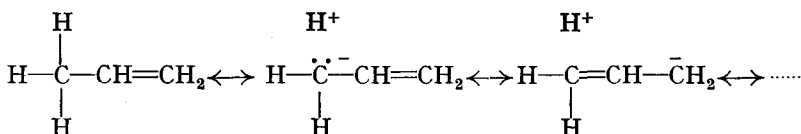


Further work showed that in all cases where the general inductive order of alkyl groups was reversed, the alkyl group was attached to an aromatic nucleus. This led Baker and Nathan (1935, 1939) to suggest that when the H—C bond is attached to an unsaturated carbon atom, the  $\sigma$ -electrons of the H—C bond become less localised by entering into partial conjugation with the attached unsaturated system, *i.e.*,



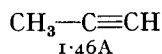
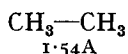
Thus there is conjugation between electrons of *single* and those of multiple bonds. This type of conjugation is known as *hyperconjugation*, and is a *permanent* effect (this name was given by Mulliken, 1941).

There are various ways of looking at the *hyperconjugative effect*. A widely used one is to regard the H—C bond as possessing partial ionic character due to resonance, e.g., propylene may be written as a resonance hybrid as follows:



From this point of view, hyperconjugation may be regarded as “*no bond resonance*”. The hydrogen atoms are not *free*; the effect is to increase the ionic character of the C—H bond, the electrons of which become partially delocalised through conjugation.

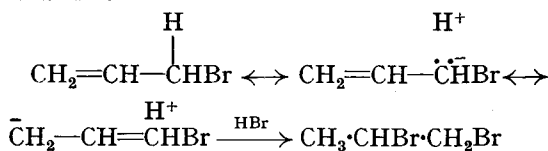
Various physical data have been explained by hyperconjugation, e.g., bond lengths:



Because of hyperconjugation, the CH<sub>3</sub>—C bond has some partial double bond character and consequently is shortened.

Also, since hyperconjugation stabilises a molecule (through resonance), propylene, for example, should be more stable than “expected”. This has been found to be so; the observed heat of hydrogenation of propylene is less than the calculated value.

Using this scheme of hyperconjugation, we are now in a position to explain the formation of the 1 : 2-dibromide from allyl bromide and hydrogen bromide by the polar mechanism.



The inductive effect of the bromine atom would tend to give the 1 : 3-dibromide (see above). If, however, the hyperconjugative effect is operating, and is *stronger* than the —I effect of the bromine atom, then the 1 : 2-dibromide will be formed.

An interesting point here is that with allyl alcohol, the —I effect of the hydroxyl group is stronger than hyperconjugative effect (p. 519).

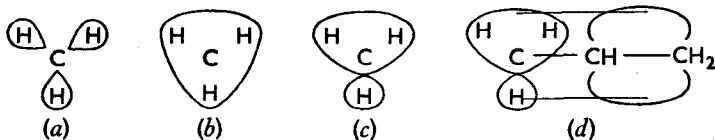


FIG. 12.2.

From the M.O. point of view, hyperconjugation may be explained as follows:  $\pi$ -Orbitals can overlap with other  $\pi$ -orbitals to produce conjugation (p. 88).  $\pi$ -Orbitals, however, can also overlap to a certain extent with adjacent  $\sigma$ -orbitals to form extended orbitals. When this occurs we have *hyperconjugation*, and this phenomenon is exhibited mainly by the hydrogen bonds in a *methyl* group when



this group is attached to an unsaturated carbon atom. The question is: how does this overlapping occur? Coulson (1942) treats the methyl group (Fig. 2a) as a "compound" atom to form a "group" orbital (Fig. b). An alternative "group" orbital may also be formed as in (c). In this arrangement, the methyl group behaves as a group with a  $\pi$ -orbital, and this can conjugate with an adjacent  $\pi$ -bond in, e.g., propylene (Fig. d). Hence, owing to partial delocalisation of bonds ( $\sigma$  and  $\pi$ ) in this way, the propylene molecule is more stable than "expected".

The unusual reactivity of the halogen atom in allyl halides may be explained as follows. If the chlorine were to ionise, the carbon atom to which it was attached now has a positive charge and has only *str* electrons. Hence the  $\pi$ -bond covering the other two carbon atoms can extend to embrace this third carbon atom. The net result is an M.O. covering *three* carbon atoms, and so the delocalisation energy will be increased, *i.e.*, the new arrangement is stabilised, and behaves as if the chlorine atom is ionic (Fig. 3).

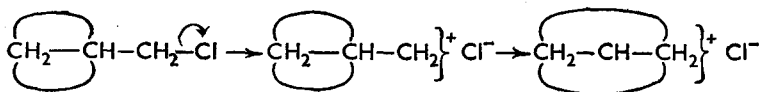


FIG. 12.3.

There is now, however, a certain amount of doubt that dipole moment data are evidence for hyperconjugation. Since the electronegativity of a carbon atom depends on its state of hybridisation, there will be a bond moment when two differently hybridised carbon atoms are linked together. Petro (1958) has calculated bond moments for several types of carbon-carbon single bonds:

Bond	Bond moment
$\text{C}(sp^3)^+-\text{C}(sp^2)^-$	0.68D
$\text{C}(sp^2)^+-\text{C}(sp)^-$	1.15D
$\text{C}(sp^3)^+-\text{C}(sp)^-$	1.48D

Ferreira (1960) has calculated the dipole moments of various molecules, e.g., toluene, propylene, etc., on these principles, and has shown that the calculated values agree well with the experimental values. Thus it appears that dipole moment evidence for hyperconjugation is not valid.

It has also been found experimentally that all C—C single bonds are *not* the same length, e.g.,

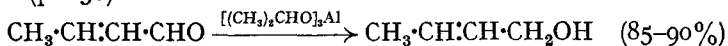
$sp^3-sp^3$	1.54Å
$sp^3-sp^2$	1.50Å
$sp^3-sp$	1.46Å

This shortening has been attributed to hyperconjugation, but it can also be explained in terms of different electronegativities of the two carbon atoms.

It is quite possible, however, since bond moment (and bond lengths) is a ground-state property, that hyperconjugation exists in excited states and in transition states of molecules, and therefore is important for the interpretation of reactivity of molecules.

Mulliken (1959) has concluded that the explanation offered above is partly right, but does not believe the  $\pi$ -delocalisation shortenings are negligible. He has made some calculations and has attributed 40 per cent. of observed shortenings to  $\pi$ -electron resonance and 60 per cent. to hybridisation differences.

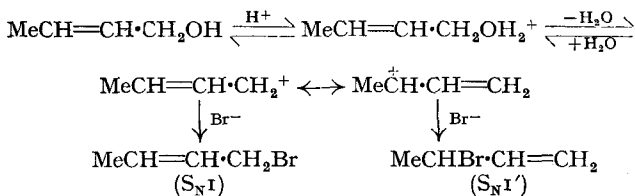
**Crotyl alcohol** (*crotonyl alcohol, but-2-en-1-ol*),  $\text{CH}_3\cdot\text{CH}:\text{CH}\cdot\text{CH}_2\text{OH}$ , may be prepared by the reduction of crotonaldehyde with aluminium *isopropoxide* (p. 150):



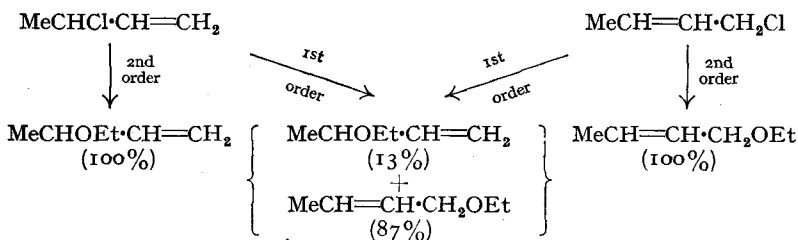
Crotyl alcohol is a colourless liquid, b.p.  $118^{\circ}$ , fairly soluble in water. When treated with hydrogen bromide, crotyl alcohol produces a mixture of crotyl and methylvinylcarbinyl bromide:



The formation of the rearranged product is an example of anionotropy, and the most widely studied example is the three-carbon system, *i.e.*, the allylic system. Nucleophilic substitution reactions of allylic halides may occur by the  $\text{S}_{\text{N}}2$  mechanism, and when this is operating, substitution proceeds normally (see below). When, however, nucleophilic substitution reactions are carried out under conditions which favour the unimolecular mechanism, then the product may be a mixture of two isomers, the rearranged product being an example of the *allylic rearrangement*. The mechanism by which this rearrangement occurs is known as  $\text{S}_{\text{N}}1'$ , and the steps involved are believed to be as follows, via a resonance hybrid cation:



There is much evidence to support this  $\text{S}_{\text{N}}1'$  mechanism, *e.g.*, Hughes *et al.* (1948) examined the conversion of  $\alpha$ -methylallyl and crotyl chloride into  $\alpha$ -methylallyl and crotyl ethyl ether by reaction with ethanolic sodium ethoxide. The concentration of the sodium ethoxide was made so small as to give first-order kinetics, or so large as to give second-order kinetics. The results were:



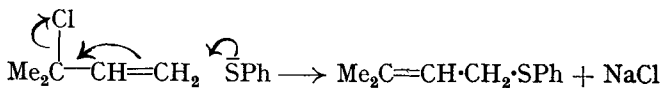
With second-order substitution, each chloride gives its own *unrearranged ether* (thus the  $\text{S}_{\text{N}}2$  mechanism). With first-order substitution, however, each chloride gives the *same* mixture of isomeric ethers. This latter result may be explained by assuming that *two* mechanisms are operating  $\text{S}_{\text{N}}1$  (without rearrangement) and  $\text{S}_{\text{N}}1'$  (with rearrangement), both proceeding through a *common* intermediate cation.

An interesting point about this reaction is the predominance of the crotyl ether whichever chloride is used as starting material. A possible answer is hyperconjugation, which can stabilise the crotyl cation but not the  $\alpha$ -methylallyl cation:

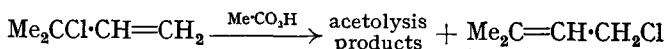


In addition to the  $\text{S}_{\text{N}}1'$  mechanism, there is also the  $\text{S}_{\text{N}}2'$ , *i.e.*, a bimolecular nucleophilic substitution with allylic rearrangement. This has been difficult

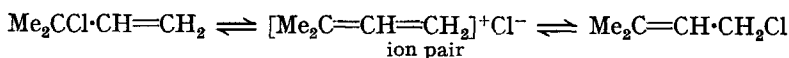
to demonstrate, but a good example of it has been given by de la Mare *et al.* (1953). These authors have suppressed the  $S_N2$  reaction by steric factors and reduced the  $S_N1$  reaction by means of a reagent of high nucleophilic activity and a solvent of low ionising power. They found that the reaction between  $\alpha$ : $\alpha$ -dimethylallyl chloride and sodium thiophenoxide in ethanol gives 62 per cent. of rearranged product by a second-order reaction (*i.e.*,  $S_N2'$ ):



One other problem that will be discussed here is the case of ion pairs in the allylic rearrangement (see also p. 109). Young *et al.* (1951) have shown that  $\alpha$ : $\alpha$ -dimethylallyl chloride in acetic acid undergoes acetolysis accompanied by rearrangement to  $\gamma$ : $\gamma$ -dimethylallyl chloride:

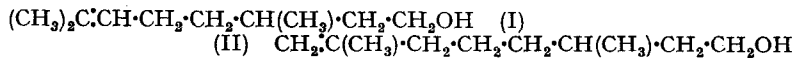


The rate of the isomerisation was shown to be proportional to the concentration of the starting chloride only. Thus a possible mechanism is the  $S_N1'$ . If this were so, then the rate of isomerisation would be affected by addition of chloride ions (since the first step is ionisation). Experiment showed that the rate was unaffected by added chloride ions, and it was also shown that when an *excess* of radioactive chloride ion was added, the rate of isomerisation was far greater than the incorporation of  $\text{Cl}^{*-}$ . It thus appears that the chloride ion is set free during the isomerisation and is mainly the "first ion" to recombine, even though the solution contains a large excess of  $\text{Cl}^{*-}$  ions. Young *et al.* explained this result by assuming that the starting chloride undergoes ionisation to form an ion-pair, and this is followed by internal return:

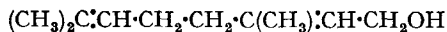


Nevertheless, some ion-pairs escape from the solvent cage, and these "free" carbonium ions are capable of undergoing acetolysis and combination with  $\text{Cl}^{*-}$ .

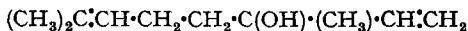
A number of unsaturated alcohols occur in *essential oils*. The essential oils are volatile oils with pleasant odours, and are obtained from various plants to which they impart their characteristic odours. They are widely used in the perfume industry. **Citronellol** occurs in citronella oil, rose oil, etc. It appears to be a mixture of the two structural isomers I and II:



**Geraniol** and **nerol** are *cis-trans* isomers of the following structure (and possibly of the structure corresponding to II above):

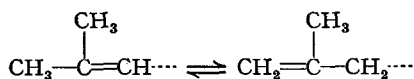


Geraniol is a constituent of geranium oil, rose oil, etc. Nerol occurs in neroli oil, etc. **Linalool**, which is an isomer of geraniol and nerol, occurs in linaloe oil, lavender oil, coriander oil, etc.:



These alcohols are the oxygen derivatives of the group of compounds known as the *open-chain terpenes*. It appears that all of these alcohols are mixtures of

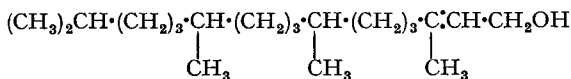
structural isomers (see citronellol, above). It is possible, however, that the two structures form a three-carbon tautomeric system:



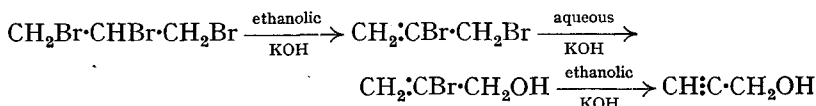
**Farnesol**, a *sesquiterpene* alcohol, occurs in rose oil, the oil from ambrette seeds, etc., and, like the terpene alcohols, is a mixture of two forms, one of which is:



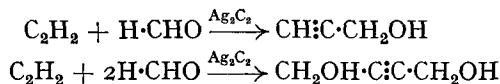
**Phytol** is an unsaturated alcohol which occurs in chlorophyll (the green colouring matter of leaves and other parts of a plant). Its structure is:



The simplest acetylenic alcohol is **propargyl alcohol** (*prop-2-yn-1-ol*),  $\text{CH}_3\text{C}\cdot\text{CH}_2\text{OH}$ . This may be prepared from 1:2:3-tribromopropane by the following series of reactions, which clearly show the difference in reactivity of the bromine atoms, and at the same time illustrate the use of aqueous and ethanolic solutions of potassium hydroxide:



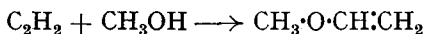
Propargyl alcohol (together with butyne-diol) is prepared by the interaction of acetylene and formaldehyde in the presence of silver or cuprous acetylide as catalyst:



Propargyl alcohol is a colourless liquid, b.p.  $114^\circ$ . It behaves in many ways like acetylene, *e.g.*, it adds on two or four bromine atoms, and forms the silver or cuprous compounds when treated with an ammoniacal solution of silver nitrate or cuprous chloride. It may be catalytically reduced to allyl and *n*-propyl alcohols; it is now being used to prepare these two compounds commercially.

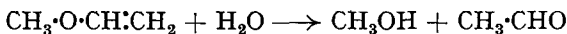
#### UNSATURATED ETHERS

The simplest unsaturated ether is methyl vinyl ether,  $\text{CH}_3\cdot\text{O}\cdot\text{CH}:\text{CH}_2$ , which is prepared industrially by passing acetylene into methanol at  $160\text{--}200^\circ$  in the presence of 1–2 per cent. potassium methoxide, and under pressure sufficient to prevent boiling:

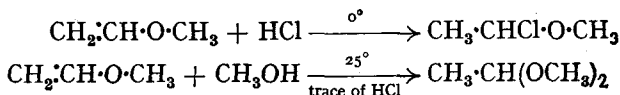


The acetylene is diluted with nitrogen to prevent explosions.

Methyl vinyl ether is a very reactive gas, b.p.  $5\text{--}6^\circ$ . It is hydrolysed rapidly by dilute acid at room temperature to give methanol and acetaldehyde (*cf.* the ethers).

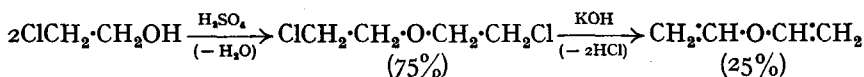


This is a potential industrial method for preparing acetaldehyde. Methyl vinyl ether is stable in alkaline solution. It undergoes many addition reactions at the double bond, *e.g.*,



It readily polymerises, and is used for making polyvinyl ether plastics.

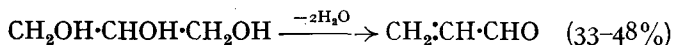
**Divinyl ether** (*vinyl ether*),  $\text{CH}_2\text{:CH}\cdot\text{O}\cdot\text{CH}\text{:CH}_2$ , may be prepared by heating ethylene chlorohydrin with sulphuric acid, and then passing the product, 2 : 2'-dichlorodiethyl ether, over potassium hydroxide at 200–240°:



Divinyl ether is a colourless liquid, b.p. 39°. It is used as an anæsthetic, being better for this purpose than diethyl ether.

#### UNSATURATED ALDEHYDES

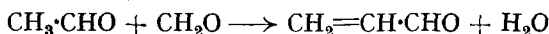
The simplest unsaturated aldehyde is **acraldehyde** (*acrolein*, *prop-2-en-1-al*),  $\text{CH}_2\text{:CH}\cdot\text{CHO}$ . This is conveniently prepared by heating glycerol with potassium hydrogen sulphate, which is the most satisfactory dehydrating agent for this reaction:



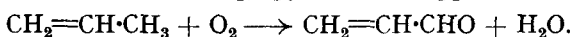
Acraldehyde may also be readily prepared by the oxidation of allyl alcohol with manganese dioxide (p. 267).

Acraldehyde is prepared industrially in many ways, *e.g.*,

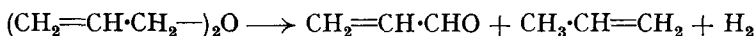
(i) by passing a mixture of acetaldehyde and formaldehyde vapour over sodium silicate as catalyst:



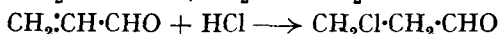
(ii) By the direct oxidation of propylene over copper oxide:



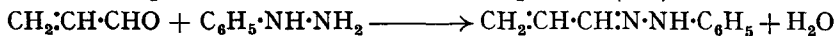
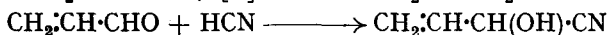
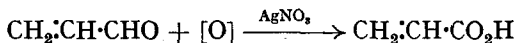
(iii) By the pyrolysis of diallyl ether:



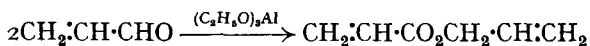
Acraldehyde is a colourless liquid, b.p. 52°, with a pungent irritating odour. It is unstable, readily polymerising to a white solid. It is an  $\alpha\beta$ -unsaturated aldehyde, and undergoes many of the usual reactions of an olefin and an aldehyde, *e.g.*, it adds on two halogen atoms or a molecule of halogen acid (contrary to Markownikoff's rule; *cf.* allyl alcohol):



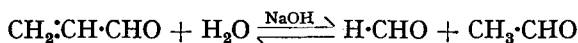
The addition of hydrogen bromide is unaffected by the presence of peroxides. Acraldehyde reduces ammoniacal silver nitrate, forms a cyanohydrin with hydrogen cyanide, and a phenylhydrazone with phenylhydrazine:



Acraldehyde undergoes the Tischenko reaction (p. 161) to form allyl acrylate:

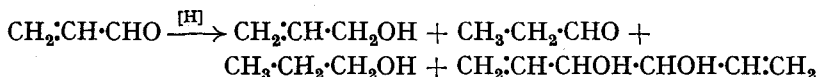


It does not, however, undergo the normal aldol condensation; instead, in the presence of alkali, cleavage of the molecule takes place:



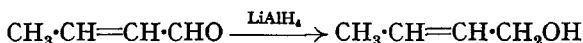
This reaction is actually the reversal of the aldol condensation, and is characteristic of  $\alpha\beta$ -unsaturated aldehydes.

When acraldehyde is reduced with metal and acid, there are obtained an unsaturated alcohol, a saturated aldehyde, a saturated alcohol, and a compound formed by bimolecular reduction:



A good yield of the bimolecular product is obtained by reducing acraldehyde with magnesium amalgam (*cf.* pinacol, p. 253). Acraldehyde is reduced by sodium amalgam to *n*-propanol and by aluminium isopropoxide (Meerwein-Ponndorf-Verley reduction, p. 150) to allyl alcohol. It should be noted that metal and acid do not usually reduce a double bond; it is only when the double bond is in the  $\alpha\beta$ -position with respect to a carbonyl group that it is reduced in this way (see also below).  $\alpha\beta$ -Unsaturated aldehydes may be catalytically reduced to unsaturated alcohols by means of a platinum catalyst in the presence of traces of ferrous sulphate and zinc acetate; the former promotes reduction of the aldehyde group and the latter inhibits reduction of the double bond (Adams *et al.*, 1927). When Raney nickel is used as catalyst at fairly low temperatures and pressures, the product is a saturated aldehyde, but at higher temperatures and pressures the product is a saturated alcohol. Broadbent *et al.* (1959) have shown that both rhenium heptaselenide and heptasulphide are good catalysts for hydrogenation. Both are resistant to poisoning, but the former saturates the carbon-oxygen double bond more easily than the carbon-carbon double bond.

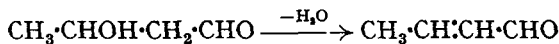
$\alpha\beta$ -Unsaturated aldehydes (and ketones) may be reduced to the unsaturated alcohols by lithium aluminium hydride, *e.g.*,



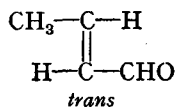
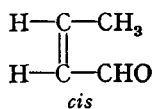
If, however, a phenyl group is attached to the  $\beta$ -carbon atom, the double bond is also reduced (see cinnamic acid, p. 690).

Acraldehyde adds on to butadiene to form a cyclic compound (see the *Diels-Alder* reaction, p. 472):

**Crotonaldehyde** (*but-2-en-1-al*),  $\text{CH}_3\cdot\text{CH}\cdot\text{CH}\cdot\text{CHO}$ , may be prepared by heating aldol alone, or better, with a dehydrating agent, *e.g.*, zinc chloride. The best yield is obtained by distilling aldol with acetic acid as catalyst:



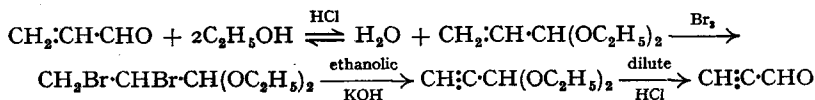
Crotonaldehyde is a colourless liquid, b.p.  $104^\circ$ . It closely resembles acraldehyde in its chemical properties. It exists, however, in two geometrical isomeric forms, *cis* and *trans*:



Catalytic reduction (Raney nickel) of crotonaldehyde in the presence of chloroform gives butyraldehyde; in the absence of chloroform, butanol is formed (Cornubert *et al.*, 1950).

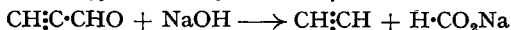
A number of unsaturated aldehydes occur naturally in the essential oils, many accompanying the corresponding unsaturated alcohol, *e.g.*, citral or geranial, neral, citronellal.

The simplest acetylenic aldehyde is **propargylaldehyde** (propiolaldehyde, propynal),  $\text{CH}_2\text{:C}\cdot\text{CHO}$ . This may be prepared from acraldehyde, the aldehyde group of which must be "protected" by acetal formation:



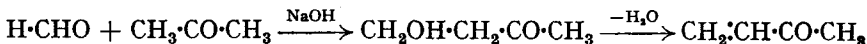
It may also be obtained by the controlled oxidation of propargyl alcohol.

Propargylaldehyde is a liquid, b.p.  $60^\circ$ , which undergoes cleavage when treated with sodium hydroxide (*cf.* acraldehyde, above):

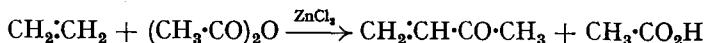


#### UNSATURATED KETONES

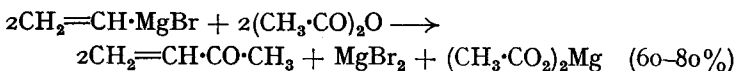
The simplest unsaturated ketone is **methyl vinyl ketone** (*but-3-en-2-one*),  $\text{CH}_3\cdot\text{CO}\cdot\text{CH}\cdot\text{CH}_2$ . This may be prepared by means of an aldol condensation between formaldehyde and acetone, the product being dehydrated by heat.



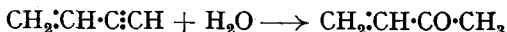
It may also be prepared by the action of acetic anhydride on ethylene in the presence of zinc chloride as catalyst:



Methyl vinyl ketone may also be prepared by the action of acetic anhydride on vinylmagnesium bromide in tetrahydrofuran at  $-60^\circ$  to  $-70^\circ$  (Martin, 1957); this is a general method for preparing vinyl ketones:

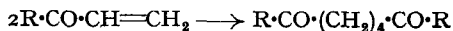


It is manufactured by hydrating vinylacetylene in the presence of dilute sulphuric acid and mercuric sulphate (*cf.* acetaldehyde, p. 166):

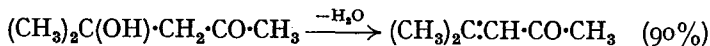


Methyl vinyl ketone is a liquid, b.p.  $79^\circ$ , which polymerises on standing. It is used commercially as the starting material for plastics.

Reduction of vinyl ketones with zinc or magnesium produces 1:6-diketones (Kossanyi, 1960):

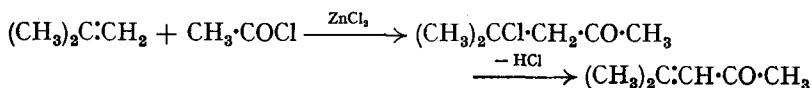


**Mesityl oxide** (4-methylpent-3-en-2-one),  $(\text{CH}_3)_2\text{C}\cdot\text{CH}\cdot\text{CO}\cdot\text{CH}_3$ , may be prepared by distilling diacetone alcohol (*q.v.*) with a trace of iodine:



Stross *et al.* (1947) have shown that mesityl oxide prepared this way is a mixture of mesityl oxide and *isomesityl oxide*,  $\text{CH}_2\text{:C}(\text{CH}_3)\cdot\text{CH}_2\cdot\text{CO}\cdot\text{CH}_3$ .

Mesityl oxide may also be prepared as follows:

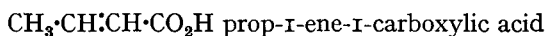






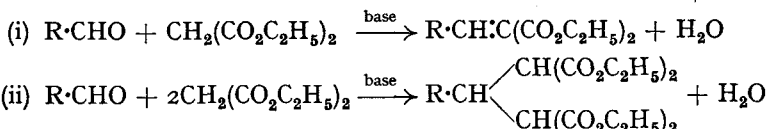


Alternatively, the acid is named as a substitution product of the olefin, *e.g.*,

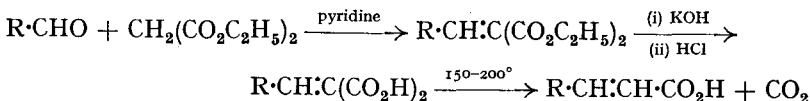


In practice the unsaturated acids are usually known by their common names (see text below).

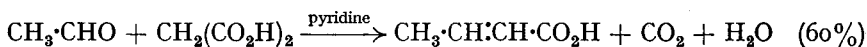
Many methods are available for preparing unsaturated monocarboxylic acids, but each one depends on the position of the double bond in the acid. A general method for preparing  $\alpha\beta$ -unsaturated acids is by the **Knoevenagel reaction** (1898). This is the reaction between aldehydes and compounds with active methylene groups in the presence of an organic base. The reaction may take place in one of two ways:



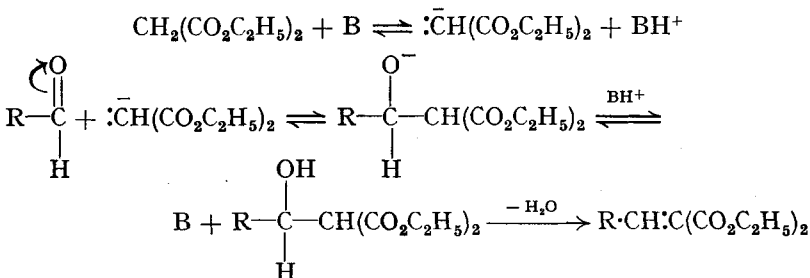
Reaction (i) is favoured by using equivalent amounts of aldehyde and ethyl malonate in the presence of pyridine (Doebner, 1900). Reaction (ii) is favoured by using excess ethyl malonate in the presence of piperidine, and when the aldehyde is aliphatic. Furthermore, it appears that the term Knoevenagel reaction is taken to mean the condensation when *unsaturated* compounds are produced. Obviously then, to prepare  $\alpha\beta$ -unsaturated acids, (i) must be used, followed by hydrolysis and heating.



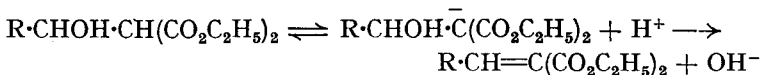
In practice, it is usually sufficient to treat the aldehyde with malonic acid in the presence of pyridine; *e.g.*, acetaldehyde gives crotonic acid:



The mechanism of this reaction has been the subject of much discussion. When a *tertiary* base, *e.g.*, pyridine, is used as catalyst, then the mechanism is believed to be similar to that of the aldol condensation (p. 157):

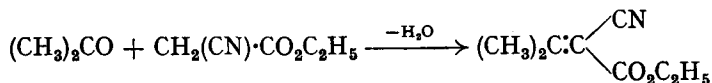


According to Zabicky (1961), the last stage proceeds as follows:



When a primary or secondary base is used as catalyst, the mechanism may still possibly be as given above, but a complication arises from the fact that carbonyl compounds can form addition products with such bases, and these addition products may therefore be intermediates in the reaction.

Ethyl malonate condenses with aldehydes only. On the other hand, ethyl cyanoacetate condenses with ketones in the presence of acetamide in glacial acetic acid solution, provided the water formed is removed continually by distillation; *e.g.*, acetone forms *isopropylidencyanoacetic ester*:

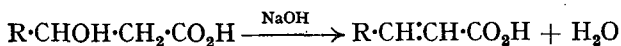
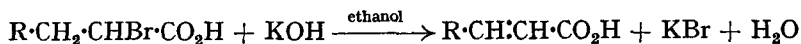


Since cyano-compounds are readily hydrolysed to the corresponding acid, the above condensation may be used to prepare  $\alpha\beta$ -unsaturated acids of the type  $\text{R}_2\text{C}:\text{CH}\cdot\text{CO}_2\text{H}$ .

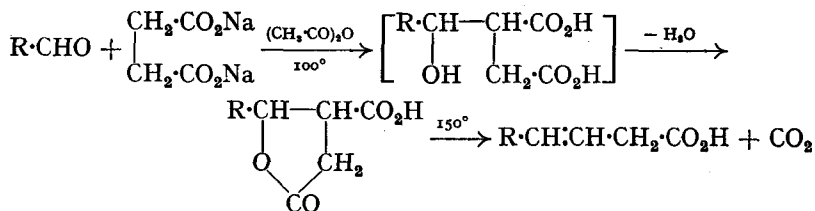
It can be seen from the foregoing that although the methylene group in ethyl malonate will react with aldehydes, it is not sufficiently "active" to react with ketones. Replacement of one carbethoxy group by a cyano-group makes the methylene group (in the cyano-ester) active enough, *i.e.*, increases the tendency for proton release, to react with ketones. Thus the cyano-group is more strongly electron-attracting than the carbethoxy group. Groups with a -I effect are usually known as *negative groups*. It is the presence of a negative group that is the common feature in compounds which tend to undergo condensation reactions, exhibit tautomerism, and show increased strength as an acid and decreased strength as a base.

Many negative groups are characterised by the presence of multiple bonds, *e.g.*,  $\text{NO}_2$ , CN, CO, etc., and it is these negative groups which give rise to an active methylene group, and to tautomerism. On the other hand, negative groups which do not contain multiple bonds, *e.g.*, F, Cl, Br, I,  $\cdot\text{OCH}_3$ , do not give rise to an active methylene group, or to tautomerism. All the negative groups, however, increase the strength of an acid and decrease the strength of a base (examples of these phenomena will be found in the text).

$\alpha\beta$ -Unsaturated acids may also be prepared by heating  $\alpha$ -bromo-acids with ethanolic potassium hydroxide, or better still, with potassium *tert.*-butoxide (Cason *et al.*, 1953); or by heating  $\beta$ -hydroxy-acids with aqueous sodium hydroxide:



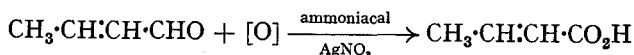
$\beta\gamma$ -Unsaturated acids may be prepared by heating an aldehyde with sodium succinate and acetic anhydride at  $100^\circ$ . The product is a  $\gamma$ -alkyl-*paraconic acid*, and when this is heated at  $150^\circ$ , it eliminates carbon dioxide to form the  $\beta\gamma$ -unsaturated acid (Fittig *et al.*, 1885):



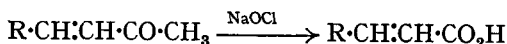
This reaction is really an extension of the Perkin reaction (see p. 651).

Unsaturated alcohols may be oxidised to the corresponding unsaturated acid, provided the double bond is protected, *e.g.*, acrylic acid from allyl alcohol (see p. 252).

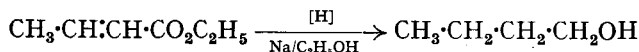
Oxidation of unsaturated aldehydes produces unsaturated acids. The oxidation, however, cannot be carried out with the usual oxidising agents, such as acid or alkaline permanganate, acid dichromate, etc., since these will attack the double bond. A useful oxidising agent for unsaturated aldehydes is ammoniacal silver nitrate (see p. 160); *e.g.*, crotonaldehyde is oxidised to crotonic acid:



Unsaturated methyl ketones may be oxidised to unsaturated acids by sodium hypochlorite (*cf.* the haloform reaction), *e.g.*,

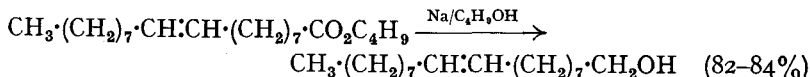


**General reactions of the unsaturated acids.** The esters of  $\alpha\beta$ -unsaturated acids undergo the same addition reactions (including the Michael condensation) at the double bond as the  $\alpha\beta$ -unsaturated ketones. When reduced by the Bouveault-Blanc method,  $\alpha\beta$ -unsaturated esters are converted into the corresponding saturated alcohol:



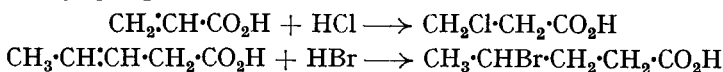
Lithium aluminium hydride, however, generally, reduces these esters to the corresponding *unsaturated* alcohols (*cf.* p. 125).

Esters in which the double bond is further removed from the ester group are reduced to the corresponding *unsaturated* alcohol (*cf.* acraldehyde, above); *e.g.*, butyl oleate is reduced to oleyl alcohol:



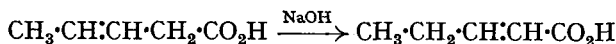
All the unsaturated acids may be reduced catalytically to saturated acids.

$\alpha\beta$ - and  $\beta\gamma$ -Unsaturated acids add on halogen acid, the halogen atom becoming attached to the unsaturated carbon atom which is further from the carboxyl group:

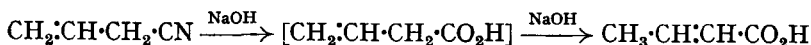


This mode of addition (which may be contrary to Markownikoff's rule, as in the case of acrylic acid) may be ascribed to the inductive effect of the carboxyl group (*cf.* allyl alcohol, etc.). On the other hand, addition of halogen acid to  $\gamma\delta$ -unsaturated acids of the type  $\text{CH}_2\cdot\text{CH}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CO}_2\text{H}$  takes place in accordance with Markownikoff's rule. This must be due to the fact that the inductive effect of the carboxyl group ceases to be felt beyond the  $\beta$ -carbon atom.

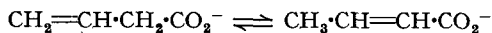
When unsaturated acids are boiled with alkali, the double bond tends to move so as to form the  $\alpha\beta$ -unsaturated acid:



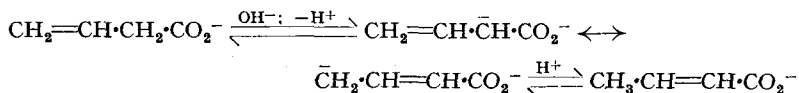
An interesting example of this migration of the double bond is the hydrolysis of allyl cyanide with boiling alkali to produce *crotonic* acid. But-3-enoic acid is probably formed first, and this then rearranges to crotonic acid:



The movement of a double bond to the  $\alpha : \beta$ -position shows that the latter acid is thermodynamically more stable, *e.g.*, Linstead *et al.* (1934) showed that the migration is reversible and that the equilibrium between the sodium salts of vinylacetic acid and crotonic acid is 98 per cent. on the side of the latter:

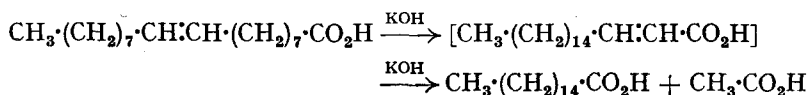


The mechanism of this shift is believed to be:



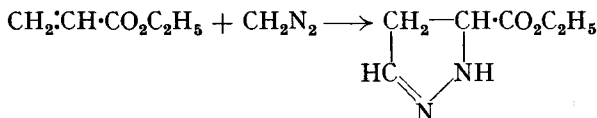
This is supported by the fact that sodium vinylacetate exchanges H for D in sodium hydroxide solution containing  $\text{D}_2\text{O}$  (Ives *et al.*, 1935); sodium crotonate also exchanges, but much more slowly (Ives, 1938).

When unsaturated acids are fused with alkali, cleavage of the chain takes place with the formation of two acids, one of which is always acetic acid. This again indicates the migration of the double bond to the  $\alpha\beta$ -position; *e.g.*, oleic acid gives acetic and palmitic acids:

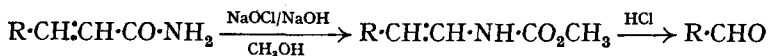


It is therefore obvious that fusion of an unsaturated acid with alkali cannot be used to determine the position of the double bond. If, however, the unsaturated acid is treated with cold dilute alkaline permanganate, or hydrogen peroxide in acetic acid (or formic acid), the double bond is hydroxylated, and the glycol formed under these conditions, *i.e.*, without migration of the double bond, may now be oxidised in the usual way (see p. 73). Alternatively, the position of the double bond may be ascertained by ozonolysis (p. 74). In view of this shift of the double bond to the  $\alpha : \beta$ -position, it therefore follows that the  $\alpha : \beta$ -unsaturated acid is thermodynamically more stable than any of the other isomeric unsaturated acids.

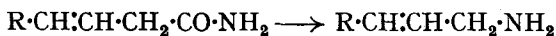
$\alpha\beta$ -Unsaturated esters add on aliphatic diazo-compounds to form *pyrazoline* derivatives; *e.g.*, acrylic ester reacts with diazomethane to give *pyrazoline-5-carboxylic ester*:



$\alpha\beta$ -Unsaturated acids may be degraded by the Hofmann method (p. 206) using a modified procedure. The  $\alpha\beta$ -unsaturated acid amide in methanol is treated with an alkaline solution of sodium hypochlorite, the urethan produced being hydrolysed in acid solution to give the *aldehyde* in good yield:

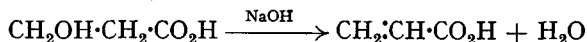


In this case, *two* carbon atoms are eliminated from the acid. On the other hand,  $\beta\gamma$ - and  $\gamma\delta$ -unsaturated acid amides eliminate *one* carbon atom to produce the corresponding unsaturated primary amine, but in poor yield:



**Acrylic acid** (*prop-2-enoic acid*),  $\text{CH}_2\text{:CH}\cdot\text{CO}_2\text{H}$ , may be prepared:

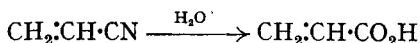
- (i) By the oxidation of allyl alcohol or acraldehyde (see p. 267).  
 (ii) By heating  $\beta$ -hydroxypropionic acid with aqueous sodium hydroxide:



Alternatively, ethylene cyanohydrin may be heated with sulphuric acid:

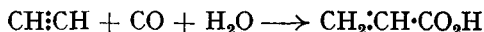


Vinyl cyanide also gives acrylic acid on hydrolysis:



It is therefore possible that the intermediate in the hydrolysis of ethylene cyanohydrin may be vinyl cyanide or  $\beta$ -hydroxypropionic acid, or both. Acrylic acid is prepared industrially with ethylene cyanohydrin (prepared from ethylene oxide and hydrogen cyanide, p. 251) as the starting material.

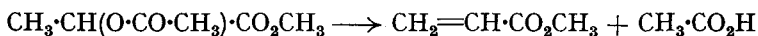
(iii) A new industrial preparation is by the interaction of acetylene, carbon monoxide and water in the presence of nickel salts as catalyst:



If an alcohol is used instead of water, the corresponding acrylic ester is obtained, *e.g.*,

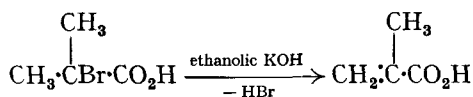


Another industrial method is by the pyrolysis of an alkyl acetyl-lactate, *e.g.*,

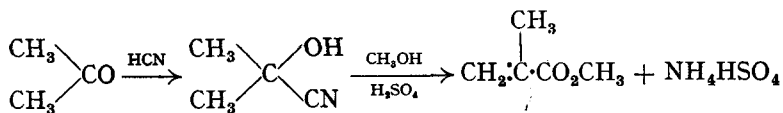


Acrylic acid is a colourless liquid, b.p.  $141^\circ$ , which is miscible with water in all proportions. On standing it slowly polymerises to a solid.

**Methacrylic acid** (2-methylprop-2-enoic acid),  $\text{CH}_2\text{:C}(\text{CH}_3)\cdot\text{CO}_2\text{H}$ , exists as colourless prisms, m.p.  $15^\circ$ . It may be prepared by removing a molecule of hydrogen bromide from  $\alpha$ -bromoisobutyric acid:



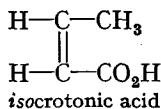
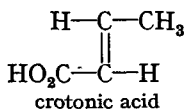
Methyl methacrylate is very important commercially, since it polymerises to polymethyl methacrylate under the influence of heat. This polymer is tough, transparent, and can be moulded; one of its trade names is *perspex*. One industrial method of preparing methyl methacrylate is as follows:



Methyl acrylate, which may be prepared by heating ethylene cyanohydrin with methanol and sulphuric acid, also polymerises, but this polymer is softer than that from the methacrylate.

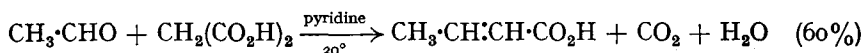
**Crotonic acid** and **isocrotonic acid** both have the same structure

$\text{CH}_3\cdot\text{CH}:\text{CH}\cdot\text{CO}_2\text{H}$  (*but-2-enoic acid*), but are geometrical isomers, crotonic acid being the *trans* isomer, and *isocrotonic* the *cis*:

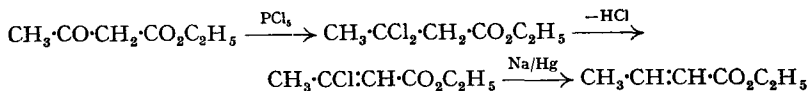


The more stable form is crotonic acid, m.p.  $72^\circ$ . *isocrotonic* acid, m.p.  $15^\circ$ , slowly changes into crotonic acid when heated at  $100^\circ$ .

**Crotonic acid** (*trans-but-2-enoic acid*) may be prepared by oxidising crotonaldehyde with ammoniacal silver nitrate; by heating  $\beta$ -hydroxybutyric acid with sodium hydroxide; or by the Knoevenagel reaction (see p. 280);

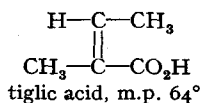
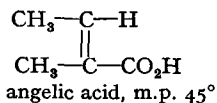


**isocrotonic acid** (*cis-but-2-enoic acid*) may be prepared by the action of sodium amalgam on  $\beta$ -chloroisocrotonic ester which is obtained from acetoacetic ester by reaction with phosphorus pentachloride:



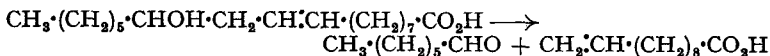
The action of sodium amalgam is particularly interesting, since it normally reduces a double bond in the  $\alpha\beta$ -position.

**Angelic and tiglic acids** are geometrical isomers with the structure  $\text{CH}_3\cdot\text{CH}:\text{C}(\text{CH}_3)\cdot\text{CO}_2\text{H}$  (*2-methylbut-2-enoic acid*):



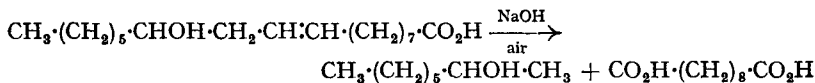
Both acids are found in nature as esters.

**Undecylenic acid** (*dec-9-ene-1-carboxylic acid*),  $\text{CH}_2\cdot\text{CH}\cdot(\text{CH}_2)_8\cdot\text{CO}_2\text{H}$ , may be obtained by the destructive distillation of *ricinoleic acid* (*11-hydroxyheptadec-8-ene-1-carboxylic acid*), which occurs as the glyceride ester in castor-oil. Heptanal is the other product, 10 per cent. yield of each being obtained:



Undecylenic acid is a solid, m.p.  $24.5^\circ$ , and is said to be a preventive and a cure for athlete's foot.

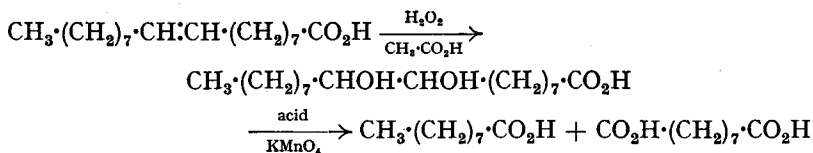
When ricinoleic acid is heated with sodium hydroxide in air, octan-2-ol and sebacic acid are obtained:



When ricinoleic acid (castor oil) is treated with concentrated sulphuric acid, it gives a complex mixture consisting of the hydrogen sulphate of ricinoleic acid in which the hydroxyl group is esterified, and a compound in which the sulphuric acid has added to the double bond: esterification and addition do not occur together in the same molecule of ricinoleic acid. The product, which is known as *Turkey-red oil*, is used as a wetting agent.

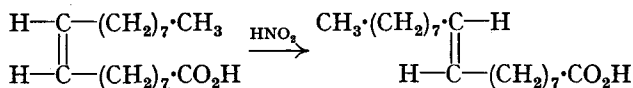
**Oleic acid** (*cis-heptadec-8-ene-1-carboxylic acid*) occurs as the glyceryl ester in oils and fats. It is a colourless oil, m.p.  $16^\circ$ , which is insoluble in

water, but soluble in ethanol and ether. Catalytic reduction converts it into stearic acid. Cold dilute alkaline permanganate, or hydrogen peroxide in acetic acid, converts oleic acid into 9 : 10-dihydroxystearic acid, which, on oxidation with, *e.g.*, acid permanganate, gives nonoic acid and azelaic acid:



This shows that the double bond in oleic acid is in the 9 : 10 position (carboxyl group being 1), and this is confirmed by ozonolysis.

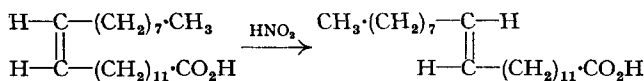
Oleic acid is the *cis* form. The *trans* form is **elaidic acid**, m.p. 51°, which may be obtained by the action of nitrous acid on oleic acid:



**Linoleic acid** (*heptadeca-8 : 11-diene-1-carboxylic acid*),  $\text{CH}_3 \cdot (\text{CH}_2)_4 \cdot \text{CH} : \text{CH} \cdot \text{CH}_2 \cdot \text{CH} : \text{CH} \cdot (\text{CH}_2)_7 \cdot \text{CO}_2\text{H}$ , b.p. 228°/14 mm., occurs as the glyceryl ester in linseed oil, hemp oil, etc.; it has been synthesised by Raphael *et al.* (1950).

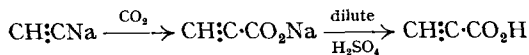
**Linolenic acid** (*heptadeca-8 : 11 : 14-triene-1-carboxylic acid*),  $\text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH} : \text{CH} \cdot \text{CH}_2 \cdot \text{CH} : \text{CH} \cdot \text{CH}_2 \cdot \text{CH} : \text{CH} \cdot (\text{CH}_2)_7 \cdot \text{CO}_2\text{H}$ , is a liquid which occurs as the glyceryl ester in, *e.g.*, poppy-seed oil. Oils containing linoleic and linolenic acids are drying oils (p. 263). Linolenic acid is the most abundant and widespread triene acid in Nature; it has been synthesised by Weedon *et al.* (1956).

**Erucic acid**, m.p. 34°, is the *cis* form of *heneicos-12-ene-1-carboxylic acid*,  $\text{CH}_3 \cdot (\text{CH}_2)_7 \cdot \text{CH} : \text{CH} \cdot (\text{CH}_2)_{11} \cdot \text{CO}_2\text{H}$ . It occurs as the glyceryl ester in various oils, *e.g.*, rape oil, cod-liver oil, etc. It is converted into the *trans* isomer **brassicic acid**, m.p. 61.5°, by the action of nitrous acid (*cf.* oleic acid, above):

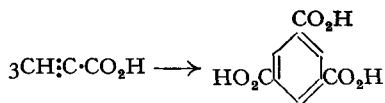


**Nervonic acid** (*tricos-14-ene-1-carboxylic acid*),  $\text{CH}_3 \cdot (\text{CH}_2)_7 \cdot \text{CH} : \text{CH} \cdot (\text{CH}_2)_{13} \cdot \text{CO}_2\text{H}$ , occurs in human brain-tissue and in fish oils. Both the *cis* and *trans* forms are known, but it appears to be the *cis* acid, m.p. 43°, which occurs naturally.

**Propiolic acid** (*propargylic acid*, *prop-2-yneic acid*),  $\text{CH}_2 : \text{C} \cdot \text{CO}_2\text{H}$ , is the simplest acetylenic carboxylic acid. It is conveniently prepared by the action of dry carbon dioxide on sodium acetylide:



It is a colourless liquid, m.p. 9°, which smells like acetic acid; it is reduced by sodium amalgam to propionic acid; it adds on halogen acid to give the  $\beta$ -halogeno-acrylic acid. It forms the silver or cuprous salt when treated with an ammoniacal solution of silver nitrate or cuprous chloride, respectively. When exposed to sunlight, it polymerises to *trimesic acid* (benzene 1 : 3 : 5-tricarboxylic acid; *cf.* acetylene):

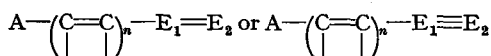


$\alpha\beta$ -Acetylenic acids are stronger acids than their ethylenic and saturated analogues due to the acetylene bond exerting a strong electron-attracting effect (*cf.* p. 96).

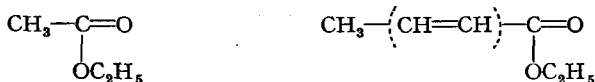


## THE PRINCIPLE OF VINYLOGY

According to Fuson (1935), the principle of vinylogy may be described as follows: If  $E_1$  and  $E_2$  represent non-metallic elements, then in the compound of the type  $A-E_1=E_2$  or  $A-E_1\equiv E_2$ , if a structural unit of the type  $\left(\begin{array}{c} \text{---C=C---} \\ | \quad | \end{array}\right)_n$  is interposed between A and  $E_1$ , the function of  $E_2$  remains qualitatively unchanged, but that of  $E_1$  may be usurped by the carbon atom attached to A. Thus

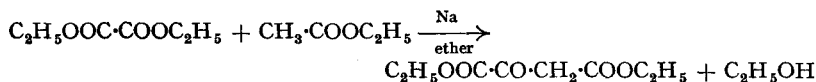


form vinylogous series. This may be illustrated by the compounds ethyl acetate and ethyl crotonate. These are vinylogues ( $n$  being equal to 1):

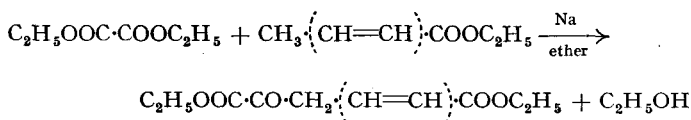


A is equivalent to  $\text{CH}_3$  and  $E_1=E_2$  to  $\begin{array}{c} \text{---C=O} \\ | \\ \text{OC}_2\text{H}_5 \end{array}$

Ethyl acetate condenses with ethyl oxalate to form *oxalacetic ester* (this, of course, is an example of the Claisen condensation):



In the same way, ethyl crotonate also condenses with ethyl oxalate:

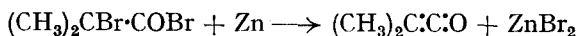


Several other examples of the application of vinylogy will be found in the text.

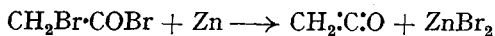
## KETENS (KETENES)

Ketens are compounds which are characterised by the presence of the grouping  $>\text{C}=\text{C}=\text{O}$ . If the compound is of the type  $\text{R}\cdot\text{CH}\cdot\text{C}\cdot\text{O}$ , it is known as an *aldoketen*; and if  $\text{R}_2\text{C}\cdot\text{C}\cdot\text{O}$ , then a *ketoketen*.

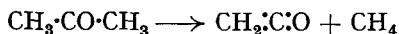
The most general method of preparing a keten is by debrominating an  $\alpha$ -bromoacyl bromide with zinc, e.g., dimethylketen from  $\alpha$ -bromoisobutyryl bromide:



The simplest member of the keten series is **keten** (*ketene*),  $\text{CH}_2\cdot\text{C}\cdot\text{O}$ . Keten may be prepared by debrominating bromoacetyl bromide with zinc:



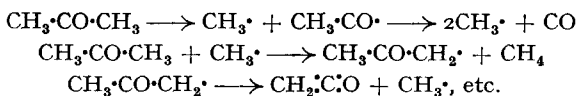
It is, however, usually prepared by the thermal decomposition of acetone (ethyl acetate or acetic anhydride may also be used as the starting material):



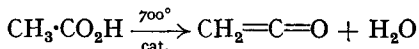
In practice, acetone vapour is passed over an electrically heated metal filament at  $700\text{--}750^\circ$ ; the filament is made of chromel wire (an alloy of 80 per cent. nickel and 20 per cent. chromium). The yield of keten is high, being usually between 90 and 95 per cent. An alternative procedure,

which gives a much lower yield (25–29 per cent.), is to pass acetone vapour through a long combustion tube filled with broken porcelain heated to redness.

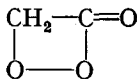
The thermal decomposition of acetone has been shown to be a free-radical chain reaction. The exact details are not known with certainty; Rice and Walters (1941) have suggested the following:



Keten is prepared industrially by passing acetone vapour through a copper tube at 700–850°, and by the decomposition of acetic acid in the presence of phosphoric acid or ethyl phosphate as catalyst:

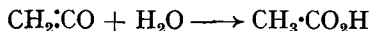


Keten is a colourless, poisonous, pungent gas, b.p.  $-41^\circ$ , which oxidises in air to the unstable peroxide, the structure of which may be as shown. Keten is a very reactive compound, and so is important as a synthetic reagent. It rapidly polymerises to *diketen*, and because of this tendency to polymerise, keten is usually used immediately when prepared.

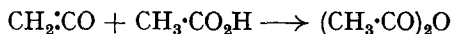


The reactions of keten are generally those of an acid anhydride; it acetylates most compounds with an active hydrogen atom (p. 198), provided the compound can be dissolved in some solvent inert to the action of keten. The yield of acetyl derivative is almost 100 per cent. (based on keten). The following reactions clearly show the acetylating property of keten:

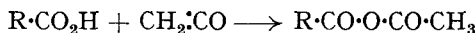
- (i) When keten is passed into water, acetic acid is formed slowly:



- (ii) When keten is passed into glacial acetic acid, acetic anhydride is formed:



By means of this reaction a mixed anhydride may be obtained, one radical of which, of course, must be the acetyl group:

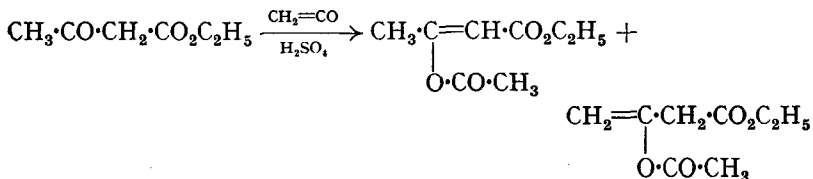


- (iii) Keten reacts with aliphatic or aromatic hydroxy-compounds:

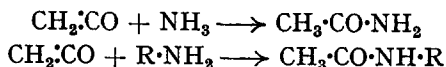


The reaction, however, is best carried out in the presence of a catalyst, e.g., sulphuric acid.

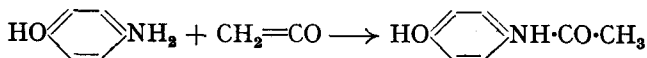
It also acetylates enolisable compounds, e.g.,



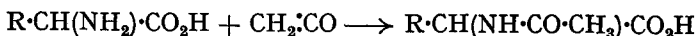
(iv) Keten reacts with ammonia to form acetamide, and with primary or secondary amines to form *N*-alkyl-acetamides:



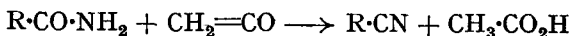
Primary amino-groups are acetylated extremely readily, and hence it is possible to acetylate this group selectively in compounds containing both an amino and hydroxyl group, *e.g.*, *p*-aminophenol:



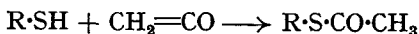
A particularly useful reaction of this type is the acetylation of amino-acids:



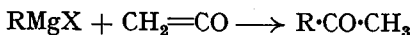
Amides are also acetylated by keten in the presence of sulphuric acid, but at elevated temperatures (in the absence of sulphuric acid) the cyanide is formed.



(v) Thiols are acetylated (preferably in the presence of sulphuric acid as catalyst):

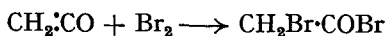


(vi) Keten reacts with Grignard reagents to form methyl ketones:

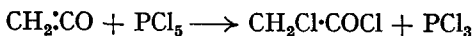


In addition to behaving as an acetylating reagent, keten behaves as an unsaturated compound, the carbonyl group showing no reactivity, *e.g.*,

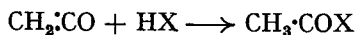
(i) Keten adds on bromine to form bromoacetyl bromide:



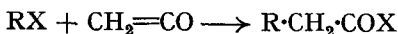
The halogeno-acetyl halide is also formed by the interaction of keten and phosphorus pentahalides:



(ii) Keten adds on halogen acid to form the acetyl halide:

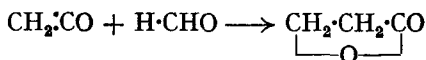


Alkyl halides also react with the keten in the presence of charcoal at 100° to form acid chlorides:



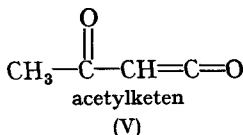
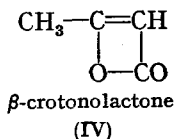
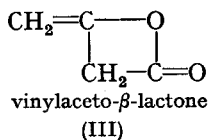
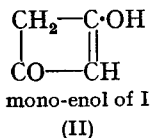
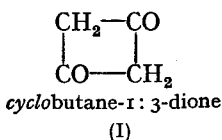
This offers a means of stepping up a series.

(iii) A particularly interesting addition reaction of keten is that with aldehydes to form  $\beta$ -lactones; *e.g.*, with formaldehyde,  $\beta$ -propiolactone is formed:



**Diketen** is readily formed by passing keten into acetone cooled in solid carbon dioxide (yield: 50–55 per cent.). Diketen is a pungent-smelling liquid, b.p. 127°, which, when strongly heated (550–600°), is depolymerised to keten.

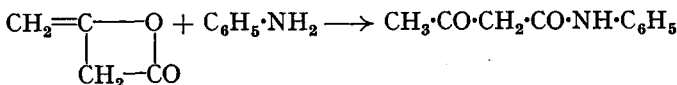
The structure of diketen is still uncertain. Various structures have been suggested, *e.g.*,



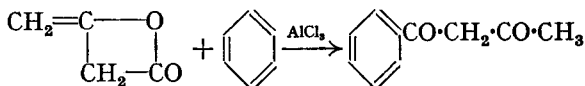
According to Whiffen and Thompson (1946), based on their work of infra-red measurements, the structure of diketen is most likely III or IV, or a mixture of both. These authors also point out that the evidence seems to favour III. This formula is also favoured by Blomquist and Baldwin (1948), who treated diketen with *N*-bromosuccimide and showed that the resulting products agree with structure III (and not with IV). Structure III is also supported by mass spectra studies of Long *et al.* (1953). Structure I has been excluded by work with isotope  $^{14}\text{C}$  (Roberts *et al.*, 1949). It is interesting to note, however, that the structure of dimethylketen dimer is 2:2:4:4-tetramethylcyclobutane-1:3-dione (*i.e.*, it corresponds to I), and the ring is planar (Robertson *et al.*, 1956).

Diketen may be further polymerised to dehydroacetic acid (p. 227).

Diketen reacts with alcohols to form esters of acetoacetic acid, and this reaction is now being used to prepare acetoacetic ester industrially (see p. 224). It also reacts with primary amines to form *N*-substituted acetoacetamides, *e.g.*, with aniline:



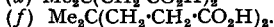
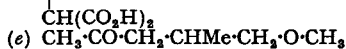
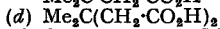
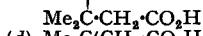
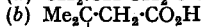
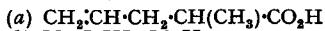
Diketen also undergoes the Friedel-Crafts reaction with benzene to form benzoylacetone:



### QUESTIONS

1. Using acetone or glycerol as the starting material, show how you would prepare:—(a) 3-methylbut-2-enoic acid, (b)  $\beta$ : $\beta$ -dimethylacrylic acid, (c)  $\beta$ -hydroxypropionic acid, (d)  $\alpha$ : $\alpha$ -dimethylsuccinic acid, (e)  $\alpha$ : $\beta$ -dibromopropionic acid, (f) glyceraldehyde.

2. Name the following compounds and suggest one synthesis for each:



3. How would you distinguish between allyl alcohol and propargyl alcohol?

4. Describe the preparation and the more important properties of:—(a) allyl alcohol, (b) allyl halides, (c) crotyl alcohol, (d) propargyl alcohol, (e) methyl vinyl ether, (f) divinyl ether, (g) crotonaldehyde, (h) propargylaldehyde, (i) methyl vinyl ketone, (j) crotonic acid, (k) propiolic acid.

5. How may acraldehyde, mesityl oxide, phorone and acrylic acid be prepared? Name the compounds and state the conditions under which they are formed when the above substances, respectively, are treated with:—(a)  $\text{Br}_2$ , (b)  $\text{HBr}$ , (c)  $\text{HCN}$ , (d)  $\text{NaOH}$ , (e)  $\text{NH}_3$ , (f)  $\text{H}_2$ , (g)  $\text{NaHSO}_3$ , (h)  $\text{NH}_2\text{OH}$ , (i)  $\text{CH}_2(\text{CO}_2\text{Et})_2$ , (j) E.A.A., (k)  $\text{CH}_2\text{N}_2$ .
6. Define and give examples of:—(a) hyperconjugation, (b) the allylic rearrangement, (c) the 1:4 mechanism, (d) Michael condensation, (e) Knoevenagel reaction, (f) negative groups, (g) geometrical isomerism, (h) vinylogy, (i) halochromic salt, (j) cyanoethylation.
7. Discuss the general methods of preparation and the more important properties of the unsaturated monocarboxylic acids. Give an account of the methods that can be used for determining the position of the double bond in an unsaturated acid.
8. Write an account of the preparation and properties of keten and diketen, including in your answer a discussion of the structure of diketen.
9. Write an account of the reduction of  $\alpha\beta$ -unsaturated carbonyl compounds.

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CHAPTER XIII  
NITROGEN COMPOUNDS

SOME compounds containing nitrogen have been described in Chapter IX, since these were regarded primarily as acid derivatives. It is now proposed to deal with many other nitrogen compounds, most of which may be regarded as alkyl nitrogen compounds.

**Hydrocyanic acid, hydrogen cyanide** (*prussic acid*), HCN, was discovered by Scheele (1782), who obtained it from bitter almonds which contain the glycoside *amygdalin*. Amygdalin, on hydrolysis with dilute acid, yields hydrogen cyanide, benzaldehyde and glucose:

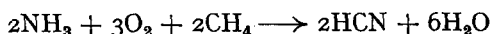


Hydrogen cyanide also occurs in the leaves of certain plants, *e.g.*, laurel. It may be prepared by heating sodium cyanide with concentrated sulphuric acid, the gas being dried over calcium chloride:

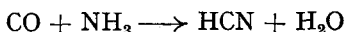


Hydrogen cyanide is prepared industrially:

(i) By passing a mixture of ammonia, air and methane over a platinum-rhodium gauze catalyst at 1000°:



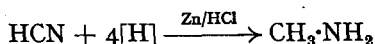
(ii) By passing a mixture of carbon monoxide and ammonia over an alumina catalyst at 500-700°:



Hydrogen cyanide is a colourless, poisonous liquid, b.p. 26°. It is a very weak acid, and is miscible in all proportions with water, ethanol and ether. It hydrolyses slowly in aqueous solution, and more rapidly in the presence of inorganic acids to form first formamide, and then ammonium formate:



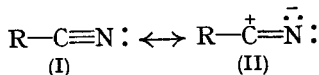
Hydrogen cyanide is reduced by nascent hydrogen to methylamine:



It is a useful reagent for certain syntheses, *e.g.*, cyanohydrins by combination with carbonyl compounds (p. 151), and in the Gattermann aldehyde synthesis (p. 647).

**Structure of hydrogen cyanide.** Hydrogen cyanide is believed to exist in two forms because it gives rise to two kinds of alkyl derivatives: the *alkyl cyanides*, R·CN, which are derivatives of *hydrogen cyanide*, HCN; and the *alkyl isocyanides*, R·NC, which are derivatives of *hydrogen isocyanide*, HNC.

The structures of HCN and R·CN, respectively, were originally believed to be H·C≡N and R·C≡N, but recent determinations of the dipole moments of the alkyl cyanides indicate that they are resonance hybrids of structures I and II, the contribution of II being about 57 per cent.:



On the other hand, infra-red studies strongly favour I.

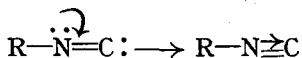
The structures of HNC and R·NC proved more difficult to elucidate. Originally, the formula of the alkyl *isocyanides* was written R—N≡C (nitrogen with a valency of five and carbon, four). This, however, was inconsistent with the chemical properties of *isocyanides*, and was soon considered unlikely. It is now known, according to the electronic theory of valency, that four bonds between nitrogen and carbon is impossible on theoretical grounds.

Normally, on addition to unsaturated compounds, the addendum adds to each atom joined by the double bond; this does not occur with *isocyanides*, the addendum adding only to the carbon atom:

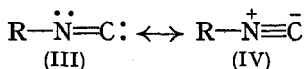


These facts led Nef (1891–1892) to suggest that *isocyanides* did not contain quadrivalent carbon but bivalent carbon. He therefore wrote their formula as R—N=C<, with two "free" valencies by means of which *isocyanides* add on the addendum to the carbon atom alone (as shown in the above examples).

Study of the dipole moments and Raman spectra of *isocyanides* indicated that bivalent carbon did not represent the true state of affairs, and led to the suggestion that the bond between the nitrogen and carbon atoms was a triple bond. If we use the electronic formula of Nef's structure, we can introduce a triple bond between the nitrogen and carbon atoms by rearranging the lone pair of the nitrogen atom to act as a donor to the carbon atom, *i.e.*,



Raman spectra of cyanides and *isocyanides* show the presence of the C≡N group. This is satisfied by the N≡C group. On the other hand, more recent work indicates that alkyl *isocyanides* are resonance hybrids of III and IV:



Furthermore, the value of the C—N—C valency bond angle has been found to be 180°, *i.e.*, these three atoms form a linear arrangement, which shows that IV makes a very large contribution to the actual state (see Ch. 11).

Thus, in view of the existence of alkyl cyanides and *isocyanides*, hydrogen cyanide is believed to be tautomeric, giving rise to the *nitrile-isonitrile diad system*:



The position, however, cannot be regarded as being completely satisfactory. It appears that only one form of acid is known, *viz.*, hydrogen cyanide; all its reaction indicate the structure H—C≡N, *e.g.*, its hydrolysis to formic acid.

#### ALKYL CYANIDES

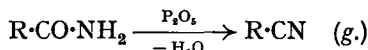
These are also known as **nitriles** or **carbonitriles**.

**Nomenclature.** This group of compounds is usually named either as the *alkyl cyanides* (*i.e.*, the alkyl derivatives of hydrogen cyanide), or as the *nitrile* of the acid which is produced on hydrolysis, the suffix *-ic* of the trivial

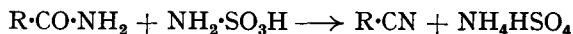
name being replaced by *-onitrile*. The following examples illustrate both systems of nomenclature:

HCN	hydrogen cyanide or formonitrile
CH <sub>3</sub> ·CN	methyl cyanide or acetonitrile
(CH <sub>3</sub> ) <sub>2</sub> CH·CN	<i>isopropyl cyanide</i> or <i>isobutyronitrile</i>

**General methods of preparation.** 1. By the dehydration of acid amides with phosphorus pentoxide:



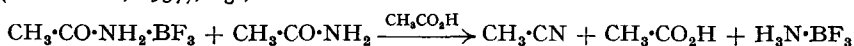
Amides may also be converted into cyanides by heating with phosphorus pentachloride or thionyl chloride. Dehydration of the amide to cyanide is also very conveniently effected by heating with sulphamic acid (Kirsanov *et al.*, 1950).



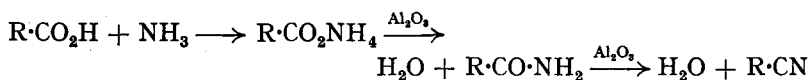
Stephens *et al.* (1955) have shown that *p*-toluenesulphonyl chloride in pyridine readily dehydrates amides to cyanides (yield: 58–76 per cent).

High molecular weight acid amides are dehydrated to the corresponding cyanide by heat alone (p. 205).

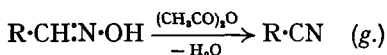
An acid amide may be converted into the cyanide by heating it with the amide-boron trifluoride complex in the presence of a small amount of carboxylic acid (Nieuwland, 1937), *e.g.*,



Cyanides are prepared industrially by passing a mixture of carboxylic acid and ammonia over alumina at 500°. This reaction probably occurs as follows:



2. By the dehydration of aldoximes with phosphorus pentoxide, or better, with acetic anhydride:

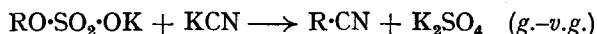


3. The most convenient method is to heat an alkyl iodide with potassium cyanide in aqueous ethanolic solution; a small amount of *isocyanide* is also obtained:

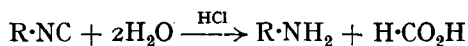


This method is satisfactory only if R is a primary or secondary alkyl radical. If it is a tertiary radical, very little cyanide is obtained, the tertiary iodide being converted into the corresponding olefin (*cf.* p. 108). Tertiary alkyl cyanides are best prepared by method 4 below.

Many cyanides, particularly the lower members, may be readily prepared by warming the potassium alkyl sulphate with potassium cyanide (some *isocyanide* is also obtained):

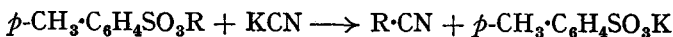


The cyanide may be freed from *isocyanide* by shaking with dilute hydrochloric acid, which hydrolyses the latter, but does not affect the former:

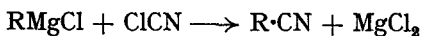




Tosylates, *i.e.*, *p*-toluenesulphonates (see p. 612), are also useful for cyanide preparation:



4. By the interaction of a Grignard reagent and cyanogen chloride:

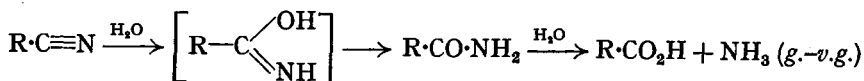


This is the best method of preparing tertiary alkyl cyanides.

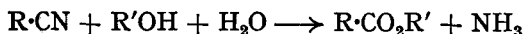
Methyl cyanide may be formed by passing a mixture of acetylene and ammonia over zirconia at 400–500°, the yield reaching as high as 99 per cent. (Amiel and Nomine, 1947.)

**General properties.** The alkyl cyanides are stable neutral substances with fairly pleasant smells, and are not as poisonous as hydrogen cyanide. The lower members are liquids which are soluble in water (with which they can form hydrogen bonds), but the solubility diminishes as the molecular weight increases. They are all readily soluble in organic solvents.

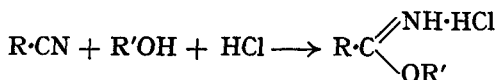
**Reactions.** 1. The alkyl cyanides are hydrolysed by acids or alkalis to the corresponding acid via the intermediate formation of an amide (see also p. 204):



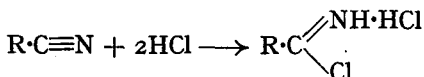
When a solution of alkyl cyanide in an alcohol is heated with concentrated sulphuric acid or hydrochloric acid, the *ester* is obtained:



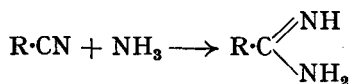
On the other hand, if dry hydrogen chloride is passed into the solution of an alkyl cyanide in anhydrous alcohol, the *imidic ester hydrochloride* is formed:



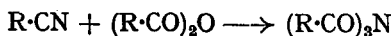
When an alkyl cyanide is treated with *dry* hydrogen chloride, the *imido-chloride* is formed:



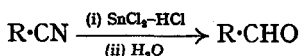
2. Alkyl cyanides combine with dry ammonia to form *amidines*:



3. Alkyl cyanides combine with acid anhydrides on heating to form *tertiary acid amides*:



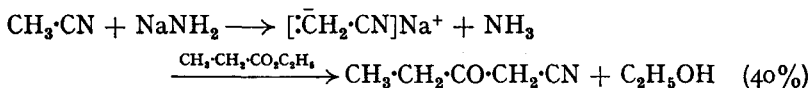
4. Alkyl cyanides may be converted into aldehydes; *e.g.*,



This, as we have seen (p. 148), is a general method for preparing aldehydes.



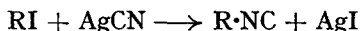
sodamide (Levine and Hauser, 1946); *e.g.*, methyl cyanide condenses with ethyl propionate to form propionylmethyl cyanide:



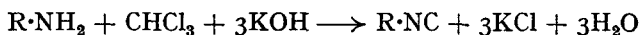
#### ALKYL *iso*CYANIDES

These are also known as *isonitriles* or *carbylamines*.

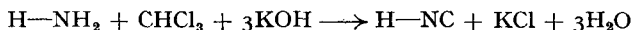
**General methods of preparation.** 1. By heating an alkyl iodide with silver cyanide in aqueous ethanolic solution: a small amount of cyanide is also formed:



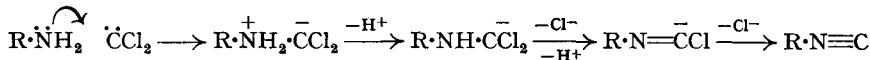
2. By heating a mixture of a primary amine and chloroform with ethanolic potassium hydroxide:



It has been argued that by analogy with this reaction, replacement of a primary amine by ammonia would lead to the formation of hydrogen *isocyanide*:

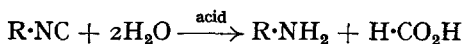


The mechanism of the *isocyanide* reaction is not certain. Robinson (1961) has suggested that the reaction proceeds via the intermediate formation of dichloromethylene, which is produced from the chloroform in alkaline solution (p. 117):

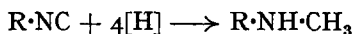


**General properties.** The alkyl *isocyanides* are poisonous, most unpleasant-smelling liquids, with lower boiling points than the isomeric cyanides. They are not very soluble in water, the nitrogen atom not having a lone pair of electrons available for hydrogen bonding.

**Reactions.** 1. Alkyl *isocyanides* are hydrolysed to an amine and formic acid by dilute acids, *but are not hydrolysed by alkalis*:

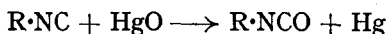
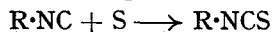
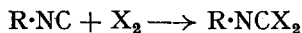


2. Alkyl *isocyanides* are reduced to secondary amines either by nascent hydrogen or by catalytic reduction:

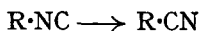


Both reactions 1 and 2 clearly indicate that the alkyl group in alkyl *isocyanides* is attached to the *nitrogen* atom of the CN group (*cf.* cyanides, above).

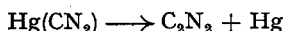
3. Alkyl *isocyanides* add on halogen to form *alkyliminocarbonyl halides*, sulphur to form *alkyl isothiocyanates*, and are readily oxidised by mercuric oxide to *alkyl isocyanates*:



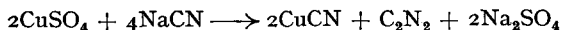
4. When alkyl *isocyanides* are heated for a long time, they rearrange to the cyanide:



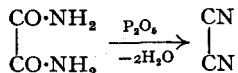
**Cyanogen** (*ethanedinitrile*),  $C_2N_2$ , may be prepared by heating the cyanides of mercury or silver:



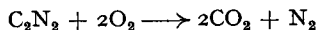
It may also be prepared by adding sodium cyanide to copper sulphate solution and heating. The cupric cyanide first formed is unstable, decomposing into cuprous cyanide and cyanogen:



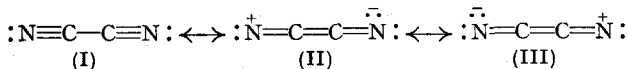
When heated with phosphorus pentoxide, oxamide is dehydrated to cyanogen:



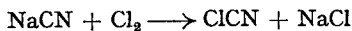
Cyanogen is a poisonous, colourless gas, b.p.  $-21^\circ$ , very soluble in water. It burns with a violet flame to give carbon dioxide and nitrogen:



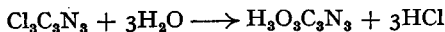
Its aqueous solution slowly decomposes to give a brown precipitate of *azulmic acid*,  $C_4H_5ON_5$ , and the solution contains ammonium oxalate, hydrogen cyanide, formic acid and urea. When cyanogen is heated at  $400^\circ$ , it polymerises to *paracyanogen*, which, at  $800^\circ$ , regenerates cyanogen. The structure of cyanogen is probably best represented as a resonance hybrid, I being the most important:



**Cyanogen chloride**,  $ClCN$ , may be prepared by passing chlorine into a cooled solution of sodium cyanide:



It is a poisonous, colourless gas, b.p.  $12^\circ$ , which is very soluble in water, ethanol and ether. It readily polymerises to *cyanuric chloride*,  $Cl_3C_3N_3$ . This is a crystalline solid, m.p.  $154^\circ$ , which is decomposed by heating with water under pressure at  $125^\circ$  to give *cyanuric acid*:

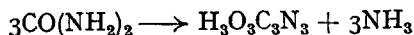


**Cyanogen bromide**,  $BrCN$ , may be prepared by adding sodium cyanide to well-cooled bromine water:

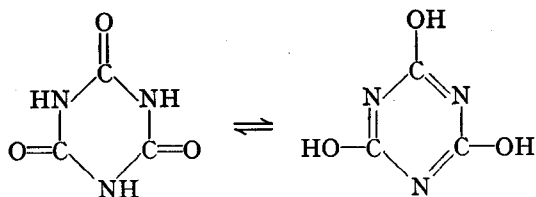


It is a colourless, crystalline solid, m.p.  $52^\circ$ , which polymerises to *cyanuric bromide*,  $Br_3C_3N_3$ . Cyanogen bromide is a useful reagent for converting tertiary amines into secondary amines (see p. 318).

**Cyanic acid**,  $HO-CN$ . Urea, on dry distillation, gives *cyanuric acid*:

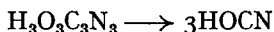


The yield is improved by heating urea with zinc chloride. Cyanuric acid is a colourless, crystalline solid, not very soluble in water, and is strongly acid, reacting as a mono-, di- and tribasic acid. It has a cyclic structure (a *triazine derivative*) and is believed to be tautomeric (*amido-imidol triad system*):

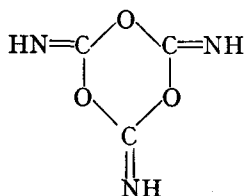


On the other hand, X-ray analysis of cyanuric acid in the solid state indicates that the acid is best represented as a resonance hybrid of the carbonyl form (amido-form). Furthermore, absorption spectra studies in neutral solution show that the same forms are present as in the solid state (Koltz and Askounis, 1947).

When cyanuric acid is heated, it does not melt but decomposes into cyanic acid vapour which, when condensed below 0°, gives a colourless condensate:



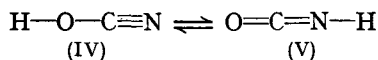
Cyanic acid is a colourless, volatile, strongly acid liquid which, above 0°, readily polymerises to cyanuric acid and *cyamelide*, which is a white solid isomeric with cyanuric acid. The structure of cyamelide is believed to be



Aqueous solutions of cyanic acid rapidly hydrolyse to give carbon dioxide and ammonia:

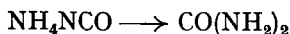


Cyanic acid was believed to be a tautomeric mixture of cyanic acid, IV, and isocyanic acid, V (amido-imidol triad system):

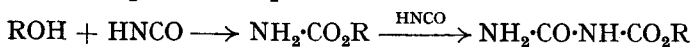


Infra-red studies, however, have indicated that cyanic acid is V; only derivatives of V are known, *e.g.*, alkyl isocyanates, R·NCO.

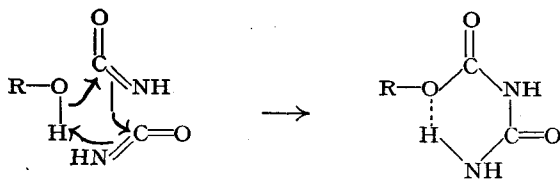
When a solution of potassium isocyanate (usually called potassium cyanate) and ammonium sulphate is evaporated to dryness, urea and potassium sulphate are obtained, the urea being formed by the molecular rearrangement of the intermediate product ammonium isocyanate:



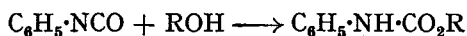
Cyanic acid reacts with alcohols to form *urethans*; excess of cyanic acid converts urethans into *allophanates*, which are esters of the unknown acid, *allophanic acid*,  $\text{NH}_2\cdot\text{CO}\cdot\text{NH}\cdot\text{CO}_2\text{H}$ :



According to Close *et al.* (1953), the formation of urethan is, if it is truly the intermediate step, not the important one in the usual preparation of allophanates. These authors suggest that allophanate formation occurs via a concerted attack of two molecules of cyanic acid to form a chelate intermediate.

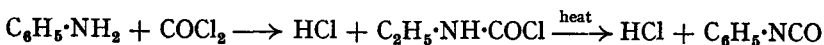


*N*-substituted urethans are formed by the reaction between alkyl or aryl *isocyanates* and an alcohol. These are well-defined crystalline solids, and so are used to characterise alcohols, phenyl and 1-naphthyl *isocyanates* being the *isocyanates* used for this purpose:



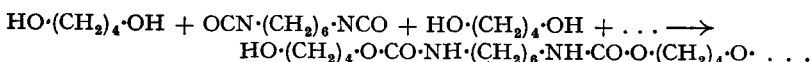
Phenyl *isocyanate* is also used to characterise primary and secondary amines, with which it forms substituted ureas (see p. 315).

Phenyl *isocyanate* is usually prepared by the action of carbonyl chloride on aniline:



This is a general method for preparing *isocyanates*; another general method is the Curtius reaction (p. 209).

Di-*isocyanates*, e.g., hexamethylene di-*isocyanate*,  $\text{OCN}\cdot(\text{CH}_2)_6\cdot\text{NCO}$ , are used to prepare polyurethan plastics by reaction with di- and polyhydroxyalcohols, e.g., tetramethylene glycol:

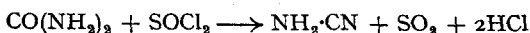


**Fulminic acid.**  $\text{HO}\cdot\text{N}\equiv\text{C}$ , may be prepared by decomposition of its salts with acid. Mercury fulminate,  $[(\text{CNO})_2\text{Hg}]_2\text{H}_2\text{O}$ , which is used as a detonator, may be prepared by dissolving mercury in nitric acid, and then adding ethanol. Free fulminic acid is unstable. It is soluble in ether, the ethereal solution also being unstable, the acid readily polymerising.

**Cyanamide**,  $\text{NH}_2\cdot\text{CN}$ , may be prepared by the action of ammonia on cyanogen chloride:

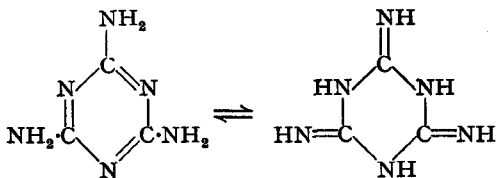


It may also be prepared by heating urea with thionyl chloride:



It is also readily prepared by the action of water and carbon dioxide on calcium cyanamide (see below).

Cyanamide is a colourless, crystalline solid, m.p.  $42^\circ$ , very soluble in water, ethanol and ether. It is converted into *guanidine* (*q.v.*) by ammonia, and into *thiourea* (*q.v.*) by hydrogen sulphide. When cyanamide is melted it forms the dimer *dicyanodiamide*  $(\text{NH}_2)_2\text{C}\cdot\text{N}\cdot\text{CN}$ , and the trimer *melamine*, which is a cyclic compound (and tautomeric):

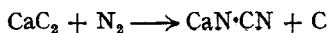


Melamine is used for making melamine-formaldehyde plastics.

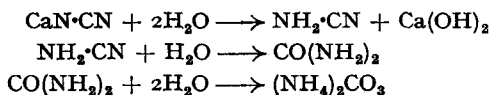
Cyanamide itself is a tautomeric compound (amidine system), and Raman spectra investigations have shown that two forms are present in equilibrium in the solid or fused state, or in solution:



Cyanamide forms salts, the most important of which is the calcium salt. This is manufactured by heating calcium carbide mixed with 10 per cent. its weight of calcium chloride in a stream of nitrogen at  $800^\circ$ :



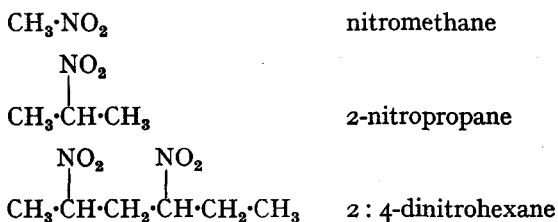
The calcium cyanamide-carbon mixture is used as a fertiliser; it is hydrolysed in the soil to cyanamide, which is then hydrolysed to urea, which, in turn, is converted into ammonium carbonate by bacteria in the soil:



Calcium cyanamide is also used to prepare urea industrially.

### NITROPARAFFINS

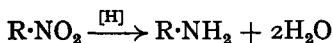
**Nomenclature.** The nitroparaffins are named as the nitro-derivative of the corresponding paraffin, the positions of the nitro-groups being indicated by numbers, *e.g.*,



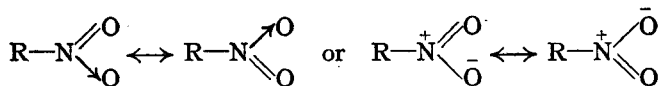
The nitroparaffins, the structure of which is  $\text{R}\cdot\text{NO}_2$ , are isomeric with the alkyl nitrites,  $\text{R}\cdot\text{O}\cdot\text{NO}$ . The evidence that may be adduced for these respective formulæ is to be found in the study of the reactions of these two groups of compounds. The reactions of the nitrites have already been described (p. 196), and those of the nitroparaffins are described below. It is, however, worth while at this stage to mention the reaction which most clearly indicates their respective structures, *viz.*, reduction. When alkyl nitrites are reduced by nascent hydrogen, an alcohol and ammonia or hydroxylamine are formed. This shows that the alkyl group in nitrites is attached to an oxygen atom:



On the other hand, when nitroparaffins are reduced, a primary amine is formed. This shows that the alkyl group is attached to the nitrogen atom, since the structure of a primary amine is known to be  $\text{R}\cdot\text{NH}_2$  from its method of preparation (see below):



The structure of the nitro-compounds was originally written  $\text{R}-\overset{\text{O}}{\parallel}{\text{N}}-\overset{\ominus}{\text{O}}$ , but work on the dipole moments indicates that they are resonance hybrids:



For most purposes, however, the original formula  $\text{R}-\overset{\text{O}}{\parallel}{\text{N}}-\overset{\ominus}{\text{O}}$  or the non-committal formula  $\text{R}\cdot\text{NO}_2$ , is satisfactory.

From the M.O. point of view, the nitro-group is conjugated (Fig. 1), and delocalisation of bonds increases its stability (the two oxygen atoms are equivalent; *cf.* the carboxylate ion, p. 184).

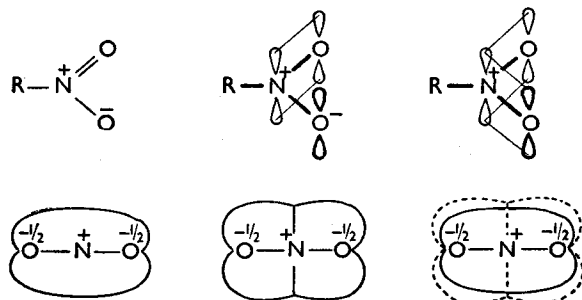


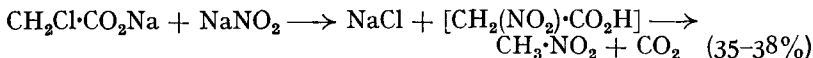
FIG. 13.1.

**General methods of preparation.** 1. By heating an alkyl halide with silver nitrite in aqueous ethanolic solution:



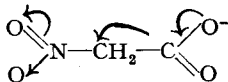
This method is only useful for the preparation of primary nitroparaffins. With *sec.*-halides the yield is about 15 per cent., and with *tert.*-halides 0–5 per cent.; the yield of nitrite increases from primary to tertiary halides (Kornblum *et al.*, 1954, 1955). Kornblum *et al.* (1956) have now described a simple new synthesis of primary and secondary nitro-compounds. These authors have shown that, contrary to general opinion, sodium nitrite reacts with alkyl halides to give good yields of nitroparaffin (55–62 per cent.) together with alkyl nitrites (25–33 per cent.). The success of the reaction depends on the use of dimethylformamide as solvent, and the addition of urea increases the solubility of sodium nitrite. Alkyl bromides and iodides are most satisfactory; the chlorides react too slowly to be useful.

2. Nitromethane may be prepared by boiling an aqueous solution of sodium nitrite with a halogeno-acetic acid, *e.g.*,



This method has no value for preparing higher nitroparaffins (Treibs *et al.*, 1954).

The ready decarboxylation of the intermediate nitroacetic acid may be explained on the assumption that the electron-attracting nitro-group facilitates the loss of carbon dioxide (*cf.* p. 177):



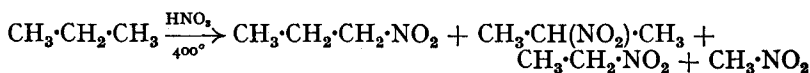
3. Until fairly recently, the preparation of nitro-compounds by direct nitration was of academic interest only, but mainly from the work of Hass and his co-workers direct nitration is now an important industrial process. Two techniques have been evolved: liquid-phase nitration and vapour-phase nitration.

In *liquid-phase nitration*, the hydrocarbon is heated with concentrated nitric acid under pressure at 140°. Nitration under these conditions is always slow, and a large amount of polynitro-compounds is produced. It



is interesting to note that a mixture of nitric and sulphuric acids is not suitable for nitrating paraffins (*cf.* aromatic hydrocarbons, p. 553).

In *vapour-phase nitration*, the hydrocarbon is heated with nitric acid (or with oxides of nitrogen) at 150–475°; each hydrocarbon has its optimum temperature, *e.g.*,



Vapour-phase nitration is more satisfactory than liquid-phase nitration.

Hass and Shechter (1947) have formulated general rules of vapour-phase nitration of paraffins (and *cycloparaffins*).

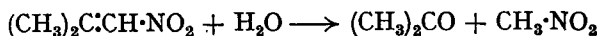
(i) Polynitro-compounds are formed only from paraffins of fairly high molecular weight.

(ii) Any hydrogen atom in the hydrocarbon is capable of replacement by a nitro-group, and the ease of replacement is tertiary hydrogen > secondary > primary. As the temperature rises, however, the ease of replacement tends to become equal.

(iii) Any alkyl group present in the paraffin can be replaced by a nitro-group, *i.e.*, chain fission takes place; *e.g.*, isopentane yields nine nitroparaffins. The fission reaction increases as the temperature rises.

(iv) Oxidation always accompanies nitration, resulting in the formation of nitro-compounds and a mixture of acids, aldehydes, ketones, alcohols, nitrites, nitroso-compounds, nitro-olefins, polymers, carbon monoxide and carbon dioxide. Catalysts such as copper, iron, platinum oxide, etc., accelerate oxidation rather than nitration.

4. Another recent method for preparing nitro-compounds is the hydrolysis of  $\alpha$ -nitro-olefins with water, acid or alkali; *e.g.*, 2-methyl-1-nitroprop-1-ene gives acetone and nitromethane in almost quantitative yield (Levy and Scaife, 1947):



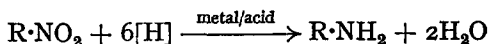
5. Kornblum *et al.* (1956) have introduced a practical synthesis of *tert.*-nitro-compounds by the oxidation of *tert.*-carbinamines with potassium permanganate:



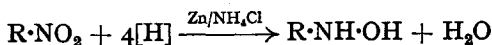
**General properties.** The nitroparaffins are colourless (when pure), pleasant-smelling liquids which are sparingly soluble in water. Most of them can be distilled at atmospheric pressure.

The nitroparaffins in commercial use at the moment are the lowest four members of the series: nitromethane, nitroethane and 1- and 2-nitropropanes. These are prepared by the vapour-phase nitration of propane, and are used as solvents for oils, fats, cellulose esters, resins and dyes.

**Reactions.** 1. Nitroparaffins are reduced in *acid* solution to primary amines:



Catalytic reduction also produces a primary amine, the yield with a Raney nickel catalyst being 90–100 per cent. When the reduction is carried out in *neutral* solution, *e.g.*, with zinc dust and ammonium chloride solution, nitro-compounds are converted into hydroxylamine derivatives:

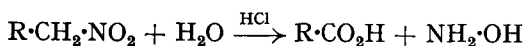


When stannous chloride and hydrochloric acid are used as the reducing agent, nitro-compounds are converted into a mixture of hydroxylamine derivative and oxime:



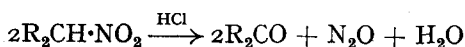
Since hydroxylamine can give rise to two types of derivatives, *e.g.*,  $R \cdot NH \cdot OH$  and  $NH_2 \cdot OR$ , it is necessary to distinguish one from the other. A common method is to name the former as the *N*-alkylhydroxylamine, and the latter as the *O*-alkylhydroxylamine, the capital letters *N* and *O*, respectively, indicating where the alkyl group is attached in the molecule.

2. Primary nitro-compounds are hydrolysed by boiling hydrochloric acid or by 85 per cent. sulphuric acid to a carboxylic acid and hydroxylamine:



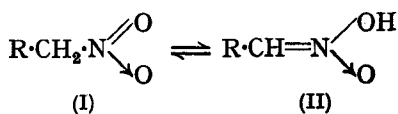
This reaction is now used for manufacturing hydroxylamine, and may become a commercial source of propionic acid (using *n*-nitropropane).

Secondary nitro-compounds are hydrolysed by boiling hydrochloric acid to ketones and nitrous oxide:



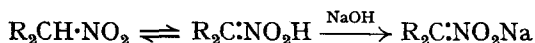
Tertiary nitro-compounds are generally unaffected by hydrochloric acid.

3. Primary and secondary nitro-compounds, *i.e.*, those containing  $\alpha$ -hydrogen atoms, are acidic in character due to tautomerism (the nitro-group is a very strong negative group and contains multiple bonds):

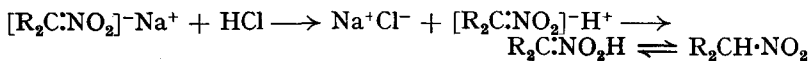


The nitro-form I is often called the *pseudo-acid* form; II is known as the *aci*-form or *nitronic acid*. This is an example of a triad system, the *nitro-acinitro* system; the equilibrium is almost completely on the left, and this may be due to the nitro-form being stabilised by resonance (of the nitro-group).

These nitronic acids do not dissolve in aqueous sodium carbonate, but do in aqueous sodium hydroxide, which disturbs the nitro-acinitro equilibrium by removing the latter form. Thus nitro-compounds behave as acids in the presence of strong alkalis, but not in their absence; hence they are said to be *pseudo-acids*:



These sodium compounds are true salts, *i.e.*, they exist as ions:  $[R_2C : NO_2]^- Na^+$ . When the sodium salt is acidified at low temperature, there is not always an immediate separation of oily drops (of the nitro-form). On standing, however, the acidified solution slowly deposits oily drops due to the slow tautomeric change of the nitronic acid into the nitro-compound. Furthermore, when the sodium salt is carefully neutralised with hydrochloric acid, the resulting solution has a conductivity which is greater than that calculated for the sodium chloride content. Hence, in addition to the sodium and chloride ions, there must be present other ions which must be those from the nitronic acid. Thus the following changes probably take place:

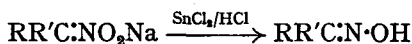


This is evidence for the existence of the nitronic acid; actually Hantzsch and Schultze (1896) isolated both forms of phenylnitromethane,  $C_6H_5 \cdot CH_2 \cdot NO_2$ , thus confirming the existence of the nitro-acinitro tautomeric system.

When the sodium salt solution of the nitronic acid is acidified with 50 per cent. sulphuric acid at room temperature, an aldehyde (from a primary nitro-compound) and a ketone (from a secondary nitro-compound) is obtained, e.g., ( $R'$  is either an alkyl radical or a hydrogen atom):

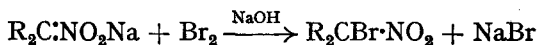


When treated with stannous chloride and hydrochloric acid, the sodium salt of the nitronic acid is reduced to the aldoxime or ketoxime:



These oximes are readily converted into the parent carbonyl compound by steam distillation or by direct hydrolysis with acid.

4. Primary and secondary nitro-compounds are readily halogenated in alkaline solution in the  $\alpha$ -position only:



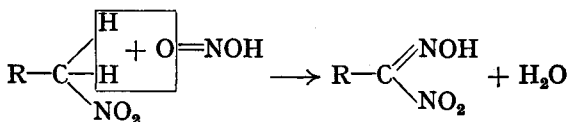
Primary nitro-compounds can form the mono- and dibromo-derivatives, whereas secondary form only the monobromo-derivative: nitromethane is exceptional in that it can form the tribromo-derivative. *Chloropicrin* (p. 117) is manufactured by the reaction between nitromethane, chlorine and sodium hydroxide.

When liquid or gaseous nitro-compounds are treated with halogen *in the absence of alkali*, indiscriminate substitution takes place resulting in the formation of the  $\alpha$ -,  $\beta$ -,  $\gamma$ -, halogeno-compounds, e.g.,

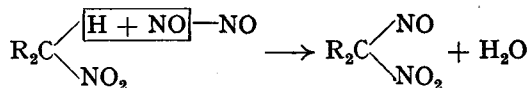


5. Nitro-compounds react with nitrous acid, the product formed depending on the nature of the alkyl group.

Primary nitro-compounds form *nitrolic acids*; these are crystalline substances which dissolve in sodium hydroxide to give red solutions:

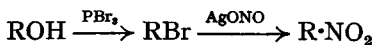


Secondary nitro-compounds form *pseudonitroles* ( $\psi$ -nitroles); these are colourless crystalline substances which dissolve in sodium hydroxide to give blue solutions (the blue colour is probably due to the presence of the nitroso-group; see below):



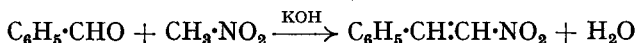
Tertiary nitro-compounds do not react with nitrous acid since they have no  $\alpha$ -hydrogen atom.

These reactions with nitrous acid are the basis of the "red, white and blue" test for the nature of monohydric alcohols (Victor Meyer *et al.*, 1874). The alcohol under investigation is treated as follows:

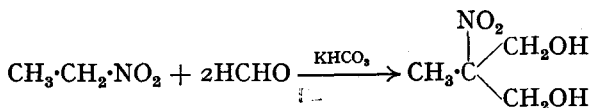


The nitro-compound is now treated with an alkaline solution of sodium nitrite, acidified with hydrochloric acid, and finally made alkaline with sodium hydroxide. The development of a red colour indicates a primary alcohol, blue colour a secondary, and the solution remaining colourless ("white"), a tertiary alcohol. This test is now only historically important.

6. Owing to the presence of active  $\alpha$ -hydrogen atoms, primary and secondary nitro-compounds undergo condensation with aldehydes; *e.g.*, (i) nitro-methane condenses with benzaldehyde in the presence of ethanolic potassium hydroxide to form *o*-nitrostryrene:

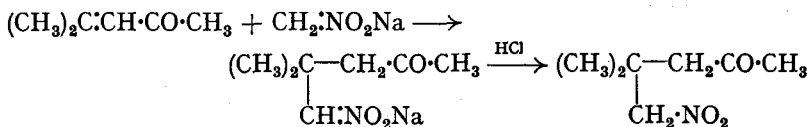


(ii) Nitroethane condenses with formaldehyde in the presence of aqueous potassium hydrogen carbonate to form the bishydroxymethyl compound, 2-methyl-2-nitropropane-1 : 3-diol (*cf.* p. 165).

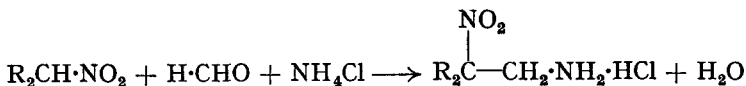


These condensations are similar to the aldol condensations, the active methylene or methyne group being produced by the adjacent nitro-group.

The sodium salts of the nitronic acids condense with  $\alpha\beta$ -unsaturated ketones (p. 279); *e.g.*, with mesityl oxide nitromethane forms 4 : 4-dimethyl-5-nitropentan-2-one:



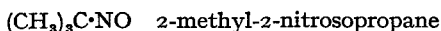
Primary and secondary nitro-compounds also undergo the **Mannich reaction** (1917). This is the condensation between formaldehyde, ammonia or a primary or secondary amine (preferably as the hydrochloride), and a compound containing at least one active hydrogen atom. In this reaction, the active hydrogen atom is replaced by an aminomethyl group or substituted aminomethyl group:



The Mannich reaction offers a means of preparing a large variety of compounds, *e.g.*, nitro-amines, diamines, etc.

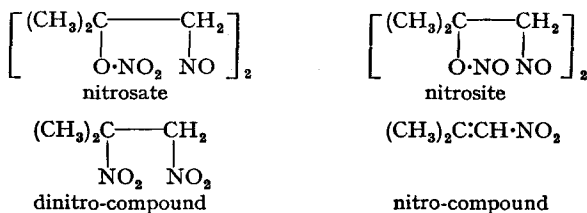
#### NITROSO-PARAFFINS

The nitroso-paraffins contain a nitroso-group,  $\text{—N=O}$ , directly attached to a carbon atom. They are named as the nitroso-derivatives of the corresponding paraffin, *e.g.*,

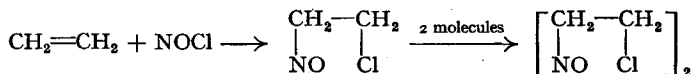


**General methods of preparation.** 1. By the addition of "nitrous fumes" to olefins. The compound formed depends on the nature of the olefin; usually a mixture is obtained, *e.g.*, Michael and Carlson (1940) treated *isobutene* with

dinitrogen tetroxide under various conditions, and believed that the following compounds were formed (see also p. 71):



2. By the addition of nitrosyl chloride or bromide to olefins, whereby olefin nitrosahalides are formed (p. 71):



Thorne (1956) has shown that, in general, structures which increase the availability of electrons at the double bond favour the formation of nitrosochlorides and nitrosates. Thus it was found that a carboxyl group fairly close to the double bond prevents formation of adducts, e.g., 4-phenylbut-3-enoic and 5-phenylpent-4-enoic acid do not form nitrosochlorides or nitrosates; oleic acid, however, forms a nitrosochloride. Furthermore, the position of a double bond in an olefin determines whether an adduct is formed, e.g., hex-1-ene does not form a nitrosochloride whereas hex-2-ene does.

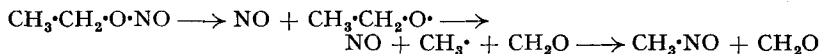
3. By the action of nitrous acid on certain types of compounds, e.g., secondary nitro-paraffins (see p. 305).

4. By the oxidation of primary amines containing a tertiary alkyl group with e.g., Caro's acid (peroxy(mon)sulphuric acid):



On the other hand, Emmons (1957) has prepared primary, secondary, and tertiary nitroso compounds by oxidation of amines with neutralised peracetic acid in methylene dichloride (yield: 33-80 per cent.).

5. Gowenlock *et al.* (1956) have prepared nitrosoparaffins (C<sub>1</sub> - C<sub>4</sub>) by the pyrolysis of alkyl nitrites, and have proposed the following mechanism (e.g., for ethyl nitrite):

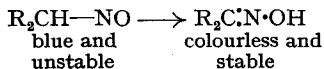


**General properties.** Nitroso-compounds, which are usually blue or green liquids, tend to associate to give colourless solids (smelling like camphor) which are dimers. These bimolecular solids regenerate the monomer when fused or when dissolved in solution. Chilton *et al.* (1955) and Gowenlock *et al.* (1955) have examined the absorption spectrum of the two solid forms of nitrosomethane, and have concluded that they are geometrical isomers (*N.B.*, a *double-bond* is

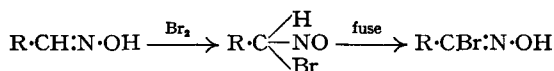


necessary for this molecule to exhibit geometrical isomerism).

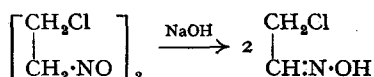
Nitroso-compounds exist as such only when the nitroso-group is attached to a carbon atom not joined to hydrogen, *i.e.*, to a tertiary carbon atom. If the nitroso-group is attached to a primary or secondary carbon atom, the nitroso-compound is generally unstable, tending to rearrange to the oxime:



This is known as the *nitroso-oximino* triad system. This system is *potentially* tautomeric, but no example is known of the isomerisation of the oxime directly to the nitroso-compound. On the other hand, when an aldoxime is treated with bromine, the bromonitroso compound is formed; this, on fusion, is converted into the isomeric bromo-oxime:



It has also been found that the bimolecular nitroso-chlorides rearrange, if possible, to the oxime when treated with sodium hydroxide:



The so-called *isonitroso*-compounds (oximino-compounds) are actually the oximes, *e.g.*, *isonitrosoacetone*,  $\text{CH}_3\cdot\text{CO}\cdot\text{CH}\cdot\text{N}\cdot\text{OH}$ , formed by the action of nitrous acid on acetone, is really the half oxime of methylglyoxal (*q.v.*).

Nitroso-compounds may be oxidised to the nitro-compound by nitric acid, and reduced to the primary amine by, *e.g.*, tin and hydrochloric acid:



### MONOAMINES

Amines are derivatives of ammonia in which one or more hydrogen atoms have been replaced by alkyl groups. The amines are classified as primary, secondary or tertiary amines according as one, two or three hydrogen atoms in the ammonia molecule have been replaced by alkyl groups. Thus the general formulæ of primary, secondary and tertiary amines may be written  $\text{R}\cdot\text{NH}_2$ ,  $\text{R}_2\text{NH}$  and  $\text{R}_3\text{N}$ , and each is characterised by the presence of the *amino-group*  $-\text{NH}_2$ , the *imino-group*  $>\text{NH}$ , and the *tertiary nitrogen atom*  $>\text{N}-$ , respectively.

In addition to the amines the tetra-alkyl derivatives of ammonium hydroxide,  $[\text{R}_4\text{N}]^+\text{OH}^-$ , are known; these are called the *quaternary ammonium hydroxides*.

**Nomenclature.** The suffix of the series is *amine*, and each member is named according to the alkyl groups attached to the nitrogen atom, *e.g.*,

$\text{CH}_3\cdot\text{NH}_2$	methylamine
$(\text{CH}_3)_2\text{NH}$	dimethylamine
$(\text{CH}_3)_3\text{N}$	trimethylamine
$(\text{C}_2\text{H}_5)_2\text{N}\cdot\text{CH}(\text{CH}_3)_2$	diethylisopropylamine

The amines are said to be "simple" when all the alkyl groups are the same, and "mixed" when the alkyl groups are different.

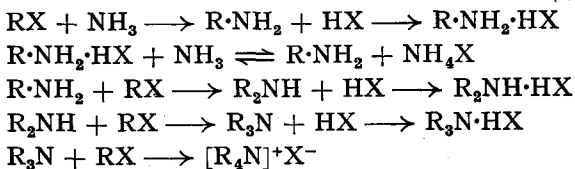
The method of naming a quaternary ammonium hydroxide is illustrated by the following examples:

$(\text{CH}_3)_4\text{NOH}$	tetramethylammonium hydroxide
$(\text{CH}_3)_3\text{N}\cdot\text{C}_2\text{H}_5\text{OH}$	ethyltrimethylammonium hydroxide

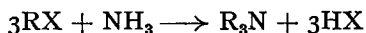
**General methods of preparation.** Many methods are available for preparing amines, but it is instructive to consider them in the following groups:

**Methods for the three classes of amines.** 1. **Hofmann's method** (1850). This is by means of *ammonolysis*, an alkyl halide and an ethanolic solution of ammonia being heated in a sealed tube at  $100^\circ$ . A mixture of all three

classes of amines is obtained, together with some quaternary ammonium compound (see p. 314 for the structure of amine salts):



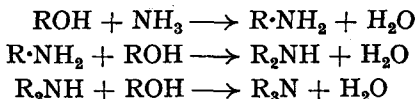
In many cases a good yield of primary amine may be obtained by using a large excess of ammonia, and a good yield of tertiary amine by using alkyl halide in slight excess required by the equation:



Carrying out the reaction in liquid ammonia (in excess) gives a better yield of primary amine than by using aqueous or ethanolic ammonia; *e.g.*, Watt and Otto (1947) found that ammonolysis of ethyl iodide by liquid ammonia in excess at 0° was complete in less than 15 minutes, and gave 46 per cent. ethylamine, 31 per cent. diethylamine and 17 per cent. triethylamine.

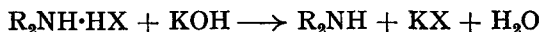
The order of reactivity of the alkyl halides in ammonolysis is alkyl iodide > bromide > chloride, and the method is limited to primary alkyl halides and the secondary halide, *isopropyl* bromide. All other secondary halides and tertiary halides eliminate a molecule of halogen acid to form the olefin and no amine when heated with ethanolic ammonia. Amines of the type  $R_3C \cdot NH_2$  are best prepared by means of a Grignard reagent (p. 357).

2. A mixture of the three types of amines may be prepared by the ammonolysis of alcohols; the alcohol and ammonia are heated under pressure in the presence of a catalyst, *e.g.*, copper chromite or alumina:



The primary amine may be obtained as the main product by using a large excess of ammonia (*cf.* method 1).

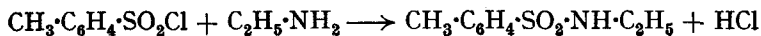
**Separation of amine mixtures.** When the mixture contains the three amine salts and the quaternary salt, it is distilled with potassium hydroxide solution. The three amines distil, leaving the quaternary salt unchanged in solution, *e.g.*,



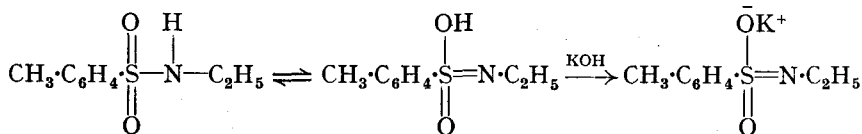
The distillate of mixed amines may now be separated into the individual amines as follows:

**Fractional distillation.** This is the most satisfactory method and is now used industrially, its success being due to the high efficiency of industrial fractionation apparatus.

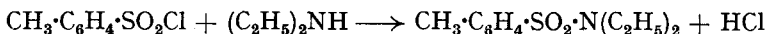
**Hinsberg's method** (1890). The mixture of amines is treated with an aromatic sulphonyl chloride. Benzenesulphonyl chloride,  $C_6H_5 \cdot SO_2Cl$ , was used originally, but has now been replaced by *p*-toluenesulphonyl chloride,  $CH_3 \cdot C_6H_4 \cdot SO_2Cl$ . After treatment with this acid chloride, the solution is made alkaline with potassium hydroxide. Primary amines form the alkyl sulphonamide, *e.g.*, ethylamine forms ethyl *p*-toluenesulphonamide:



These sulphonamides are soluble in potassium hydroxide solution, possibly due to the formation of the soluble potassium salt of the enol form of the sulphonamide:



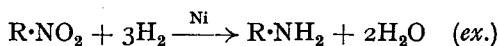
Secondary amines form dialkyl sulphonamides, which are insoluble in potassium hydroxide solution because these sulphonamides are incapable of tautomerism (there is no  $\alpha$ -hydrogen atom adjacent to the negative group); e.g., diethylamine forms diethyl *p*-toluenesulphonamide:



Tertiary amines do not react with *p*-toluenesulphonyl chloride.

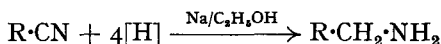
The alkaline solution is distilled, and the tertiary amine thereupon distils off. The residual liquid is filtered: the filtrate contains the primary amine derivative which, on acidification, gives the alkyl sulphonamide; the residual solid is the dialkyl sulphonamide. The amines are regenerated from the sulphonamides by refluxing with 70 per cent. sulphuric acid or 25 per cent. hydrochloric acid.

**Preparation of primary amines.** 1. By the reduction of nitro-compounds with metal and acid, or with hydrogen and a nickel catalyst:



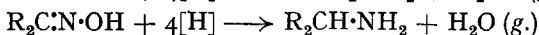
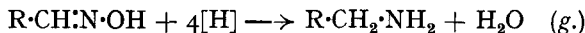
This method is becoming increasingly important since more aliphatic nitro-compounds are becoming available and is particularly useful for preparing amino-alcohols from the starting materials obtained by the condensation between formaldehyde and nitro-compounds (see p. 306).

2. (i) By the reduction of alkyl cyanides:

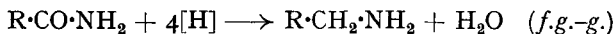


This method is particularly useful for the preparation of high molecular weight amines, since the cyanides are readily prepared from the long-chain fatty acids.

(ii) By the reduction of oximes with sodium and ethanol, or catalytically:



(iii) By the reduction of amides with sodium and ethanol, or catalytically:

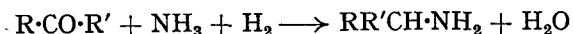


In all cases there are also obtained varying amounts of secondary amine as by-products, which increase in quantity when the reduction is carried out catalytically (see alkyl cyanides, p. 296). Reeve *et al.* (1956), however, have found that Raney cobalt (and Raney nickel) generally gives a primary amine in high purity by the reduction of oximes. On the other hand, nitro-compounds, cyanides, oximes and amides may be reduced by lithium aluminium hydride to primary amines unaccompanied by secondary amines.

3. By passing a mixture of aldehyde or ketone and a large excess of ammonia and hydrogen under pressure (20–150 atm.) over Raney nickel

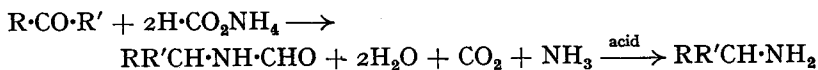


at 40–150°. The reaction may also be carried out at 3 atmospheres in the presence of excess ammonium chloride and Adams' platinum catalyst:

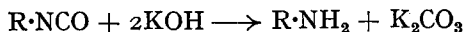


Small amounts of secondary and tertiary amines are obtained as by-products. This process of introducing alkyl groups into ammonia or primary or secondary amines by means of an aldehyde or ketone in the presence of a reducing agent is known as *reductive alkylation*.

4. By the *Leuckart reaction* (p. 156):

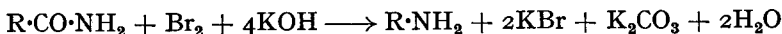


5. By the hydrolysis of alkyl *isocyanates* with boiling alkali (Wurtz, 1849):



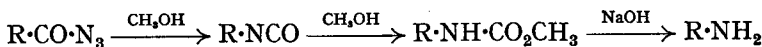
This method is not very useful in practice owing to the inaccessibility of the *isocyanates*. It is, however, historically important because Wurtz discovered amines by this reaction. He at first thought he had obtained ammonia, but subsequently found the gas was inflammable.

6. By *Hofmann's degradation method* (p. 206):



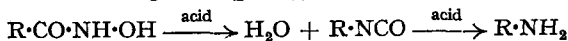
This is generally the most convenient method of preparing primary amines.

7. By the *Curtius reaction* (p. 209):



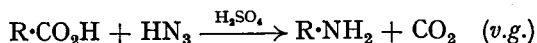
This method of preparing primary amines works well for all members of the series.

8. By the *Lossen rearrangement* (p. 207):



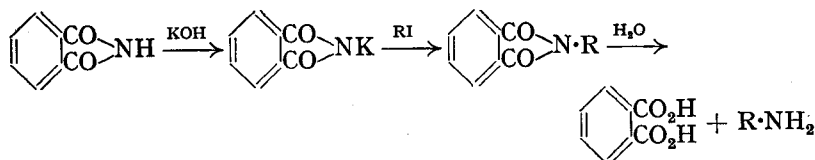
This has very little importance as a practical method.

9. The *Schmidt reaction* (1923). This reaction is carried out by shaking a solution of a carboxylic acid in concentrated sulphuric acid with a chloroform solution of hydrazoic acid (*cf.* p. 178).

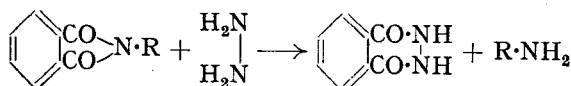


This method generally gives better yields of primary amines than the Hofmann or Curtius reaction, but it is somewhat dangerous because of the explosive and poisonous character of the hydrazoic acid.

10. **Gabriel's phthalimide synthesis** (1887). In this method phthalimide is converted, by means of ethanolic potassium hydroxide, into its salt potassiumphthalimide, which, on heating with an alkyl halide, gives the *N*-alkylphthalimide. This is then hydrolysed to phthalic acid and a primary amine by heating with 20 per cent. hydrochloric acid under pressure, or by refluxing with potassium hydroxide solution:

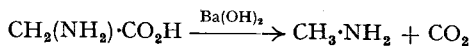


When hydrolysis is difficult, the alkylphthalimide can be treated with hydrazine to give the amine (Ing, 1926):



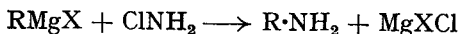
Gabriel's synthesis is a very useful method since it gives a pure primary amine.

11. *Decarboxylation of amino-acids.* This is carried out by distilling the amino-acid with barium hydroxide; e.g., glycine gives methylamine:



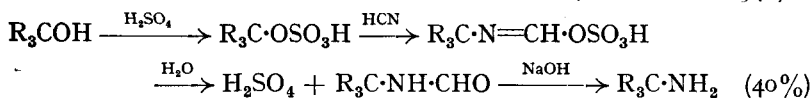
Decarboxylation of amino-acids may also be effected by bacteria, especially putrefying bacteria (many of which occur in the intestines).

12. By means of a Grignard reagent and chloramine. The product is pure:



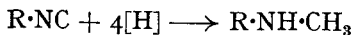
Alternatively, a primary amine may be prepared by interaction of a Grignard reagent and *O*-methylhydroxylamine (see p. 357).

13. A good method for preparing primary amines containing a *tert.*-alkyl group is to add a *tert.*-alcohol (or an alkene) to acetic acid in which is dissolved sodium cyanide, and then add sulphuric acid (Ritter *et al.*, 1948):



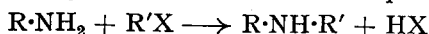
The *N*-alkylformamide produced is hydrolysed with sodium hydroxide.

**Preparation of secondary amines.** 1. By the reduction of an alkyl isocyanide:

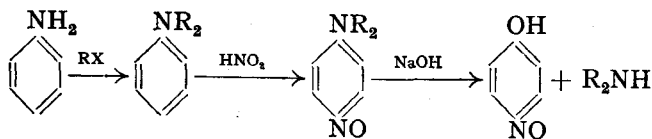


The amine produced always contains a methyl group as one radical; the method is of academic interest only.

2. By heating a primary amine with the calculated quantity of alkyl halide:



3. Aniline is heated with an alkyl halide, and the product, dialkylaniline, is treated with nitrous acid; the *p*-nitroso-dialkylaniline so formed is then boiled with sodium hydroxide solution. A pure secondary amine and *p*-nitrosophenol are produced:



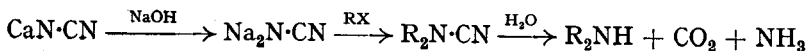
This is one of the best methods of preparing pure secondary amines.

4. By the catalytic reduction of a Schiff's base, which is formed by interaction of a primary amine and an aldehyde (Henze and Humphreys, 1942).

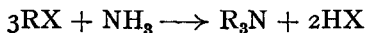


Secondary amines prepared this way usually contain an aromatic group as one of the radicals (R is generally the phenyl radical, C<sub>6</sub>H<sub>5</sub>·).

5. By the hydrolysis of a dialkyl cyanamide with acid or alkali:

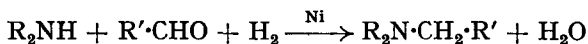


**Preparation of tertiary amines.** 1. The best method of preparation is to heat an ethanolic solution of ammonia with alkyl halide which is used in slight excess required by the equation:

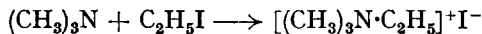


When the reaction mixture is made alkaline and distilled, the tertiary amine is obtained. The residual quaternary compound may be distilled *in vacuo* to yield more tertiary amine (see quaternary compounds, p. 318).

2. By the reduction of a carbonyl compound (in excess) in the presence of hydrogen, ammonia or a primary or secondary amine, with Raney nickel as catalyst (*cf.* primary amines, method 3), *e.g.*,



**Preparation of quaternary compounds.** There is only one satisfactory method of preparing quaternary compounds, *viz.*, by heating ammonia with a very large excess of alkyl halide; a primary, secondary or tertiary amine may be used instead of ammonia. The starting materials will depend on the nature of the desired quaternary compound, *e.g.*, ethyltrimethylammonium iodide may be prepared by heating trimethylamine with ethyl iodide:



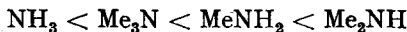
**General properties of the amines.** The lower members are gases, soluble in water (with which they can form hydrogen bonds). These are followed by members which are liquids, and finally by members which are solids. The solubility in water decreases as their molecular weight increases. All the volatile members have a powerful fishy smell, and are combustible.

The reactions of an amine depend very largely on the class of that amine.

**Reactions given by all three classes of amines.** 1. All the amines are basic, and they are stronger bases than ammonia.



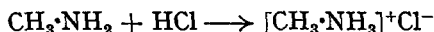
One factor that controls the basicity of amines will be the availability of the lone pair for protonation. At first sight, it would appear that as the number of alkyl groups increases, then because of their + I effect, the lone pair will become more available, thereby increasing the basicity of the amine. This, however, is not the case, as can be seen from the following order of basicity:



The reason for this order is not clear. It has been suggested that a steric factor operates. Addition of the proton increases crowding and so sets up strain, which will be greatest in the tertiary amine, and consequently the stability of this molecule is decreased, *i.e.*, its basicity is reduced. However, when we consider that the three bonding pairs and the lone pair all occupy  $sp^3$  orbitals, and that a lone pair causes crowding of bonding pairs (p. 29), it would seem that protonation should *relieve* crowding by transforming the lone pair into a bonding pair.

All the 'onium ions carry a positive charge and so are solvated. The greater the ion, the less will be the solvation and so the less stabilised is the ion. It seems possible that in going from  $Me_2NH$  to  $Me_3N$ , although the availability of the lone pair is increased, the ion has now grown sufficiently in size at this stage to become less solvated and so the stabilisation lost due to this decrease in solvation is greater than the inductive effect making the lone pair available for protonation.

2. All the amines combine with acids to form salts, *e.g.*, methylamine combines with hydrochloric acid to form *methylammonium chloride*:

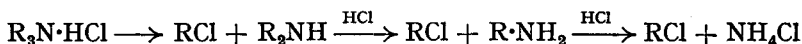


The nitrogen is quadricovalent unielectrovalent in amine salts; but to show their relationship to the amines, their salts are often written as, *e.g.*,  $\text{CH}_3\cdot\text{NH}_2\cdot\text{HCl}$ , methylamine hydrochloride;  $[(\text{C}_2\text{H}_5)_2\text{NH}]_2\cdot\text{H}_2\text{SO}_4$ , diethylamine sulphate.

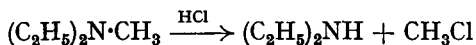
Amine salts of certain complex acids, particularly chloroplatinic acid, are used for the determination of the molecular weights of amines (see p. 5).

3. All the amines combine with alkyl halides to form alkyl-substituted ammonium halides with more alkyl groups than the amine used.

4. When an amine salt is heated at high temperature, a molecule of alkyl halide is eliminated (*i.e.*, reverse of reaction 3, above):

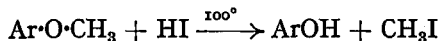


If the tertiary amine is a mixed amine, it is the smallest alkyl group that is eliminated first:



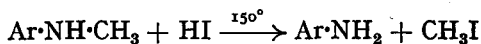
This is the basis of estimating the *methylimino-group*,  $\text{>N}\cdot\text{CH}_3$ , in natural substances such as alkaloids.

When the methyl ether of a high boiling hydroxy compound is heated with concentrated hydriodic acid at  $100^\circ$ , methyl iodide is formed (*cf.* p. 142):



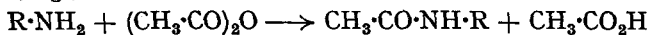
This is the **Zeisel method** for the quantitative estimation of methoxyl groups (p. 637).

When the temperature is raised to  $150^\circ$ , *N*-methyl groups are converted into methyl iodide:



This is the **Herzig-Meyer method** for the quantitative estimation of methylimino-groups. Thus methoxyl and methylimino-groups can be estimated separately when both are present in the same compound.

**Reactions given by primary and secondary amines.** 1. Primary and secondary amines react with acid chlorides or anhydrides to form the *N*-alkyl acid amide, *e.g.*,

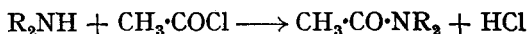


These monoacetyl derivatives are easily prepared and, since they are usually well-defined crystalline solids, are used to characterise primary amines.

It is difficult to prepare the diacetyl derivative; excess of the acetylating agent and high temperature, however, often yields the diacetyl derivative:



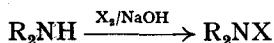
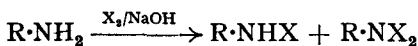
Secondary amines, obviously, can form only the monoacetyl derivative:



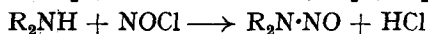
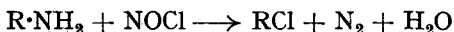
The acetylated amines are neutral substances which do not form salts with inorganic acids. It is the presence of the acetyl group, a negative group, which decreases the basic strength of the amine (see p. 569).

Sulphonyl chlorides also react with primary and secondary amines to form *N*-alkyl sulphonamides (see the Hinsberg separation, above).

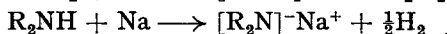
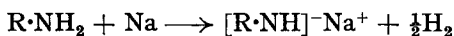
2. Halogens, in the presence of alkali, react with primary and secondary amines to form halogeno-amines. Primary amines form the mono- or dihalogeno-derivative according to the amount of halogen used:



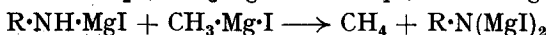
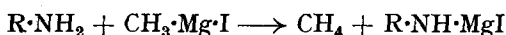
3. Primary amines react with nitrosyl chloride to form an alkyl chloride: secondary amines are converted into a nitrosamine:



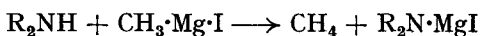
4. Primary and secondary amines form sodium salts when heated with sodium:



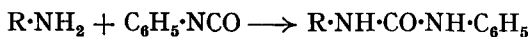
5. Primary amines react in two stages with Grignard reagents, the first stage taking place at room temperature, the second only at high temperature:



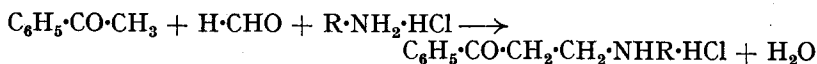
Secondary amines, since they contain only one active hydrogen atom, can only react with one molecule of a Grignard reagent:



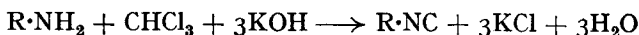
6. Primary and secondary amines form substituted ureas with phenyl isocyanate, and may be characterised by these derivatives:



7. Primary and secondary amines can participate in the Mannich reaction (p. 306), e.g.,

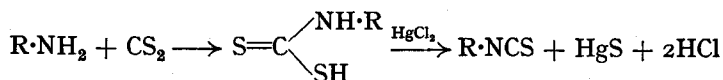


**Reactions given by primary amines.** 1. Primary amines form isocyanides when heated with chloroform and ethanolic potassium hydroxide:



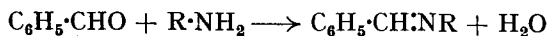
This reaction is used as a test for primary amines (or for chloroform).

2. When warmed with carbon disulphide, primary amines form a *dithiocarbamic acid*, which is decomposed by mercuric chloride to the *alkyl isothiocyanate*:

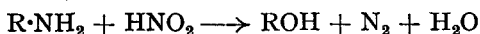


This is known as the *Hofmann mustard oil reaction*, and may be used as a test for primary amines.

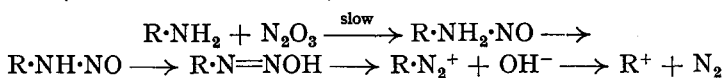
3. Primary amines combine with aromatic aldehydes to form *Schiff bases*:



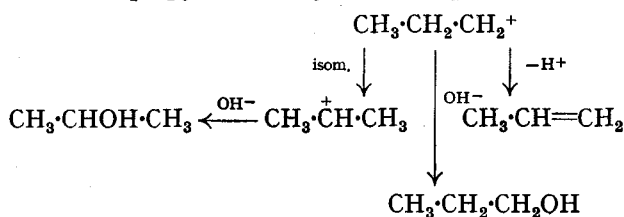
4. Primary amines react with nitrous acid with the evolution of nitrogen. The equation is usually written:



The reaction, however, is far more complicated than this equation indicates. According to Whitmore (1941), methylamine does not form any methanol at all when treated with nitrous acid; dimethyl ether is produced. Ethylamine gives 60 per cent. of ethanol, and *n*-propylamine 7 per cent. of *n*-propanol, 32 per cent. of *isopropanol* and 28 per cent. of propylene. Linne-mann (1868) had claimed to have obtained methanol in 50 per cent. yield from methylamine. Austin (1960) has examined the deamination of methylamine in detail and showed (using *no* excess of inorganic acid) that the following compounds are formed: methanol, methyl nitrite (major product), methyl chloride, nitromethane, and methylnitric acid ( $NO_2 \cdot CH=NOH$ ). Austin has shown that nitrous acid, as such, is *not* a participant in the initial interaction with the amine; the effective nitrosating reagent is dinitrogen trioxide (or  $NOX$ ;  $X=Cl, Br, I$ ); thus:

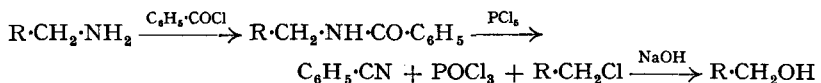


The products from *n*-propylamine may thus be explained as follows:

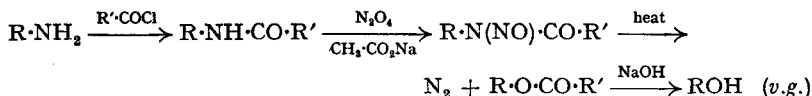


Whatever are the products formed by the action of nitrous acid on a primary amine, nitrogen is always evolved. Thus this reaction may be used as a test for primary amines, since none of the other classes of amines liberates nitrogen.

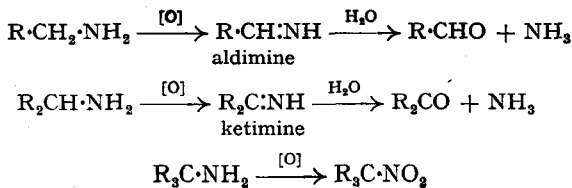
Primary amines may be converted into the corresponding alcohols in good yields by means of the von Braun method (see also p. 762):



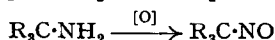
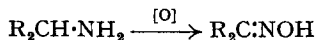
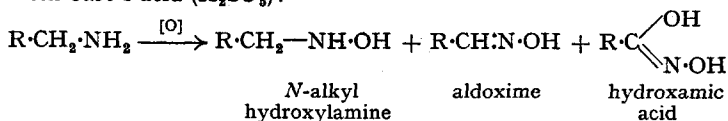
White (1954) has introduced a new method for the deamination of aliphatic amines:



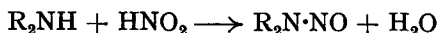
5. *Oxidation of primary amines.* The products obtained depend on the oxidising agent used, and on the nature of the alkyl group, *e.g.*, (i) with potassium permanganate:



(ii) with Caro's acid ( $\text{H}_2\text{SO}_5$ ):

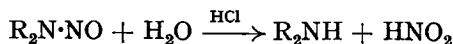


**Reactions given by secondary amines.** 1. Secondary amines react with nitrous acid to form insoluble oily *nitrosamines*; *nitrogen is not evolved*:

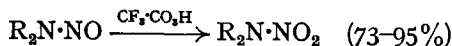


Nitrosamines are yellow neutral oils which are steam-volatile. When warmed with a crystal of phenol and a few drops of concentrated sulphuric acid, nitrosamines form a green solution which, when made alkaline with aqueous sodium hydroxide, turns deep blue. This procedure may be used as a test for secondary amines; it is known as *Liebermann's nitroso reaction*.

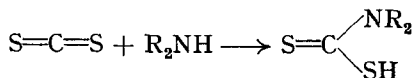
Nitrosamines are readily hydrolysed to the amine by boiling with dilute hydrochloric acid:



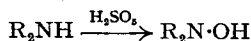
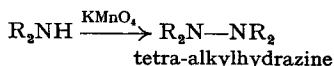
Peroxytrifluoroacetic acid converts secondary nitrosamines into nitramines (Emmons, 1954):



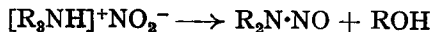
2. When warmed with carbon disulphide, secondary amines form a *dithiocarbamic acid*, which is *not* decomposed by mercuric chloride to the alkyl *isothiocyanate* (*cf.* primary amines):



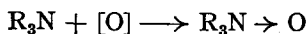
3. Secondary amines may be oxidised, the product depending on the oxidising agent used, *e.g.*,



**Reactions given by tertiary amines.** 1. Tertiary amines dissolve in *cold* nitrous acid to form the nitrite salt,  $\text{R}_3\text{N}\cdot\text{HNO}_2$  or  $[\text{R}_3\text{NH}]^+\text{NO}_2^-$ . When this solution is warmed, the nitrite decomposes to form a nitrosamine and alcohol:

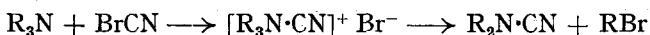


2. Tertiary amines are not affected by potassium permanganate, but are oxidised to the *amine oxide* by Caro's acid or by hydrogen peroxide:

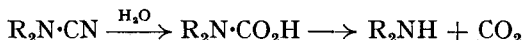


These amine oxides are basic and exist as  $[\text{R}_3\text{N}\cdot\text{OH}]^+\text{OH}^-$  in solution. When the solution is evaporated to dryness, the dihydrate,  $\text{R}_3\text{NO}\cdot 2\text{H}_2\text{O}$ , is obtained as crystals. These, when carefully heated *in vacuo*, are converted into the anhydrous amine oxide,  $\text{R}_3\text{NO}$ . Amine oxides form addition compounds with gaseous hydrogen halide, *e.g.*,  $[\text{R}_3\text{N}\cdot\text{OH}]^+\text{Cl}^-$ , and with alkyl halides, *e.g.*,  $[\text{R}_3\text{N}\cdot\text{OR}]^+\text{Cl}^-$ .

3. Tertiary amines react with cyanogen bromide to form a *dialkyl cyanamide*:



The dialkyl cyanamides are readily hydrolysed by acid or alkali to a secondary amine:



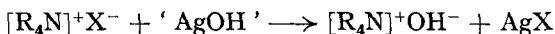
This method therefore offers a means of converting a tertiary amine into a secondary, but is mainly used to open the ring of a cyclic amine containing a tertiary nitrogen atom (see p. 762).

#### QUATERNARY AMMONIUM COMPOUNDS

The quaternary ammonium salts are white crystalline solids, soluble in water, and completely dissociated in solution (the nitrogen is quadricovalent unielectrovalent). When a quaternary ammonium halide is heated *in vacuo*, it gives the tertiary amine:



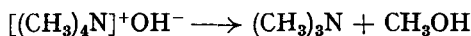
When a quaternary ammonium halide is treated with moist silver oxide, the quaternary ammonium hydroxide is produced:



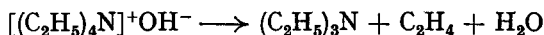
This change may also be effected by treating the quaternary ammonium halide with a methanolic solution of potassium hydroxide. Potassium halide, which is precipitated, is removed by filtration, and the solvent then evaporated from the filtrate. It is important to note that the quaternary ammonium hydroxide is not liberated by *aqueous* potassium hydroxide.

The quaternary ammonium hydroxides are white deliquescent crystalline solids which are as strongly basic as sodium and potassium hydroxides (all exist as ions in the solid state). Their solutions absorb carbon dioxide, and will liberate ammonia from its salts.

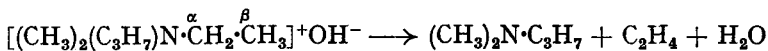
The thermal decomposition of quaternary ammonium hydroxides is a very important reaction. Only tetramethylammonium hydroxide decomposes to give an alcohol:



All other quaternary ammonium hydroxides give an olefin and water, *e.g.*,



If the quaternary ammonium hydroxide contains different alkyl groups of which one is methyl, then the methyl group is *always* retained by the nitrogen, and an olefin and water are formed. Furthermore, if the ethyl group is one of the radicals, then ethylene is formed preferentially to any other olefin (*Hofmann's rule*). Water is always eliminated by the combination of the hydroxyl ion with a  $\beta$ -hydrogen atom of one of the alkyl groups (preferably ethyl):



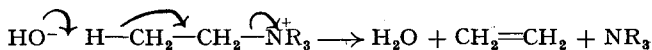
If there is no  $\beta$ -hydrogen in the quaternary hydroxide, *e.g.*, tetramethylammonium hydroxide, then no olefin is formed.

The above reaction is the basis of the *Hofmann exhaustive methylation method* (1851). In certain cases it is used to prepare unsaturated compounds

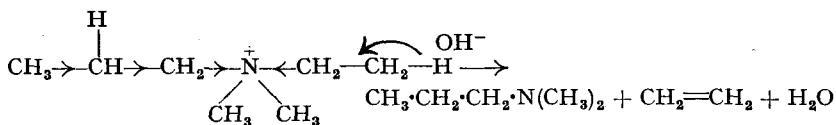


of known structure, *e.g.*, benzene (see p. 506), but it is generally used to ascertain the nature of the carbon skeleton of cyclic compounds containing a nitrogen atom in the ring (see p. 762).

According to Ingold *et al.* (1927, 1933) the reaction proceeds by a bimolecular elimination (E2) mechanism:



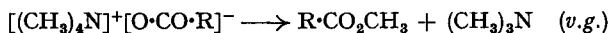
The reason for the preferential elimination of ethylene has been explained as follows (Ingold *et al.*, 1927). The positive charge on the nitrogen atom produces an inductive effect which causes positive charges to be produced on neighbouring carbon atoms. This weakens the C—H bonds sufficiently for a  $\beta$ -proton to be eliminated by the E2 mechanism.



Since the terminal methyl group of the *n*-propyl radical is electron-releasing, the positive charge induced on the  $\beta$ -carbon atom (of the propyl group) is partially neutralised. This "tightens" the bonding of these  $\beta$ -hydrogen atoms, and so a less tightly bound  $\beta$ -hydrogen atom in the ethyl radical is eliminated preferentially with the formation of ethylene.

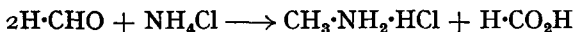
As can be seen from the foregoing account, the formation of ethylene (and, in general, the least branched olefin) is attributed to the polar factor. Brown *et al.* (1956), however, have concluded from their work that the Hofmann type of elimination must be attributed to the large steric requirements of the group undergoing elimination and not to the positive charge on the 'onium group (*cf.* Saytzeff's rule, p. 111).

Another interesting application of the method of exhaustive methylation is the preparation of methyl esters of acids which are difficult to esterify by the usual methods. The acid is converted into the quaternary methylammonium salt by titration with tetramethylammonium hydroxide in methanolic solution; the salt, on heating at 200–300°, is decomposed into the methyl ester and trimethylamine (Prelog and Piantanida, 1936):



*Methylamine*, *dimethylamine* and *trimethylamine* may be prepared by any of the general methods, but are conveniently prepared by special methods.

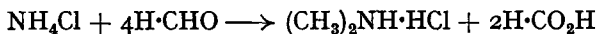
**Methylamine:** By heating ammonium chloride with two equivalents of formaldehyde (in formalin soln); the yield is 45–51 per cent. based on the ammonium chloride:



It is prepared industrially by passing a mixture of methanol and ammonia over a catalyst, and separating the mixture by fractional distillation (see p. 309).

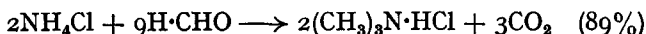
Methylamine is a gas, b.p.  $-7.6^\circ$ , which is used as a refrigerant.

**Dimethylamine:** By heating ammonium chloride with about four equivalents of formaldehyde (in formalin solution):

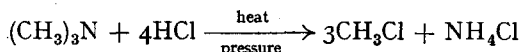


It is a gas, b.p.  $7^\circ$ .

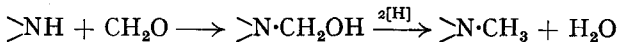
**Trimethylamine:** By heating a solid mixture of ammonium chloride and paraformaldehyde:



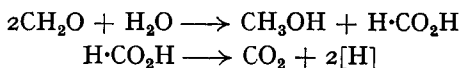
It is a gas, b.p.  $3.5^{\circ}$ . It occurs in sugar residues, and is used as a source of methyl chloride:



N-methylation of primary and secondary amines can readily be effected by formaldehyde (formalin solution); the mechanism may be:



The  $2[\text{H}]$  is produced according to the following reactions:



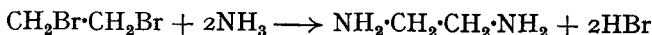
Carbon dioxide is always evolved in these reactions.

The long-chain amines, prepared by the catalytic reduction of alkyl cyanides (from fatty acids and ammonia), are used as antioxidants, sterilising agents and flotation agents.

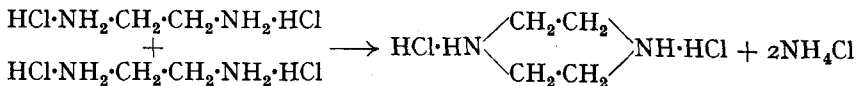
#### DIAMINES

Diamines may be prepared by methods similar to those for the monoamines, using polymethylene halides instead of alkyl halides.

**Ethylenediamine.**  $\text{NH}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{NH}_2$ , may be prepared by heating, under pressure, ethylene bromide with a large excess of ammonia:

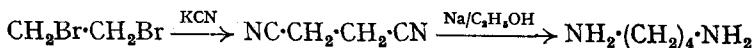


It is a colourless liquid, b.p.  $118^{\circ}$ , soluble in water. It forms *piperazine* when its hydrochloride is heated:

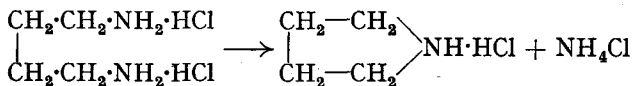


Ethylenediamine forms chelate compounds with many metals, e.g., cobalt.

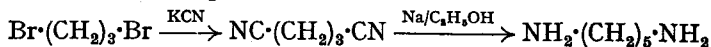
**Putrescine, tetramethylenediamine,**  $\text{NH}_2\cdot(\text{CH}_2)_4\cdot\text{NH}_2$ , is formed by the putrefaction of proteins (in flesh). It may be prepared as follows:



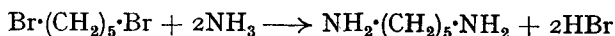
It is a poisonous solid, m.p.  $27^{\circ}$ , with a disagreeable odour, and is soluble in water. When its hydrochloride is heated, *pyrrolidine* is formed:



**Cadaverine, pentamethylenediamine,**  $\text{NH}_2\cdot(\text{CH}_2)_5\cdot\text{NH}_2$ , is formed by the putrefaction of proteins (in flesh). It may be prepared by an analogous method to that used for putrescine:

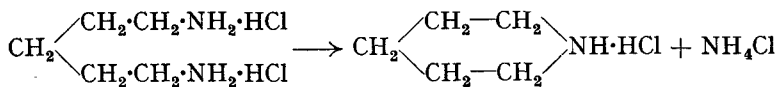


It is, however, prepared more conveniently by heating pentamethylene bromide with an excess of ammonia:

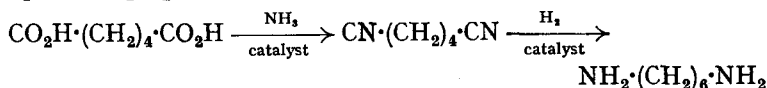


The starting material pentamethylene bromide is readily obtained from piperidine (see p. 762).

Cadaverine is a poisonous, syrupy, fuming liquid, b.p. 178–180°, with a disagreeable odour, and is soluble in water. When its hydrochloride is heated, piperidine is formed:



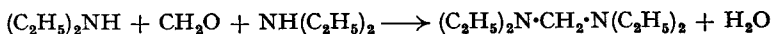
**Hexamethylenediamine** is manufactured by the catalytic hydrogenation of adiponitrile prepared from adipic acid:



It is a colourless crystalline solid, m.p. 39°, and is used in the manufacture of *nylon* (p. 379).

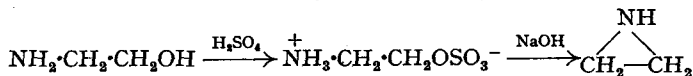
**Spermine**, a deliquescent crystalline solid which is isolated from human sperm, is a tetramine:  $\text{NH}_2 \cdot (\text{CH}_2)_3 \cdot \text{NH} \cdot (\text{CH}_2)_4 \cdot \text{NH} \cdot (\text{CH}_2)_3 \cdot \text{NH}_2$ .

Diamines with two amino-groups attached to the same carbon atom are unknown (*cf.* the group  $\text{C}(\text{OH})_2$ , p. 168). On the other hand, *N*-substituted derivatives have been prepared, *e.g.*, tetraethylmethylenediamine:

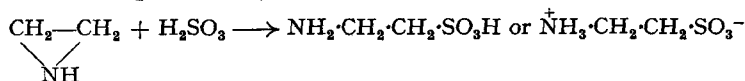


#### UNSATURATED AMINES

The simplest unsaturated amine would be vinylamine (ethenylamine) if it existed. All attempts to prepare it result in the formation of the cyclic compound **ethyleneimine (aziridine)**, and a good method is to treat 2-aminoethanol with sulphuric acid and then to heat the product with aqueous sodium hydroxide.

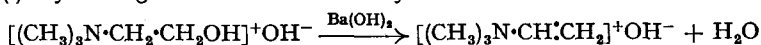


Thus this compound is a three-membered heterocyclic ring. Ethyleneimine is a syrupy liquid, b.p. 56°, with a strong ammoniacal odour; it is miscible with water, and is strongly basic. It combines with sulphurous acid to form *taurine* (2-aminoethanesulphonic acid), which occurs in human bile:

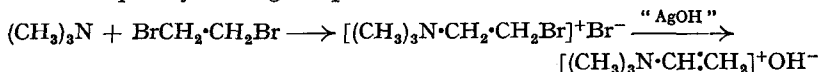


**Neurine** (*trimethylvinylammonium hydroxide*),  $[(\text{CH}_3)_3\text{N} \cdot \text{CH} : \text{CH}_2]^+ \text{OH}^-$ , is found in the brain. It may be prepared:

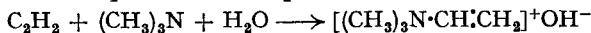
(i) By boiling choline with barium hydroxide solution:



(ii) By heating trimethylamine and ethylene bromide (one molecule of each), and subsequently heating the product with silver oxide in water:

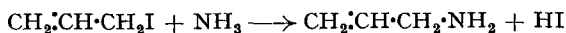


(iii) A very interesting synthesis is by the interaction of acetylene and trimethylamine under pressure, in the presence of water at 60°:

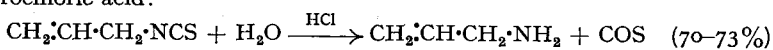


Neurine is a very poisonous syrupy liquid.

**Allylamine** (*2-propenylamine*),  $\text{CH}_2 = \text{CH} \cdot \text{CH}_2 \cdot \text{NH}_2$ , may be prepared by heating allyl iodide with ammonia:



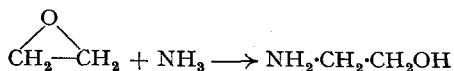
It is more conveniently prepared by boiling allyl isothiocyanate with dilute hydrochloric acid:



It is a colourless liquid, b.p.  $53^\circ$ , with an ammoniacal smell, and is miscible with water.

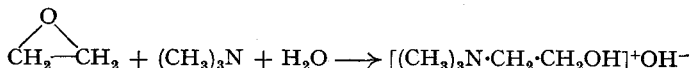
#### AMINOALCOHOLS

The simplest aminoalcohol is **2-aminoethanol**,  $\text{NH}_2\cdot\text{CH}_2\cdot\text{CH}_2\text{OH}$  (*cholamine*, *ethanolamine*, *2-hydroxyethylamine*). It occurs in kephalins (p. 263), and is best prepared by the action of ethylene oxide on excess of ammonia.



It is a viscous liquid, b.p.  $171^\circ$ , miscible with water, and is strongly basic.

**Choline** (*2-hydroxyethyltrimethylammonium hydroxide*) occurs in lecithins (p. 263); it is best prepared by the action of ethylene oxide on trimethylamine in aqueous solution:



It is a colourless viscous liquid, soluble in water, and is strongly basic. It forms neurine when boiled with barium hydroxide solution (see above). It is present in the vitamin B complex; it is a growth factor in chicks.

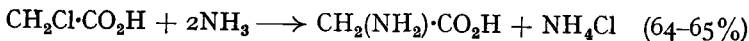
#### AMINO-ACIDS

Amino-acids are derivatives of the carboxylic acids in which a hydrogen atom in the carbon chain has been replaced by an amino-group. The amino-group may occupy the  $\alpha$ - or  $\beta$ - or  $\gamma$ - . . . position; there may also be two or more amino-groups present in the chain.

The three basic classes of foods are: proteins, fats and carbohydrates. The proteins are nitrogenous substances which occur in most cells of the animal body; they also occur in plants. When hydrolysed by strong inorganic acids or by enzymes, proteins yield a mixture of amino-acids, all of which are  $\alpha$ -amino-acids. The number of amino-acids so far obtained appears to be about twenty-five, of which about ten are essential, *i.e.*, a deficiency in any one growth in young animals, and may even cause death.

The amino-acids are classified in several ways; Table VI shows a convenient classification; the letters *g*, *l* and *e* which follow the name of the acid indicate that the acid is respectively of general occurrence, lesser occurrence, and essential (in man).

In this book we shall consider in detail only the simplest amino-acid, **glycine** (*aminoacetic acid*, *glycocoll*),  $\text{CH}_2(\text{NH}_2)\cdot\text{CO}_2\text{H}$ . This acid is found in many proteins, and occurs in certain animal excretions, usually in combination, *e.g.*, *hippuric acid* (in horses' urine),  $\text{C}_6\text{H}_5\cdot\text{CO}\cdot\text{NH}\cdot\text{CH}_2\cdot\text{CO}_2\text{H}$ . Glycine may be readily prepared by the action of concentrated ammonium hydroxide solution on chloroacetic acid:



It may also be prepared pure by Gabriel's phthalimide synthesis (p. 311):

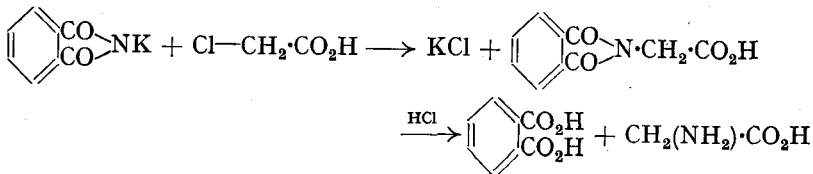
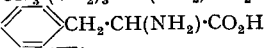
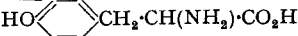
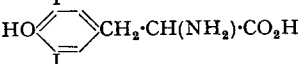
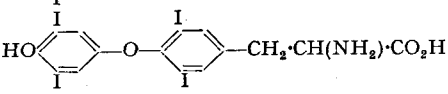
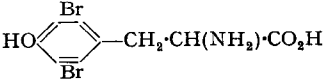
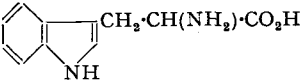
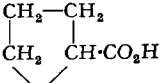
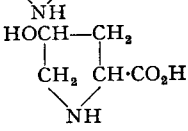
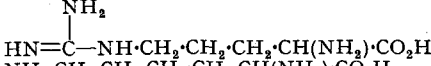



TABLE VI

Name	Formula
<b>Neutral Amino-acids (one amino-group and one carboxyl group)</b>	
1. Glycine ( <i>g</i> )	$\text{CH}_2(\text{NH}_2) \cdot \text{CO}_2\text{H}$
2. Alanine ( <i>g</i> )	$\text{CH}_3 \cdot \text{CH}(\text{NH}_2) \cdot \text{CO}_2\text{H}$
3. Valine ( <i>g, e</i> )	$(\text{CH}_3)_2\text{CH} \cdot \text{CH}(\text{NH}_2) \cdot \text{CO}_2\text{H}$
4. Leucine ( <i>g, e</i> )	$(\text{CH}_3)_2\text{CH} \cdot \text{CH}_2 \cdot \text{CH}(\text{NH}_2) \cdot \text{CO}_2\text{H}$
5. <i>iso</i> Leucine ( <i>g, e</i> )	$(\text{C}_2\text{H}_5)_2\text{CH} \cdot \text{CH}(\text{NH}_2) \cdot \text{CO}_2\text{H}$
6. Norleucine ( <i>l</i> )	$\text{CH}_3 \cdot (\text{CH}_2)_3 \cdot \text{CH}(\text{NH}_2) \cdot \text{CO}_2\text{H}$
7. Phenylalanine ( <i>g, e</i> )	
8. Tyrosine ( <i>g</i> )	
9. Serine ( <i>g</i> )	$\text{HOCH}_2 \cdot \text{CH}(\text{NH}_2) \cdot \text{CO}_2\text{H}$
10. Cysteine ( <i>g</i> )	$\text{HS} \cdot \text{CH}_2 \cdot \text{CH}(\text{NH}_2) \cdot \text{CO}_2\text{H}$
11. Cystine ( <i>g</i> )	$(-\text{S}-\text{CH}_2 \cdot \text{CH}(\text{NH}_2) \cdot \text{CO}_2\text{H})_2$
12. Threonine ( <i>g, e</i> )	$\text{CH}_3 \cdot \text{CHOH} \cdot \text{CH}(\text{NH}_2) \cdot \text{CO}_2\text{H}$
13. Methionine ( <i>g, e</i> )	$\text{CH}_3 \cdot \text{S} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}(\text{NH}_2) \cdot \text{CO}_2\text{H}$
14. Di-iodotyrosine or iodogorgic acid ( <i>l</i> )	
15. Thyroxine ( <i>l</i> )	
16. Dibromotyrosine ( <i>l</i> )	
17. Tryptophan ( <i>g, e</i> )	
18. Proline ( <i>g</i> )	
19. Hydroxyproline ( <i>l</i> )	
<b>Acidic Amino-acids (one amino-group and two carboxyl groups)</b>	
20. Aspartic acid ( <i>g</i> )	$\text{CO}_2\text{H} \cdot \text{CH}_2 \cdot \text{CH}(\text{NH}_2) \cdot \text{CO}_2\text{H}$
21. Glutamic acid ( <i>g</i> )	$\text{CO}_2\text{H} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}(\text{NH}_2) \cdot \text{CO}_2\text{H}$
22. $\beta$ -Hydroxyglutamic acid ( <i>l</i> ) <sup>1</sup>	$\text{CO}_2\text{H} \cdot \text{CH}_2 \cdot \text{CHOH} \cdot \text{CH}(\text{NH}_2) \cdot \text{CO}_2\text{H}$
<b>Basic Amino-acids (two amino-groups and one carboxyl group)</b>	
23. Ornithine *	$\text{NH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}(\text{NH}_2) \cdot \text{CO}_2\text{H}$
24. Arginine ( <i>g, e</i> )	
25. Lysine ( <i>g, e</i> )	$\text{NH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}(\text{NH}_2) \cdot \text{CO}_2\text{H}$
26. Histidine ( <i>g, e</i> )	

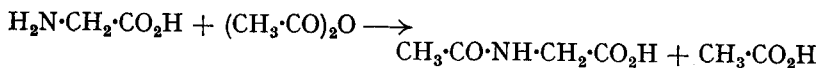
\* Ornithine is probably not present in proteins, but is formed by the hydrolysis of arginine.

<sup>1</sup> Occurrence in proteins uncertain.

Glycine exists as white prisms which melt, with decomposition, at 289–292°. It has a sweet taste, and is soluble in water but insoluble in ethanol and ether. Since it contains an amino-group and a carboxyl group, it combines the properties of a base and an acid, *i.e.*, it is *amphoteric*. The following reactions are typical of all  $\alpha$ -amino-acids.

**Reactions characteristic of the amino-group.** 1. Glycine forms salts with strong inorganic acids, *e.g.*,  $\text{Cl}^-(\text{H}_3\text{N}^+\text{CH}_2\text{CO}_2\text{H})$

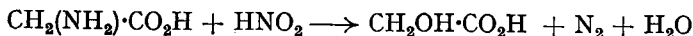
2. Glycine reacts with acetyl chloride or acetic anhydride to give the acetyl derivative:



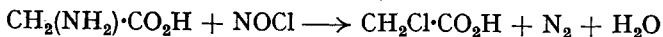
Similarly, with benzoyl chloride, it forms benzoylglycine (hippuric acid; see above).

These acylated derivatives are acidic, the basic character of the amino-group being effectively eliminated by the presence of the negative group attached to the nitrogen (see p. 569).

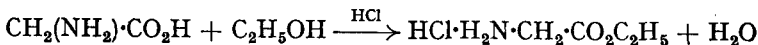
3. When glycine is treated with nitrous acid, nitrogen is evolved and glycollic acid is formed:



4. Nitrosyl chloride (or bromide) reacts with glycine to form chloro- (or bromo-) acetic acid:

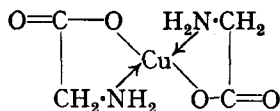


**Reactions characteristic of the carboxyl group.** 1. Glycine may be esterified by an alcohol in the presence of inorganic acid, *e.g.*,

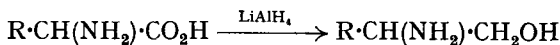


The ester is liberated from its hydrochloride by alkali.

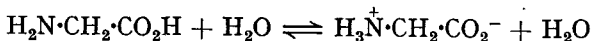
2. Glycine forms metallic salts when its aqueous solution is warmed with a metallic oxide or hydroxide. These salts are chelate compounds, *e.g.*, the copper salt (deep blue needles) is:



3. Amino-acids may be reduced to aminoalcohols by lithium aluminium hydride (Vogel *et al.*, 1952).



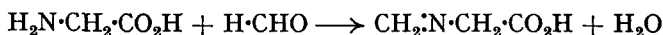
**Reactions due to both the amino- and carboxyl groups.** 1. When measured in aqueous solution, the dipole moment of glycine is found to have a large value. To account for this large value it has been suggested that glycine exists, in solution, as an *inner salt*:



Such a double charged ion is known, in addition to an inner salt, as a *zwitterion*, *ampholyte*, or a *dipolar ion*. This dipolar ion structure also accounts for the absence of acidic and basic properties of an amino-acid (the carboxyl

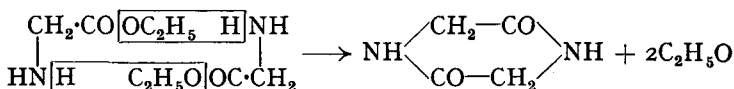
and amino-groups of the *same* molecule neutralising each other to form a salt). The properties of crystalline glycine, *e.g.*, its high melting point and its insolubility in hydrocarbon solvents, also indicate that it exists as the inner salt in the solid state.

Owing to its amphoteric character, glycine cannot be titrated directly with alkali. When formalin solution is added to glycine, methyleneglycine is formed (reaction probably more complex):

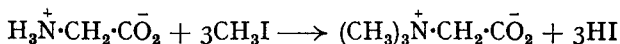


This is a strong acid (the basic character of the amino-group being now suppressed), and can be titrated with sodium hydroxide. This method is known as the *Sørensen titration*.

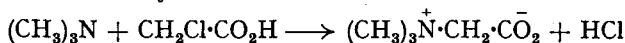
2. When heated, glycine forms *diketopiperazine*; glycine esters give a better yield:



**Betaines.** These are the trialkyl derivatives of glycine, which exist as dipolar ions of formula  $\text{R}_3\text{N}^+\text{C}\bar{\text{O}}_2$ . Betaine itself is the trimethyl derivative, and may be prepared by heating glycine with methyl iodide in methanolic solution:



It is more conveniently prepared by warming an aqueous solution of chloroacetic acid with trimethylamine:



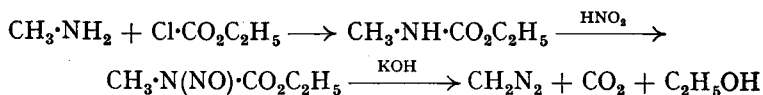
Betaine is a solid, m.p.  $300^\circ$  (with decomposition). It occurs in nature, especially in plant juices. It behaves as a base, *e.g.*, with hydrochloric acid it forms the stable crystalline hydrochloride,  $\text{Cl}^- (\text{CH}_3)_3\text{N}^+\text{CH}_2\cdot\text{CO}_2\text{H}$ .

#### ALIPHATIC DIAZO-COMPOUNDS

The aliphatic diazo-compounds are characterised by the presence of the group  $>\text{CN}_2$ .

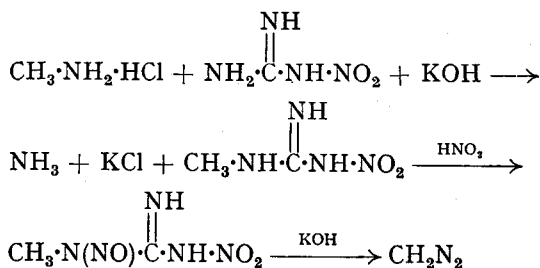
**Diazomethane**,  $\text{CH}_2\text{N}_2$ , may be prepared in various ways; the first is of historical importance, and the others are very convenient methods.

*Method of Von Pechmann* (1894). Methylamine is treated with ethyl chloroformate to give *N*-methylurethan which, on treatment with nitrous acid in ethereal solution, forms *N*-methyl-*N*-nitroso-urethan. This, on warming with methanolic potassium hydroxide, decomposes into diazomethane, which is collected on cooled ether:

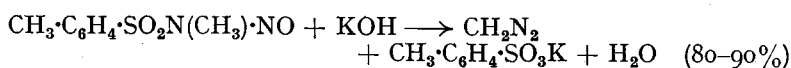


*Method of McKay* (1948). Methylamine hydrochloride and nitroguanidine are allowed to react in potassium hydroxide solution, the product *N*-methyl-*N'*-nitroguanidine treated with nitrous acid, and the

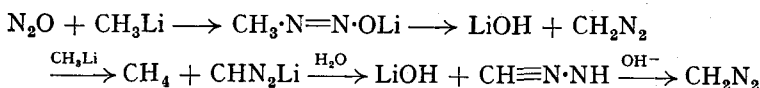
*N*-methyl-*N*-nitroso-*N'*-nitroguanidine so produced is then warmed with potassium hydroxide:



*Method of Backer et al.* (1951). The nitroso-derivative of *p*-toluene-*N*-methylsulphonamide is distilled with ethanolic potassium hydroxide:



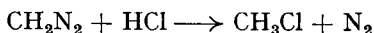
*Method of Müller et al.* (1955). Nitrous oxide is passed into an ethereal solution of methyl-lithium, and the precipitate decomposed in ether with aqueous potassium hydroxide:



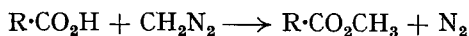
Diazomethane is a yellow, poisonous gas; liquid diazomethane, b.p.  $-24^\circ$ , is explosive. The gas is soluble in ether, and since the ethereal solution is fairly safe to handle, reactions with diazomethane are usually carried out in ethereal solution. Diazomethane is neutral; it is reduced by sodium amalgam to methylhydrazine  $\text{CH}_3 \cdot \text{NH} \cdot \text{NH}_2$ .

**Reactions.** i. Diazomethane is widely used as a methylating agent for hydroxyl groups. In these reactions nitrogen is always liberated.

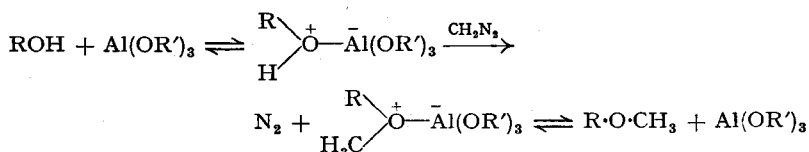
It reacts with halogen acid to form a methyl halide, *e.g.*,



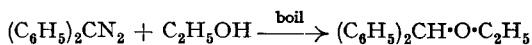
Diazomethane methylates *acidic* hydroxyl groups very readily: carboxylic acids, sulphonic acids, phenols, and enols, *e.g.*,



Alcohols can also be methylated by diazomethane in the presence of a suitable catalyst, *e.g.*, an aluminium alkoxide.

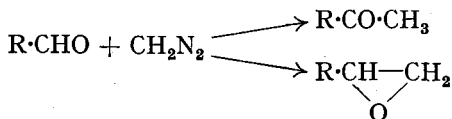


Alcohols may, however, be attacked directly by certain diazo-compounds, *e.g.*, diphenyldiazomethane:

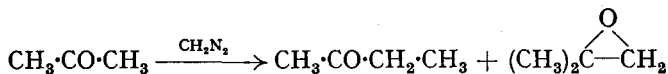




Diazomethane also reacts with aldehydes, converting them into methyl ketones; but in some cases the ethylene oxide derivative is formed, particularly when R is a negative group.

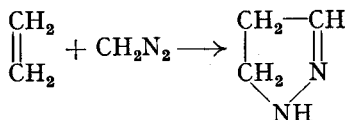


Ketones also react in a similar manner, but only in the presence of water as catalyst; e.g., acetone forms both the higher ketone and the ethylene oxide derivative:

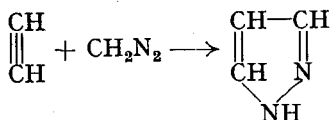


Certain cyclic ketones undergo ring expansion when treated with diazomethane (p. 479).

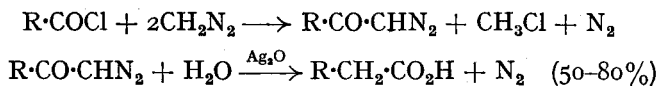
2. Diazomethane adds on to ethylenic compounds to form *pyrazoline* derivatives (cf.  $\alpha\beta$ -unsaturated esters, p. 283); with ethylene, *pyrazoline* is formed:



Diazomethane also adds on to acetylenic compounds, in this case to form *pyrazole* derivatives; with acetylene, *pyrazole* is formed:

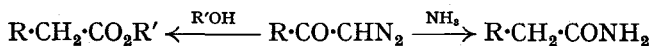


3. Diazomethane is used in the **Arndt-Eistert synthesis** (1935). This is a means of converting an acid (aliphatic, aromatic, alicyclic, or heterocyclic) into the next higher homologue. The acid chloride is treated with diazomethane (2 molecules), and the resulting *diazoketone* is warmed with water in the presence of silver oxide as catalyst:

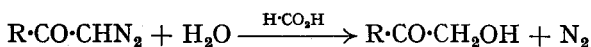


This rearrangement of the diazoketone is usually referred to as the **Wolff rearrangement** (1912).

Diazoketones react with alcohols and ammonia in the presence of silver oxide as catalyst to form esters and amides, respectively:

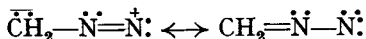


In the absence of a catalyst and in the presence of water and formic acid, diazoketones form hydroxymethyl ketones:

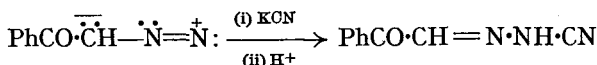




The first two forms make the greatest contribution, but Huisgen (1955) believes that the following two resonance structures also contribute to some extent:



The interesting point here is that the first of these two structures could behave as an electrophilic reagent at the terminal nitrogen atom. There is some evidence to support this, *e.g.*, diazoacetophenone reacts with aqueous potassium cyanide solution as follows (Wolff, 1902):



**Diazoacetic ester** (*ethyl diazoacetate*),  $\text{CHN}_2\cdot\text{CO}_2\text{C}_2\text{H}_5$ , may be readily prepared by treating a cooled solution of the hydrochloride of ethyl glycine ester with cold sodium nitrite solution:

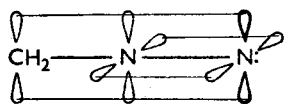
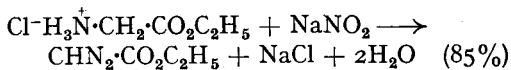
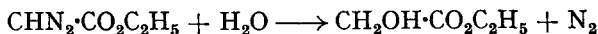


FIG. 13.2.

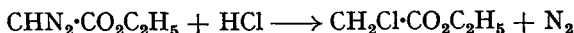


It is a yellow oil, b.p.  $141^\circ/720$  mm., insoluble in water, soluble in ethanol and ether.

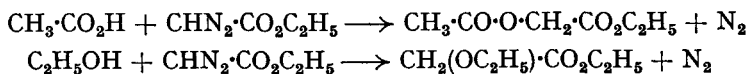
The reactions of diazoacetic ester are similar to those of diazomethane. It is reduced by zinc dust and acetic acid to ammonia and glycine. When boiled with dilute halogen acid, it eliminates nitrogen to form glycollic ester:



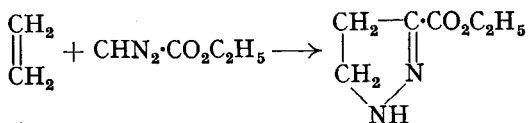
When, however, diazoacetic ester is warmed with *concentrated* halogen acid, ethyl halogeno-acetate is formed, *e.g.*,



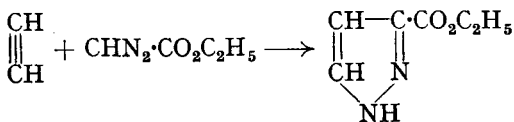
Diazoacetic ester reacts with compounds containing an active hydrogen atom, *e.g.*, it forms acetylglycollic ester with acetic acid, and the ethyl ether of glycollic ester with ethanol:



It reacts with ethylenic compounds to form *pyrazoline* derivatives, *e.g.*, with ethylene it forms pyrazoline-3-carboxylic ester:



With acetylenic compounds it forms *pyrazole* derivatives, *e.g.*, with acetylene, it gives pyrazole-3-carboxylic ester:



## QUESTIONS

1. Draw up an analytical table to show how you would distinguish between aqueous solutions of  $\text{AcNH}_2 \cdot \text{HCl}$ ,  $\text{MeNH}_2 \cdot \text{HCl}$ ,  $\text{Me}_2\text{NH} \cdot \text{HCl}$ ,  $\text{Me}_3\text{N} \cdot \text{HCl}$ ,  $\text{Me}_4\text{NCl}$ .
2. Write out the structures and names of the isomeric amines of formula  $\text{C}_4\text{H}_{11}\text{N}$ .
3. Discuss the problem of hydrogen cyanide as a tautomeric mixture, including in your answer an account of the structures of the alkyl cyanides and isocyanides.
4. Describe the methods for preparing MeCN. Name the compounds and state the conditions under which they are formed when MeCN is treated with: (a) NaOH, (b) HCl, (c) ROH + HCl, (d)  $\text{NH}_3$ , (e)  $\text{Ac}_2\text{O}$ , (f)  $\text{SnCl}_2$ , (g) H, (h)  $\text{RMgBr}$ , (i) Na, (j)  $\text{AcOEt}$ .
5. Write an account of the preparation and properties of cyanic acid and its related compounds.
6. How may  $\text{EtNO}_2$  be prepared? Name the compounds and state the conditions under which they are formed when  $\text{MeNO}_2$  is treated with:—(a) H, (b) HCl, (c) NaOH, (d) NaOH followed by  $\text{H}_2\text{SO}_4$ , (e) NaOH followed by  $\text{SnCl}_2/\text{HCl}$ , (f)  $\text{Br}_2$ , (g)  $\text{HNO}_2$ , (h)  $\text{H} \cdot \text{CHO}$ , (i)  $\text{C}_6\text{H}_5 \cdot \text{CHO}$ , (j)  $\text{CH}_2 \cdot \text{CH} \cdot \text{CO} \cdot \text{CH}_3$ .
7. Suggest as many methods as you can:—(a) for separating the three classes of amines, (b) for distinguishing between the three classes of nitro-compounds.
8. Discuss the various methods whereby:—(a) a primary amine may be converted into a secondary, and vice-versa, (b) a secondary amine into a tertiary, and vice-versa, (c) EtOH into *n*-PrOH, and vice-versa.
9. Write an account of the general methods for preparing amines. Name the compounds and state the conditions under which they are formed when  $\text{Et} \cdot \text{NH}_2$ ,  $\text{Et}_2\text{NH}$ ,  $\text{Et}_3\text{N}$ , respectively, are treated with:—(a)  $\text{H}_2\text{O}$ , (b)  $\text{H}_2\text{SO}_4$ , (c) MeI, (d)  $\text{AcCl}$ , (e)  $\text{Br}_2$ , (f)  $\text{NOCl}$ , (g) Na, (h)  $\text{MeMgI}$ , (i)  $\text{C}_6\text{H}_5 \cdot \text{NCO}$ , (j)  $\text{CS}_2$ , (k)  $\text{C}_6\text{H}_5 \cdot \text{CHO}$ , (l)  $\text{HNO}_2$ , (m)  $\text{KMnO}_4$ , (n)  $\text{H}_2\text{SO}_5$ , (o)  $\text{BrCN}$ .
10. Write an account of the preparation and properties of the quaternary ammonium hydroxides.
11. Describe the preparation and properties of:—(a) ethylenediamine, (b) putrescine, (c) cadaverine, (d) aziridine, (e) neurine, (f) allylamine, (g) choline, (h) choline.
12. Suggest one synthesis for each of the following:—(a)  $\text{CH}_3 \cdot \text{CH}(\text{NH}_2) \cdot \text{CH}_2 \cdot \text{NH}_2$ , (b)  $\text{Me}_2\text{C}(\text{NH}_2) \cdot \text{CH}_2\text{OH}$ , (c)  $\text{NH}_2 \cdot (\text{CH}_2)_3 \cdot \text{CHOH} \cdot \text{CH}_3$ , (d)  $\text{Me}_2\text{N} \cdot \text{NH}_2$ , (e)  $\text{Me}_2\text{N} \cdot \text{OH}$ , (f) spermine.
13. Describe the preparation and properties of glycine. What are betaines?
14. Describe the preparation of:—(a)  $\text{CH}_2\text{N}_2$ , (b)  $\text{CHN}_2 \cdot \text{CO}_2\text{Et}$ . Discuss their structures. Name the compounds and state the conditions under which they are formed when  $\text{CH}_2\text{N}_2$  and  $\text{CHN}_2 \cdot \text{CO}_2\text{Et}$ , respectively, are treated with:—(a) HBr, (b)  $\text{AcOH}$ , (c)  $\text{Et} \cdot \text{SO}_3\text{H}$ , (d) EtOH, (e)  $\text{Et} \cdot \text{NH}_2$ , (f)  $\text{AcNH}_2$ , (g)  $\text{CH}_3 \cdot \text{CHO}$ , (h)  $\text{Me}_2\text{CO}$ , (i)  $\text{C}_2\text{H}_4$ , (j)  $\text{C}_2\text{H}_2$ , (k)  $\text{EtO}_2\text{C} \cdot \text{CH} = \text{CH} \cdot \text{CO}_2\text{Et}$ .
15. Define and give examples of:—(a) tautomerism, (b) pseudo-acids, (c) Mannich reaction, (d) Schmidt's reaction, (e) Gabriel's synthesis, (f) Zeisel method, (g) Herzig-Meyer method, (h) Liebermann's nitroso-reaction, (i) Hofmann's exhaustive methylation method, (j) Sørensen titration, (k) Arndt-Eistert synthesis, (l) reductive alkylation.

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CHAPTER XIV  
ALIPHATIC COMPOUNDS OF  
SULPHUR, PHOSPHORUS, ARSENIC AND SILICON

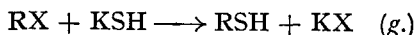
SULPHUR COMPOUNDS

**Mercaptans or thioalcohols, RSH.** These compounds occur in petroleum and give rise to "sour petrol".

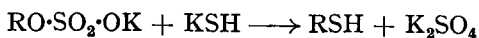
**Nomenclature.** One method is to name them as alkyl *mercaptans*, the —SH group being known as the *mercapto* or *sulph-hydryl group*. On the other hand, according to the I.U.P.A.C. system of nomenclature, the —SH group is known as the *thiol* group, and the suffix of the series is *thiol*. This method of naming the mercaptans arises from the fact that they are the sulphur analogues of the alcohols, the usual procedure of showing that an oxygen atom has been replaced by a sulphur atom being indicated by the prefix *thio*.

$\text{CH}_3\cdot\text{SH}$	methyl mercaptan	methanethiol
$\text{C}_2\text{H}_5\cdot\text{SH}$	ethyl mercaptan	ethanethiol
$(\text{CH}_3)_2\text{CH}\cdot\text{CH}_2\cdot\text{SH}$	<i>isobutyl</i> mercaptan	2-methylpropanethiol

**General methods of preparation.** One method is to heat an alkyl halide with potassium hydrogen sulphide in ethanolic solution:

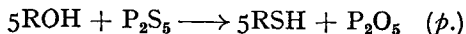


Alternatively, a potassium alkyl sulphate may be distilled with potassium hydrogen sulphide (the yield of thioalcohol is variable):

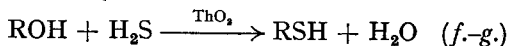


Tosylates may also be used instead of the alkyl sulphates (*cf.* the alkyl cyanides, p. 295).

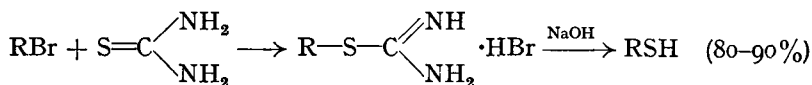
Another method depends on the direct replacement of oxygen in an alcohol by sulphur. This may be carried out by heating the alcohol with phosphorus pentasulphide:



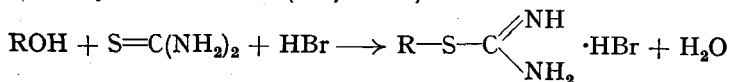
A more satisfactory method of replacing the oxygen by sulphur is to pass a mixture of alcohol vapour and hydrogen sulphide over a thoria catalyst at 400°:



The best method for preparing thioalcohols is to decompose an *S-alkylisothiuronium salt* with alkali; these salts may be prepared by interaction of an alkyl halide (preferably the bromide or iodide) and thiourea:



On the other hand, Frank and Smith (1946) have found that the *S-alkylisothiuronium salt* may be prepared by heating an alcohol and thiourea with 48 per cent. hydrobromic acid (for 7 hours):

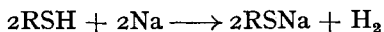


The yields are as good as those when the alkyl bromide is used, and so eliminate the step of converting the alcohol into the alkyl bromide.

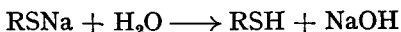
**General properties.** The thiols, except methanethiol, which is a gas, are colourless volatile liquids with disagreeable smells. Their boiling points are lower than those of the corresponding alcohols; this is probably due to the fact that they are very little associated, hydrogen bonding not readily taking place between hydrogen and sulphur. The thiols are also less soluble in water than the corresponding alcohols, again, no doubt, due to their inability to form hydrogen bonds with water. They are more strongly acidic than the alcohols; this is to be expected, since the thiols are the alkyl derivatives of hydrogen sulphide, which is a stronger acid than water, of which the alcohols may be regarded as alkyl derivatives.

**Reactions.** The thioalcohols resemble the alcohols in many ways (sulphur and oxygen occur in the same periodic group); the main difference is their behaviour towards oxidising agents.

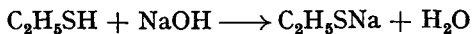
1. Thiols form mercaptides with the evolution of hydrogen when treated with alkali metals:



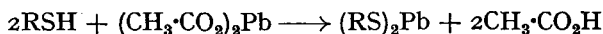
These alkali mercaptides are salts:  $[\text{RS}]^-\text{Na}^+$ , and are decomposed by water:



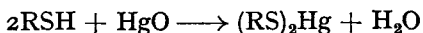
This reaction is reversible for the low-molecular-weight thiols, since these dissolve in aqueous alkali, *e.g.*,



2. Thiols precipitate mercaptides when treated with an aqueous solution of the salt of a heavy metal, *e.g.*,

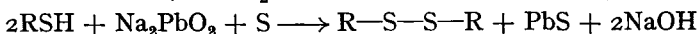
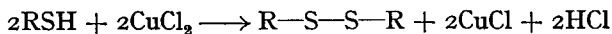


Thiols also attack mercuric oxide in aqueous solution to form the mercury mercaptide:

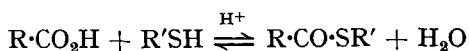


It is this reaction which is the origin of the name mercaptans (*mercurius*, mercury; *captans*, seizing). These heavy metals mercaptides are *covalent* compounds.

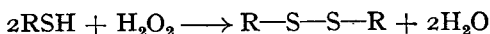
An aqueous solution of cupric chloride or an alkaline solution of sodium plumbite containing sulphur ("doctor solution") converts thiols into disulphides:



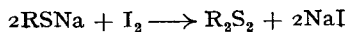
3. Thiols react with carboxylic acids, preferably in the presence of inorganic acid, to form a *thioester*:



4. Thiols may be oxidised, the nature of the product depending on the oxidising agent used. Mild oxidation with, *e.g.*, air, hydrogen peroxide, cupric chloride or sodium hypochlorite results in the formation of *dialkyl-disulphides*:



Dialkyl-disulphides may also be prepared by the action of iodine on sodium mercaptides:

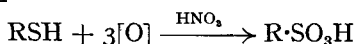


Field *et al.* (1958) have shown that lead tetra-acetate oxidises thiols to disulphides:

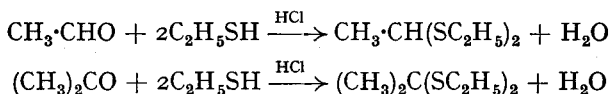


These disulphides have an unpleasant smell (not as unpleasant as that of thiols), and their formation by the oxidation of thiols is known as "sweetening" (p. 58). Allyl disulphide,  $(\text{CH}_2\cdot\text{CH}\cdot\text{CH}_2)_2\text{S}_2$ , occurs in garlic. Disulphides are reduced to thiols by lithium aluminium hydride.

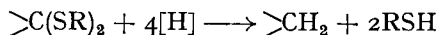
When oxidised with vigorous oxidising agents, *e.g.*, nitric acid, thiols are converted into *sulphonic acids*:



5. Thiols readily combine with aldehydes and ketones, in the presence of hydrochloric acid, to form *mercaptals* and *mercaptols* respectively; *e.g.*, ethanethiol forms diethylmethyl mercaptal with acetaldehyde, and diethylidimethyl mercaptal with acetone (see also sulphones, below):



Refluxing mercaptals (and mercaptols) with ethanol in the presence of freshly prepared Raney nickel replaces the thiol group by hydrogen (Wolfrom *et al.*, 1944):

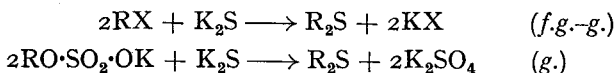


Thus a carbonyl group can be converted into a methylene group (*cf.* the Clemmensen and Wolff-Kishner reductions).

The aldehyde group may be "protected" in *acid* solution by conversion into a mercaptal, and can be regenerated by treatment of the latter with mercuric chloride in the presence of cadmium carbonate (*cf.* acetals, p. 161).

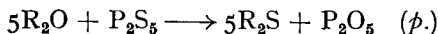
**Thioethers or alkyl sulphides,  $\text{R}_2\text{S}$ .** These are the sulphur analogues of the ethers, from which they differ considerably in a number of ways.

**General methods of preparation.** 1. By heating potassium sulphide with an alkyl halide or a potassium alkyl sulphate:

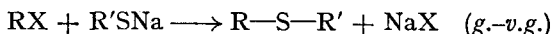


Tosylates may also be used instead of the alkyl sulphates.

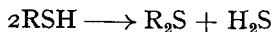
2. Heating an ether with phosphorus pentasulphide:



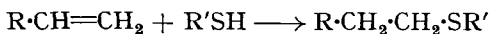
3. By heating an alkyl halide with a sodium mercaptide (*cf.* Williamson's synthesis, p. 141):



4. By passing a thiol over a mixture of alumina and zinc sulphide at 300°:

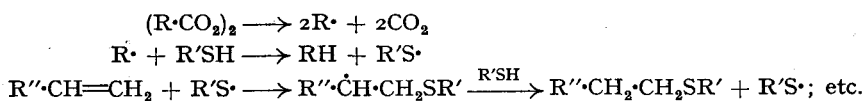


5. By the addition of a thiol to an olefin in the presence of peroxides; in the absence of the latter very little reaction occurs (Kharasch *et al.*, 1939):

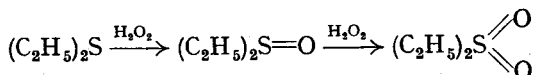




This reaction probably occurs by a free-radical mechanism:



**General properties and reactions.** The thioethers are unpleasant-smelling oils, insoluble in water but soluble in organic solvents. Chemically they are comparatively inert. They may be oxidised to *sulphoxides* which, on further oxidation, are converted into *sulphones*: e.g., ethyl sulphide, on oxidation with hydrogen peroxide in glacial acetic acid, gives first diethyl sulphoxide and then diethyl sulphone:

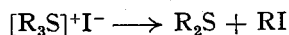


Other oxidising agents which bring about the same changes are potassium permanganate, nitric acid, perbenzoic acid, etc.

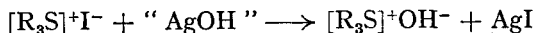
Originally, sulphur was thought to be quadrivalent in sulphoxides and sexavalent in sulphones. Then, to conform with the "octet" theory, the valencies were changed to 3 and 4, respectively, the oxygen atoms now being linked by co-ordinate bonds. More recently, however, bond length measurements of the S—O bond in sulphoxides and sulphones indicate that these bonds are almost all double bonds. M.O. calculations have also shown that the S—O bond is largely double in character and that the  $3d$  orbitals of the sulphur atom are involved in the formation of this bond (Moffitt, 1950).

The valency shell of sulphur is  $(3s)^2(3p)^4$ . Also the nature of hybridisation used is decided by the number of  $\sigma$ -electrons and lone pairs in the atom in the bonded state (p. 28). Unless one wishes to consider multiple bonds as "bent" bonds, electrons in  $\pi$ -bonds (double or triple) are not counted when deciding the type of hybridisation. In sulphides, each R group supplies one electron, and since the S atom has 6 valency electrons, the bond orbitals are  $sp^3$ , two being occupied by bonding pairs, and two by lone pairs, i.e.,  $\text{R}_2\ddot{\text{S}}$ . In sulphonium salts, the halide ion takes its bonding pair, and the R group uses one of the lone pairs of the sulphur atom, i.e.,  $\text{R}_3\ddot{\text{S}}^+\text{X}^-$ . In sulphoxides,  $\text{R}_2\ddot{\text{S}}=\text{O}$ , the orbitals are still  $sp^3$ , but here the R groups are joined by  $\sigma$ -bonds, the oxygen atom by a  $\sigma$  and  $\pi_{d-p}$  bond (one of the sulphur electrons has been promoted to  $3d$ ), and a lone pair remains in the fourth  $sp^3$  orbital. In sulphones,  $\text{R}_2\text{S} \begin{array}{l} \text{O} \\ // \\ \text{O} \end{array}$ , there are four  $\sigma$ -bonds and two  $\pi_{d-p}$  bonds (one to each oxygen atom).

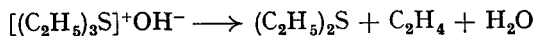
The alkyl sulphides form various addition products, e.g., with bromine the alkyl sulphide dibromide is formed,  $\text{R}_2\text{SBr}_2$ . Alkyl sulphides also combine with a molecule of alkyl halide to form *sulphonium salts*, in which the sulphur is tervalent unielectrovalent, e.g., the formula of triethylsulphonium iodide is  $(\text{C}_2\text{H}_5)_3\ddot{\text{S}}^+\text{I}^-$ . When a sulphonium salt is heated, it decomposes into alkyl sulphide and alkyl halide (cf. quaternary ammonium salts, p. 318):



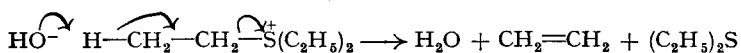
When they are treated with moist silver oxide, the *sulphonium hydroxide* is formed:



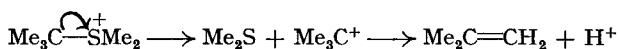
Sulphonium hydroxides are strongly basic, and on heating form alkyl sulphide and olefin, e.g.,



This is believed to occur by an E2 mechanism (*cf.* p. 319):

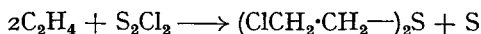


This reaction can also occur by the E1 mechanism provided the alkyl groups are of a suitable type, *e.g.*, *t*-butyldimethylsulphonium chloride in alkaline solution decomposes by the E1 mechanism:

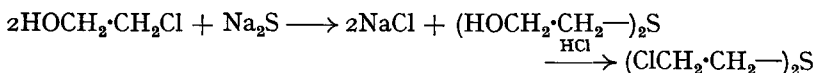


Challenger *et al.* (1948) have isolated dimethyl- $\beta$ -carboxyethylsulphonium chloride,  $[(\text{CH}_3)_2\overset{+}{\text{S}}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CO}_2\text{H}]\bar{\text{Cl}}$ , from natural sources.

**Mustard gas**, 2 : 2'-dichlorodiethyl sulphide, bis(2-chloroethyl) sulphide,  $(\text{ClCH}_2\cdot\text{CH}_2)_2\text{S}$ , may be prepared by the action of sulphur monochloride on ethylene:

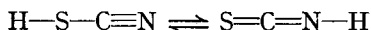


It may also be prepared, in a purer state, by heating ethylene chlorohydrin with sodium sulphide, and treating the product with hydrochloric acid:



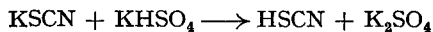
Mustard gas is an oily liquid, b.p. 215–217°, with a mustard-like smell. It is almost insoluble in water, but soluble in most organic solvents. It is a poison, and a vesicant.

**Thiocyanic acid, isothiocyanic acid and their derivatives.** Thiocyanic acid appears to be a tautomeric substance, the equilibrium mixture of thiocyanic acid, HSCN, and isothiocyanic acid, HNCS. Spectroscopic studies of thiocyanic acid indicate the structure HNCS (Beard *et al.*, 1947):



Salts and esters of both forms are known (*cf.* cyanic acid, p. 299).

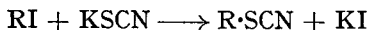
Thiocyanic acid may be prepared by heating a mixture of potassium thiocyanate and potassium hydrogen sulphate:



Thiocyanic acid distils over as a colourless liquid, m.p. 5°. It is soluble in water, ethanol and ether in all proportions. Its dilute aqueous solutions are fairly stable, the concentrated solutions decomposing to form carbonyl sulphide and ammonia:



**Alkyl thiocyanates**, R·SCN, may be prepared by heating potassium thiocyanate with an alkyl halide (or tosyl ester, p. 612):



They may also be prepared by the action of cyanogen chloride on a lead mercaptide:

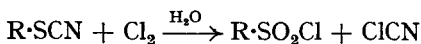


The alkyl thiocyanates are fairly stable volatile oils, with a slight odour of garlic. They are oxidised to sulphonic acids by concentrated nitric acid, and reduced to thiols by, *e.g.*, zinc and sulphuric acid; both of these re-

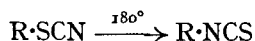
actions show that the alkyl radical in alkyl thiocyanates is directly attached to sulphur:



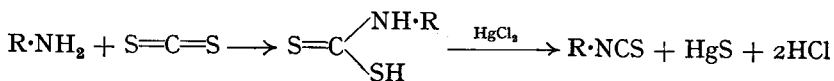
They are converted into sulphonyl chlorides by chlorine water.



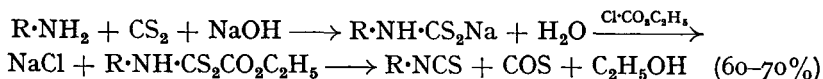
When heated at  $180^\circ$ , alkyl thiocyanates rearrange to the alkyl *isothiocyanate*:



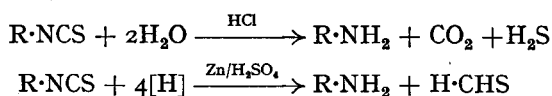
**Alkyl isothiocyanates** or **mustard oils**,  $\text{R}\cdot\text{NCS}$ , may be prepared by heating alkyl thiocyanates at  $180^\circ$ , but a much more satisfactory method is the **Hofmann mustard-oil reaction** (1868), which is carried out by heating a mixture of a primary amine, carbon disulphide and mercuric chloride. The mechanism is uncertain; it may be via the formation of a *dithio-carbamic acid salt* (see p. 390 for further details):



Another convenient method is to add an aqueous solution of a primary amine to carbon disulphide in sodium hydroxide solution, and then ethyl chloroformate:



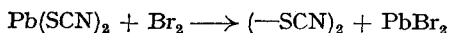
The alkyl *isothiocyanates* are liquids with a powerful mustard smell; they are lachrymatory and vesicatory. They are hydrolysed to primary amines when heated with hydrochloric acid, and reduced to primary amines and thioformaldehyde by, *e.g.*, zinc and sulphuric acid; both of these reactions show that the alkyl radical in alkyl *isothiocyanates* is directly attached to nitrogen:



**Allyl isothiocyanate** (*allyl mustard oil*),  $\text{CH}_2\cdot\text{CH}\cdot\text{CH}_2\cdot\text{NCS}$ , occurs in mustard seed as the glucoside *sinigrin*, which, on hydrolysis by acid or by the enzyme *myrosin* (which is found in mustard seeds), gives allyl *isothiocyanate*, glucose and potassium hydrogen sulphate. Allyl *isothiocyanate* is a colourless oil, b.p.  $151^\circ$ , and is the substance which gives mustard its characteristic odour and taste. It is lachrymatory and vesicatory, and is a convenient starting material for the preparation of allylamine.

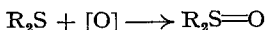
Gmelin *et al.* (1955) have isolated  $\text{CH}_3\cdot\text{S}\cdot(\text{CH}_2)_4\cdot\text{NCS}$  and  $\text{CH}_3\cdot\text{S}\cdot(\text{CH}_2)_3\cdot\text{NCS}$  from natural sources.

**Thiocyanogen**,  $(-\text{SCN})_2$ , may be prepared by treating lead thiocyanate with bromine in ethereal solution at  $0^\circ$ .



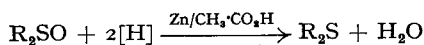
Thiocyanogen is a gas and resembles the halogens in that it adds on to double bonds (*thiocyanation*).

**Alkyl sulphoxides**,  $R_2S=O$ , may be prepared by oxidising alkyl sulphides with the *theoretical* amount of hydrogen peroxide (in acetic acid) or with *dilute* nitric acid:



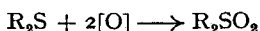
The state of oxidation depends largely on the conditions, and usually a mixture of sulphoxide and sulphone is obtained. Chromium trioxide in acetic acid appears to be specific for oxidation to sulphoxide (Knoll, 1926), and Edwards *et al.* (1954) have shown that saturated (and unsaturated) aliphatic sulphides may be oxidised to sulphoxides by chromium trioxide in pyridine or with manganese dioxide in light petroleum (yield: 49–74 per cent.). Alkyl sulphides are also readily oxidised by liquid dinitrogen tetroxide to sulphoxides, and there is no further oxidation to sulphone (yield: 90 per cent.; Addison *et al.*, 1956).

The sulphoxides are odourless, relatively unstable solids, soluble in water, ethanol and ether, and are feebly basic, *e.g.*, they form salts with hydrochloric acid. The structure of these salts is uncertain; it may be  $[R_2S-OH]^+Cl^-$ . Sulphoxides are reduced to sulphides by zinc and acetic acid:

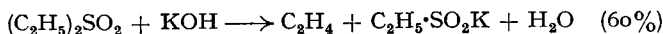


Dimethyl sulphoxide may be used as an oxidising agent for certain compounds, *e.g.*, phenacyl bromide (see p. 661).

**Alkyl sulphones**,  $R_2S \begin{array}{l} \diagup O \\ \diagdown O \end{array}$ , may be prepared by oxidising alkyl sulphides with hydrogen peroxide *in excess* (in acetic acid) or with *concentrated* nitric acid:

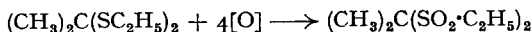


They are colourless, odourless, very stable solids, soluble in water; they are very resistant to reduction, but some sulphones (and sulphoxides) are reduced to sulphide by lithium aluminium hydride. Many sulphones produce sulphonic acids when fused with potassium hydroxide at 200°, *e.g.*,



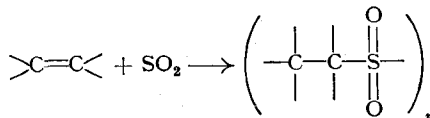
This reaction may be used to prepare aliphatic sulphonic acids.

A very important sulphone is **sulphonal** [2 : 2-bis(ethylsulphonyl)-propane], which may be prepared by the oxidation of dimethyldiethyl mercaptol with potassium permanganate:



Sulphonal is a colourless solid, m.p. 126°, stable to acids and alkalis. It has been used as an hypnotic.

Sulphur dioxide adds on to unsaturated compounds to form long linear polymers known as *polysulphones*, the valency of the sulphur changing from 4 to 6:

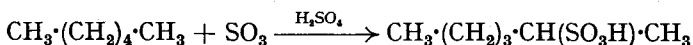


The reaction takes place in the liquid phase at room temperature under the influence of light, or in the presence of a catalyst such as silver nitrate or peracetic acid. The properties of the polysulphones depend on the nature of the olefin used; all polysulphones, however, are thermoplastic, resinous substances which are insoluble in water, acids and most organic solvents.

**Sulphonic acids**,  $R \cdot SO_3H$ . The aliphatic sulphonic acids are named either as alkylsulphonic acids or as alkanesulphonic acids; in the latter case the sulphonic acid group is considered as a substituent group, *e.g.*,

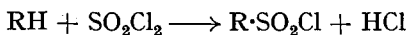
$\text{CH}_3\cdot\text{SO}_3\text{H}$	methylsulphonic acid or methanesulphonic acid
$\text{CH}_3\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{SO}_3\text{H}$	<i>n</i> -propylsulphonic acid or propane-1-sulphonic acid
$(\text{CH}_3)_2\text{CH}\cdot\text{SO}_3\text{H}$	isopropylsulphonic acid or propane-2-sulphonic acid

**General methods of preparation.** 1. By the action of fuming sulphuric acid or chlorosulphonic acid on a paraffin. The sulphonic acid group enters the chain, probably at the second carbon atom, *e.g.*,

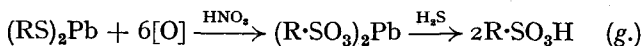


Sulphuric acid itself has no action; it is the free sulphur trioxide that is the sulphonating reagent.

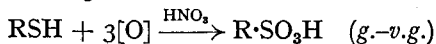
2. By the action of sulphuryl chloride on a hydrocarbon in the presence of light and a catalyst, *e.g.*, pyridine, at 40–60°. The sulphonyl chloride is obtained, often in high yield; the sulphonyl chloride group appears to enter mainly at the second carbon atom, but varying amounts of product with this group at the first carbon are also obtained:



3. By the oxidation of a lead mercaptide with concentrated nitric acid, the lead sulphionate produced being converted into the free acid by hydrogen sulphide:

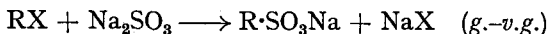


In practice it is usually more convenient to use a thiol or a thiocyanate as the starting material, *e.g.*,

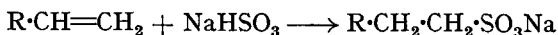


This method is most satisfactory, in that the position of the sulphonic acid group is known with certainty (the position of the mercapto or thiocyanate group being determined by the nature of the alkyl halide used in the preparation of the thiol or thiocyanate).

4. The **Strecker reaction** (1868). This reaction is carried out by heating an alkyl halide with sodium sulphite; the sodium salt of the sulphonic acid is produced:

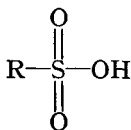


5. Sodium hydrogen sulphite adds on to olefins in the presence of peroxides to form sulphonic acids (Kharasch *et al.*, 1939).

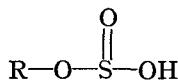


6. By the oxidation of *S*-alkylisothiuronium salts (p. 390).

**General properties and reactions.** The sulphonic acids are generally thick liquids, soluble in water. They are isomeric with the alkyl hydrogen sulphites:



alkylsulphonic acid



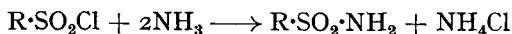
alkyl hydrogen sulphite

The alkyl hydrogen sulphites are esters readily hydrolysed by alkali; the sulphonic acids are not hydrolysed, but form salts with alkali. Many of the reactions of the sulphonic acids and their methods of preparation show that in these acids the sulphur is directly attached to the alkyl group.

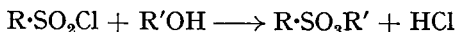
The sulphonic acids are strong acids, forming salts with metallic hydroxides or carbonates; the lead and barium salts are very soluble in water. They form the acid chloride, the sulphonyl chloride, when treated with phosphorus pentachloride (see p. 610):



These sulphonyl chlorides are only very slowly hydrolysed by water (*cf.* acyl chlorides); they react readily with concentrated aqueous ammonia to form *sulphonamides*:



Sulphonyl chlorides also react with alcohols to form esters:

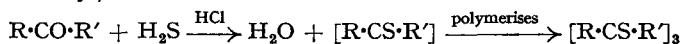


Alkyl sulphonates *cannot* be produced by heating a mixture of sulphonic acid and alcohol; *no esterification takes place*. Sulphonyl chlorides are reduced by lithium aluminium hydride to thiols (Marvel *et al.*, 1950).

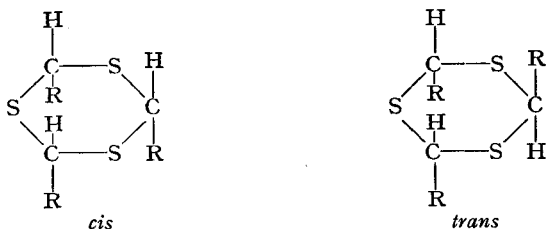
The sulphonic acids undergo many double-decomposition reactions (see the aromatic sulphonic acids, p. 608). There are, however, two important differences between aliphatic and aromatic sulphonic acids. In the former, the sulphonic acid group (*a*) is not eliminated by heating with hydrochloric acid, and (*b*) is hardly replaced, if at all, by hydroxyl when fused with alkali.

**Thioaldehydes and thioketones.** These readily polymerise to the trimer and the isolation of the monomer is difficult, and impossible in some cases, *e.g.*, thioformaldehyde.

Thioaldehydes and thioketones may be prepared by the action of hydrogen sulphide on an aldehyde or ketone in the presence of hydrochloric acid, *e.g.*, ( $\text{R}' = \text{H}$  or alkyl):

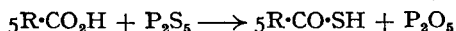


These trimers are cyclic compounds (1 : 3 : 5-*trithians*), and many of those of the thioaldehydes have been isolated in two forms. Baumann and Fromm (1891) suggested that the two forms were geometrical isomers, the *cis* form being the one with the three hydrogen atoms all on the same side of the plane:



Schönberg and Barakat (1947), however, believe that the ring is not planar, but puckered, and that the two forms are related to each other as "chair" and "boat" forms (*cf. cyclohexane*, p. 488). Hassell and Viervoll (1947) have shown by electron diffraction studies that the ring is puckered and that it is of the "chair" type. If this is so, then the existence of the two forms can be explained by *cis-trans* isomerism.

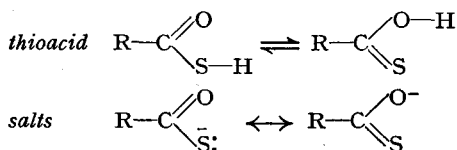
**Thioacids**,  $\text{R}\cdot\text{CO}\cdot\text{SH}$ , may be prepared by the action of phosphorus pentasulphide on a carboxylic acid:



The thioacids have a most disagreeable odour, and slowly decompose in air. They have lower boiling points and are less soluble in water than the corresponding oxygen compounds; they are soluble in most organic solvents.

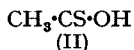
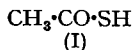
In most of their reactions, the thioacids and their salts behave as if they

contained the mercapto-group, but in a few reactions they behave as if they contained a hydroxyl group. This may be accounted for by tautomerism for the acid and resonance for the salts:



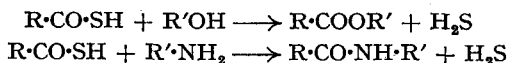
The existence of the acid as a tautomeric mixture is supported by the preparation of both the *O*- and *S*-esters.

**Nomenclature.** The methods of nomenclature are illustrated by the following example:

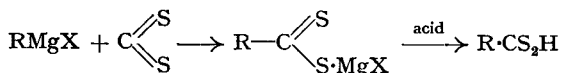


According to the trivial system of nomenclature, both I and II are named as thioacetic acid. According to the I.U.P.A.C. rules, the suffix *-oic* of the corresponding oxygen acid is changed to *thioic*. Thus both I and II are named either as ethanethioic acid or methanecarbothioic acid. On the other hand, the suffix *-thiolic* is used if it is certain that the oxygen of the hydroxyl group is replaced by sulphur, and the suffix *thionic* if it is the oxygen of the carbonyl group. Thus I is ethanethiolic acid or methanecarbothiolic acid, and II is ethanethionic or methanecarbothionic acid.

The most characteristic reaction of the thioacids is their extreme readiness to acylate alcohols and amines:



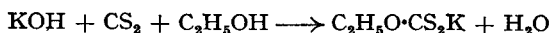
**Dithioacids**,  $\text{R}\cdot\text{CS}_2\text{H}$ , may be prepared by the action of a Grignard reagent on carbon disulphide:



**Nomenclature.** The methods of nomenclature are illustrated by the following example:

$\text{CH}_3\cdot\text{CS}_2\text{H}$  is named as dithioacetic acid, ethanethionthiolic acid or methanecarbothioic acid.

A very important dithioacid is **dithiocarbonic acid**,  $\text{HO}\cdot\text{CS}_2\text{H}$ . The free acid is unknown, but many of its derivatives have been prepared, *e.g.*, *potassium xanthate* may be prepared by the reaction between potassium hydroxide, ethanol and carbon disulphide:



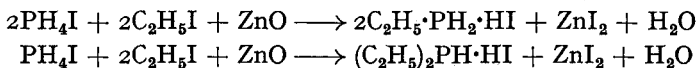
The name **xanthate** is derived from the property of these compounds, giving a *yellow* precipitate of copper xanthate with copper salt (Greek: *xanthos*, yellow).

**Vulcanisation of rubber.** This process is carried out by heating crude rubber with 4–5 per cent. sulphur and certain organic compounds which accelerate the reaction between the rubber and sulphur. These organic compounds are known as *accelerators*, and all contain sulphur or nitrogen, or both. Vulcanising rubber causes the rubber to lose its stickiness, makes it no longer sensitive to temperature changes, causes it to retain its elasticity over a wide temperature range, and increases its tensile strength. The function of the sulphur appears to be to cross-link the long hydrocarbon chains in crude rubber.

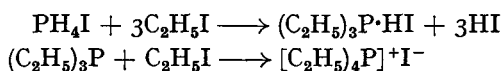
## PHOSPHORUS COMPOUNDS

**Alkyl-phosphines.** All three classes of phosphines are known, the tertiary phosphines being the commonest; the quaternary phosphonium compounds are also known.

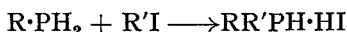
**General methods of preparation.** 1. Primary and secondary phosphines are produced when phosphonium iodide is heated with alkyl halide in the presence of zinc oxide, *e.g.*, ethyl and diethylphosphine:



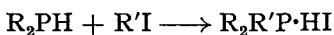
If the reaction is carried out in the *absence* of zinc oxide, the tertiary phosphines and quaternary phosphonium compounds are produced, *e.g.*, triethylphosphine and tetraethylphosphonium iodide:



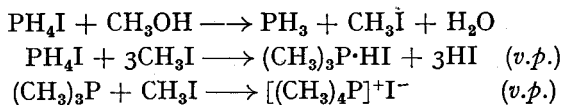
Secondary phosphines may be prepared by heating a primary phosphine with the calculated amount of alkyl halide:



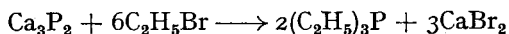
Tertiary phosphines may be prepared from secondary in a similar manner:



2. A mixture of tertiary phosphine and quaternary phosphonium compound is produced when phosphonium iodide is heated with one of the lower alcohols or lower ethers, *e.g.*,



A small amount of tertiary phosphine is produced when a metallic phosphide is heated with alkyl halide, *e.g.*,

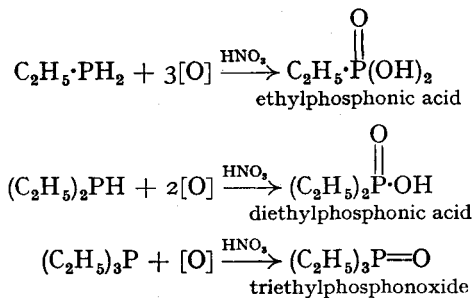


A very small amount of quaternary phosphonium compound is produced when phosphorus is heated with an alkyl halide or an alcohol.

3. Tertiary phosphines are prepared most conveniently by the action of excess Grignard reagent on phosphorus trihalide:



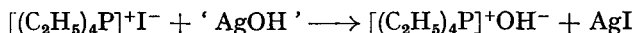
**General properties and reactions.** Except for methylphosphine (a gas), all the alkyl-phosphines are colourless, unpleasant-smelling liquids. They resemble the corresponding nitrogen compounds in many ways, but differ in being less basic and more easily oxidised, *e.g.*,



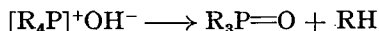


In naming organic acids and oxides derived from phosphorus, arsenic or antimony, the syllable -on denotes the quinquevalent and -in the tervalent state of the central atom (*British Chemical Abstracts*, 1948).

When quaternary phosphonium halides are treated with moist silver oxide, the quaternary phosphonium hydroxide is produced:



The quaternary phosphonium hydroxides are strongly basic, comparable in strength with the quaternary ammonium hydroxides and sodium hydroxide. When heated they form the trialkyl-phosphonoxide and a hydrocarbon (*cf.*  $R_4NOH$ , p. 318).



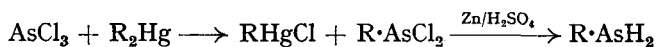
Phosphorus differs from nitrogen in being able to expand its valency shell to form a decet; compounds of the type  $R_3PX_2$  have been prepared (*cf.* phosphorus pentahalides). Arsenic also forms compounds of this type. Wittig *et al.* (1948) have prepared pentaphenylphosphorus,  $(C_6H_5)_5P$ .

Triphenylphosphine (which is now obtainable commercially) is used to prepare triphenylphosphine methylene, which is used in the Wittig reaction (p. 64):

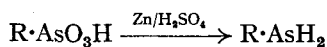


#### ARSENIC COMPOUNDS

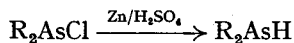
**Alkyl-arsines.** There are primary, secondary and tertiary arsines, and quaternary arsonium compounds. Primary arsines may be prepared by the action of dialkyl-mercury on arsenic trichloride and reducing the product, alkyl-dichloroarsine, with zinc and sulphuric acid:



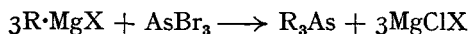
Alternatively, they may be prepared by reducing an alkyl-arsonic acid with zinc and sulphuric acid:



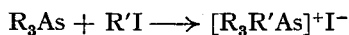
Secondary arsines may be prepared by the reduction of dialkyl-chloroarsine:



Tertiary arsines may be prepared by the action of excess Grignard reagent on arsenic tribromide:

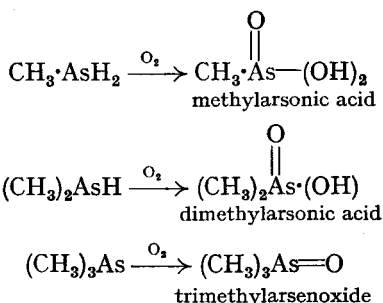


Quaternary arsonium halides may be prepared by the addition of alkyl halide to a tertiary arsine:

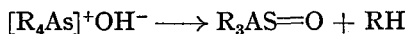


**General properties and reactions.** Except for methylarsine (a gas), the alkyl-arsines are colourless poisonous liquids with a garlic smell. They

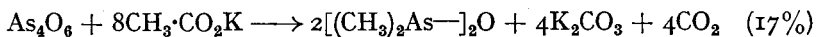
have practically no basic properties, and do not form salts with inorganic acids. They are readily oxidised when exposed to air:



Quaternary arsonium halides form the corresponding hydroxide when treated with moist silver oxide. These hydroxides are strongly basic and, on heating, decompose into the trialkyl-arsonoxide and hydrocarbon (*cf.*  $\text{R}_4\text{POH}$ ):



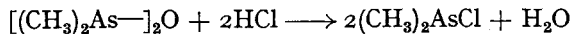
**Cacodyl oxide** (*dimethylarsin oxide*),  $(\text{CH}_3)_2\text{As} \text{---} \text{O} \text{---} \text{As}(\text{CH}_3)_2$ . Cadet (1760) distilled a mixture of equal parts of arsenious oxide and potassium acetate, and obtained a vile-smelling, spontaneously inflammable oil, which subsequently became known as *Cadet's liquid*:



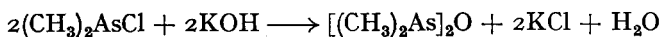
This reaction was later investigated by Bunsen (1837-1843), who showed that Cadet's liquid was a mixture of *cacodyl oxide* and *cacodyl*,  $(\text{CH}_3)_2\text{As} \text{---} \text{As}(\text{CH}_3)_2$ . It was Berzelius who proposed the name *cacodyl* (Greek: *kakodes*, stinking).

A better method for preparing cacodyl oxide is to pass a mixture of the vapours of arsenious oxide and acetic acid over an alkali metal acetate catalyst at 300-400° (yield: 66 per cent., Fuson and Shive, 1947).

Cacodyl oxide is an extremely poisonous liquid, b.p. 150°, insoluble in ethanol and ether. It is not spontaneously inflammable when pure; its inflammability is due to the presence of cacodyl. Cacodyl oxide is feebly basic, reacting with hydrochloric acid to form **cacodyl chloride** (*dimethylchloroarsine*), b.p. 109°:



Pure cacodyl oxide may be prepared by heating cacodyl chloride with potassium hydroxide:

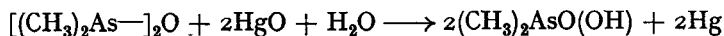


**Cacodyl** (*tetramethyldiarsine*),  $[(\text{CH}_3)_2\text{As} \text{---}]_2$ , may be prepared by heating cacodyl chloride with zinc in an atmosphere of carbon dioxide (*cf.* Wurtz reaction):



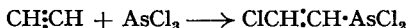
It is a colourless poisonous liquid, b.p. 170°, spontaneously inflammable in air, giving carbon dioxide, water and arsenious oxide.

**Cacodylic acid** (*dimethylarsonic acid*),  $(\text{CH}_3)_2\text{AsO} \cdot (\text{OH})$ , is formed when cacodyl oxide is oxidised with moist mercuric oxide:

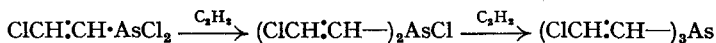


It is a crystalline odourless substance, m.p. 200°, soluble in water, the aqueous solution being acid to phenolphthalein. Cacodylic acid reacts with hydrogen sulphide to form *cacodyl sulphide*,  $[(\text{CH}_3)_2\text{As}-]_2\text{S}$ .

**Lewisite** (*dichloro-β-chlorovinylarsine*),  $\text{ClCH}_2\text{CH}\cdot\text{AsCl}_2$ , may be prepared by passing acetylene into arsenic trichloride in the presence of anhydrous aluminium chloride:

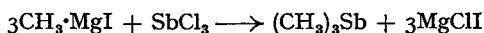


Continued action of acetylene produces bis(β-chlorovinyl)chloroarsine and finally tris(β-chlorovinyl)arsine:



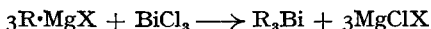
Lewisite is a liquid, b.p. 190° (with decomposition), and is a powerful vesicant.

**Antimony compounds.** Antimony forms only tertiary stibines and quaternary stibonium compounds. Tertiary stibines may be prepared by the action of a Grignard reagent on antimony trichloride, *e.g.*, trimethylstibine:

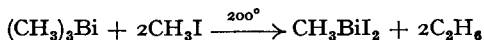


Trimethylstibine slowly adds on methyl iodide to form tetramethylstibonium iodide,  $[(\text{CH}_3)_4\text{Sb}]^+\text{I}^-$ , which, on treatment with moist silver oxide, forms tetramethylstibonium hydroxide,  $[(\text{CH}_3)_4\text{Sb}]^+\text{OH}^-$ . The quaternary stibonium compounds closely resemble the corresponding arsenic compounds.

**Bismuth compounds.** The organo-bismuth compounds resemble the organo-compounds of mercury, lead and tin in reactivity, *i.e.*, they are true organo-metallic compounds (p. 348). Only tertiary bismuthines are known, and these are best prepared by the action of a Grignard reagent on bismuth trichloride:



Tertiary bismuthines do *not* add on a molecule of alkyl halide; generally, they react to form an alkyl-halogeno-bismuthine, *e.g.*, trimethylbismuthine, when heated with methyl iodide at 200°, forms methyl-di-iodo-bismuthine and ethane:



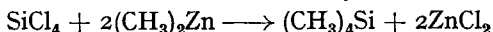
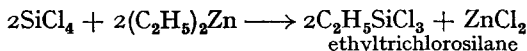
Pentaphenylbismuth,  $(\text{C}_6\text{H}_5)_5\text{Bi}$ , has now been prepared by Wittig *et al.* (1952); it is an unstable solid.

## SILICON COMPOUNDS

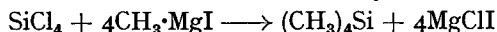
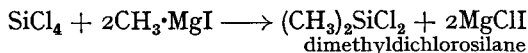
The organo compounds of silicon have come into prominence in recent years due to the discovery that resins could be prepared from them.

**Alkyl-silanes.** These are silicon hydrides (silanes) in which one or more hydrogen atoms have been replaced by an alkyl group, *e.g.*,  $\text{C}_2\text{H}_5\text{SiH}_3$ , ethylsilane;  $(\text{CH}_3)_4\text{Si}$ , tetramethylsilane.

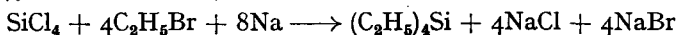
**General methods of preparation.** 1. By the action of a dialkyl-zinc on silicon tetrachloride (Friedel and Crafts, 1863):



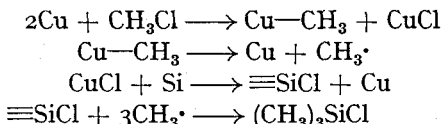
2. By the action of a Grignard reagent on silicon tetrachloride (Kipping, 1904):



3. By heating a mixture of silicon tetrachloride and alkyl bromide with sodium (*cf.* Wurtz reaction):



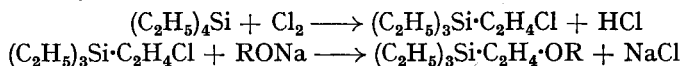
4. By passing alkyl halide vapour over a mixture of silicon and copper at  $350^\circ$  (Patnode and Rochow, 1945); *e.g.*, methyl chloride gives a mixture of methyltrichlorosilane, dimethyldichlorosilane, trimethylchlorosilane and methyldichlorosilane, of which the first two predominate. This reaction has been shown to take place via the formation of methylcopper, which then undergoes homolytic fission to give a methyl free radical (Hurd and Rochow, 1945):



5. By passing a mixture of alkyl halide vapour and silicon tetrachloride over an aluminium or zinc catalyst at  $400^\circ$ . The same mixture is obtained as in method 4; and probably the mechanism is the same.

Methods 1, 4 and 5 are used on a large scale for preparing the intermediates required for the preparation of silicones (see below).

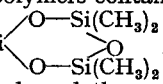
**General properties and reactions.** The alkylsilanes are colourless oils, stable in air, and are not affected by acids or alkalis. The alkyl groups in tetra-alkylsilanes may be chlorinated, and these chlorinated compounds undergo many of the reactions characteristic of the alkyl halides, *e.g.*,

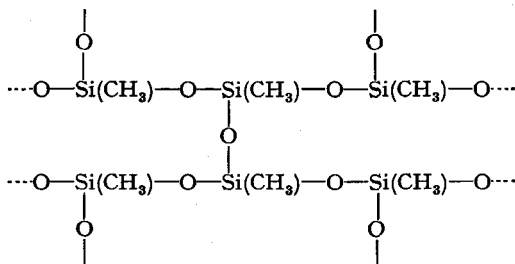


**Alkyl-halogenosilanes** may be prepared by any of the above methods (1-5). They are usually colourless oily liquids that fume in the air due to their ready hydrolysis to silanols.

**Silanols.** Hydrolysis of trialkyl-chlorosilanes, dialkyldichlorosilanes and alkyl-trichlorosilanes gives the *silanols*,  $\text{R}_3\text{SiOH}$ , *silanediols*,  $\text{R}_2\text{Si}(\text{OH})_2$ , and *silanetriols*,  $\text{RSi}(\text{OH})_3$ , respectively.

Trialkyl silanols are colourless stable liquids, many of which have a camphor-like odour. On the other hand, the silanediols and silanetriols are unstable, eliminating water to form polymers. Hydrolysis is carried out by dissolving the alkyl-chlorosilane in a solvent, and mixing with another solvent containing water. Under these conditions hydrolysis is slow: rapid hydrolysis leads to gel formation. The hydroxy-compounds are polymerised by heating.

Hydrolysis of dimethyldichlorosilane produces cyclic polymers containing 3-9 oxygen atoms in the ring, *e.g.*, the trimer,  $(\text{CH}_3)_2\text{Si}$  ; linear polymers,  $\text{HOSi}(\text{CH}_3)_2\cdot[\text{OSi}(\text{CH}_3)_2]_n\cdot\text{OH}$ , are also obtained, and the value of  $n$  may be increased by treating with sulphuric acid, resulting in higher polymers which are viscous liquids or soft plastics. Hydrolysis of methyltrichlorosilane results in the formation of amorphous powders or hard brittle solids. These polymers consist of linear, cyclic and cross-linked structures, depending on the conditions of the hydrolysis; *e.g.*, the end product of the dehydration process is cross-linked:



Thus by controlling the conditions of hydrolysis, and using mixtures of intermediates, polymers with different properties can be obtained. These polymers are known as the **silicones**. Silicones may be roughly classified as follows:

- (i) *Silicone fluids*: used in high-temperature baths and diffusion pumps, as hydraulic fluids, and form water-repellent surfaces.
- (ii) *Silicone rubbers*: used as electrical insulators.
- (iii) *Silicone greases*: used as lubricants at high and low temperatures.
- (iv) *Silicone resins*: used as electrical insulators.

### QUESTIONS

1. How may EtSH be prepared? Name the compounds and state the conditions under which they are formed when EtSH is treated with:—(a) Na, (b) KOH, (c)  $(\text{AcO})_2\text{Pb}$ , (d) HgO, (e)  $\text{Na}_2\text{PbO}_2$ , (f) AcOH, (g)  $\text{H}_2\text{O}_2$ , (h) NaOCl, (i)  $\text{HNO}_3$ , (j)  $\text{CH}_3\cdot\text{CHO}$ , (l)  $\text{Me}_2\text{CO}$ .
2. Describe the preparation and properties of:—(a)  $\text{Et}_2\text{S}$ , (b)  $(\text{ClCH}_2\text{CH}_2)_2\text{S}$ , (c)  $\text{Me}\cdot\text{SCN}$ , (d)  $\text{CH}_2\cdot\text{CH}\cdot\text{CH}_2\cdot\text{NCS}$ , (e)  $\text{Et}_2\text{SO}$ , (f)  $\text{Me}_2\text{SO}$ , (g)  $\text{Me}_2\text{C}(\text{SO}_2\text{Et})_2$ .
3. Discuss the structures of the sulphoxides, sulphones, sulphonium salts, trimeric thioaldehydes and thioacids.
4. Suggest one synthesis for each of the following:—(a)  $\text{Me}\cdot\text{NH}\cdot\text{CS}\cdot\text{OEt}$ , (b)  $\text{Me}\cdot\text{NH}\cdot\text{CS}\cdot\text{NH}\cdot\text{Et}$ , (c)  $\text{Et}\cdot\text{NH}\cdot\text{CS}_2\cdot\text{Me}$ . What would each of these give on vigorous hydrolysis?
5. Compare and contrast the methods of preparation and the properties of the *onium* compounds of N, S, P and As.
6. How may  $\text{Et}\cdot\text{SO}_3\text{H}$  be prepared? How may this be distinguished from  $\text{EtO}\cdot\text{SO}_3\text{H}$ ? How may  $\text{Et}\cdot\text{SO}_3\text{H}$  be converted into:—(a)  $\text{Et}\cdot\text{SO}_2\text{Cl}$ , (b)  $\text{Et}\cdot\text{SO}_3\text{Na}$ , (c)  $(\text{Et}\cdot\text{SO}_2)_2\text{Pb}$ , (d)  $\text{Et}\cdot\text{SO}_2\text{Et}$ , (e)  $\text{Et}\cdot\text{SO}_2\cdot\text{NH}_2$ , (f)  $\text{Et}\cdot\text{SO}_2\cdot\text{NH}\cdot\text{Et}$ ?
7. Compare and contrast the methods of preparation and the properties of the phosphines and arsines.
8. Write an account of the preparation and properties of the cacodyl compounds, and discuss the part played by these compounds in the history of organic chemistry.
9. Write an account of the preparation and properties of the tetra-alkyl-silanes and the alkyl-chlorosilanes, and discuss the use of organo-silicon compounds in industry.

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CHAPTER XV  
ORGANO-METALLIC COMPOUNDS

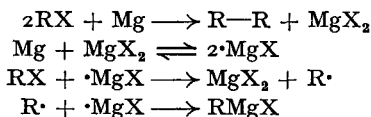
GENERALLY speaking, organo-metallic compounds are those organic compounds in which a metal is directly joined to carbon (see, however, alkali metals, p. 361). The most widely studied and the most useful are the magnesium compounds, but in recent years the organo-compounds of sodium and lithium have been studied in great detail; the lithium compounds in particular are becoming increasingly important in synthetic work.

THE GRIGNARD REAGENTS

The alkyl-magnesium halides,  $R-Mg-X$ , or Grignard reagents, introduced by Grignard in 1900, are extremely valuable in laboratory organic syntheses, and recently are being used on a large scale (*cf.* silicon compounds, p. 345). A Grignard reagent is generally prepared by reaction between magnesium (1 atom) and alkyl halide (1 molecule) in dry, alcohol-free ether.



The mechanism of the formation of a Grignard reagent is still not clear. A free radical mechanism has been suggested (Gomberg and Bachmann, 1927; *cf.* triphenylmethyl bromide, p. 702). The reaction starts by the formation of a trace of magnesium halide (Wurtz reaction) and then proceeds as follows:

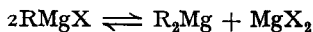


The ethereal solution of the Grignard reagent is generally used in all reactions. Other solvents besides ether may be used, *e.g.*, tertiary amines, tetrahydrofuran and the dimethyl ether of ethylene glycol. Tetrahydrofuran is being used increasingly as a solvent, since it has been found that it increases the reactivity of organic halides towards magnesium. Dimethyl sulphate also reacts readily with magnesium in tetrahydrofuran to give  $CH_3Mg\cdot SO_4CH_3$  (Normant *et al.*, 1957). The reactions of this new reagent appear to be similar to those of  $CH_3MgX$ .

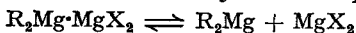
The ease with which an alkyl halide forms a Grignard reagent depends on a number of factors. It has been found that for a given alkyl radical the ease of formation is alkyl iodide > bromide > chloride. It has also been found that the formation of a Grignard reagent becomes increasingly difficult as the number of carbon atoms in the alkyl group increases, *i.e.*, the ease of formation is  $CH_3X > C_2H_5X > C_3H_7X > \dots$ . Since tertiary alkyl iodides readily eliminate hydrogen iodide with the formation of an olefin, tertiary alkyl chlorides are used.

Normant (1953, 1957) has shown that Grignard reagents can be prepared from vinyl and aryl halides if tetrahydrofuran is used as solvent.

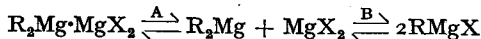
**Structure of Grignard reagents.** The structure of the Grignard reagent in ethereal solution has been the subject of much research. Grignard *et al.* (1901), in their attempt to isolate the Grignard reagent, showed that the compound contained ether (which they called "ether of crystallisation"). Since this time many formulæ have been proposed, among which is the one by Jolibois (1912), who suggested that the Grignard reagent was the loose molecular complex  $R_2Mg\cdot MgX_2$ . On the other hand, Schlenk *et al.* (1929) suggested the following equilibrium:



These authors found that a mixture of equivalent amounts of dialkylmagnesium and magnesium halide behaved exactly as a Grignard reagent. This, however, can be explained by the dissociation of the Jolibois complex:



Ubbelohde *et al.* (1955) have confirmed that  $RMgX$  is dimerised and solvated in ether. Thus the following equilibria are possible:



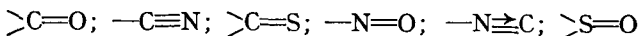
These equilibria have been examined by Dessy *et al.* (1957). Since an equimolecular mixture of diethylmagnesium and magnesium bromide in ether shows the same kinetics towards 1-hexyne as the ordinarily prepared Grignard solution, it seems reasonable to suppose that both involve the same or similar complexes. When  $^{26}MgBr_2$  was mixed with  $R_2Mg$ , and subsequently the  $MgBr_2$  precipitated with dioxan, 95 per cent. recovery of the  $^{26}Mg$  was obtained. If equilibrium B were involved, then a 50 per cent. recovery would have been expected. Thus a better formulation of the Grignard reagent appears to be  $R_2Mg \cdot MgX_2$  and equilibrium A.

In this book, the formula  $RMgX$  will be used to designate a Grignard reagent.

**Reactions of the Grignard reagents.** When working with Grignard reagents, it is usual to add the other reactant (often in ethereal solution) slowly to the Grignard solution or vice-versa, and after a short time, decompose the magnesium complex with water or dilute acid; the yields are usually *g.-v.g.*

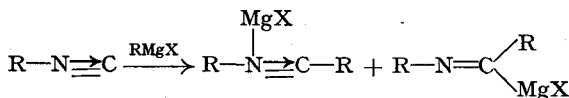
The majority of Grignard reactions fall into two groups.

(i) *Addition of the Grignard reagent to a compound containing any of the following groups (containing multiple bonds):*



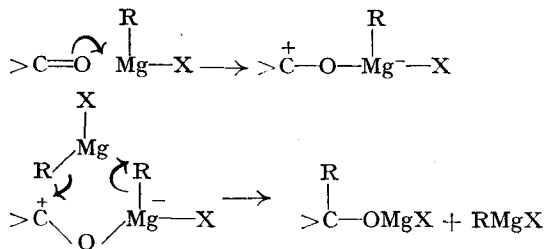
In each case the alkyl group of  $RMgX$  adds on to the atom with the lower electron-affinity, and the fragment  $MgX$  to the atom with the higher. It is important to note that a Grignard reagent does *not* add on to two carbon atoms joined by a double or triple bond.

The addition of a Grignard reagent to an *isocyanide* is exceptional in that both  $R$  and  $MgX$  add on to some extent to the carbon atom:



In the case of the *azo-group*,  $-N=N-$ , the fragment  $MgX$  adds on to each nitrogen atom and the alkyl group,  $R$  or  $C_nH_{2n+1}$ , is eliminated as  $R-R$ ,  $C_nH_{2n}$  and  $C_nH_{2n+2}$ .

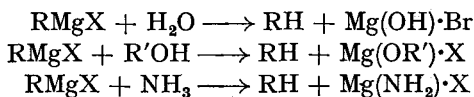
The most important group is the carbonyl group. The mechanism of addition of Grignard reagents to this group has been the subject of much discussion, and it cannot be said that the mechanism is settled. A favoured theory is the cyclic-addition mechanism (Swain *et al.*, 1951):



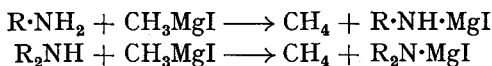
One molecule of the Grignard reagent co-ordinates with the carbonyl compound at the oxygen atom, thereby increasing the polarity of the C=O bond, and then a second molecule of Grignard reagent donates its R group to the carbonyl carbon atom.

Kharasch *et al.* (1941, 1944) have shown that in the presence of a small amount of cobaltous chloride the Grignard reaction takes place by a free-radical mechanism. It appears that traces of metal impurities may bring about a free-radical mechanism and thereby lead to an abnormal reaction of the Grignard reagent; even a trace of free magnesium may be sufficient (see diphenyl, p. 698).

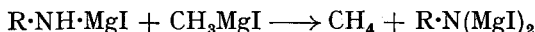
(ii) *Double decomposition with compounds containing an active hydrogen atom or a reactive halogen atom.* We shall consider only the former at this stage (see p. 354 for an example of the latter). As we have seen, an active hydrogen atom is one joined to oxygen, nitrogen or sulphur. When such compounds react with a Grignard reagent, the alkyl group is converted into the paraffin, *e.g.*,



All reactions with compounds containing an active hydrogen atom result in the quantitative yield of hydrocarbon. Thus this type of reaction is valuable for the determination of the number of active hydrogen atoms in a compound. The procedure is known as the **Zerewitinoff active hydrogen determination** (1907), and methylmagnesium iodide is normally used as the Grignard reagent. The methane which is liberated is measured (by volume), one molecule of methane being equivalent to one active hydrogen atom, *e.g.*,

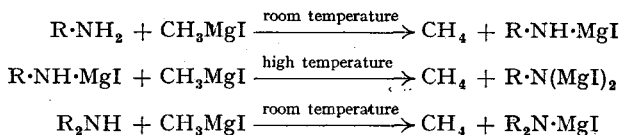


Only one hydrogen atom in a primary amine reacts at room temperature. At a sufficiently high temperature, the active hydrogen atom in the magnesium derivative of the primary amine will react with a further molecule of methylmagnesium iodide:



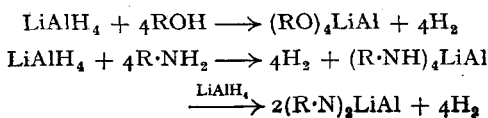
It is therefore possible to estimate the number of amino- and imino-groups in compounds containing both. It is not possible to get a high enough temperature for the second reaction with ether; a satisfactory solvent for the complete Zerewitinoff determination is pyridine (Lehman and Basch, 1945).

The Zerewitinoff determination can be used to distinguish between primary, secondary and tertiary amines:



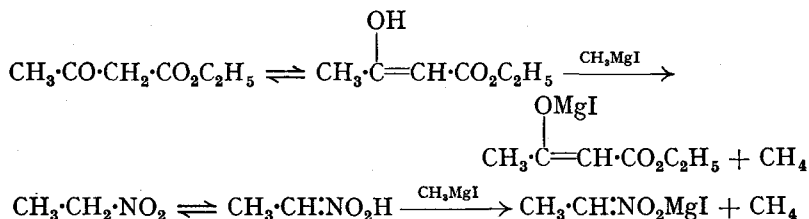
Thus a primary amine ultimately gives two molecules of methane, a secondary one, and a tertiary none (no reaction).

Lithium aluminium hydride also reacts with compounds containing active hydrogen, and so may be used for analytical determinations, *e.g.*,



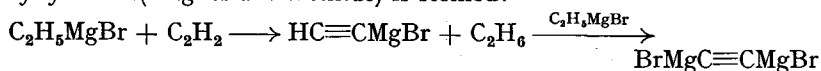


The enolic form of a compound, since it contains an active hydrogen atom, reacts with a Grignard reagent, *e.g.*, acetoacetic ester and nitroethane:



In both cases the methane will not be liberated immediately, but at a rate depending on the speed of the conversion of keto into enol.

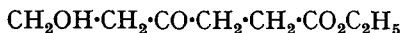
The hydrogen atom in the  $\equiv\text{CH}$  group is also active with respect to a Grignard reagent (to be expected, since it is acidic, p. 96). Thus, when acetylene is passed through an ether solution of ethylmagnesium bromide, ethynylenebis(magnesium bromide) is formed:



The second step can be avoided by adding the Grignard solution to tetrahydrofuran saturated with acetylene (Jones *et al.*, 1956).

**Order of reactivity of functional groups.** In most cases of syntheses in which a Grignard reagent is used, the other compound has only one functional group, and consequently the reaction takes place in one direction only. Occasionally it is necessary to carry out a synthesis with a compound containing two (or possibly more) functional groups. If an excess of Grignard reagent is used, then both groups react as would be expected. It has been found experimentally that the reactivity of different groups is not equal, and hence when one equivalent of Grignard reagent is added, two competitive reactions take place simultaneously, but at different rates, resulting in two products in unequal amounts. Experiments have shown that an active hydrogen reacts very much faster than any other group; so much so, in fact, that a compound containing an active hydrogen and another group, reacts with one equivalent of a Grignard reagent as if it had only one reactive group, the active hydrogen.

Experiments have also shown that the reactivity of the carbonyl group in aldehydes is somewhat greater than in ketones. The carbonyl group in both aldehydes and ketones, however, is much more reactive than in acyl chlorides and esters, the latter being less reactive than the former. Finally, the carbonyl group in all the types of compounds named above is more reactive than a halogen atom of the alkyl halide type (which is not to be confused with the halogen in an acyl chloride; see p. 355). The foregoing general rules may be illustrated with the compound:



One molecule of  $\text{RMgX}$  would react exclusively with the hydroxyl group; a second molecule of  $\text{RMgX}$  with the keto-group; and a third molecule with the carboxyl group.

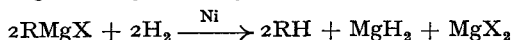
#### SYNTHETIC USES OF THE GRIGNARD REAGENTS

**Hydrocarbons.** When a Grignard reagent is treated with any compound containing active hydrogen, a hydrocarbon is produced; in practice, water or dilute acid is used:

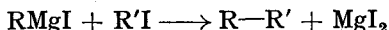


Since alkyl halides are readily prepared from alcohols, it becomes a relatively simple matter to convert an alcohol (saturated or unsaturated) into the corresponding hydrocarbon.

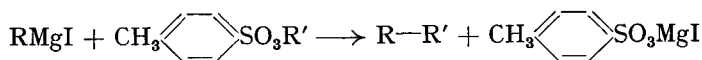
The alkyl group of a Grignard reagent may also be converted into the parent paraffin by reducing the Grignard reagent catalytically:



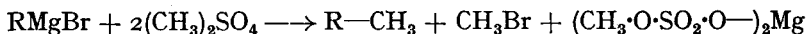
Hydrocarbons containing more carbon atoms than the Grignard reagent may be prepared by treating the latter with an alkyl halide. This is an example of the reaction between a Grignard reagent and a compound containing a reactive halogen atom:



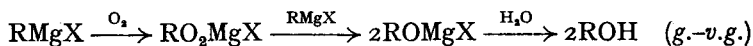
The yield of R-R' is very good only if R' is allyl or t-alkyl radical. On the other hand, a good yield of R-R', where R' is any alkyl radical, may be obtained by using *p*-toluenesulphonic esters as the alkylating agent:



When R' is either a methyl or ethyl group, methyl or ethyl sulphate, respectively, may be used:



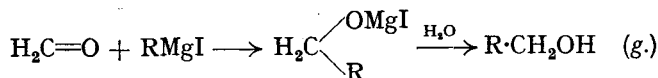
**Primary alcohols.** A Grignard reagent may be used to synthesise an alcohol by treating it with dry oxygen and decomposing the product with water:



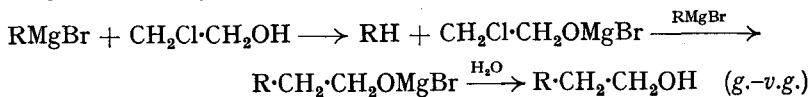
This method (which can be used for all three classes of alcohols) is little used in practice since an alkyl halide may be converted into the corresponding alcohol by simpler means (p. 106). The method, however, is useful for converting aryl halides into phenols.

Walling *et al.* (1955) have isolated peroxides (yield: 30–90 per cent.) by the slow addition of a Grignard reagent to oxygen-saturated solvents at  $-70^\circ$ . This supports the above mechanism (suggested by Porter *et al.*, 1920). Peroxides have not been isolated from aromatic Grignard reagents, but their presence has, however, been detected.

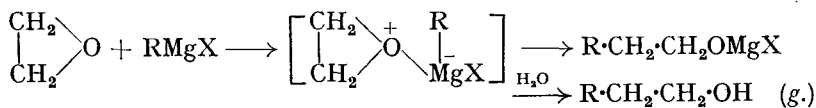
When a Grignard reagent (in ethereal solution) is treated with formaldehyde gas, or when a Grignard reagent in, *e.g.*, di-*n*-butyl ether (b.p.  $141^\circ$ ), is refluxed with paraformaldehyde, a primary alcohol is obtained by decomposing the magnesium complex with dilute acid:



On the other hand, a primary alcohol containing *two* carbon atoms more than the Grignard alkyl radical can be prepared by adding one molecule of ethylene chlorohydrin to two molecules of Grignard reagent.

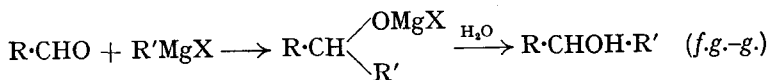


Two molecules of Grignard reagent are not necessary if ethylene oxide is used instead of ethylene chlorohydrin. Ethylene oxide is added to the well-cooled Grignard solution, the mixture allowed to stand for several hours, the ether then distilled off and the residue treated with ice-cold water:



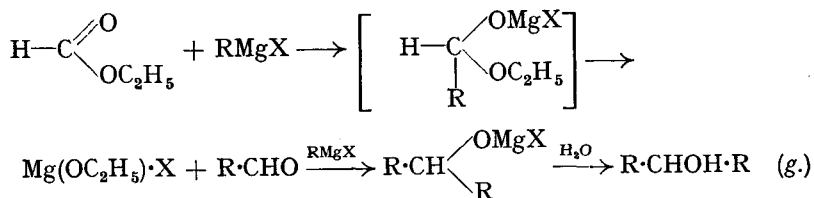
Care must be taken in carrying out this reaction since, when all the ether has been distilled, a vigorous reaction often occurs apparently due to the rearrangement of the intermediate complex (an oxonium salt). This vigorous reaction may be avoided by distilling off some of the ether, adding benzene, and then distilling until the temperature of the vapour reaches 65°.

**Secondary alcohols.** When a Grignard reagent is treated with any aldehyde other than formaldehyde, a secondary alcohol is formed:

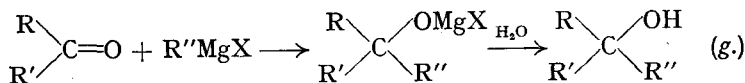


It can be seen that the secondary alcohol R·CHOH·R', is obtained whether we start with R·CHO and R'MgX, or R'·CHO and RMgX. Which pair we use is generally a matter of their relative accessibility.

Secondary alcohols may also be prepared by interaction of a Grignard reagent (2 molecules) and ethyl formate (1 molecule). The mechanism of the reaction is still not certain; one which is widely accepted is that an aldehyde is formed as an intermediate product, and subsequently reacts with another molecule of Grignard reagent to form the secondary alcohol (see aldehydes, below):



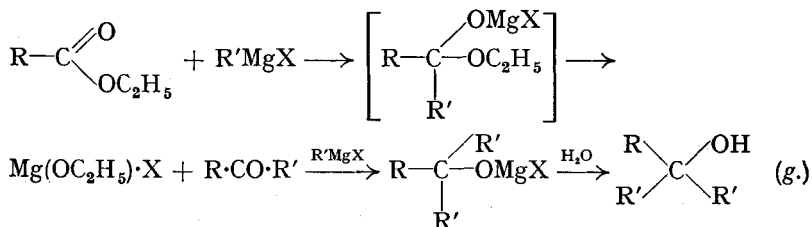
**Tertiary alcohols.** A tertiary alcohol may be prepared by the action of a Grignard reagent on a ketone:



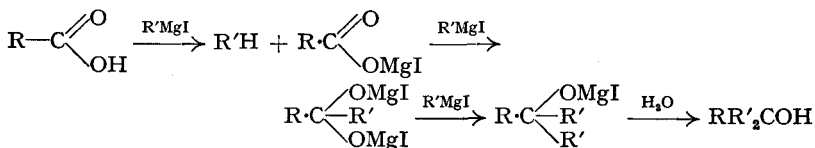
By this means a tertiary alcohol with three different alkyl groups may be prepared, and the starting materials may be any of the following pairs of compounds: R·CO·R' and R''MgX; R·CO·R'' and R'MgX, or R'·CO·R'' and RMgX (*cf.* secondary alcohols).

Tertiary alcohols containing at least two identical alkyl groups may be

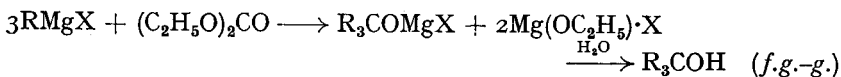
prepared by the reaction between a Grignard reagent (2 molecules) and any ester (1 molecule) other than formic ester (*cf.* secondary alcohols):



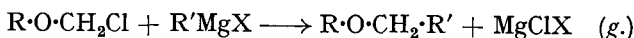
Similar results may be achieved by using an acid and a slight excess of Grignard reagent, *i.e.*, more than three molecules (Huston *et al.*, 1946):



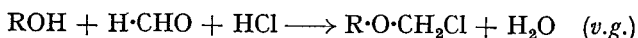
Tertiary alcohols containing three identical alkyl groups may be prepared by the reaction between a Grignard reagent (3 molecules) and ethyl carbonate (1 molecule):



**Ethers.** The preparation of an ether using a Grignard reagent is another example of the reaction between the latter and a compound containing a reactive halogen atom (*cf.* hydrocarbons); the method consists in adding an  $\alpha$ -monochloroether to a Grignard reagent, *e.g.*,

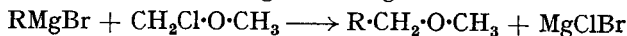
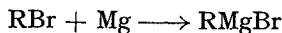
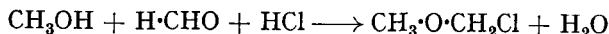


Chloroethers of the type  $\text{R}\cdot\text{O}\cdot\text{CH}_2\text{Cl}$  are readily prepared by passing hydrogen chloride into a cooled mixture of formalin solution and an alcohol:

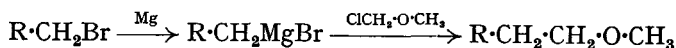


A particularly useful chloroether is monochlorodimethyl ether, by means of which it is possible to ascend both the ether and alcohol series.

The following equations illustrate how it may be used:

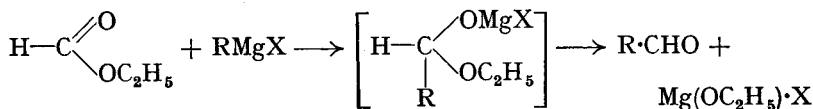


When refluxed with constant-boiling hydrobromic acid, this ether gives the alkyl bromide  $\text{R}\cdot\text{CH}_2\text{Br}$  and methyl bromide (see p. 142). The alkyl bromide may be hydrolysed to the corresponding alcohol,  $\text{R}\cdot\text{CH}_2\text{OH}$ , or may be converted into the ether  $\text{R}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{O}\cdot\text{CH}_3$ :



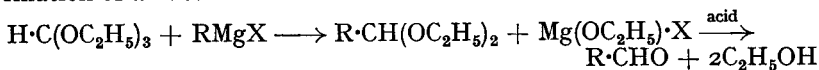
**Aldehydes.** An aldehyde may be prepared by the reaction between a Grignard reagent (1 molecule) and ethyl formate (1 molecule). If the

Grignard reagent is in excess, a secondary alcohol is formed (see above). Hence, to avoid this as much as possible, the Grignard reagent is added to the ester:



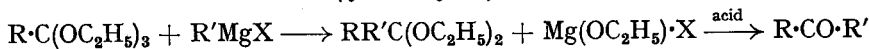
Isolation of the aldehyde supports the mechanism given for the formation of a secondary alcohol when the Grignard reagent is in excess (see secondary alcohols).

In the preparation of an aldehyde by this method it is impossible to avoid the formation of some secondary alcohol as well. If, however, ethyl orthoformate is used instead of ethyl formate, a better yield of aldehyde is obtained, since the formation of secondary alcohol is prevented by the formation of an acetal:

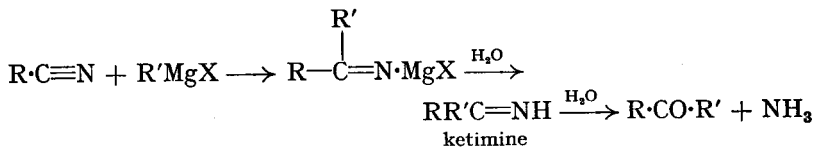


Aldehydes may also be prepared by the reaction between a Grignard reagent and hydrogen cyanide or formamide (see ketones, below).

**Ketones.** Ketones *cannot* be prepared by the reaction between a Grignard reagent (1 molecule) and any ester (1 molecule) other than formic ester, since it is rarely possible to stop the reaction at the first stage (as can be done for the preparation of an aldehyde using ethyl formate). It is possible, however, to prepare a ketone (as its ketal) by using any orthoester other than orthoformic ester (*cf.* aldehydes):



Ketones may be prepared by adding an alkyl cyanide to a Grignard reagent, and decomposing the complex with dilute acid; methyl cyanide is the only alkyl cyanide which does not form a ketone:



The starting materials may be either R·CN and R'MgX, or R'·CN and RMgX. If hydrogen cyanide is used instead of an alkyl cyanide (R=H), an aldehyde is formed.

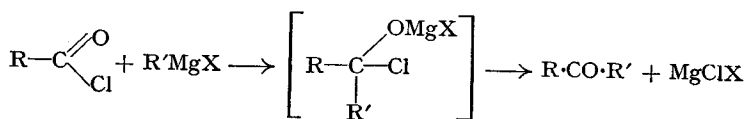
Acyl chlorides (1 molecule) react rapidly with Grignard reagents (1 molecule) to form ketones:



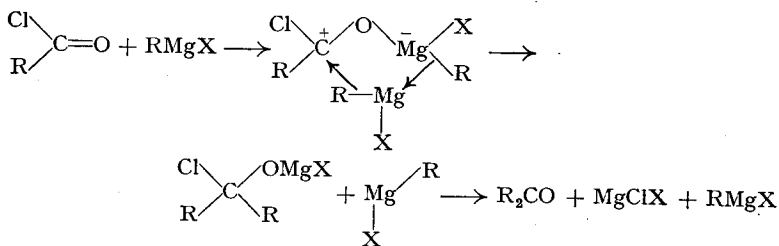
Tertiary alcohol is also formed, due to the action of the Grignard reagent on the ketone produced. The best conditions for the preparation of straight-chain ketones is the addition of one molecule of Grignard reagent to one or more molecules of acyl chloride at  $-65^\circ$  in the presence of a small amount of ferric chloride. For branched-chain ketones the temperature can be about  $5^\circ$  (Percival *et al.*, 1953).

The mechanism of the reaction is not certain, but it appears to be additive and not double decomposition, since the reactivity of acyl halides with a Grignard reagent is acyl fluoride > chloride > bromide > iodide (Entemann and

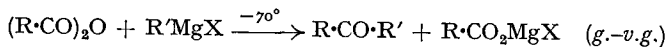
Johnson, 1933); this order is opposite to that of the reactivity of the halogen atom in acyl halides. Thus the reaction may be formulated:



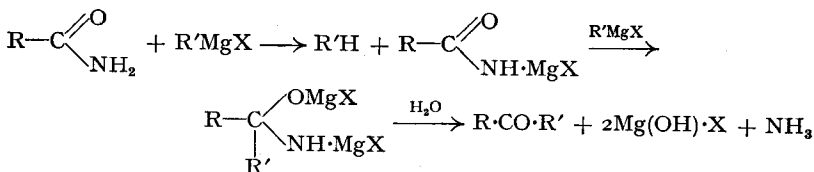
On the other hand, Morrison *et al.* (1954) propose the following mechanism, a second molecule attacking the Grignard-acyl halide complex (*cf.* p. 349):



Acid anhydrides also form ketones, the reaction being best carried out at about  $-70^\circ$ :

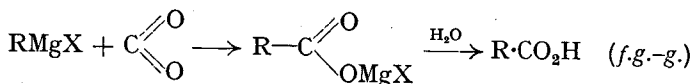


Amides and *N*-substituted amides react with Grignard reagents to form ketones:



This reaction necessitates the use of two molecules of Grignard reagent, and is therefore of very little practical importance. Formamide gives rise to the formation of an aldehyde.

**Acids.** When a Grignard reagent is treated with solid carbon dioxide and the complex decomposed with dilute acid, a monocarboxylic acid is obtained:

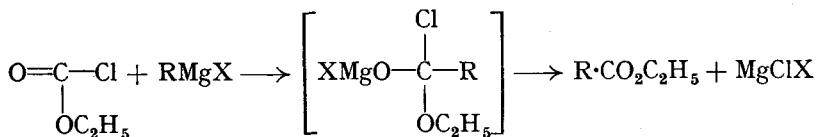


Solid carbon dioxide is used in order to attain a low temperature ( $-70^\circ$ ); if the reaction is carried out with carbon dioxide at room temperature, the product is mainly a mixture of ketone and tertiary alcohol. High yields of acid are also obtained by the addition of the Grignard reagent to powdered solid carbon dioxide in ether (Hussey, 1951). On the other hand, a good yield of acid may also be obtained by passing carbon dioxide into the Grignard solution cooled to  $0^\circ$ .

The above method is particularly useful for preparing acids of the type  $\text{R}_3\text{C}\cdot\text{CO}_2\text{H}$ , which usually cannot be prepared by the cyanide synthesis using a tertiary alkyl halide (p. 294). It may also be noted that this method offers a means of ascending the acid series.

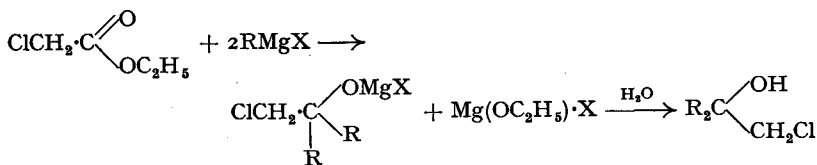
**Esters.** When a Grignard reagent (1 molecule) reacts with ethyl chloroformate (1 molecule) an ester is formed. Since chloroformic ester is the

half-acid chloride of carbonic acid, the reaction probably takes place by an additive mechanism (see ketones):

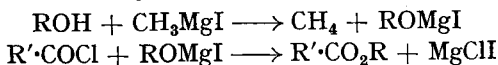


To avoid as far as possible reaction of the Grignard reagent with the carbethoxy group of the carboxylic ester produced, the ethyl chloroformate is kept in excess by adding to it the Grignard reagent.

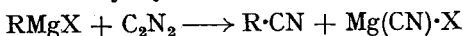
Chloroformic ester is an acid chloride; ethyl chloroacetate is not. When the latter is treated with a Grignard reagent (2 molecules), a chloro-tertiary alcohol is produced, the carbonyl group of the carbethoxy being more reactive than the chlorine atom of the alkyl halide type:



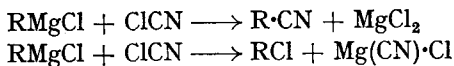
A very useful method for preparing esters of tertiary alcohols is to treat the tertiary alcohol with a Grignard reagent, and then add an acyl chloride, which reacts with the alkoxy-magnesium halide left in the solution:



**Alkyl cyanides.** Cyanogen (1 molecule) reacts with a Grignard reagent (1 molecule) to form an alkyl cyanide:



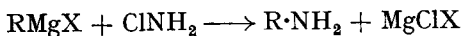
Alkyl cyanides are also formed, together with alkyl chloride, when a Grignard reagent (1 molecule) is added to an ethereal solution of cyanogen chloride (1 molecule); the latter should always be in excess, since the alkyl cyanide produced tends to react with the Grignard reagent (*cf.* aldehydes and esters):



This reaction is probably the best method for preparing tertiary alkyl cyanides.

Only cyanogen chloride reacts to form an alkyl cyanide, and the best yield is obtained when the halogen atom in the Grignard reagent is chlorine. Cyanogen bromide and iodide react with Grignard reagents to form the alkyl bromide and iodide, respectively; no alkyl cyanide is formed at all (Coleman *et al.*, 1928, 1929).

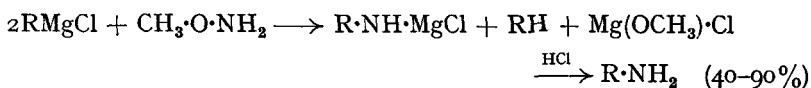
**Primary amines.** A primary amine is formed by the reaction between a Grignard reagent and chloramine:



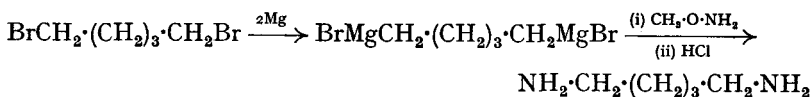
This is one of the best methods for preparing primary amines containing a tertiary alkyl group. The yields are usually low. This is not unexpected when we consider the very great reactivity of active hydrogen; in fact, it is surprising that we get any amine at all.

A much more satisfactory method for preparing pure primary amines is the reaction between *O*-methylhydroxylamine and a Grignard reagent

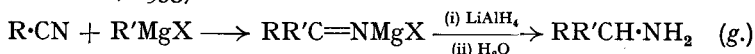
which may be either the alkyl-magnesium chloride or bromide, but *not* iodide (Brown and Jones, 1946):



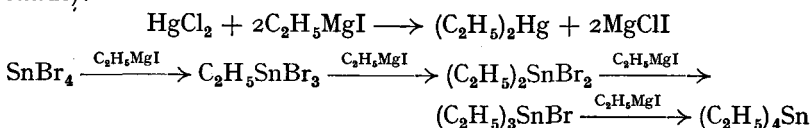
This reaction is also applicable to the preparation of certain diamines (see also p. 360), *e.g.*, cadaverine:



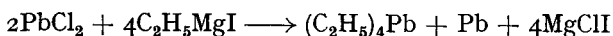
Primary amines may also be prepared by reducing the adducts formed between cyanides and Grignard reagents with lithium aluminium hydride (Pohland *et al.*, 1953).



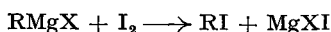
**Organic-metallic and organo non-metallic compounds.** These compounds may be prepared by interaction of a Grignard reagent and an inorganic halide, the former acting as an alkylating reagent. Some examples have already been mentioned, *e.g.*, the alkyl-phosphines, arsines, and silanes; these are regarded as organic compounds of non-metallic elements. Examples of the formation of organo-metallic compounds are diethyl-mercury (from mercuric chloride) and the ethyl-tin compounds (from stannic bromide):



A particularly interesting example is the formation of *tetraethyl-lead* from *lead dichloride*:



**Alkyl iodides.** Alkyl iodides are formed when a Grignard reagent—the alkyl-magnesium chloride or bromide—is treated with iodine:

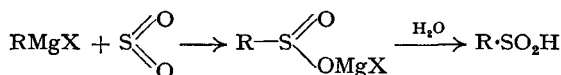


This reaction provides a good method for preparing alkyl iodides from the corresponding chloride or bromide.

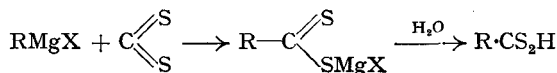
**Thioalcohols.** These may be prepared by the action of sulphur on a Grignard reagent:



**Sulphinic acids.** When sulphur dioxide is passed into a well-cooled Grignard solution, a sulphinic acid (as its magnesium complex) is formed:



**Dithioic acids.** These may be prepared by the action of carbon disulphide on a Grignard reagent (*cf.* carboxylic and sulphinic acids):



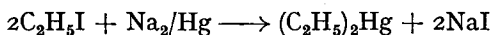




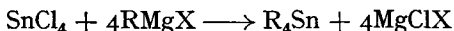


dimethylmercury;  $(C_2H_5)_4Pb$ , tetraethyl-lead. They are not generally isolated, but are used directly as intermediates, and their preparation is usually carried out in an atmosphere of nitrogen.

**General methods of preparation.** 1. By heating an alkyl halide with an alloy, *e.g.*, diethylmercury from ethyl iodide and sodium amalgam:

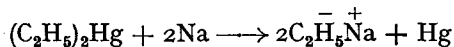


2. By the reaction between a Grignard reagent and a metallic halide, *e.g.*,

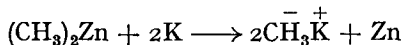


This method may be used to prepare the organo-compounds of those metals which have a lower electrode potential than magnesium. Generally, an organo-metallic compound may be prepared by the reaction between a dialkyl-metal of *higher* electrode potential and the chloride of a metal of *lower* electrode potential.

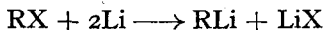
3. A metal of *higher* electrode potential generally reacts with the dialkyl-metal of *lower* electrode potential, *e.g.*,



**Alkali group of metals.** The organo-alkali compounds are generally best prepared by the action of the alkali metal on a dialkyl-mercury or zinc compound (method 3, above), *e.g.*,



Lithium compounds, however, are best prepared by heating an alkyl halide with lithium (Ziegler, 1930):



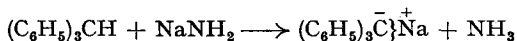
Alkyl chlorides are generally the most satisfactory; the iodides usually undergo the Wurtz reaction. On the other hand, aryl bromides and iodides give good yields of the lithium compound. Many organo-lithium compounds, however, cannot be prepared by this method, but may readily be prepared by the following exchange reaction ("indirect metalation"):



The most satisfactory radical (R) for this purpose is *n*-butyl. Another important method is by metalation (see p. 539).

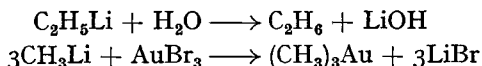
The alkyl sodium and potassium compounds are insoluble, colourless, highly reactive solids. They are electrovalent compounds, *i.e.*, salts. The lithium compounds are colourless liquids or readily fusible solids, and are covalent, *e.g.*,  $CH_3Li$ , but, according to the nature of the alkyl group, they may have partial ionic character, *e.g.*, *n*-butyl-lithium. Owing to their covalent nature, lithium compounds are more stable and less reactive than those of sodium and potassium.

An important organo-sodium compound is triphenylmethylsodium,  $(C_6H_5)_3CNa$ , which may be prepared by the action of sodamide on triphenylmethane in liquid ammonia solution:

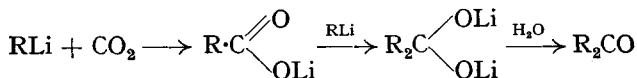


It is a very good reagent for bringing about condensation reactions (see, *e.g.*, p. 230).

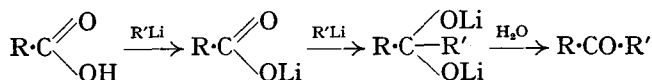
From the practical point of view, lithium compounds are the most satisfactory to use in organic synthesis, since they are very easily prepared and, being covalent, dissolve in organic solvents. Generally speaking the lithium compounds (and those of sodium and potassium) behave like the Grignard reagents, but the lithium compounds are usually more reactive; *e.g.*,



With carbon dioxide a good yield of ketone is obtained:

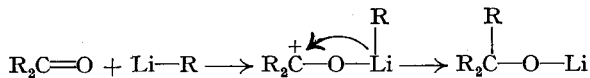


A ketone is also the main product when a carboxylic acid is used as starting material:



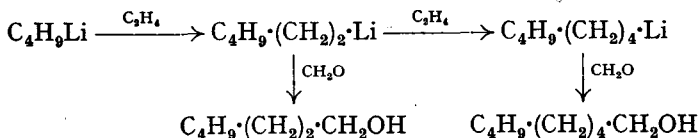
Lithium compounds also react with aldehydes and ketones to give alcohols in better yields than with Grignard reagents.

According to Swain *et al.* (1950), the addition of organolithium compounds to carbonyl compounds proceeds as follows:



Some authors believe that Grignard reagents also behave in this way (*cf.* p. 349).

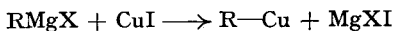
The main difference between lithium compounds and Grignard reagents is that the former can add on to the C=C grouping, *e.g.*, Ziegler *et al.* (1950) have shown that *n*-butyl-lithium adds on to ethylene under high pressure, and that after the addition of formaldehyde a mixture of alcohols (C<sub>7</sub>-C<sub>13</sub>) is obtained, *e.g.*,



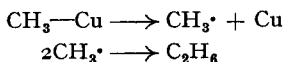
This offers a means of stepping up a series.

It should also be noted that lithium forms lithium alkenyls with various vinyl halides. This offers a means of preparing unsaturated compounds such as alcohols, ketones and acids. Lithium acetylides may also be prepared and used in synthetic work.

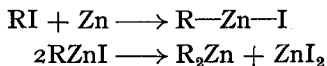
**Copper group of metals** (*copper, silver and gold*). The alkyl derivatives of the copper group are best prepared by the reaction between a Grignard reagent and the metal halide, *e.g.*,



Their most characteristic reaction is their ready decomposition, which possibly takes place via the formation of free radicals, *e.g.*,



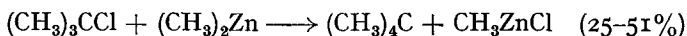
**Organo-zinc compounds.** The dialkyl-zinc compounds were the first organo-metallic compounds to be prepared; they were discovered by Frankland (1849) in an attempt to prepare the ethyl radical by removing iodine from ethyl iodide by means of zinc. The alkyl iodide is heated with zinc in an atmosphere of carbon dioxide, and the product, alkyl-zinc iodide, is distilled in an atmosphere of carbon dioxide:



The yield of dialkyl-zinc may be increased by carrying out the distillation *in vacuo* (50–90 per cent.). Krug *et al.* (1954) have shown that the dialkyl-zincs are best prepared by reaction between an alkyl bromide or iodide and a zinc-copper couple prepared by heating a mixture of zinc dust and cupric acetate.

The alkyl-zinc compounds are volatile liquids, spontaneously inflammable in air (hence the necessity to use an atmosphere of carbon dioxide in their preparation). They have an unpleasant smell, and burn the skin. The alkyl-zinc compounds have been used in various synthetic reactions (they behave like the Grignard reagents), but owing to the difficulty in handling them, and because better synthetic reagents are known, *e.g.*, the Grignard reagent, the use of the alkyl-zinc compounds is restricted to three synthetic preparations:

(i) *Preparation of hydrocarbons containing a quaternary carbon atom; e.g., neopentane* may be prepared by the action of dimethylzinc on *tert.*-butyl chloride:

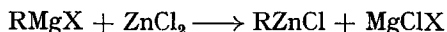


Apparently dialkyl-zinc compounds do not react with primary or secondary alkyl halides.

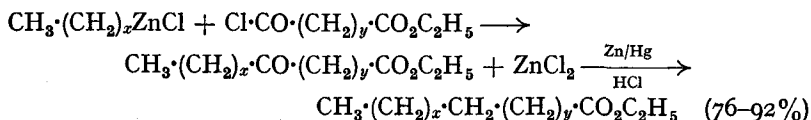
(ii) *Preparation of ketones.* Alkyl-zinc compounds react with acyl chlorides to form ketones:



The success of this method depends on the fact that the ketone can be isolated in good yield because dialkyl-zinc compounds react very slowly with ketones (*cf.* Grignard reagent, p. 355). Even so, the dialkyl cadmium compounds are replacing the zinc compounds in the preparation of ketones (see below). An alkyl-zinc chloride may be prepared by reaction between a Grignard reagent and zinc chloride:

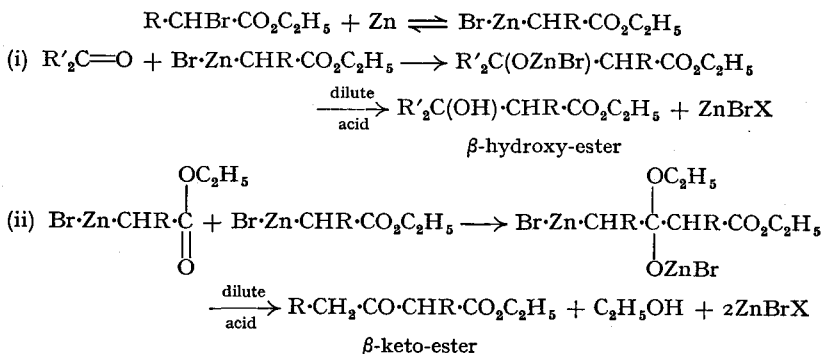


Jones (1947) used these compounds to prepare long-chain fatty acids (*cf.* p. 231). He prepared a keto-ester by reaction between an alkyl-zinc chloride and the acid chloride-ester derivative of a dicarboxylic acid, and reduced the keto-ester by the Clemmensen method:



(iii) The **Reformatsky reaction** (1887). The Reformatsky reaction is the reaction between an  $\alpha$ -bromoacid ester and a carbonyl compound (aldehyde, ketone or ester) in the presence of zinc to form a  $\beta$ -hydroxy-ester. The

reaction is best carried out by adding zinc to a mixture of bromoacid ester and carbonyl compound, and then warming. According to Dippy *et al.* (1951), the Reformatsky reaction proceeds as follows:

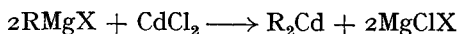


Which of the two reactions predominates depends on the structure of the carbonyl compound. If this is a ketone and the two R' groups are very large, *i.e.*, the carbonyl group is sterically hindered, the main reaction proceeds via (ii). When the carbonyl compound is an aldehyde (one R'=H), the main reaction proceeds via (i).

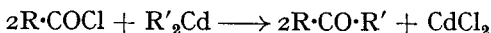
A few cases of  $\beta$ -haloesters undergoing the Reformatsky reaction are known, but the yields are low.

The preparation of a Grignard reagent from a bromoacid ester is not practical, since the organo-magnesium compound formed immediately reacts with the ester group of a second molecule.

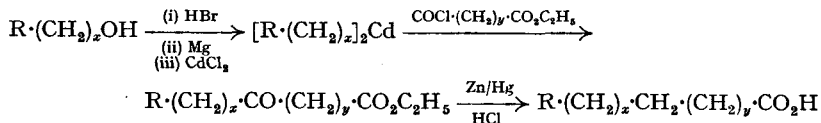
**Organo-cadmium compounds.** Dialkyl-cadmium compounds may be prepared by the action of a Grignard reagent on cadmium chloride:



These compounds may be used to prepare simple ketones or polyfunctional compounds containing a keto-group. The reaction is carried out by treating an acyl chloride with dialkyl-cadmium, the yield being as high as 98 per cent. (better than with dialkyl-zinc). The high yields of ketone are due to the fact that dialkyl-cadmium compounds show very little tendency to react with a carbonyl group (but see below):

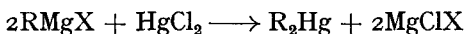


This ketone synthesis may be used to synthesise long-chain fatty acids as follows:



Syntheses with organocadmium compounds have always been carried out with the cadmium compounds prepared *in situ* (see above). Kollonitsch (1960) has shown that *pure* dimethylcadmium does *not* react with benzoyl chloride. This author believes that the successful use of organocadmium compounds requires a "salt effect", and has shown that magnesium salts generated in the preparation of the organocadmium compounds had this effect. It was also shown that organocadmium compounds react with aldehydes in the presence of magnesium salts to give secondary alcohols.

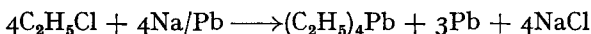
**Organo-mercury compounds.** Dialkyl-mercury compounds are best prepared by the reaction between a Grignard reagent and mercuric chloride:



They are poisonous liquids, *not* spontaneously inflammable in air; they are *not* decomposed by water, but are by dilute acids (*cf.* magnesium and zinc compounds).

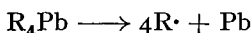
An important reaction involving the use of mercury is **mercuration**. This process is the introduction of a *mercuri-acid group*, of which the commonest is the *acetoxo-mercuri* group,  $-\text{HgO}\cdot\text{CO}\cdot\text{CH}_3$ . Mercuration has some interesting applications in aromatic chemistry, and will be discussed later (p. 539).

**Organo-lead compounds.** The only organo-lead compound which is important is tetraethyl-lead. This is prepared industrially by heating ethyl chloride with a sodium alloy under pressure:



Tetraethyl-lead is a liquid, b.p. about  $200^\circ$ , insoluble in water but soluble in ether. It is used for raising the octane number of petrol (see p. 57). To prevent lead being deposited in the cylinder head when such "doped" petrol is used (1 part tetraethyl-lead per thousand parts petrol), a small amount of ethylene bromide is added. The lead is thereby converted into lead dibromide, which is sufficiently volatile to be removed with the exhaust gases.

Tetramethyl- and tetraethyl-lead have been used by Paneth and his co-workers (1929, 1931) to prepare *free methyl* and *ethyl radicals*. The vapour of the tetra-alkyl-lead in a stream of hydrogen or nitrogen, under reduced pressure (1–2 mm.), was carried through a tube (gas velocity about 10–15 metres per sec.) heated at a point A (Fig. 1) to  $600\text{--}800^\circ$ :



The decomposition into lead was shown by the deposition of a lead mirror at point A. The presence of free methyl or ethyl radicals was shown by the disappearance of a lead mirror previously deposited at a point B farther along the tube and kept at room temperature; hydrocarbons do not attack lead. If the distance between A and B was greater than



FIG. 15.1.

32 cm., the mirror at B did not disappear. This showed that the free alkyl radicals have a very short life; calculations based on experiment have shown that their half life period is about 0.006 sec.

**Free radicals.** There are two types of free radicals, long-life and short-life free radicals. The former are stabilised by resonance (see p. 703), whereas the latter exist only as reactive intermediates in reactions.

The removal of metallic mirrors is now a well-established technique for the detection and identification of free radicals produced in the decomposition of organic compounds. The rate of removal of the mirrors is usually followed photometrically, the opacity of the mirror being matched against that of a standard. This procedure has been modified by measuring the electrical conductivity of the mirror (Whittingham, 1947).

Thermal decomposition is a general method for producing free radicals in the gaseous phase. Another general method (for producing free radicals in the gaseous phase or in solution) is photochemical decomposition. Thus photolysis of tetramethyl-lead, dimethylmercury, and dimethylzinc gives

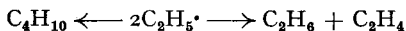
rise to free methyl radicals; *e.g.*, Leighton and Mortensen (1936) showed that a mirror of radioactive lead was attacked by a stream of tetramethyl-lead vapour which had been irradiated. Photolysis of alkyl iodides produces free alkyl radicals and iodine atoms, *e.g.*, West (1935) showed that the photochemical decomposition products of methyl iodide converted *para* hydrogen (the two nuclei have opposite spins) into *ortho* hydrogen (parallel spins). Free radicals can often be detected by the conversion of *para* hydrogen into *ortho*. They may also often be detected by combination with nitric oxide (see p. 703). The method of paramagnetic resonance is also being used to detect and measure free-radical concentrations (*inter alia*, Ingram *et al.*, 1954).

When the light-irradiation time is extremely short, and examination of the reactive free radicals is rapidly carried out before they have a chance to disappear, the process is known as *flash photolysis*. An alternative method is to carry out the experiment under conditions where the free radicals have a long life-time. In this case, the radicals are known *frozen free radicals*, and one method of preparation is in solution in a rigid unreactive medium at low temperature; under these conditions the free radicals cannot diffuse together and react. A widely used medium is a mixture of ether, ethanol, and *isopentane* cooled in liquid nitrogen.

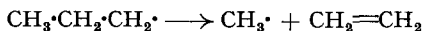
Other methods for preparing free radicals (in the gaseous phase or in solution) are by the action of a metal on a halide (see, *e.g.*, p. 703), or the catalytic effect of certain compounds, notably organic peroxides (see, *e.g.*, p. 68). Free radicals may also be *formed* in solution during electrolysis (p. 52); their formation has been used to explain the course of electrolysis in many cases.

The reactions of free radicals may be classified into three groups:

(i) *Inter-radical reactions* in which the radicals combine or undergo disproportionation, *e.g.*,

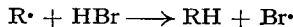


(ii) *Radical decomposition*, *e.g.*,



The tendency for a free radical to decompose into a smaller radical increases with increase in chain-length. The free methyl radical is stable up to 1000°. The free ethyl radical is not so stable, and radicals higher than ethyl readily decompose into methyl or ethyl radicals and an olefin.

(iii) *Radical-molecule reactions*. Examples of this type are: (a) displacement reactions, *e.g.*,



(b) Radical induced polymerisations; these are chain reactions and involve addition to a multiple bond (see p. 78).

The configuration of alkyl free-radicals is not certain. Herzberg *et al.* (1956) have examined the spectra of  $\text{CH}_3\cdot$  and  $\text{CD}_3\cdot$ , and have concluded that in the ground state the radical deviates slightly from a planar configuration, whereas it is planar in all observed excited states.

## QUESTIONS

1. Write an account of the preparation of Grignard reagents and discuss their structure.

2. Give examples of the use of a Grignard reagent in preparing:—(a) a saturated hydrocarbon, (b) an unsaturated hydrocarbon, (c) a primary alcohol, (d) a secondary alcohol, (e) a tertiary alcohol, (f) an ether, (g) an aldehyde, (h) a ketone, (i) a carboxylic acid, (j) an ester, (k) a cyanide, (l) a primary amine, (m) an organo-metallic compound.

3. Show, by means of equations, how you would convert *n*-BuOH into:—(a) *n*-AmOH, (b) hexan-2-ol, (c) heptan-1-ol, (d) di-*n*-Bu carbinol, (e) 3-methylheptan-3-ol.



4. Suggest a synthesis for each of the following:—(a)  $\text{Me}_2\text{CBr}\cdot\text{CH}_2\text{Br}$ , (b)  $\text{Et}_2\text{CCl}\cdot\text{Me}$ , (c)  $\text{Me}_2\cdot\text{CH}\cdot\text{CH}_2\cdot\text{CH}_3$ , (d)  $\text{CH}_3\cdot\text{CH}_2\cdot\text{CHBr}\cdot\text{CH}_2\cdot\text{CH}_3$ , (e)  $\text{Me}_2\text{CH}\cdot\text{CHOH}\cdot\text{CH}_2\cdot\text{Me}$ , (f)  $\text{MeEtisoPrCOH}$ , (g)  $(\text{Me}_2\text{CH})_3\text{COH}$ .
5. Starting with  $\text{AcOH}$ ,  $\text{MeOH}$  and  $\text{EtOH}$  and any inorganic material you think necessary, show how you would synthesise:—(a)  $\text{Me}_2\text{CH}\cdot\text{C}(\text{OH})\text{Me}_2$ , (b)  $\text{EtCHMe}\cdot\text{CHBr}\cdot\text{Me}$ , (c)  $\text{Me}_3\text{C}\cdot\text{CO}_2\text{H}$ , (d)  $\text{Et}_3\text{C}(\text{OH})\cdot\text{CH}_2\text{OH}$ , (e)  $\text{CH}_3\cdot\text{CHOH}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CO}_2\text{Et}$ , (f)  $\text{CH}_2\text{Cl}\cdot\text{CH}_2\cdot\text{CO}\cdot\text{CH}_3$ .
6. Describe the preparation and properties of:—(a)  $\text{EtNa}$ , (b)  $(\text{C}_6\text{H}_5)_3\text{CNa}$ , (c)  $\text{EtLi}$ , (d)  $\text{Me}_2\text{Zn}$ , (e)  $\text{Et}_2\text{Cd}$ , (f)  $\text{Me}_2\text{Hg}$ , (g)  $\text{Et}_4\text{Pb}$ .
7. Define and give examples of:—(a) The Zerewitinoff active hydrogen determination, (b) the steric effect, (c) the Reformatsky reaction, (d) mercuration.
8. Write an account of the preparation and properties of the free alkyl radicals.

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