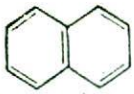
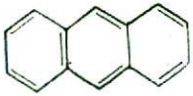
Chapter **46**

Fused Polynuclear Aromatic Hydrocarbons

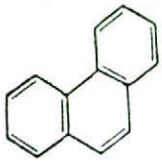
Fused or condensed aromatic hydrocarbons contain more than one ring and have two carbons shared by two (or three) aromatic rings. The most important members of this class are naphthalene, anthracene and phenanthrene.



NAPHTHALENE



ANTHRACENE



PHENANTHRENE

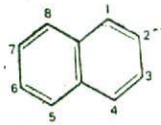
Naphthalene has two carbon atoms shared by two rings (indicated by thick dots). Anthracene and phenanthrene have two pairs of carbon atoms shared by two rings, each pair being shared by a separate pair of rings.

NAPHTHALENE

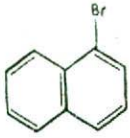
Naphthalene is the largest single constituent (6 to 10 per cent) of coal-tar. It is obtained industrially by chilling the middle oil fraction (bp 170-230°C), when crude naphthalene crystallises out. It is purified by washing it successively with dilute sulphuric acid (to remove basic impurities), sodium hydroxide (to remove acidic impurities), and water. Finally the solid is sublimed or steam-distilled to give pure naphthalene.

NOMENCLATURE OF NAPHTHALENE DERIVATIVES

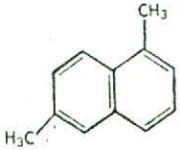
In naming derivatives of naphthalene, the numbering system shown below is used. The numbers selected to denote the position of a substituent on the naphthalene rings should be as small as possible.



NAPHTHALENE



1-BROMONAPHTHALENE



1,6-DIMETHYLNAPHTHALENE

An alternative nomenclature system is occasionally used when there is only one substituent on the naphthalene skeleton. This system uses the Greek letters α (alpha) and β (beta) to designate the two possible orientations of the single substituent.



NAPHTHALENE α-NITRONAPHTHALENE β-BROMONAPHTHALENE

STRUCTURE OF NAPHTHALENE

All ten carbon atoms in naphthalene are sp^2 hybridized. The sp^2 hybrid orbitals overlap with each other and with s orbitals of the eight hydrogen atoms forming C—C and C—H σ bonds (Fig. 46·1). Since the σ bonds result from the overlap of trigonal sp^2 orbitals, all carbon and hydrogen atoms in naphthalene lie in one plane. This has been confirmed by X-ray diffraction studies.

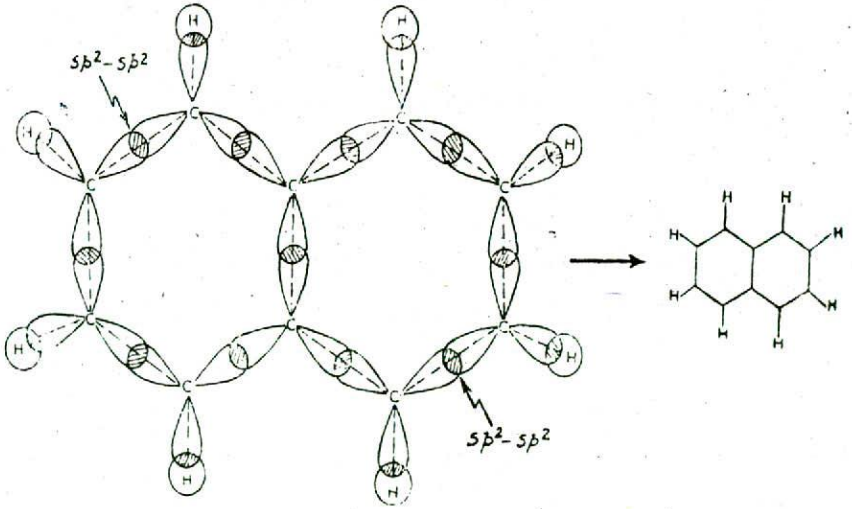


Fig. 46·1, Formation of the σ bonds in naphthalene.

Also each carbon atom in naphthalene possesses an unhybridized p orbital containing one electron. These p orbitals are perpendicular to the plane containing the σ bonds. The lateral overlap of the p orbitals produces a π molecular orbital containing ten electrons (Fig. 46·2). One half of this π molecular orbital lies above and the other half lies below the plane of the σ bonds. Naphthalene shows aromatic properties because the resulting π molecular orbital satisfies the Huckel's rule ($n=2$ in $4n+2$).

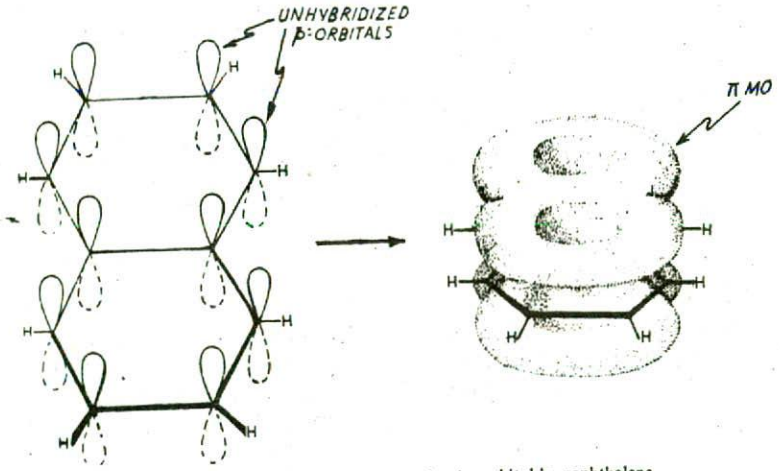
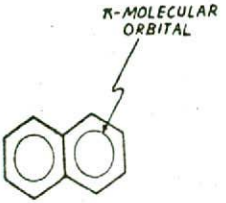
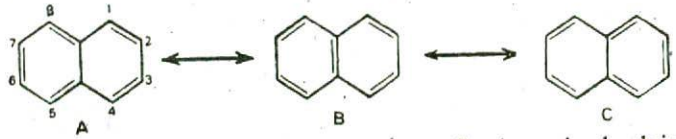


Fig. 46·2 Formation of the π molecular orbital in naphthalene.

A common shorthand representation of naphthalene is simply two fused hexagons with a circle inside each hexagon. The circles represent the π molecular orbital.



According to the resonance theory, naphthalene is considered to be a hybrid of the following *three* canonical forms.



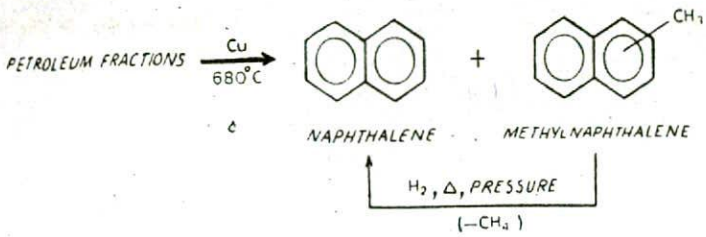
X-Ray diffraction studies show that, unlike benzene, all carbon-carbon bonds in naphthalene are not of the same length. In particular, the C1–C2 bond is considerably shorter (1·36 Å) than the C2–C3 bond (1 40 Å). This difference can be understood if we examine the three resonance forms given above. Notice that the C1–C2 bond is double in two structures (A and B) and single in only one (*C*); whereas the C2–C3 bond is single in two structures (A and B) and double in only one (*C*). We would, therefore, expect the C1–C2 bond to have more double-bond character (shorter bond length), and the C2–C3 bond to have more single-bond character (longer bond length).

The resonance energy of naphthalene is about 61 Kcal/mole. This value is less than twice the amount of a single benzene ring (36 Kcal/mole). As a result, naphthalene is somewhat less aromatic (more reactive) than benzene.

SYNTHESIS OF NAPHTHALENE

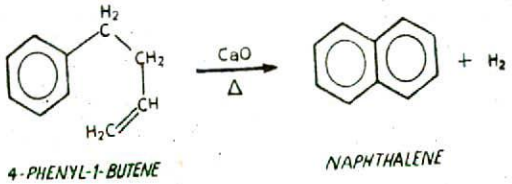
Naphthalene may be obtained :

(1) **From Petroleum.** When petroleum fractions are passed over copper catalyst at 590° C, naphthalene and methylnaphthalenes are formed. Methylnaphthalenes are separated and converted into naphthalene by heating with hydrogen under pressure (*dealkylation*).

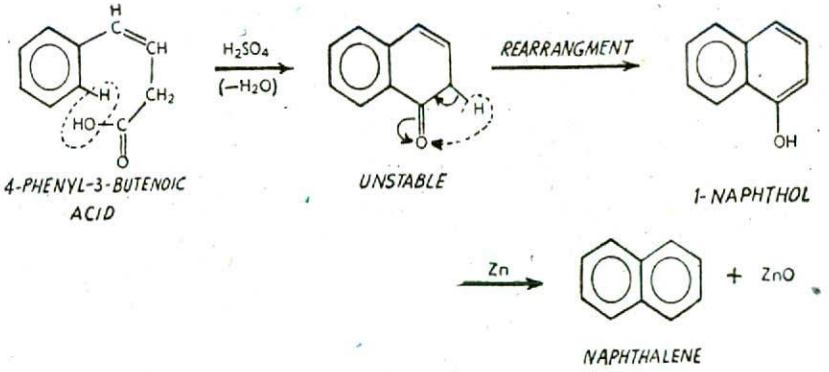


Prior to 1960 all naphthalene came from coal-tar, but now almost half of it is produced from petroleum by the above method.

(2) **From 4-Phenyl-1-butene.** When 4-phenyl-1-butene is passed over red hot calcium oxide, naphthalene is obtained.

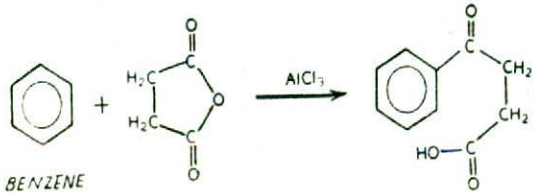


(3) **From 4-Phenyl-3-butenoic Acid.** When 4-phenyl-3-butenoic acid is heated with concentrated sulphuric acid, 1-naphthol is formed. This on distillation with zinc dust gives naphthalene.

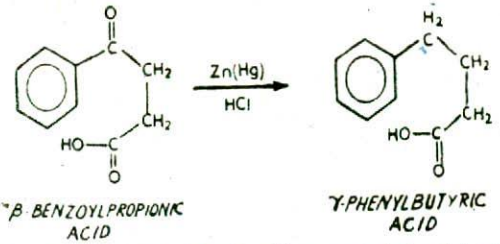


(4) **By Haworth Synthesis.** This involves the following five steps :

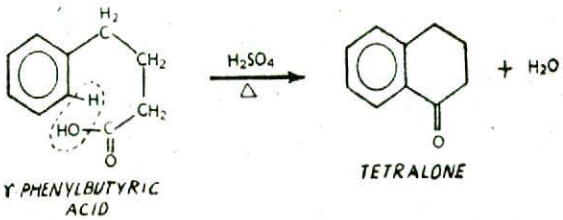
Step 1. Benzene and succinic anhydride are heated in the presence of aluminium chloride to form β-benzoylpropionic acid. (*Friedel-Crafts Acylation*)



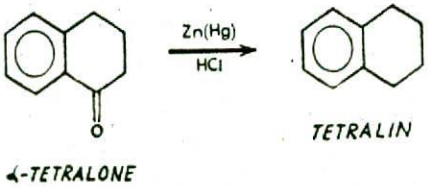
Step 2. β-Benzoylpropionic acid is treated with amalgamated zinc in the presence of hydrochloric acid to give γ-phenylbutyric acid. (*Clemmensen Reduction*)



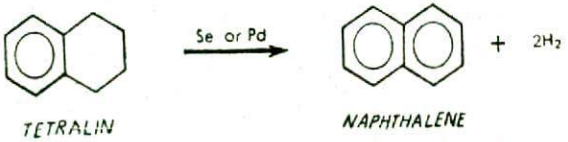
Step 3. γ-Phenylbutyric acid is heated with concentrated sulphuric acid or polyphosphoric acid to form α-tetralone. (*Ring-closure Reaction*)



Step 4. α-Tetralone is heated with amalgamated zinc and hydrochloric acid to give tetralin. (*Clemmensen Reduction*)



Step 5. Tetralin is heated with selenium or palladium to yield naphthalene (*Aromatization Reaction*).



Substituted naphthalenes can be obtained by using toluene, bromobenzene, or anisole instead of benzene in *Step* (*1*).

PROPERTIES OF NAPHTHALENE

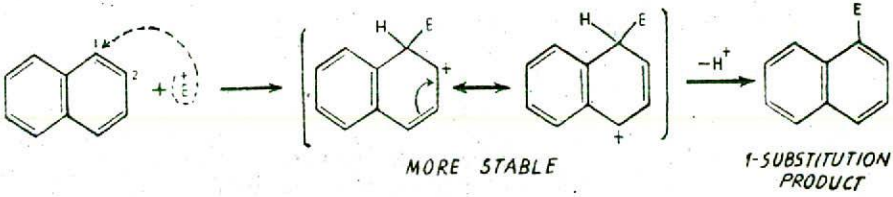
(*Physical*). Naphthalene is a colourless crystalline solid. It melts at 82°C and boils at 218°C. Naphthalene is insoluble in water, but dissolves in ether, benzene, and hot ethanol. It sublimes readily when warmed and is volatile with steam. Naphthalene has a characteristic 'moth ball' odour.

(*Chemical*). Some of the important chemical reactions of naphthalene are described below.

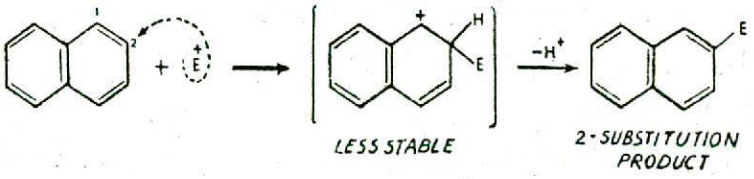
A. ELECTROPHILIC SUBSTITUTION REACTIONS

Naphthalene, like benzene, undergoes electrophilic substitution reactions. Substitution occurs primarily at C-1 (α-position). This can be understood if we examine the intermediate carbonium ion. Two resonance froms can be written for the intermediate carbonium ion obtained from the attack at C-1 (without involving the other ring), whereas only one such form is possible for substitution at C-2. E^+ in the following equations represents an electrophile.

Attack at C-1

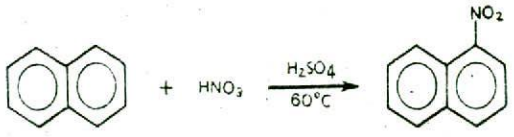


Attack at C-2



Consequently the former intermediate is more stable and the product with a substituent at C-1 predominates. Substitution at C-2 (β-position) occurs only when the reactions are carried at higher temperatures or when bulkier solvents are used.

(1) **Nitration.** Naphthalene undergoes nitration with concentrated nitric acid in the presence of sulphuric acid at 60° C to produce 1-nitronaphthalene.

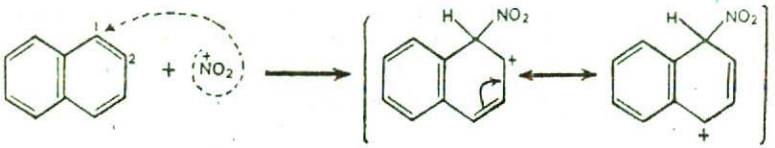


MECHANISM. The mechanism of this reaction involves the following three steps :

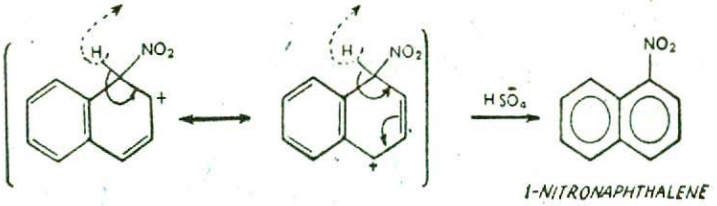
Step 1. The electrophile ($\overset{+}{N}O_2$) is generated.

$$2H_2SO_4 + HONO_2 \longrightarrow \overset{+}{N}O_2 + 2\overset{-}{H}SO_4 + \overset{+}{H_3}O$$

Step 2. The electrophile attacks naphthalene at C-1 to form the resonance-stabilised carbonium ion (only those resonance forms are shown below which do not involve the other ring).

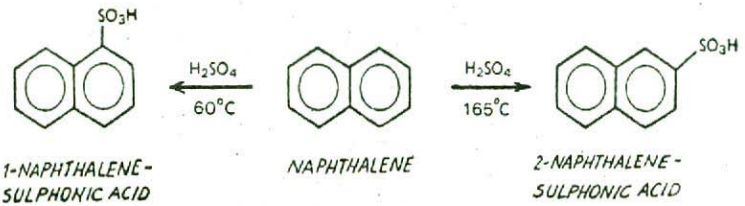


Step 3. A hydrogen ion is eliminated to yield 1-nitronaphthalene.

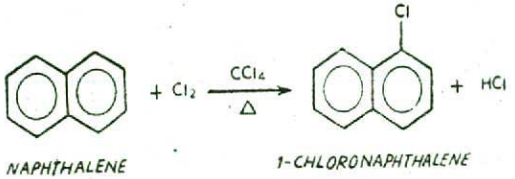


Similar steps may be written for other electrophilic substitution reactions of naphthalene.

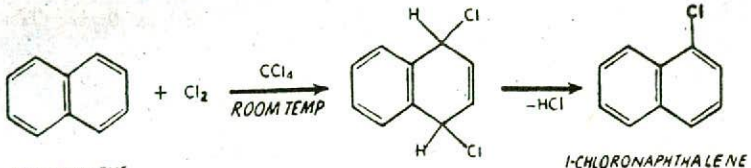
(2) **Sulphonation.** Naphthalene undergoes sulphonation with concentrated sulphuric acid at 60°C to form 1-naphthalenesulphonic acid If the reaction is carried at 165°C, 2-naphthalene-sulphonic acid is obtained.



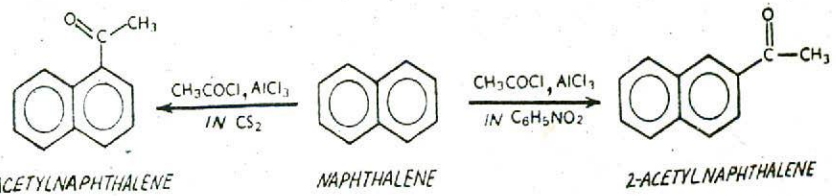
(3) **Halogenation.** Naphthalene undergoes chlorination or bromination in boiling carbon tetrachloride to give 1-chloronaphthalene. Unlike benzene, no Lewis acid catalyst is required.



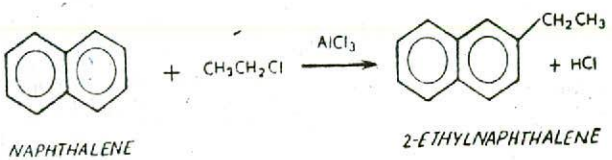
When the above reaction is carried at room temperature, naphthalene dichloride (1, 4-addition product) is obtained. On heating, naphthalene dichloride loses HCl to yield 1-chloronaphthalene.



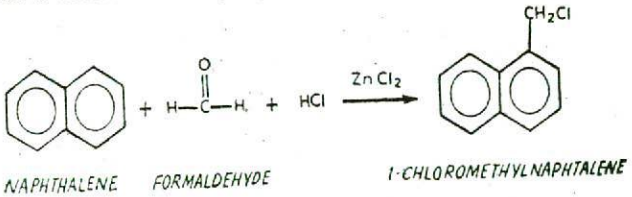
(4) **Friedel-Crafts Acylation.** Naphthalene undergoes acylation with acetyl chloride and aluminium chloride in carbon disulphide to give 1-acetylnaphthalene. When nitrobenzene is used as a solvent, 2 acetylnaphthalene is obtained.



(5) **Friedel-Crafts Alkylation.** Naphthalene undergoes alkylation with alkyl halides (methyl halides do not react) in the presence of aluminium chloride to give 2-alkylnaphthalenes.



(6) **Chloromethylation.** Naphthalene reacts with formaldehyde and HCl in the presence of zinc chloride to form 1-chloromethylnaphthalene.

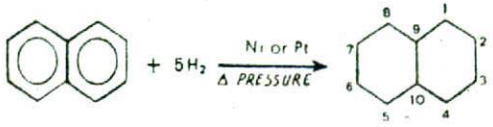


B. OTHER REACTIONS

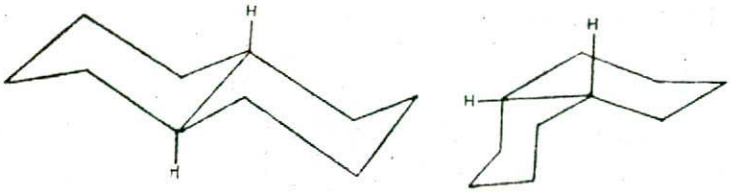
(7) **Reduction.** Naphthalene undergoes reduction more readily than benzene. With sodium and ethyl alcohol (bp 78°C) it gives 1,4-dialin or 1,4-dihydronaphthalene With sodium and isopentanol (bp 130°C) it gives tetralin or 1,2,3,4-tetrahydronaphthalene.



Catalytic reduction completely hydrogenates both rings and produces decalin or decahydronaphthalene.



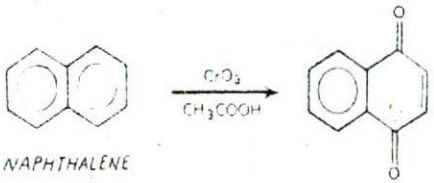
Decalin consists of two cyclohexane molecules (in chair forms) fused together along a common side. It exists in *cis* and *trans* isomeric forms which differ in the space relationship of hydrogen atoms at C-9 and C-10 positions. When nickel is used as a catalyst, the main product is *trans*-decalin. When platinum is used as a catalyst, the main product is *cis*-decalin. Decalin sold commercially is the mixture of both these forms, and is used as a solvent in the varnish and lacquer trade.



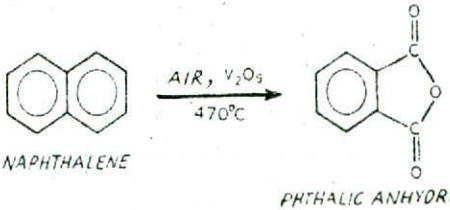
trans-decalin (bp 185°C)

cis-decalin (bp 195°C)

(8) **Oxidation.** Naphthalene is much more easily oxidised than benzene. With chromium trioxide in acetic acid at room temperature, it gives 1,4-naphthaquinone.



Oxidation of naphthalene with oxygen and vanadium pentoxide at 475°C yields phthalic anhydride. This method is used industrially.



Phthalic acid is an important industrial material. It is used in the manufacture of resins paints, dyes and plastics.

Uses. Naphthalene as 'moth balls' has been used to protect woolen goods from moths for many years. Recently, *p*-dichlorobenzene has replaced naphthalene in the manufacture of moth balls, as it has a less abnoxious odour. It is used for increasing the illuminating power of coal gas. Naphthalene is used in the manufacture of phthalic anhydride, carbaryl for insecticides, 2-naphthol, dyes, and several medicinal products.

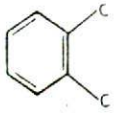
Classical Derivation of the Structure of Naphthalene

The structure of naphthalene was arrived at from a consideration of facts and conclusions such as the following.

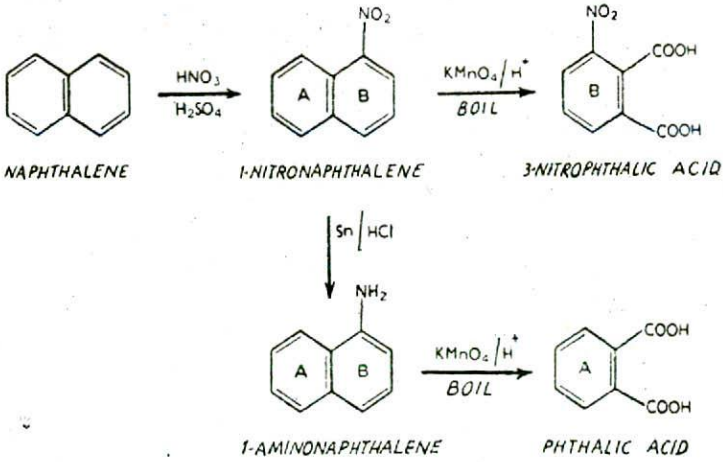
(1) Elemental analysis and molecular weight determinations show that the molecular formula of naphthalene is $C_{10}H_8$.

(2) Dipole moment of naphthalene is zero. This indicates that the naphthalene molecule is symmetrical.

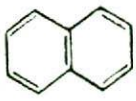
(3) Oxidation of naphthalene with oxygen and vanadium pentoxide at 470°C yields phthalic anhydride. This indicates the presence of a benzene ring with two *ortho* side-chains in the molecule.



(4) Nitration of naphthalene produces a nitronaphthalene which when oxidised gives 3-nitrophthalic acid. Reduction of the nitronaphthalene gives an aminonaphthalene which when oxidised yields only phthalic acid.



The electrophilic nitro group stabilises the benzene ring to which it is attached (ring B), and the other benzene ring is preferentially oxidised. On the other hand, the nucleophilic amino group makes the benzene ring to which it is attached (ring B) more susceptible to oxidation. These results clearly indicate that naphthalene consists of two fused benzene rings.



NAPHTHALENE

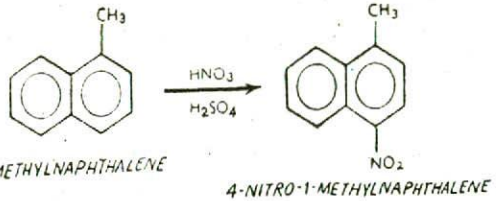
The above structure of naphthalene has been confirmed by several synthesis (p 1144).

Naphthalene is a hybrid of three resonance structures. These structures along with molecular orbital picture are given on page 1143.

Substitution in Naphthalene Derivatives

The introduction of a second substituent into the naphthalene ring follows essentially the same rules as for benzene. The nature of the group already present determines the position of the entering group.

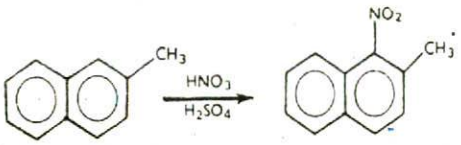
Rule 1. If the first group is an *ortho-para* director in the benzene sense (*e.g.*, —OH, $-NH_2$, $-CH_3$) and is located at C-1, it will direct the incoming group to the C-2 or C-4 positions.



1-METHYLNAPHTHALENE

4-NITRO-1-METHYLNAPHTHALENE

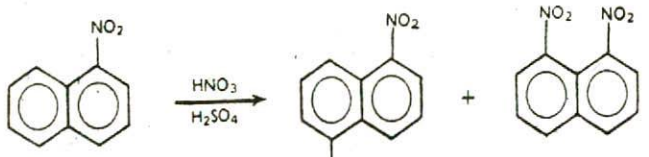
Rule 2. If the first group is *ortho para* director and is located at C-2, it will direct the incoming group to the C-1 position.



2-METHYL NAPHTHALENE

1-NITRO-2-METHYLNAPHTHALENE

Rule 3. If the first group is a *meta* director (*e.g.*, $-NO_2$, $-SO_3H$, —COOH) and is located at C-1 or C-2, it will direct the incoming group to the C-5 or C-8 positions in the other ring.



1-NITRONAPHTHALENE

1,5-DINITRO-NAPHTHALENE

1,8-DINITRO NAPHTHALENE

The above rules do not always hold in sulphonation. In this case the reaction is reversible and at high temperatures tends to take place at a β-position in either ring.

IMPORTANT DERIVATIVES OF NAPHTHALENE

NAPHTHOLS

The hydroxy derivatives of naphthalene are known as naphthols.

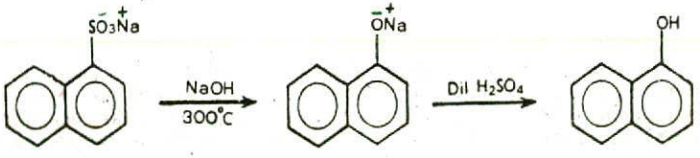


1-NAPHTHOL (α-NAPHTHOL) 2-NAPHTHOL (β-NAPHTHOL)

1-Naphthol (α-*Naphthol*)

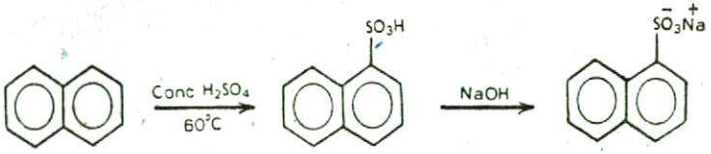
Preparation. 1-Naphthol may be obtained:

(1) *From Sodium 1-Naphthalenesulphonate.* When sodium 1-naphthalenesulphonate is fused with sodium hydroxide at 300° C, it gives sodium 1-naphthoxide. Treatment of this with dilute sulphuric acid yields 1-naphthol.



SODIUM 1-NAPHTHALENE SULPHONATE — SODIUM 1-NAPHTHOXIDE — 1-NAPHTHOL

Sodium 1-naphthalenesulphonate used in the above reaction may be obtained from naphthalene as shown below.



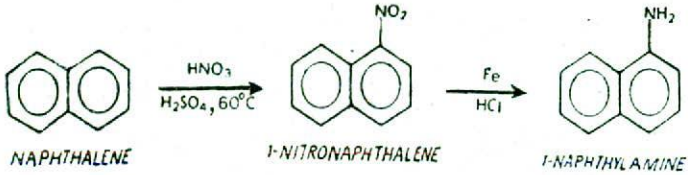
NAPHTHALENE — 1-NAPHTHALENE SULPHONIC ACID — SODIUM 1-NAPHTHALENE SULPHONATE

(2) *From 1-Naphthylamine.* When 1-naphthylamine is heated with dilute sulphuric acid at 300° C under pressure, 1-naphthol is formed.



1-NAPHTHYLAMINE — 1-NAPHTHOL

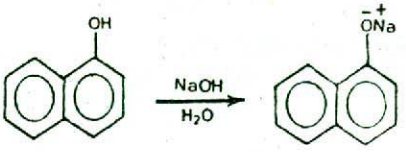
1-Naphthylamine used in the above reaction may be prepared from naphthalene as shown below.



Properties. (*Physical*). 1-Naphthol is a colourless solid, mp 94° C. It is only slightly soluble in water, but dissolves readily in ethanol and ether.

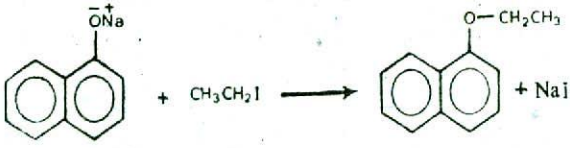
(*Chemical*). 1-Naphthol resembles phenol in its chemical properties.

(1) **Acidic Character.** 1-Naphthol is a weak acid. It dissolves in sodium hydroxide or sodium carbonate solution owing to the formation of water-soluble sodium 1-naphthoxide.

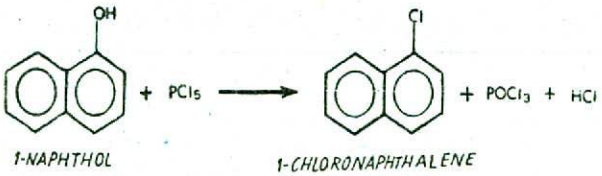


The reason for the weak acidic character of 1-naphthol is that it ionises in water to yield a resonance stabilized naphthoxide ion. However, it is a stronger acid than phenol. The increased acidity is due to the greater stability of the naphthoxide ion as compared to the phenoxide ion. In the naphthoxide ion the negative charge is delocalized over two aromatic rings, whereas in the phenoxide ion it is delocalized over one ring.

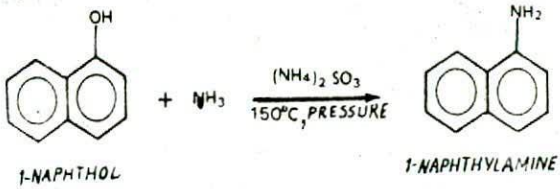
When sodium 1-naphthoxide is heated with alkyl halides, the corresponding ethers are formed. (*Williamson's synthesis*)



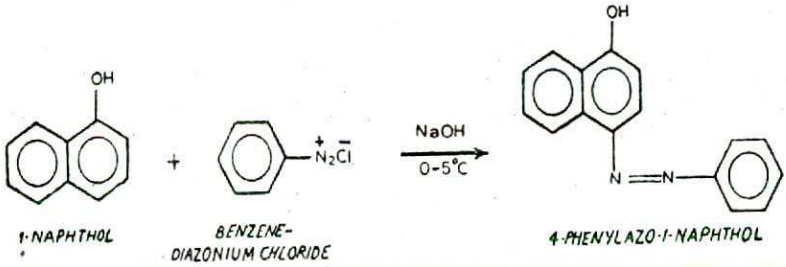
(2) **Reaction with Phosphorous Pentachloride.** 1-Naphthol reacts with PCl_5 to form 1-chloronaphthalene.



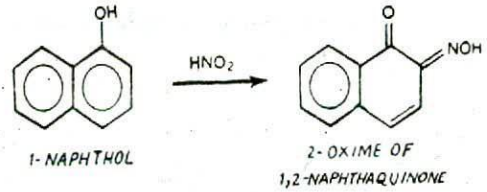
(3) **Bucherer Reaction.** The reversible conversion of a naphthol into the corresponding naphthylamine is called the *Bucherer Reaction*. 1-Naphthol reacts with ammonia and ammonium sulphite at 150° C under pressure to yield 1-naphthylamine.



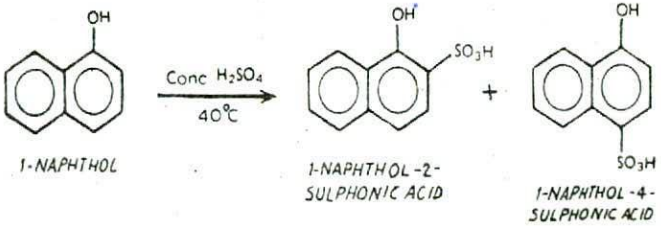
(4) **Azo-coupling.** 1-Naphthol reacts with benzenediazonium chloride in a weakly alkaline solution at 0-5°C to give 4-phenylazo-1-naphthol.



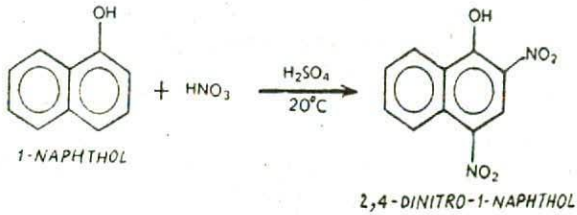
(5) **Reaction with Nitrous Acid.** 1-Naphthol reacts with nitrous acid to give 2-oxime of 1, 2-naphthaquinone.



(6) **Sulphonation.** 1-Naphthol reacts with concentrated sulphuric acid at 40°C to yield a mixture of 1-naphthol-2-sulphonic acid (*Schaeffer's acid*) and 1-naphthol-4-sulphonic acid (*Nevile-Winther's acid*). Both these sulphonic acids are used in the manufacture of azo dyes.

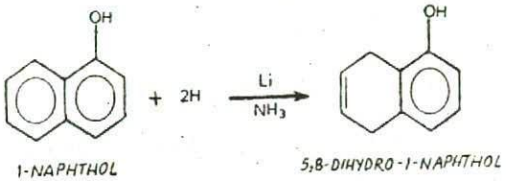


(7) **Nitration.** 1-Naphthol reacts with concentrated nitric acid and sulphuric acid at 20° C to give 2, 4-dinitronaphthol.

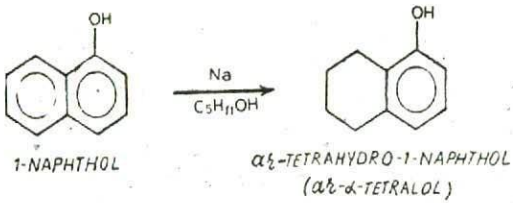


The sodium salt of 2, 4-dinitro-1-naphthol is known as *Martius Yellow*. It is used as a dye for wool and silk.

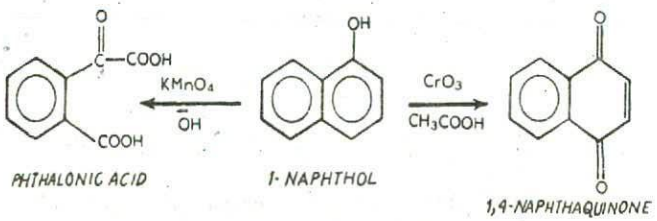
(8) **Reduction**. 1-Naphthol undergoes reduction with lithium metal in liquid ammonia to yield 5, 8-dihydro-1-naphthol. (*Birch Reduction*)



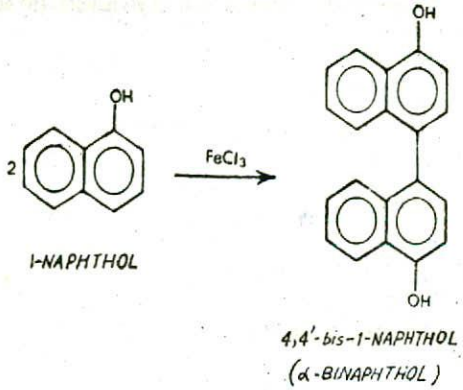
Reduction of 1-naphthol with sodium and isopentanol gives *ar*-tetrahydro-1-naphthol or *ar*-α-tetralol. In these names the prefix *ar*- stands for *aromatic* and indicates that the four hydrogen aroms are not in the ring containing the —OH group.



(9) **Oxidation**. 1-Naphthol reduces ammonical silver nitrate. It is oxidised by chromium trioxide in acetic acid to 1, 4-naphthaquinone, and by alkaline potassium permanganate to phthalonic acid.



Oxidation o 1-naphthol with ferric chloride yields a blue-violet precipitate of 4, 4′-*bis*-1-naphthol or α-binaphthol.



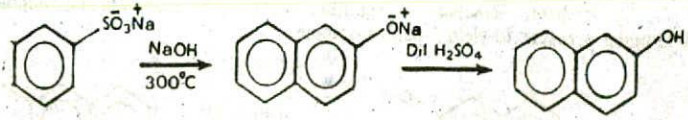
1-NAPHTHOL

4,4'-bis-1-NAPHTHOL
(α-BINAPHTHOL)

Uses. 1-Naphthol is used in the manufacture of insecticides and dyes.

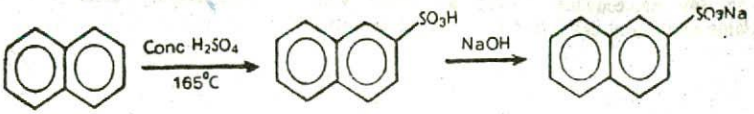
2-Naphthol (*β-Naphthol*).

Preparation. 2-Naphthol is obtained by fusing sodium 2-naphthalenesulphonate with sodium hydroxide at 300°C. Sodium 2-naphthoxide is formed which on treatment with dilute sulphuric acid yields 2-naphthol.



SODIUM 2-NAPHTHALENESULPHONATE — SODIUM 2-NAPHTHOXIDE — 2-NAPHTHOL

Sodium 2-naphthalenesulphonate used in the above reaction may be prepared from naphthalene as shown below.

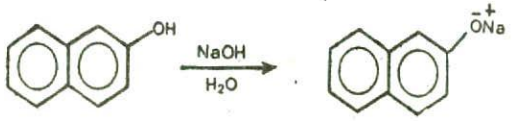


NAPHTHALENE — 2-NAPHTHALENE SULPHONIC ACID — SODIUM 2-NAPHTHALENE SULPHONATE

Properties. (*Physical*). 2-Naphthol is a colourless solid, mp 123°C. It is only slightly soluble in water, but dissolves in ether and ethanol.

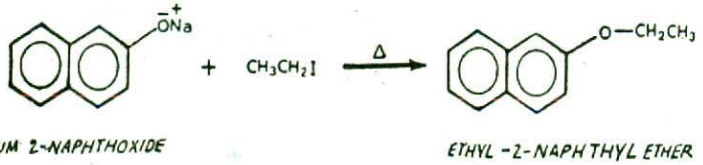
(*Chemical*). 2-Naphthol resembles 1-naphthol in its chemical properties.

(1) **Acidic Character.** Like 1-naphthol, it is also a stronger acid than phenol. It dissolves in sodium hydroxide or sodium carbonate solution to give water-soluble sodium 2-naphthoxide.



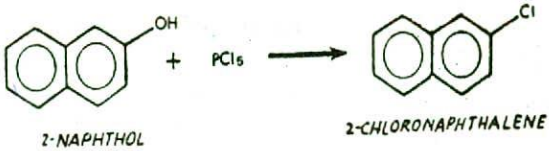
2-NAPHTHOL — SODIUM 2-NAPHTHOXIDE

When sodium 2-naphthoxide is treated with alkyl halides, the corresponding ethers are obtained. (*Williamson's Synthesis*)

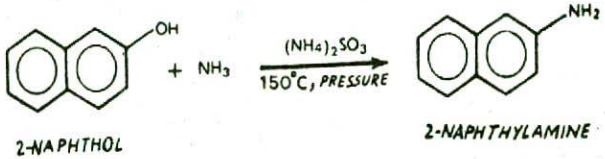


Ethyl 2-naphthyl ether is known as *nerolin*. It is used as a perfume in artificial neroli oil and *eau de Cologne*.

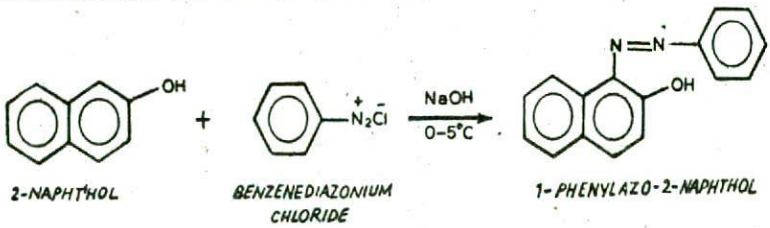
(2) **Reaction with Phosphorous Pentachloride.** 2-Naphthol reacts with PCl_5 to give 2-chloronaphthalene.



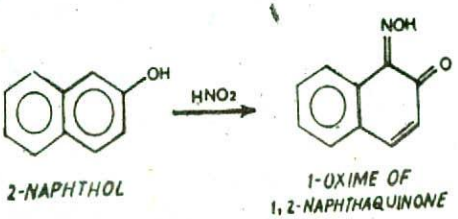
(3) **Bucherer Reaction.** 2-Naphthol reacts with ammonia and ammonium sulphite at 150°C under pressure to yield 2-naphthylamine.



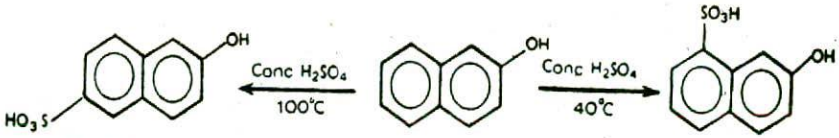
(4) **Azo-coupling.** 2-Naphthol reacts with benzenediazonium chloride in a weakly alklaine solution at 0-5°C to form 1-phenylazo-2-naphthol.



(5) **Reaction with Nitrous acid.** 2-Naphthol reacts with nitrous acid to give 1-oxime of 1, 2-naphthaquinone.

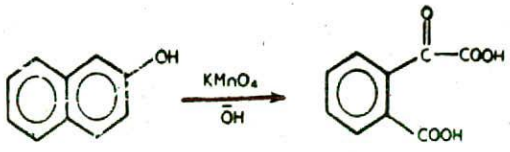


(6) **Sulphonation.** 2-Naphthol reacts with concentrated sulphuric acid at 40°C to yield 2-naphthol-8-sulphonic acid (*Crocein acid*). When this reaction is carried at 100° C, crocein acid undergoes rearrangement to give 2-naphthol-6-sulphonic acid (*Schaeffer's β-acid*). Both these sulphonic acids are used in the manufacture of azo dyes.



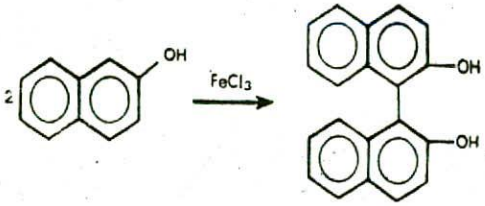
2-NAPHTHOL-6-SULPHONIC ACID — 2-NAPHTHOL — 2-NAPHTHOL-8-SULPHONIC ACID

(7) **Oxidation.** 2-Naphthol reduces ammonical silver nitrate. It is oxidised by alkaline potassium permanganate to phthalonic acid.



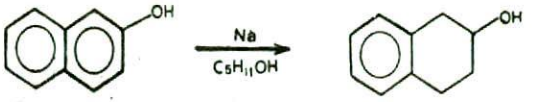
2-NAPHTHOL — PHTHALONIC ACID

Oxidation of 2-naphthol with ferric chloride yields a green precipitate of 1,1'-*bis*-2-naphthol or β-binphathol.



1,1'-BIS-2-NAPHTHOL (β-BINAPHTHOL)

(8) **Reduction.** 2-Naphthol undergoes reduction with sodium and isopentanol to give *ac*-tetrahydro-2-naphthol or *ac*-β-tetralol. In these names the prefix *ac*-stands for *alicyclic* and indicates that the four hydrogen atoms are in the ring containing the —OH group.

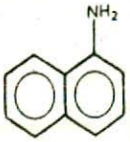


2-NAPHTHOL — ac-TETRAHYDRO-2-NAPHTHOL (ac-β-TETRALOL)

Uses. 2-Naphthol is used : (*1*) for making dyes ; (*2*) as an antioxidant in the manufacture of synthetic rubber ; (*3*) as an antiseptic in the treatment of skin diseases ; and (*4*) for preparing its methyl and ethyl ethers (*nerolins*), which are extensively used in perfumery.

NAPHTHYLAMINES

The amino derivatives of naphthalene are known as the naphthylamines.



1-NAPHTHYLAMINE
(α-NAPHTHYLAMINE)



2-NAPHTHYLAMINE
(β-NAPHTHYLAMINE)

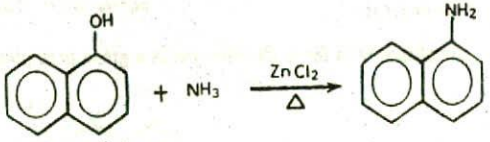
1-Naphthylamine (α-*Naphthylamine*)

Preparation. 1-Naphthylamine may be obtained :

(*1*) By the reduction of 1-nitronaphthalene with iron and hydrochloric acid. (*Commercial method*)

(*2*) By heating 1-naphthol with ammonia and ammonium sulphite at 150°C under pressure. (*Bucherer reaction*)

(*3*) By heating 1-naphthol with ammonia and zinc chloride at 260° C.

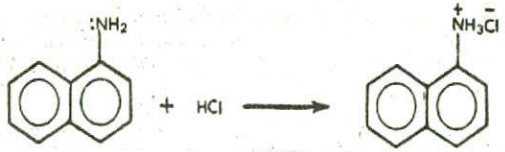


1-NAPHTHOL 1-NAPHTHYLAMINE

Properties. (*Physical*). 1-Naphthylamine is a colourless solid, mp 50° C. It turns brown on exposure to air. 1-Naphthylamine is only slightly soluble in water, but dissolves readily in ethanol and ether. It has an unpleasant odour.

(*Chemical*). 1-Naphthylamine resembles aniline in its chemical properties.

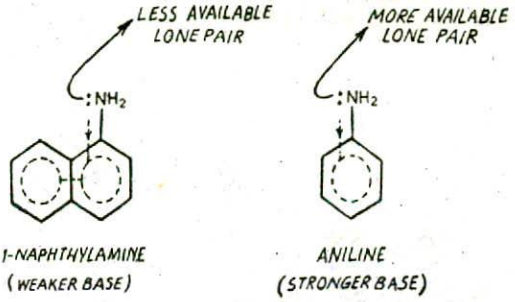
1. **Basic Character.** 1-Naphthylamine is a weak base ($pK_a = 3{\cdot}9$). It dissloves in acids to form the corresponding salts.



1-NAPHTHYLAMINE 1-NAPHTHYLAMMONIUM CHLORIDE

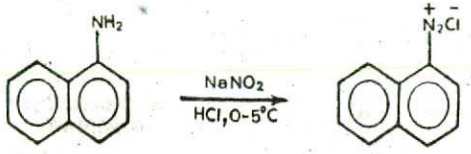
The reason for the weak basic character of 1-naphthylamine is that the lone pair of electrons on nitrogen is involved in the formation of the delocalized π molecular orbital and is not readily available for the formation of a new covalent bond with proton.

1-Naphthylamine is a slightly weaker base than aniline ($pK_a = 4{\cdot}6$). This is due to the more extensive delocalization in the case of 1-naphthylamine.

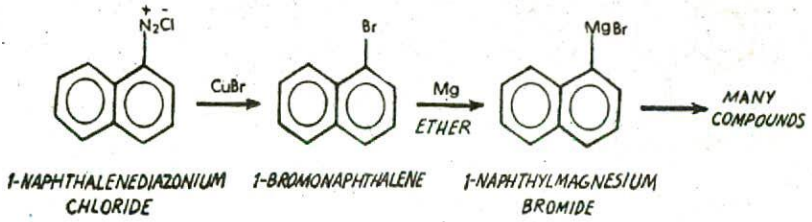


In 1-naphthylamine the lone pair of electrons on nitrogen is delocalized over two rings, whereas in aniline it is delocalized over one ring. As a result, the lone pair in 1-naphthylamine is even less available for the formation of a new bond with proton.

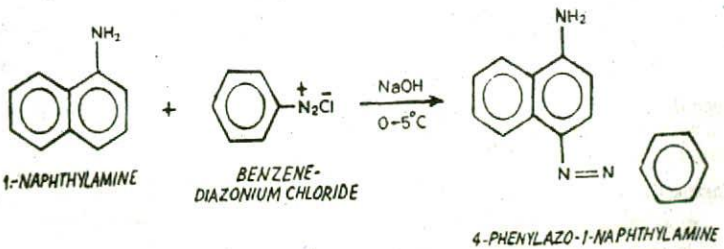
(2) **Diazotization.** 1-Naphthylamine reacts with sodium nitrite in excess hydrochloric acid at 0-5°C to yield 1-naphthalenediazonium chloride.



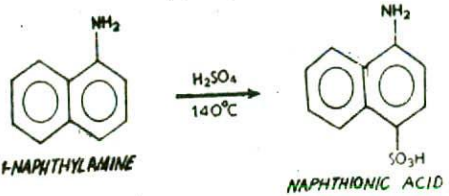
Like other diazonium salts, 1-naphthalenediazonium chloride couples with phenols and aromatic amines. It may also be converted into a large number of 1-substituted naphthalene derivatives by the reactions we have already studied. For example,



(3) **Azo-coupling.** 1-Naphthylamine reacts with benzenediazonium chloride in a weakly alkaline solution at 0—5°C to give 4-phen. azo-1-naphthylamine.

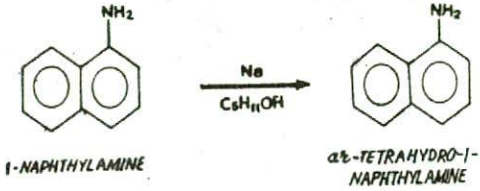


(4) **Sulphonation.** 1-Naphthylamine reacts with concentrated sulphuric acid at 140°C to give 1-naphthylamine-4-sulphonic acid or naphthionic acid.

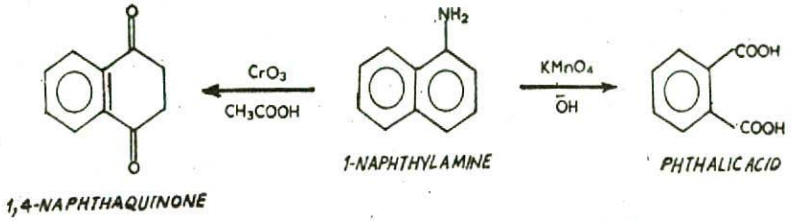


Naphthionic acid is used in the manufacture of *Congo Red.*

(5) **Reduction.** 1-Naphthylamine undergoes reduction with sodium and isopentanol to give *ar*-tetrahydro-1-naphthylamine (5,6,7,8-tetrahydro-1-naphthylamine).



(6) **Oxidation.** 1-Naphthylamine reduces ammoniacal silver nitrate. It is oxidised by chromium trioxide in acetic acid to 1,4-naphthaquinone, and by alkaline potassium permanganate to phthalic acid.



1-Naphthylamine gives a blue precipitate with ferric chloride.

Use. 1-Naphthylamine is used in the manufacture of dyes.

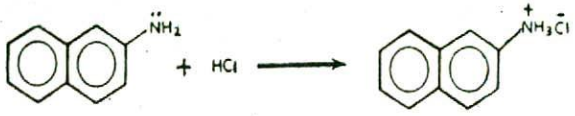
2-Naphthylamine (β-*Naphthylamine*)

Preparation. 2-Naphthylamine is obtained industrially by the Bucherer reaction. In this method 2-naphthol is heated with ammonia and ammonium sulphite at 150° C under pressure.

Properties. (*Physical*). 2-Naphthylamine is a colourless solid, mp 112°C. It is only slightly soluble in water, but dissolves in ether and ethanol. 2-Naphthylamine is not sold in the open market because prolonged exposure to it leads to bladdar tumors.

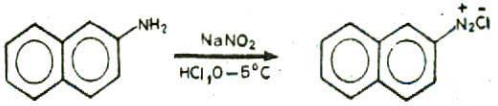
(*Chemical*). 2-Naphthylamine resembles 1-naphthylamine in its chemical properties

(1) **Basic Character.** 2-Naphthylamine ($pK_a = 4{\cdot}1$) is also a weaker base than aniline and dissolves in acids to give the corresponding salts.



2-NAPHTHYLAMINE 2-NAPHTHYLAMMONIUM CHLORIDE

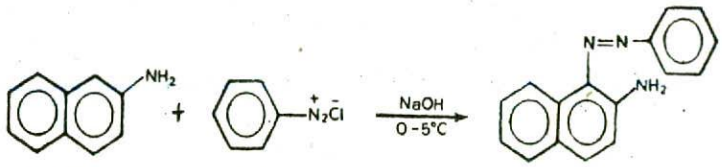
(2) **Diazotization.** 2-Naphthylamine reacts with sodium nitrite in excess hydrochloric acid at 0-5°C to yield 2-naphthalenediazonium chloride.



2-NAPHTHYLAMINE 2-NAPHTHALENEDIAZONIUM CHLORIDE

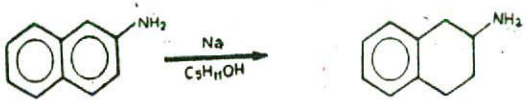
2-Naphthalenediazonium chloride couples with phenols and aromatic amines and can be converted into a large number of 2-substituted naphthalene derivatives.

(3) **Azo-coupling.** 2-Naphthylamine reacts with benzenediazonium chloride in a weakly alkaline solution at 0-5°C to give 1-phenylazo-2-naphthylamine.



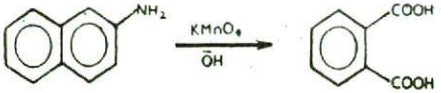
2-NAPHTHYLAMINE BENZENE-DIAZONIUM CHLORIDE 1-PHENYLAZO-2-NAPHTHYLAMINE

(4) **Reduction.** 2-Naphthylamine undergoes reduction with sodium and isopentanol to yield *ac*-tetrahydro-2-naphthylamine (1,2,3,4-tetrahydro-2-naphthylamine).



2-NAPHTHYLAMINE ac-TETRAHYDRO-1-NAPHTHYLAMINE

(5) **Oxidation.** 2-Naphthylamine reduces ammonical silver nitrate. Like 1-napthylamine, it undergoes reduction with alkaline potassium permanganate to give phthalic acid.



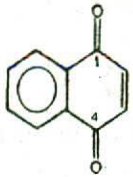
2-NAPHTHYLAMINE PHTHALIC ACID

2-Naphthylamine gives no colouration with ferric chloride.

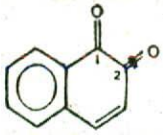
Use. 2-Naphthylamine is used in the manufacture of dyes.

NAPHTHAQUINONES

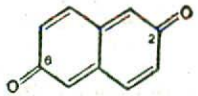
Three naphthaquinones are known :



1,4-NAPHTHAQUINONE
(α-NAPHTHAQUINONE)



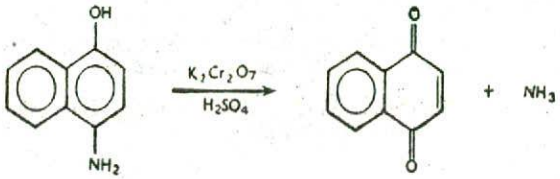
1,2-NAPHTHAQUINONE
(β-NAPHTHAQUINONE)



2,6-NAPHTHAQUINONE
(AMPHI-NAPHTHAQUINONE)

1,4-Naphthaquinone (α-*Naphthaquinone*)

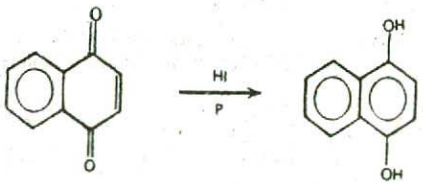
It is obtained by the oxidation of 4-amino-1-naphthol with potassium dichromate and sulphuric acid.



4-AMINO-1-NAPHTHOL 1,4-NAPHTHAQUINONE

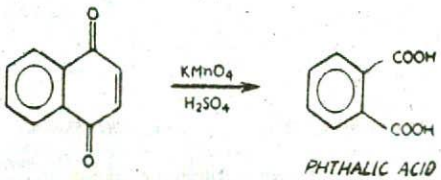
1,4-Naphthaquinone may also be prepared by the oxidation of naphthalene with chromium trioxide in glacial acetic acid.

1,4-Naphthaquinone is a yellow crystalline solid, mp 125°C. It is volatile with steam. It is reduced by hydriodic acid and red phosphorous to 1,4-dihydroxynaphthalene



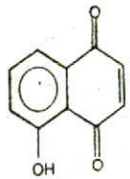
1,4-NAPHTHAQUINONE 1,4-DIHYDROXYNAPHTHALENE

Oxidation of 1,4-naphthaquinone with potassium permanganate and dilute sulphuric acid gives phthalic acid.

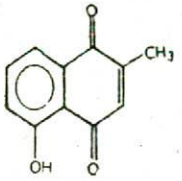


1,4-NAPHTHAQUINONE PHTHALIC ACID

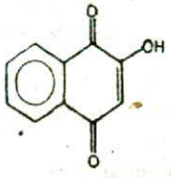
A number of 1,4-naphthaquinone derivatives have been isolated from plant and animal sources. For example, *juglone* (5-hydroxy-1,4-naphthaquinone) is found in the shells of walnuts. *Plumbagin* (2-methyl-5-hydroxy-1,4-naphthaquinone) is isolated from the roots of various species of *plumbago*. *Lawsone* (2-hydroxy-1,4-naphthaquinone) is obtained from the henna plant and is used in the manufacture of henna hair dyes.



JUGLONE

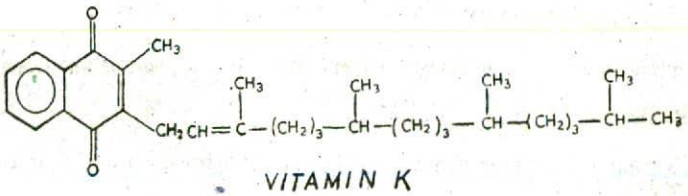


PLUMBAGIN



LAUSONE

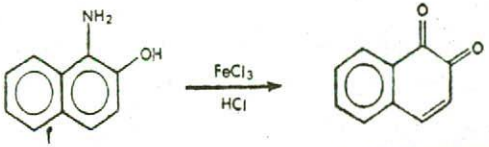
Vitamin K is found in leafy vegetables and is essential for the proper coagulation of blood. It is a derivative of 2-methyl-1,4-naphthaquinone (menadione).



VITAMIN K

1,2-Naphthaquinone (β-*Naphthaquinone*)

1,2-Naphthaquinone is obtained by the oxidation of 1-amino-2-naphthol with ferric chloride or potassium dichromate and dilute sulphuric acid.



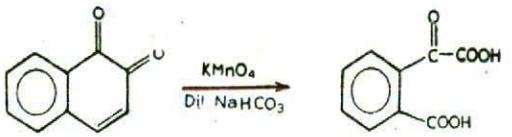
1-AMINO-2-NAPHTHOL *1,2-NAPHTHAQUINONE*

1,2-Naphthaquinone is a red crystalline solid, mp 115° C (with decomposition). It is non-volatile with steam. It is reduced by hydriodic acid alone to 1,2-dihydroxynaphthalene.



1,2-NAPHTHAQUINONE *1,2-DIHYDROXYNAPHTHALENE*

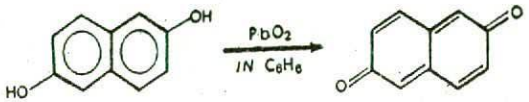
Oxidation of 1,2-naphthaquinone with potassium permanganate in dilute bicarbonate solution gives phthalonic acid.



1,2-NAPHTHAQUINONE PHTHALONIC ACID

2,6-Naphthaquinone (*Amphi-naphthaquinone*)

2,6-Naphthaquinone is obtained by oxidising 2,6-dihydroxynaphthalene with activated lead dioxide in warm benzene.

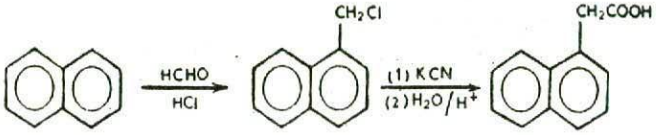


2,6-DIHYDROXYNAPHTHALENE 2,6-NAPHTHAQUINONE

2,6-Naphthaquinone is an orange solid, mp 135° C. It is non-volatile with steam.

α-Naphthylacetic Acid

α-Naphthylacetic acid is obtained by the chloromethylation of naphthalene, conversion to nitrile, and hydrolysis.



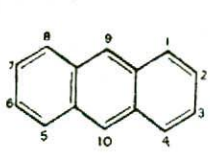
NAPHTHALENE 1-CHLOROMETHYLNAPHTHALENE α-NAPHTHYLACETIC ACID

α-Naphthylacetic acid is used as an 'apple set' spray to reduce the premature dropping of fruit from the tree ; one application near the end of growing season holds the apples on the tree for one or two weeks α-Naphthylacetic acid is also used as a spray to delay the flowering of fruit trees until the danger of frost is past, and as a spray to keep potatoes from sprouting. When sprayed on tomatoes and cucumbers, it causes the production of seedless fruits.

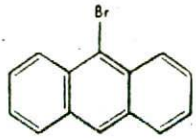
ANTHRACENE

Anthracene occurs in coal-tar (less than 1 per cent) and is obtained from the green oil fraction (bp 270-360°C). On cooling this fraction crude anthracene crystallizes out. Crude anthracene contains phenanthrene and carbazole as impurities. It is purified by washing it successively with solvent naphtha (to remove phenanthrene) and pyridine (to remove carbazole). Finally the solid is sublimed to give pure anthracene .

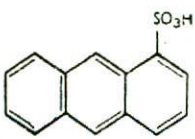
In naming derivatives of anthracene, the numbering system shown below is used. The numbers selected to denote the position of a substituent on the anthracene rings should be as small as possible.



ANTHRACENE



9-BROMOANTHRACENE



1-ANTHRACENESULPHONIC ACID

STRUCTURE OF ANTHRACENE

All fourteen carbon atoms in anthracene are sp^2 hybridized. The sp^2 hybrid orbitals overlap with each other and with s orbitals of the ten hydrogen atoms forming C—C and C–H σ bonds. Since the bonds result from the overlap of trigonal sp^2 orbitals, all carbon and hydrogen atoms in anthracene lie in the same plane. This has been confirmed by X-ray diffraction studies

Also each carbon atom in anthracene possesses an unhybridized p orbital containing one electron. These p orbitals are perpendicular to the plane of the σ bonds. The lateral overlap of these p orbitals produces a π molecular orbital containing fourteen electrons (Fig. 46·3). One half of this π molecular orbital lies above and the other half lies below the plane of the σ bonds. Anthracene shows aromatic properties because the resulting π molecular orbital satisfies the Huckel's rule ($n=3$ in $4n+2$).

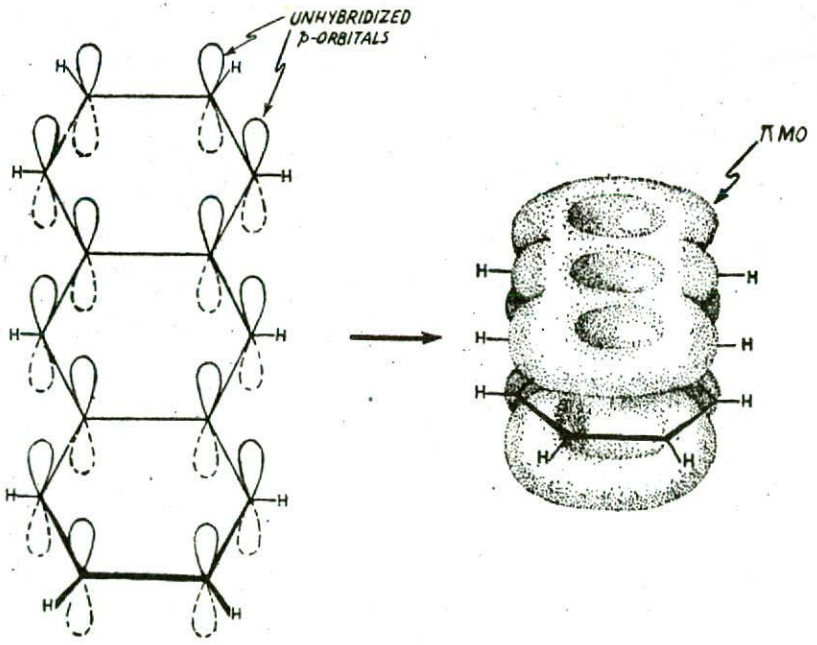
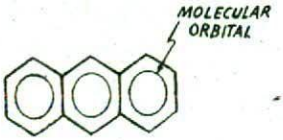
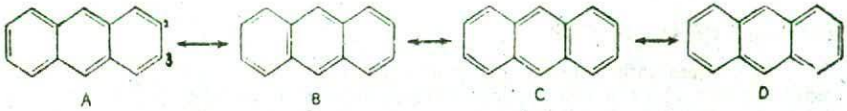


Fig. 46·3. Formatian of π molecular orbital in anthracene.

A common shorthand representation of anthracene is simply three linearly fused hexagons with a circle inside each hexagon. The circles represent the π molecular orbitals.



According to the resonance theory, anthracene is considered to be a hybrid of the following *four* canonical forms.



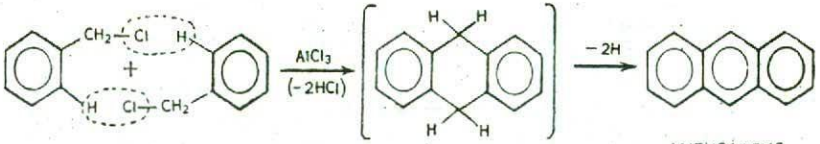
X-Ray diffraction studies show that, like naphthalene, all carbon-carbon bonds in anthracene are not of the same length. In particular, the C1—C2 bond is considerably shorter (1·37Å) than the C2—C3 bond (1·42 Å). This difference in bond lengths can be understood if we examine the four resonance forms given above. Notice that the C1—C2 bond is double in three structures (A, B and C) and single in only one (D) ; whereas the C2—C3 bond is single in three structurres (A, B and C), and double in only one (D). We would, therefore, expect the C1—C2 bond to have more double-bond character (shorter bond length), and the C2—C3 bond to have more single-bond character (longer bond length).

The resonance energy of anthracene is 84 Kcal/mole. This averages to 28 Kcal/mole per ring, which is substantially lower than that of benzene (36 Kcal/mole). As a result, anthracene is much less aromatic than benzene and behaves more like an unsaturated aliphatic hydrocarbon.

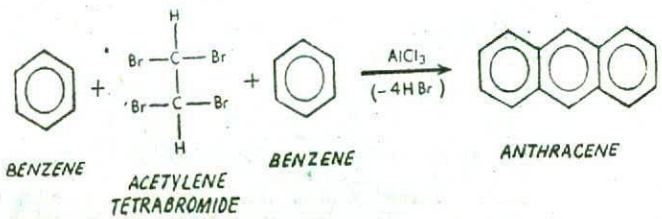
SYNTHESIS OF ANTHRACENE

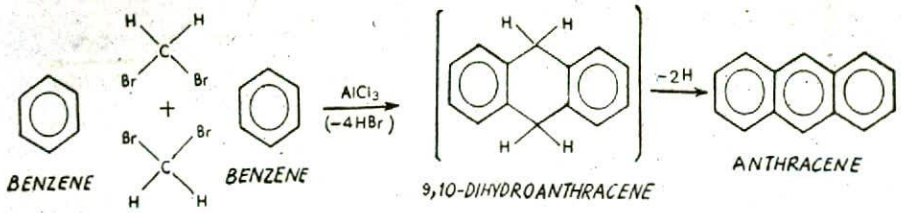
Anthracene may be obtained :

(1) **By Friedel-Crafts Reactions.** Benzyl chloride reacts with itself to form 9,10-dihydroanthracene, which readily loses two hydrogen atoms to yield anthracene.

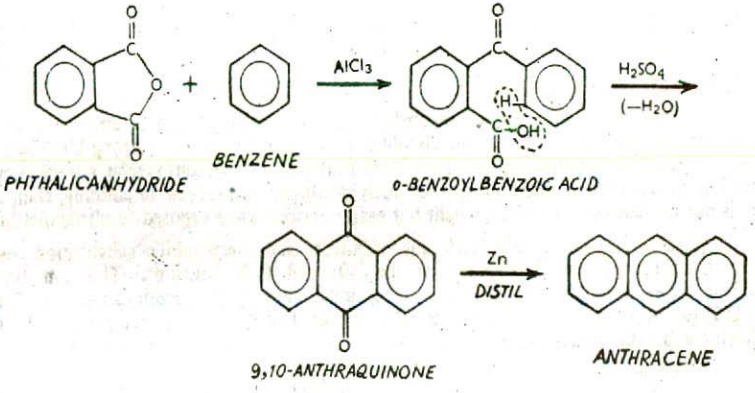


Anthracene may also be prepared by the Friedel-Crafts reaction between benzene and 1,1,2,2-tetrabromoethane (acetylene tetrabromide), or between benzene and dibromomethane.

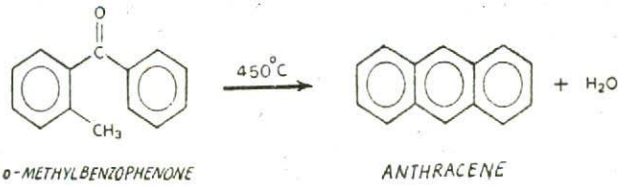




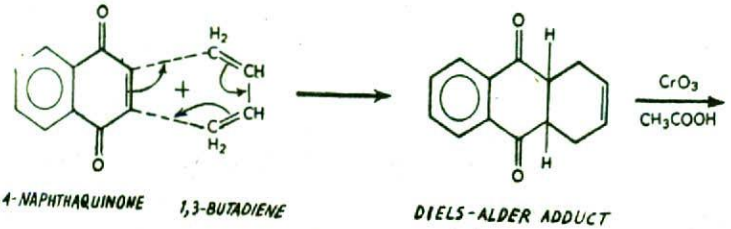
(2) **By Haworth Synthesis.** This involves the treatment of benzene with phthalic anhydride in the presence of aluminium chloride to form *o*-benzoylbenzoic acid. This is then heated with concentrated sulphuric acid to give 9,10-anthraquinone. Distillation of the anthraquinone with zinc dust yields anthracene.

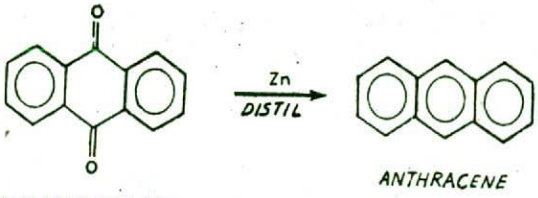


(3) **By Elbs Reaction.** The conversion of a diaryl ketone containing a methyl or methylene group *ortho* to the carbonyl function is known as the *Elbs Reaction*. For example, when *o*-methylbenzophenone is heated at 450°C, anthracene is formed.



(4) **By Diels-Alder Reacton.** This involves the reaction of 1,4-naphthaquinone with 1,3-butadiene. The product of this reaction is oxidised with chromium trioxide in glacial acetic acid to form 9,10-anthraquinone. Distillation of anthraquinone with zinc dust yields anthracene.



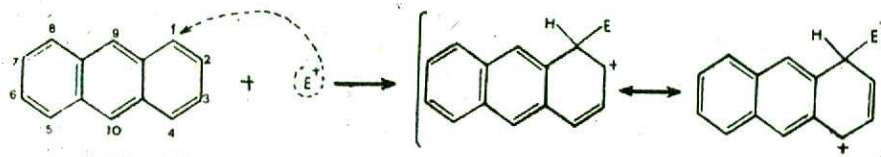


PROPERTIES OF ANTHRACENE

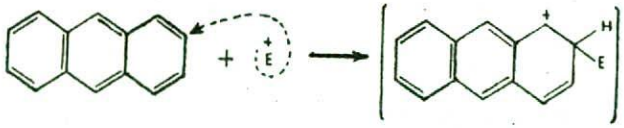
(*Physical*). Anthracene is a colourless solid. It melts at 218°C and boils at 340°C. Anthracene is insoluble in water, but dissolves in benzene. It shows a strong blue fluorescence when exposed to ultraviolet light. This fluorescent property of anthracene is used in criminal detection work, since a small amount of finely powdered anthracene on clothing, skin, money, etc., is not detected under ordinary light but easily noticed when exposed to ultraviolet light.

(*Chemical*). Anthracene undergoes addition and electrophilic substitution reactions. These reactions preferentially occur at the C-9 and C-10 positions. This can be understood if we examine the intermediate carbonium ions obtained from attack at C-1, C-2, and C-9 (all other positions are equivalent to either 1 or 2 or 9 by symmetry). E^+ in the following equations represents an electrophile.

Attack at C-1



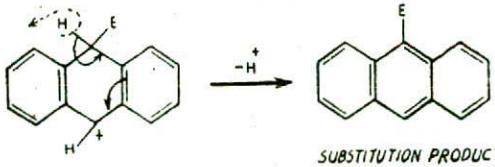
Attack at C-2



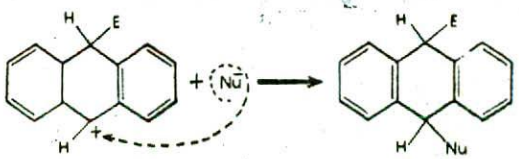
Attack at C-9



Attack at C-9 yields a carbonium ion intermediate in which two benzene rings are retained ; whereas attack at C-1 or C-2 yields an intermediate in which a naphthalene system is retained. The former intermediate is more stable and its formation favoured because the resonance energy of two benzene rings ($2 \times 36 = 72$ Kcal) exceeds that of naphthalene (61 Kcal). This carbonium ion intermediate can lose a proton to give the corresponding substitution product, or it can react with a nucleophile to form the 9,10-addition product. $\bar{N}u$ in the following equations represents a nucleophile.



SUBSTITUTION PRODUCT

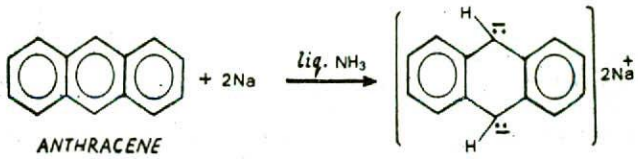


ADDITION PRODUCT

Substitution at C-1 or C-2 occurs only when the reaction is reversible (as in the case of sulphonation).

The main chemical reactions of anthracene are described below.

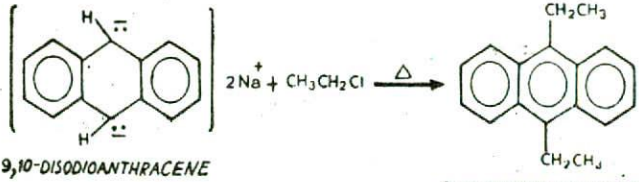
(1) **Reaction with Sodium**. Anthracene reacts with metallic sodium in liquid ammonia to form a deep blue 9,10-disodioanthracene.



ANTHRACENE

9,10-DISODIOANTHRACENE
(DEEP BLUE)

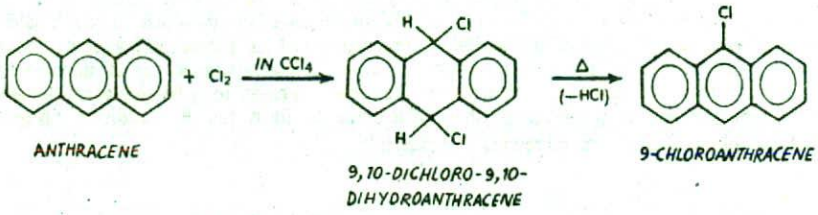
When the disodio-derativve is heated with an alkyl halide, it gives the corresponding 9,10-dialkylanthracene.



9,10-DISODIOANTHRACENE

9,10-DIETHYLANTHRACENE

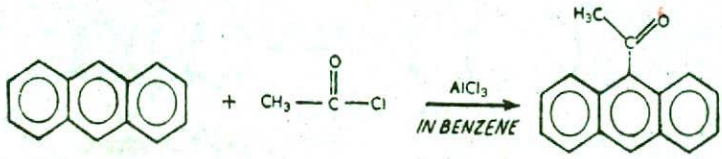
(2) **Reaction with Halogens**. Anthracene reacts with chlorine in carbon tetrachloride at room temperature to give 9,10-dichloro-9,10-dihydroanthracene (an addition product). On heating, this addition product loses a molecule of hydrogen chloride by 1,4-elimination to form 9-chloroanthracene (a substitution product).



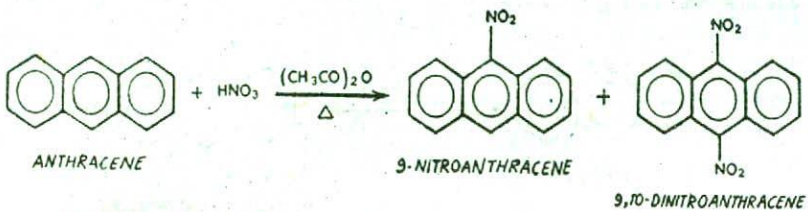
9-Chloroanthracene may also be obtained by chlorinating anthracene at 100°C, or by treating anthracene with cupric chloride in CCl_4.

Bromine reacts similarly.

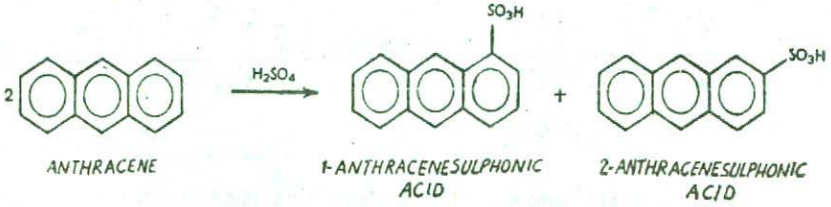
(3) **Friedel-Crafts Acylation**. Anthracene undergoes acylation with acetyl chloride and aluminium chloride in benzene to form 9-acetylanthracene.



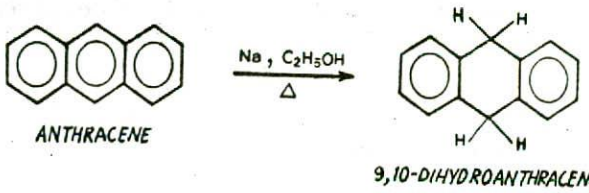
(4) **Nitration**. Anthracene undergoes nitration with concentrated nitric acid in acetic anhydride at room temperature to yield a mixture of 9-nitroanthracene and 9,10-dinitroanthracene. The usual nitrating mixture ($HNO_3 + H_2SO_4$) is not used because it leads to the formation of 9,10-anthraquinone by oxidation.



(5) **Sulphonation**. Anthracene undergoes sulphonation with concentrated sulphuric acid to yield a mixture of 1-anthracenesulphonic acid and 2-anthracenesulphonic acid. At lower temperatures 1-anthracenesulphonic acid is the major product ; where as at higher temperatures 2-anthracenesulphonic acid is the major product.



(6) **Reduction**. Anthracene undergoes reduction with sodium and ethyl alcohol to form 9,10-dihydroanthracene.



ANTHRACENE

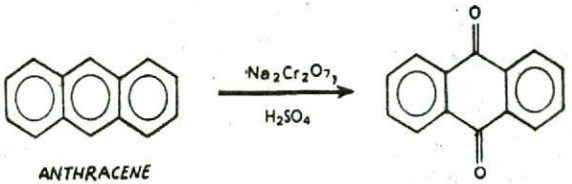
9,10-DIHYDROANTHRACENE

Catalytic reduction using nickel at 225°C first gives 9,10-hydroanthracene, and on continued hydrogenation this is converted into 1,2,3,4-tetrahydroanthracene and 1,2,3,4, 5,6,7,8-octahydroanthracene. Notice that the 9,10-hydrogen atoms migrate to the neighbouring ring.



9,10-DIHYDROANTHRACENE 1,2,3,4-TETRAHYDROANTHRACENE 1,2,3,4,5,6,7,8-OCTA-HYDROANTHRACENE

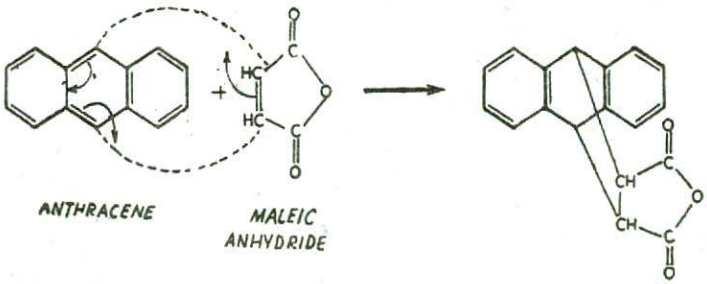
(7) **Oxidation.** Anthracene undergoes oxidation with sodium dichromate and sulphuric acid to form 9,10-anthraquinone. Other oxidising agents like nitric acid and air in the presence of V_2O_5 also lead to the formation of 9,10-anthraquinone.



ANTHRACENE

ANTHRAQUINONE (9,10-ANTHRAQUINONE)

(8) **Diels-Alder Reaction.** Anthracene undergoes a Diels-Alder reaction with maleic anhydride to yield the corresponding adduct.



ANTHRACENE MALEIC ANHYDRIDE

DIELS-ALDER ADDUCT

Use. Anthracene is used in the manufacture of anthraquinone.

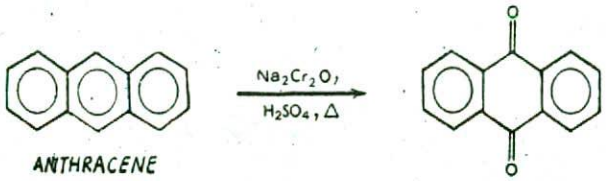
IMPORTANT DERIVATIVES OF ANTHRACENE

Anthraquinone (*9,10-Anthraquinone*)

Three quinones of anthracene are known. They are the 1,2-, 1,4-, and 9,10-anthraquinone. 9, 10-Anthraquinone is of considerable industrial importance and is usually referred to simply as anthraquinone.

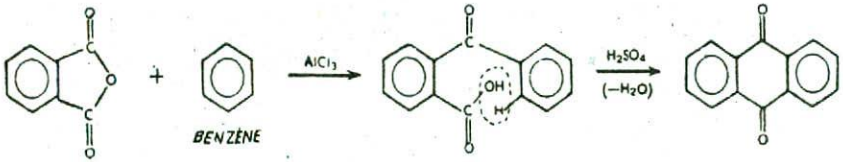
Preparation. Anthraquinone may be obtained :

(1) FROM ANTHRACENE. When anthracene is oxidised with sodium dichromate and sulphuric acid, or air in the presence of vanadium pentoxide at about 400°C, anthraquinone is formed



ANTHRACENE 9,10-ANTHRAQUINONE

(2) FROM BENZENE AND PHTHALIC ACID. When benzene is treated with phthalic anhydride in the presence of aluminium chloride, *o*-benzoylbenzoic acid is formed. Treatment of this with concentrated sulphuric acid yields anthraquinone.



PHTHALIC ANHYDRIDE BENZENE *o*-BENZOYLBENZOIC ACID ANTHRAQUINONE

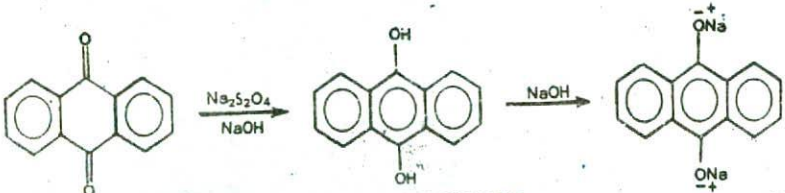
This process is used commercially. The derivatives of benzene and phthalic anhydride may be used to produce substituted anthraquinones.

Properties. (*Physical*). Anthraquinone is a pale yellow solid, mp 286°C. It is insoluble in water, but dissolves in boiling benzene.

(*Chemical*). Anthraquinone shows very little resemblance to *p*-benzoquinone *e.g.*, it has no smell, is not volatile, and is resistant to oxidising agents. This is probably because the carbonyl double bonds are each part of an aromatic system. It behaves more like an unreactive aromatic ketone.

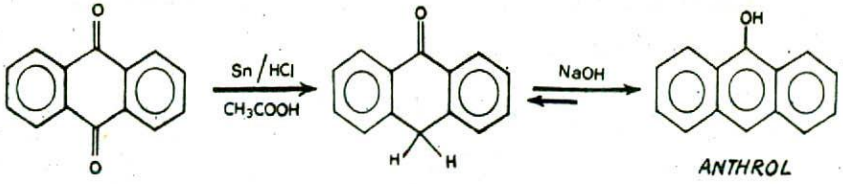
Some of the important chemical properties of anthraquinone are described below.

(1) **Reduction.** Anthraquinone undergoes reduction with alkaline sodium hydrosulphite ($Na_2S_2O_4$) or zinc and alkali to form 9,10-dihydroxyanthracene. This dissolves in alkali to yield a disodium salt of 9,10-dihydroxyanthracene, which is blood-red in colour. Its formation may be used as a test for anthraquinone. When the red solution is exposed to air and shaken, anthraquinone crystallizes out.



ANTHRAQUINONE 9,10-DIHYDROXYANTHRACENE DISODIUM SALT OF 9,10-DIHYDROXYANTHRACENE

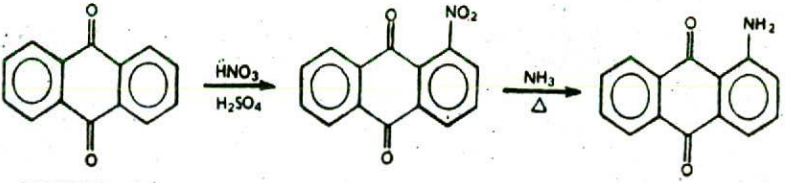
Reduction of anthraquinone with tin and hydrochloric acid in glacial acetic acid yields anthrone which tautomerizes to anthrol (9-hydroxyanthracene) with boiling alkali.



ANTHRAQUINONE ANTHRONE ANTHROL

Anthraquinone is reduced to anthracene by heating with concentrated hydriodic acid at 150°C or distilling with zinc dust.

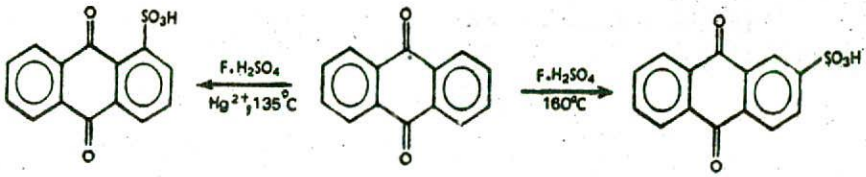
(2) **Nitration.** Anthraquinone undergoes nitration with concentrated nitric acid in the presence of sulphuric acid to form 1-nitroanthraquinone. Prolonged heating yields a mixture of 1,5- and 1,8-dinitroanthraquinones. When 1-nitroanthraquinone is heated with ammonia, 1-aminoanthraquinone is formed.



ANTHRAQUINONE 1-NITROANTHRAQUINONE 1-AMINOANTHRAQUINONE

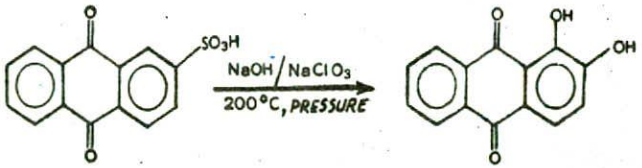
1-Aminoanthraquinone is used in the manufacture of indathrene dyes.

(3) **Sulphonation.** Anthraquinone undergoes sulphonation with fuming sulphuric acid at 160°C to give 2-anthraquinonesulphonic acid. Prolonged heating yields a mixture of 2,6- and 2,7-anthraquinonedisulphonic acids. If sulphonation is carried in the presence of mercuric sulphate catalyst at 135°C, 1-anthraquinonesulphonic acid is obtained. Prolonged heating in this case yields a mixture of 1, 5- and 1,8-anthraquinonedisulphonic acids.



1-ANTHRAQUINONE-SULPHONIC ACID ANTHRAQUINONE 2-ANTHRAQUINONE-SULPHONIC ACID

When 2-anthraquinonesulphonic acid is fused with sodium hydroxide and sodium chlorate ($NaClO_3$) at 200°C under pressure, *alizarin* is formed.



2-ANTHRAQUINONE-SULPHONIC ACID ALIZARIN (1,2-DIHYDROXYANTHRAQUINONE)

Anthraquinone does not undergo Friedel-Crafts reaction.

Uses. Anthraquinone is used in the manufacture of alizarin and several other dyes.

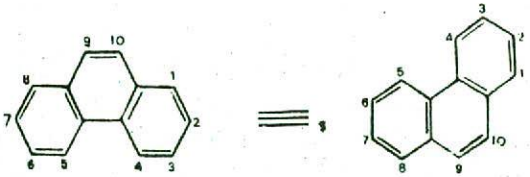
Alizarin (*1,2-dihydroxyanthraquinone*)

The structure, preparation, and properties of alizarin are discussed in the chapter on *Colour, Dyes, and Pigments.*

PHENANTHRENE

Phenanthrene is an isomer of anthracene. It may be obtained, along with anthracene, from the green oil fraction of coal-tar. On cooling this fraction we get a solid mass which contains phenanthrene, anthracene, and carbazole. Treatment of this with solvent naphtha dissolves phenanthrene. Evaporation of this solution yields crude phenanthrene, which may be purified by recrystallization of the picrate from ethanol.

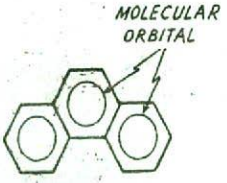
In naming derivatives of phenanthrene, the numbering system shown below is used. As before, the numbers selected to denote the position of a substituent on phenanthrene rings should be as small as possible.



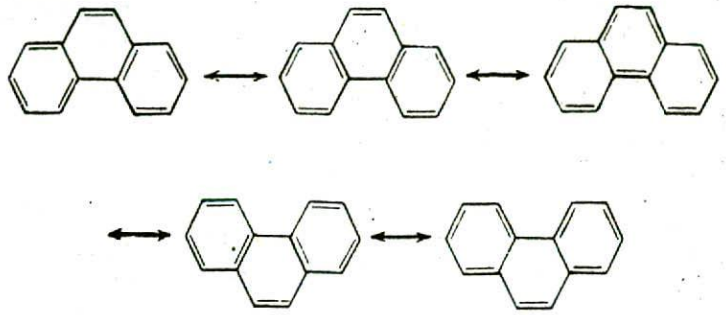
STRUCTURE OF PHENANTHRENE

Like anthracene, phenanthrene is a planar molecule. All fourteen carbon atoms are sp^2 hybridized. The sp^2 orbitals overlap with each other and with s orbitals of ten hydrogen atoms to form C—C and C—H σ bonds. Each carbon atom also possesses a p orbital and these are perpendicular to the plane containing the σ bonds. The lateral overlap of these p orbitals produces a π molecular orbital containing ten electrons. Phenanthrene shows aromatic properties because the resulting π molecular orbital satisfies the Huckel's rule ($n=3$ in $4n+2$).

A common shorthand representation of phenanthrene is simply three hexagons fused in angular fashion with a circle inside each hexagon. The circles represent the π molecular orbital.



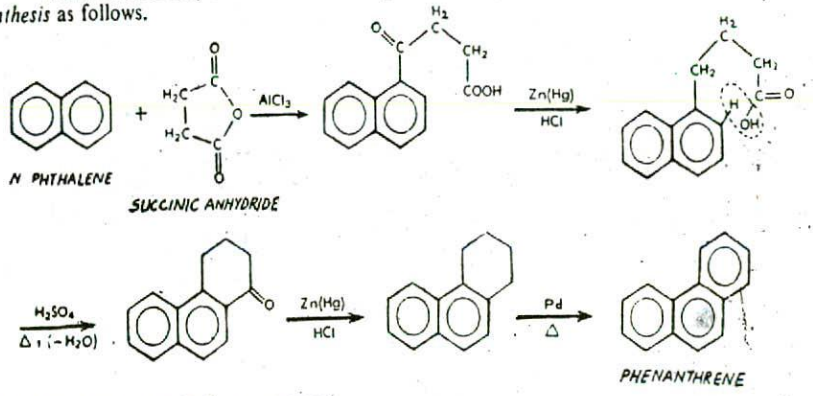
Phenanthrene is considered to be a hybrid of the following *five* resonance forms :



The resonance energy of phenanthrene is 92 Kcal/mole.

SYNTHESIS OF PHENANTHRENE

Phenanthrene may be obtained from naphthalene and succinic anhydride by the *Haworth synthesis* as follows.



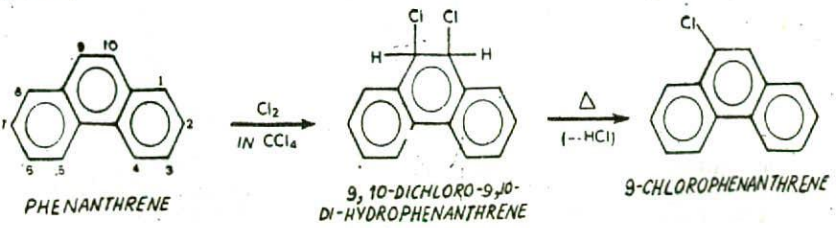
PROPERTIES OF PHENANTHRENE

(*Physical*). Phenanthrene is a colourless solid, mp 100°C. It is insoluble in water, but dissolves readily in ethanol, benzene, and ether. Phenanthrene gives blue fluorescence in benzene solution.

(*Chemical*). Phenanthrene undergoes oxidation, addition, and electrophilic substitution reactions. As with anthracene, these reactions preferentially occur at the C-9 and C-10 positions.

Some of the important reactions of phenanthrene are described below.

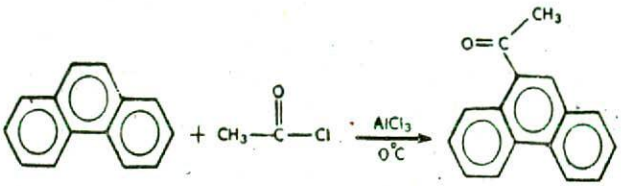
(1) **Reaction with Halogens.** Phenanthrene reacts with chlorine in carbon tetrachloride at room temperature to give 9,10-dichloro-9,10-dihydrophenanthrene (an addition product). On heating this loses a molecule of hydrogen chloride to yield 9-chlorophenanthrene (a substitution product).



9-Chlorophenanthrene may also be obtained by treatment of phenanthrene with chlorine in the presence of $FeCl_3$.

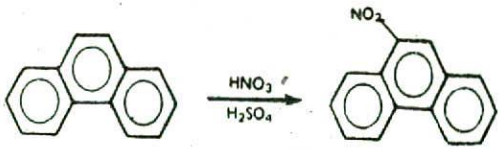
Bromine reacts similarly.

(2) **Friedel-Crafts Acylation**. Phenanthrene undergoes acylation with acetyl chloride in the presence of aluminium chloride at 0°C to give 9-acetylphenanthrene.



PHENANTHRENE 9-ACETYLPHENANTHRENE

(3) **Nitration**. Phenanthrene undergoes nitration with concentrated nitric acid and sulphuric acid to yield 9-nitrophenanthrene.



PHENANTHRENE 9-NITROPHENANTHRENE

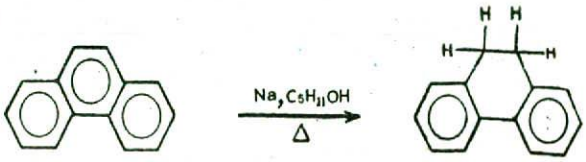
(4) **Sulphonation**. Phenanthrene reacts with concentrated sulphuric acid at 120°C to give a mixture of 2-phenanthrenesulphonic acid and 3-phenanthrenesulphonic acid. Notice that, like anthracene, substitution does not occur at C-9.



PHENANTHRENE 2-PHENANTHRENESULPHONIC ACID

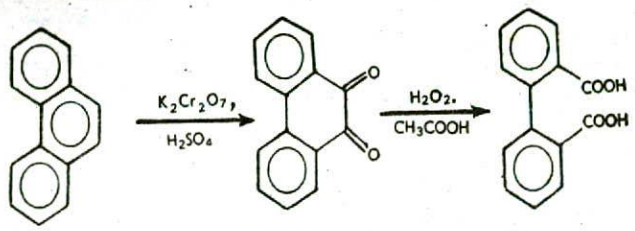
3-PHENANTHRENESULPHONIC ACID

(5) **Reduction**. Phenanthrene undergoes reduction with sodium and isopentanol to form 9,10-dihydrophenanthrene.



PHENANTHRENE 9,10-DIHYDROPHENANTHRENE

(6) **Oxidation**. Phenanthrene undergoes oxidation with potassium dichromate and sulphuric acid or chromium trioxide in acetic acid to form 9,10-phenanthraquinone (mp 206° C). Further oxidation of this with hydrogen peroxide in acetic acid gives diphenic acid.



PHENANTHRENE 9,10-PHENANTHRAQUINONE DIPHENIC ACID

Phenanthrene is of little industrial importance but phenanthrene ring systems are found widely distributed in natural compounds such as carcinogenic (meaning cancer-producing) hydrocarbons, bile acids, sex harmones, morphine alkaloids, and cholestrol.

QUESTIONS

1. Discuss the structure of naphthalene. *(Dibrugarh BSc Hons, 1994)*
2. How does the structure of diphenyl differ from that of naphthalene ?
3. Discuss the structure of naphthalene. How will you convert it into : (*a*) 1-Naphthol, (*b*) 2-Naphthol, and (*c*) 2-Naphthylamine. *(Gauhati BSc Hons, 1993)*
4. How is naphthalene obtained from coal-tar ? *(Magadh BSc Hons, 1993)*
5. How will you synthesise naphthalene ? *(Madurai BSc, 1994)*
6. Write a note on : Haworth's synthesis of naphthalene. *(Aligarh BSc Hons, 1993)*
7. Write a note on : Electrophilic substitution in naphthalene.
8. How would you explain that the electrophilic substitution in naphthalene takes place at position 1 ? *(Karnataka BSc, 1994)*
9. Why does chlorination of naphthalene takes place at the α-position ? *(Marathwada BSc1993)*
10. Explain : Nitration of naphthalene takes place exclusively in the α-position. *(Nagpur BSc III, 1994)*
11. Describe the reactions of naphthalene.
12. Complete the following reactions :
    (*a*) Naphthalene + Conc. H_2SO_4 at 40°C →
    (*b*) Naphthalene + Conc. H_2SO_4 at 160°C →
    (*c*) Naphthalene + Na + C_2H_5OH →
13. What is Bucherer reaction ? Give two differences between phenols and naphthols. *(South Gujarat BSc, 1994)*
14. What happens when naphthalene is oxidised with chromic acid ? *(Delhi BSc Hons, 1993)*
15. What happens when naphthalene vapours mixed with air is passed over heated vanadium pentoxide ? *(Annamalai BSc, 1993)*
16. What is the product of oxidation of naphthalene with potassium permanganate ? *(Madras BSc, 1993)*
17. How will you synthesise the following compounds from naphthalene ?
    (*a*) α-Naphthol ; (*b*) β-Naphthol ; (*c*) α-Naphthylamine ; (*d*) β-Naphthylamine ; (*e*) Tetralin (*f*) β-Naphthoic acid ; (*g*) Phthalic acid ; and (*h*) Phthalimide.
18. Discuss the structure of anthracene. *(Jammu BSc, 1993)*
19. How is anthracene isolated from coal-tar ?
20. Outline the method of preparation and properties of anthracene.
21. Describe the preparation, properties, and structure of anthracene.
22. Explain : In anthracene, the 9,10-positions are usually attacked ? *(Bundelkhand BSc Hons, 1993)*

23. How will you synthesise the following compounds from anthracene ?
(*a*) Alizarin ; and (*b*) Anthraquinone.

24. How will you synthesise :
(*a*) Anthracene ; and (*b*) 9-Methylanthracene (*Sambalpur BSc Hons, 1994*)

25. Discuss the structure of phenanthrene.

26. Describe Haworth's method for the synthesis of phenanthrene. (*Kerala BSc III, 1994*)

27. What is the product of oxidation of phenanthrene by $K_2Cr_2O_7/H_2SO_4$.

Chapter **47**

Heterocyclic Compounds

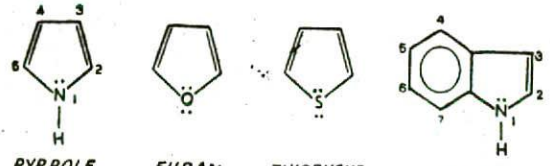
Heterocyclic compounds are those cyclic compounds in which one or more of the ring carbons are replaced by another atom. The non-carbon atoms in such rings are referred to as *hetero atoms*. The most common hetero atoms are nitrogen, oxygen and sulphur, but other atoms such as boron, phosphorous, or silicon can also be members of heterocyclic rings

A number of substances which are heterocyclic compounds according to the above definition have already been discussed in earlier chapters *e.g.*, ethylene oxide, succinic anhydride, lactones, and cyclic carbohydrates. These compounds are readily formed from open-chain substances and are easily converted into open-chain derivatives. The heterocyclic compounds which we are about to consider here are much more stable and possess aromatic properties. A variety of such heterocyclic compounds of different ring sizes are known. In this chapter we will restrict our study to the most important ones which are made of five- and six-membered rings.

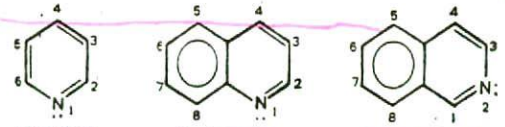
NOMENCLATURE

The simple heterocyclic compounds are called by well established *common names*. However, the more complex rings which are not within the scope of this book are named more systematically. The common names of some of the most important five- and six-membered heterocyclic ring compounds are given below.

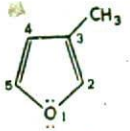
Five-Membered Rings :



Six-Membeted Rings :

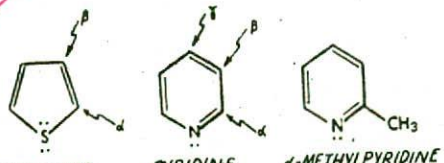


Notice that the rings containing nitrogen usually end with *-ole* if five-membered and with *-ine* if six-membered. The hetero atom is always numberd as 1 (isoquinoline is an exception), and in such a way as to keep the substituent numbers as low as possible.



3-METHYLFURAN 2-BROMOPYRIDINE

The carbon atoms next to the hetero atom are sometimes referred to as the α-carbon atoms and those further away as β- and γ-carbon atoms. This method is used only for naming simple derivatives or to indicate the equivalence of positions.



THIOPHENE PYRIDINE α-METHYLPYRIDINE (2-METHYLPYRIDINE)

FIVE-MEMBERED RINGS

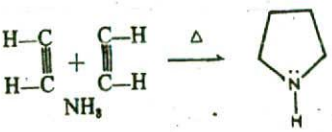
PYRROLE, 

It is an important five-membered heterocyclic compound because many naturally occurring substances contain the pyrrole ring *e.g.*, chlorophyll, hemoglobin, and some of the alkaloids. Pyrrole derives its name from the fact that its vapours produce a bright red colour when brought in contact with a pine splint moistened with concentrated hydrochloric acid (Gr, *pyrros*, fiery + *oleum*, oil).

Pyrrole occurs in coal-tar and in bone oil (Dippel's oil). The latter is obtained by the dry distillation, or pyrolysis, of animal by-products such as horns, hooves, and bones. It may be isolated from bone oil by first washing it with dilute sulphuric acid to remove the basic substances, and then with dilute alkali to remove the acidic substances. It is next subjected to fractional distillation. The fraction passing over between 100°C to 150°C contains pyrrole, which may be removed by boiling with potassium hydroxide. The potassium salt is formed which on steam distillation gives pyrrole. This is finally purified by distillation.

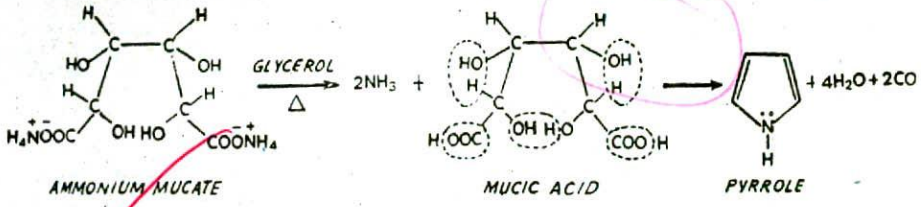
Preparation. Pyrrole may be obtained :

(1) By passing a mixture of acetylene and ammonia through a red-hot tube.

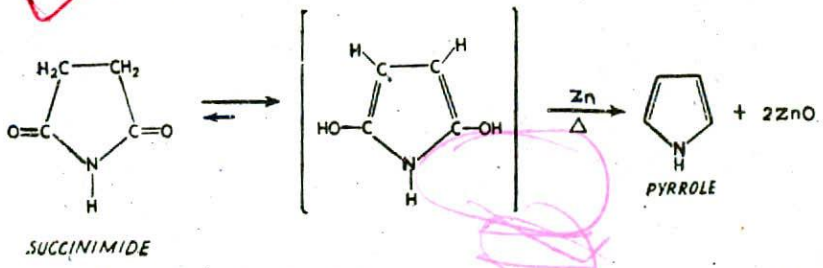


pyrrole

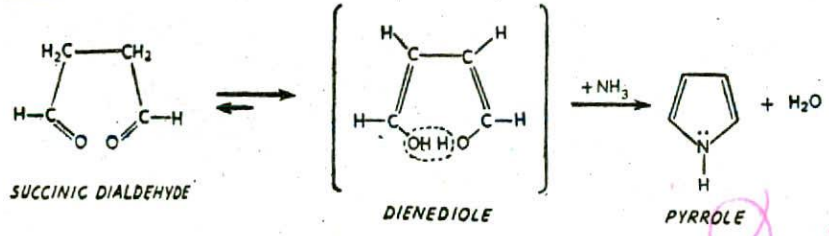
(2) By heating ammonium mucate with glycerol at 200°C. At this temperature, ammonium mucate is dissociated into mucic acid and ammonia. The acid then undergoes dehydration, decarboxylation, and ring-closure by reaction with ammonia.



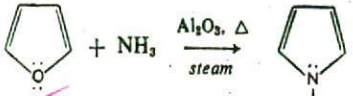
(3) By heating succinimide with zinc dust.



(4) By warming succinic dialdehyde with ammonia.



(5) By passing a mixture of furan, ammonia, and steam over aluminium oxide catalyst at 480—490°C. (*Commercial Method*)



Structure of Pyrrole. In pyrrole the nitrogen atom and the four carbon atoms are sp^2 hybridized. The sp^2 hybrid orbitals overlap with each other and with s atomic orbitals of the five hydrogen atoms forming C—C, C—N, C—H, and N—H σ bonds as shown in Fig. 47·1. All these σ bonds lie in one plane.

Also each carbon atom and the nitrogen atom possesses an unhybridized p atomic orbital and these are perpendicular to the plane of the σ bonds. The p orbitals on carbons contain one electron each and the p orbital on nitrogen contains two electrons (the lone pair). The lateral overlap of these p orbitals produces a π molecular orbital containing *six* electrons (Fig. 47·2), an arrangement that is frequently referred to as an Aromatic Sextet. Pyrrole shows aromatic properties or aromaticity because the resulting π molecular orbital satisfies the Huckel's rule ($n=1$ in $4n+2$).

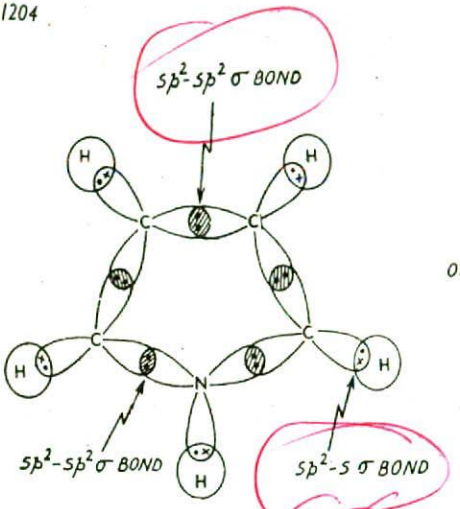


Fig. 47·1 Formation of σ bonds in pyrrole.

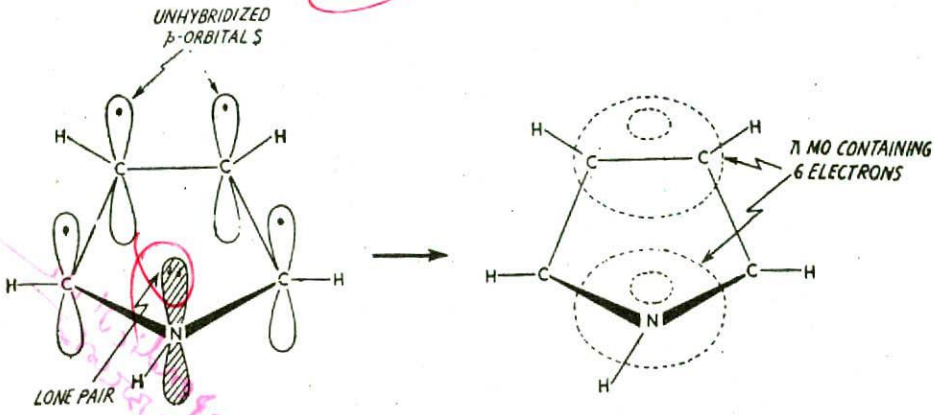


Fig. 47·2. The unhybridized *p* orbitals in pyrrole overlap with each other to form a delocalized π molecular orbital above and below the plane containing the σ bonds.

A common shorthand representation of pyrrole is simply pentagon, a five-membered ring, with a circle inside (Fig. 47·3). The circle represents the π molecular orbital.

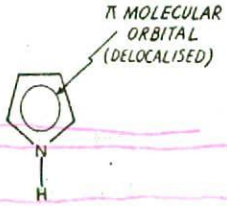
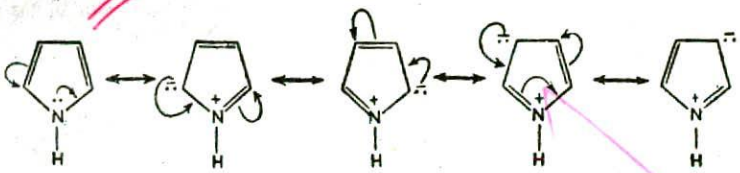


Fig. 47·3. Simplified representation of pyrrole.

According to the resonance theory, pyrrole is considered to be hybrid of the following canonical forms.



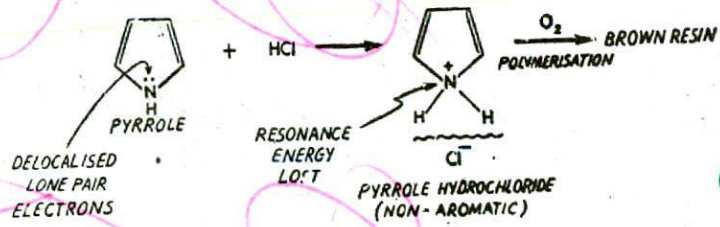
Notice that as a result of donation of electrons by the nitrogen atom, the carbon atoms of the pyrrole ring have gained in electron density. That is, they have become negatively charged. This enables pyrrole to participate in electrophilic substitution reactions.

Measurement of bond lengths by X-ray analysis confirms the hybrid character of the pyrrole molecule. In particular, the C—N bond (1·38 Å), which is shorter than a normal C—N *single* bond (1·48 Å), seems to possess significant *double* bond character.

Properties *Physical*). Pyrrole is colourless liquid, bp 131°C, which rapidly turns brown on exposure to air. Its odour is like that of chloroform. Pyrrole is sparingly soluble in water but dissolves in ethanol and ether.

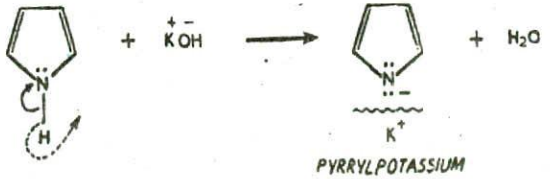
(*Chemical*). The main chemical properties of pyrrole are described below.

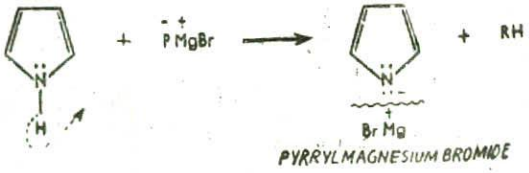
(1) **Basic Character.** Pyrrole is a weak base (pK_a=3·4). It reacts with dilute hydrochloric acid to give a crystalline hydrochloride. This salt is stable in the absence of oxygen :



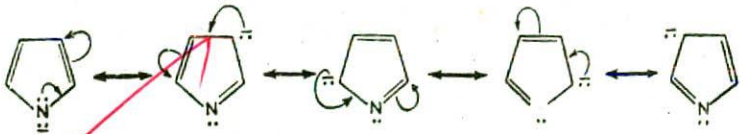
otherwise polymerisation rapidly occurs to produce a brown resin. The reason for the weak basic character of pyrrole is that the lone pair of electrons on nitrogen is involved in the formation of the delocalized π molecular orbital and is not available for the formation of a new bond with proton. Furthermore, if a proton is added to the nitrogen atom by reaction with an acid, the resulting structure ceases to be aromatic and the resonance energy is lost. This makes the pyrrole cation very unstable in comparison to the free pyrrole and indicates why pyrrole is a weak base. Also, the pyrrole cation behaves as a typical conjugated diene and undergoes polymerisation readily.

(2) **Acidic Character.** Pyrrole is not only a weak base but also a very weak acid (pK_a=15). This is shown by its reactions with solid potassium hydroxide and Grignard reagents.



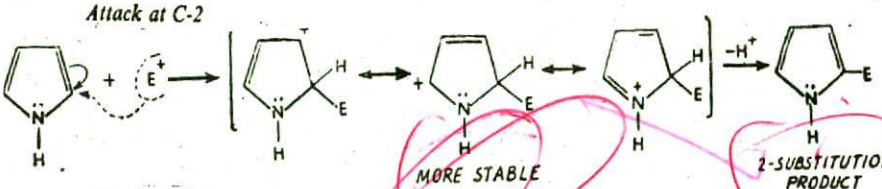


The reason for the acidic character of pyrrole is that the electron pair delocalization from nitrogen makes it positively charged and increases the possibility of proton abstraction giving pyrryl anion. Furthermore, the pyrryl anion is stabilized by delocalization of the negative charge over the ring. The resonance forms of pyrryl anion are given below.

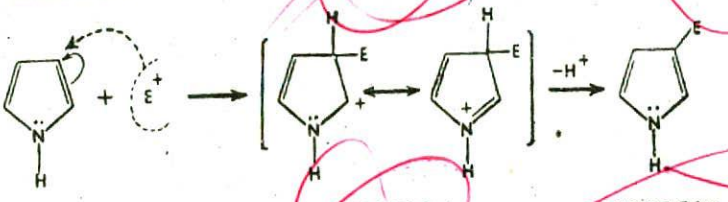


(3) **Electrophilic Substitutions.** Pyrrole undergoes electrophilic substitution reactions primarily at *C-2*. This is understandable if we examine the intermediate cation. Three resonance forms can be written for the intermediate obtained from attack at *C-2*, whereas only two such forms are possible for substitution at *C-3*. E^+ in the following equations represents an electrophile.

Attack at C-2



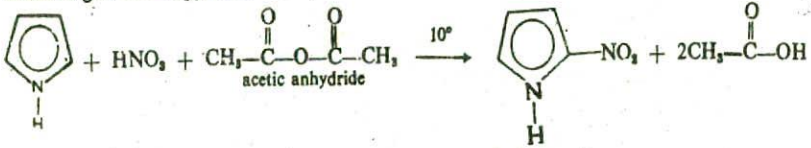
Attack at C-3



Consequently the former intermediate is more stable and the product with a substituent at *C-2* predominates. Substitution at *C-3* occurs only when both the 2-positions (that is, α and α') are blocked. The same reasoning is applicable for the electrophilic substitutions in furan and thiophene.

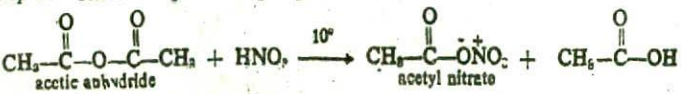
Electrophilic substitution reactions of pyrrole are not carried in the presence of strong acids or reagents which give rise to strong acids, because under such conditions pyrrole undergoes polymerisation and resinification.

(*a*) **Nitration.** Pyrrole can be nitrated by a *cold* solution of nitric acid in acetic anhydride to give 2-nitropyrrole.

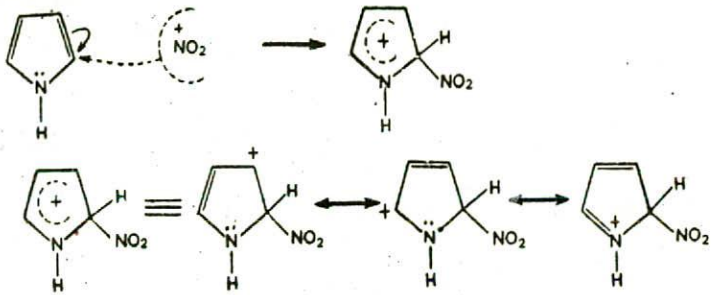


MECHANISM. The mechanism of this reaction involves the following *three* steps-

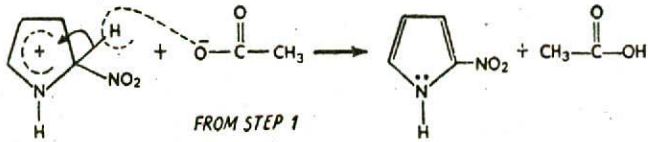
Step 1. The electrophile $\overset{+}{N}O_2$ is generated



Step 2. The electrophile attacks pyrrole at *C-2* to form the resonance-stabilised cation



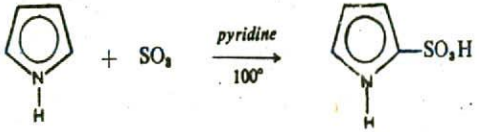
Step 3. A hydrogen ion is eliminated to yield *2-nitropyrrole*



2-NITROPYRROLE

Similar sequences may be written for other electrophilic substitution reactions of pyrrole

(*b*) **Sulphonation.** Pyrrole may be sulphonated with sulphur trioxide in pyridine at about 100°C to yield pyrrole-2-sulphonic acid.



pyrrole-2-sulphonic acid

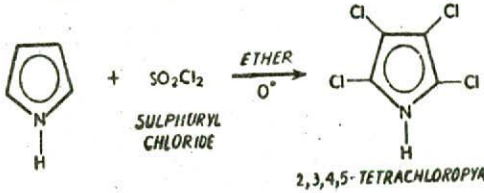
(*c*) **Halogenation.** Halogenation reactions of pyrrole proceed with great vigour and require careful control of reaction conditions.

(*i*) Chlorination is carried out with sulphuryl chloride in ether at 0°C.

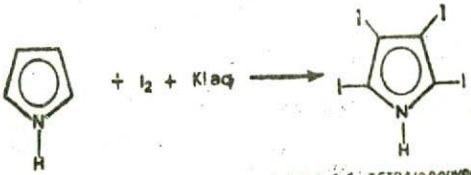
(*ii*) Bromination with bromine in ethanol at 0°C.

(*iii*) Iodination with iodine in an aqueous solution of potassium iodide.

In each case the tetrahalogen derivative is obtained.



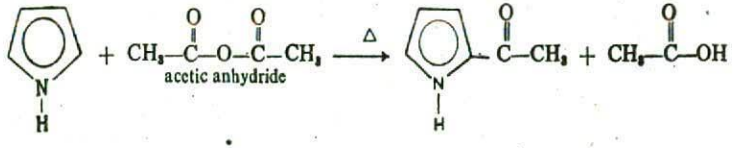
2,3,4,5-TETRACHLOROPYRROLE



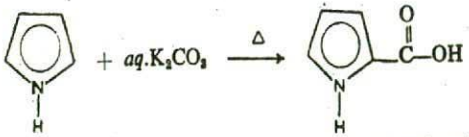
2,3,4,5-TETRAIODOPYRROLE

2,3,4,5-Tetraiodopyrrole possesses antiseptic properties and is used in medicine under the name *iodol*.

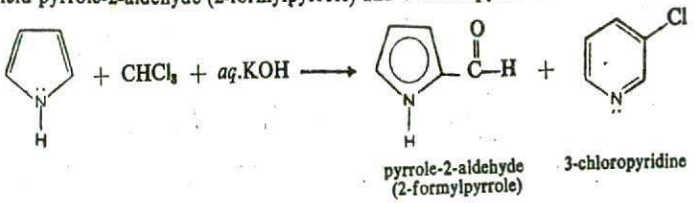
(*d*) **Friedel-Crafts Acylation.** Pyrrole may be acetylated with acetic anhydride at 250°C to give 2-acetylpyrrole. Notice that no catalyst is required in this reaction.



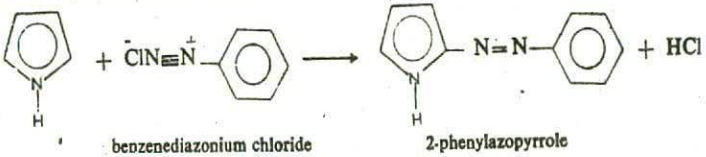
(*e*) **Kolbe-Schmitt Carboxylation.** Pyrrole reacts with aqueous potassium carbonate at 100°C to give pyrrole-2-carboxylic acid.



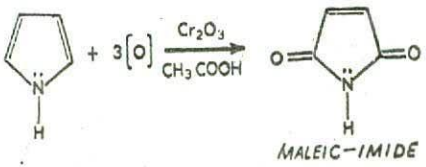
(*f*) **Reimer-Tiemann Formylation.** Pyrrole reacts with chloroform in the presence of alkali to yield pyrrole-2-aldehyde (2-formylpyrrole) and 3-chloropyridine.



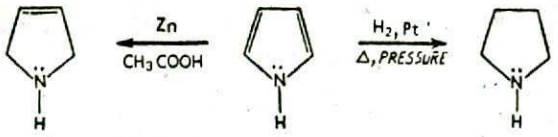
(*g*) **Diazo Coupling.** Pyrrole couples with benzenediazonium chloride in a weakly acidic solution to give 2-phenylazopyrrole.



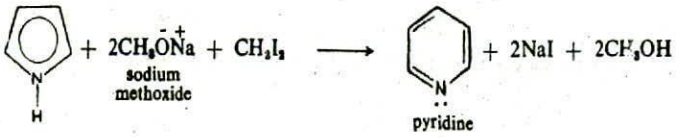
(4) **Oxidation.** Pyrrole is oxidised by chromium trioxide in acetic acid to give the imide of maleic acid.



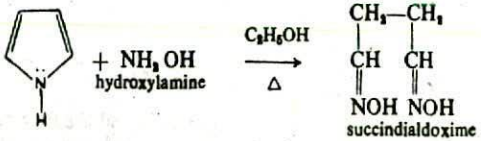
(5) **Reduction.** Mild reduction of pyrrole with zinc and acetic acid yields 3-pyrroline (2,5-dihydropyrrole). Catalytic reduction completely hydrogenates the ring system and produces pyrrolidine.



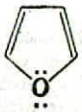
(6) **Ring Expansion Reaction.** When treated with sodium methoxide and methylene iodide, pyrrole undergoes ring expansion forming pyridine.



(7) **Ring Opening Reaction.** When treated with hot ethanolic hydroxylamine, pyrrole undergoes ring opening forming the dioxime of succindialdehyde.



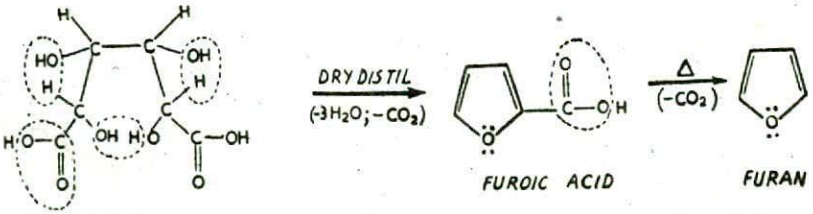
FURAN AND ITS DERIVATIVES

FURAN, 

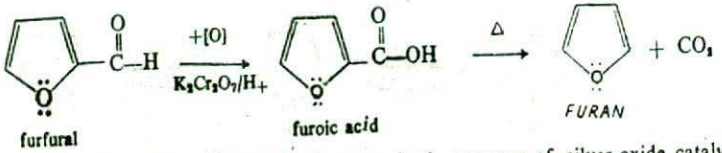
Furan is the oxygen-containing counterpart of pyrrole. It occurs together with its methyl homologues in wood-tar. Its vapours produce a green colour when brought in contact with a pine splint moistened with concentrated hydrochloric acid.

Preparation. Furan may be obtained :

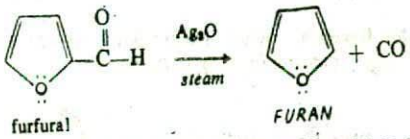
(1) By dry-distillation of mucic acid and heating the product, furoic acid (furan-2-carboxylic acid), at 200—300°C.



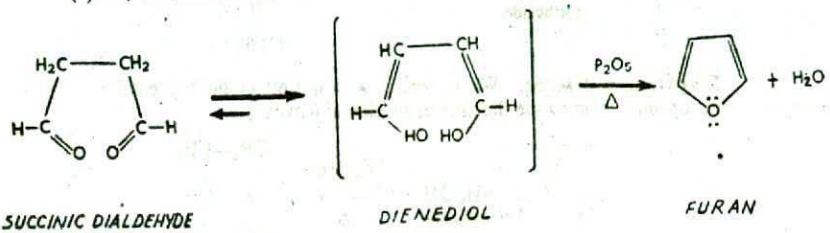
(2) By oxidation of furfural with potassium dichromate to give furoic acid and subsequent decarboxylation at 200—300°C.



(3) By decarbonylation of furfural in steam in the presence of silver oxide catalyst. (*Commercial*)



(4) By dehydration of succinic dialdehyde by heating with P_2O_5 or $ZnCl_2$.



Structure of Furan. In furan the oxygen atom and the four carbon atoms are sp^2 hybridized. The sp^2 hybrid orbitals overlap with each other and with *s* orbitals of four hydrogen atoms forming C—C, C—O, and C—H σ bonds as shown in Fig. 47·4. Notice that sp^2 orbital of oxygen is completely filled. The electrons residing in this orbital make up one of the two lone pair electrons of oxygen.

Also each carbon atom and the oxygen atom possesses an unhybridized *p* orbital and these are perpendicular to the plane containing the σ bonds. The *p* orbitals on carbons contain one electron each and *p* orbitals on oxygen contains an unshared pair of electrons (the other lone pair). The lateral overlap of these *p* orbitals produces a π molecular orbital containing *six* electrons (Fig.47 5). Furan shows aromatic properties because the resulting π molecular orbital, like pyrrole, also satisfies the Huckel's rule ($n = 1$ in $4n+2$).

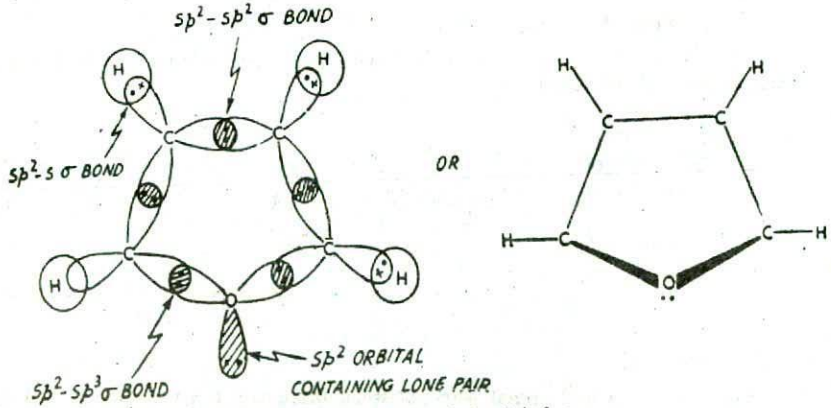


Fig. 47·4 Formation of σ bonds in furan.

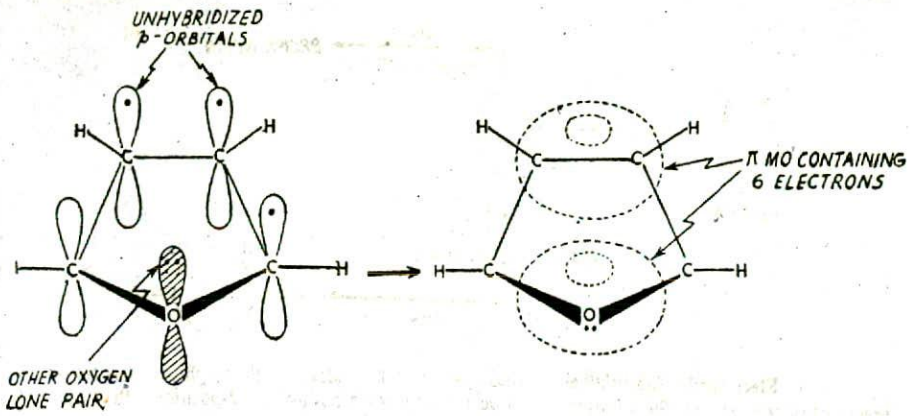


Fig. 47·5 Formation of π molecular orbital in furan.

A common shorthand representation of furan is simply pentagon with a circle inside (Fig. 47·6). The circle represents the π molecular orbital.

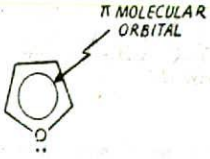
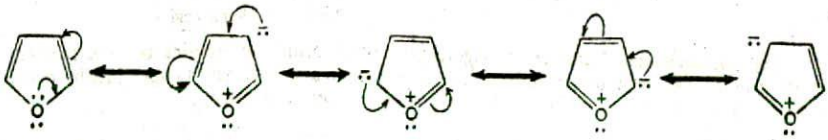


Fig. 47·6. Simplified representation of furan.

According to the resonance theory, furan is considered to be hybrid of the following canonical forms.

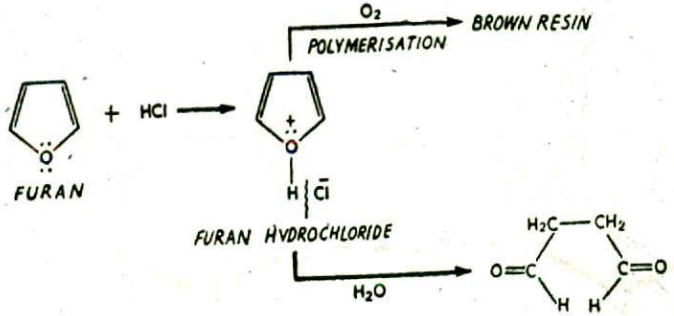


Measurement of bond lengths by X-ray analysis confirms the hybrid character of the furanmolecule. In particular, the C—O bond (1·37 Å), which is shorter than a normal C—O single bond (1·43 Å), possesses significant double bond character.

Properties. (*Physical*). Furan is a colourless liquid, bp 32°C, with a chloroform like smell. It is only slightly soluble in water, but dissolves in most organic solvents.

(*Chemical*). Some of the important chemical reactions of furan are :

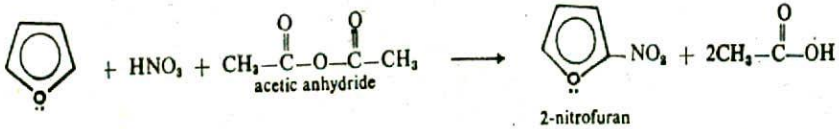
(1) **Basic Character.** Furan, like pyrrole, is a weak base. It forms unstable salts with mineral acids. These salts may either polymerize to produce a brown resin or undergo hydrolysis to yield succindialdehyde.



(2) **Electrophilic Substitutions.** Furan, like pyrrole, undergoes electrophilic substitution reactions mainly at *C-2*. Substitution at *C-3* occurs only when both of the 2-positions (that is, α and α′) are already blocked.

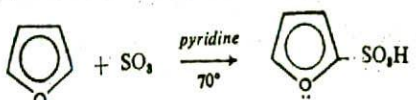
Electrophilic substitution reactions of furan are not carried in the presence of strong acids, because under such conditions it undergoes polymerisation.

(*a*) **Nitration.** Furan can be nitrated with a hot solution of nitric acid in acetic anhydride to form 2-nitrofuran.



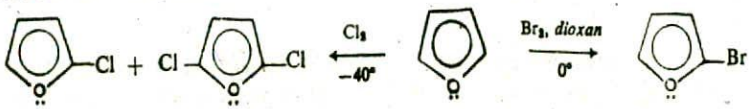
2-nitrofuran

(*b*) **Sulphonation.** Furan may be sulphonated by sulphur trioxide in pyridine at 70°C to yield furan-2-sulphonic acid.



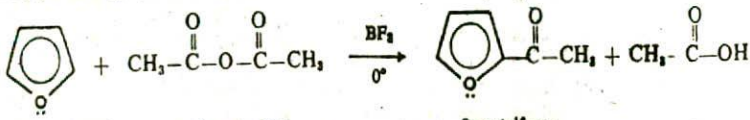
furan-2-sulphonic acid

(*c*) **Halogenation.** Furan reacts vigorously with chlorine and bromine at room temperature to give polyhalogenated products, but does not react at all with iodine. Much milder conditions have to be used to obtain *monochloro* or *monobromo* derivatives.



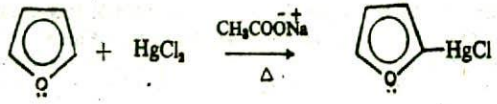
2-chlorofuran 2,5-dichlorofuran 2-bromofuran

(*d*) **Friedel-Crafts Acylation.** Furan can be acetylated with acetic anyhydride in the presence of BF_3 (or $SnCl_4$) at 0° to yield 2-acetylfuran.



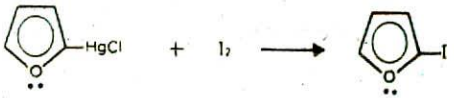
acetic anhydride 2-acetylfuran

(*e*) **Mercuration.** Furan undergoes mercuration on heating with mercuric chloride in aqueous sodium acetate to yield 2-chloromercurifuran.

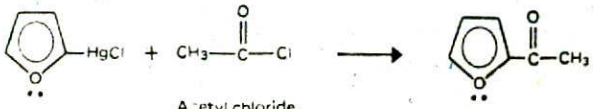


2-chloromercurifuran

2-Chloromercurifuran is useful in synthesis, because the mercuri-group is readily replaced by iodine or bromine and by an acyl group.

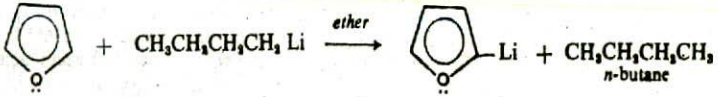


2-Chloromercurifuran 2-Iodofuran



Acetyl chloride 2-Acetylfuran

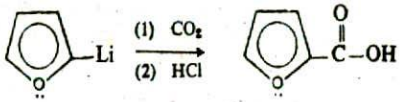
(*f*) **Reaction with *n*-Butyl-lithium.** Furan reacts with *n*-butyl-lithium in ether to give 2-furan-lithium.



n-butane

2-furan-lithium

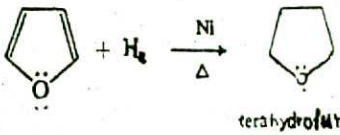
2-Furan-lithium undergoes many of the usual reactions of organolithium compounds. For example, it combines with carbon dioxide to form furoic acid (furan-2-carboxylic acid)



2-furan-lithium furoic acid

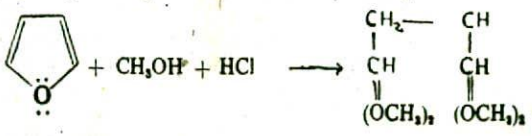
(*g*) **Diazo Coupling.** Furan is not sufficiently reactive to couple with benzenediazonium chloride.

(3) **Reduction.** Furan is reduced by hydrogen in the presence of nickel to produce tetrahydrofuran.



tetrahydrofuran

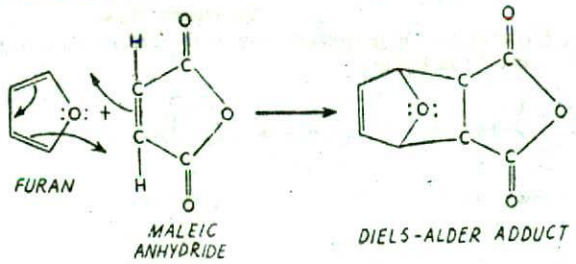
(4) **Ring-opening Reaction.** When treated with methanol and hydrochloric acid, furan undergoes ring-opening forming the diacetal of succindialdehyd



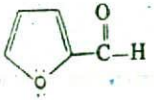
diacetal of succindialdehyde

Hydrolysis of furan with dilute hydrochloric acid also leads to ring-opening

(5) **Reaction with Maleic Anhydride** (*Diels-Alder Reaction*). Furan has sufficient diene character to undergo Diels-Alder reaction with maleic anhyride to form an addition product. The addition occurs across *C-2* and *C-5*. Pyrrole and thiophene do not give this reaction.



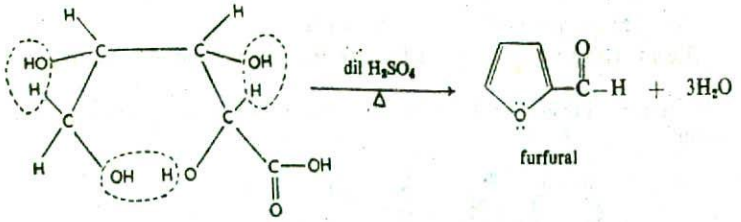
Use. Furan is used in the manufacture of tetrahydrofuran.

FURFURAL, *Furan-2-aldehyde, 2-Formylfuran,* 

Furfural is the most important derivative of furan. It derives its name from the fact that it was first obtained by boiling bran with dilute acid (L., *Furfur*, bran). Furfural produces a green colour when brought in contact with a pine splint moistened with concentrated hydrochloric acid. It also produces an intense red colour when heated with aniline and acetic acid.

The group, $-C_4H_3O$ *e.g.*,  , is called *furyl*.

Preparation. Furfural is obtained commercially by the acid catalysed dehydration of pentoses, five-carbon sugars, found as polymers in oat hulls, corn cobs, bran, and straw. Oat hulls give the highest yield.

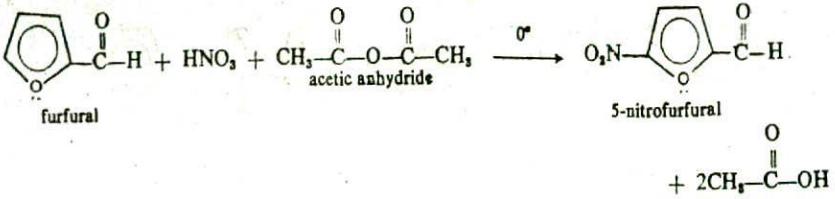


Properties. (*Physical*). Furfural is a colourless oil with a pleasant characteristic odour, bp 162°C. It is only slightly soluble in water, but it is miscible with most organic solvents. Furan is oxidised by air, the colour changing through shades of yellow and brown to almost black. These changes can be prevented by storing in the absence of oxygen or by adding antioxidant like hydroquinone.

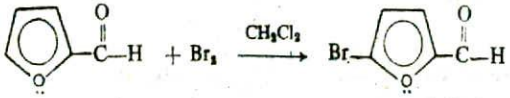
(*Chemical*). Furfural closely resembles benzaldehyde in chemical behaviour. It undergoes electrophilic substitution at the other available 2 (or α) position, that is, at *C-5*. Furfural is much more stable than furan towards acidic reagents.

Some of the important reactions of furfural are described below.

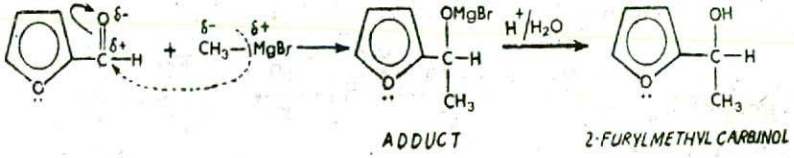
(1) **Nitration.** Furfural can be nitrated by a *cold* solution of nitric acid in acetic anhydride to yield 5-nitrofurfural.



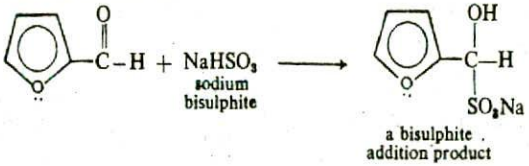
(2) **Bromination**. Furfural reacts with bromine in dichloromethane (methylene chloride) to give 5-bromofurfural.



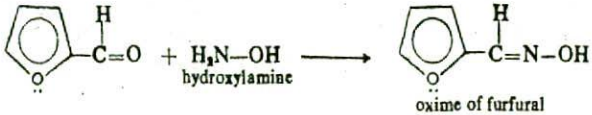
(3) **Grignard Addition.** The Grignard reagents add to the carbonyl group of furfural to form a product which on hydrolysis yields secondary alcohols. For example, with methylmagnesium bromide, 2-furylmethylcarbinol is obtained.



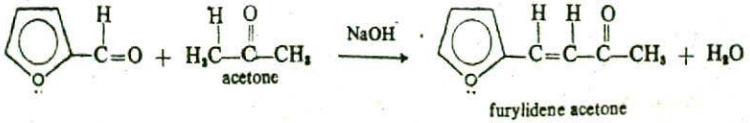
(4) **Bisulphite Addition.** Sodium bisulphite adds to the carbonyl group of furfural to form a bisulphite addition product.



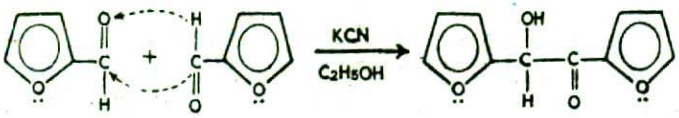
(5) **Reaction with Hydroxylamine.** Furfural condenses with hydroxylamine to form an oxime.



(6) **Reaction with Acetone** (*Claisen-Schmidt Condensation*). Furfural condenses with acetone in the presence of a base to give furylidene acetone.

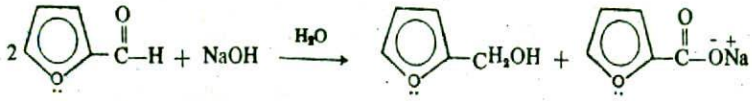


(7) **Reaction with ethanolic Potassium Cyanide.** Furfural undergoes benzoin type condensation with ethanolic potassium cyanide to form *furoin*.



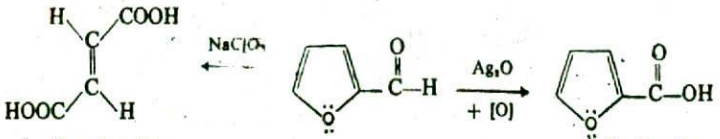
FURFURAL (2 MOLES) FUROIN

(8) **Reaction with Sodium Hydroxide** (*Cannizzaro Reaction*). Furfual undergoes self-oxidation and reduction with aqueous sodium hydroxide to yield a mixture of furfuryl alcohol and sodium salt of furoic acid.



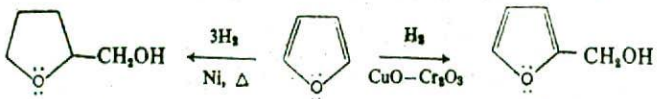
furfuryl alcohol sodium furoate

(9) **Oxidation**. Furfural may be oxidised by silver oxide or dilute potassium permanganate to give furoic acid. When a stronger oxidising agent like potassium chlorate is used, furfural undergoes ring opening, forming fumaric acid.



fumaric acid furoic acid

(10) **Reduction**. Furfural may be reduced with : (*i*) hydrogen and $CuO\text{-}CrO_3$ to give furfuryl alcohol; and (*ii*) hydrogen and nickel to form tetrahydrofurfuryl alcohol. Notice that in the first reaction only the carbonyl group is hydrogenated, but in the second case both ring and the carbonyl group are reduced.



tetrahydrofurfuryl alcohol FURAN furfuryl alcohol

Uses. Furfural is used : (1) as a wash in poultry houses to kill lice; (2) as a solvent for refining lubricating oils, and for removing butadiene from its mixture with butenes and butane; (3) in the manufacture of resins (*phenol-furfural resins*) of the Bakelite type; (4) as a solvent for cellulose esters; (5) as a paint remover; and (6) in the production of furan and many of its derivatives.

TETRAHYDROFURAN,

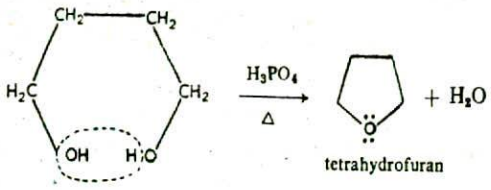


Tetrahydrofuran is another important derivative of furan. It is a saturated cyclic ether and is commonly designated as **THF**. It does not occur in nature.

Preparation. Tetrahydrofuran may be obtained :

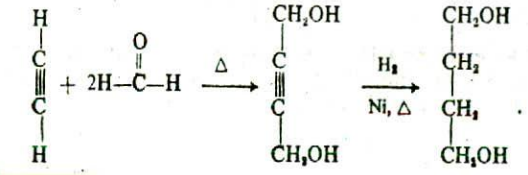
(1) By catalytic hydrogenation of furan.

(2) By acid catalysed dehydration of 1, 4-butanediol. (*Commercial*)



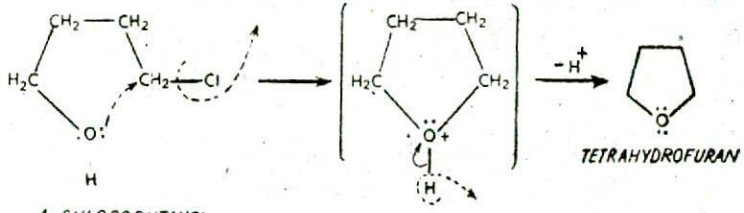
1,4-butanediol

1,4-Butanediol used in this reaction is obtained by the condensation of acetylene with formaldehyde to form 2-butyne-1,4-diol. This on hydrogenation in the presence of a catalyst yields 1,4-butanediol.



acetylene 2-butyne-1,4-diol 1,4-butanediol

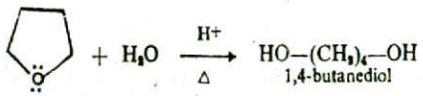
(3) By treatment of 4-chlorobutanol with water. In the presence of water 4-chlorobutanol undergoes intramolecular S_N2 reaction with ring closure to yield teterahydrofuran.



4-CHLOROBUTANOL

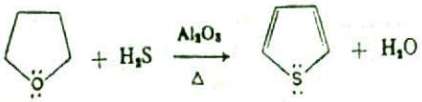
Properties. Tetrahodrofuran is a *poisonous* volatile liquid, bp 66°C. It is miscible with both water and most organic solvents. Some of its important reactions are given below

(1) **Hydrolysis.** Tetrahydrofuran undergoes hydrolysis in the presence of dilute sulphuric acid to yield 1,4-butanediol.



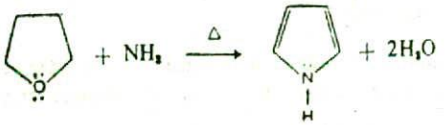
tetrahydrofuran

(2) **Reaction with Hydrogen Sulphide.** Tetrahydrofuran reacts with hydrogen sulphid in the presence of aluminium oxide at 300° to give tetrahydrothiophene



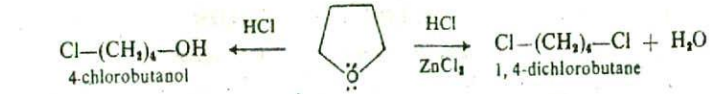
tetrahydrothiophene

(3) **Reaction with Ammonia.** Tetrahydrofuran reacts with ammonia at 300°C to form tetrahydropyrrole.



tetrahydropyrrole
(*pyrrolidine*)

(4) **Reaction with Hydrochloric Acid.** Tetrahydrofuran reacts with hydrochloric acid to give 4-chlorobutanol (tetramethylene chlorohydrin). When the reaction is carried out in the presence of $ZnCl_2$, 1,4-dichlorobutane is obtained.

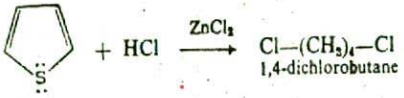


Uses. Tetrahydrofuran is used : (1) as a solvent in the preparation of Grignard reagents and its reactions; and (2) in the manufacture *nylon 6-6* and 1,3-butadiene.

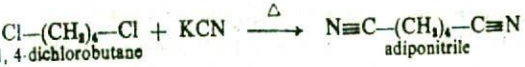
COMMERCIAL CONVERSION OF TETRAHYHROFURAN INTO NYLON 6-6

This involves the following five steps.

Step 1. Tetrahydrofuran is treated with HCl in the presence of $ZnCl_2$ to form 1,4-dichlorobutane.

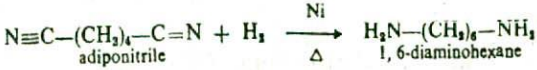


Step 2. 1,4-Dichlorobutane is heated with potassium cyanide to give adiponitrile.

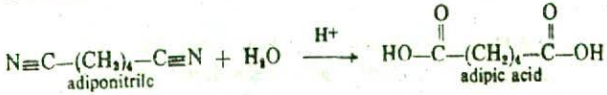


The adiponitrile so obtained is divided into *two* portions.

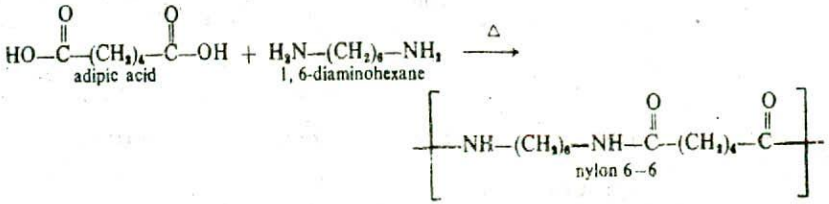
Step 3. One portion of adiponitrile is reduced in the presence of a catalyst to form 1,6-diaminohexane (**hexamethylenediamine**).



Step 4. The other portion of adiponitrile is hydrolysed in the presence of an acid catalyst to give adipic acid.



Step 5. Adipic acid and 1,6-diaminohexane are finally condensed at 280°C to yield *Nylon* 6-6.



This variety of nylon is known as *Nylon 6-6*, because diamine and the dicarboxylic acid contain *six* carbons each.

THIOPHENE, ***Thiophen,*** 

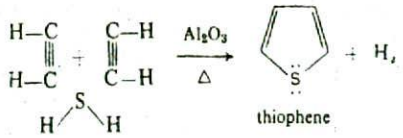
Thiophene is the sulphur containing counterpart of furan. It occurs in the light oil fraction of coal-tar and is usually present as an impurity in commercial benzene. The boiling points of thiophene and benzene are so close together that they cannot be separated by distillation.

Thiophene may be separated from benzene by shaking the mixture with cold concentrated sulphuric acid. Thiophene reacts to form thiophene-2-sulphonic acid, which is soluble in sulphuric acid. It can also be removed by refluxing the mixture with mercuric acetate which mercurates thiophene with much greater ease. Thiophene can be regenerated from the organomercury compound by heating with hydrochloric acid. The best method of removing thiophene from benzene is by shaking with Raney nickel.

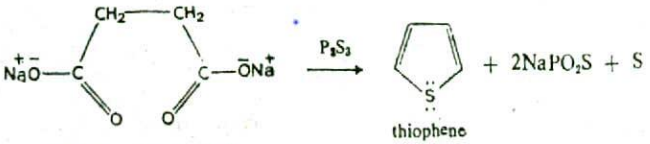
Thiophene gives a blue-green colour when it is added to a solution of isatin in sulphuric acid.

Preparation. Thiophene may be obtained :

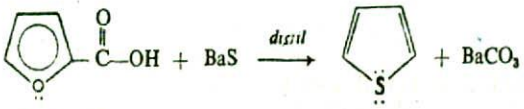
(1) By passing a mixture of acetylene and hydrogen sulphide through a tube containing aluminium oxide at 400°C.



(2) By heating sodium succinate with phosphorous trisulphide.

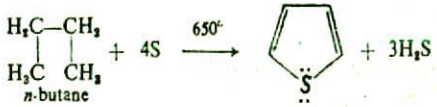


(3) By distillation of furoic acid with barium sulphide.



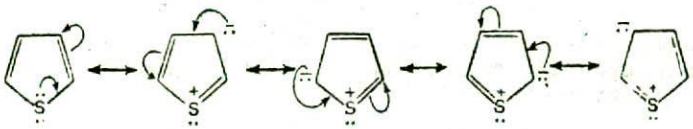
furoic acid thiophene

(4) By reaction of sulphur with *n*-butane in the gas phase at 650°C. (*Commercial*)

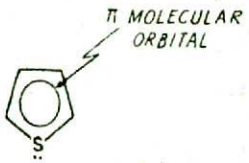


n-butane thiophene

Structure of Thiophene. The structure of thiophene is similar to that of furan. It is considered to be resonance hybrid of the following canonical forms,



and can be represented simply by a pentagon with a circle inside. The circle represents the π molecular orbital containing six electrons (*Aromatic Sextet*).

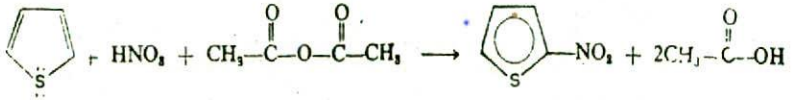


Properties (*Physical*). Thiophene is a colourless liquid, bp 84°C, with an odour very similar to that of benzene. It is insoluble in water, but miscible with most organic solvents.

(*Chemical*). Thiophene does not show any basic properties. It is much more stable to acids than either pyrrole or furan. Thiophene does not undergo the Diels-Alder reaction. However, some of its important reactions are described below.

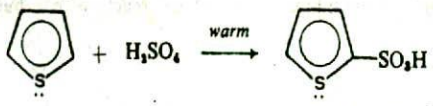
(1) **Electrophilic Substitutions**. Thiophene, like furan and pyrrole, undergoes electrophilic substitution reactions primarily at *C-2*. Substitution at *C-3* occurs only when both of the 2-positions (that is, α and α′) are already occupied.

(*a*) **Nitration**. Thiophene can be nitrated by solution of nitric acid in acetic anhydride to yield 2-nitrothiophene.



2-nitrothiophene

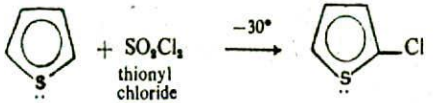
(*b*) **Sulphonation**. Thiophene undergoes sulphonation with concentrated sulphuric acid to give thiophene-2-sulphonic acid.



thiophene-2-sulphonic acid

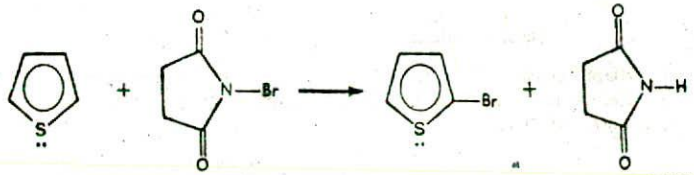
(*c*) **Halogenation**. Thiophene reacts vigorously with chlorine and bromine at room temperature to give polyhalogenated products but *does not* react at all with iodine. Much milder conditions have to be used to obtain monosubstituted derivatives.

Chlorination :

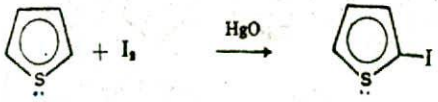


2-chlorothiophene

Bromination :

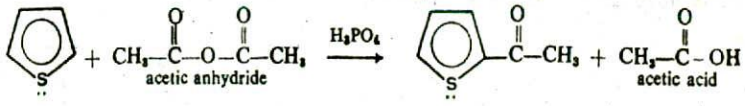


Iodination :



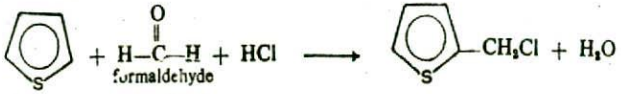
2-iodothiophene

(*d*) **Friedel-Crafts Acylation**. Thiophene may be acetylated with acetic anhydride in the presence of phosphoric acid, or with acetyl chloride in the presence of $SnCl_4$ to yield 2-acetylthiophene.



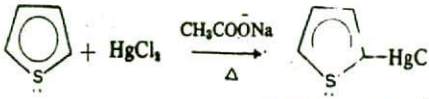
2-acetylthiophene

(*e*) **Chloromethylation**. Thiophene reacts with formaldehyde and hydrochloric acid to give 2-chloromethylthiophene.



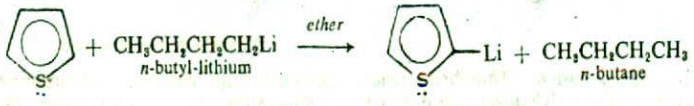
2-chl: eth; hiopi

(*f*) **Mercuration**. Thiophene undergoes mercuration with mercuric chloride in aqueous sodium acetate to produce 2-chloromercurithiophene.



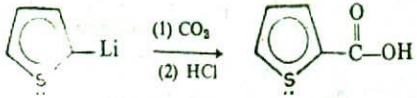
2-chlorome ophen

(*g*) **Reaction with *n*-Butyl-lithium.** Thiophene reacts with n-butyl-lithium to yield the 2-lithium derivative



2-thiophene-lithium

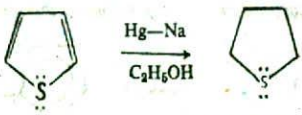
2-Thiophene-lithium can be used to prepare various 2-substituted thiophenes. For example, it reacts with carbon dioxide to form thiophene-2-carboxylic acid.



2-thiophene-lithium thiophene-2-carboxylic acid

(*h*) **Diazo Coupling.** Thiophene does not react with benzenediazonium chloride.

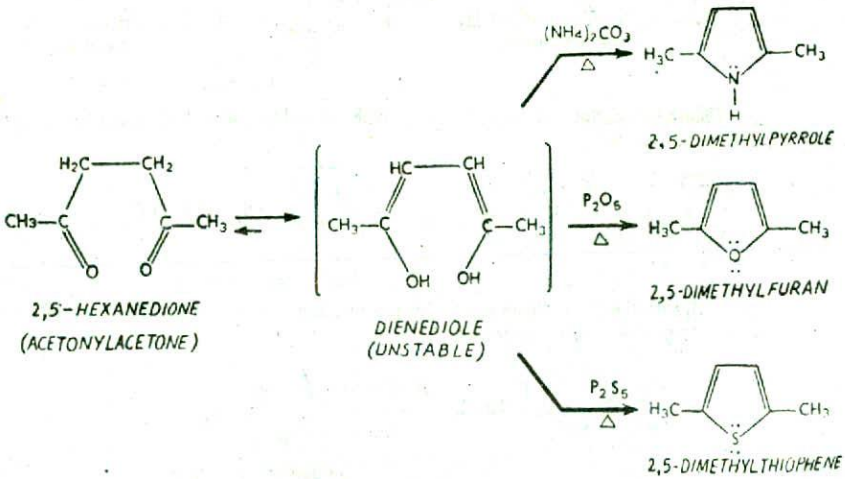
(2) **Reduction.** Thiophene may be hydrogenated by means of sodium amalgam and ethanol to tetrahydrothiophene.



tetrahydrothiophene

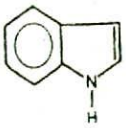
General Methods for Preparing Five-membered Heterocyclic Compounds

Five-membered heterocyclic compounds may be obtained from 1,4-diketones by ring closure. For example, 2,5-dimethyl derivatives of pyrrole, furan, and thiophene may be obtained from 2,5-hexanedione as shown below.



INDOLE AND ITS DERIVATIVES

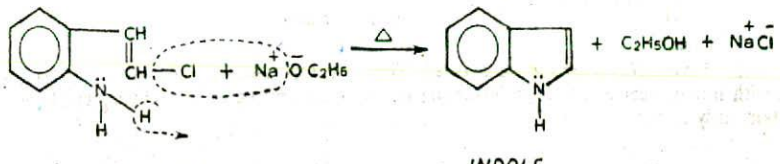
INDOLE, α, β-**Benzopyrrole,**



Indole consists of a benzene ring fused to the α, β positions of a pyrrole ring. It derives its name from the fact that it was first obtained by distilling oxindole, a degradation product of indigo, with zinc dust. Indole occurs in coal-tar and in the oils of jasmine and orange blossoms. It is also found as a part of the total structure of a number of alkaloids and amino acids *e.g.*, serotonin, reserpine, and tryptophan. Indole, like pyrrole, produces red colour with a pine splint moistened with concentrated hydrochloric acid.

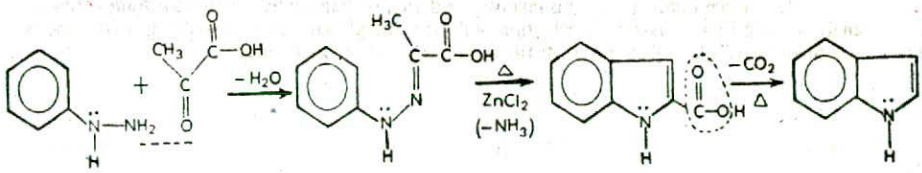
Preparation. Indole may be obtained :

(1) *By the Lipp Synthesis.* In this method *o*-amino-ω-chlorostyrene is heated with sodium ethoxide at 160—170°C.



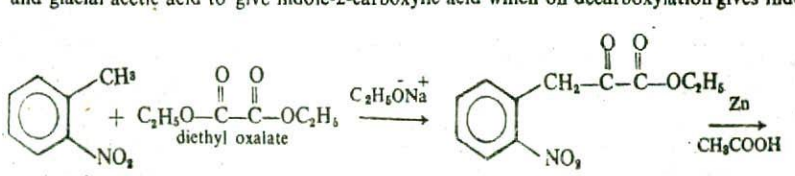
O-AMINO-ω-CHLOROSTYRENE *INDOLE*

(2) *By the Fischer Indole Synthesis.* In this method pyruvic acid is first treated with phenylhydrazine to form the corresponding phenylhydrazone. The hydrazone is heated with anhydrous zinc chloride or polyphosphoric acid ($H_3PO_4 + P_2O_5$) to give indole-2-carboxylic acid which on decarboxylation yields indole.

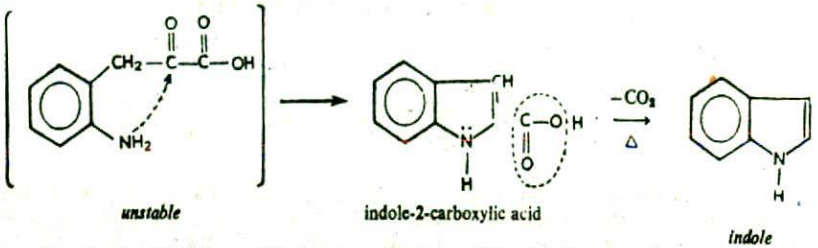


PHENYLHYDRAZINE *PYRUVIC ACID* *A PHENYLHYDRAZONE* *INDOLE-2-CARBOXYLIC ACID* *INDOLE*

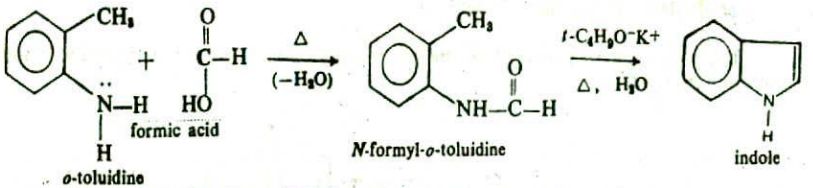
(3) *By the Reissert Synthesis.* In this method *o*-nitrotoluene is condensed with diethyl oxalate in the presence of a base to form a 2-*keto*-ester. This is then reduced with zinc and glacial acetic acid to give indole-2-carboxylic acid which on decarboxylation gives indole.



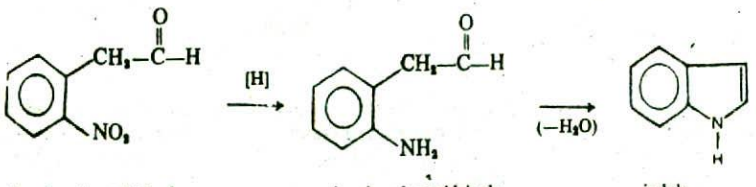
o-nitrotoluene 2-*keto*-ester



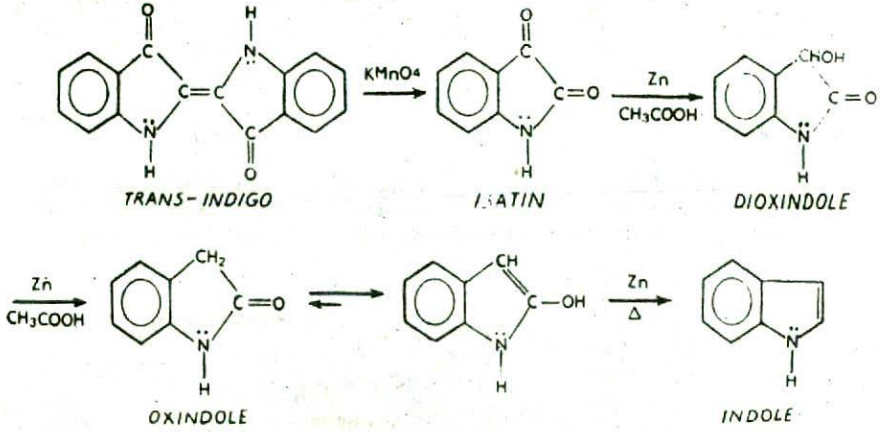
(4) *From o-Toluidine.* This involves treatment of *o*-toluidine with formic acid to form *N*-formyl-*o*-toluidine. This undergoes dehydration on heating with potassium *t*-butoxide to yield indole.



(5) *From o-Nitrophenylacetaldehyde.* This involves reductionof *o*-nitrophenylacetalde hyde with iron powder and sodium bisulphite to give *o*-aminophenylacetaldehyde, which cyclises spontaneously to yield indole.

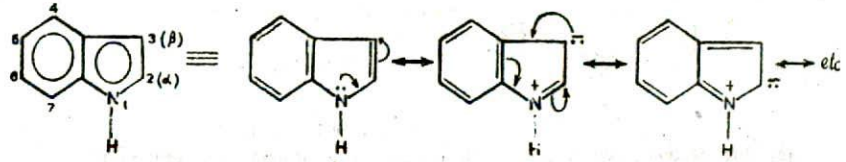


(6) *From trans-Indigo* This involves oxidation of trans-indigo with potassium permanganate to form isatin. Isatin on reduction with zinc and glacial acetic acid first gives dioxindole and finally oxindole. This is next distilled with zinc dust to give indole.



Structure of Indole. Like pyrrole, all ring atoms in indole (*eight* carbons + *one* nitrogen) are sp^2 hybridized. The sp^2 hybrid orbitals overlap with each other and with *s* orbitals of hydrogens to form C—C, C—N, C—H, and N—H σ bonds. Each ring atom also possesses a *p* orbital and these are perpendicular to the plane containing the σ bonds. The *p* orbitals on carbons contain one electron each and the *p* orbital on nitrogen contains two electrons (the lone pair). The lateral overlap of these *p* orbitals produces a π molecular orbitial containing *ten* electrons. Indole shows aromatic properties because the resulting π molecular orbital satisfies the Huckel's rule ($n=2$ in $4n+2$).

Indole is considered to be hybrid of several canonical forms, some of which are shown below.



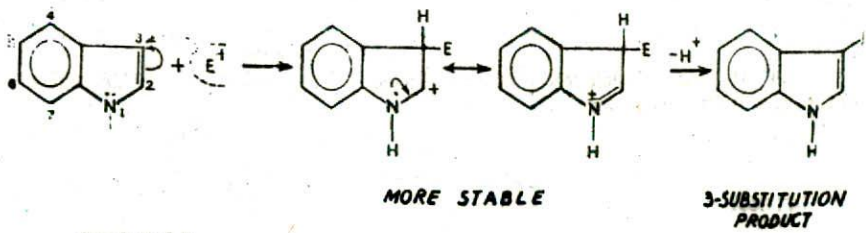
Properties (*Physical*). Indole is a colourless, volatile solid, mp 52°C. It is sparingly soluble in *cold* water, but dissolves in hot water and most organic solvents. Indole has a powerful odour which is pleasant and flowery in low concentrations. It is, in fact, used commercially as a perfume base. In contrast, indole and its 3-methyl derivative (*Skatole*) are responsible for the strong offensive odour of faeces.

(*Chemical*) Some of the important reactions of indole are given below :

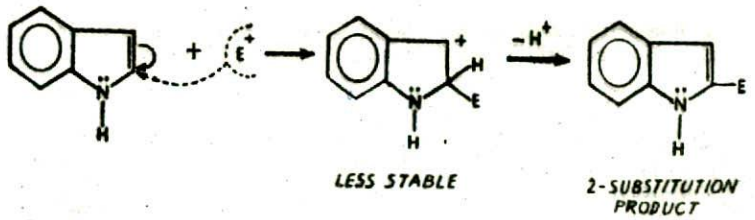
(1) **Basic and Acidic Character** Like pyrrole, indole is a weak base and also a weak acid. It is polymerised by strong acids and reacts with potassium hydroxide and Grignard reagents.

(2) **Electrophilic Substitutions.** Unlike pyrrole, indole undergoes electrophilic substitution at *C-3*. This is because *two* resonance forms can be written for intermediate cation obtained from attack at *C-3* (without disturbing the benzene ring), whereas only one such form is possible for substitution at *C-2*.

Attack at C-3

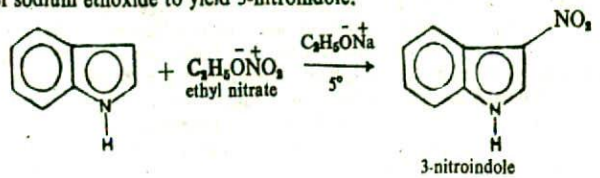


Attack at C-2



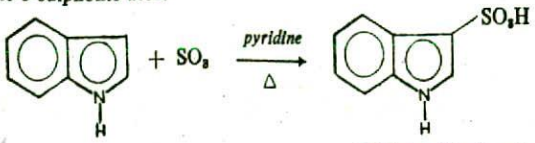
Consequently the former intermediate is more stable and the product with a substitu- *C-3* predominates. Substitution at *C-2* occurs only when the 3-position is already

(*a*) **Nitration.** Indole may be nitrated at low temperature with ethyl nitrate in the presence of sodium ethoxide to yield 3-nitroindole.



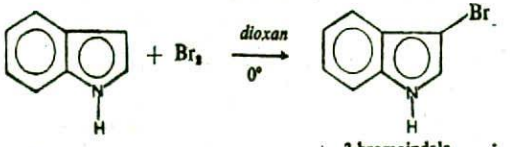
3-nitroindole

(*b*) **Sulphonation.** Indole undergoes sulphonation with sulphur trioxide in pyridine at 110°C to give indole-3-sulphonic acid.



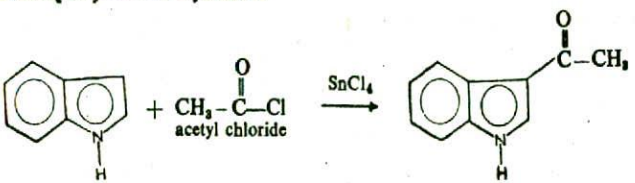
indole-3-sulphonic acid

(*c*) **Bromination.** Indole can be brominated with bromine in dioxan at 0°C to form 3-bromoindole.



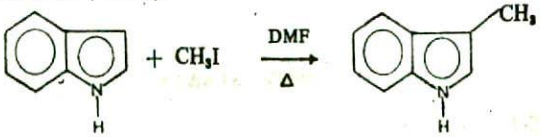
3-bromoindale

(*d*) **Friedel-Crafts Acylation.** Indole may be acetylated with acetyl chloride in the presence of $SnCl_4$ to yield 3-acetylindole.



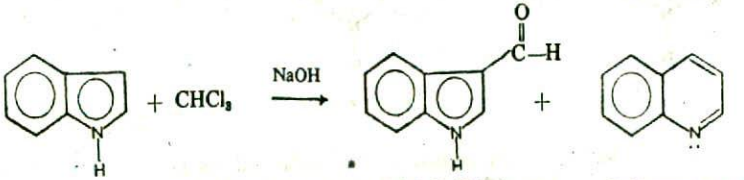
3-acetylindole

(*e*) **Alkylation.** Indole reacts with methyl iodide in dimethyl sulphoxide (*DMF*) at about 80°C to give 3-methylindole (*skatole*).



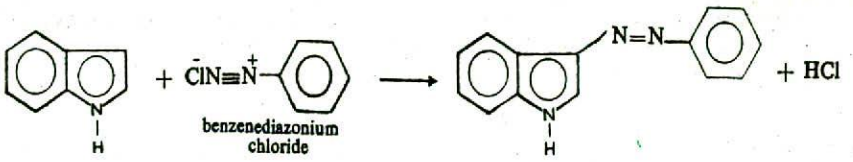
3-methylindole

(*f*) **Reimer-Tiemann Formylation.** Indole reacts with chloroform in the presence of alkali to yield indole-3-aldehyde (3-formylindole) and 3-chloroquinoline.



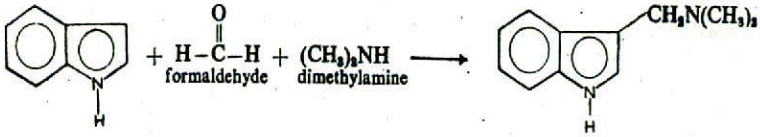
indole-3-aldehyde 3-chloroquinoline

(*g*) **Diazo Coupling.** Indole couples with benzenediazonium chloride in a weakly acidic solution to yield 3-phenylazoindole.



3-phenylazoindiole

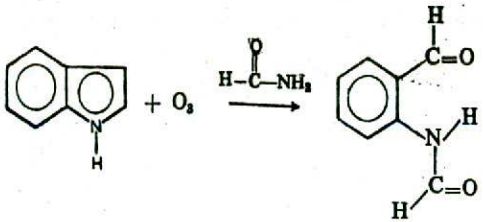
(*h*) **Mannich Reaction.** Indole undergoes Mannich reaction with formaldehyde and dimethylamine to give 3-dimethylaminomethylindole (*Gramine*).



3-dimethylaminomethylindole (gramine)

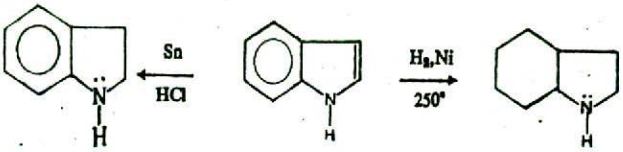
Gramine also occurs naturally in sprouting barley.

(3) **Oxidation.** Indole may be oxidised by ozone in formamide to give 2-formamidobenzaldehyde. Notice that this product is obtained by cleavage of the 2,3-bond in indole.



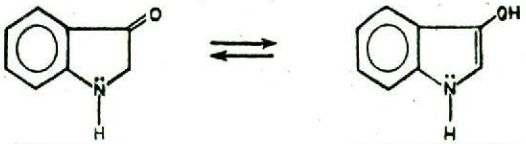
2-formamidobenzaldehyde

(4) **Reduction.** Mild reduction of indole with zinc (or tin) and hydrochloric acid yields 2,3-dihydroindole (*Indoline*). Catalytic reduction hydrogenates both rings and produces ocatahydroindole.



2,3-dihydroindole octahydroindole

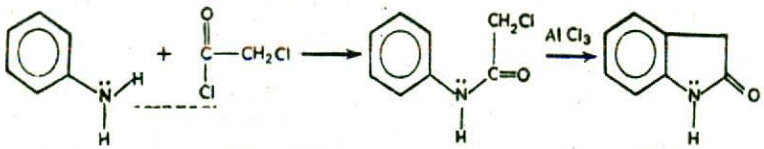
Indoxyl. It is an unstable yellow solid, mp 85°C, which is isomeric with 3-hydroxyindole.



INDOXYL 3-HYDROXYINDOLE

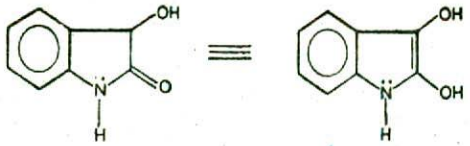
Indoxyl gives a red colour with ferric chloride and is *resinified* by concentrated hydrochloric acid. It is easily oxidised in alkaline solution by air (autoxidation) to give the dyestuff indigo. Indoxyl gives indole on distillation with zinc dust.

Oxindole. It is a colourless solid, mp 126-7°C. Oxindole may be obtained from aniline and chloroacetyl chloride as shown below.



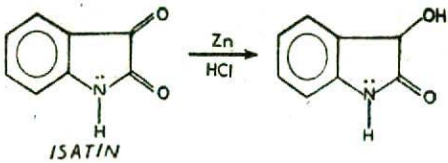
ANILINE CHLOROACETYL CHLORIDE OXINDOLE

Dioxindole. It is a colourless solid, mp 180°C, which is tautomeric with 2,3-dihydroxyindole.



DIOXINDOLE (3-HYDROXYOXINDOLE) 2,3-DIHYDROXYINDOLE

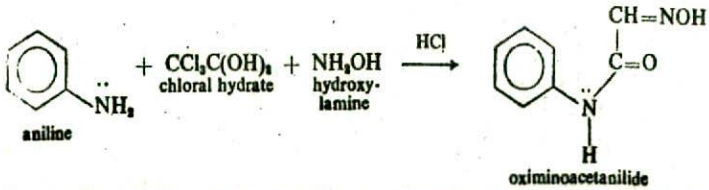
Dioxindole can be obtained by reducing isatin with zinc and hydrochloric acid.



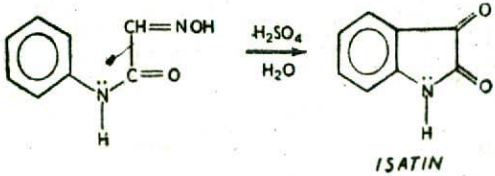
ISATIN

Isatin. It was first obtained by the oxidation with nitric acid. Today isatin is prepared from aniline by the following *two* steps.

Step 1. Treatment of solution of aniline in concentrated hydrochloric acid with chloral hydrate and hydroxylamine, produces crystals of oximinoacetanilide.

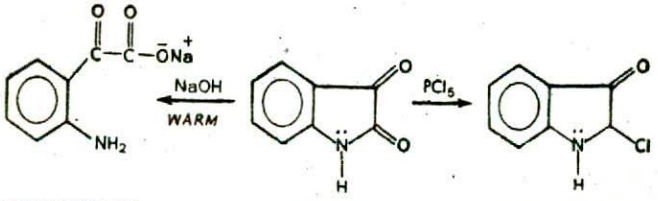


Step 2. Treatment oximinoacetanilide crystals with sulphuric acid yields isatin by ring closure.



ISATIN

Isatin is a red crystalline solid mp 200-201°C. It is sparingly soluble in water, but dissolves in ethanol. Isatin reacts with phosphorous pentachloride to form isatin chloride, and with sodium hydroxide to yield isatinic acid as sodium salt.



SODIUM SALT OF ISATINIC ACID *ISATIN* *ISATIN CHLORIDE*

SIX-MEMBERED RINGS

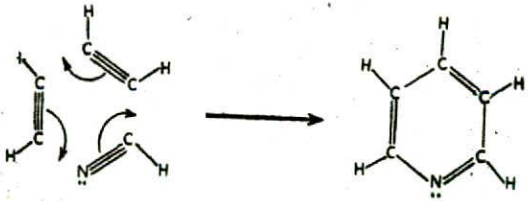
PYRIDINE,



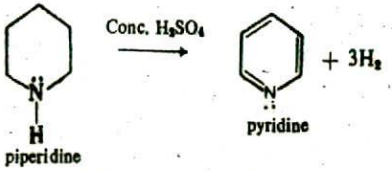
Pyridine is the most important of the heterocyclic ring systems. It occurs along with pyrrole in bone oil and in the light oil fraction (bp up to 170°C) of coal-tar. It can be isolated from the latter by extracting it with dilute sulphuric acid. This removes pyridine and other bases in the acid layer as soluble sulphates. The acid layer is then treated with sodium hydroxide when a dark brown liquid separates. Pyridine is obtained from this oily liquid by fractional distillation.

Preparation. Pyridine may be obtained :

(1) By passing a mixture of acetylene and hydrogen cyanide through a red-hot tube.

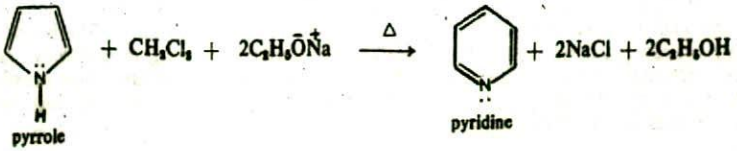


(2) By dehydrogenation of piperidine with concentrated sulphuric acid at 300°C or with nitrobenzene at 260°C.



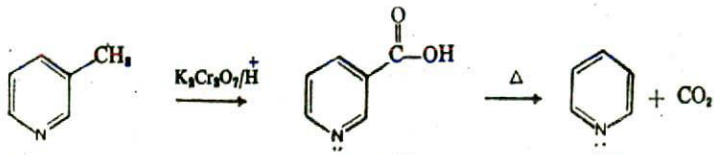
piperidine pyridine

(3) By heating pyrrole with dichloromethane in the presence of sodium ethoxide.



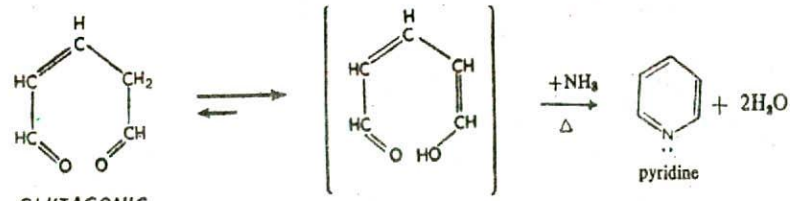
pyrrole pyridine

(4) *From β-Picoline (3-Methylpyridine).* This involves oxidation of β-picoline with potassium dichromate and sulphuric acid to give nicotinic acid (pyridine-3-carboxylic acid). Nicotinic acid on decarboxylation with calcium oxide yields pyridine.



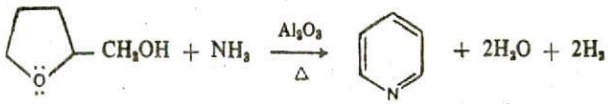
β-picoline nicotinic acid pyridine

(5) By heating glutaconic aldehyde with ammonia.



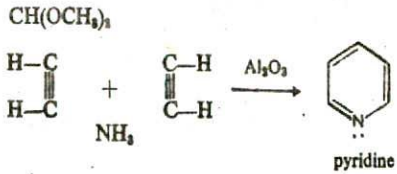
GLUTACONIC ALDEHYDE pyridine

(6) By heating tetrahydrofurfuryl alcohol with ammonia in the presence of aluminium oxide at 500°C. (*Commercial Method*)



Tetrahydrofurfuryl alcohol pyridine

(7) By reaction of acetylene with ammonia and formaldehyde dimethylacetal in the presence of aluminium oxide at 500°C. (*Commercial Method*)



pyridine

Structure of Pyridine. In pyridine all ring atoms (*five* carbons + *one* nitrogen), are sp^2 hybridized. Two of the sp^2 orbitals on each atom overlap with each other to form the C—C and C—N σ bonds. The third sp^2 orbital on each carbon atom overlaps with an *s* orbital from hydrogen to form the C—H σ bonds; the third sp^2 orbital on nitrogen is occupied by the nitrogen lone pair electrons (Fig. 47·7). All σ bonds in pyridine lie in one plane and all bond angles are approximately equal to 120°C.

Also each ring atom in pyridine possesses an unhybridized *p* orbital (containing *one* electron) and these are perpendicular to the plane containing the σ bonds. The lateral overlap of the *p* orbitals produces a delocalized π molecular orbital containing six electrons (Aromatic Sextet). One half of this π molecular orbital lies above and the other half below the plane of σ bonds (Fig. 47·8). Pyridine shows some aromatic properties because the resulting molecular orbital satisfies the Huckel's rule ($n=1$ in $4n+2$).

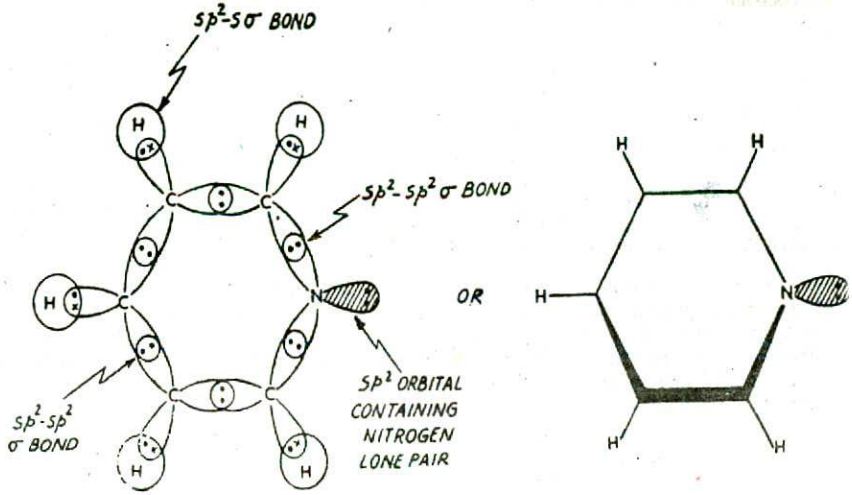


Fig. 47·7. Formation of σ bonds in pyridine.

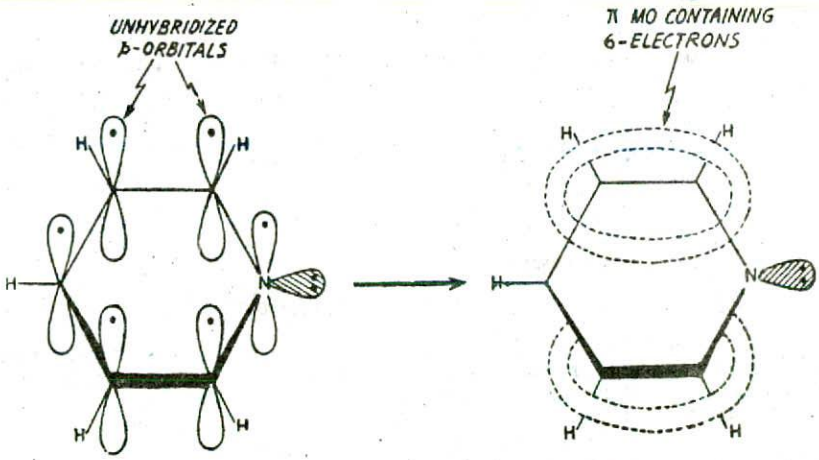


Fig. 47·8. The unhybridized *p* orbitals in pyridine overlap with each other to form a delocalized π molecular orbital above and below the plane of σ bonds. The nitrogen lone pair electrons being in sp^2 hybrid orbital do not interact with π molecular orbital.

A common shorthand representation of pyridine is simply hexagon, a six-membered ring, with a circle inside (Fig. 47·9). The circle again represents the π molecular orbital.

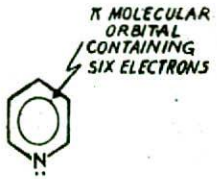
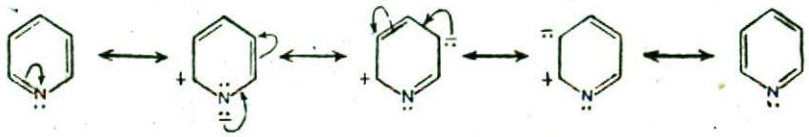


Fig. 47·9. Simplified representation of pyridine.

According to the resonance theory, pyridine is considered to be hybrid of the following five contributing structures.



Measurement of bond lengths by X-ray analysis confirms the hybrid nature of the pyridine molecule. The C—C and C—N bond lengths of 1·39 Å and 1·37 Å are intermediate between those corresponding to a *single* and a *double* bond.

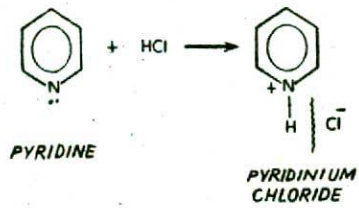
Properties (*Physical*). Pyridine is a colourless liquid, bp 115C°. It has a very characteristic pungent and disgusting odour. Pyridine is miscible with water and most organic solvents. It is very hygroscopic. Pyridine reacts with sodium and so should be dried over solid potassium hydroxide or barium oxide. The presence of water in pyridine can be detected easily by adding pure benzoyl chloride. If water is present, a precipitate of benzoic anhydride will be formed immediately.

Almost all classes of organic compounds are soluble in pyridine, even many of the high melting solids which scarcely dissolve in solvents such as ethanol and benzene. It is consequently used as a solvent.

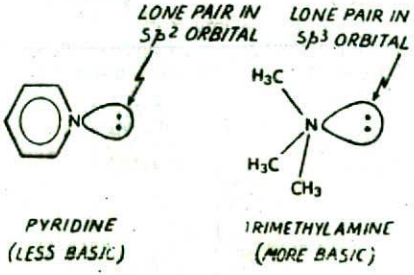
Pyridine forms an azeotrope with water, which boils at 92–93°C.

(*Chemical*). The main chemical reactions of pyridine are described below.

(1) **Basic Character**. Pyridine behaves as a base ($pK_a = 5·2$). It reacts with acids to form fairly stable salts.

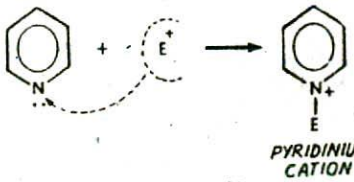


The reason for the basic character of pyridine is that the nitrogen lone pair being in sp^2 hybrid orbital is not involved in the formation of the delocalized π molecular orbital. It is readily available for the formation of a new N—H bond with proton. Pyridine is a stronger base than pyrrole (or aniline) in which the basicity is reduced by delocalization of the nitrogen lone pair. On the other hand, pyridine is a considerably weaker base than trimethylamine (a typical aliphatic tertiary amine).



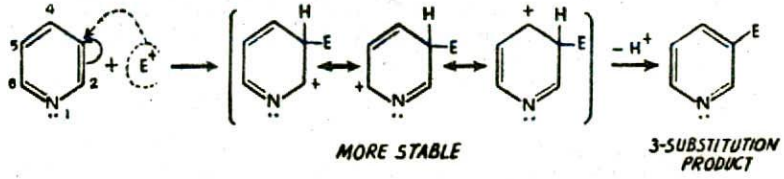
This is probably due to the difference in the nature of hybrid orbitals containing the nitrogen lone pair in the two molecules. In pyridine it is an sp^2 orbital; in trimethylamine it is an sp^3 orbital. Recall that sp^2 orbitals are smaller (due to more *s* character) than the sp^3 orbitals. This means that the lone pair of electrons on nitrogen in pyridine is more closely associated with the nitrogen nucleus. It is, therefore, less available for the formation of a bond with proton and consequently the relative bascity is reduced.

(2) **Electrophilic Substitutions.** Pyridine is considerably less reactive than benzene towards electrophilic substitution. This is so as : (*i*) the nitrogen atom in pyridine, because of its electronegativity lowers the electron density around the ring carbons ; and (*ii*) the usual electrophiles can coordinate with the lone pair of electrons on nitrogen to form resonance stabilized pyridinium salts.

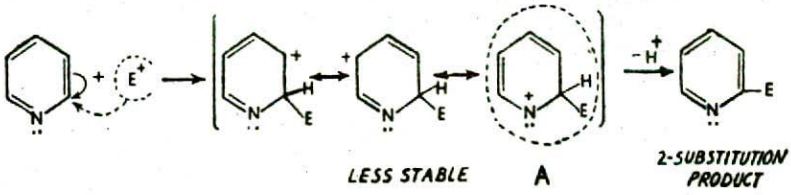


Pyridine, however, does undergo electrophilic substitution reactions when extremely vigorous reaction conditions are used. Substitution occurs almost exclusively at *C-3* (β-position). This can be understood if we follow our guide of examining the intermediate cation.

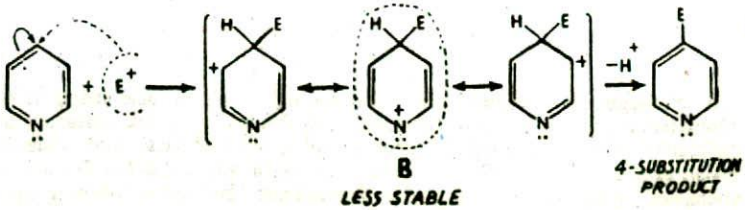
Attack at C-3



Attack at C-2

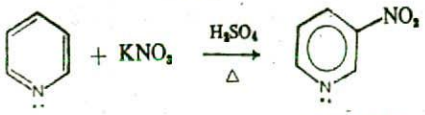


Attack at C-4



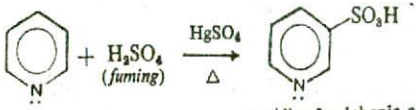
The contributing forms (*A*) and (*B*) which result from attack at *C-2* and *C-4* respectively are energetically unfavourable and may be ignored. This is because the nitrogen atom in these forms has only *six* electrons. Thus, the intermediates arising from attack at *C-2* and *C-4* have two resonance forms each. Consequently the product with a substituent at *C-3* predominates. If *C-3* is already blocked, substitution will occur at the other available β-position, that is, at *C-5*.

(*a*) **Nitration.** Pyridine undergoes nitration (in poor yield) with potassium nitrate in the presence of sulphuric acid at 300°C to yield 3-nitropyridine.



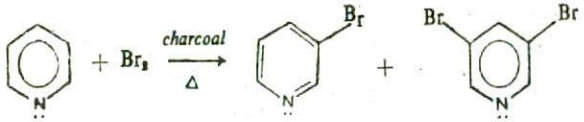
3-nitropyridine

(*b*) **Sulphonation.** Pyridine undergoes sulphonation with fuming sulphuric acid in the presence of mercuric sulphate at 230°C to give pyridine-3-sulphonic acid.



pyridine-3-sulphonic acid

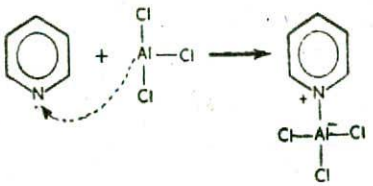
(*c*) **Bromination.** Pyridine may be brominated by passing the vapours of pyridine and bromine over charcoal catalyst at 300°C to yield 3-bromopyridine and 3,5-dibromopyridine.



3-bromopyridine 3, 5-dibromopyridine

When temperature of 500°C is used, a mixture of 2-bromopyridine and 2,6-dibromopyridine is obtained. At this temperature substitution probably occurs by a free radical mechanism, the active agent being bromine atom obtained by homolysis of bromine molecule.

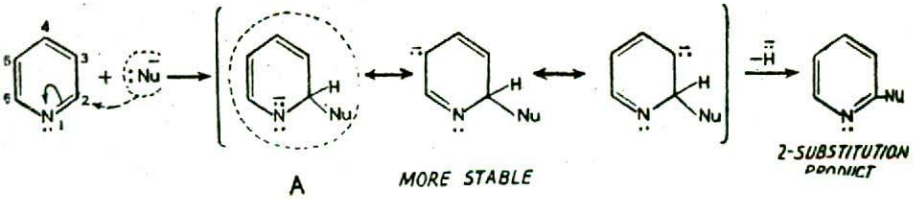
(*d*) **Friedel-Crafts Acylation and Alkylation.** Pyridine does not undergo Friedel-Crafts acylation and alkylation. This is because the Lewis acids (*e.g.*, $AlCl_3$) which are used as catalysts in these reactions coordinate with the lone pair of electrons on nitrogen.



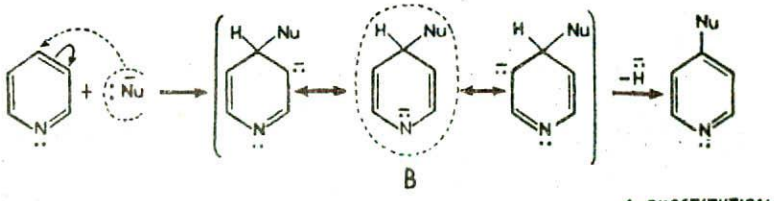
PYRIDINE-ALUMINIUM COMPLEX

(3) **Nucleophilic Substitutions.** Unlike benzene and pyrrole, pyridine undergoes nucleophilic substitution reactions. The same electronegativity that makes pyridine unreactive toward electrophilic substitution makes it highly reactive toward nucleophilic substitution. Substitution occurs mainly at *C-2* (or at *C-4* if *C-2* is blocked) Preference of attack at *C-2* or *C-4* over *C-3* is again rationalised on the basis of stabilities of intermediates. Nu: in the following equations, represents a nucleophile.

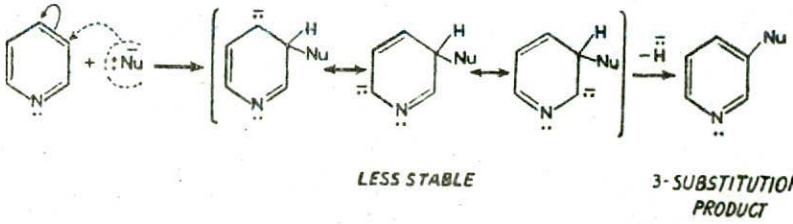
Attack at C-2



Attack at C-4

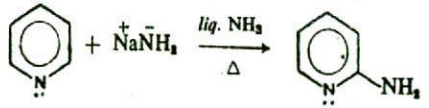


Attack at C-3



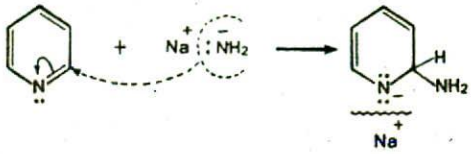
Notice that attack at *C-2* and *C-4* in pyridine involves intermediates (*A* and *B*) in which the negative charge is spread over nitrogen (more electronegative than carbon) as well as carbons. This leads to the enhanced stability of these intermediates. Consequently the products with substituents at *C-2* and *C-4* predominate.

(*a*) **Reaction with Sodamide** (*Chichibabin Reaction*). Pyridine reacts with sodamide in liquid ammonia at about 100°C to form 2-aminopyridine.

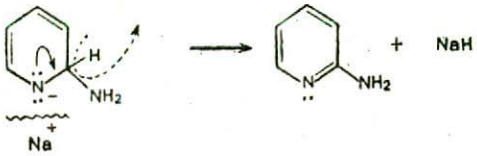


MECHANISM. The mechanism of the above reaction involves the following *three* steps.

Step 1. The nucleophile ($:\bar{N}H_2$) attacks the *C*-2 position in pyridine.



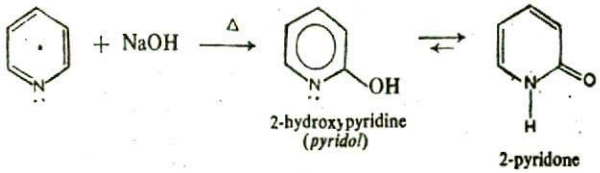
Step 2. Hydride ion (:H) is eliminated as sodium hydride to yield *2-aminopyridine.*



Step 3. Sodium hydride is removed by reaction with liquid ammonia to give back sodamide.

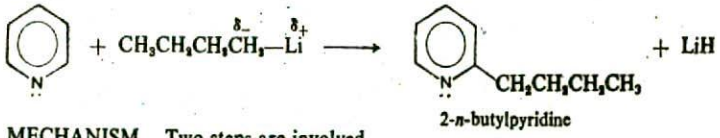
$$NaH + NH_3 \longrightarrow \overset{+}{N}a\overset{-}{N}H_2 + H_2$$

(*b*) **Reaction with Sodium Hydroxide.** Pyridine reacts with sodium hydroxide at 300°C to yield an equilibrium mixture of 2-hydroxypyridine and 2-pyridone. The reaction is carried out in the presence of oxygen (or air).



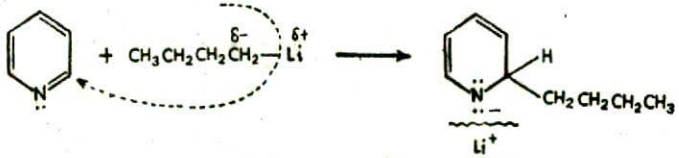
Infra-red studies indicate that 2-hydroxypyridine is present only in small amount, and 2-pyridone is the major product.

(*c*) **Reaction with *n*-Butyl-lithium.** Pyridine reacts with *n*-Butyl-lithium at 100°C to give 2-*n*-butylpyridine.

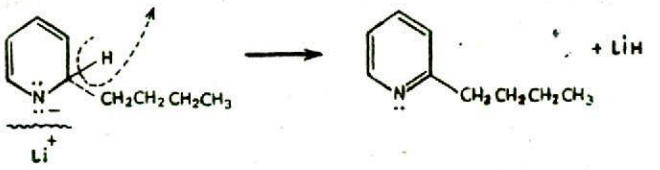


MECHANISM. Two steps are involved.

Step 1. The nucleophile ($CH_3\bar{C}HCH_2CH_3$) attacks the C-2 position in pyridine.

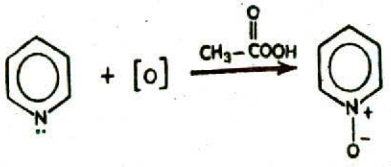


Step 2. Hydride ion (:H) is eliminated as lithium hydride to yield 2-*n*-butylpyridine.



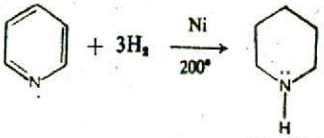
2-*n*-butylpyridine

(4) **Oxidation.** Like benzene, pyridine is quite stable towards mild oxidising agents. It does not react with chromic acid or nitric acid. However, it may be oxidised by peracetic acid to give pyridine-*N*-oxide.



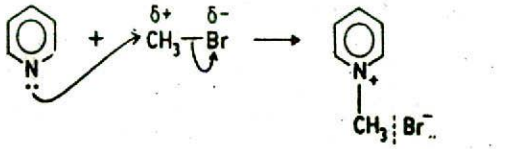
PYRIDINE-N-OXIDE
(PYRIDINE-1-OXIDE)

(5) **Reduction.** Pyrrole undergoes reduction with lithium aluminium hydride ($LiAlH_4$), or hydrogen in the presence of nickel catalyst to form piperidine.



piperidine

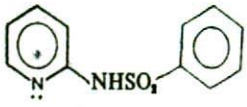
(6) **Reaction with Alkyl Halides.** Pyridine reacts with alkyl halides to form *N*-alkyl pyridinium halides. For example, with methyl bromide it yields crystalline *N*-methylpyridinium bromide.



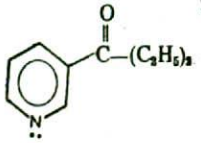
N-METHYLPYRIDINIUM BROMIDE
(1-methylpyridinium bromide)

Uses. Pyridine is used : (1) in organic synthesis as a basic solvent, whereby it not only exerts a catalytic action but also can combine with acids produced in reactions. For example, acylation and benzoylation takes place smoothly in pyridine solution; (2) to *denature* ethyl alcohol; and (3) as a starting material in the preparation of sulphapyridine, Zelan, and niacin.

Sulphapyridine and Coramine. Sulphapyridine is a colourless crystalline solid, mp 191-193°C. Although it is known to have severe side-effects, sulphapyridine has been used in the treatment of pneumonia, genorrhoea and other infectious diseases.



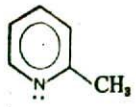
sulphapyridine



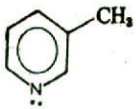
coramine

Coramine is widely used as a respiratory stimulant.

Picolines. The monomethyl derivatives of pyridine are called *picolines*. They occur in bone oil and in coal-tar, and are obtained from the latter source. There are three isomeric picolines, known as the α-, β-, and γ-picolines, or the 2-, 3-, and 4-methylpyridines.



α-picoline
(*2-methylpyridine*)
bp 129·4°

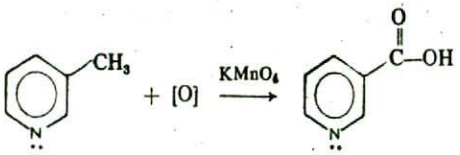


β-picoline
(*3-methylpyridine*)
bp 143·5°



γ-picoline
(*4-methylpyridine*)
bp 143·0°

Picolines undergo oxidation with potassium permanganate to yield carboxy derivatives of pyridine. For example, β-picoline gives nicotinic acid.

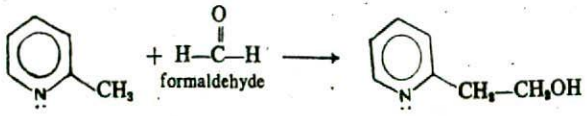


β-picoline

nicotinic acid
(*pyridine-3-carboxylic acid*)

2-Vinylpyridine. It may be obtained from α-picoline (2-methylpyridine) by the following *two* steps.

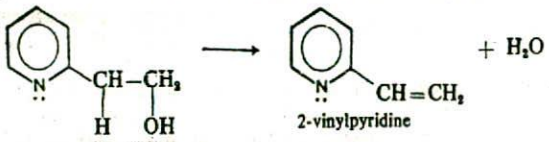
Step 1. α-Picoline is condensed with formaldehyde to form 2-β-hydroxyethylpyridine.



α-picoline

2-β-hydroxyethylpyridine

Step 2. Dehydration of 2-β-hydroxyethylpyridine yields 2-vinylpyridine.



2-β-hydroxyethylpyridine

2-vinylpyridine

2-Vinylpyridine undergoes polymerization in the same way as styrene. The copolymerization of 2-vinylpyridine and butadiene yields elastomers which adhere well to nylon fibres and are used in the manufacture of automobile tyres. Incorporation of 2-vinylpyridine during the

polymerization of acrylonitrile produces polyacrylonitrile (*PAN*) fibres which have basic properties, and thus are easily dyed with acid dyes.

PIPERIDINE,

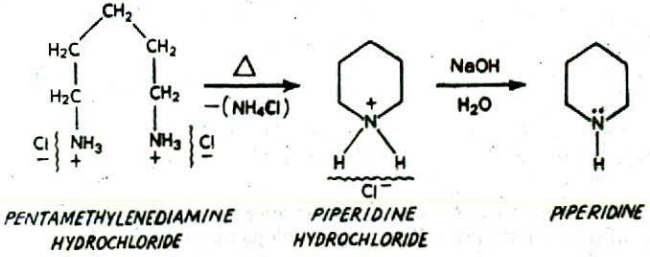


Piperidine derives its name from the fact that it was first obtained by the hydrolysis of piperine, one of the alkaloids of pepper.

Preparation. Piperidine may be obtained :

(1) By the hydrogenation of pyridine over nickel at about 200°C.

(2) From pentamethylenediamine hydrochloride by the following steps.



Structure of Piperidine. In piperidine all ring atoms (*five* carbons+*one* nitrogen) are sp^3 hybridized, and all bond angles are approximately equal to 109°28′. It is a non-planar molecule and preferably adopts a conformation analogous to the chair form of cyclohexane (Fig. 47·10).

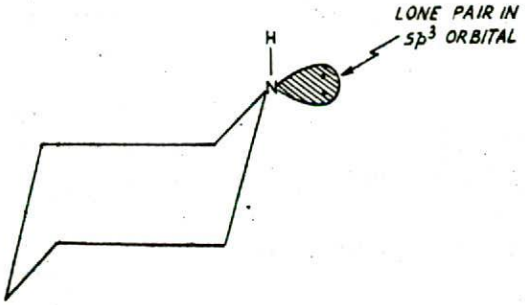


Fig.47·0. Chair form of piperidine.

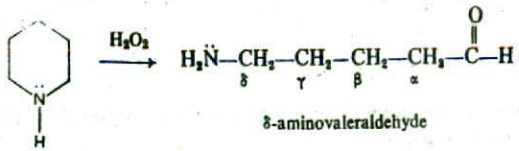
Properties. Piperidine is a colourless liquid, bp 106°C, which has an amine-like smell. It is miscible with water, and most organic solvents. Piperidine is a much stronger base than pyridine or ammonia ($pK_a = 11·2$). It forms salts with acids.

Piperidine behaves like a typical secondary amine in its chemical behaviour. It reacts with acetyl chloride, benzoyl chloride, alkyl halides, and nitrous acid in the same manner as secondary aliphatic amines do. On heating with concentrated sulphuric acid to 300°C, it is oxidised to pyridine.

Uses. Piperidine is used : (1) as a catalyst for a number of reactions, for example, the condensation of aldehydes with malonic acid; and (2) as an accelerator in the vulcanization of rubber.

Methods of Opening Heterocyclic Rings. A number of methods (in which piperidine is taken as an example) are described below for opening of heterocyclic rings. They are of great value in the determination of the structure of heterocyclic compounds.

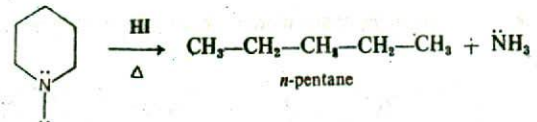
(1) *By Oxidation.* This involves treatment with hydrogen peroxide.



piperidine

δ-aminovaleraldehyde

(2) *By Reduction.* This involves treatment with hydriodic acid at about 300°C.

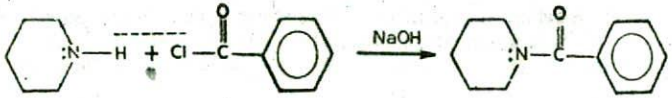


piperidine

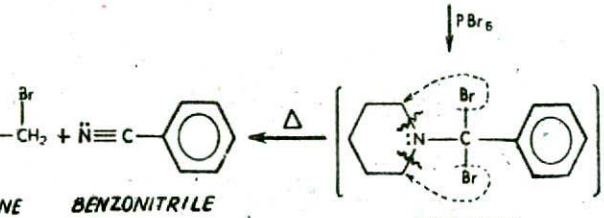
n-pentane

(3) *By Hofmann's Method of Exhaustive Methylation.* This is based on the observation that many quaternary ammonium hydroxides on heating lose water to give an unsaturated hydrocarbon and a tertiary amine.

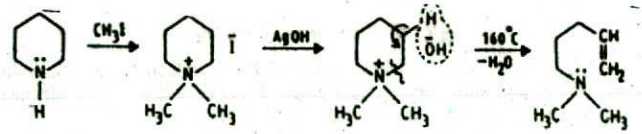
(4) *By Von Braun's Method.* This involves treatment with benzoyl chloride to form the *N*-benzoyl derivative, which is subsequently treated with phosphorous pentabromide

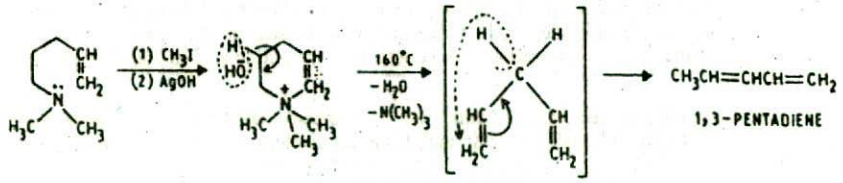


PIPERIDINE BENZOYL CHLORIDE N-BENZOYLPIPERIDINE



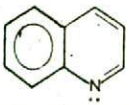
1,5-DIBROMOPENTANE BENZONITRILE





UNSTABLE

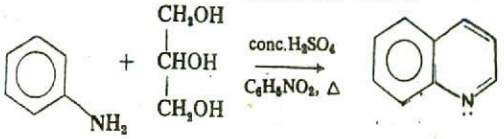
1,3-PENTADIENE

QUINOLINE, *α, β-Benzopyridine,* 

Quinoline consists of a benzene ring fused to the α, β positions of a pyridine ring. It derives its name from the fact that it was first obtained by heating the famous antimalarial alkaloid *quinine*, with alkali. Quinoline occurs in coal-tar, bone oil, and in *angostura* bark.

Preparation. Quinoline may be obtained :

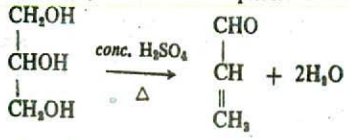
(1) *By Skraup Synthesis.* In this reaction, a mixture of aniline and glycerol is heated in the presence of sulphuric acid and a mild oxidising agent, usually nitrobenzene or arsenic pentoxide. The reaction is exothermic and tends to become very violent. Ferrous sulphate or boric acid is generally added to make the reaction less violent.



aniline glycerol quinoline

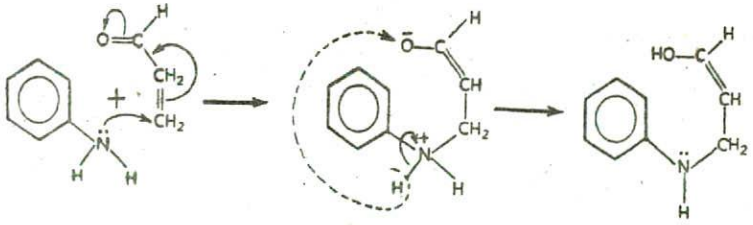
MECHANISM. The mechanism of this reaction is not completely understood. However, it is believed that it proceeds by the following steps.

Step 1. Glycerol undergoes dehydration with sulphuric acid to give acrolein.



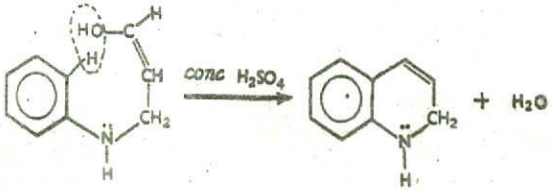
glycerol acrolein

Step 2. Aniline adds to acrolein (1,4-addition) to give (A).



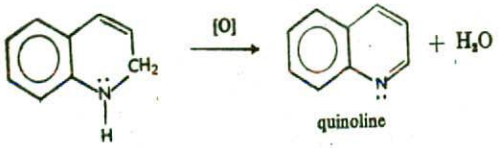
(A)

Step 3. (A) Undergoes ring closure in the presence of sulphuric acid to form 1,2-dihydroquinoline.



(A) 1,2-dihydroquipoline

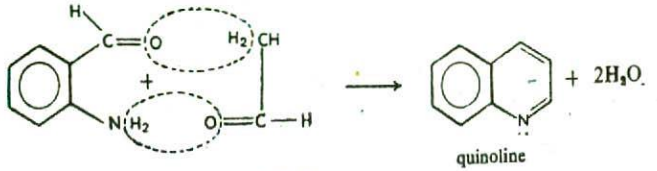
Step 4. 1,2-Dihydroquinoline undergoes oxidation with nitrobenzene to finally yield quinoline. Nitrobenzene itself is reduced to aniline which is reused in step (2).



1, 2-dihydroquinoline

This synthesis is used for the commercial preparation of quinoline. It is also important bacause by starting with substituted anilines, substituted quinolines can be made.

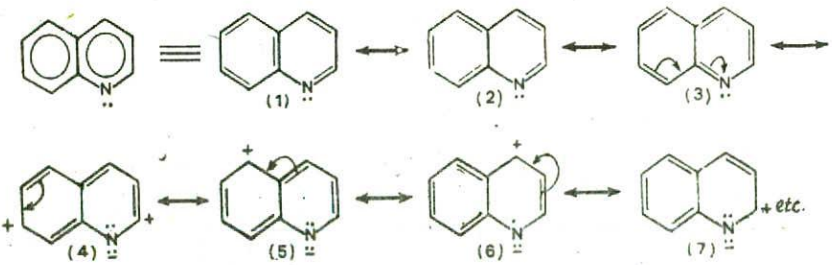
(2) *By the Friedlander Synthesis.* This involves the condensation of *o*-aminobenzalde hyde with acetaldehyde in the presence of an alkali.



O-AMINOBENZAL-DEHYDE ACETALDEHYDE

Structure of Quinoline. All ring atoms in quinoline are sp^2 hybridized. As in the case of pyridine, the nitrogen lone pair electrons reside in an sp^2 orbital, and are not involved in the formation of the delocalized π molecular orbital. It shows aromatic properties because its π orbital contains *ten* electrons and satisfies the Huckel's rule ($n=2$ in $4n+2$).

Quinoline is considered to be the hybrid of the following canonical forms.

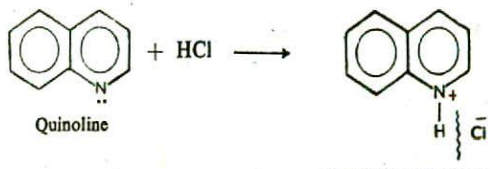


The first three structures are similar to the Kekule structures written for naphthalene. The last four, which are polar structures, show the effect of the electron-attracting nitrogen atom on the molecule.

Properties (*Physical*). Quinoline is a colourless liquid, bp 237°C. It turns yellow on standing, and has pyridine-like smell. Quinoline is miscible with most organic solvents, and dissolves in water to about 0·7 per cent at room temperature.

(*Chemical*). The main chemical properties of quinoline are described below.

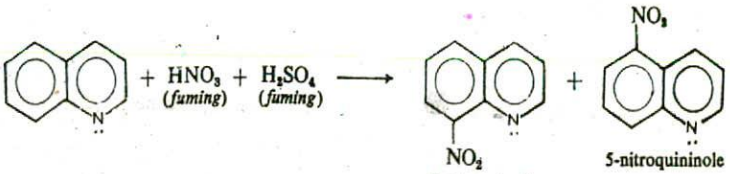
(1) **Basic Character.** Quinoline is a slightly weaker base (pK_a=4·94) than pyridine (pK_a=5·2). It reacts with acids to yield salts which are sparingly soluble in water.



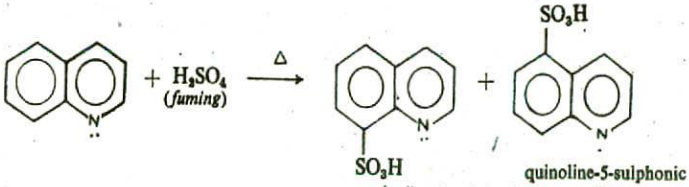
QUINOLINIUM CHLORIDE

(2) **Electrophilic Substitutions.** Quinoline undergoes electrophilic substitution reactions only under vigorous conditions, as was the case with pyridine. Substitution occurs at C-8 and C-5.

(*a*) **Nitration.** Quinoline undergoes nitration with fuming nitric acid in the presence of fuming sulphuric acid to give a mixture of 8-nitroquinoline and 5-nitroquinoline.

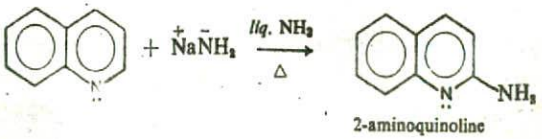


(*b*) **Sulphonation.** Quinoline may be sulphonated with fuming sulphuric acid at 220°C to yield a mixture of quinoline-8-sulphonic acid and quinoline-5-sulphonic acid.

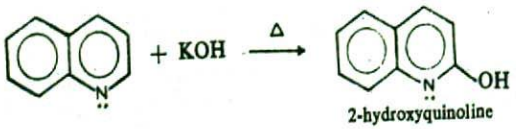


(3) **Nucleophilic Substitutions.** Like pyridine, quinoline undergoes nucleophilic substitution reactions. Substitution occurs at C-2 (or at C-4 if C-2 is blocked).

(*a*) **Reaction with Sodamide.** Quinoline reacts with sodamide in liquid ammonia at about 100°C to form 2-aminoquinoline.

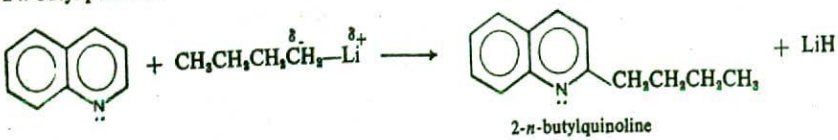


(*b*) **Reaction with Potassium Hydroxide.** Quinoline reacts with potassium hydroxide at 220°C to give 2-hydroxyquinoline.



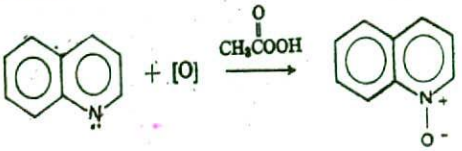
2-hydroxyquinoline

(c) **Reaction with *n*-Butyl-lithium.** Quinoline reacts with *n*-butyl-lithium to yield 2-*n*-butylquinoline.



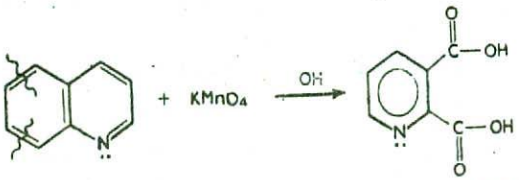
2-*n*-butylquinoline

(4) **Oxidation.** Quinoline is oxidised by peracetic acid to give quinoline-*N*-oxide.



QUINOLINE-N-OXIDE

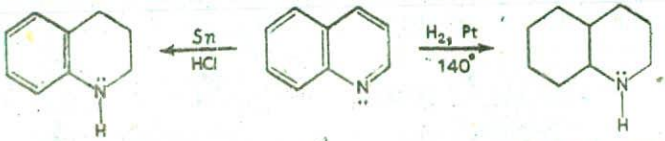
Oxidation with alkaline potassium permanganate yields pyridine-2,3-dicarboxylic acid.



PYRIDINE-2,3-DICARBOXYLIC ACID
(QUINOLINIC ACID)

The above reaction provides a major clue to the structure of quinoline because it shows the position of ring fusion relative to the nitrogen atom.

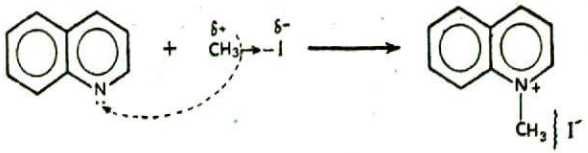
(5) **Reduction.** Mild reduction of quinoline with tin and hydrochloric acid gives 1,2,3,4-tetrahydroquinoline. Reduction with hydrogen and platinum catalyst produces decahydroquinoline.



1,2,3,4-TETRAHYDRO-QUINOLINE

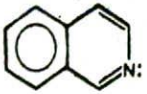
DECAHYDROQUINOLINE

(6) **Reaction with Alkyl Halides.** Quinoline reacts with alkyl halides to give *N*-alkylquinolinium halides. For example, with methyl iodide it yields *N*-methylquinolinium iodide.



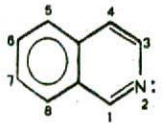
N-METHYLQUINOLIUM IODIDE
(1-METHYLQUINOLIUM IODIDE)

Uses. Quinoline is used : (1) in organic synthesis as a high-boiling basic solvent, whereby it not only exerts a catalytic action but also can combine with acids produced in reactions; (2) in the manufacture of pharmaceuticals, dyes and insecticides.

ISOQUINOLINE, β,γ-*Benzopyridine,* 

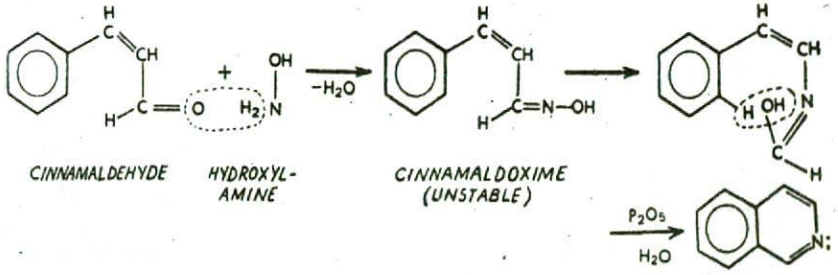
Isoquinoline consists of a benzene ring fused to the β, γ positions of a pyridine ring. It is isomeric with quinoline. Isoquinoline occurs in coal-tar and in bone oil. It is isolated from coal-tar in the form of a sparingly soluble sulphate. Isoquinoline is also found as part of the total structure of a number of alkaloids *e.g.*, papaverine and morphine.

Isoquinoline is one of the very few heterocyclic compounds in which numbering of the ring atoms does not start on the *hetero* atom. As in the case of naphthalene, the numbering starts adjacent to the benzene ring.



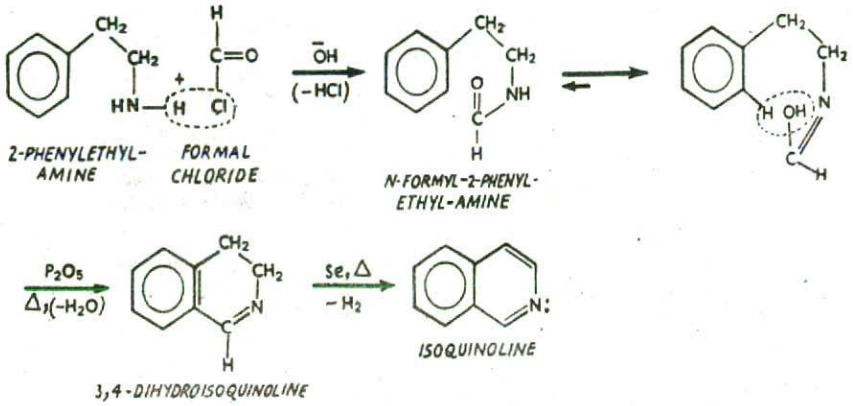
Preparation. Isoquinoline can be prepared :

(1) *From Cinnamaldehyde.* This involves condensation of cinnamaldehyde with hydroxylamine to form the corresponding oxime. The oxime is then heated with phosphorus pentoxide to yield isoquinoline. It is believed that the oxime first undergoes rearrangement which is then followed by ring closure.



CINNAMALDEHYDE *HYDROXYL-AMINE* *CINNAMALDOXIME (UNSTABLE)*

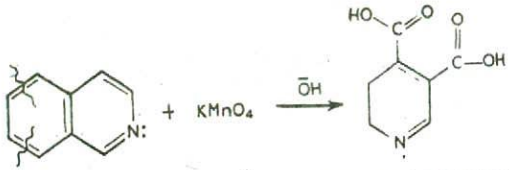
(2) *By the Bischler-Napieralski Synthesis.* In this reaction, 2-phenylethylamine is first treated with formyl chloride in the presence of a base to form *N*-formyl-2-phenylethylamine. This amide is next heated with phosphorous pentoxide in pyridine to give 3,4-dihydroisoquinoline which on oxidation (dehydrogenation) with palladium or selenium yields isoquinoline



Properties. Isoquinoline is a colourless solid (mp 26°C; bp 243°C) with a smell like that of benzaldehyde. It is volatile in steam, sparingly soluble in water, and is soluble in many organic solvents. It turns yellow on normal storage.

Isoquinoline ($pK_a = 5{\cdot}14$) is a stronger base than quinoline. It forms stable salts with acids.

Isoquinoline resembles quinoline in most of its chemical properties. Like quinoline, it undergoes electrophilic substitution at C-5 and C-8. It is oxidised by alkaline potassium permanganate to give pyridine-3,4-dicarboxylic acid (*Cinchomeronic acid*).



Oxidation with peracetic acid gives the *N*-oxide. Mild reduction of isoquinoline with tin and hydrochloric acid yields 1,2,3,4-tetrahydroisoquinoline. Reduction with hydrogen and platinium catalyst produces decahydroisoquinoline.

QUESTIONS

1. Write the structural formulas of pyrrole, pyridine, and thiophene. How is thiophene separated from benzene and how do you test for thiophene in benzene? Mention the properties of thiophene.
2. How would you prepare pyrrole? What are its chief uses?
3. How is pyridine obtained? Discuss its structure and mention its uses.
4. Discuss briefly the structures and comparative chemistry of pyridine and benzene.
5. How is pyridine prepared? How can it be converted into:

   (*a*) Pyridine-2-sulphonic acid; (*b*) piperidine; (*c*) 2-aminopyridine; and (*d*) pyridinium chloride.
6. Discuss briefly the chemistry of furan and pyrrole. How can a compound belonging to each of these ring systems be synthesised?
7. Draw the Molecular Orbital Picture of pyrrole (or pyridine), labelling each of the orbitals involved, and showing all bond angles.

8 Explain: (*i*) Electrophilic substitution in the case of furan takes place preferentially at 2 or 5 positions
(*ii*) Pyrrole is weakly acidic whereas pyridine is weakly basic. (*Udaipur BSc III, 1980*)

9. (*a*) In addition to electrophilic substitution reaction, what other types of reactions are given by furan ? Give suitable examples.
(*b*) Explain why furan is more reactive at position 2 than at position 3.
(*c*) Compare the bascicity and reactivity of pyrrole and pyridine. (*Banaras BSc III, 1980*)

10. Give any two reactions in which pyrrole resembles phenol. (*Calicut BSc III, 1980*)

11. Discuss the MO structure of Pyrrole. (*Punjab BSc Chem Engg, 1980*)

12. (*a*) Give one method for the preparation of Pyrrole, Furan and Thiophene.
(*b*) How are these classified as aromatic compounds ?
(*c*) How will you synthesise the following compounds :—
(*i*) 2-Aminopyridine (*ii*) 3-Aminopyridine (*Punjab BSc III, 1980*)

13. Describe one method of preparation and one property of any two of the following:
(*i*) Furan (*ii*) Thiophene (*iii*) Pyrrole.
(*Bombay BSc, 1980*)

14. Discuss the electrophilic substitution in Pyridine. (*Himachal BSc III, 1980*)

15. Explain Electrophilic and Nucleophilic substitution in Pyridine with the help of one example in each case. (*Kurukshetra BSc III, 1980*)

16. Pyrrole is weaker base than Pyridine. Explain. (*Guru Nanak Dev BSc III, 1980*)

17. (*a*) Show the steps involved in the preparation of furan from aldopentose. Give structural formulae.
(*b*) Indicate the steps in any one method of preparation of isoquinoline. (*Kerala BSc III, 1980*)

18. What are heterocyclic compounds ? How is pyridine isolated from coal tar ? How does pyridine react with:
(*i*) hot conc. H_2SO_4 (*ii*) Na/C_2H_5OH (*iii*) Br_2 ?
(*Delhi BSc III, 1980*)

19. Give methods of synthesis and discuss aromativity and orientation in:—
(*i*) Pyridine (*ii*) Isoquinoline. (*Baroda BSc III, 1980*)

20. Give one method of synthesis of pyridine and isoquinoline. (*Bangalore BSc III, 1980*)

21. (*a*) Describe important properties of pyrrole and pyridine.
(*b*) On the basis of Huckel's Rule account for the aromaticity in thiophene and benzene.
(*Gorakhpur BSc H, 1981*)

22. What are heterocyclic compounds ? Describe the important reactions of Pyridine and establish its structure. (*Aligarh BSc Hons, 1980*)

23. (*a*) Give the synthesis of: Furan, Pyrrole and Thiophene from 1,4-diketone.
(*b*) Starting with pyrrole, how will you get the following:
(*i*) 1-Nitropyrrole (*ii*) 2-Acetylpyrrole (*iii*) Pyrrole-2-sulphonic acid.
(*c*) Why is pyridine more basic than pyrrole ? (*Punjabi BSc II, 1981*)

24. (*a*) What are heterocyclic compounds ? Why are some of them classified as aromatic compounds ?
(*b*) Give resonance forms of Furan. (*Osmania BSc III, 1981*)

25. Justify the statement that Pyrrole, Thiophene and Furan are superaromatic compounds. How are these synthesised ? (*Rajasthan BSc III, 1981*)

26. How does pyridine react with:—
(*i*) HI at 300°C (*ii*) Sodamide ? (*Saugar BSc III, 1981*)

27. (*a*) Predict the products of reaction with pyrrole of the following reagents:
(*i*) Nitric acid in Acetic anhydride at —10°.
(*ii*) Sulphur trioxide in Pyridine.
(*iii*) Benezenediazonium chloride.
(*iv*) Bromine in alcohol.
(*b*) Give reason to justify pyridine is more basic than pyrrole. (*Maharishi Dayanand BSc III, 1981*)

28. (*a*) Illustrate the reactions which could be used to elucidate the structure of Pyridine.
(*b*) In what respects does the α-position of pyridine resemble closely the ortho or para position in nitrobenezene ? (*Kurukshetra BSc III, 1981*)

29. (*a*) Discuss the nucleophilic substitution reactions of pyridine.
(*b*) How will you explain:
(*i*) Electrophilic substitution in pyridine occurs chiefly in position 3 whereas it takes place in position 2 in pyrrole.
(*ii*) Greater basicity of pyridine as compared to that of pyrrole. (*Punjab BSc III, 1981*)

30. (*a*) Explain the following:—
(*i*) Electrophilic substitution in Pyrrole takes place at 2-position, whereas in Pyridine it is

at 3-position.

(*ii*) Pyridine is more basic than pyrrole.

(*iii*) Discuss the oribital picture of Pyridine. (*Himachal BSc III, 1981*)

31 What are heterocyclic compounds ? Describe the resonance hybrid in pyrrole. (*Himachal BSc III, 1982*)

32. (*a*) Give principal products of reaction of Pyrrole with the following reagents:

(*i*) Nitric acid in acetic anhydride at —10°C.

(*ii*) Chromium trioxide in sulphuric acid.

(*iii*) Potassium iodide-iodine solution.

(*iv*) Phenyldiazonium chloride. (*Guru Nanak Dev BSc III, 1982*)

33. Describe the preparation of furan. Discuss its aromatic character. How would you prepare the following compounds from furan :

(*a*) Tetrahydrofuran

(*b*) 2-Nitrofuran (*Dibrugarh BSc Hons, 1994*)

34. Explain the aromaticity of pyrrole. (*Cochin BSc, 1993*)

35. Explain : Pyridine is a much stronger base than pyrrole. (*Bangalore BSc III, 1993*)

36. Explain : Piperidine is a stronger base than pyridine. (*Delhi BSc Hons, 1994*)

37. Explain with the help of orbital diagram that nonbonding electron pair at nitrogen in pyridine is not involved in delocalisation. (*Sambalpur BSc Hons, 1994*)

38. Describe the synthesis of :

(*a*) Pyridine ; (*b*) Pyrrole ; (*c*) Furan ; (*d*) Quinoline ; and (*e*) Isoquinoline

39. How will you synthesise 3-aminopyridine from β-picoline. (*Madras BSc, 1994*)

Hint. Use the following steps: (*i*) $KMnO_4$; (*ii*) $SOCl_2$; (*iii*) NH_3; and (*iv*) NaOBr.

40. How will you synthesise 8-ethylquinoline from benzene ? (*Lucknow BSc, 1993*)

Hint. Use the following steps : (*i*) $CH_3CH_2Cl/AlCl_3$; (*ii*) HNO_3/H_2SO_4; (*iii*) H_2/Ni or Sn/HCl; and (iv) glycerol (Skraup synthesis).

41. Write a note on : Molecular orbital structure of pyrrole. (*Karnataka BSc, 1993*)

Chapter **48**

Alkaloids

The term alkaloid, meaning *'alkali-like'* has been used to designate :

The compounds of plant origin having one or more basic nitrogen atoms in heterocyclic ring systems, which induce pronounced physiological activity in animals and man.

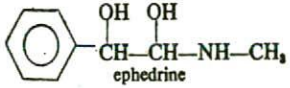
The above definition of the alkaloids is by no means perfect and does not cover all compounds classed as alkaloids.

(1) *Piperine*, the alkaloid of pepper, is not basic and has practically no physiological activity.

(2) Purines such as caffeine (in coffee and tea) and theobromine (in cocoa bean), which stimulate the nervous system, and are heterocycles containing nitrogens, conform to the definition of alkaloids but are frequently not included in this class.

(3) *Opium* (containing the alkaloid *morphine*) and *hashish* or *bhang*, are both habit-forming drugs, yet the active principle of the latter does not contain nitrogen.

(4) Ephedrine is a straight-chain alkaloid that is produced by animal glands, and has marked physiological activity.



ephedrine

In fact, no precise definition of the term 'alkaloid' is possible but in general it designates compounds having the following common features :

(*a*) They are found in plants, although a few are of animal origin

(*b*) They are basic in character and show marked physiological activity ;

(*c*) They have heterocyclic rings containing nitrogen as a part of their structures.

As stated above, most of the alkaloids induce physiological responses when administered to man and animals. Thus the active principles of some of the oldest drugs and medicines known to man were alkaloids. This made the study of alkaloids particularly fascinating for thousands of years. By now over 2,500 alkaloids have been isolated, and their structures elucidated. The search for new and useful ones continues even today.

OCCURRENCE AND ISOLATION

Alkaloids occur chiefly in plants of the dicotyledons families and are localised in seeds, leaves, bark, or root of the plant. Each site may contain several closely related alkaloids. They occur largely as salts of common plant acids such as acetic acid, oxalic acid, lactic acid, malic acid, tartaric acid, citric acid or of certain special organic acids.

79 (45-52/1982)

For extraction of alkaloids, the plant material is macerated. If the material is rich in fat (seeds) it is first extracted with ligroin or petroleum ether for their removal. The plant residue is then extracted with methanol and the cellulosic material separated by filtration. The filtrate is evaporated to give the crude plant extract. This is then dissolved in dilute acid and extracted with ether. The acid solution of the alkaloid salts is then basified and extracted with ether. Evaporation of ether solution gives a solid mixture of crude alkaloids. It is then subjected to fractional crystallisation for separation into individual pure alkaloids. In modern practice the isolation is effected by column chromatography, gas chromatography and by counter current distribution. The general scheme for the extraction of alkaloids is illustrated in Fig. 48·1.

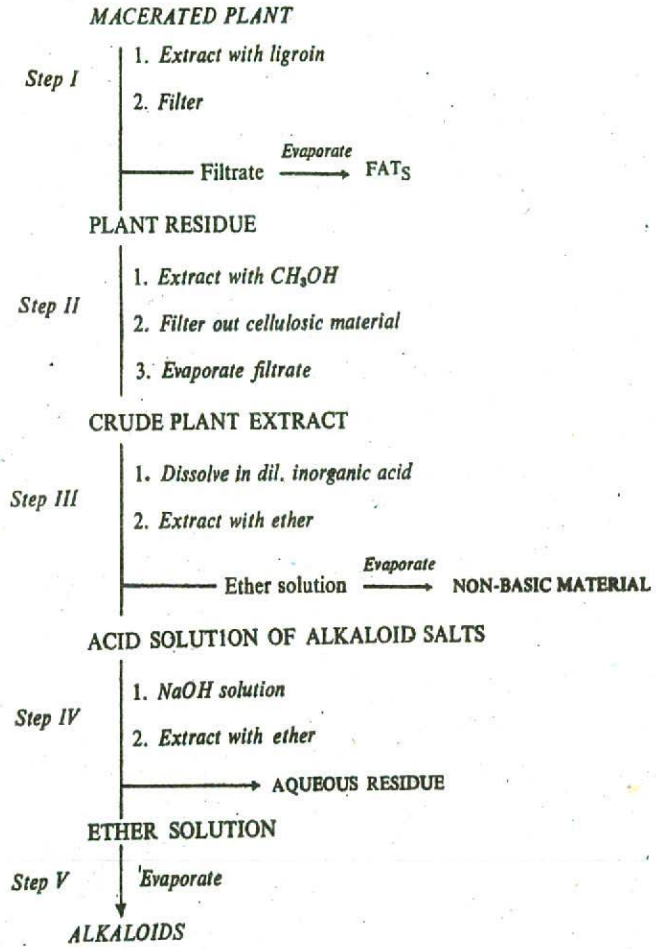


Fig. 48·1 Procedure for the isolation Alkaloids from Plants.

The Ion Exchange Method. Recently an entirely new technique based on the ion exchange principle for the isolation of alkaloids has been developed. The alkaloids react with H^+ ion to form a covalent bond by exchange with a positive ion, and are adsorbed smoothly on a hydrogen ion exchanger. They are then removed from the exchanger by regeneration with alkali together with a suitable solvent as ethanol or acetone

GENERAL PROPERTIES

(1) Alkaloids are usually colourless, crystalline, non-volatile solids, while a few of them (*coniine*, *nicotine*) are liquids.

(2) Except the liquid alkaloids which are soluble in water, the rest are insoluble in water but dissolve readily in ethanol, ether, chloroform and benzene.

(3) They are optically active, the majority being laevorotatory.

(4) They are basic with a bitter taste, and dissolve in mineral acids to form salts.

(5) **Physiological Activity.** Most of them possess marked physiological activity when orally administered : *coniine* is a violet poison ; *quinine* is an antimalarial ; *cocaine* acts as local anaesthetic ; *morphine* relieves pain ; *atrophine* dialates pupil of the eye ; and so on.

(6) **Basic Character.** The molecule of an alkaloid contains one or more basic nitrogen atoms. Most alkaloids are tertiary monoacid bases, while a few are secondary bases. Thus they form well defined crystalline salts with mineral acids, the hydrochloride and nitrate being generally readily soluble in water.

Alkaloidal Reagents. The solutions of alkaloids in dilute minerals acids when treated with certain reagents form insoluble precipitates, often having characteristic colours and melting points. Such reagents as are used for identification of alkaloids are frequently spoken of as *Alkaloidal* reagents. The common ones are :

Chloroplatinic acid, H_2PtCl_6 : Phosphomolybdic acid; Phosphotungstic acid; Picric acid, Tannic acid· Potassium mercuric iodide, $HgCl_2$ —KI (*Mayer's reagent*); Potassium bismuth iodide, $KBiI_4$ (*Dragendroff's reagent*); Potassium cadmium iodide. $KCdI_3$ (*Marme's reagent*) : Potassium iodide solution in iodine, KI_3.

The same alkaliodal reagents may be used for the precipitation of proteins and other complex substances of basic nature.

CLASSIFICATION ; A BRIEF SURVEY

Alkaloids are so numerous and involve such a variety of molecular structure that their rational classification is difficult. However, the best approach to the problem is to group them into families, depending on the type of heterocyclic ring system present in the molecule. Very often a number of alkaloids having similar structure are found in the same plant and also show resemblance in the properties. Alkaloids are also named as a group after the name of the plant from which they are isolated.

For historical reasons as also because of their structural complexities, the nomenclature of alkaloids has not been systematised. The names of individual members are, therefore, generally derived from the name of the plant in which they occur, or from their characteristic physiological activity.

The various classes of alkaloids according to the heterocyclic ring system they contain are listed below.

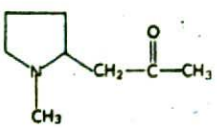
(*i*) *Pyrrolidine alkaloids* ;
(*ii*) *Piperidine alkaloids* ;
(*iii*) *Pyridine-Pyrrolidine alkaloids* ;
(*iv*) *Pyridine-Piperidine alkaloids* ;
(*v*) *Quinoline alkaloids* ;
(*vi*) *Isoquinoline alkaloids* ;
(*vii*) *Indole alkaloids*.

In the following treatment we will discuss the above classes taking examples of the familiar members. In most of these cases we will also give concisely the structure, the source and the characteristic physiological activity. The detailed study of the important alkaloids however, will be taken up separately at a later stage.

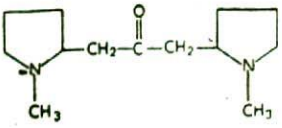
(1) **Pyrrolidine Alkaloids.** They contain the pyrrolidine (tetrahydropyrrole) ring system *e.g.*, *Hygrine* and *Cuscohygrine*.



PYRROLIDINE



HYGRINE



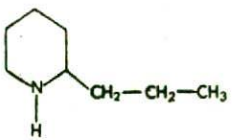
CUSCOHYGRINE

Hygrine is isolated from the leaves of the Peruvian Coca shrub. *Cuscohygrine* is found in 'cusco leaves'.

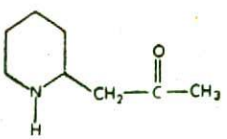
(2) **Piperidine Alkaloids.** They have piperidine (hexahydropyridine) as the heterocyclic structural unit *e.g.*, *Coniine*, *Isopelletierine*, *Lobeline*, and *Piperine*.



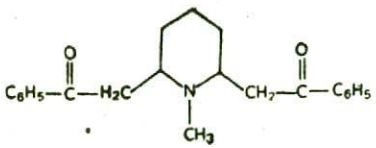
PIPERIDINE



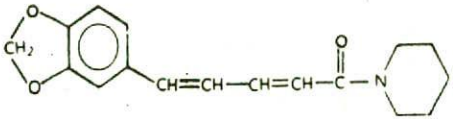
CONIINE



ISOPELLETIERINE



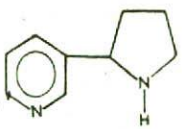
LOBELINE



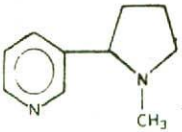
PIPERINE

Coniine occurs in the oil of hemlock and is poison to humans. *Isopelletierine* is isolated from bark of pomegranate tree. *Lobeline*, obtained from the seeds of Indian tobacco is used in medicine as a respiratory stimulant and as a tobacco substitute.

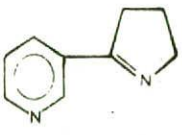
(3) **Pyrrolidine- yridine Alkaloids.** The heterocyclic ring system present in these alkaloids is pyrrolidine-pyridine. Examples are *nicotine* or *myosmine*.



PYRROLIDINE-PYRIDINE



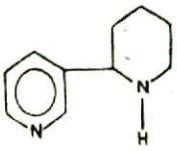
NICOTINE



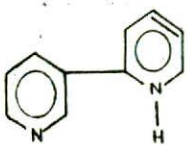
MYSOMINE

Nicotine is isolated from tobacco leaf. It is highly toxic which in very small doses causes respiratory stimulation, and in large doses causes respiratory failure and de h. *Mysomine* also occurs in tobacco and aroma of tobacco smoke is due to it.

(4) **Pyridine-Piperidine Alkaloids.** This family of alkaloids contains a pyridine ring system joined to a piperidine ring system. The implest member is *Anabasine*, the chief alkaloid isolated from the poisonous Asiatic plant, *Anabasis aphyllan.* Another alkaloid of this class is Anatabine.

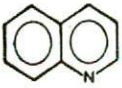


ANABASINE

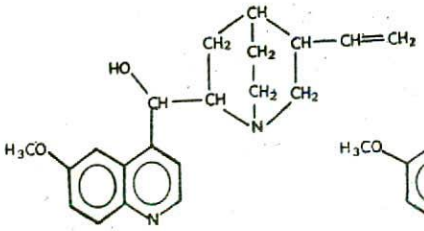


ANATABINE

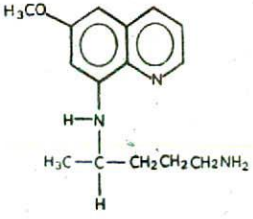
(5) **Quinoline Alkaloids.** These have the basic heterocyclic ring system quinoline *e.g.*, quinine and primaquinine.



QUINOLINE



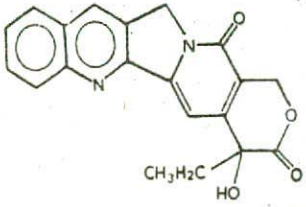
QUININE



PRIMAQUININE

Quinine occurs in the bark of Cinchona tree. It has been used for centuries for treatment of malaria. Synthetic drugs such as primaquinine have largely replaced quinine as an antimalarial.

A recently isolated alkaloid of this group is camptothecin found in chinese tree *Camptotheca acuminata Nyssacae.* This is known to possess antileukemic and antitumor activity in animals.

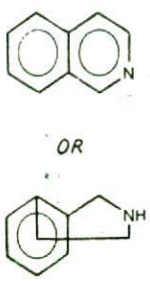


CAMPTOTHECIN

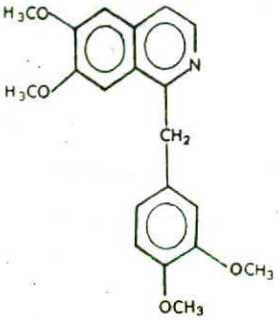
(6) **Isoquinoline Alkaloids.** They contain the heterocyclic ring system isoquinoline *e.g.*, papaverine and morphine.

Papaverine is isolated from the unripe seed capsule of the opium poppy. It finds use as medicine in the treatment of spasms of the stomach or intestines.

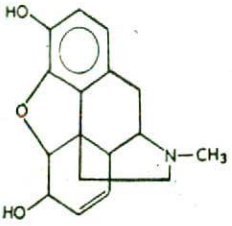
Morphine is isolated from opium. It is used in medicine as hypnotic (sleep producing) and (pain releiving). Unfortunately, prolonged intake of morphine leads to addiction and hence it use is sharply restricted.



ISOQUINOLINE

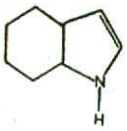


PAPAVERINE

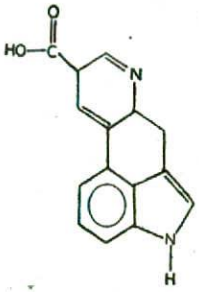


MORPHINE

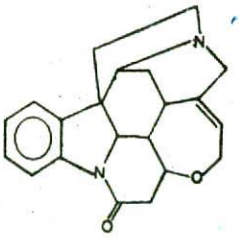
(7) **Indole Alkaloids.** Alkaloids based upon the indole skeleton are widely distributed in nature. The physiological action of these substances may rest in the fact that derivatives of indole play important roles in the chemistry of the brain.



INDOLE
(BASIC SKELETON)



LYSERGIC ACID



STRYCHNINE

Lysergic acid, isolated from the fungus *Claviceps purpurea*, is the best known alkaloid of this class. In small regulated amounts, it is used in the treatment of migrane headaches as also for the induction of uterine contraction in childbirth. The dimethylamide of lysergic acid (LSD) is the most potent psychotomimetic substance known. It has varied effects on humans, producing colour hallicuninations and psychotic states similar to those of schizophrenia.

Another indole alkaloid is strychnine which is isolated from the seed of *strychnos* nuxvomica. It is extremely poisonous and is used for exterminating vermin. Its structure was elucidated in 1948 and this was followed by its total synthesis by R.B. Woodward.

DETERMINATION OF STRUCTURE

Alkaloids mostly have complex molecular stucture the determination of which is both tedious and challenging. This needs a careful and systematic approach. The usual procedure is as follows.

(1) **Determination of Molecular Formula.** The molecular formula of the given unkown alkaloid is first determined by suitable methods described before.

(2) **Detection of Groups.** The presence of various functional groups in the molecule is ascertained by applying specific tests.

A. NATURE OF OXYGEN FUNCTIONS

Oxygen is usually present as alcoholic, phenolic, carbonyl, carboxyl, methoxy or ester group.

(*a*) *Hydroxyl group OH.* The alkaloid is treated with acetic anhydride, acetyl chloride or benzoyl chloride to detect the presence of hydroxyl group (Note that $-NH_2$ group also reacts with these reagents). The —OH group may be phenolic or alcoholic. It is phenolic if the alkaloid—

(*i*) gives a colouration with ferric chloride.

(*ii*) is soluble in sodium hydroxide and is reprecipitated by carbon dioxide.

If the above tests are given in negative, the —OH group is alcoholic. Primary alcoholic group, CH_2OH, forms esters and on oxidation yields aldehydes. The secondary alcoholic group, $>CHOH$, forms esters and on oxidation gives a ketone.

(*b*) *Carboxyl group COOH.* The presence of carboxyl group is indicated by the formation of salts and esters, and the evolution of carbon dioxide with sodium bicarbonate solution.

(*c*) *Methoxy group, $-OCH_3$.* This group produces methyl iodide on heating with hydriodic acid.

$$-OCH_3 + HI \longrightarrow -OH + CH_3I$$

(*d*) *Carbonyl group, $>C=O$.* The presence of carbonyl group is detected by the formation of oxime and hydrazone.

(*e*) *Ester group, $-CO-OR$.* The alkaloid containing the ester group gives an acid and an alcohol on hydrolysis.

B. NATURE OF NITROGEN FUNCTIONS

(*a*) *Amino group, $-NH_2$.* The alkaloids containing an amino group form salts with acids. The nature of the amino group is decided on the basis of the following reactions.

(*i*) Aliphatic $-NH_2$ group reacts with nitrous acid to give a primary alcohol with the evolution of nitrogen.

(*ii*) Aromatic $-NH_2$ group forms diazonic salts and dyes by coupling reactions.

(*iii*) Secondary amino group, —NH—, reacts with nitrous acid to form nitrosoamines.

(*iv*) Tertiary amino group, >N—, reacts with methyl iodide to form quaternary salts.

(*b*) *Amide group, $-CONH_2$.* Upon hydrolysis, the alkaloids containing an amide group yield the corresponding carboxylic acid and ammonia.

C. PRESENCE OF UNSATURATION

The presence of unsaturation in alkaloids is indicated by treatment with bromine water or dilute alkaline potassium permanganate. Reduction with sodium amalgam, sodium and ethanol, hydriodic acid, or tin and hydrochloric acid also shows the presence of unsaturation.

(3) **Estimation of Groups.** The estimation of various groups detected as above, is carried as follows.

(*a*) *Hydroxyl groups.* The number of hydroxyl groups is determined by acetylating the alkaloid and hydrolysing the acetyl derivative with a known volume of IN–NaOH.

$$R-OH \xrightarrow{CH_3COCl} R-COCH_3 \xrightarrow{NaOH} R-OH + CH_3COONa$$

The excess of alkali is estimated by titration with a standard solution of hoydrochloric acid. The number of acetyl groups or hydroxyl groups can be calculated from the volume of alkali used for hydrolysis.

(*b*) *Carboxyl groups.* The number of carboxyl groups may be determined volumetrically by titration against a standard barium hydroxide solution using phenolphthalein as indicator or gravimetrically by 'Silver salt method'.

(*c*) *Methoxy groups* (Zeisel's method). The number of methoxy groups is estimated by heating the alkaloid with concentrated hydriodic acid. The methyl iodide evolved is absorbed in ethanolic silver nitrate when silver iodide is precipitated.

$$R(OCH_3)n + nHI \longrightarrow R(OH)n + nCH_3I$$
$$nCH_3I + nAgNO_3 \longrightarrow nAgI + nCH_3NO_3$$

The precipitate of silver iodide is boiled with nitric acid, filtered, washed, dried and weighed. From the weight of the pricipitate formed, the number of methoxy groups can be calculated.

(*d*) *$-NH_2$, $>NH$ and $-N<$ groups.* These can be estimated : (*i*) by forming the hydrochloride and titrating its aqueous solution against N/10 KOH using phenolphthalein as indicator ; and (*ii*) by the platinichloride method described before.

(4) **Degradation**. The alkaloid is decomposed by treating with suitable reagents to give simpler compounds which can be identified easily.

Hydrolysis. An alkaloid containing an ester or amide group gives simpler products on hydrolysis. For example, piperine gives piperidine and piperic acid on hydrolysis.

$$\underset{\text{piperine}}{C_{11}H_9O_2-CO-NH_2} + H_2O \longrightarrow \underset{\text{piperic acid}}{C_{11}H_9O_2-CO-OH} + \underset{\text{piperidine}}{C_5H_{10}-NH}$$

From this we infer that piperine is an amide of piperic acid.

(*ii*) *Oxidation.* Oxidation of alkaliod with potassium permanganate, potassium dichromate, or with hydrogen peroxide can bring about several changes, Thus with potassium permanganate the molecule may be oxidised away leaving a COOH group at the root.

(*iii*) *Distillation with Zinc dust.* When distilled with zinc dust, many alkaloids yield the parent compound, or are dehydrogenated. Thus morphine on distillation with zinc dust gives phenanthrene, indicating the presence of the latter as the basic skeleton in the molecule. Coniine yields conyrine by the loss of a molecule of hydrogen.

(*iv*) *Exhaustive Methylation.* This is an important method used to find a recognisable moiety in an unknown alkaloid. This is acomplished by degradation of the alkaloid by the following steps.

(*a*) The heterocyclic ring of the alkaloid is reduced if unsaturated.

(*b*) The alkaloid (or the reduced alkaloid) is treated with excess of methyl iodide when the >NH of the ring system is methylated and then converted to the respective quaternary ammonium iodide.

$$\underset{\text{imino group}}{>N-H} \xrightarrow[\textit{methylation}]{CH_3I} \underset{\text{methyl derivative}}{>N-CH_3} \xrightarrow{+CH_3I} \underset{\text{4° amm iodide}}{>\overset{+}{N}\begin{matrix}CH_3\\CH_3\end{matrix}\Big]\overset{-}{I}}$$

(*c*) The quatenary ammonium iodide is changed to the corresponding hydroxide by reaction with moist silver oxide (AgOH).

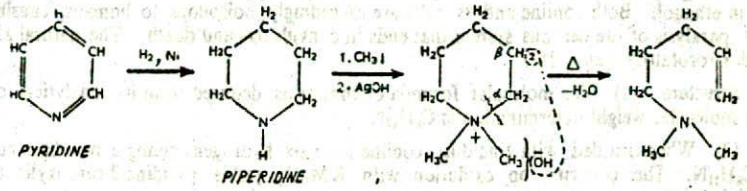
$$>\overset{+}{N}\begin{matrix}CH_3\\CH_3\end{matrix}\Big]\overset{-}{I} \xrightarrow{AgOH} >\overset{+}{N}\begin{matrix}CH_3\\CH_3\end{matrix}\Big]\overset{-}{OH} + AgI$$

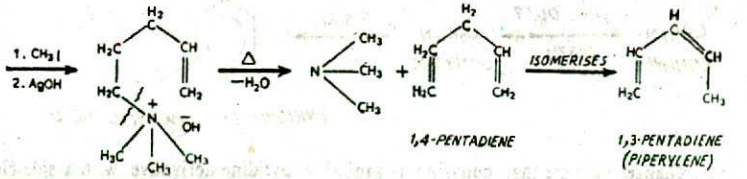
4° amm hydroxide

(*d*) The quaternary ammonium hydroxide on pyrolysis splits out a molecule of water the OH group extracting a H atom from the β-position with respect to N atom. As a result, the C—N bond on the side of the β-hydrogen concerned ruptures to give an open chain unsaturated amine.

(*e*) The above sequence of reaction listed in steps *a*, *b*, *c*, *d* are repeated with excess of CH_3I when rupture of the second C—N bond occurs and N atom is eliminated as $(CH_3)_3N$. The unsaturated hydrocarbon left behind, which often isomerises to a conjugated diene, is identified by the usual analytical methods.

The overall process mentioned in the steps above involving repeated methylation to get the degradation end-products is called Exhaustive Methylation. The nature of these products helps in arriving at the structure of the parent alkaloid. This may be illustrated by taking example of pyridine ring system.





Thus the mode of linking in the ring system is established. The method has been best exploited in the elucidation of structure of *coniine.*

Hofmann's exhaustive methylation method is applicable as long as β-hydrogen is available for elimination of H_2O, otherwise it fails. Thus it does not apply in case of quinoline and isoquinoline derivatives.

(5) **Newer Physical Methods.** In conjunction with the chemical methods mentioned earlier more recent and sophisticated techniques are now frequently used to elucidate the structure of alkaloids. In fact, in some cases the structure of alkaloid has been given even without carrying out any chemical work.

(*i*) *Infrared Spectra* are used to detect the presence of many functional groups ;

(*ii*) *Ultraviolet Spectra* are employed so as to project the possible type of structures present in the molecule.

(*iii*) *X-Ray Analysis* has provided a means to fit in the various structural units indicated to be present in the molecule, thus givining a sure procedure to give the final structure of the alkaloid accurately.

(*iv*) ***NMR Spectroscopy.*** **It is a more recent and sophisticated method for detecting many functional groups such as olken. protons, *N*—, *O*—, and *C*—methyl groups. The presence of heterocyclic ring systems *e.g.*, pyrrole, pyridine, quinoline, isoquinoline indole etc., is clearly proved by NMR spectroscopic method.**

(6) Synthesis. The analytical procedure discussed above will project the tentative structure for the alkaloid under investigation. Because of the aforesaid physical methods, which are sure and accurate, the confirmation of the structure by synthesis of the alkaloid is no longer that important. Nevertheless, synthesis will ever remain a fruitful method for confirming the proposed structure as it might as well provide a newer way of obtaining an alkaloid rather than depending only on a natural source.

CONIINE

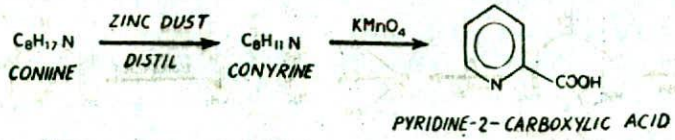
It is the principal toxic substance present in the hemlock herb (*Conium maculatum*) and is now of historical interest only. The extract of hemlock containing coniine was used as official state poison by Greeks for the execution of criminals. The famous philosopher Socrates was put to death in 400 B.C. by being required to drink hemlock extract.

Isolation. The seeds of hemlock are powdered and distilled with sodium hydroxide solution. Coniine is then recovered from the distillate by on extraction with ether. The ethereal extract on evaporation leaves behind the alkaloid.

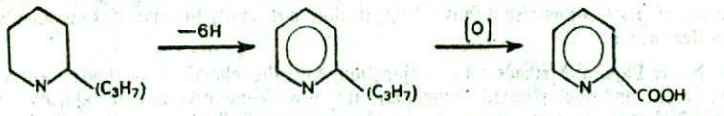
Properties. Coniine is a colourless, strongly alkaline liquid, bp 167°C. It has an unpleasant odour recalling a mouse, and has a burning taste. It is sparingly soluble in water but dissolves readily in ethanol. Both coniine and its salts are exceedingly poisonous to humans, causing a gradual paralysis of the nervous system that ends in convulsions and death. The natural alkaloid is dextrorotatory, $[\alpha]_D = 15{\cdot}7°$.

Structure. (1) The molecular formula of coniine as deduced from its analytical data and the molecular weight determination is $C_8H_{17}N$.

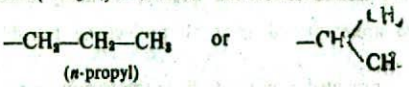
(2) When distilled with zinc dust coniine loses six hydrogens giving a new base conyrine, $C_8H_{11}N$. The conyrine on oxidation with $KMnO_4$ yields pyridine-2-carboxylic acid (α-picolinic acid).



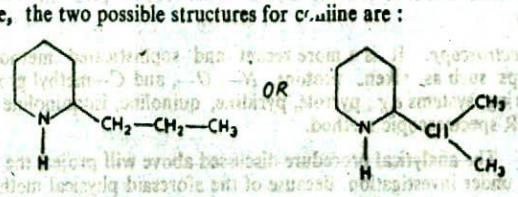
These changes indicate that conyrine is probably pyridine derivative with a side-chain in 2-position which upon oxidation would be capable of producing pyridine-2-carboxylic acid. Again, since conyrine is obtained from coniine by loss of six hydrogens the latter compound could be the corresponding piperidine derivative. Thus we can depict the above reactions as :



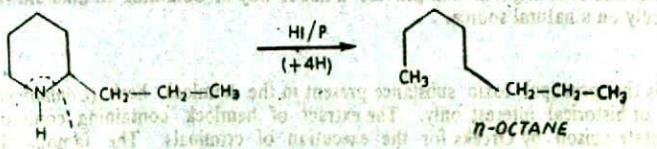
The side-chain ($-C_3H_7$) in coniine can be represented in two ways.



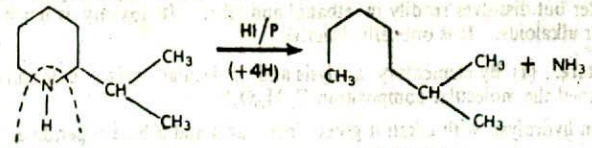
Therefore, the two possible structures for coniine are :



(3) On heating with hydriodic acid and phosphorus, coniine is reduced to give *n*-octane. This shows that the side-chain is *n*-propyl and not isopropyl.

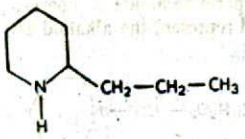


Had the chain been isopropyl, the expected product would have been isooctane.



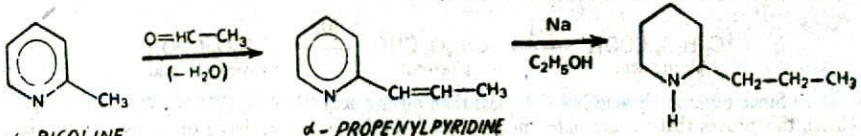
2-ISOPROPYL PIPERIDINE ISOOCTANE

Therefore, it stands to reason that coniine has the structure :



(4) An additional evidence for the above structure of coniine is afforded by the exhaustive methylation of the alkaloid which gives an alkene, *conylene* (C_8H_{14}) with the elimination of nitrogen as $(CH_3)_3N$. The conylene can be reduced to form *n*-octane.

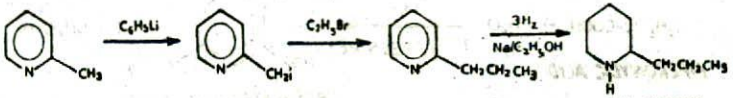
(5) The structure of coniine was finally confirmed by *Landenburg's Synthesis* (1886). The condensation of α-picoline (2-methylpyridine) with acetaldehyde at 250°C forms 2-propenylpyridine, which on reduction with sodium and ethanol yields (±)-coniine.



α - PICOLINE α - PROPENYLPYRIDINE (±) CONIINE

(±)-Coniine so obtained is resolved by forming salts with (+)-tartaric acid and fractional crystallisation. The salt of (+)-coniine being less soluble crystallises out first. This on treatment with alkali gave free (+)-coniine which was found to be identical with the natural alkaloid.

The structure of coniine has also been confirmed by another synthesis effected by *Bergmann* in 1932.



α- PICOLINE CONYRINE (±)- CONIINE

The product is a racemate which is resolved to give (+)-coniine as described before.

PIPERINE

This alkaloid occurs in the ripe fruit (white pepper) and in the unripe fruit (black pepper) of *Piper nigrum*. It occurs in the kernel of the black pepper to the extent of 5 to 10 per cent and was isolated from this source by Oerstedt (1819).

Extraction. Piperine is obtained by extracting the powdered black peppers with ethanol. The extract is evaporated and the solvent free residue is treated with NaOH solution to remove resin. The insoluble residue is again dissolved in warm ethanol (or ether). From the solution, piperine crystallises out on cooling.

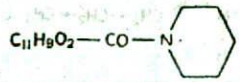
Properties. Piperine froms beautiful colourless crystals, mp 128—129·5°C. It is neutral to litmus and has the characteristic sharp flavour and taste of black pepper. It is difficultly soluble in water but dissolves readily in ethanol and ether. Its toxicity is much feeble as compared to other alkaloids. It is optically inactive.

Structure. (1) By elementary analysis and molecular weight determination, piperine has been assigned the molecular composition $C_{17}H_{19}O_3N$.

(2) On hydrolysis with alkali it gives piperic acid and a base piperidine.

$$\underset{\text{piperine}}{C_{17}H_{19}O_3N} + H_2O \xrightarrow[\text{boil}]{\text{NaOH}} \underset{\text{piperic acid}}{C_{11}H_9O_2{-}COOH} + \underset{\text{piperidine}}{C_5H_{10}NH}$$

Obviously, piperine is the piperidine amide of piperic acid. The structure of piperidine is already known and hence we could represent the alkaloid as :



(PIPERIDINE AMIDE)

Thus to have a complete picture of the structure of piperine, we should know the structure of piperic acid.

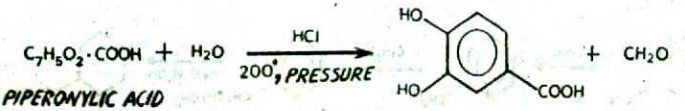
(3) *Structure of Piperic acid.* (*a*) Piperic acid on oxidation with potassium permanganate first gives piperonal and then piperonylic acid.

$$\underset{\text{piperic acid}}{C_{11}H_9O_2.COOH} \xrightarrow{[O]} \underset{\text{piperonal}}{C_7H_5O_2.CHO} \xrightarrow{[O]} \underset{\text{piperonylic acid}}{C_7H_5O_2.COOH}$$

Since piperonylic acid has C_4H_4 less than piperic acid ($C_{11}H_9O_2.COOH - C_7H_5O_2.COOH = C_4H_4$), this proves that the aromatic moiety $C_7H_5O_2$ in the molecule, has a single side chain and the fragment C_4H_4 is knocked out during oxidation. Thus piperic acid could be written as $C_7H_5O_2{-}C_4H_4{-}COOH$ and the above reaction yielding piperonylic acid explained as follows.

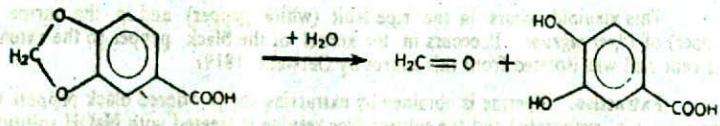
$$\underset{\text{piperic acid}}{C_7H_5O_2{-}C_4H_4{-}COOH} \xrightarrow[-(C_4H_4)]{[O]} \underset{\text{piperonylic acid}}{C_7H_5O_2{-}COOH}$$

(*b*) The structure of piperonylic acid follows from the fact that on heating with hydrochloric acid at 200°C under pressure forms protocatechuic acid and formaldehyde.



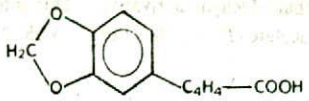
PIPERONYLIC ACID *PROTOCATECHUIC ACID*

Since one carbon has been eliminated as CH_2O and as a result two free OH groups appeared in protocatechuic acid, it follows that piperonylic acid is 3, 4-methylenedioxybenzoic acid. The above reaction can be visualised to have proceeded as follows.

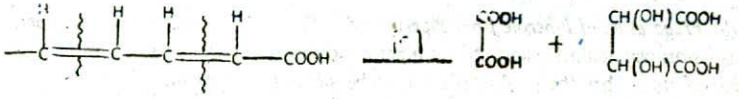


3, 4 - METHYLENEDIOXY-BENZOIC ACID *PROTOCATECHUIC ACID*

(*c*) As indicated in step (*a*) above, the structure of piperic acid may now be written as.

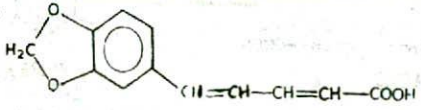


(*d*) The structure of the side-chain in piperic acid becomes clear from the fact that : (*i*) it takes up readily four bromine atoms showing the presence of two double bonds; (*ii*) on careful oxidation with $KMnO_4$ it decomposes to form a molecule of tartaric acid and oxalic acid each, indicating the presence of two bonds in alternate positions.



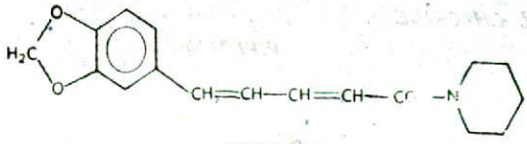
SIDE CHAIN OXALIC ACID TARTANIC ACID

Hence the complete structure of piperic acid can be written as



PIPERIC ACID

(4) Knowing the molecular structure of piperic acid and piperidine the structural formula of piperine can be derived by joining the two as amide (*See step 3c*)

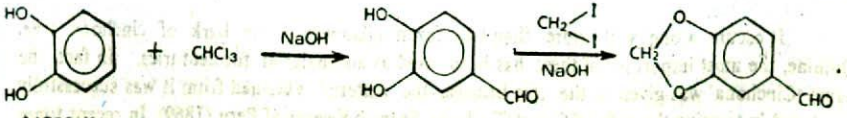


PIPERINE
(PIPERIDINE AMIDE OF PIPERIC ACID)

(5) The synthetic evidence for the structure of piperine was afforded by first synthesicing piperic acid and then preparing from it the alkaloid.

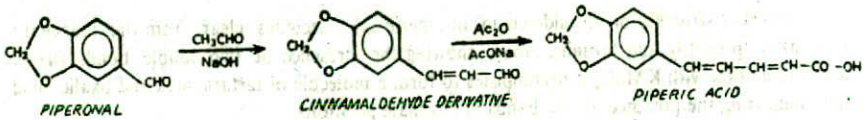
(*a*) *The Synthesis of Piperic acid* (Landenburg and Scholtz, 1894).

(*i*) Piperonal is obtained from catechol by Reimer-Tiemann reaction.

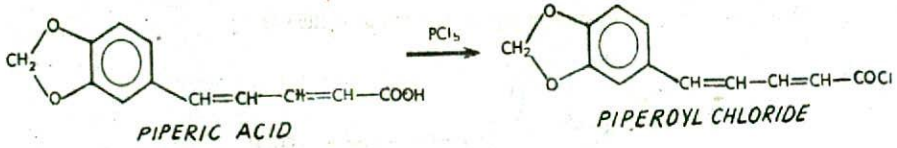


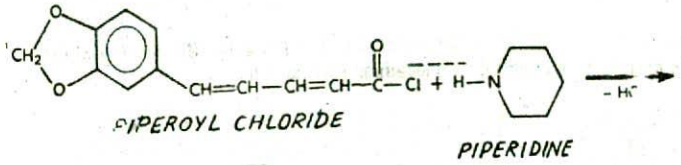
CATECHOL PIPERONAL

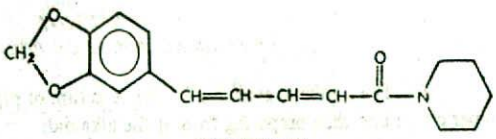
(*ii*) Pipernal is condensed with acetaldehyde in the presence of sodium hydroxide *Claisen Condensation*) to give cinnamaldehyde derivative. This is then heated with acetic anhydride in the presence of sodium acetate (*Perkin Reaction*) to yield piperic acid



(*b*) *Preparation of Piperine from Piperic acid.* This is done by first reacting piperic acid with phosphorus pentachloride so as to get piperoyl chloride. This is heated with piperidine in benzene solution when the product is found to be identical with natural piperine.







QUININE

It occurs along with more than two dozen alkaloids in the bark of cinchona tree. Quinine, the most important of these has been used as antimalarial for centuries. In fact, the name 'Cinchona' was given to the tree because the material obtained from it was successfully employed in treating the wife of Count Cinchona, Spanish Viceroy of Peru (1869). In recent times the main source of quinine has been plantations in the Dutch East Indies, chiefly Java.

Isolation. The finely powdered cinchona bark is extracted with benzene or toluene in the presence of alkali. It is present in the bark as ester of quininic qunitannic acids and passes into the solvent extract after being liberated by alkali. The mixture of alkaloids is then extracted from the solvent layer by dilute sulphuric acid. When the acid extract so obtained is neutralised with alkali, the sparingly soluble quinine sulphate precipitates out. The other minor alkaloids present left behind are precipitated from the filtrate with excess of alkali.

Quinine was synthesised by Woodward and Doering (USA) in 1944, but a commercially feasible process has never been realised.

Properties. Quinine is a white solid, mp 177°C, which crystallises with three molecules of water to form the trihydrate, mp 57°C. It has an intensely bitter taste. The alkaloid is very sparingly soluble in water but dissolves in organic solvents such as benzene, toluene, chloroform, ether etc. The natural quinine is leavorotatory, $[\alpha]_D = -158°$. It is very weakly dibasic but forms well-defined salts with acids *e.g.*, quinine sulphate and quinine hydrochloride.

$(C_{20}H_{24}H_2N_2)_2H_2SO_4 . 8H_2O$ — quinine sulphate

$C_{20}H_{24}O_2N_2HCl . 2H_2O$ — quinine hydrochloride

Quinine has a specific property of fighing down malarial parasites in the human body. The drug is suppressive but not curative. Quinine and its salts were used for long as antimalarials. The alkaloid is also an antipyretic, that is, it lowers the body temperature in high fever. Quinine has now been replaced by more effective and less toxic medicines as *atebrin*, *plasmochin*.

Structure. (1) The molecular formula of quinine is $C_{20}H_{24}N_2O_2$.

(2) It adds two molecules of CH_3I to form di-quaternary salt which suggests that both the N atoms present in the molecule are tertiary.

$$\underset{\text{quinine}}{C_{20}H_{24}N_2O_2} + 2CH_3I \longrightarrow \underset{\text{di-quaternary salt}}{C_{20}H_{24}N_2O_2.2CH_3I}$$

(3) Quinine readily forms the acetyl derivative and chloro compound on treatment with acetic anhydride and phosphorus pentachloride respectively. Therefore, it contains one —OH group.

(4) On mild oxidation the alkaloid is converted into a ketone, *quininone*, without loss of any carbon. This shows that the —OH group is present as secondary alcohol group.

$$\underset{\text{quinine}}{[C_{20}H_{23}N_2O]}>CHOH \xrightarrow{[O]} \underset{\text{quininone}}{[C_{20}H_{23}N_2O]}>CO + H_2O$$

(5) On heating with hydrochloric acid, quinine loses one carbon atom as CH_3Cl, indicating that the second oxygen in the molecule is present as methoxy ($-OCH_3$) group.

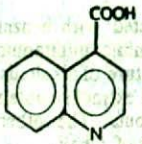
$$\underset{\text{quinine}}{\left[C_{18}H_{21}N_2O\right]}\!\!>\!\!C\!-\!OCH_3 \xrightarrow[\Delta]{HCl} \underset{\text{cinchonine}}{\left[C_{18}H_{21}N_2O\right]}\!\!>\!\!N\!-\!OH + CH_3Cl$$

(6) It adds one molecule of Br_2 or halogen acids, showing the presence of a double bond in the molecule. Also, quinine on oxidation with $KMnO_4$ yields a monocarboxylic acid and formic acid, which confirms the presence of double bond in a vinyl group ($-CH=CH_2$).

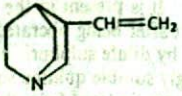
$$\underset{\text{quinine}}{[C_{18}H_{21}N_2O_2]}-CH=CH_2 + Br_2 \longrightarrow \underset{\text{dibromide}}{[C_{18}H_{21}N_2O_2]}-\overset{Br}{\underset{|}{CH}}-\overset{Br}{\underset{|}{CH_2}}$$

$$[C_{18}H_{21}N_2O_2]-CH=CH_2 \xrightarrow[KMnO_4]{[O]} \underset{\text{monocarboxylic acid}}{[C_{18}H_{21}N_2O_2]-COOH} + \underset{\text{formic acid}}{HCOOH}$$

(7) Quinine on vigorous oxidation with chromic acid yields quininic acid and 3-vinylquinuclidine.

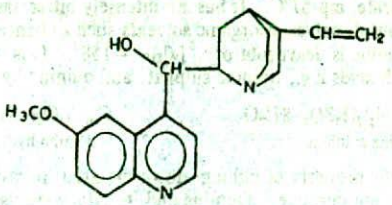


QUININIC ACID



3-VINYL-QUINUCLIDINE

(8) The above reactions supplemented by more evidence of complex nature have shown that quinine has the structure.



QUININE

NICOTINE

Nicotine is the chief alkaloid of tobacco plant (*Nicotina tabacum*). It occurs in the plant leaves as salts of malic acid and citric acid to the extent of 4 to 5 per cent. The alkaloid was named after the Frenchman *Nicot* who introduced tobacco in France in 1560.

Isolation. (1) Waste parts of the tobacco plant are finely powdered and extracted with dilute acid. The water-soluble salts of alkaloids are thus removed in solution, leaving the insoluble cellulose, chlorophyll etc behind.

(2) The acid extract is then made basic with lime or sodium hydroxide, and steam-distilled. Steam-distillation separates the nicotine from water-soluble nonvolatile materials (sugars, inorganic salts etc).

(3) The distillate is acidified to about pH 3 with solid oxalic acid and concentrated to a syrup. On cooling, the crystalline salt of nicotine and oxalic acid separates. Other alkaloids not forming slightly soluble oxalates are left in the solution.

(4) The crystalline nicotine oxalate is then transferred to a separating funnel and treated with excess of aqueous KOH. The nicotine thus set free rises to the surface as a brown oil, and separated by extraction with ether.

(5) The ethereal solution of the alkaloid is dried over solid anhydrous KOH, and the ether evaporated. For further purification, the residue is fractionally distilled under vacuum.

Properties. (1) Nicotine is one of the few alkaloids known to exist in a liquid form; colourless, bp 246°C.

(2) It has a tobacco-like smell and a burning 'alkaline' taste.

(3) It is soluble in water and also in organic solvents such as ethanol, ether and benzene.

(4) The natural alkaloid is laevorotatory, $[\alpha]_D = -169°$.

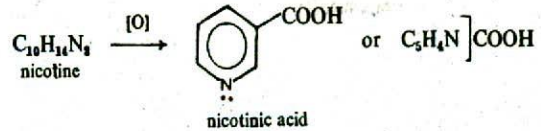
(5) It is a deadly poison to animals and is used commercially as an insecticidal spray for plants and animals.

(6) In small quantities, nicotine stimulates the nervous system for a while, which is followed by depression. A low nicotine-content tobacco is used for smoking purposes even-though it is definitely injurious to health, causing diseases like asthma and lung cancer.

Structure. (1) Elemental analysis and molecular weight determination leads to the molecular formula $C_{10}H_{14}N_2$ for nicotine.

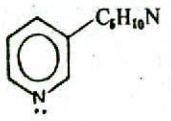
(2) It absorbs two molecules of CH_3I, suggesting the tertiary nature of both the nitrogen atoms.

(3) On ozidation with chromic acid, nicotine yields nicotinic acid (pyridine-3-carboxylic acid).



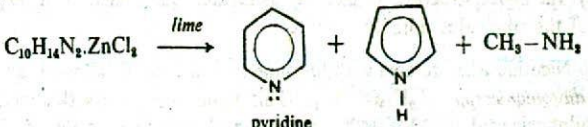
nicotinic acid

This shows that the alkaloid contains a pyridine nucleus with a side-chain at the 3-position. That is, the side-chain has the composition $(C_{10}H_{14}N_2 - C_5H_4N) = C_5H_{10}N$. Therefore, the formula for nicotine may be written as :



From the above formula it is evident that the side-chain must be saturated.

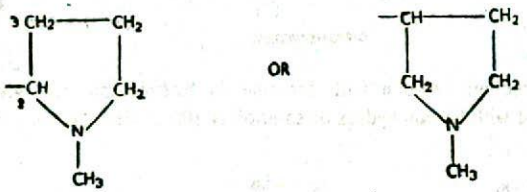
(4) *Nature and Position of the side-chain.* (*i*) The alkaloid forms an addition compound with zinc chloride, $C_{10}H_{14}N_2.ZnCl_2$, which when heated with lime yields pyridine, pyrrole, and methylamine.



pyridine pyrrole

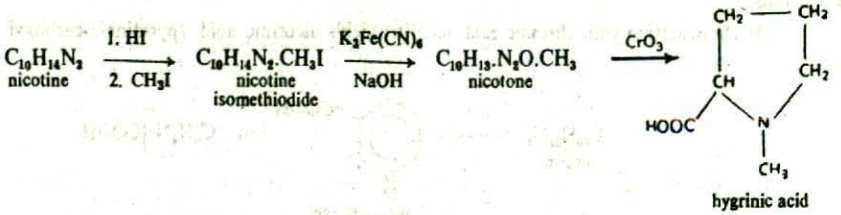
This suggests that the side-chain, $C_5H_{10}N$, is a pyrrole derivative.

(*ii*) When heated with concentrated hydriodic acid at 200—300°C (Herzig and Meyer), nicotine yields CH_3I, showing that methyl group is attached to *N*-atom. Therefore, it appears that the side-chain could be *N*-methylpyrrolidine.



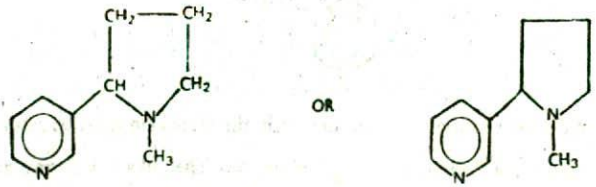
However, the point of attachment of the side-chain to the pyridine nucleus could be C_3 or C_2 as shown above.

(*iii*) Nicotine hydriodide when treated with CH_3I, forms nicotine isomethiodide which on oxidation with potassium ferricyanide yields *nicotone*. This on further oxidation with chromium trioxide produces *hygrinic acid*.



The formation of hygrinic acid as above proves beyond doubt that the side-chain, *N*-methylpyrrolidine, is attached to the pyridine nucleus through C_2.

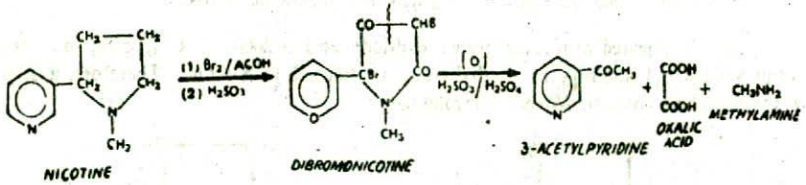
(5) From the foregoing considerations the structural formula of nicotine may be written



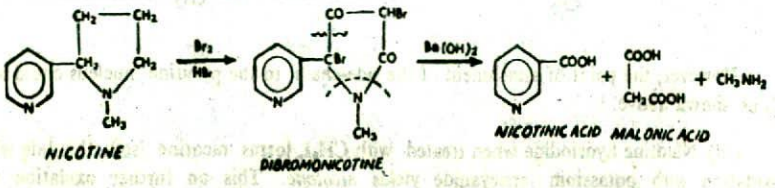
(N-METHYLPYRROLIDINE-2-PYRIDINE)

(6) The above structure of nicotine is further confirmed as it explains the following reactions of the alkaloid admirably.

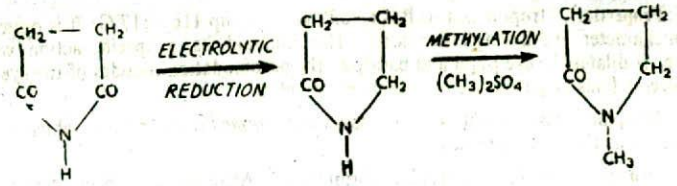
(*i*) Nicotine when treated with bromine in acetic acid followed by aqueous sulphurous acid gives *dibromonicotine*, $C_{10}H_{10}ON_2Br_2$. This upon oxidation with a mixture of sulphurous acid and sulphuric acid at 130—140°, yields 3-acetylpyridine, oxalic acid and methylamine (Pinner, 1892).



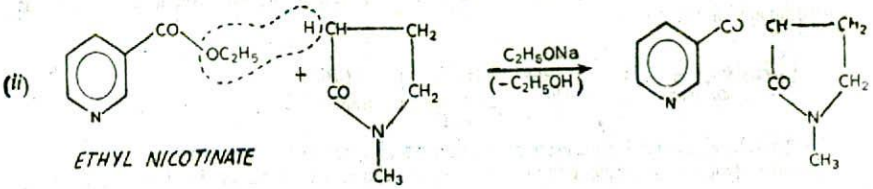
(*ii*) Nicotine on reaction with bromine in hydrobromic acid gives which when heated with barium hydroxide solution at 100°C, yields nicotinic acid, malonic acid and methymine.



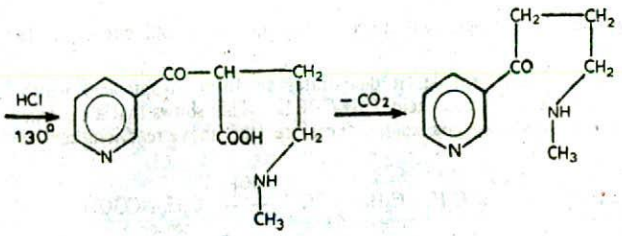
(7) Finally, the structure of nicotine was confirmed by the following synthesis accomplished by Spath (1928).



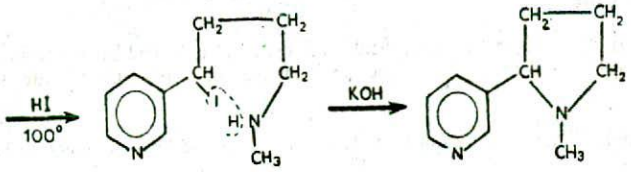
SUCCINIMIDE 2-PYRROLIDONE



ETHYL NICOTINATE



β-KETONIC ACID (UNSTABLE)



(±)-NICOTINE

(*iii*) The racemic alkaloid obtained is resolved by means of (+)-tartaric acid to get (—)-nicotine which is found to be identical with the natural alkaloid.

ATROPINE

This alkaloid is present in the stems and roots of the plant *Atropa belladonna* (the "deadly night shade") in traces. It is believed that the original alkaloid is (—)-hyocyamine, which is usually racemised to the optically acitive form, atropine, during isolation.

Isolation. Atropine is obtained by treating the plant juice with alkali, followed by extraction with ether. The crude alkaloid is purified through oxalate formation, fractional recrystallisation, and treatment o f the salt with alkali.

Atropine is invariably prepared in the laboratory as well as commercially by the recemisation of (-)-hyocyamine by heat or alkali.

Properties. Atropine is a white crystalline solid, mp 116—117°C. It is optically inactive, basic in character, and having bitter taste. This alkaloid has a specific action when dropped into eye. It dilates the eye pupil and paralyses the accomodation muscles of the eye temporarily. Therefore, it finds extensive use in ophthalmic practice.

Atropine is also used in medicine as an *antispasmodic*, a substance which relieves muscle spasms such as those of intestines.

Structure. (1) The molecular formula of Atropine has been determined to be $C_{17}H_{23}NO_3$.

(2) The alkaloid on hydrolysis with HCl at 130°C or with alkali at 60°C, yields (±)-tropic acid and tropine.

$$\underset{\text{atropine}}{C_{17}H_{23}NO_3} + H_2O \xrightarrow[130^\circ]{H^+} \underset{\substack{(\pm)\text{-tropic}\\ \text{acid}}}{C_9H_{10}O_3} + \underset{\text{tropine}}{C_8H_{15}NO}$$

Therefore, atropine is an ester of tropic acid and tropine (tropine tropate). If we can elucidate the structure of tropic acid and tropine, we can easily construct the structural formula for atropine.

(3) STRUCTURE OF TROPIC ACID

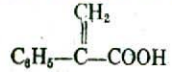
(*i*) It has the molecular formula $C_9H_{10}O_3$.

(*ii*) As shown by the usual tests, tropic acid molecule has one —OH and one —COOH group.

(*iii*) When heated with barium hydroxide, it dehydrates to form atropic acid, which upon oxidation with chromic acid yields benzoic acid, C_6H_5COOH. This shows that a benzene nucleus is present in tropic acid as also in atropic acid. Therefore, the above reactions can be represented as :

$$\underset{\text{tropic acid}}{C_6H_5—C_2H_3OH—COOH} \xrightarrow{-H_2O} \underset{\text{atropic acid}}{C_6H_5—C_2H_2—COOH} \xrightarrow{[O]} \underset{\text{benzoic acid}}{C_6H_5—COOH}$$

The two possible structures for atropic acid are :

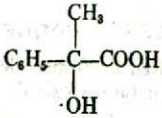


I

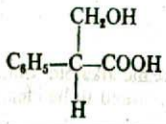


II

We know that structure II is cinnamic acid and hence atropic acid has structure I. Theoretically we can get the formula of tropic acid by adding a molecule of water to CH_2‖—C— unit in structure I. Since it can be done in two ways, tropic acid can be assigned the structure III or IV.



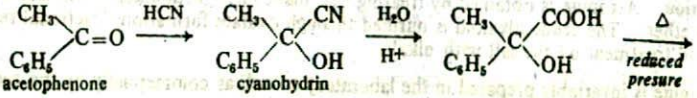
III

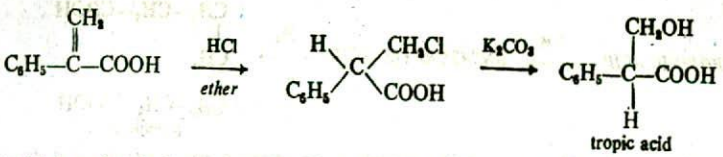


IV

The structure IV represents tropic acid since structure III is known to represent *atrolactic acid.*

(*iv*) The structure of tropic acid has been confirmed by the following synthesis (Mackenzie, Wood, 1919).





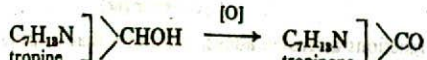
The product is found to be identical with the tropic acid obtained by the hydrolysis of natural alkaloid.

(4) STRUCTURE OF TROPINE

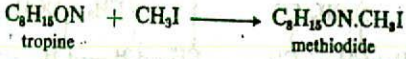
(*i*) The molecular formula of tropine has been found to be $C_8H_{15}NO$.

(*ii*) As shown by the usual tests, it contains one —OH group.

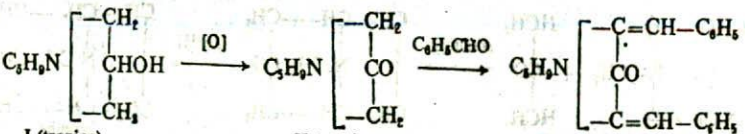
(*iii*) On oxidation with chromic acid, tropine gives a ketone *tropinone*, indicating the presence of secondary alcoholic —OH group.



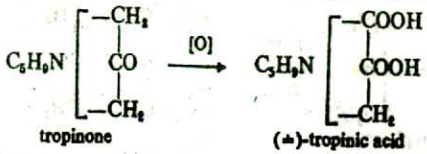
(*iv*) Tropine takes one molecule of methyl iodide, demonstrating the presence of a tertiary N-atom.



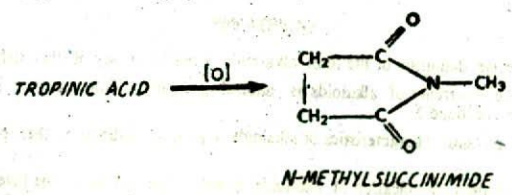
(*v*) Willstalter observed that tropinone (obtained by oxidation of tropine) reacts with benzaldehyde to form dibenzylidene derivative, suggesting that the keto group is flanked by two methylene groups, $—CH_2—CO—CH_2—$. Therefore, tropinone can be written as II and tropine as I which explains the reaction as below.



(*vi*) Tropinone on chromic acid oxidation gives (±)-tropinic acid containing the same number of carbon atoms. This shows that tropinone is a cyclic ketone.



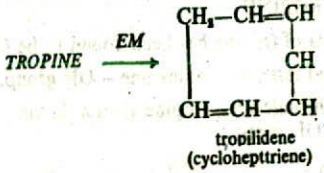
(*vii*) Tropinic acid upon further oxidation yields *N*-methylsuccinimide, indicating the presence of *N*-methylpyrrolidine ring system.



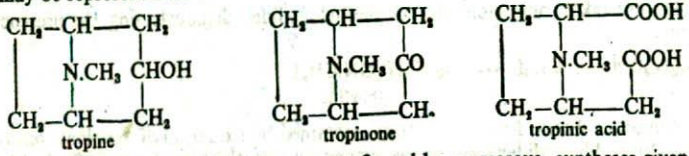
(*viii*) Tropinic acid on exhaustive methylation (*EM*), leads to the formation of an unsaturated dicarboxylic acid which on hydrogenation gives primelic acid.



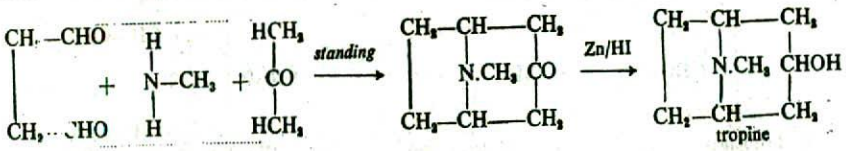
Hence tropinic acid must contain a straight chain of seven carbon atoms and tropinone a seven-carbon ring. The presence of seven-carbon ring is further supported by the fact that tropine when subjected to exhaustive methylation yields tropilidene (cycloheptriene).



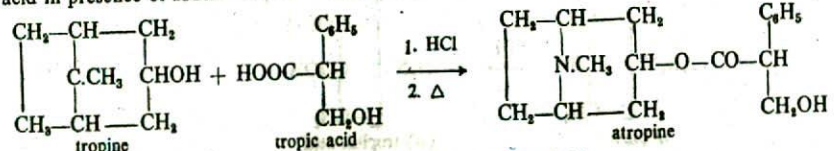
(*ix*) From the reactions discussed above, it follows that tropine, tropinone and tropinic acid may be represented as :



(*x*) The structure of tropine was confirmed by numerous syntheses given from time to time. Robinson synthesised tropine as follows.



(5) Finally the structure of atropine is established by combining tropine with tropic acid in presence of HCl.



The product obtained is identical with the natural alkaloid.

QUESTIONS

1. Give a precise definition of the term 'alkaloid'. Could you say if this definition is 'perfect'?

2. Discuss the occurrence of alkaloids as natural products. How are they isolated from plant material in which they are found?

3. Give the physical characteristics of alkaloids in general, elaborating their physiological activity and basic character.

4. Give the modern classification of alkaloids based on the nature of the heterocyclic ring system present in their molecular structure. Give at least one example of each type, also mentioning its source and specific physiological activity.

5. Write a brief note on the following alkaloids: primaquinine, camptothecin, papaverine, morphine, and LSD.

6. Give an outline of the procedures followed for the determination of the structure of alkaloids. Make a special mention of the more sophisticated physical methods introduced recently for the elucidation of structure of alkaloids.

7. Write a note on 'Exhaustive Methylation Degradation method' as applied to find out the heterocyclic moiety present in the molecule of an unknown alkaloid.

8. Describe the occurrence, isolation and properties of coniine. How was its structure determined ?

9. What are alkaloids ? How are they isolated from natural products ? *(North Eastern Hill BSc Hons, 1993)*

10. Discuss the extraction of alkaloids from plants and their general properties. *(Baroda BSc, 1993)*

11. What are alkaloids ? How are they classified ? Write the structural formula of coniine. *(Karnataka BSc III, 1993)*

12. What are alkaloids ? What are the general methods for the elucidation of structure of alkaloids ? *(Sambalpur BSc Hons, 1994)*

13. What are alkaloids ? Write the structure of atropine. How is tropic acid obtained from atropine ? Give evidence for the structure of tropic acid. *(Kerala BSc, 1993; Bombay BSc, 1994)*

14. Write a note on : Exhaustive methylation. *(Andhra BSc, 1994)*

15. Write a note on : Alkaloidal reagents. *(South Gujarat BSc III, 1993)*

16. Give the synthesis of the following compounds :
(*a*) Coniine ; (*b*) Piperic acid ; and (*c*) Nicotine *(Madras BSc, 1994)*

17. Describe how the structure of nicotine was established. *(Berhampur BSc, 1992)*

18. Describe how the structure of quinine was established. *(Andhra BSc, 1993)*

19. Describe how the structure of coniine was established. *(Madurai BSc, 1994)*

20. Describe how the structure of piperine was established. *(North Bengal BSc Hons, 1994)*

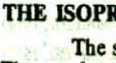
Chapter 49

Terpenes

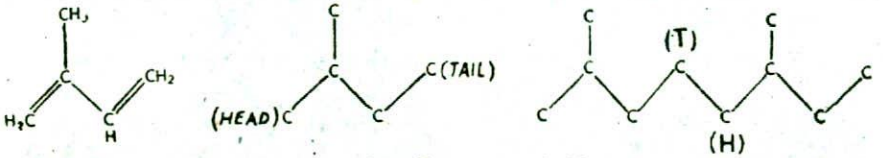
Many of the fragrant components of plants are volatile with steam and may be isolated by steam distillation, solvent extraction, or other treatment of the plant. These components are called the **Essential oils**. They are widely used in the perfumery, food flavourings, and medicines. The essential oils are not pure single compounds. They usually consist of mixtures of hydrocarbons containing 10, 15, 20, 30 or 40 carbon atoms or their oxygenated derivatives. These individual compoents of essential oils are called the **Terpenes** or **Terpenoids**.

THE ISOPRENE RULE

The structure of terpenes is based on a basic "building block" of five carbon atoms. Their carbon skeletons can be constructed by linking together of C_5 units branched at the second carbon atom. The **Isoperene Rule** states that terpene skeletons are formed by linking together



units (*isoprene units*) through carbon atoms 1 and 4 (*head-to-tail*), carbon atoms 1 and 1 (*head-to-head*), carbon atoms 4 and 4 (*tail-to-tail*) or combination thereof. The head-to-tail arrangement is most common. This isoprene rule has proved to be of great value in deriving the structure of terpenes.



Examples of some common terpenes are shown in Fig. 49·1. Dashed lines are used to indicate how the formulas can be divided into isoprene units.

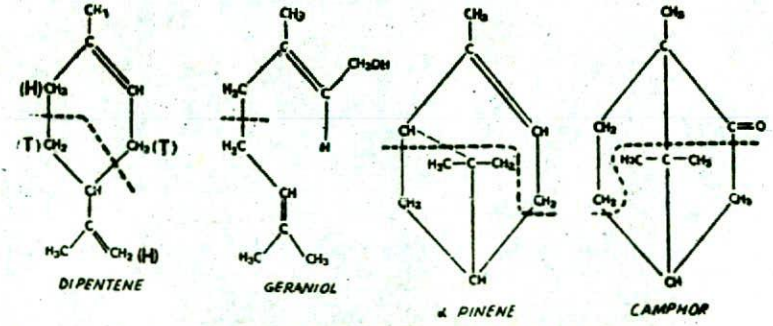


Fig. 49·1 Some common terpenes and their division into isoprene units.

ISOLATION OF TERPENES

Terpenes are isolated from *essential oils* present in plants. The essential oil is extracted from the plant tissues by four methods : (1) *Steam distillation* ; (2) *Digestion with solvents* ; (3) *Expression* ; *and* (4) *Adsorption in purified fats.* Method (1) is the one most widely used. The plant tissue is mascerated and then steam distilled. If a particular terpene is decomposed under these conditions, it may be removed by extraction with light petrol at 50°C and the solvent distilled under reduced pressure. Alternatively, the method of adsorption in fats may be employed. For example, the flower petals are spread over molten fat until the latter is saturated with essential oil. The fat is then digested with ethanol to remove the essential oil from it.

Essential oils obtained from plants as above usually contain a number of terpenes which are separated by *fractional distillation* or *chromatography.* Gas chromatography has been particularly useful.

PROPERTIES OF TERPENES

(*Physical*). Most of the terpenes are colourless fragrant liquids having a boiling point between 150°and 200° C. They are lighter than water and are readily volatile in steam. They dissolve in organic solvents, but usually not in water. Most of them are optically active although their is no prevailing direction of rotation ; some are *dextro*, others are *laevo.*

(*Chemical*). Most of the terpenes being unsaturated hydrocarbons, are highly reactive. They undergo addition reactions with hydrogen bromide, bromine, hydrogen, nitrosyl chloride, and ozone. They also form characteristic addition compounds with NO_2 and NOBr, which are used in their identification. Most terpenes are oxidised easily and tend to resinify upon exposure to air.

CLASSIFICATION OF TERPENES

Terpenes are classified according to the number of isoprene units they contain. The classes found in nature are listed in Table 49·1.

Table 49·1. Classes of Terpenes

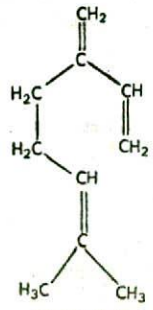
Class	*Number of Carbon Atoms*	*Number of Isoprene Units*
Monoterpenes	10	2
Sesquiterpenes	15	3
Diterpenes	20	4
Triterpenes	30	6
Tetraterpenes	40	8
Polyterpenes	$5n$	n

A. MONOTERPENES (C_{10})

The *monoterpenes* contain ten carbon atoms (two isoprene units). They may occur as *open-chain* (acyclic), *monocyclic or bicyclic* compounds. Some of the important members of this class are described below.

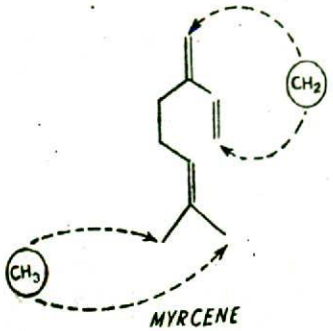
MYRCENE, *2-Methyl-6-methylene-2,7-octadiene,* $C_{10}H_{16}$

Myrcene is an open-chain monoterpene hydrocarbon. It is found in verbena and bay oils.



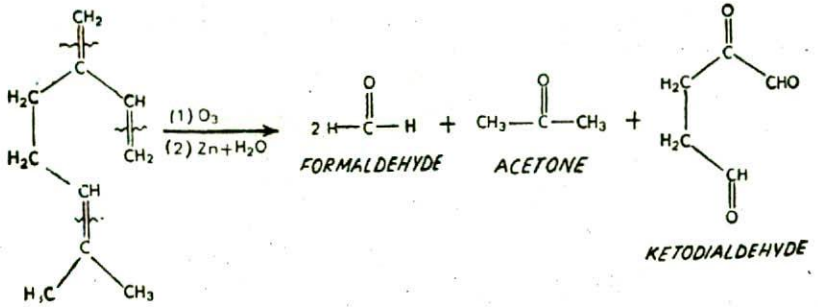
MYRCENE

For simplicity, the structures of terpenes are frequently written with line formulas. A corner is meant to represent a carbon atom with appropriate number of hydrogens. A line branching off the structure represents a methyl group, not a hydrogen Thus the above structure of myrcene may be written as :



MYRCENE

Myrcene is a liquid, bp 166—8°C. It undergoes catalytic hydrogenation to form decane, $C_{10}H_{22}$. It reacts with maleic anhydride to yield the corresponding Diels-Alder adduct. Myrcene undergoes ozonolyis to give a mixture of formaldehyde, acetone, and a ketodialdehyde.



CITRAL, *3, 7-Dimethyl-2,6-octadien-1-al*, $C_{10}H_{16}O$

Citral is widely distributed and occurs to the extent of 70 to 80 per cent in lemongrass oil. It is also found in oil of orange, oil of lemon (6 to 7 per cent) and in citronella oil.

Isolation.

The essential oil containing citral is treated with sodium bisulphite solution, when crystalline citral bisulphite derivative is obtained. This derivative is then hydrolysed with sodium carbonate to give pure citral.

Structure of Citral

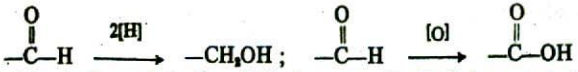
The structure of citral has been deduced from the consideration of facts and conclusions such as the following :

(1) Elemental analysis and molecular weight determinations show that the molecular formula of citral is $C_{10}H_{16}O$.

(2) Citral reacts with bromine (2 molecules) to form a tetrabromide derivative. This indicates the presence of two carbon-carbon double bonds in the citral molecule.

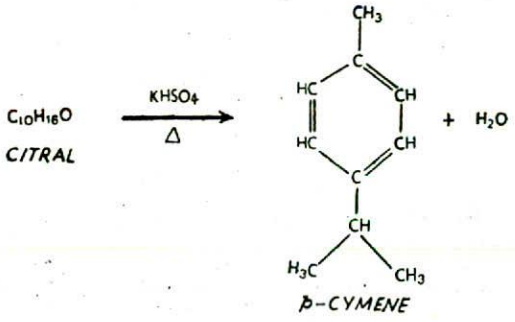
(3) Citral reacts with hydroxylamine to form an oxime. It also adds sodium bisulphite. These reactions indicate the presence of an aldehyde (—CHO) or a ketone (—CO—) group.

(4) Citral undergoes reduction with sodium amalgam and water to give a primary alcohol *geraniol*, $C_{10}H_{18}O$. It undergoes oxidation with the silver oxide to yield *geranic acid*, $C_{10}H_{16}O_2$, containing the same number of carbons. These reactions indicate the presence of an aldehyde group.

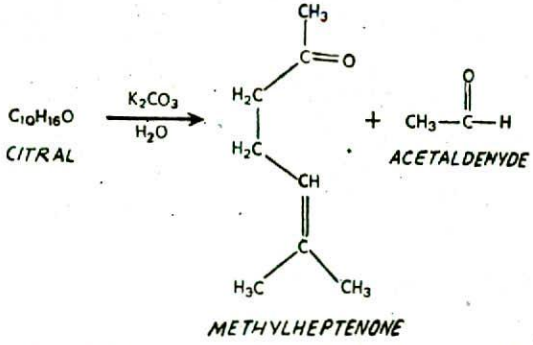


UV Studies indicate that the aldehyde group in citral is present as a part of an α, β-unsaturated carbonyl system.

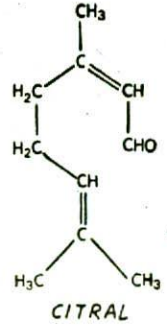
(5) When citral is heated with potassium bisulphate, it is converted to *p*-cymene. This indicates the relative positions of methyl and isopropyl groups in the citral molecule.



(6) Citral undergoes hydrolysis with potassium carbonate to give 2-methyl-2-hepten-6-one (methylheptenone) and acetaldehyde.

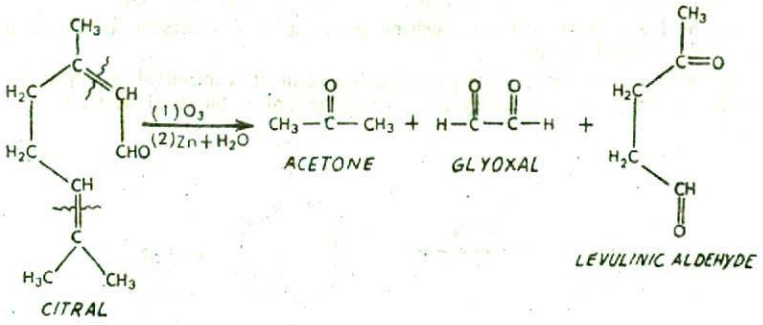


The above evidence indicates that citral has the following structural formula :



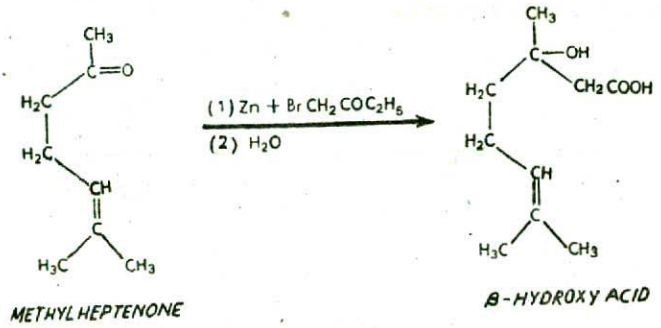
This structure of citral has been confirmed by its ozonolysis and synthesis from 2-methyl-2-hepten-6-one.

Ozonolysis of Citral. Citral undergoes ozonolysis to give acetone, glyoxal, and levulinic aldehyde. This reaction clearly establishes the positions of the two carbon-carbon double bonds in the citral molecule.

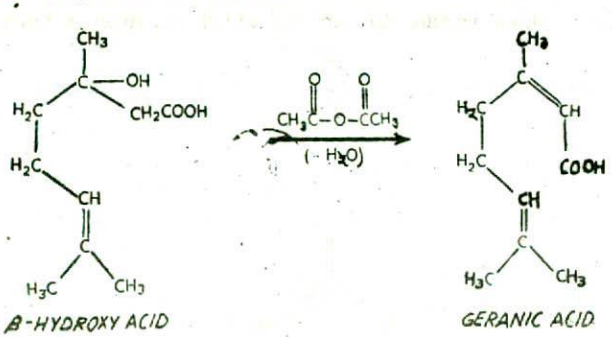


Synthesis of Citral. Citral can be synthesized from 2-methyl-2-hepten-6-one (methylheptenone) by the following three steps.

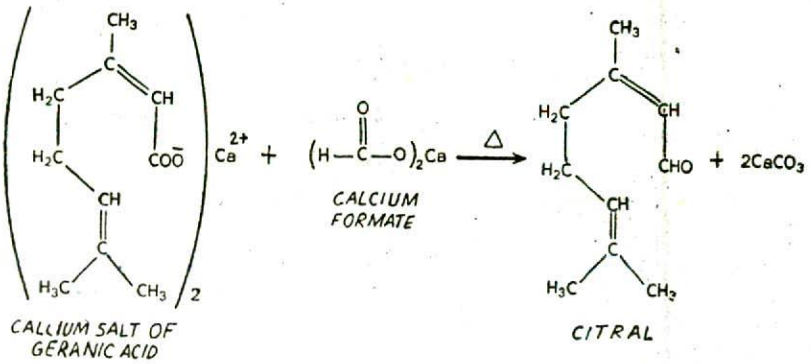
Step 1. Methylheptenone is subjected to Reformatsky reaction and hydrolysis to give a β-hydroxy acid.



Step 2. Dehydration of β-hydroxy acid with acetic anhydride gives geranic acid.

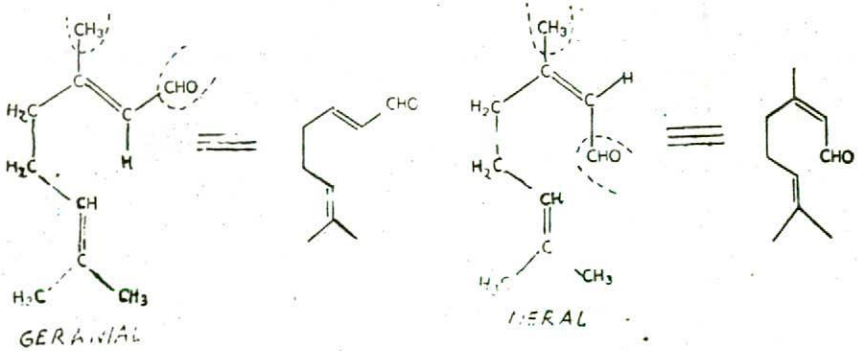


Step 3. Distillation of a mixture containing the calcium salt of geranic acid and calcium formate yields citral.



Geometrical Isomerism in Citral

Citral exists in two geometrical forms, known as citral-*a* (*geranial*) and citral-*b* (*neral*).



In geranial the methyl and the aldehyde groups are *cis* to each other and in neral they are *trans*. Both these forms occur together in varying amounts in natural oils. The unqualified term *citral* usually refers to the mixture. The configurations of these two isomers have been determined from a consideration of the rate of cyclisation of their corresponding alcohols.

Properties of Citral

(*Physical*). Geranial and neral are yellow liquids with the same boiling point, 118°C/20 mm.

(*Chemical*). Geranial and neral give the same chemical reactions, that is, the reactions of alkenes and aldehydes. Some of the important reactions of these isomers are listed in Fig. 49·2.

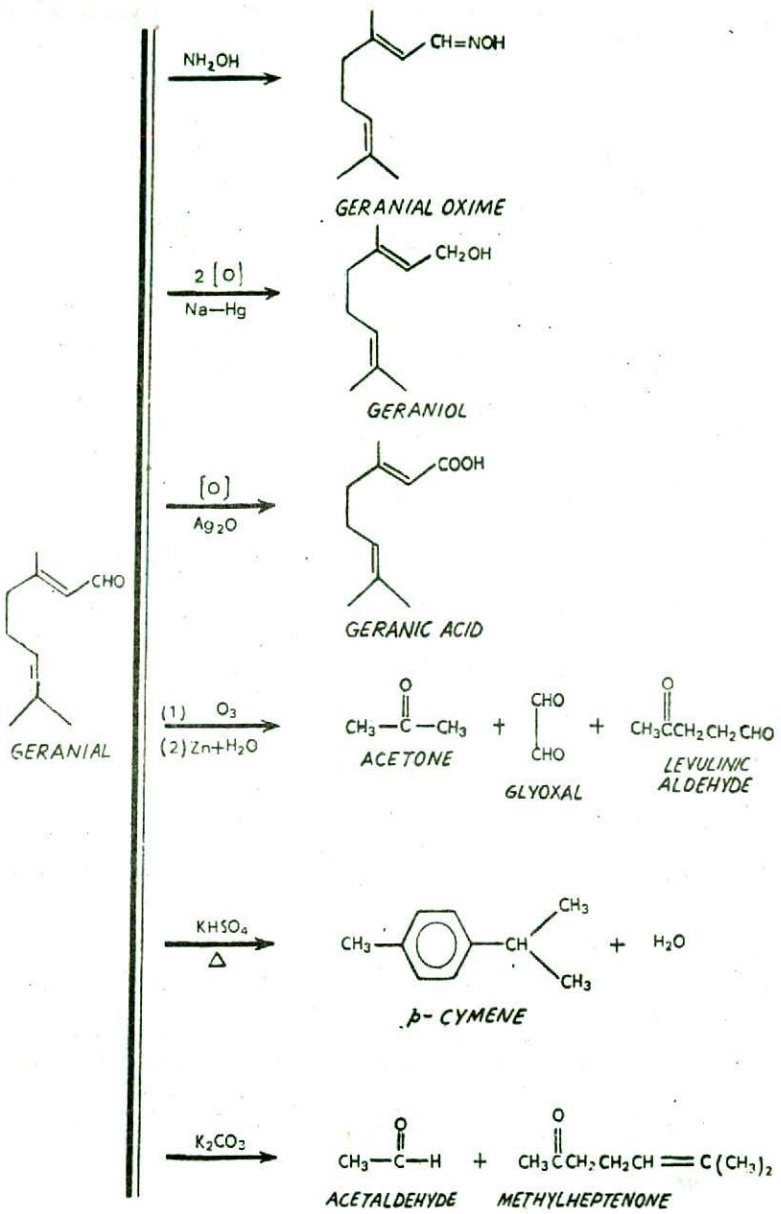


Fig. 49·2 Some important reactions of geranial. These reactions are also given by neral.

Uses of Citral

Geranial and neral are used for scenting cosmetics, perfumes, soaps and in lemon flavours. Geranial is also used in the manufacture of geraniol.

GERANIOL, *3,7-Dimethyl-2,6-octadien-1-ol*, $C_{10}H_{18}O$

Geraniol is the alcohol corresponding to geranial. It is found in the oils of rose (40 to 50 per cent), palmarosa (70 to 80 per cent), geranium, eucalyptus, and citronella.

Isolation

Geraniol is obtained from the cheap oil of palmarosa. The oil is treated with anhydrous calcium chloride with which geraniol forms a crystalline addition product. This crystalline addition product is then decomposed with water to give pure geraniol.

Structure of Geraniol

The structure of geraniol has been deduced as follows :

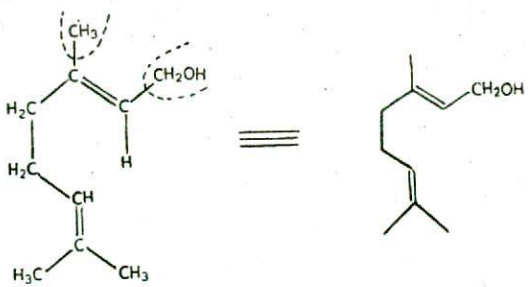
(1) Elemental analysis and molecular weight determinations show that the molecular formula of geraniol is $C_{10}H_{18}O$.

(2) Geraniol reacts with bromine (2 molecules) to form the tetrabromo derivative (2,3,6,7-tetrabromo-3,7-dimethyl-1-octanol). This indicates the presence of two carbon-carbon double bonds in the geraniol molecule.

(3) Geraniol does not form an oxime with hydroxylamine. This indicates the absence of an aldehyde (—CHO) or a ketone (—CO—) group.

(4) Geraniol can be obtained by the reduction of citral-*a* (geranial) with sodium amalgam or with ethyl or isopropyl alcohol in the presence of an aluminium alkoxide catalyst (*Meerwein-Ponndorf-Verley reduction*). Geraniol also undergoes oxidation to give citral-*a*. These reactions indicate the presence of a primary alcohol group in geraniol and its relationship with citral-*a*.

The above facts clearly show that geraniol has the following structure. Notice that the methyl and the $—CH_2OH$ groups are *cis* to each other.



GERANIOL

Properties of Geraniol

(*Physical*). Geraniol is colourless liquid with a sweet rosy odour. It boils at 230°C. Geraniol is insoluble in water but dissolves in ethanol.

(*Chemical*). Geraniol gives the reactions of alkenes and primary alcohols. Some of its important reactions are listed in Fig. 49·3.

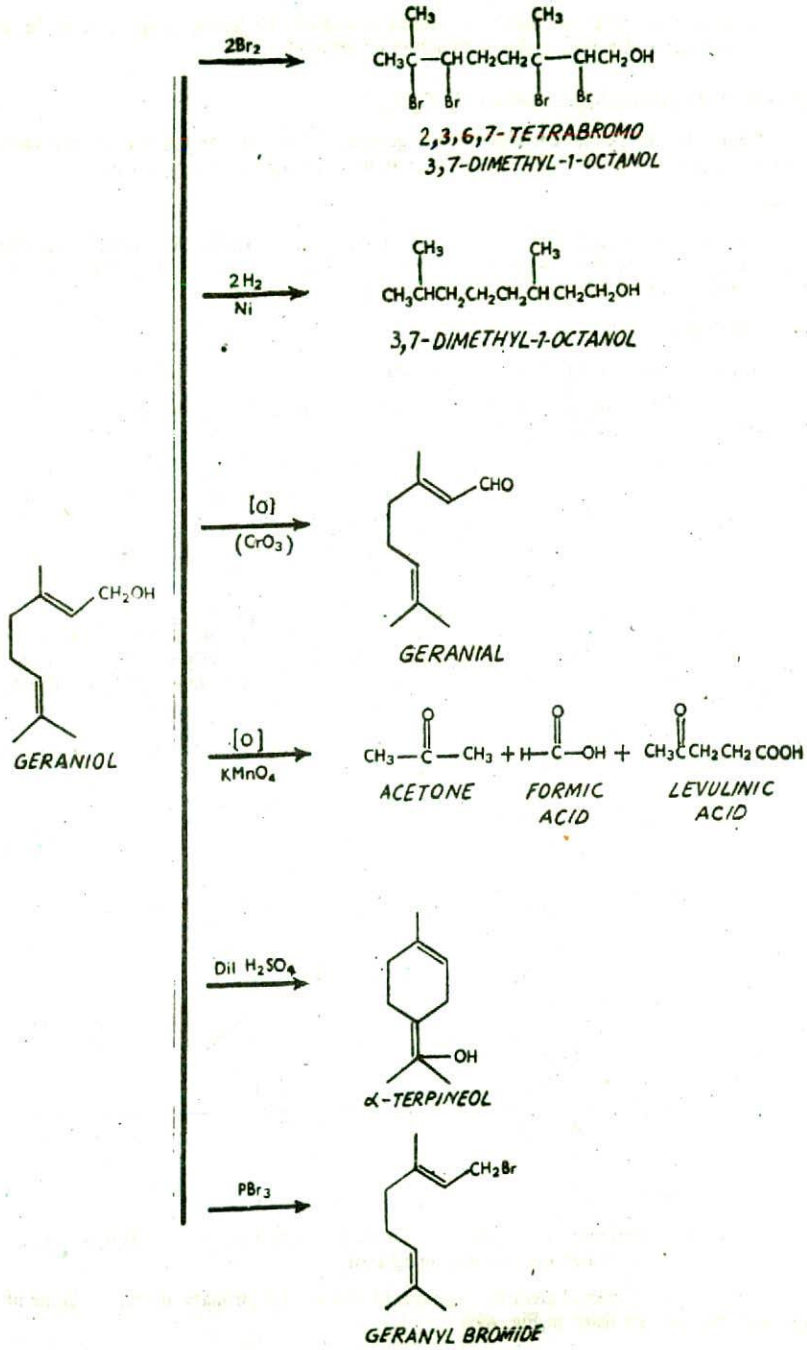


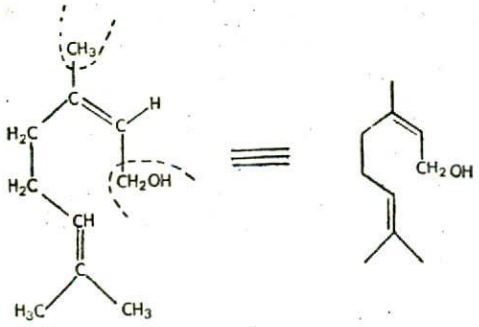
Fig. 49·3. Some important reactions of geraniol.

Uses of Geraniol

Geraniol is used in the manufacture of artificial rose scents. It is widely used in perfume, cosmetic, and flavour industries. It is also used as an agent for luring insects into traps.

NEROL, *3,7-Dimethyl-2,6-octadien-1-ol,* $C_{10}H_{18}O$

Nerol is the alcohol corresponding to neral. It is found in *neroli oil* (orange blossom oil) and *oil of bergamot.*



NEROL

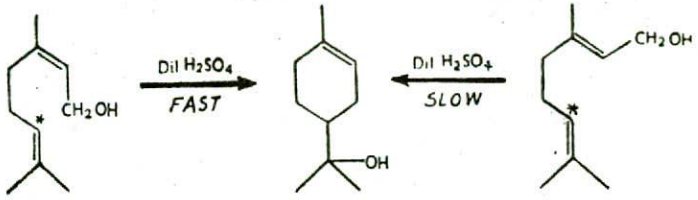
Notice that nerol is the geometric isomer of geraniol. In nerol the methyl and the $-CH_2OH$ groups are *trans* to each other and in geraniol they are *cis*.

Nerol is a colourless liquid, bp 225°C. It has a rose-like odour. Its chemical properties are similar to those of geraniol.

Nerol is used in the preparation of artificial rose scents.

Determination of the Configurations of Nerol and Geraniol

The configurations of nerol and geraniol have been determined from a consideration of their reaction with dilute (5 per cent) sulphuric acid. Both isomers undergo cyclization with this reagent to give α-terpineol.

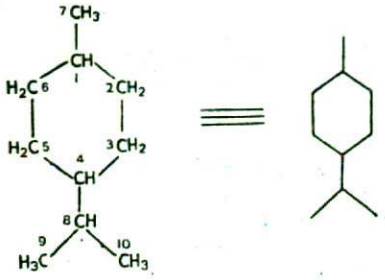


NEROL α-TERPINEOL GERANIOL

Nerol undergoes cyclization *nine* times faster than geraniol. This indicates that the $-CH_2OH$ group in nerol must be nearer to the carbon (*) which is involved in ring formation.

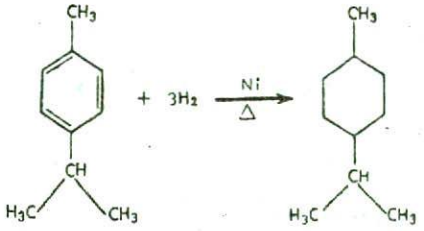
***p*-MENTHANE,** *4-Isopropyl-1-methylcyclohexane,* $C_{10}H_{20}$

p-Menthane is a monocyclic monoterpene. For naming other such terpenes, *p*-menthane is used as the parent substance. The positions of the substituents and double bonds are indicated by numbers, the conventional method of numbering being shown below.



p-MENTHANE

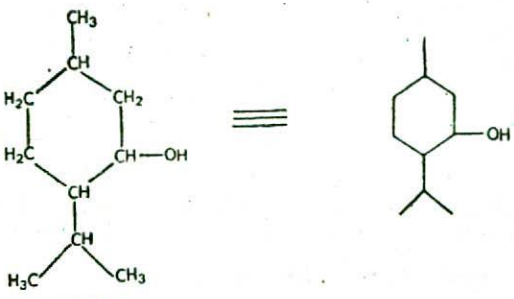
p-Menthane does not occur in nature. It is obtained by the catalytic hydrogenation of *p*-cymene or limonene.



p-CYMENE *p*-MENTHANE

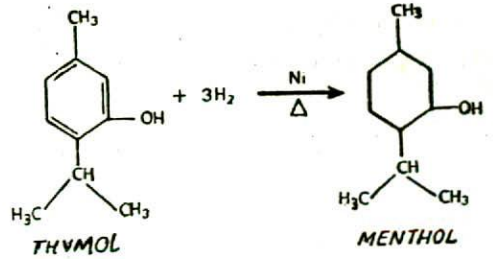
MENTHOL, *3-p-Menthanol, 3-Hydroxy-4-isopropyl-1-methylcyclohexane*, $C_{10}H_{20}O$

Menthol occurs in the oil of peppermint to the extent of 80 per cent. When this oil is cooled, crystals of menthol are obtained.



MENTHOL

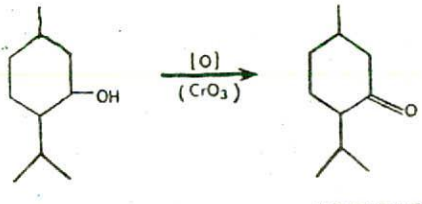
Synthesis. **Menthol is prepared by catalytic hydrogenation of thymol.**



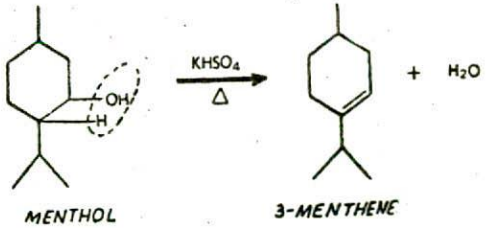
Properties (*Physical*). Menthol found in the oil of peppermint is laevorotatory. It is a colourless solid with a strong minty odour and cooling taste. It melts at 42°C and boils at 216°C. Synthetic menthol is a (±)-mixture

(*Chemical*). Menthol gives the reactions of a cyclic secondary alcohol.

(1) It undergoes oxidation with chromic acid to give the corresponding ketone *menthone* (3-*p*-menthanone; bp 207°C).



(2) It undergoes dehydration with potassium bisulphate to form 3-menthene (3-*p*-menthene; bp 168°C) by removal of the —OH group from C-3 and the hydrogen atom from C-4.



(3) It undergoes reduction with hydriodic acid to yield *p*-menthane.

Uses. Menthol is used in pharmaceutical preparations because of its anaesthetic and antiseptic action. When used in inhalers (*Vicks Inhalers*), its vapours have a cooling and mildly anaesthetic action upon inflamed nasal tissue. Menthol is used in face creams, shaving creams, tooth pastes, and ointments because of the cooling sensation that it imparts to the skin It is also used in candles, chewing gums, and certain brands of cigarettes.

LIMONENE, *1,8-p-Menthadiene*, $C_{10}H_{16}$

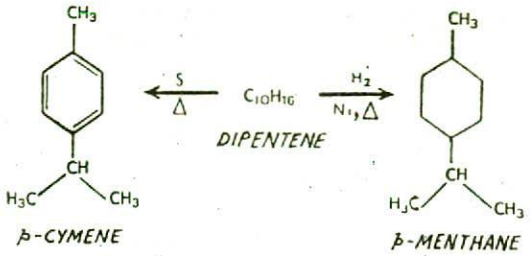
Limonene is an important monoterpene hydrocarbon. It is optically active (+)-Limonene occurs in the oils of orange, lemon, caraway, and lemongrass. (−)-Limonene is found in pine needles and in peppermint oil. (±)-Limonene, also known as dipentene, occurs in turpentine oil Of these three optical isomers dipentene is the most important.

Structure. The structure of dipentene (or limonene) has been derived as follows.

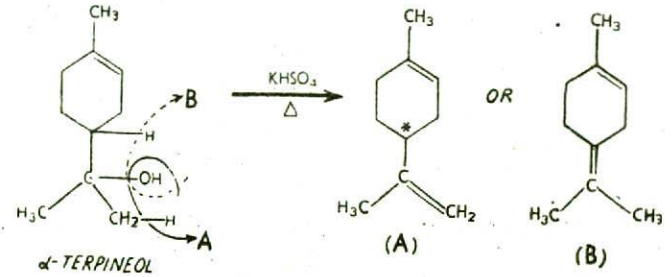
(1) Elemental analysis and molecular weight determinations show that the molecular formula of dipentene is $C_{10}H_{16}$.

(2 Dipentene reacts with bromine (2 molecules) to form a crystalline tetrabromide (mp 105°C). It also reacts with hydrogen bromide (2 molecules) to give the corresponding dihydrobromide. These reactions indicate the presence of two carbon-carbon double bonds in the dipentene molecule.

(3) Dipentene undergoes dehydrogenation over heated sulphur to yield *p*-cymene. It also undergoes catalytic hydrogenation to give *p*-menthane. These reactions tell us about the nature of the carbon framework of dipentene.

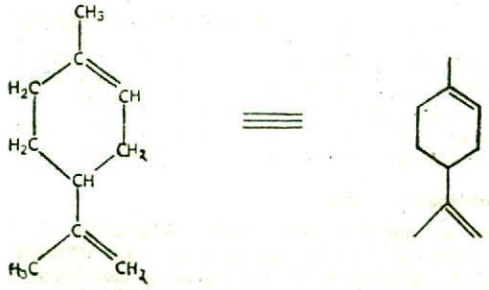


(4) Dipentene can be obtained by dehydration of α-terpineol with potassium bisulphate or oxalic acid. The elimination of water molecule can take place in two ways, giving (A) or (B).



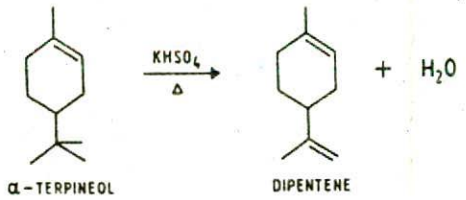
Structure (A) can show optical activity because it contains an asymmetric carbon atom (*). (B) cannot be optically active because it is a symmetrical molecule. Therefore (A) represents optically active limonene or its racemic modification dipentene.

The above facts clearly show that dipentene has the following structure.

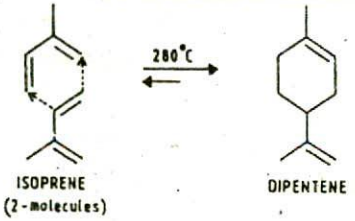


Synthesis. Dipentene may be obtained :

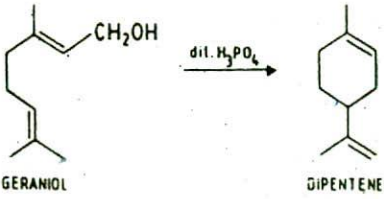
(1) By heating α-terpineol with potassium bisulphate.



(2) By heating isoprene in a sealed tube at 280° C.



(3) By heating geraniol with dilute phosphoric acid.



Properties (*Physical*). Dipentene is a liquid, bp 170·3°C/695 mm. It has a lemon-like odour. It is insoluble in water but dissolves in ethyl alcohol and diethyl ether.

(*Chemical*). Dipentene gives the reactions of alkadienes. Some of its important reactions are listed in Fig. 49·4.

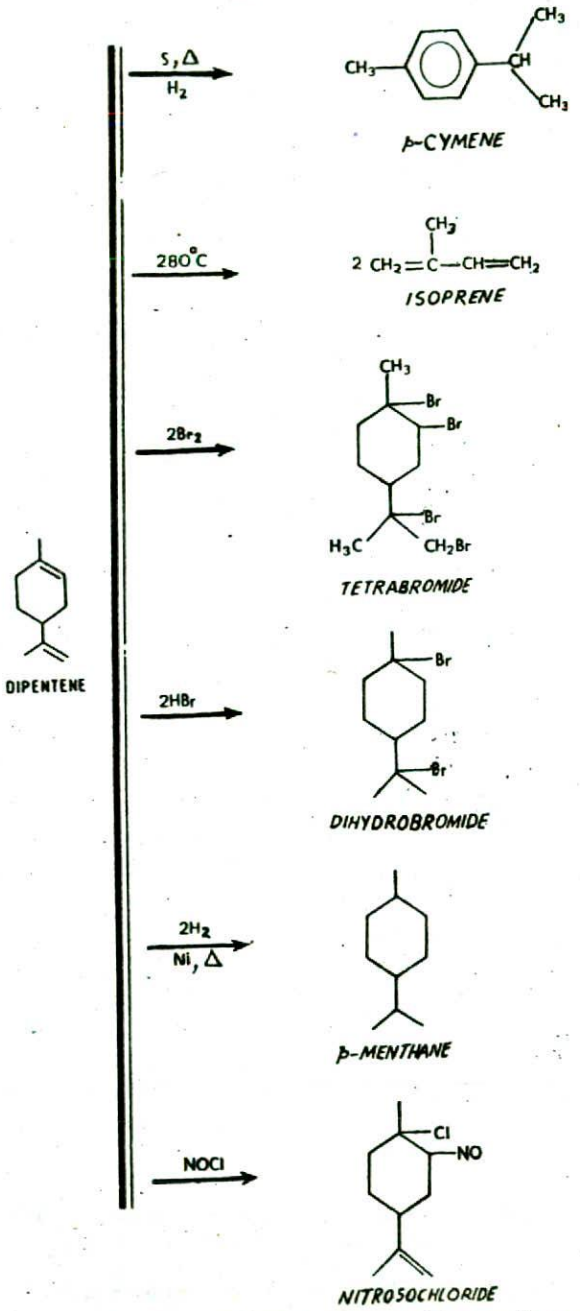
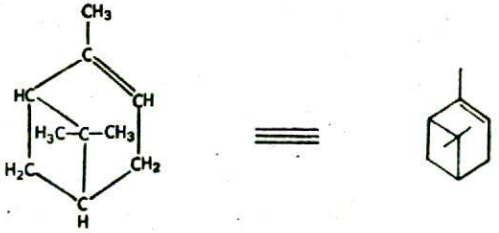


Fig. 49·4. Some important reactions of dipentene. These reactions are also given by limonene.

Uses. Dipentene is used as a flavour in foods, beverages, and pharmaceutical preparations. It is also used in the manufacture of resins, isoprene, *p*-cymene, and *p*-menthane.

α-PINENE, $C_{10}H_{16}$

α-Pinene is a bicyclic monoterpene. It is present in nearly all essential oils. The most common source of α-pinene is turpentine in which it occurs in both (+)- and (−)-forms.



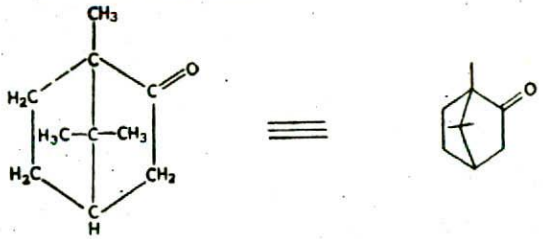
α-PINENE

α-Pinene is a liquid, bp 154—6° C. It gives the reactions of alkenes. α-Pinene reacts with dry hydrogen chloride to form colourless crystalline pinene chloride, $C_{10}H_{17}Cl$ (mp 131°C.) This crystalline compound has a faint camphor-like odour and is known as *artificial camphor*.

Turpentine oil which is mostly pinene is used as a solvent for resins, as a thinner for paints and varnishes, and in the commercial synthesis of camphor.

CAMPHOR, $C_{10}H_{16}O$

Camphor is obtained by steam distillation of wood, leaves, or bark of the camphor tree. This tree grows mainly in Japan and Formosa.



CAMPHOR

Commercially, camphor is obtained from α-pinene by the series of reactions shown in Fig. 49·5.

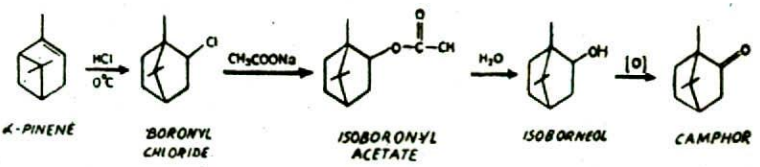


Fig. 49·5. Commercial synthesis of camphor.

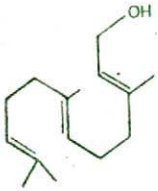
Camphor is a colourless, crystalline solid. It has a characteristic strong odour. It melts at 179°C and boils at 207°C. Despite its high melting point, camphor sublimes at room temperature. It occurs in both the (+)- and (−)-forms.

Cmphor is a ketone and shows the properties characteristic of the carbonyl group. For examaple, it forms an oxime with hydroxylamine. It is reduced by sodium and alcohol to a secondary alcohol *borneol* (mp 209°C; bp 213°C).

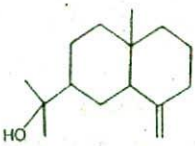
Camphor is used as a plastisizer for cellulose nitrate (*smokeless powder*). It is used in pharmaceutical preparations because of its analgesic, stimulant, expectorant, antiseptic, and carminative effects. In the chemical laboratories, it is a convenient solvent for the determination of molecular weights, since its cryoscopic constant of 40 is unusually high. It is also used as a moth repellent, in embalming fluids, and as a preservative in cosmetics.

B. SESQUITERPENES (C_{15})

The sesquiterpenes contain fifteen carbons (three terpene units). Like the monoterpenes, they can be found either as open-chain compounds, such as *farnesol*, an oil found in flowers, or as cyclic compounds, such as *eudesmol*, found in eucalyptus oil.



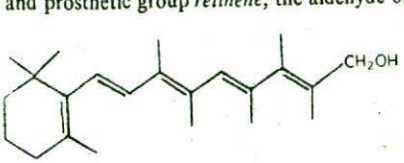
FARNESOL



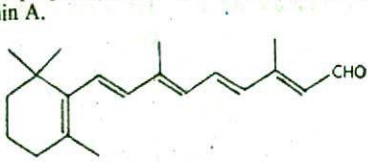
EUDESMOL

C. DITERPENES (C_{20})

The diterpenes contain twenty carbons (four isoprene units). **Vitamin A**, found in fish liver oils, is a monocyclic diterpene. It is required for the production in our eyes of visual purple (rhodopsin), which is necessary for sight. Visual purple is composed of a protein complex and prosthetic group *retinene*, the aldehyde of vitamin A.

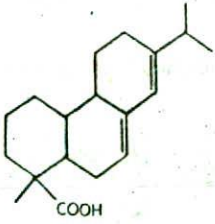


VITAMIN A



RETINENE

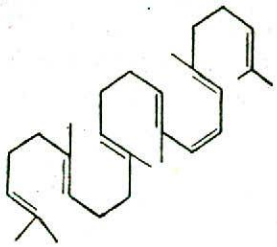
Abietic acid is a tricyclic diterpene. It is the chief constituent of pine resin.



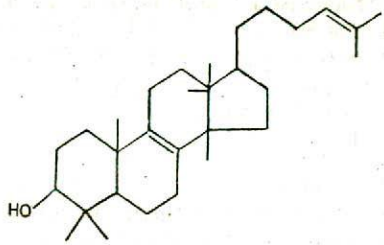
ABIETIC ACID

D. TRITERPENES (C_{30})

The triterpenes contain thirty carbons (six isoprene units). Examples of triterpenes are *squalene* and *lanosterol*. These compounds are important intermediates in the biosynthesis of of steroids. Squalene is also found in shark liver oil and lanosterol in lanolin (wool fat), which is used extensively in hair dressing formulations.



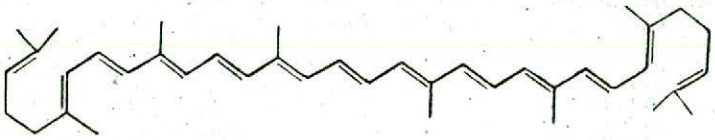
SQUALENE



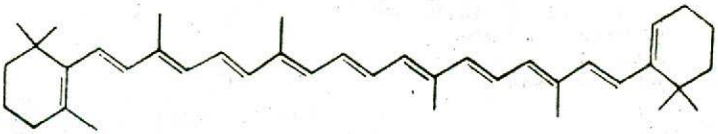
LANOSTEROL

E. TETRATERPENES (C_{40})

The tetraterpenes contain forty carbons (eight isoprene units). They are responsible for colouring of many food stuffs, such as tomatoes, carrots, corn, egg yolk, watermelon, and so on. The colour is caused by long conjugated polyene chains in these terpenes. Examples of tetraterpenes are **lycopene** and **β-carotene**. Lycopene is responsible for the red colour of ripe tomatoes and watermelon. β-Carotene imparts orange colour to carrots.



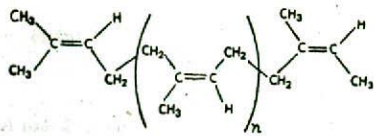
LYCOPENE



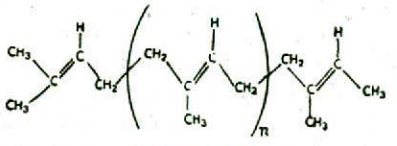
β-CAROTENE

F. POLYTERPENES (C_n)

The two most important polyterpenes are **natural rubber** and **gutta-percha**. In natural rubber, the double bonds of the repeating isoprene units are *cis*; the molecules are able to bend back and forth a little so that the rubber can stretch. Gutta-percha has the *trans* structure. It is hard and non-rubbery. Gutta-percha is extensively used in electrical insulation and dentistry.



NATURAL RUBBER



GUTTA-PERCHA

QUESTIONS

1. **What are terpenes? How are they classified? Write the formulas for several terpenes of both open-chain and cyclic types and by means of dotted lines show the relation of each compound to isoprene.**
2. **What are essential oils? How are they isolated from natural sources?**
3. **Three constituents of essential oils have the common molecular formula, $C_{10}H_{16}O$. Upon reduction they take up respectively *six*, *four*, or *two* atoms of hydrogen per molecule. Name some compounds corresponding to these data.**

4. Tell how the structure of *citral* has been established.
5. How can citral be synthesized from 2-methyl-2-hepten-6-one ?
6. Predict the major product(s), if any, of the reaction of *citral* with each of the following reagents :
   (*a*) NH_2OH
   (*b*) (*i*) O_3; (*ii*) $Zn + H_2O$
   (*c*) Ag_2O
   (*d*) $K_2CO_3 + H_2O$
   (*e*) $KHSO_4$, heat.
7. Tell how the structure of *geraniol* has been established.
8. How can *geraniol* be obtained from citral ?
9. Predict the major product(s), if any, of the reaction of *geraniol* with each of the following reagents :
   (*a*) Dil. H_2SO_4
   (*b*) H_2/Ni
   (*c*) Br_2
   (*d*) $KMnO_4$
   (*e*) PCl_3
10. Geraniol and nerol are geometric isomers. How will you determine their configurations ?
11. Describe how the structure of *dipentene* has been established.
12. How can *dipentene* be prepared from α-terpineol or isoprene ?
13. Predict the major product(s), if any, of the reaction of *dipentene* with each of the following reagents :
   (a) S, heat
   (*b*) H_2/Ni
   (*c*) NOCl
   (*d*) HBr
   (*e*) Heat at 280°C
14. Show how the following compounds could be synthesized from the indicated starting materials.
   (*a*) Geraniol *from* citral-*a*
   (*b*) Citral *from* 2-methyl-2-hepten-6-one
   (*c*) α-Terpineol *from* geraniol
   (*d*) Menthol *from* thymol
   (*e*) Camphor *from* α-pinene

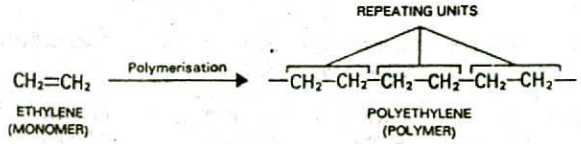
15. Write a note on : Isoprene rule. (*Bombay BSc, 1993*)
16. What are terpenes ? How are they classified ? (*Anna BSc, 1993; Madurai BSc, 1994*)
17. Outline the synthesis of (*a*) α-Terpineol ; and (*b*) Camphor
18. Describe how the structure of citral was established. (*South Gujarat BSc III, 1994*)
19. Describe how the structure of geraniol was established.
20. Describe how the structure of dipentene was established. (*Bombay BSc, 1994*)
21. How will you establish that
   (*a*) Dipentene contains two double bonds.
   (*b*) Citral contains an aldehyde group. (*Madurai BSc, 1993*)
22. (*a*) How are terpenes classified ?
   (*b*) Show that citral is an α, β-unsaturated aldehyde.
   (*c*) Write structures of different geometrical isomers of citral. (*Delhi BSc Hons, 1994*)

Chapter **50**

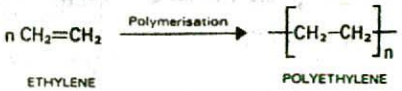
Synthetic Polymers

The development of modern technology has brought tremendous changes to our life-styles in the last 30 years. One of the most significant changes has been the gradual replacement of natural materials, such as wood, wool and cotton with man-made synthetic polymers. For better or worse, we are becoming a *'plastic'* society. In this chapter we will study how polymers are made and how they are used.

Polymers are high molecular weight compounds, whose structures are composed of a large number of simple repeating units. The repeating units are usually obtained from low molecular weight, simple compounds, referred to as monomers. The conversion process, monomer to polymer, is known as 'polymerisation'. The formation of polyethylene is an example of this process.



The equations for polymerisation are represented as shown below, where *n* stands for a large number.



Frequently, the end-groups of polymers are unknown – they may arise from impurities in the reaction mixture. In some cases, the end-groups can be controlled. The properties of a polymer are governed almost entirely by the bulk of the polymer molecule rather than the end-groups. To emphasise the basic structure of the polymer, it is customary not to include the end-groups in the formula.

Polymers are said to be **linear**, if the repeating units are joined together like links in a chain. The chains may be **branched**, or joined together by **cross-links**, or both (Fig. 50.1). More extensive cross-linking may lead to the formation of a three dimensional **cross-linked** or **net-work polymer**.

There are two main types of polymerisation processes : **addition polymerisation** and **condensation polymerisation.** In addition polymerisation, all atoms in the monomer are present in the polymer, but condensation polymerisation is characterised by the elimination of small molecules, such as water, methyl alcohol, carbon dioxide, etc.

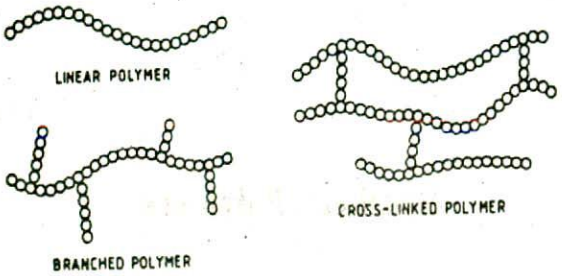


Fig. 50.1 Linear, branched and cross-linked polymers.

ADDITION POLYMERS

Addition polymers are formed by combination of alkene monomers to produce a single huge molecule only. Examples are :

(1) **Polyethylene (Polythene).** It is obtained by polymerising ethylene. The reaction is carried at 200°C and 1000 atm. pressure, with small amount of oxygen as a catalyst. At this temperature, the oxygen reacts with ethylene to form peroxides, which initiate the polymerisation reaction.



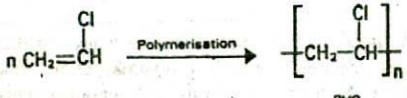
End–use. Polyethylene is used in packaging, houseware, such as buckets and dustbins, carpet backing, cable insulation and flexible bottles.

(2) **Polypropylene.** It is obtained by polymerising propylene. The reaction is carried at 50–120°C and 3 atm. pressure, in the presence of aluminiumtrialkyl-titanium tetrachloride (Ziegler catalyst).



End–use. Polypropylene is used in making houseware, medical equipment (can be sterilised), toys, electronic components, tubing and pipes, fibres and filaments, coating.

(3) **Polyvinyl Chloride (PVC).** It is obtained by polymerising vinyl chloride. The reaction is carried at 80°C and 10 atm. pressure, with small amount of benzoyl peroxide (or lauroyl peroxide) as a free-radical catalyst.

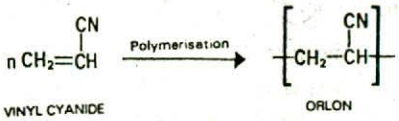


Vinyl chloride is prepared from acetylene by treatment with HCl in the presence of $HgCl_2$.



End–use. PVC is widely used in imitation leathers, floor coverings, corrugated roofing material, and gramophone records. With the addition of a plasticizer, the polymer has a rubber-like texture. This is used in squeeze bottles, pipes, etc.

(4) **Orlon (Acrilan).** It is obtained by polymerising vinyl cyanide. The reaction is carried at 40°C and atmospheric pressure with small amount of benzoyl peroxide (or potassium persulphate) as a free-radical catalyst.



Vinyl cyanide was once prepared by treating acetylene with HCN in the presence of $Ba(CN)_2$.

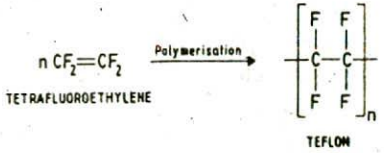
$$HC \equiv CH + HCN \xrightarrow{Ba(CN)_2} CH_2=CHCN + 6H_2O$$

Now it is prepared by a cheaper process which involves catalytic oxidation of propene in the presence of ammonia.

$$2CH_3CH=CH_2 + 3O_2 + 2NH_3 \xrightarrow[\text{catalyst}]{450^\circ C} 2CH_2=CHCN + 6H_2O$$

End–use. Orlon is used as a synthetic textile fibre in clothing and carpeting.

(5) **Teflon (PTEF or Fluon).** It is obtained by polymerising tetrafluoroethylene. The reaction is carried at 30–40°C and under pressure with benzoyl peroxide (or potassium persulphate) as a free-radical catalyst.

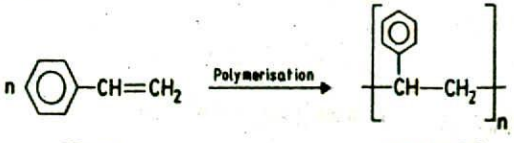


Tetrafluoroethylene is prepared by treating chlorodifluoromethane with HCl at 900°C.

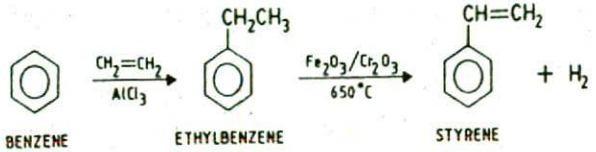
$$2CHClF_2 \xrightarrow{900^\circ C} CF_2=CF_2 + 2HCl$$

End–use. Teflon is familiar because of its use as non-stick coating, particularly for cooking utensils. *Nirlep non-stick frying pans have teflon coating.* Because of its low chemical reactivity, excellent toughness, electrical and heat resistance, teflon is used as insulation for electrical items and in the manufacture of gaskets and valves.

(6) **Polystyrene.** It is obtained by heating styrene alone at 132°C or in the presence of dibenzoyl peroxide catalyst at 50°C.



Styrene is prepared from benzene by the following reactions :



End-use. Polystyrene is used in the manufacture of food containers, cosmetic bottles, television cabinets, plastic cups, packaging and toys.

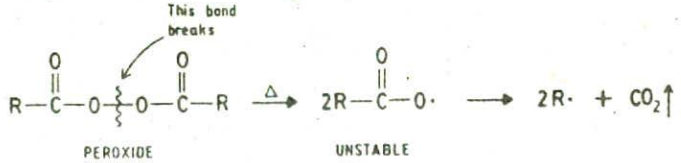
MECHANISM OF ADDITION POLYMERISATION

Addition polymerisation takes place either by a free-radical *or* ionic mechanism depending upon the reagents employed.

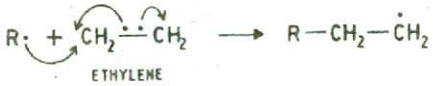
Free-Radical Polymerisation

Free-radical polymerisation is catalysed by organic peroxides or other reagents which decompose to give free radicals. Following steps are involved :

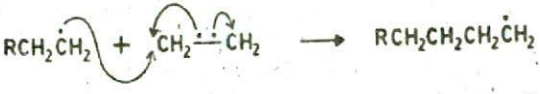
(1) **Chain Initiation**. Organic peroxides undergo homolytic fission to give free radicals.



(2) **Chain Propagation**. Free radical produced in the above step adds to an alkene molecule to form a new free radical.



This free radical can attack another alkene molecule and so on.



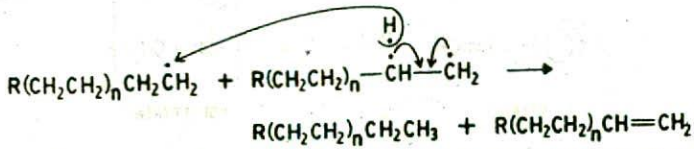
$$RCH_2\dot{C}H_2 + nCH_2{=}CH_2 \longrightarrow R(CH_2CH_2)_n CH_2\dot{C}H_2$$

(3) **Chain Termination**. The chain can be interrupted when two free radical chains combine, or by disproportionation.

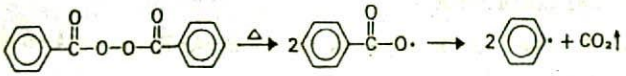
COMBINATION :

$$2R(CH_2CH_2)_n CH_2\dot{C}H_2 \longrightarrow R(CH_2CH_2)_n CH_2CH_2 : CH_2CH_2(CH_2CH_2)_n R$$

DISPROPORTIONATION :



Note. Benzoyl or *t*-butyl peroxides are common reagents for free-radical polymerisations.





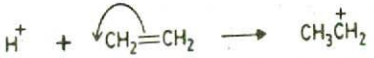
Phenyl or methyl free radicals will then initiate free-radical polymerisation.

Polymerisation of unsaturated monomers is complicated in practice by several factors that greatly affect the properties of the product. One such problem is that free-radical polymerisation yields a product that is not linear, but has numerous branches in it. Branches arise when the free-radical end of a growing chain abstracts a hydrogen atom from the middle of a chain to yield an internal radical site that continues the polymerisation.

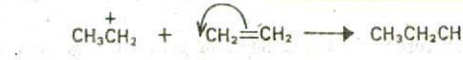
Ionic Polymerisation

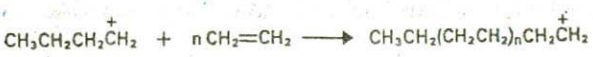
Ionic polymerisation is initiated by acids such as H_2SO_4, HF, or BF_3 with trace of water ($BF_3 + H_2O = HOBF_3H^+$). Following steps are involved :

(1) **Chain Initiation**. Proton adds to the carbon-carbon double bond of alkene to give a stable carbonium ion.

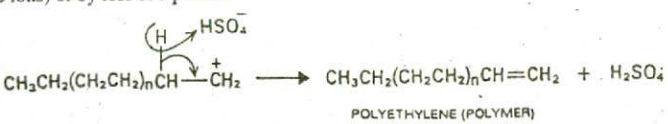


(2) **Chain Propagation**. The carbonium ion adds to another molecule of alkene to produce a new carbonium ion, which can similarly add to another molecule of alkene and so on.





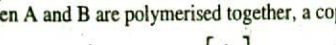
(3) **Chain Termination**. The chain reaction can be interrupted by combination with an anion (negative ions) or by loss of a proton.



For simplicity, ethylene has been used to illustrate the free-radical and ionic mechanisms of addition polymerisation. The reactions require pressures of about 1000 atmospheres at 200°C. Much lower pressures and temperatures can be used with Ziegler catalysts which consist of a trialkyl aluminium and titanium tetrachloride in an inert solvent. The polyethylene produced by Ziegler polymerisation has higher density than polyethylene obtained from high pressure free-radical polymerisation and has the important advantage that it will withstand boiling water without softening.

COPOLYMERS

Copolymers are produced by polymerising two or more different monomers. Consider the polymerisation of monomers A and B. When allowed to react separately, each gives a homopolymer. When A and B are polymerised together, a copolymer is formed.





Copolymer structure my be either alternating, in which a definite structural pattern may be observed, or random.

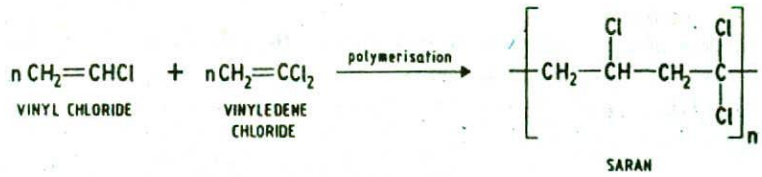
ALTERNATING COPOLYMER:

$$nA + nB \longrightarrow -A-B-A-B-A-B-A-B-A-B-A-B-A-B-A-B-A-$$

RANDOM COPOLYMER :

$$nA + nB \longrightarrow -A-A-B-A-B-B-A-B-A-A-B-A-B-A-A-B-B-$$

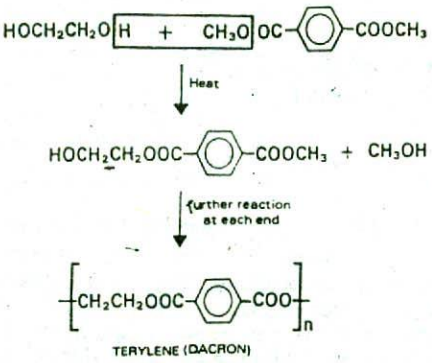
Saran is an important copolymer. It is obtained by treatment of vinyl chloride with vinylidene chloride in the presence of benzoyl peroxide or lauroyl peroxide catalyst. Saran is used to make tough food wrap that is very effective moisture barrier. Automobile upholstery can also be fabricated from saran.



CONDENSATION POLYMERS

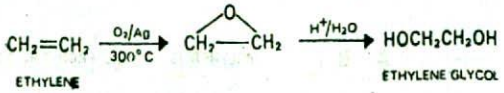
Condensation polymers are formed by combination of monomers with the elimination of simple molecules such as H_2O or CH_3OH. There are two main types of condensation polymers : *polyesters* or *polyamides*.

(a) **Terylene (Dacron or Teron)** is the most important polyester. It is prepared by heating ethylene glycol with dimethyl terephthalate at 270–285°C in the presence of metal oxides.

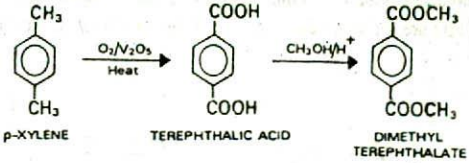


The polymer melt can be spun into fibres and combined with such naturally occurring fibres as cotton. The combination of cotton and polyester yields a fabric (*e.g.*, 60/40 cloth), that dries quickly without wrinkling, yet still retains the coolness and comfort of 100% cotton. Polyesters have revolutionised the cloth industry.

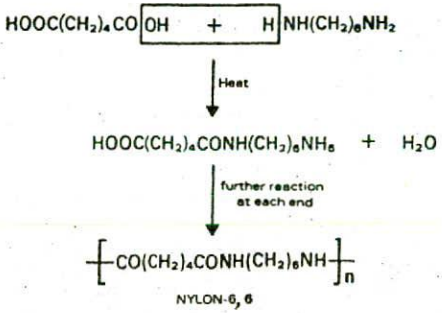
Ethylene glycol is manufactured by catalytic oxidation of ethylene to ethylene oxide which is then treated with dilute acid.



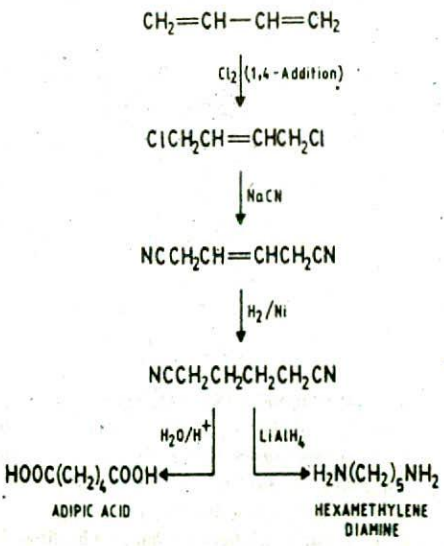
Dimethyl terephthalate is obtained by catalytic oxidation of *p*-xylene followed by esterification of the resultant acid.



(*b*) **Nylon-6,6** is the most important polyamide. It is obtained by heating adipic acid with hexamethylene under nitrogen at 180–220°C. Nylon-6,6 derives its name from its starting materials, adipic acid and hexamethylene, both of which have *six* carbons.



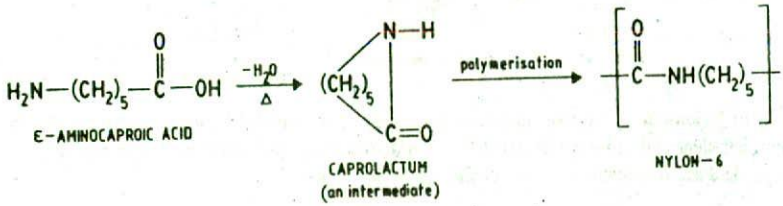
Both starting materials can be prepared from 1,3-butadiene.



Nylon-6,6 was developed as a synthetic fibre for the production of stockings and other wearing apparel. It was introduced to the public at the New York World's Fair in 1939. It is used to make fibres for clothing and carpeting, filaments for fishing lines and ropes, bristles for brushes, and

molded objects such as gears and bearings. For the better application no lubrication is required, because nylon surfaces are inherently slippery.

A similar polyamide, **Nylon-6**, is obtained by heating aminocaproic acid under nitrogen at 220-260°C. Nylon-6 fibres are widely used in carpets and, more recently, in water desalination units.



Because of their ability to form hydrogen-bonds between the polymer chains (Fig. 50.2), nylons show unusually high strength and make excellent fibres.

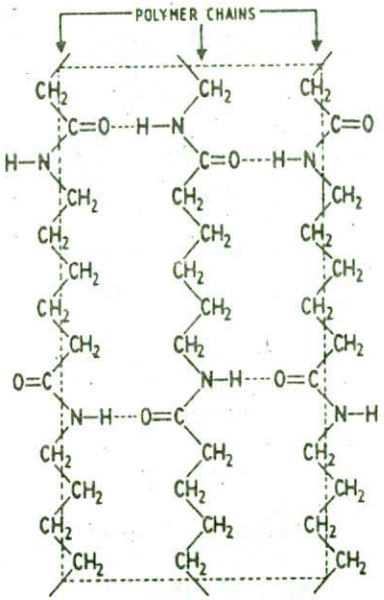


Fig. 50.2. Structure of hydrogen-bonding in Nylon-6.

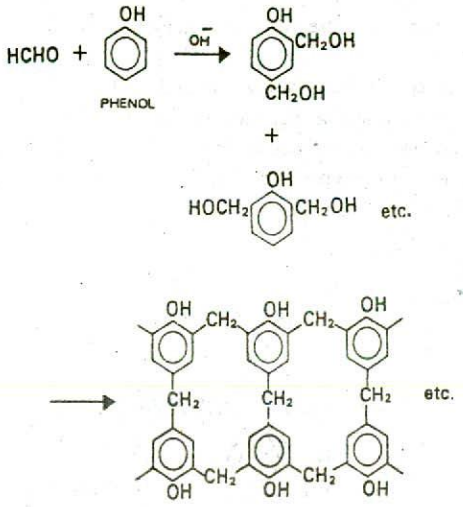
THERMOPLASTIC AND THERMOSETTING POLYMERS

A thermoplastic polymer is one which softens on heating and becomes rigid again on cooling. This is because there are weak attractive forces between the long polymer molecules and these are readily disrupted on heating. Most addition polymers and some condensation polymers are thermoplastic. *Examples are : Nylon, Polythene and Polystyrene.*

A thermosetting polymer is one which becomes hard on heating. It cannot be softened by heating. Polymers of this type are often prepared in two stages. The first stage is the formation of long chain molecules which are capable of further reaction with each other. These intermediate polymers usually flow and can be placed in moulds. Colouring is often added at this stage.

The second stage is the application of heat which cause a reaction to occur between the chains, thus producing a complex-network polymer. *Examples are : Phenolic resins, Epoxy resins, Polyurethanes and Alkyd resins.*

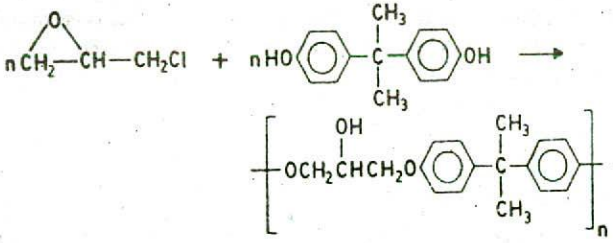
(a) **Phenolic Resins.** These polymers are made by condensation of phenols with formaldehyde. For example, when phenol is treated with excess formaldehyde and alkali catalyst, short chain polymers are first formed. On heating, these chains increase in length which finally cross-link to give a hard, insoluble thermosetting plastic *Bakelite*.



BAKELITE

Bakelite is widely used for making molded products such as handles on electrical and cooking utensils ; electrical plates and switches, appliances ; and as a bonding adhesive in plywood.

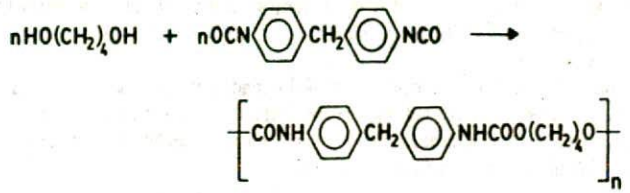
(b) **Epoxy Resins.** These polymers, which are known for their bonding properties, are used in adhesives such as *Araldite*. Epoxy resins are prepared by condensation of excess chloroepoxyalkanes with dihyric phenols in the presence of NaOH catalyst at 50–60°C. For example,



The polymer produced is cross-linked by heating with certain amines, when terminal epoxy groups of the chains react with the amine, cross-linking the chains.

Epoxy resins are extensively used to bind glass, porcelain, metal and wood. These resins, because of their inertness, hardness and flexibility make excellent protective coatings. Fibreglass boat hulls, for example, have a metal frame coated with a thick layer of spun glass trapped in a set of epoxy resin.

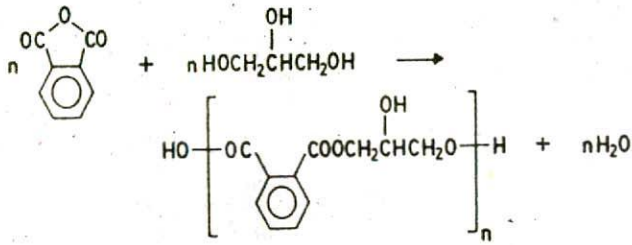
(c) **Polyurethanes.** These polymers are prepared by reaction of diisocyanates and diols in the presence of stannic chloride or stannous octoate at 50–100°C.



If triols and di- or triisocyanates are used, cross-linking can take place to give a thermosetting polymer.

Polyurethanes can be spun into elastic fibres such as **Spandex**. If they are formed in the presence of a low-boiling liquid that will readily vaporise as the reactants are heated, a semirigid polyurethane foam results. Polyurethane foams are used in construction and interior decoration of buildings.

(d) **Alkyd Resins.** These are polymers derived from alcohols and acids/anhydrides. Glyptal resin (a typical alkyd resin) is obtained by heating phthalic anhydride and glycerol at 180°C.



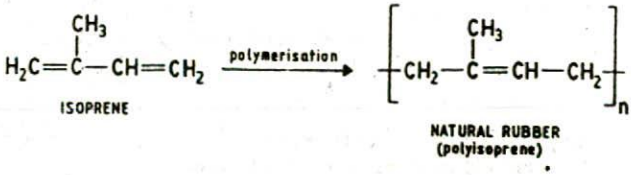
This can be dissolved in a suitable solvent and applied as a surface coating. On heating, the solvent evaporates and a hard, smooth, protective surface results, owing to cross-linking of the chains.

Glyptals are mainly used as bonding resins and in alkyd paints.

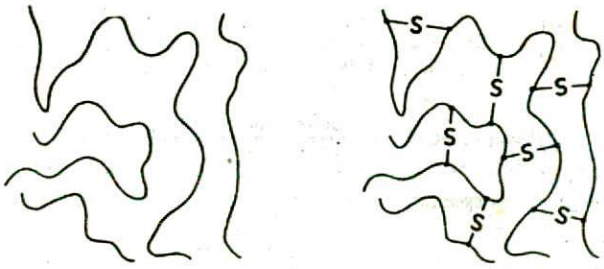
NATURAL AND SYNTHETIC RUBBERS

(1) Natural Rubber

With the expansion of motor-car industry the demand for rubber increased enormously. Organic chemists found that rubber is a hydrocarbon polymer built up from the monomer isoprene. *Natural rubber is polyisoprene.*



Raw rubber obtained from **latex** tapped from the rubber tree, particularly *Hevea brasiliensis*, does not possess the characteristic of the rubber with which we are familiar. In order to give it strength and elasticity, it is vulcanised. In the vulcanisation process, raw rubber is mixed with small amounts of sulphur and heated. The sulphur reacts with the polymer molecules forming a cross-linked network.

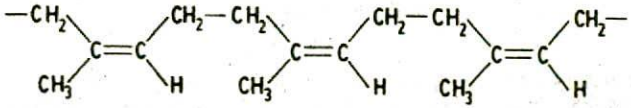


UNVULCANISED RUBBER VULCANISED RUBBER

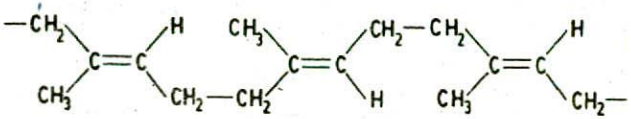
This cross-linking gives mechanical strength to the rubber. In addition, fillers such as carbon black and zinc oxide are usually added to the crude rubber before vulcanisation in order to improve its wearing characteristics.

The recurring double bonds in isoprene and butadiene polymers make it possible to have polymers with specific spatial orientation as a result of *cis-trans* isomerism. Recall that two carbon atoms joined by a double bond are not free to rotate and thus give rise to *cis-trans* isomerism. An isoprene polymer can have all *cis*, all *trans*, or a *random* distribution of *cis* and *trans* configurations about the double bonds.

Natural rubber is *cis*-polyisoprene with an all *cis* configuration about the carbon-carbon double bonds. Gutta-percha, also obtained from plants, is an all *trans*-polyisoprene. Although these two polymers have the same composition, their properties are radically different. The *cis* natural rubber is a soft, elastic material whereas the *trans* gutta-percha is a tough, nonelastic, hornlike substance. Gutta-percha is used for electrical insulation, and in dentistry.



ALL cis CONFIGURATION OF NATURAL RUBBER

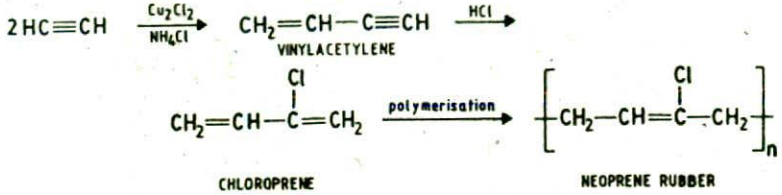


ALL trans CONFIGURATION OF GUTTA-PERCHA

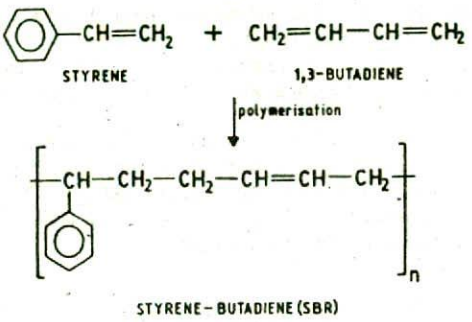
Only random or nonstereospecific polymers are obtained by free radical polymerisation. Synthetic polyisoprenes made by free radical polymerisation are much inferior to natural rubber, since they contain both *cis* and *trans* isomers. But Ziegler-Natta catalysts [*for example*, $(C_2H_5)_3Al/TiCl_4$] allow polymerisation to proceed by an ionic mechanism, producing stereochemically controlled polymers. Ziegler-Natta catalysts made possible the synthesis of polyisoprene with all *cis* configuration and with properties fully comparable to those of natural rubber.

(2) **Synthetic Rubber**

(a) **Neoprene (Polychloroprene).** It was the first synthetic rubber manufactured on a large scale. Neoprene is obtained from chloroprene in the presence of benzoyl peroxide catalyst at 60–80°C. The monomer, chloroprene, is prepared from acetylene. Neoprene is particularly resistant to chemical action. It is used in the manufacture of containers for corrosive chemicals and hoses for petrol and oil.

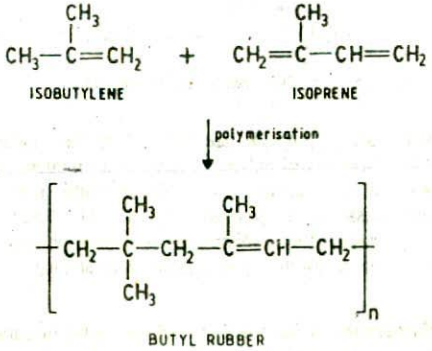


(b) **Styrene-Butadiene Rubber (also called SBR or Bunna S).** It is a copolymer made from styrene and 1,3-butadiene in emulsion at about 47°C, using potassium persulphate as the initiator.



SBR has its major use in making tires, shoe soles and inside wall of buildings.

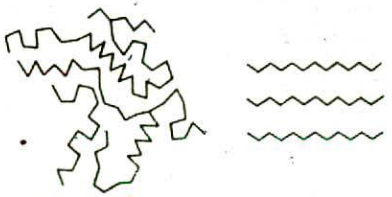
(c) **Butyl Rubber.** It is a copolymer made from isobutylene and isoprene. The polymerisation is carried out at −80 to −100°C in methyl chloride as solvent and with anhydrous aluminium chloride as catalyst. Butyl rubber is used for making inner tubes for tires, motor and for other vibration-damping applications.



POLYMER PROPERTIES AND STRUCTURE

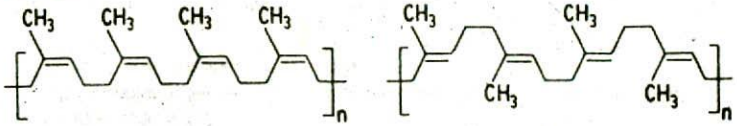
Properties of polymers depend upon their molecular weight, branching and stereochemistry. For example, as the molecular weight increases in a given family, the tensile strength increases markedly. Like other organic molecules, polymers may have functional groups and asymmetric centres. They can undergo hydrogen-bonding and dipole-dipole interactions. The chemical composition of a polymer chain is known as its **primary structure**. How the chain is arranged in relation to itself and to other chains is called the **secondary structure**. This secondary structure is as important to the properties of a polymer as its chemical composition.

A polymer may be a tangled mass of continuous chains or branched chains. The result is a soft amorphous solid such as soft rubber. On the other hand, a polymer may be composed of continuous chains held together by hydrogen bonds or by other dipole-dipole attractions. This type of polymer structure lends itself to fibres or hard, moldable plastics. A more-ordered polymer is said to have a higher degree of **crystallinity** than the amorphous, or noncrystalline, polymer.



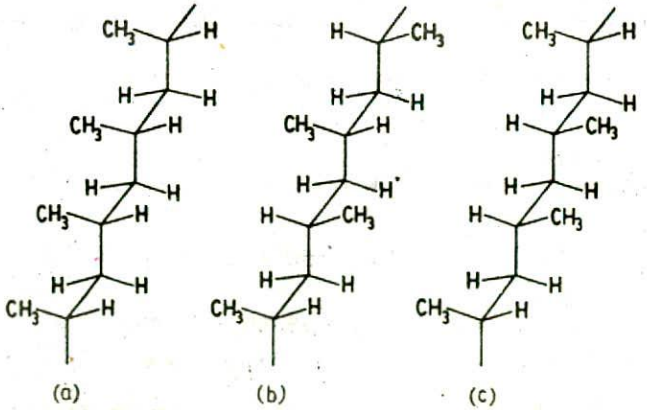
A NONCRYSTALLINE POLYMER A CRYSTALLINE POLYMER

The differences in properties between crystalline and non-crystalline polymers are beautifully demonstrated by gutta-percha and natural rubber. Gutta-percha is a highly crystalline polymer, while natural rubber has a molecular shape that does not lend itself to an ordered, crystalline arrangement.



NATURAL RUBBER (cis-polyisoprene) GUTTA-PERCHA (trans-polyisoprene)

Let us consider the polymerisation of propylene. There are three types of product that could result from the polymerisation of propylene.



(a) (b) (c)

Fig. 50.3. Isotactic (*a*), Syndiotactic (*b*), and Atactic (*c*) forms of Polypropylene.

This polymer in which all methyl groups are on the same side of the zig-zag carbon chain is called **isotactic**. The polymer in which the methyl groups regularly alternate on opposite sides of the chain is called **syndiotactic.** The polymer in which the methyl groups are randomly oriented is called **atactic** (Fig. 50.3). Because of their orderly arrangements, the chains of *isotactic* and *syndiotactic* polymers can lie closer and the polymers are more crystalline. On the other hand, *atactic* ...mer is soft and amorphous.

QUESTIONS

1. Explain what is meant by each of the following terms :

   (*a*) Polymer (*b*) Monomer
   (*c*) Copolymer (*d*) Homopolymer
   (*e*) Addition polymer (*f*) Condensation polymer
   (*g*) Thermoplastic polymer (*h*) Thermosetting polymer

2. State the key differences between :

   (*a*) Addition polymerisation and Condensation polymerisation
   (*b*) Copolymers and Homopolymers
   (*c*) Syndiotactic polymers and Isotactic polymers
   (*d*) Isotactic polymers and Atactic polymers

3. Write notes on :

   (*a*) Addition polymers *(Banaras BSc, 1993)*
   (*b*) Condensation polymers *(Jiwaji BSc, 1994)*
   (*c*) Synthetic rubbers *(Saugar BSc, 1994)*
   (*d*) Vulcanisation *(Pondicherry BSc, 1994)*

4. Give the names of the monomers that are used to produce :

   (*a*) Dacron (*b*) Orlon (*c*) Bakelite
   (*d*) Nylon-6,6 (*e*) Teflon

Answer :

POLYMER	MONOMER
Dacron	Dimethyl terephthalate + ethylene glycol
Orlon	Vinyl cyanide
Bakelite	Formaldehyde + phenol
Nylon-6,6	Adipic acid + hexamethylene diamine

5. How do thermoplastic polymers differ from thermosetting polymers ? Give two examples of each type.
   (North Eastern Hill BSc Hons, 1994)

6. Classify the following polymers on the basis of the action of heat on them : Bakelite, Nylon, Dacron, and Polyethylene.

Answer. Nylon, Dacron and Polyethylene are thermoplastic polymers. Bakelite is a thermosetting polymer.

7. Discuss the structure of natural rubber.

8. Write a step-by-step mechanism for the polymerisation of ethylene in the presence of an organic peroxide.
   (Delhi BSc Hons, 1993)

9. Discuss the mechanism for the polymerisation of propylene in the presence of H_2SO_4 (or HF) catalyst.
   (Gauhati BSc Hons, 1994)

Answer. Following steps are involved :

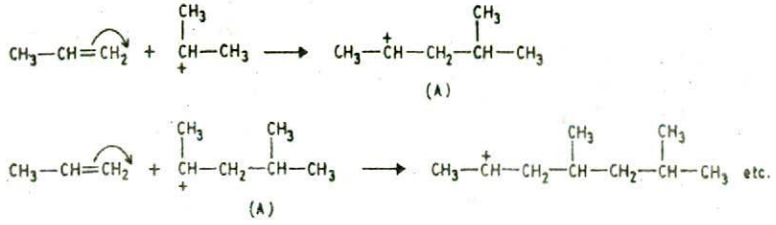
Chain Initiation. Proton from H_2SO_4 or HF adds to the C=C bond of propylene to give a stable 2° carbonium ion.

$$H_2SO_4 \longrightarrow H^+ + HSO_4^-$$

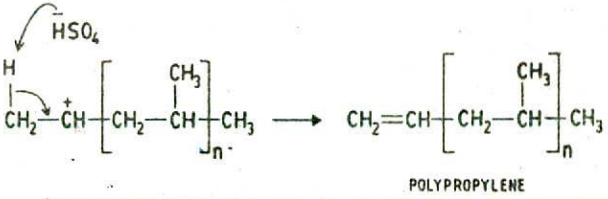
$$CH_3-CH=CH_2 + H^+ \longrightarrow CH_3-\overset{+}{C}H-CH_3$$

2° CARBONIUM ION

Chain Propagation. The carbonium ion adds to another propylene molecule to form a new carbonium ion, which can similarly add to another molecule of propylene and so on.



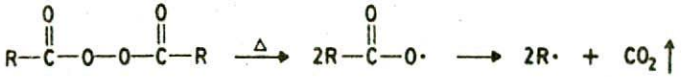
Chain Termination. The chain reaction can be terminated by transfer of a proton from the carbonium ion to HSO_4^-, forming a terminal C=C bond.



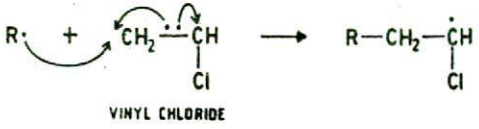
10. Write a step-by-step mechanism for the polymerisation of vinyl chloride in the presence of an organic peroxide. *(Osmania BSc Hons, 1994)*

Answer. Following steps are involved:

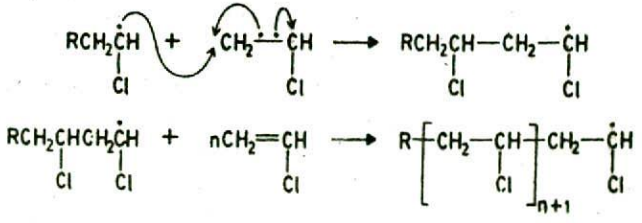
Chain Initiation. Organic peroxides decompose to give free radicals.



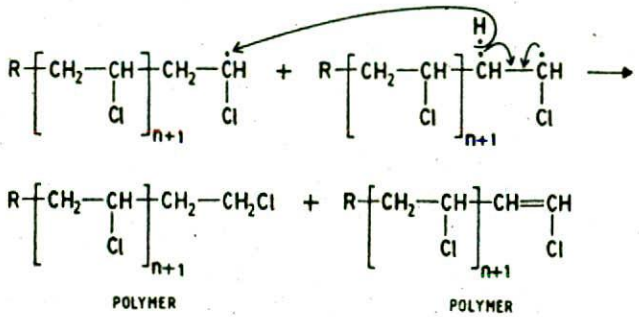
Chain Propagation. Free radical produced in the above step adds to a vinyl chloride molecule to form a new free radical.



This free radical can attack another vinyl chloride molecule and so on.



Chain Termination. The chain reaction can be interrupted when the free radicals combine *or* by disproportionation.



11. How will you synthesise the following polymers from the indicated starting materials :

(*a*) Polythene from ethylene
(*b*) Polyvinyl chloride (PVC) from acetylene
(*c*) Polystyrene from benzene *(Meerut BSc, 1993)*
(*d*) Dacron from ethylene and *p*-xylene
(*e*) Bakelite from phenol *(Vikram BSc, 1993)*
(*f*) Nylon-6,6 from 1,3-Butadiene *(Agra BSc, 1994)*
(*g*) Neoprene from acetylene *(Bundelkhand BSc, 1994)*

12. Define the term 'polymerisation'. Compound (*A*) was found to have the composition : Carbon = 38.4%, Hydrogen = 4.8% ; and Chlorine = 56.8%. Boiling with aqueous NaOH produced no effect on (*A*). Boiling with alcoholic NaOH produced unsaturated hydrocarbon, (*B*). Two successive treatments of (*B*) with sodium in liquid ammonia and methyl iodide gave a dimethyl derivative. On addition of benzoyl peroxide, (*A*) polymerised rapidly to give (*C*). Identify the compounds (*A*), (*B*), and (*C*), and explain the reactions involved. (C = 12 ; H = 1 ; Cl = 35.5)

Answer. (*A*) is $CH_2 = CHCl$; (*B*) is $HC \equiv CH$; (*C*) is $-(CH_2-\underset{Cl}{\underset{|}{CH}})_n-$

Chapter **51**

Spectroscopy

Until about 1940, chemists interested in the detailed structure of molecules had to work mainly by inference from their reactions. Elemental analysis and chemical tests, such as Lucas test, Tollens' test, the iodoform test, and the Hinsberg test, to name a few, were the sole sources of evidence for assigning composition and functional groups. Although chemical tests are useful, they are time-consuming and somewhat uncertain, sometimes require a large amount of sample, and are destructive (the analysis destroys or chemically modifies the sample). Today we can obtain a great deal of information directly from molecules by the spectroscopic methods. *Compared to chemical analysis, spectroscopic methods are faster and more accurate, require less sample, and are usually non-destructive.*

We define spectorscopy as an area of study that probes molecular structure with electromagnetic radiation. The instruments used in such studies are called spectrometers. We shall study several types of spectroscopy as they relate to organic molecules. To do that, we must first understand how electromagnetic radiation interacts with molecules.

ELECTROMAGNETIC RADIATION AND MOLECULES

Electromagnetic radiation is a form of energy with wave properties. The electromagnetic spectrum consists of a range of electromagnetic vibrations, which differ in certain of their wave dimensions. Figure 51.1 shows a plot of the amplitude of an electromagnetic wave against its progression (wave profile).

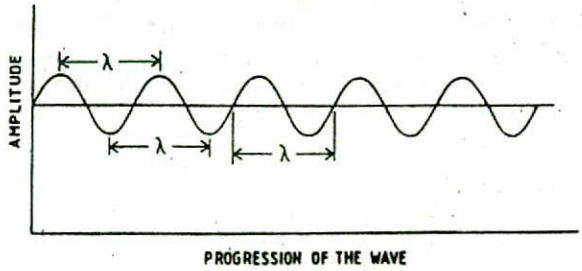


Fig. 51.1. Plot of the amplitude of an electromagnetic wave against its progression (a wave profile).

The distance between two successive amplitude maxima or minima (or other corresponding points) is the wavelength, designated by the symbol λ (Greek letter *labda*). The number of wavelengths that pass a given point each second is the frequency of the wave, designated by ν (Greek letter *nu*). Thus, the frequency is the reciprocal of the time elapsed (T) between the passage of two successive maxima or minima (Eq.1)

$$\nu = \frac{1}{T} \quad (\textit{that is, wavelengths per unit time}) \qquad \ldots(1)$$

To understand these relationships, you may consider a wavelength as one cycle of a wave, that is the distance between two successive corresponding points on the wave profile (Fig. 51.1). This makes the frequency the number of cycles that pass an observer in a specified unit of time. Since a wavelength λ takes a time T to pass a given point, the velocity (C) of the wave is λ divided by T (Eq. 2).

$$C = \frac{\lambda}{T} \quad (\textit{that is, units of length per unit of time}) \qquad ...(2)$$

In terms of the frequency of the wave, the velocity equals the product of wavelength and wave frequency (Eqs. 3 and 4).

$$T = \frac{1}{\nu} \quad (\textit{From Eq. 1}) \qquad ...(3)$$

$$C = \lambda\nu \quad \left(\textit{by substituting } \frac{1}{\nu} \textit{ for } T \textit{ in Eq. 2}\right) \qquad ...(4)$$

The velocity (or speed) of light and other forms of electromagnetic radiation has the constant value of 3×10^{10} cm per sec (in vacuum). Therefore, dividing Eq. 4 by λ shows that frequency and wavelength are inversely proportional to each other and the proportionality constant (C) is the speed of light (Eq. 5).

$$\nu = \frac{C}{\lambda} \qquad ...(5)$$

This means that electromagnetic radiation with a long wavelength has a low frequency ; a short wavelength means a high frequency.

Wavelengths are most often measured in centimeters (cm), nanometers (nm), or angstroms (Å). The relationship between these units and other units of length is :

$$1 \text{ cm} = 10 \text{ mm} = 10^{-2} \text{ m}$$

$$1 \text{ nm} = 10^{-6} \text{ mm} = 10^{-7} \text{ cm} = 10^{-9} \text{ m}$$

$$1 \text{ Å} = 10^{-1} \text{ nm} = 10^{-7} \text{ mm} = 10^{-8} \text{ cm} = 10^{-10} \text{ m}$$

The units most used to express frequency are cycles (or vibrations, that is, wavelengths) per second (cps), hertz (Hz ; 1 Hz = 1 cps), and reciprocal centimeters (cm^{-1}). The last designation is called a **wave number** and equals the reciprocal of the wavelength in centimeters ($1/\lambda$ in centimeters). Thus, a wave number of 4,000 cm^{-1} corresponds to a wavelength of 0.00025 cm and tells us the number of waves (cycles) per centimeter. The shorter the wavelength, the larger the wave number. In other words, the wave number increases as the frequency increases. Note, however, that the units of wave number are reciprocal centimeters (cm^{-1}), not cycles per second or hertz.

The Electromagnetic Spectrum

Table 51.1 shows the wavelengths associated with the various ranges of the electromagnetic spectrum. Table 51.2 shows the wavelengths and frequencies associated with the regions of the electromagnetic spectrum, which are of interest to organic chemists.

Table 51.1. The electromagnetic spectrum.

Radiation Description		Approximate Wavelength (λ)
Short-wavelength end	Cosmic rays	0.00005 nm
	Gamma rays	0.001–0.14 nm
	X rays	0.01–10 nm
	Ultraviolet	10–400 nm
	Visible	400–750 nm
	Infrared	750–500,000 nm (0.5 mm)
	Microwave	500,000–300,000,000 nm (30 cm)
Long-wavelength end	Radio waves.	30 cm–100,000 m

Table 51.2. The infrared, visible and ultraviolet regions of the electromagnetic spectrum.

Wavelength (nm)	Frequency (cm^{-1})	Description (Colour) of the Radiation
500,000–750	20–13,333	Infrared
750–620	13,333–16,129	Visible (red)
620–590	16,129–16,949	Visible (orange)
590–570	16,949–17,543	Visible (yellow)
570–500	17,543–20,000	Visible (green)
500–450	20,000–22,222	Visible (blue)
450–400	22,222–25,000	Visible (violet)
400–10	25,000–10^5	Ultraviolet

Notice that the visible spectrum extends from approximately 750 nm to 400 nm. As pointed out in *Chapter 45*, compounds that absorb electromagnetic radiation in the visible region are coloured. The colour they transmit comes from the visible wavelengths that are *not* absorbed, the ones that reflect off the compound. Colourless compounds do not absorb radiation in the visible region, but most do absorb in either the infrared or ultraviolet regions or in both. As we shall soon see, measuring absorptions in the infrared, visible and ultraviolet regions of the electromagnetic spectrum provides information about the structure of compounds.

When a compound absorbs electromagnetic radiation, matter and radiation energy (waves) interact. We can explain this interaction on the basis of quantum theory. Radiation energy interacting with matter behaves as though it consisted of *bundles of energy* called *quanta*. The amount of energy in each *bundle* or *quantum*, is given by the following equation :

$$E = h\nu \qquad \ldots(6)$$

where, E is the energy of a quantum, ν is the frequency of the radiation that produced it and h is Planck's constant ($h = 6.62 \times 10^{-27}$ erg sec). This relationship between frequency and energy expresses quantitatively what we have already stated qualitatively : **The higher the frequency of the radiation, the greater is its energy.** Quanta in the high-frequency (shorter-wavelength) ultraviolet region, for example, contain much more energy than quanta in the lower-frequency (longer-wavelength) infrared region.

A quantum of energy ($h\nu$) is also called a photon. Molecules can interact with photons in several ways, depending on the frequency of the photon and the structure of the particular molecule the photon strikes. Certain photons can increase the **rotational energy** of molecules, that is, the energy associated with the rotation of atoms around bonds. Other, more energetic photons contain precisely the energy needed to increase the **vibrational energy**, that is, the energy associated with the motions of atoms relative to one another, such as bond bendings and stretchings. Photons of even greater energy can be absorbed by increasing the **electronic energy**, that is, by exciting the electrons in a molecule to higher energy levels.

Rotational, vibrational and electronic energy are *quantised*. This means that molecules have discrete rotational, vibrational and electronic energy levels. The energies of molecules can be only at these quantised levels; they can never be at *in between* levels. A representation of rotational, vibrational and electronic energy levels is shown in Fig. 51.2.

Moving from a lower rotational state to a higher one requires the input of precise amounts of energy. Hence, molecules can absorb only certain frequencies of electromagnetic radiation ($h\nu_{ROT}$). Likewise, an increase in vibrational energy demands photons with particular energies ($h\nu_{VIB}$), but these photons must be of higher energy (hence, higher frequency) than those that can produce a change in rotational energy level. Again, though, the molecule can absorb only *certain* frequencies. This is also true for electronic energy levels, which are much more widely separated than even vibrational levels. Typically, in terms of calories per mole, electronic energy state transitions demand photons that are two or three powers of 10 (10^2 to 10^3) more energetic than those needed for vibrational transitions. It turns out that rotational-vibrational transitions require photons in the infrared (IR) region, whereas electronic transitions require photons in the ultraviolet and visible (UV-VIS) regions.

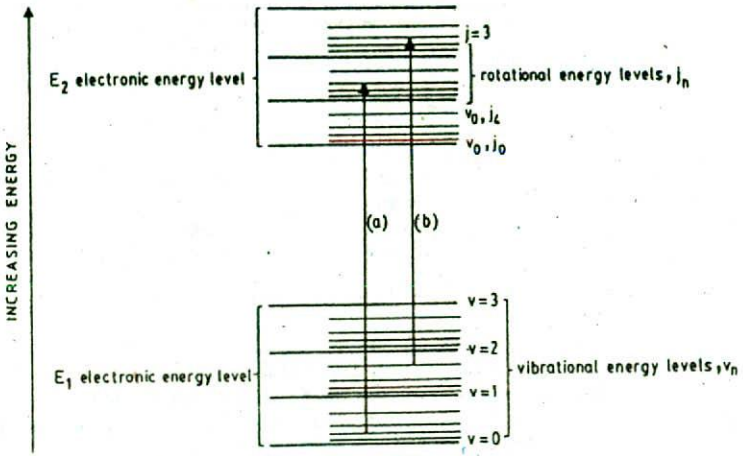


Fig. 51.2. A representation of electronic, vibrational and rotational energy levels.
Arrow (*a*) shows an electronic transition from $E = 1, v = 0, j = 2$ upto $E = 2, v = 1, j = 3$.
Arrow (*b*) shows the electronic transition from $E = 1, v = 1, j = 4$ upto $E = 2, v = 2, j = 3$.

To Summarise :

1. Electromagnetic radiation is a form of energy with wave properties.
2. Wavelength (λ) and frequency (ν) are inversely proportional.
3. The wavenumber (cm^{-1}) is the reciprocal of the wavelength in centimeters.
4. Absorptions in the ultraviolet, visible and infrared portions of the electromagnetic spectrum provide useful structural infromation about organic compounds.
5. Photons are quanta of energy.
6. The energy (E) of a photon is equal to $h\nu$ where h is Planck's constant.
7. The electronic, vibrational and rotational energy levels of a molecule are quantised ; only certain photons can be absorbed.
8. Electronic transitions require UV–VIS photons ; vibrational-rotational transitions require IR photons.

ULTRAVIOLET–VISIBLE (UV-VIS) SPECTROSCOPY

An instrument for measuring the interaction of molecules with ultraviolet and visible light is called a UV-VIS spectrometer. Such an instrument has :

1. **A light source** that can produce ultraviolet and visible radiation.
2. **A monochromator** that separates light of many wavelengths into light of a single (or at least only a few) wavelength.
3. **A sample compartment** where a sample can be placed, so that the light of known wavelength can pass through it.
4. **A detector** that can analyse the light passing through a sample and tell if and when any absorption takes place.
5. **A recorder** to make a continuous scan of the UV-VIS spectrum. The recorder pen moves across a stationary piece of chart paper, or the paper moves and the pen responds from a fixed position. In either case, the recorder traces a peak whenever the sample absorbs light. The paper is calibrated with wavelength markings (usually in nanometers) on the horizontal axis and radiation intensity markings on the vertical axis.

There is a variety of ways to measure the absorption intensity. We shall use the **molar absorptivity**, ε (Greek letter epsilon) or its logarithm, log ε. The molar absorptivity or molar

extinction coefficient, as it is called, equals the absorbance of a compound (a measure of the light absorbing power) divided by the product of its concentration and the thickness of the sample cell that contains it. This is called *Beer-Lambert law.*

$$\varepsilon = \frac{A}{c} \times l \qquad \ldots(7)$$

where, ε = molar absorptivity

A = absorbance

c = concentration in moles per liter

l = thickness of sample cell in centimeters

The absorbance (also called *optical density*) in turn, equals the logarithm of the ratio of the light intensity before it passes through a solution of an absorbing compound (I_0) and after it emerges from the solution (I).

$$A = \log \frac{I_0}{I} \qquad \ldots(8)$$

Peaks in ultraviolet and visible spectra are often quite broad. That is, they span many wavelengths. It is convenient to specify the molar absorptivity (ε) at the wavelength of greatest intensity of absorption within a broad peak. That wavelength is given the symbol λ_{max}, and the molar absorption at this wavelength is ε_{max} (replaced for convenience by log ε if ε is very large). Figure 51.3 shows the UV spectrum of 4-methyl-3-buten-2-one in methyl alcohol.

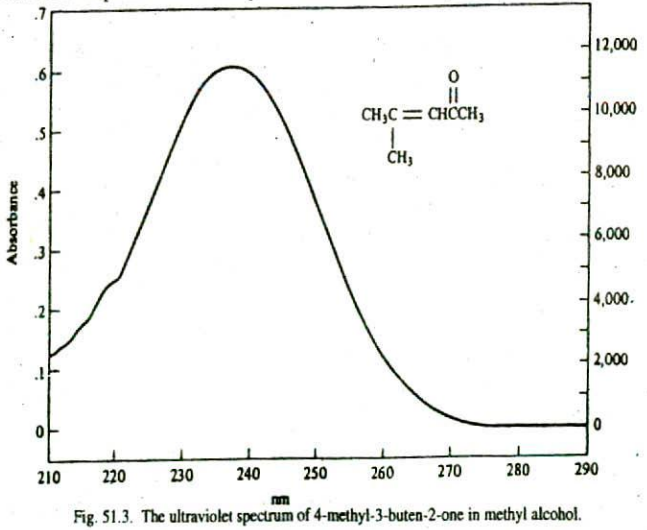


Fig. 51.3. The ultraviolet spectrum of 4-methyl-3-buten-2-one in methyl alcohol.

Interpretation of UV Spectrum

Since most organic compounds are colourless, the visible region of the spectrum (400–750 nm) is of limited value, but the ultraviolet region, especially the wavelengths from 200–400 nm, is very helpful as a guide to the presence of certain functional groups, particularly the unsaturated ones. The photons in UV light have the proper energy to raise the electrons to higher energy levels, higher levels than they normally occupy in their **ground state.** These higher energy levels are called **excited states.** When a photon kicks an electron from its ground state to an excited state, the process is called **electron excitation.**

As a rule, one unsaturated grouping is not sufficient for very intense absorption in the 200–400 nm region. Isolated C = O, C = N, N = O, N = N groups do have absorption bands in this region, but compared to compounds with conjugated multiple bonds, a singly unsaturated compound will absorb weakly (ε usually not more than 200). Compounds containing conjugated π bond system show very intense bands ; ε is often in thousands ($\log \varepsilon = 3–4$), tens of thousands ($\log \varepsilon = 4–5$), and even hundreds of thousands ($\log \varepsilon = 5–6$).

Groups that cause light to be absorbed are called chromophores. Table 51.3 gives partial list of simple, unconjugated, pi-bonded chromphores, some specific examples which contain these chromophores, and their λ_{max} and ε_{max} values. Notice that there are not many compounds that have absorption bands (λ_{max}) in the 200–400 nm range and those that do, absorb very weakly in this region.

Table 51.3. Ultraviolet absorptions of some simple chromophores.

Chromophore	Example(s)	Position λ_{max} (nm)	Intensity ϵ_{max}
 (vinyl group)	$H_2C{=}CH_2$	170	15,500
	$CH_3(CH_2)_4CH{=}CH_2$	175	13,000
$-C{\equiv}C-$ (acetylenic group)	$CH_3CH_2CH_2{-}C{\equiv}C{-}CH_3$	178 195 223	10,000 2,000 150
 (carbonyl group)	$CH_3{-}\overset{\overset{O}{\|}}{C}{-}H$	160 180 290	20,000 10,000 17
	$CH_3{-}\overset{\overset{O}{\|}}{C}{-}CH_3$	166 189 280	16,000 900 15
	$CH_3{-}\overset{\overset{O}{\|}}{C}{-}OH$	208	30
	$CH_3{-}\overset{\overset{O}{\|}}{C}{-}NH_2$	220	60
	$CH_3{-}\overset{\overset{O}{\|}}{C}{-}OCH_3$	210	60
 (nitro group)	$CH_3CH_2CH_2CH_2{-}N{=}O$	201 274	5,000 17
$-\ddot{N}{=}\ddot{N}-$ (azo group)	$CH_3{-}N{=}N{-}CH_3$	338	5

Functional groups that contain no π bonds but do have lone-pair (nonbonding) electrons on atoms such as oxygen (as in alcohols), nitrogen (as in amines) and halogen (as in alkyl halides behave similarly (Table 51.4).

Table 51.4. Ultraviolet absorption caused by lone-pair (nonbonding) electrons.

Location of the Nonbonding Electrons	Example	λ_{max}	ϵ_{max}
Oxygen	$CH_3\ddot{O}H$	183 nm	150
Nitrogen	$(CH_3)_3N$:	227 nm	900
Halogen	$CH_3\ddot{I}$:	258 nm	378

The real diagnostic value of ultraviolet and visible spectroscopy, however, is to detect conjugated unsaturated groupings. Tables 51.5 and 51.6 list a number of conjugated chromophores (and compounds that contain them) that show characteristic absorptions in the useful UV-VIS region.

Table 51.5. Ultraviolet absorptions of conjugated chromophores (Aliphatic Compounds).

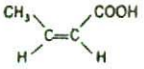
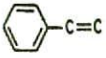
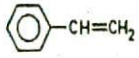
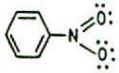
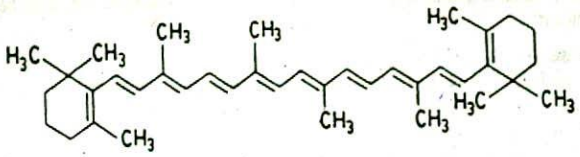
		Absorption	
Chromophore(s)	Example(s)	Approximate Position λ_{max} (nm)	Approximate Intensity ϵ_{max}
C=C—C=C	$CH_2{=}CH{-}CH{=}CH_2$	217	21,000
$(C{=}C)_n$	$CH_2{=}CH{-}CH{=}CH{-}CH{=}CH_2$ ($n = 3$)	270	40,000
	$CH_2{=}CH{-}(CH{=}CH)_2{-}CH{=}CH_2$ ($n = 4$)	310	60,000
	$CH_2{=}CH{-}(CH{=}CH)_4{-}CH_2{=}CH_2$ ($n = 6$)	380	150,000
	$CH_2{=}CH{-}(CH{=}CH)_6{-}CH{=}CH_2$ ($n = 8$)	415	200,000
C=C—C(=O)—	$CH_2{=}CH{-}C(=O){-}H$	218 320	18,000 30
		206 242	13,500 250
	$CH_2{=}CH{-}C(=O){-}CH_3$	213 320	7,000 30
$(C{=}C)_n$—C(=O)—	$CH_3{-}(CH{=}CH)_2{-}C(=O){-}H$	270	27,000
	$CH_3{-}(CH{=}CH)_4{-}C(=O){-}H$	343	40,000
	$CH_3{-}(CH{=}CH)_6{-}C(=O){-}H$	393	63,000
	$CH_3{-}(CH{=}CH)_7{-}C(=O){-}H$	415	65,000

Table 51.6. Ultraviolet absorptions of conjugated chromophores (Aromatic Compounds).

CHROMOPHORE(S)	EXAMPLE(S)	ABSORPTION: APPROXIMATE POSITION λ_{max}(nm)	ABSORPTION: APPROXIMATE INTENSITY ε_{max}
		184 203 255	47,000 7,000 230
		206 261	7,000 225
		211 270	6,000 15,000
		217 269	6,400 1,500
		230 280	8,600 1,400
		248 280	14,000 800
		250	11,400
		246	10,000
		230 272	11,600 950
		270	7,800

The most striking feature of the data in Tables 51.5 and 51.6 is the **conjugation effect.** Extended conjugation shifts the λ_{max} towards longer wavelengths (toward the so called *red end* of the spectrum). It also increases the intensity of absorption. That is, the magnitude of ε increases. The effect of extended conjugation was recognised long before spectrometers were available because long enough extension shifts the absorption into the visible region and gives the compound a visible colour complementary to the one it absorbs. Consider the example of the yellow pigment β-carotene, which occurs in carrots. The molecule has eleven carbon-carbon double bonds.



β – CAROTENE

This extended conjugation causes absorption in the blue-violet region of the spectrum. More precisely, β-carotene has strong absorption bands centered at about 450 nm and 480 nm (ε = 140,000 and 120,000, respectively). Molecules of β-carotene "extract" from white light the wavelengths covered by these absorption bands and transmit the rest. The wavelengths they transmit appear yellow to the human eye.

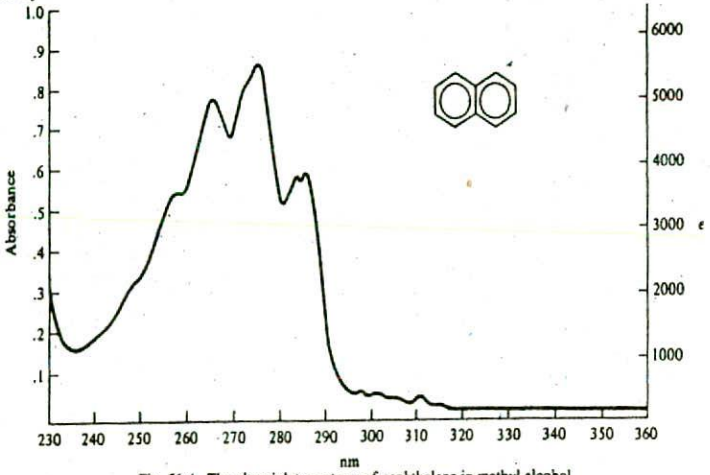
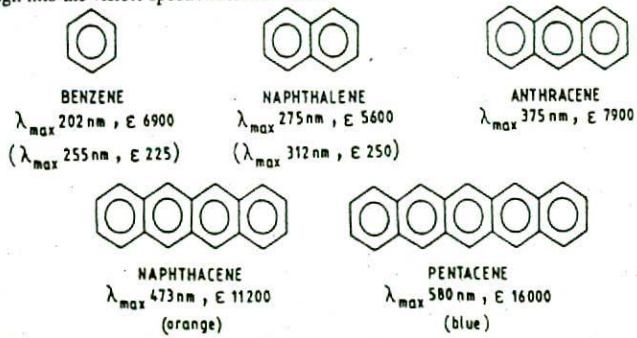


Fig. 51.4. The ultraviolet spectrum of naphthalene in methyl alcohol.

Figure 51.4 shows the UV spectrum of naphthalene. Absorptions of aromatic compounds move to longer wavelengths with increasing size of conjugated system. For example, pentacene absorbs far enough into the visible spectrum to look blue.



Use of UV-VIS Spectral Data in Quantitative Analysis

The UV-VIS spectral data can be used to measure concentration (how much compound is present). If the compound is known, one of the easiest ways to do this is to plot absorption intensity against concentration using solutions of known concentration prepared from pure authentic samples of the compound. Once the plot is made, the absorption intensity of the solution of unknown

concentration is measured and located on the plot. The concentration can then be read on the concentration axis.

To Summarise :

1. The molar absorptivity (ε) of a compound is a measure of its light-absorbing power.
2. Conjugated molecules give strong UV-VIS absorption bands.
3. Chromophores are groups that cause light absorption.
4. Extended conjugation results in more intense absorption at longer wavelengths.
5. UV-VIS data can be used both qualitatively and quantitatively.

INFRARED (IR) SPECTROSCOPY

The most useful region of the infrared radiation extends from above 2.5 to 16 microns (1 micron = 1 micrometer = 10^{-6} meter). It is more customary, however, to use wavenumbers to specify the positions of absorptions. The wavenumber of a particular radiation is the number of waves per centimeter, which is simply one divided by the wavelength (λ) in centimeters.

$$\text{Wavenumber} = \frac{1}{\text{Wavelength in cm}}$$

An infrared spectrum is usually presented as a plot of the percentage of radiation of each wavelength transmitted through the sample (0% transmission corresponds to total absorption by the sample). Figure 51.5 shows a typical infrared spectrum.

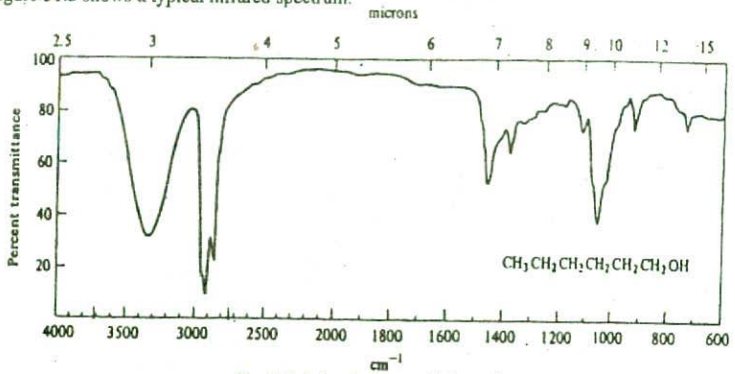


Fig. 51.5. Infrared spectrum of 1-hexanol.

An infrared spectrometer, an instrument whose essential components are shown in Fig. 51.6, is used to obtain the spectrum.

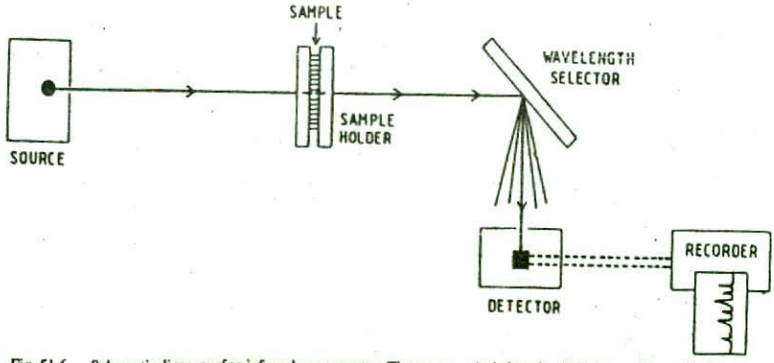


Fig. 51.6. Schematic diagram of an infrared spectrometer. The source emits infrared radiation spanning a wide frequency range. A wavelength selector permits only a particular wavelength of radiation transmitted by the sample to fall on a detector at a given time. The detector measures the intensity of radiation and a plot of this intensity for each wavelength is traced on paper by a recorder.

The infrared spectra shown in this chapter are of the layers of liquid organic compounds held between two plates of sodium chloride (sodium chloride does not absorb in this spectral region). Spectra can also be taken of gases or of compounds dissolved in a solvent. When a solvent is used, absorption due to the solvent must be subtracted. Spectrometers ordinarily do this by measuring the difference between the absorption of radiation by two sample cells - one containing the solution of the compound, the other containing only solvent. A routine infrared spectrum takes only a few minutes and a few milligrams of sample.

What happens to a molecule when it absorbs infrared radiation ? The bond lengths and angles for molecules are actually in constant motion relative to one another. Those motions that stretch bonds and deform bond angles are known as molecular vibrations. Figure 51.7 shows some of these vibrations. *Stretching vibrations change distances between adjacent atoms. Bending vibrations change bond angles.*

On absorption of a photon of infrared radiation, a molecule is excited to a higher energy level in which vibrational transitions are more energetic. To some extent, vibrational transitions involve all parts of a molecule. Some transitions, however, are relatively localised, involving mainly two or. at the most, a few atoms. As a result, some structural features lead to infrared absorptions that appear in a narrow frequency range, regardless of the structure of the remainder of the molecule. Such characteristic absorptions make infrared spectra useful in providing structural information about compounds of unknown structure.

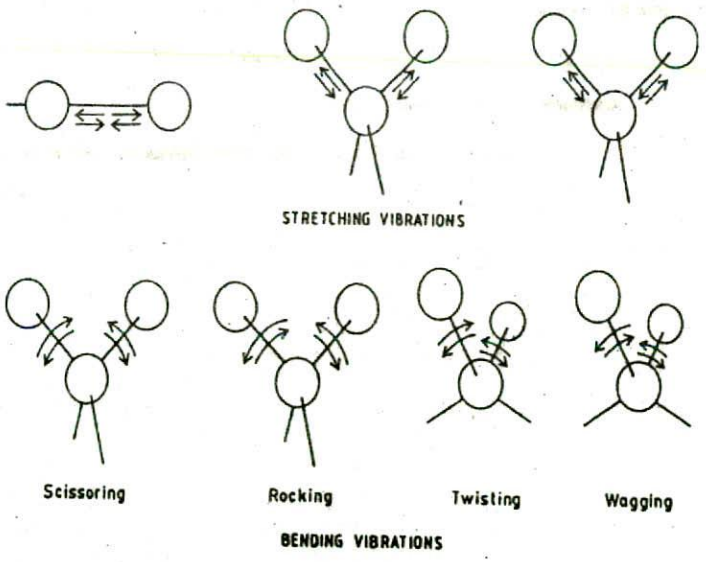
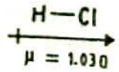


Fig. 51.7. Stretching and bending vibrations involving only a few atoms.

For a vibration to result in absorption, it must change the dipole moment of the molecule. It is fortunate that this selection rule applies, since it reduces the complexity of IR spectra, which nonetheless contain more peaks than do UV-VIS spectra. The dipole moment (μ) is a vector quantity that expresses, in units called Debye (D), the net charge polarisation in a molecule. For example, hydrogen chloride has a dipole moment of slightly more than 1D.



The positive end is toward H ; the negative end is toward Cl. Most bonds in organic molecules have bond moments (individual dipoles) that contribute to the net dipole moment. In some cases, however, individual bond moments can cancel each other out. Thus, while methyl chloride has a dipole moment, carbon tetrachloride does not.

Interpretation of IR Spectra

Bending vibrations require less energetic photons than do stretching vibrations. Therefore, they occur at lower frequencies (lower wave numbers).

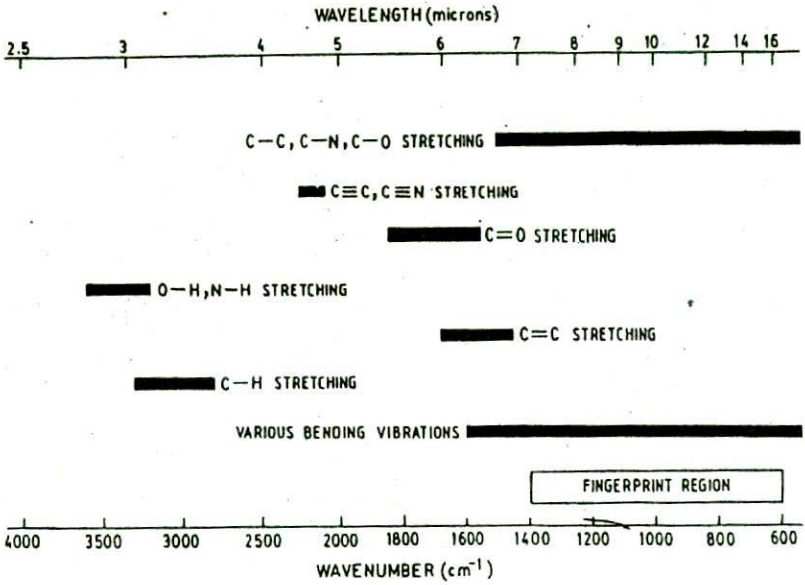


Fig. 51.8. Regions of stretching and bending vibrations.

Figure 51.8 shows some typical frequency regions. Particularly useful are the stretching vibrations of bonds involving the very light hydrogen atom (C–H, O–H, N–H), and multiple bonds (C=C, C=O, C≡C, C≡N). Stretching vibrations involving single bonds between two heavy atoms (C–C, C–N, C–O) tend to be more associated with movements involving many atoms and to appear in broader frequency ranges. Moreover, these absorptions fall in regions also occupied by bending vibrations. The region from about 1400 to 600 cm^{-1} is called the **finger print region.** It is often difficult to assign all absorptions in this region to particular structural features. Yet like the *finger print* of an individual, the absorption of an organic molecule in this region is complex and unique.

Table 51.7 lists in more detail some important stretching vibrations. With this information we can begin to relate some of the features of spectra to the structural features responsible for them.

The first two spectra in Figure 51.9 lack significant absorptions between 2800 and 1500 cm^{-1} Therefore multiple bonds are absent. The fairly sharp absorptions in the 2970 to 2850 cm^{-1} region are characteristic of C–H stretching vibrations of a saturated carbon. Although these spectra of isomeric alkanes have many similarities, they are unmistakably different, particularly in the *finger print* region.

Table 51.7. Characteristic infrared absorption frequenceis for some common structural units.

Bond	Functional class		Absorption range (cm^{-1}) (intensity of absorption)[a]	Notes
C—H	alkane (—C—H)		2850–2970 (m–s)	
	alkene (C=C(H)—)		3010–3100 (m)	
	alkyne (C≡C—H)		3290–3320 (s)	
	aromatic (Ar—H)		3000–3100 (m)	
	aldehyde (O=C—H)		2720–2850 (m)	sometimes two absorptions in this region
O—H	alcohol	free	3600–3640 (s)	sharp
		hydrogen bonded	3200–3600 (s)	generally broad
	carboxylic acid	hydrogen bonded	2500–3500 (m)	several broad, overlapping absorptions
N–H	amines, amides		3300–3500 (m)	
C=C	alkenes		1600–1680 (v)	
	aromatic rings		1450–1600	3 to 4 absorptions in this region
			near 1660 (v)	these absorptions vary considerably in intensity
			near 1580 (v)	
			near 1500 (v)	
			near 1450 (s)	overlaps with C—C bending vibrations
C≡C			2100–2260 (v)	
C≡N			2210–2260 (m)	
C—O	alcohols, ethers, carboxylic acids, esters		1050–1350 (s)	
C=O	aldehydes, ketones carboxylic acids, esters, amides, acyl halides		1550–1850 (s)	
C—N	amines		1020–1360 (s)	
C—Cl			800–600 (s)	
C—Br			600–500 (s)	

[a] The following abbreviations are used to indicate the intensity of absorption: s, strong; m, medium; w, weak; v, variable

Reconsider the spectrum in Figure 51.5. It resembles the spectra of the alkanes but also has a strong, broad, band at 3340 cm^{-1}. This absorption is typical of the O–H stretching vibration of a hydroxyl group. The particularly great width of this absorption is due to the presence of a number of different hydrogen-bonded species, each having a somewhat different absorption frequency.

The spectra in Figures 51.9(*c*) and 51.10(*a*) are of the carbonyl compounds, consistent with this, both spectra have strong absorption characteristic of a carbonyl group at about 1700 cm^{-1}. The first compound can be identified readily as an aldehyde because of the absorption at 2720 cm^{-1} typical of the C–H stretching of a –CHO grouping. The other compound must be a ketone.

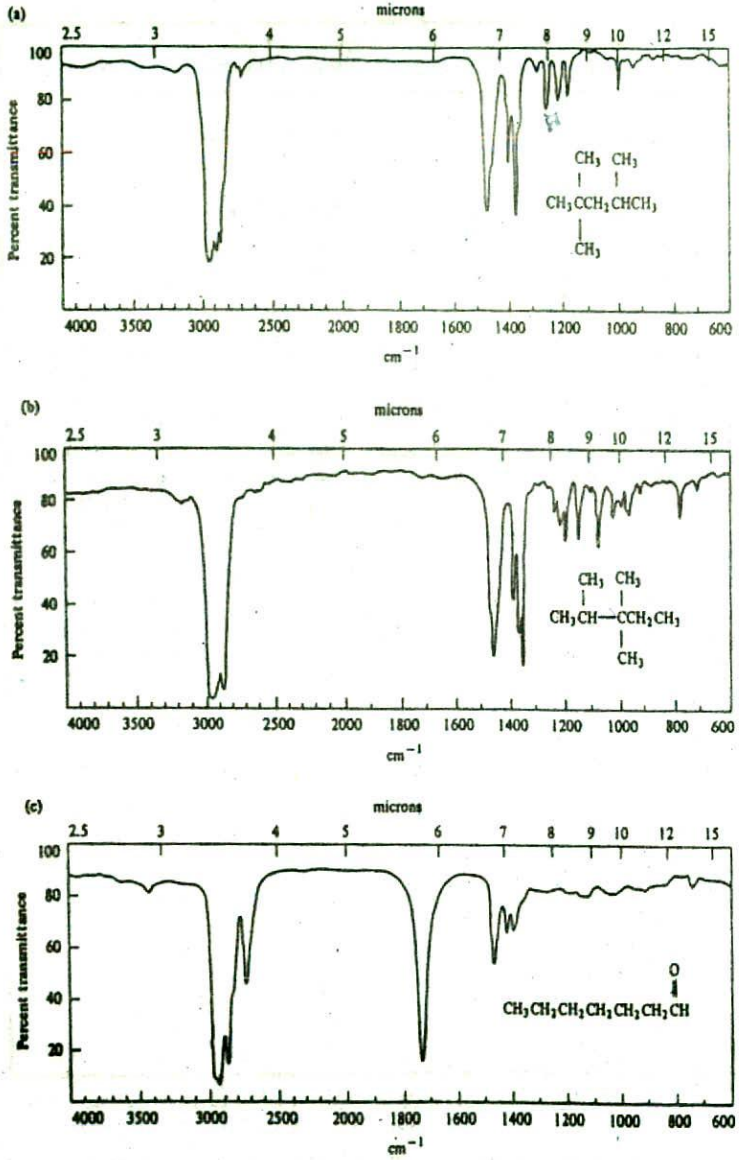


Fig. 51.9. Infrared spectra of (*a*) 2,2,4-trimethylpentane; (*b*) 2,3,3-trimethylpentane; (*c*) heptanal.

A sharp absorption at 2220 cm^{-1} in the spectrum in Figure 51.10(*b*) is characteristic of a triple bond. The presence of an aromatic ring is indicated by the group of absorptions between 1600 and 1450 cm^{-1} and is consistent with the absorption at 3060 cm^{-1} typical of = C–H stretching vibrations.

The very broad absorption in the 2500 to 3500 cm^{-1} region of the spectrum in Figure 51.10(*c*), along with the strong carbonyl absorption at 1710 cm^{-1}, is representative of a carboxylic acid.

In attempting to deduce structural information about an unknown compound from its infrared spectrum, our approach should be to look for the presence or absence of absorptions having the frequencies characteristic of certain functional groupings. For example, a compound thought to be a ketone must show a carbonyl stretching band in the 1550–1850 cm^{-1} region. If it lacks the band, it is not a ketone. Infrared spectroscopy is also used extensively to identify samples of already known compounds. Identical infrared spectra are identical in a large number of features (Just as are identical fingerprints) and almost certainly are of the same compound.

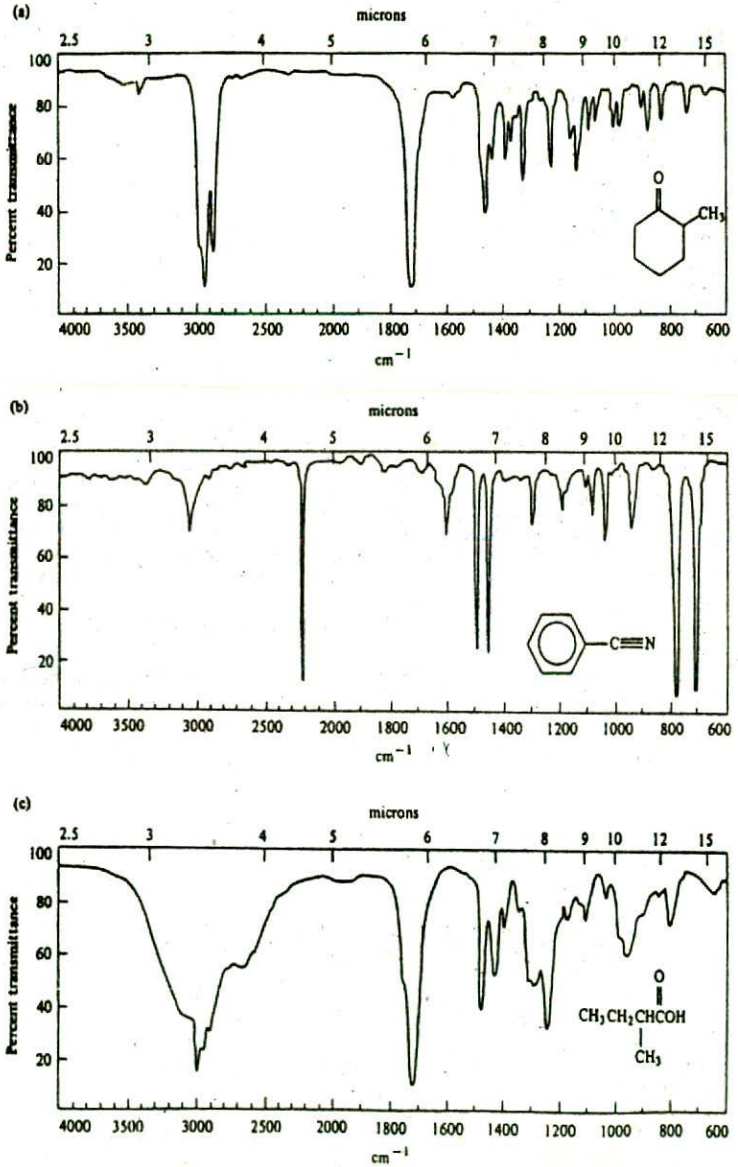


Fig. 5.10. Infrared spectra of (*a*) 2-methylcyclohexanone; (*b*) benzonitrile; and (*c*) 2-methylbutanoic acid.

To Summarise :

1. Absorption in the infrared results in vibrational excitations of bonds.
2. Different types of bonds require differing amounts of energy for vibrational excitations.
3. In an infrared spectrum, the region 1500 – 4000 cm^{-1} is useful for determination of functional groups, while the region beyond this is the *fingerprint* region.
4. Polar groups usually exhibit stronger peaks in the infrared spectrum than nonpolar groups. The absorption positions of –OH, –NH, and $-NH_2$ (a double peak), –COOH, and C=O are particularly distinctive.

NUCLEAR MAGNETIC RESONANCE (NMR) SPECTROSCOPY

Nuclear magnetic resonance (NMR) spectroscopy measures the energy absorbed when certain nuclei undergo **nuclear spin transitions.** These transitions involve photons of much less energy than those associated with electronic or vibrational transitions. Photons in the radio frequency region of the spectrum have the proper energy but only for selected nuclei.

Atomic nuclei have a property called the **spin number, I.** Nuclei that have an odd atomic number (*number of protons*) or an odd mass number (*protons + neutrons*) or both an odd atomic number and an odd mass number have spin numbers that are not zero ($I \neq 0$). Ordinary hydrogen (^1H, one proton, no neutrons in the nucleus, mass number = 1) is an example of an element whose nucleus has a spin number of $\frac{1}{2}$. The carbon-12 isotope (^{12}C), which has 6 protons and 6 neutrons in its nucleus, has $I = 0$. Carbon-13 (^{13}C) has 6 protons and 7 neutrons and, like ^1H, a spin number of $\frac{1}{2}$. **Only nuclei with non-zero values for I will give NMR spectra.**

Organic chemists deal mainly with ^1H nuclear magnetic resonance and we shall concentrate on this topic. The spectra of other nuclei, however, especially ^{13}C, can provide useful information too. One problem is that the *NMR active* nuclei (other than ^1H) of greatest use to an organic chemist are ^{13}C ($I = \frac{1}{2}$), ^{15}N ($I = \frac{1}{2}$), and ^{17}O ($I = \frac{5}{2}$). The natural abundance of these isotopes is so low that a suitable NMR spectrum requires special instrumentation or synthetic isotope enrichment.

One can think of nuclei with $I \neq 0$ as spinning tops carrying charge. Each such nucleus has a characteristic **magnetic dipole moment**, which we can represent as an arrow, →. A nucleus with a magnetic moment is like a small magnet with a certain magnetic strength (μ) and with a north and south pole. Let the arrow head be the north pole and the tail of the arrow the south pole. When there is no external magnetic field, a collection of such nuclear magnets will be randomly oriented. In a magnetic field, however, each magnet will orient itself in one of a limited number of ways. In other words, the orientations are quantised.

The numerical value of I shows how many ways a nucleus can be oriented in an external magnetic field. The number of orientations equals $2I + 1$. Thus, both ^1H and ^{13}C can assume $2(\frac{1}{2}) + 1 = 2$ orientations. Two, and only two, orientations are allowed. These nuclei will line up either with the field (↓) or against the field (↑) (Fig. 51.11).

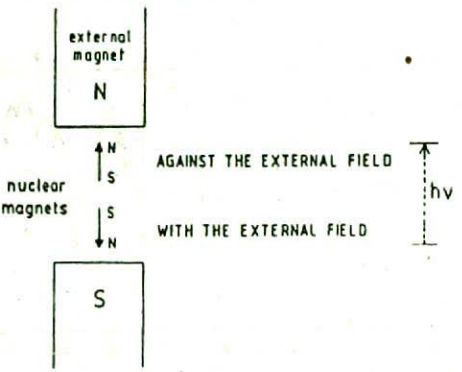


Fig. 51.11. Representation of nuclear magnets in an external magnetic field.

The two orientations have different energies. The amount of energy required to move from one orientation to another, hν, will depend on the strength of the external field, H, and on μ, the strength (magnitude) of the nuclear moment. For nuclei in which $I = \frac{1}{2}$, the relationship is expressed by the following equation :

$$E = h\nu = 2\mu H \qquad \ldots(9)$$

It turns out that at a magnetic field strength (H) of about 14,000 gauss ^{1}H nuclei require photons with a frequency of 60 million hertz (60 MHz), while ^{13}C nuclei require a frequency of about 15 MHz*. When the magnetic field strength and the radiation frequency match so that energy from the radiation is absorbed, the nuclei are said to be in *resonance with the radiation*.

An NMR spectrometer can be designed either to scan through appropriate frequencies (ν) at a set magnetic field strength (H) or to scan through a range of magnetic field strengths at a set frequency. Either way gives a match-up that will put the nuclei in resonance. In practice, the latter method is usually used ; the magnetic strength is slowly increased, while the sample is bombarded with set radio frequency. Common frequencies are 60 MHz and 100 MHz.

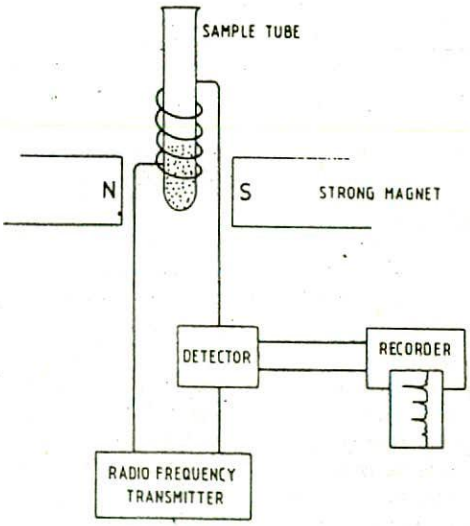


Fig. 51.12. Schematic diagram of an NMR spectrometer.

Fig. 5.12 shows the essential features of an NMR spectrometer. The sample is placed between the poles of a powerful magnet and is surrounded by a coil connected to a radio frequency transmitter. In effect, the spectrometer measures and records the amount of radio frequency radiation absorbed by the sample as the magnetic field strength is altered. Spectra are ordinarily taken of compounds in solution, although they can be of pure liquids. Commonly used solvents include those like CCl_4 that have no hydrogens to give interfering absorptions. Because deuterium (^{2}H *or* D)

---

*60 million Hz = 60 mega Hz = 60 MHz or 60 Mc (Mc = megacycles per second). Recall that $\nu = c/\lambda$; therefore $\lambda = c/\nu$. Also, since 60 MHz = 6×10^{7} cycles per sec. and $c = 3 \times 10^{10}$ cm/sec.

$$\lambda = \frac{3 \times 10^{10} \text{ cm/sec}}{6 \times 10^{7} \text{ cycles/sec}} = 0.5 \times 10^{3} \text{ cm/cycle} = 500 \text{ cm} = 5 \text{ m}$$

Thus, the photons involved in nuclear magnetic resonance have rather long wavelengths.

absorbs in a very different region than hydrogen, such solvents as $CDCl_3$, in which all H's have been replaced by D's, are also widely used. A few tenths of a milliliter of a 5 to 10% solution sufficies for routine spectra. The recorder plots absorption intensity against relative absorption frequency, giving the NMR spectrum. Figure 51.13 shows an example of a 60 MHz spectrum.

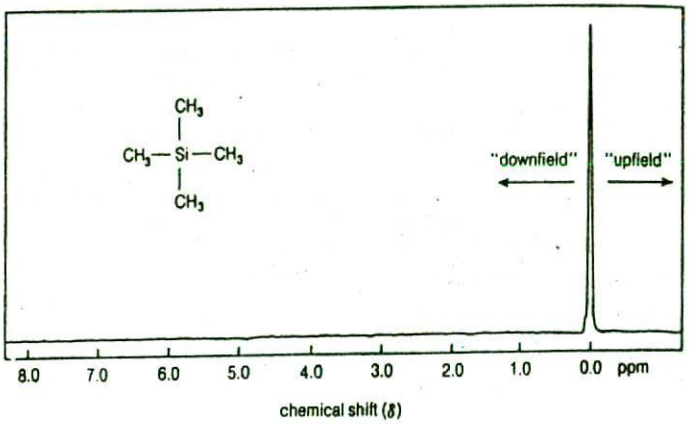


Fig. 51.13. The NMR spectrum of tetramethylsilane (TMS). The chemical shift of TMS protons is 0.00 ppm by definition.

Interpretation of NMR Spectra

Figure 51.13 shows the NMR spectrum of tetramethylsilane, $(CH_3)_4Si$. It turns out that the protons in tetramethylsilane (TMS) absorb at a high field strength relative to other protons. Thus the TMS signal is used to calibrate NMR spectra. Since nearly all proton signals are on the same (downfield) side of the TMS signal, concern about plus or minus shifts is eliminated. *TMS is a good standard because it is relatively inert, soluble in most organic solvents and volatile enough (bp 27°C) to be easily removed after the spectrum is obtained.* Usually a small amount of TMS is added directly to a sample before the sample is run. The difference in frequency units between the sharp TMS peak and the absorption signal of another proton is called the **chemical shift.**

It may seem confusing that the location of absorption peaks is specified on a frequency scale when we have said that the frequency is usually held constant and the magnetic field strength is varied. Typically the field strength is varied, but the electronic components of the spectrometer and recorder translate this to a print-out that tells us the energy of a particular absorption in hertz relative to that of some reference such as TMS. We still say that TMS is at the "high field" end of the spectrum, however, and that most other protons absorb "downfield" from the protons of TMS.

Chemical Shift. The chemical shift is expressed as a fraction of the operating frequency of the NMR spectrometer. The units therefore will be hertz per million hertz (Hz/MHz) or, in other words, parts per million (ppm) on what is called the **delta** (δ) **scale**.

On the δ scale the chemical shift of the TMS protons is arbitrarily set at 0. Another, older scale is the tau (τ) scale. On the τ scale the TMS signal is set at 10. It is easy to interconvert δ and τ scale values ($\tau = 10 - \delta$) and ($\delta = 10 - \tau$), both of which are still used.

Different hydrogen nuclei have different chemical shifts. For example, the dioxane protons absorb well downfield from the TMS protons (Fig. 51.14). Also, most organic compounds give NMR spectra that show at least several peaks. Consider the protons in 1,2-dibromo-2-methylpropane, which give an NMR spectrum with two peaks (Fig. 51.15). These observations prompt an important question: *Why do the chemical shifts of various hydrogen nuclei differ ?*

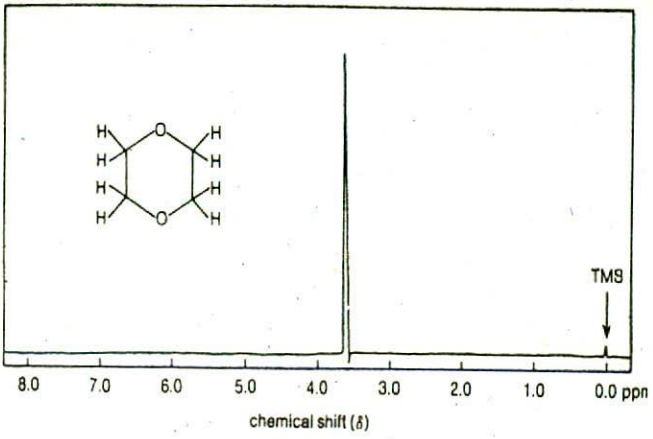


Fig. 51.14. The NMR spectrum of dioxane.

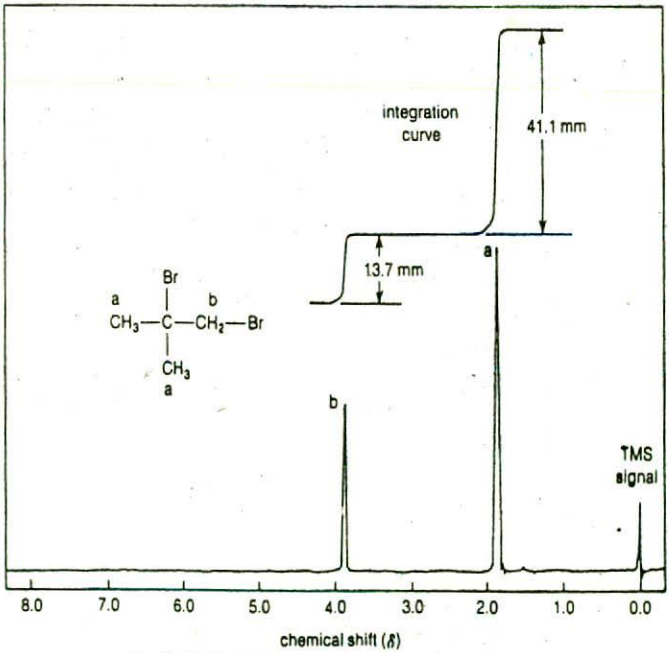


Fig. 51.15. The NMR spectrum of 1,2-dibromo-2-methylpropane.

An atomic nucleus in a molecule is not insulated from its surroundings. Around it are other nuclei, which are themselves like tiny magnets, each with its own small magnetic field. There are also negatively charged electrons in the vicinity of each nucleus and these have magnetic moments too. Therefore, what any nucleus "feels" in an external magnetic field is affected by the small local fields of other nuclei and electrons near it. Some of the small local fields near a nucleus slightly increase the effect of the external field, but others decrease it. The extent to which electrons shield the nucleus – that is, modify the effect of the external field on it – is especially important in determining chemical shifts.

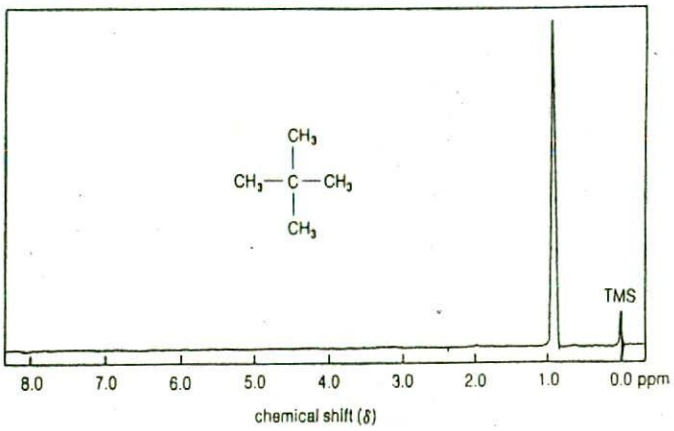
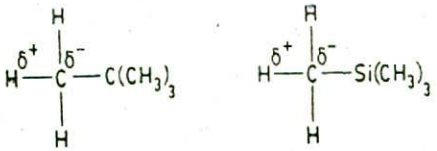


Fig. 51.16. The NMR spectrum of 2,2-dimethylpropane.

Let us compare protons of TMS to those in 2,2-dimethylpropane (Fig. 51.16). The 2,2-dimethylpropane protons absorb 55 Hz downfield from TMS at 60 MHz ($\delta = 0.92$). First of all, since both TMS and 2,2-dimethylpropane have 12 hydrogens, why is there only one peak in the NMR spectrum of each of these compounds ? The answer is that chemically equivalent hydrogens give identical chemical shifts. This is the same as saying that hydrogens in identical environments will absorb at the same field strength at a set frequency. All the hydrogens in TMS are in the same environment. Each hydrgoen in TMS is attached to a carbon that is also bonded to two other hydrogens and an $-Si(CH_3)_3$ group. The situation is similar for hydrogens in 2,2-dimethylpropane, except that a carbon replaces silicon as the central atom. Thus, the NMR spectra of both of these compounds have a single peak.

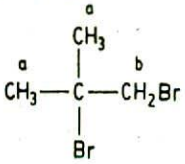
The hydrogens in TMS absorb at a higher field than those in 2,2-dimethylpropane because silicon is less electronegative than carbon. Silicon pulls electron density *less strongly* from its attached methyl groups than does the central carbon in 2,2-dimethylpropane. This means that the electrons in the C–H bonds in 2,2-dimethylpropane are more polarised toward the carbon of the methyl group than the electrons in TMS are polarised toward silicon. Thus δ^+, the partial positive charge on each hydrogen, is greater in 2,2-dimethylpropane than in TMS.



In other words, the electron density around the 2,2-dimethylpropane hydrogens has decreased relative to that around the TMS hydrogens. The electrons in 2,2-dimethylpropane shield the hydrogens less. We say that these protons are *deshielded* relative to TMS. The more deshielded a proton is, the further downfield it resonates. In effect, since electrons shield the hydrogens in TMS more than they do those in 2,2-dimethylpropane it takes a higher applied external field to get them into resonance at 60 MHz.

Number of Signals. *Shielding and deshielding by the local environment is what makes protons in non-identical environments have different chemical shifts.* With this basic principle in mind,

let us consider the 1,2-dibromo-2-methylpropane molecule again. Its NMR spectrum has two kinds of protons in the molecule. (Remember that all protons are fundamentallly identical. This is just a convenient way of saying protons are in two different environments).



1,2-DIBROMO-2-METHYLPROPANE

Closer look of the above formula shows that one kind of proton is the set of six methyl group protons (labelled **a**) all of which are chemically equivalent. Another kind is the pair of equivalent methylene hydrogens (labelled **b**). Now the question is, which peak in Figure 51.15 represents the **a** protons and which **b**? Two aspects of the spectrum provide an answer : the relative chemical shift and the relative intensity of peaks.

Bromine is an electronegative element. Therefore, it should have a strong deshielding effect. This effect should be experienced more strongly on the methylene protons **b** because they are bonded to a carbon which is, in turn, directly bonded to a bromine. The methyl protons do not experience the deshielding effect as strongly. This is because these protons are bonded to the carbon which is one carbon removed from a bromine. The intervening tertiary carbon *insulates* the methyl protons **a** to some extent from the pull of the bromine atom attached to it. The **b** protons are similarly *insulated* from the *pull* of the bromine attached to the tertiary carbon, but they are not so insulated from the bromine attached to the primary carbon. Our conclusion is that since the methylene protons are more deshielded, they ought to appear more downfield. Therefore, we would like to assign them to the shorter of the two peaks in the NMR spectrum (Fig. 51.15). The taller peak, would then be assigned to the **a** protons.

Peak intensity and Integration curve. The relative sizes of the two peaks in the spectrum of 1, 2-dibromo-2-methylpropane (Fig. 51.15) also indicates how they should be assigned. More precisely, *the area under the peaks is proportional to the number of protons responsible for the signal.* The formula has six methyl protons and two methylene protons. The relative area under the peaks **a** and **b** are in a 6 : 2 (3 : 1) ratio, which confirms our assignment on the basis of relative electron shielding. The areas (or integrals) of peaks can be obtained electronically with NMR instruments. A step-like curve is traced over each signal and the heights of the various steps are proportional to the areas under the peaks. Figure 51.15 shows the integration curve traced over the peaks.

Number of Proton Neighbours. In addition to the information from chemical shift, the number of signals and peak integration, an NMR spectrum also indicates the number of protons.

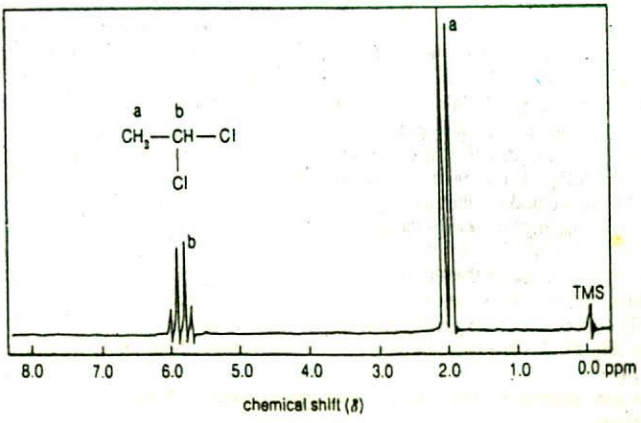


Fig. 51.17. The NMR spectrum of 1,1-dichloroethane.

The signal of a particular proton is affected by neighbouring protons with different chemical shifts. For example, consider the NMR spectrum of 1,1-dichloroethane (Fig. 51.17). The signals clearly fall into two groups, one group at higher field that integrates for *three* protons and another group considerably downfield that integrates for only *one*.. There is no question about the assignment ; the methyl group protons must be upfield pair of peaks (called a **doublet**) and the four downfield peaks (called a quartet) must be due to the $-CHCl_2$ proton. But why do the signals split ?

The nomenclature of split signals is as follows : One peak = singlet (s); two peaks = doublet (d); three peaks = triplet (t) ; four peaks = quartet (q). More than four peaks is usually called a multiplet (m).

Spin-Spin Coupling. The three equivalent methyl group protons in 1,1-dichloroethane are affected by the way in which the single proton on the adjacent carbon interacts with the applied magnetic field. If this proton lines up *with* the external field, then the effective field strength experienced by the neighbouring methyl protons is enhanced slightly. If the $-CHCl_2$ proton lines up *against* the applied magnetic field, it substracts slightly from the strength of the field affecting the methyl protons. In effect, the methyl protons can experience two very slightly different fields depending on whether the neighbouring proton is either *with* or *against* the applied field. Therefore, in a collection of molecules resonance can occur at two slightly different frequencies, and the sample will produce a *doublet* absorption signal rather than a *singlet* signal. This effect is known as *spin-spin coupling*.

The effect of methyl protons on the appearance of the $-CHCl_2$ proton signal in 1,2-dichloroethane is somewhat more complicated, but is a logical (if reversed) extension of the spin-spin coupling concept first described. The three methyl protons can interact with the applied field in four ways (Fig. 51.18). An upward pointing arrow (↑) represents alignment with the field. A downward pointing arrow (↓) represents alignment against the field.

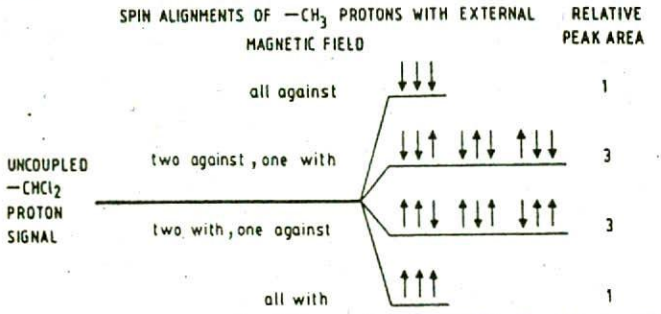
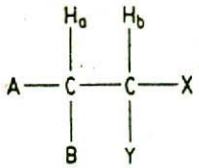


Fig. 51.18. Spin-Spin Coupling. Splitting of the $-CHCl_2$ proton signal in CH_3-CHCl_2 by the neighbouring $-CH_3$ group.

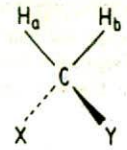
As shown in Figure 51.18, there are *three ways* to align the three methyl protons so that *two* are either with or against the external field. The permutations for this mode are two mirror-image sets, each having a relative weighting of 3. However there is only *one way* to arrange them so that *all* are either with or against the external field. This produces two mirror–image sets, each with a relative weighting of 1. The net effect is to split the signal into four peaks with each of the two inside peaks having three times the area of each of the two outside peaks. The amount of splitting (distance between individual peaks) is constant within the peaks of the quartet and is identical to the splitting observed for the two peaks of the methyl proton doublet.

Spin-spin coupling thus reveals the number of neighbouring hydrogens a particular proton has. A simple expression of this fact is that N equivalent neighbours produce $N + 1$ peaks. In using this rule it is important to realise that the neighbours must be equivalent to each other, but must not be equivalent to (that is, in the same environment as) the protons they are to split. Equivalent protons do not split each other. Consequently, the methyl group protons in 1,1-dichloroethane do not split each other (Fig. 51.17). Similarly, the protons on adjacent carbons in dioxane do not split each other (Fig. 51.14).

Spin-spin coupling is often associated with non-equivalent protons on neighbouring carbons (1,2-coupling).



1,2-COUPLING



1,1- COUPLING

There are fewer examples of spin-spin coupling between non-equivalent protons on the same carbon (1,1-coupling). Spin-spin splitting is not often seen when hydrogens are separated by more than two other atoms.

Table 51.8. Approximate chemical shifts for different kinds of protons.

Location of hydrogen	Chemical shift (δ)	
$R-CH_3$	0.8–1.0	alkanes (R = saturated alkyl)
$R-CH_2-R$	1.2–1.4	
$R-\underset{R}{CH}-R$	1.5–1.7	
$>C=C<_{H}^{H}$	4.6–5.0	
$>C=C<_{R}^{H}$	5.1–5.8	(R = saturated alkyl)
$-C\equiv C-H$	1.7–3.3	
$Ar-H$	6.5–8.0	
$>C=C<_{R}^{CH_3}$	1.6–1.8	(R = H or saturated alkyl)
$Ar-CH_3$	2.1–2.5	
$-\overset{O}{\overset{\|}{C}}-CH_3$	1.9–2.6	aldehydes, ketones, esters, acetic acid
$>N-CH_3$	2.2–2.9	amines, amides
$-O-CH_3$	3.3–3.9	methanol, ethers, esters
$Cl-CH_3$	3.1	
$Br-CH_3$	2.7	
$-\overset{O}{\overset{\|}{C}}-H$	9.2–10.2	aldehydes
ROH	0.5–5.5	alcohols
ArOH	4–8	phenols
$-\overset{O}{\overset{\|}{C}}-OH$	10–13	carboxylic acids
$>NH$	0.5–5.0	amines

Table 51.8 lists some approximate chemical shifts for different kinds of protons. It is apparent that the typical kinds of protons found in organic structures span a range of about 10 ppm on the δ scale. There is a good separation of some types of protons. For example, vinyl and aromatic protons absorb well down field from the saturated C–H types. A knowledge of the approximate chemical

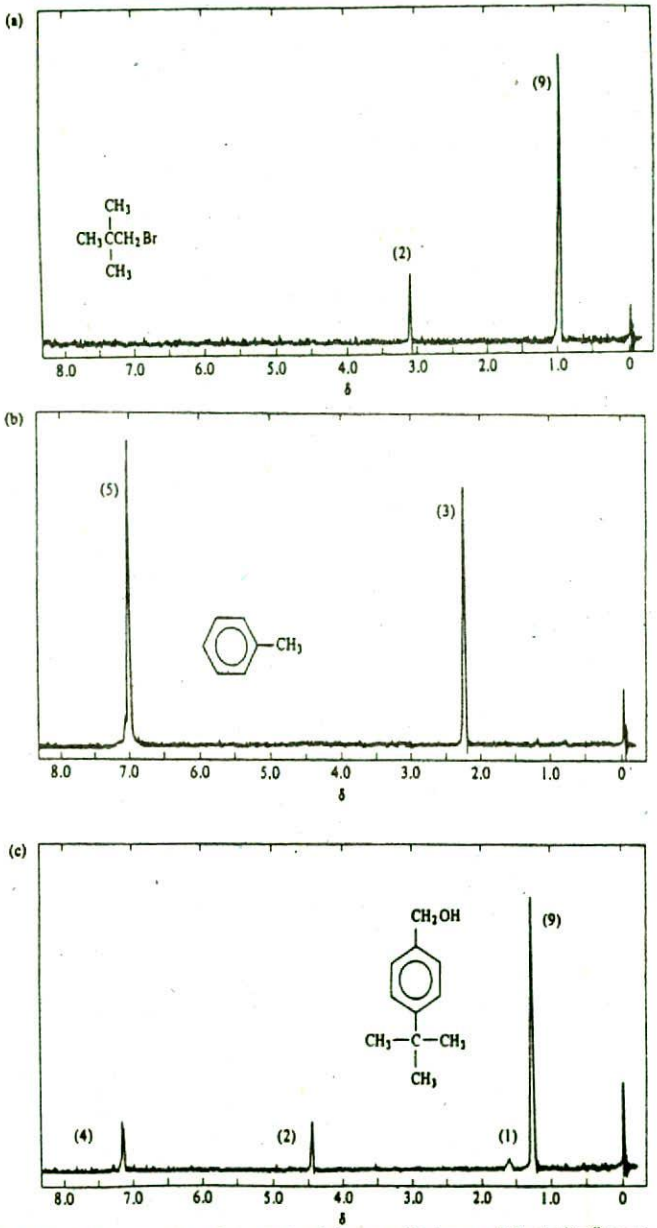


Fig. 51.19. NMR spectra of (*a*) 1-bromo-2,2-dimethylpropane ; (*b*) toluene; and (*c*) *p*-*tert*-butylbenzene. Relative areas of absorptions are indicated by the numbers in parentheses.

shift *plus* consideration of shielding and deshielding effects allows us to predict where a signal for a particular kind of proton should appear. Similarly, consideration of spin-spin coupling allows one to predict the detailed form of the various signals. More examples of NMR spectra are shown in Figures 51.19 and 51.20.

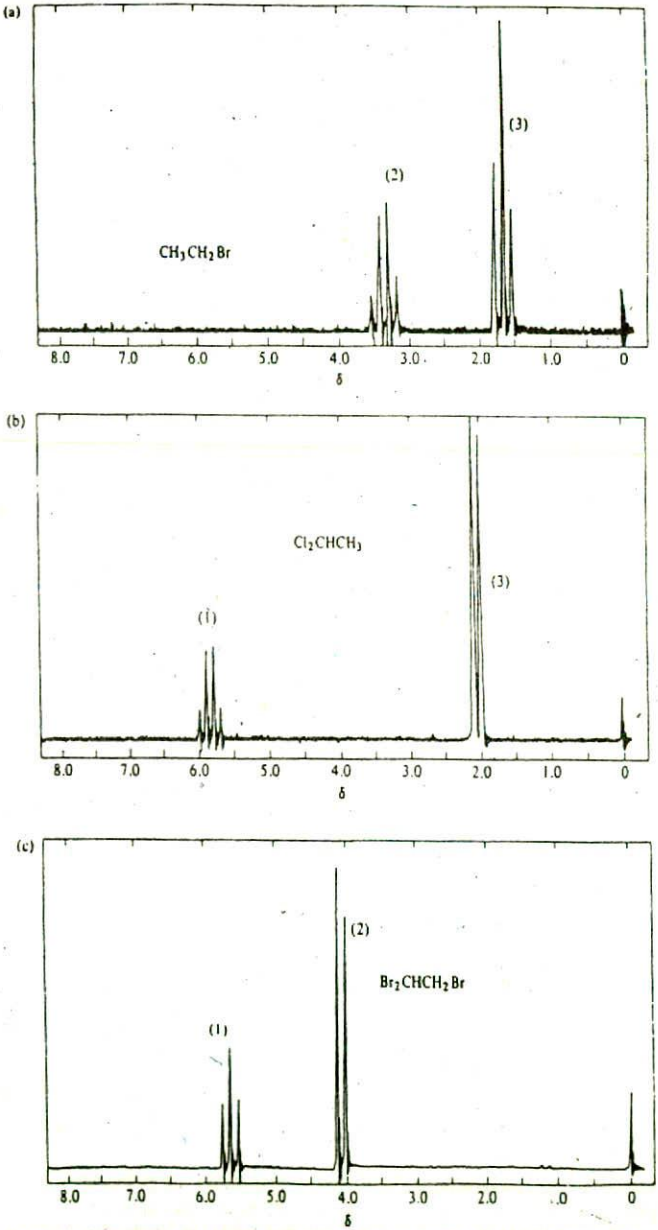


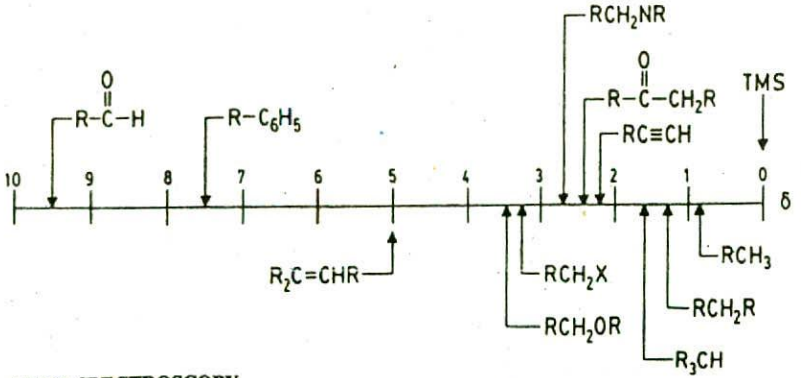
Fig. 51.20. NMR spectra of (*a*) ethyl bromide; (*b*) 1,1-dichloroethane ; and (*c*) 1,1,2-tribromoethane. Relative areas of absorptions are indicated by the numbers in parentheses.

To Summarise :

1. NMR spectroscopy measures absorption of radio frequency photons when nuclear spin transitions take place in a magnetic field.
2. Tetramethylsilane (TMS) is used as a reference for NMR because its hydrogens have a very highfield chemical shift.
3. The chemical shift of the TMS protons is assigned a value of 0 on the delta (δ) scale. Most other protons absorb downfield and have chemical shifts from 0 to 10.
4. The local environment of hydrogen affects its chemical shift.
5. Chemically eqnivalent hydrogens have identical chemical shifts.
6. The more deshielded a proton, the more downfield from TMS is its chemical shift. Always measure split signals at the centre of the multiplet.
7. The intergral of a signal (area under the peak or peaks) is proportional to the number of protons producing the signal.
8. Protons with the same chemical shift do not split each other.
9. Protons with different chemical shifts split one another if they are separated by no more than two other atoms.
10. The number of peaks resulting from spin-spin coupling is $N + 1$ where N is the number of equivalent neighbouring protons.
11. The approximate relative areas of peaks in a multiplet can be predicted by using Pascal's triangle (a memory device used in algebra to remember the binomial coefficients). The triangle may be extended to any size using only addition.

n	Pascal's Triangle	Example
0	1	n = number of neighbouring protons
1	1 1	For n = 2, triplet is expected
2	1 2 1	From triangle, triplet areas = 1:2:1
3	1 3 3 1	
4	1 4 6 4 1	
5	1 5 10 10 5 1	

12. Some typical proton chemical shifts are show below for ready reference.



MASS SPECTROSCOPY

Mass spectroscopy is a technique that allows us to measure the molecular weight (mass) of a compound. In addition, we can obtain valuable structural information about unknowns by measuring the masses of the fragments produced when high-energy molecules fly apart. Fig. 51.21 shows the most common type of mass spectrometer.

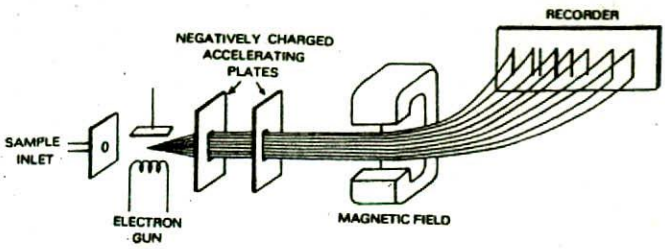
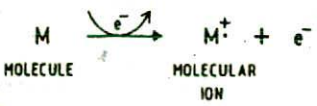


Fig. 51.21. Schematic diagram of a mass spectrometer.

A small amount of sample is introduced into the mass spectrometer and bombarded with a stream of high-energy electrons. The energy of the beam of electrons is usually 70 *eV* (electron volts) or 1600 kcal/mole. When a high-energy electron strikes an organic molecule it disloges one of the electrons of the molecule, producing a positively charged ion called the **molecular ion**.



The molecular ion is not only a cation, but because it contains an odd number of electrons, it also is a free radical. Thus it belongs to a general group of ions called radical cations.

In addition to causing ionisation, electron bombardment transfers such a large amount of energy to the sample molecules that the molecular ions fragment; they literally fly apart into numerous smaller pieces some of which retain a positive charge, and some of which are neutral. The fragments then pass through a strong magnetic field, where they are deflected according to their mass-to-charge ratio (*m/e*). Neutral fragments are not deflected by the magnetic field and are lost on the walls of the instrument. Positively charged fragments, however, are sorted by the spectrometer onto a detector, which records them as peaks at the proper ratios. Since the number of charges, *e*, is usually 1, the peaks represent the masses of the ions. The mass spectrum of a compound is usually presented as a bar graph with *m/e* values (unit masses) on the *x*-axis, and intensity (number of ions of a given *m/e* striking the detector) on the *y*-axis.

The highest peak is called the **base peak** and is arbitrarily assigned an intensity of 100%. Fig. 51.22 shows the mass spectra of methane and propane.

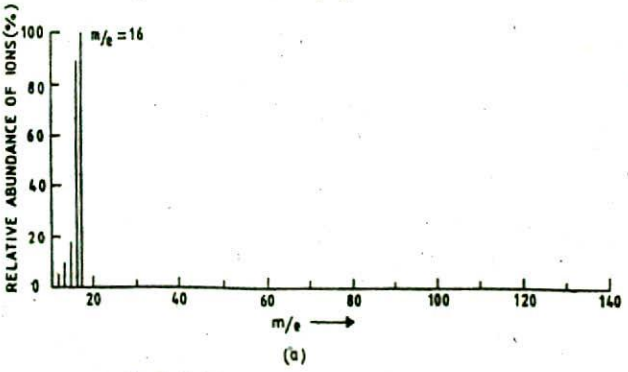
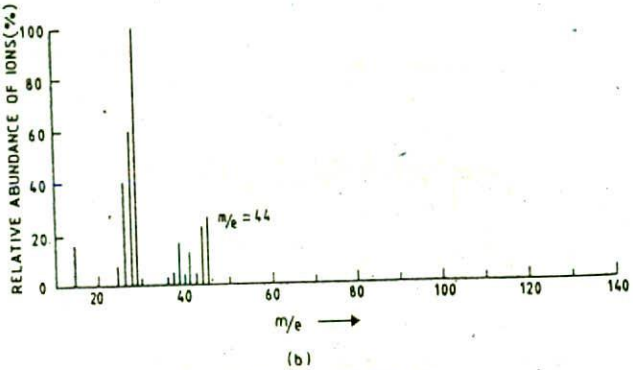


Fig. 51.22. Mass spectra of (*a*) methane (CH_4, MW = 16),

The mass spectrum of methane is quite simple, since few fragmentations are possible. As Figure 51.22(*a*) shows, the base peak has *m/e* = 16, which corresponds to the unfragmented methane

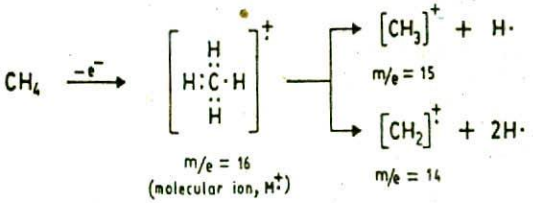


(b)

Fig. 51.22. (*b*) propane (C_3H_8, MW = 44).

moleculear ion ($M^{+\cdot}$). The mass spectrum also shows ions at *m/e* = 15 and 14, corresponding to cleavage of the molecular ion into CH_3^+ and CH_2^+ fragments.

For larger molecules, the fragmentation patterns are usually complex and the molecular ion is often not the highest (base) peak. For example, the mass spectrum of propane (Fig. 51.22*b*) has a molecular ion (*m/e* = 44) only about 30% as high as the base peak at *m/e* = 29. In addition, many other fragment ions are noticed.



Interpretation of Mass Spectra

The most important information that can be obtained by studying the mass spectrum of a compound is its molecular weight (MW). For example, if we were given three unlabelled bottles containing hexane (MW = 86), 1-hexene (MW = 84), and 1-hexyne (MW = 82), mass spectroscopy would readily distinguish between them. We must keep in mind, however, that not all compounds show a molecular ion in the mass spectrum. Although $M^{+\cdot}$ is usually easy to identify if it is abundant, certain compounds such as 2,2-dimethylpropane fragment so readily that no molecular ion is observed (Fig. 51.23).

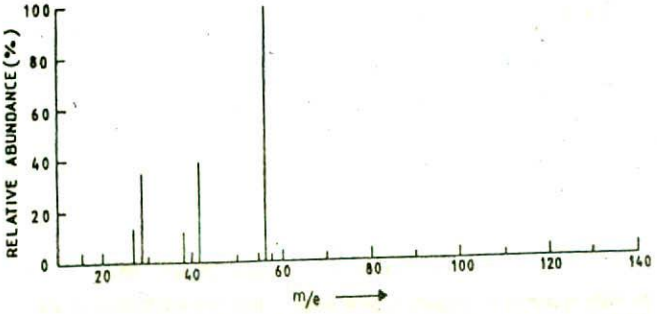


Fig. 51.23. Mass spectrum of 2,2-dimethylpropane (C_5H_{12}, MW = 72).

(*c*) $CH_3(CH_2)_4CH_3$ *and* $CH_3(CH_2)_5CH_3$
(*d*) $CH_3CH_2OCH_2CH_3$ *and* $CH_3CH_2\underset{\displaystyle OH}{\underset{|}{C}}HCH_2CH_3$

Answer

(*a*) *UV Spectroscopy.* Since its double bonds are not conjugated, the second isomer will not give an absorption at a wavelength above 200 nm. However, the first isomer has conjugated double bonds and will give an absorption characteristic of a conjugated diene.

(*b*) *NMR Spectroscopy.* The first compound will give only one absorption. The second will give two absorptions (a doublet and a quartet).

(*c*) *Mass Spectroscopy.* The two compounds have different molecular weight and their molecular ions will therefore be different. Decane will have a peak at 142 and undecane will have a peak at 156. Note that IR, UV and NMR spectra of these compounds will be similar.

(*d*) *IR Spectroscopy.* The alcohol will have a peak for the O–H absorption in the 3200–3600 cm^{-1} region. The ether will have no absorption in that area.

6. A bottle of cyclohexane is known to be contaminated with benzene. At 254 nm, benzene has a molar absorptivity of 204 and cyclohexane has a molar absorptivity of zero. A UV spectrum of the contaminated cyclohexane taken in a 2.0 cm cell shows an absorbance of 0.07. What is the molar concentration of benzene ?

Answer. 0.00017 *M* (Apply Beer–Lambert Law).

7. Cyclopentanone (0.043 *M* in a 1.0 cm cell) has λ_{max} at 288 nm with an absorbance of 0.85. What is the molar absorptivity of cyclopentanone at 288 nm ?

Answer. 19.7 (Apply Beer-Lambert Law).

8. The unsaturated aldehydes $CH_3(CH{=}CH)_nCH{=}O$ have UV absorption spectra that depend on the value of *n*, the λ_{max} being 220, 270, 312 and 343 nm as *n* changes from 1 to 4. Explain.

Answer. As the number of double bonds increase, so too does the extent of conjugation. Hence the absorption maximum moves to longer and longer wavelengths.

9. Which one of the following compounds will absorb ultraviolet light at the longest wavelength ?

(*a*) $CH_2{=}CH{-}CH{=}CHCH_2OH$

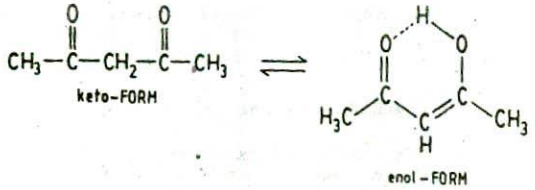
(*b*) $CH_2{=}CH{-}CH{=}CH{-}\overset{\displaystyle O}{\overset{\|}{C}}{-}H$

(*c*) $CH_2{=}CH{-}\underset{\displaystyle OH}{\underset{|}{C}}H{-}CH{=}CH_2$

Answer. (*b*) will absorb at the longest wavelength because two double bonds and the carbonyl double bond are conjugated. (*a*) has only two conjugated double bonds, and (*c*) has no conjugated double bonds.

10. The compound $CH_3\overset{\displaystyle O}{\overset{\|}{C}}CH_2\overset{\displaystyle O}{\overset{\|}{C}}CH_3$ exists in equilibrium with at tautomer. Its solutions show a strong UV absorption with a λ_{max} at 272 nm. What is the structure of the tautomer ? How could infrared spectroscopy be used to confirm your suggestion?

Answer. The methylene protons, being between the two carbonyl groups, are the most acidic protons in the molecule and most likely to tautomerise :



The enol form has a conjugated system which is responsible for the long wavelength UV absorption. The infrared spectrum of the enol form should show O–H (hydorgen bonded) stretch and C=C stretch, both not present in the keto form.

11. How would you distinguish between the following pairs of compounds by IR spectroscopy ?

(*a*) $CH_3CH_2CH_2N(CH_3)_2$ *and* $CH_3CH_2CH_2NH_2$
(*b*) $CH_3CH_2CH_2COOH$ *and* $CH_3CH_2COOCH_3$
(*c*) $CH_3CH_2COCH_3$ *and* $CH_3CH_2COOCH_3$

Answer. (*a*) $CH_3CH_2CH_2NH_2$ shows N–H absorption at 3300–3500 cm^{-1} while $CH_3CH_2CH_2N(CH_3)_2$ does not.

(*b*) $CH_3CH_2CH_2COOH$ shows O–H absorption at 2500–3500 cm^{-1} while $CH_3CH_2CH_2COOCH_3$ does not.

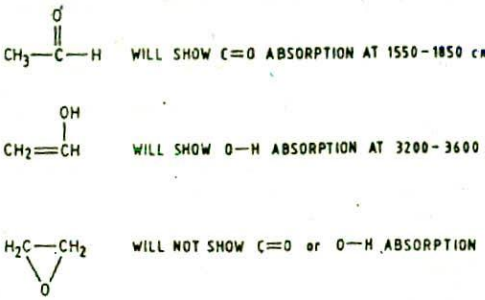
(*c*) $CH_3CH_2COOCH_3$ shows C–O absorption at 1050–1350 cm^{-1} while $CH_3CH_2COCH_3$ does not.

12. Briefly describe the main difference between the IR spectra of ethylene glycol ($HOCH_2CH_2OH$) and acetic acid (CH_3COOH).

Answer. Ethylene glycol will show strong O–H absorption at ~ 3500 cm^{-1}. It will not show carbonyl absorption. Acetic acid will show O–H absorption at ~ 3500 cm^{-1} and carbonyl (C=O) absorption at 1700 cm^{-1}.

13. Draw three isomers of molecular formula C_2H_4O. Describe how, using their IR spectra, one could distinguish among them.

Answer. The *3* isomers are :



14. How can the members of each pair of compounds be distinguished by a glance at their IR spectra ?

(*a*) $CH_3CH_2OCH_2CH_3$	*and*	$CH_3CH_2CH_2CH_2OH$
(*b*) $(CH_3)_3N$	*and*	$CH_3CH_2CH_2NH_2$
(*c*) $CH_3CH_2C{\equiv}CH$	*and*	$CH_3CH_2CH_2{=}CH_2$
(*d*) $CH_3CH_2CH_2COOH$	*and*	$CH_3CH_2COOCH_3$

Answer. (*a*) The alcohol will have a band in the 3200–3600 cm^{-1} region, characteristic of O–H;

(*b*) The primary amine will show an N–H absorption at 3300–3500 cm^{-1}, but the tertiary amine will not ;

(*c*) The first compound an alkyne will have a band in the 2100–2260 cm^{-1} region characteristic of C≡C, while alkene will show a band in the 1600–1680 cm^{-1} region characteristic of C=C ; and

(*d*) The first compound, a carboxylic acid, will show a broad O–H absorption at 2500–3500 cm^{-1}.

15. A very dilute solution of ethyl alcohol in carbon tetrachloride shows a sharp infrared band at 3600 cm^{-1}. As the solution is made more concentrated, a new, rather broad band appears at 3200–3600 cm^{-1}. Eventually the sharp band disappears and is replaced entirely by the broad band. Explain.

Answer. These infrared data provide direct evidence for hydrogen bonding in alcohols. In dilute solution the alcohol molecules are isolated, being surrounded by inert solvent molecules. The sharp band at 3600 cm^{-1} is due to the O–H stretching frequency in an isolated ethyl alcohol molecule. As the concentration of ethyl alcohol is increased, alcohol molecules come in contact with one another to form hydrogen bonds. Hydrogen-bonded O–H has a variable length (as the proton is transferred back and forth between oxygen atoms). Consequently, hydrogen-bonded O–H absorbs at a lower frequency and with a broader range (3200–3600 cm^{-1}) than the isolated O–H group.

16. Explain why the IR spectrum of glucose shows no significant absorption in the C=O stretching vibration region.

Answer. Glucose exists more than 99% in pyranose forms, which have no carbonyl group.

17. Two compounds, (A) and (B), have the same molecular formula C_2H_6O. They have different IR spectra. Compound (A) shows a strong/broad absorption at 3400 cm^{-1}, while compound (B) does not. Suggest formulas for (A) and (B) which account for the difference.

Answer. (*A*) is Ethyl alcohol (CH_3CH_2OH); (B) is Dimethyl ether (CH_3OCH_3). The strong absorption at 3400 cm^{-1} in (A) is due to the O–H bond.

18. How many NMR signals would be observed for each of the following compounds ? In other words, how many different kinds of protons are present ? Ignore any multiplicities resulting from spin-spin coupling.

(*a*) Chloroform (*b*) Acetone (*c*) Acetaldehyde
(*d*) Tetrahydrofuran (*e*) 2-Butanone (*f*) Ethyl acetate

Answer. (*a*) One signal (*b*) One signal (*c*) Two signals
(*d*) Two signals (*e*) Three signals (*f*) Three signals

19. How many NMR signals do you expect in each of the following compounds :

(*a*) 1,1-Dichloromethane (*b*) Ethyl bromide (*c*) 1,1-Dichloroethane
(*d*) *n*-Butane (*e*) Neopentane (*f*) Allyl alcohol
(*g*) Toluene (*h*) Propanal

Answer. (*a*) Two signals (*b*) Two signals (*c*) Two signals
(*d*) Two signals (*e*) One signal (*f*) Four signals
(*g*) Two signals (*h*) Three signals

20. How many signals would be expected in NMR spectrum of each of the following compounds :

(*a*) CH_3Br (*b*) CH_3CH_2Br

(*c*) $CH_3CH_2CH_2Br$ (*d*) $CH_3CH(Br)CH_3$

(*e*) $(CH_3)_4C$ (*f*) $(CH_3)_3CCl$

Answer. (*a*) One signal (*b*) Two signals (*c*) Three signals

(*d*) Two signals (*e*) One signal (*f*) One signal

21. How would you distinguish between the following pairs of compounds by NMR spectroscopy ?

(*a*) $CH_3-\overset{\overset{O}{\|}}{C}-CH_3$ *and* $CH_3CH_2-\overset{\overset{O}{\|}}{C}-H$

(*b*) $CH_3-\overset{\overset{O}{\|}}{C}-CH_3$ *and* $CH_3-\overset{\overset{O}{\|}}{C}-OCH_3$

Answer. (*a*) CH_3COCH_3 will give only one signal, while CH_3CH_2CHO will give three signals.

(*b*) CH_3COCH_3 will give only one signal, while CH_3COOCH_3 will give two signals.

22. What are the main differences in the NMR spectra of :

(*a*) $CH_3-\overset{\overset{O}{\|}}{C}-CH_3$

(*b*) $CH_3CH_2-\overset{\overset{O}{\|}}{C}-H$

(*c*) $CH_2{=}CH-CH_2OH$

Answer. (*a*) shows one NMR signal; (*b*) shows three NMR signals ; and (*c*) shows four NMR signals.

23. Draw the structure of a compound with each of the following molecular formulas that will show only one peak in its NMR spectrum :

(*a*) $C_2H_4Cl_2$ (*b*) C_5H_{12}

(*c*) C_2H_6O (*d*) C_4H_6

Answer. Possible structures are :

(*a*) $CH_3-\overset{\overset{Cl}{|}}{\underset{\underset{Cl}{|}}{C}}-CH_3$ (*b*) $CH_3-\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{C}}-CH_3$

(*c*) CH_3-O-CH_3 (*d*) $CH_3C\equiv CCH_3$

24. Indicate how the members of each group of isomeric compounds can be distinguished by a quick glance at their NMR spectra.

(*a*) $CH_3-\overset{\overset{O}{\|}}{C}-CH_3$ *and* $CH_3-\overset{\overset{O}{\|}}{C}-H$

(*b*) $CH_3CH_2OCH_2CH_3$ *and* $CH_3CH_2CH_2CH_2OH$

(*c*) $BrCH_2CH_2Br$ *and* CH_3CHBr_2

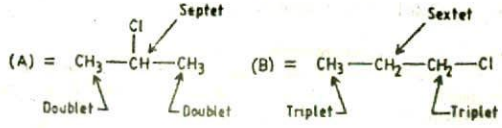
Answer. (*a*) Propionaldehyde exhibits three absorptions, but acetone only one ;

(*b*) Diethyl ether will give a simple spectrum with two absorptions in a 3:2 ratio, but butanol will give a complex spectrum with five different kinds of absorptions in a ratio 3:2:2:2:1; and

(*c*) 1,2-Dibromethane will give only one absorption, while, 1,1-Dibromethane will give two peaks in a ratio of 3:1.

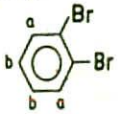
25. A chemist has two isomeric chloropropanes, (A) and (B). The NMR spectrum of (A) shows a doublet and a septet (seven peaks), while that of (B) shows two triplets and sextet (six peaks). Identify the structure of (A) and (B).

Answer. (A) is 2-chloropropane, and (B) is 1-chloropropane.

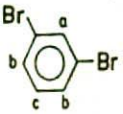


26. How will you distinguish between the three dibromobenzenes by their NMR spectra ?

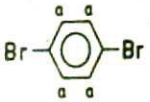
Answer. *o*-Dibromobenzene will show two peaks; *m*-dibromobenzene will show three peaks; and *p*-dibromobenzene will show only one peak.



o-DIBROMOBENZENE
(two peaks)
1 : 1



m-DIBROMOBENZENE
(three peaks)
1 : 2 : 1



p-DIBROMOBENZENE
(one peak)

27. Give a structure consistent with the following NMR data :

(*a*) Molecular Formula = CH_4O
- *a* Singlet at δ 1.43, 1H
- *b* Singlet at δ 3.47, 3H

(*b*) Molecular Formula = $C_4H_8O_2$
- *a* Triplet at δ 1.05, 3H
- *b* Singlet at δ 2.13, 3H
- *c* Quartet at δ 2.47, 2H

(*c*) Molecular Formula = $C_4H_8O_2$
- *a* Triplet at δ 1.25, 3H
- *b* Singlet at δ 2.03, 3H
- *c* Quartet at δ 4,12, 2H

(*d*) Molecular Formula = $C_4H_{10}O$
- *a* Singlet at δ 1.28, 9H
- *b* Singlet at δ 1.35, 9H

(*e*) Molecular Formula = $C_2H_3Cl_3$
- *a* Doublet at δ 3.95,2H
- *b* Triplet at δ 5.72,1H

(*f*) Molecular Formula C_3H_7Br
- *a* Doublet at δ 1.71, 6H
- *b* Septet at δ 4.32, 1H

Answer. (*a*) is Methyl alcohol = $\overset{b}{CH_3}–\overset{a}{OH}$

(*b*) is 2-Butanone = $\overset{a}{CH_3}–\overset{c}{CH_2}–\overset{O}{\overset{||}{C}}–\overset{b}{CH_3}$

(*c*) is Ethyl acetate = $\overset{b}{CH_3}–\overset{O}{\overset{||}{C}}–\overset{c}{O}\overset{a}{CH_2CH_3}$

(*d*) is *t*-Butyl alcohol = $\overset{a}{(CH_3)_3}C–\overset{b}{OH}$

(*e*) is 1,1,2-Trichloroethane = $\overset{a}{CH_2}\overset{b}{ClCHCl_2}$

(*f*) is 2-Bromopropane = $\overset{a}{(CH_3)_2}\overset{b}{CHBr}$

28. Write as many possible formulas as you can for hydrocarbons that show the following molecular ions in their mass spectra :

(*a*) $M^+ = 64$ (*b*) $M^+ = 186$ (*c*) $M^+ = 158$

Answer. In this problem we are given that all compounds represent hydrocarbons.

(*a*) For $M^+ = 64$, possible molecular formula is C_5H_4

(*b*) For $M^+ = 186$, possible formulas are $C_{14}H_{18}$ and $C_{13}H_6$

(*c*) For $M^+ = 158$, possible formula is $C_{12}H_{14}$

29. Consider the mass spectrum of Ethylbenzene. What causes the peak *m/e* = 106 ? The base peak in the mass spectrum is at *m/e* = 91. What species do you believe has a *m/e* = 91 ? Explain. The mass spectrum also contains *m/e* peaks at 78 and 77. Explain.

Answer. The *m/e* = 106 is the molecular ion peak, which is the molecular weight of ethylbenzene. The *m/e* = 91 peak is due to the benzyl, $C_6H_5–CH_2^+$, carbonium ion (very stable to resonance). *m/e* = 78 is due to benzene, C_6H_6; and *m/e* = 77 is due to the phenyl ion, $C_6H_5^+$.

30. Write notes on :

(*a*) UV spectroscopy (*Karnataka BSc, 1994*)
(*b*) IR spectroscopy (*Panjab BSc, 1993; Madras BSc, 1994*)
(*c*) NMR spectroscopy (*Kerala BSc II, 1992; Baroda BSc, 1993; Delhi BSc Hons, 1994*)
(*d*) Mass spectroscopy (*Poona BSc III, 1994*)

31. Of the two compounds, ethylene and butadiene, which absorbs at longer wavelength in UV spectroscopy. (*Delhi BSc Hons, 1993*)

Answer. Butadiene ($CH_2=CH–CH=CH_2$) will absorb at longer wavelength because of conjugation.

32. A chemist prepared 1,3,5-hexatriene and 1,5-hexadiene and placed them in separate flasks but forgot to label them. How would you proceed to identify the two compounds by UV spectroscopy ? (*Kerala BSc 1994*)

Answer. 1,3,5-Hexatriene ($CH_2=CHCH=CHCH=CH_2$) will have higher λ_{max} than 1,5-hexadiene ($CH_2=CHCH_2CH_2CH=CH_2$). This is because 1,3,5-hexatriene is conjugated; whereas 1,5-hexadiene is not.

33. How will you distinguish between the following pairs of compounds on the basis of IR spectroscopy :

(*a*) Ethyl alcohol and diethyl ether.

(*b*) Acetic acid and ethyl acetate. (*Andhra BSc III, 1993*)

Answer. (*a*) Ethyl alcohol shows a strong/broad absorption at 3200–3600 cm^{-1} (due to O–H bond) while diethyl ether does not; and (*b*) Acetic acid shows a strong/broad absorption at 2500–3500 cm^{-1} (due to O–H bond) while ethyl acetate does not.

34. Explain the importance of the finger print region in IR spectroscopy. How would you use IR spectroscopy to distinguish between diethyl ether and acetone ? *(Punjab BSc. 1994)*

35. Indicate how can you use IR spectroscopy to distinguish between the following pairs of compounds :

(*a*) $C_6H_5-\overset{\overset{O}{\|}}{C}-NH_2$ *and* $C_6H_5-\overset{\overset{O}{\|}}{C}-NHCH_3$

(*b*) CH_3CH_2OH *and* CH_3-O-CH_3 *(Magadh BSc Hons, 1994)*

36. How IR spectroscopy is used to distinguish between :

(*a*) $R-\overset{\overset{O}{\|}}{C}-NHR$ *and* $R-CH_2-NHR$

(*b*) R–OH *and* $R-NH_2$ *(Baroda BSc, 1994)*

37. Distinguish between the following pairs with the help of IR spectroscopy :

(*a*) Saturated *and* α,β-unsaturated ketones

(*b*) Ketone *and* aldehyde

(*c*) Carboxylic acid *and* ketone *(Kerala BSc, III, 1994)*

38. Explain : (*a*) The NMR spectra is useful in deciding the structures of ethanol and 1,3-dichloropropane, and (*b*) IR spectra is useful in determining the structures of acetophenone and 2,4-dimethylpentane. *(Anna BSc, 1993)*

39. (*a*) What do you understand by shielding and deshielding effect in the NMR spectrum ?

(*b*) Explain why do the protons of CH_3CH_2Br not resonate at the same field strength ?

(*c*) How are the τ (tau) and δ (delta) scales related ?

(Poona BSc, 1994)

40. How many NMR signals do you expect from each of the following compounds. Indicate also the splitting pattern of the various signals.

(*a*) CH_3OCH_3 (*b*) $CH_3OCH_2CH_3$ (*c*) CH_3CH_2OH

(Punjab BSc, 1993)

Answer. (*a*) One signal (singlet); (*b*) Three signals (singlet, quartet, triplet); and (*c*) Two signals (singlet, quartet).

41. How many NMR signals do you expect from each :

(*a*) $CH_3CH_2CH_2Br$ (*b*) $C_6H_5CH_2CH_2CH_3$

(*c*) CH_3OCH_3 (*d*) $H_2C{=}CH-CH_2OH$

(Kerala BSc, 1993)

42. How many different kinds of protons are there in the NMR spectrum of the following compounds :

(*a*) $CH_3CH_2CH_3$ (*b*) CH_3OCH_3

(*c*) $C_6H_5-CH_2CH_3$ (*d*) $CH_3-\overset{\overset{O}{\|}}{C}-CH_2CH_3$

(Delhi BSc Hons, 1994)

43. The NMR spectrum of a compound C_4H_9Br consists of a single sharp line. What is the structure of the compound? *(Poona BSc, 1994)*

Answer. The compound is *tert*-Butyl bromide, $(CH_3)_3CBr$.

44. Give a structure consistent with the following NMR data :

Molecular Formula = $C_3H_5Cl_3$

(*a*) Singlet at δ 2.20, 3H (*b*) Singlet at δ 4.02, 2H

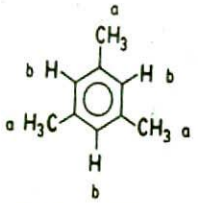
Answer. $CH_2Cl-CCl_2-CH_3$

45. Suggest a structure consistent with the following NMR data :

Molecular Formula = C_9H_{12}

(*a*) Singlet at δ 6.78, 3H (*b*) Singlet at δ 2.25, 9H

Answer. The compound is :



MESITYLENE

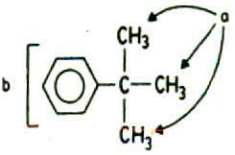
46. Give the structure consistent with following NMR data :

Molecular Formula = $C_{10}H_{14}$

(*a*) Singlet δ 1.30, 9H

(*b*) Singlet δ 7.28, 5H *(Kerala BSc III, 1991)*

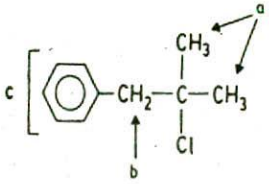
Answer. The compopund is :



t-BUTYLBENZENE

47. Give the structure consistent with the following NMR data :
Molecular Formula = $C_{10}H_{13}Cl$
(*a*) Singlet at δ 1.57, 6H (*b*) Singlet at δ 3.07, 2H (*c*) Singlet at δ 7.27, 5H *(Punjab BSc, 1993)*

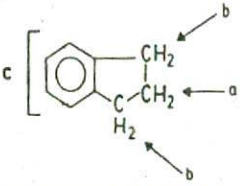
Answer. The compound is :



2-CHLORO-2-METHYL-1-PHENYLPROPANE

48. A hydrocarbon C_9H_{10} gave an NMR spectrum with threee signals :
(*a*) Quintet δ 2.04, 2H (*b*) Triplet δ 2.91, 4H (*c*) Singlet δ 7.17, 4H *(Poona BSc, 1994)*

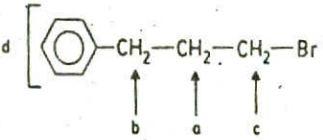
Answer. The hydrocarbon is :



INDANE

49. Suggest a suitable structure consistent with the following NMR data :
Molecular Formula = $C_9H_{11}Br$
(*a*) δ 2.15 (2H, Quintet) (*b*) δ 2.25 (2H, Triplet)
(*c*) δ 3.28 (2H, Triplet) (*d*) δ 7.25 (5H, Singlet) *(Sambalpur BSc Hons, 1993)*

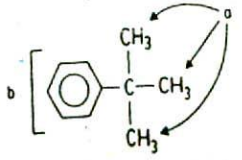
Answer. The compound is:



3-BROMO-1-PHENYLPROPANE

50. Suggest a structure consistent with the following NMR data :
Molecular Formula = $C_{10}H_{14}$
(*a*) Singlet at δ 7.12, 5H (*b*) Doublet at δ 2.45, 2H
(*c*) Multiplet at δ 1.86, 1H (*d*) Doublet at δ 0.86, 6H *(Nehu BSc Hons, 1994)*

Answer. The Compound is :



t-BUTYLBENZENE