PERIYAR INSTITUTE OF DISTANCE EDUCATION
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SALEM – 636 011

B.Sc. CHEMISTRYs
THIRD YEAR
PAPER – V : ORGANIC CHEMISTRY

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B.Sc. CHEMISTRY

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PAPER – V : ORGANIC CHEMISTRY

UNIT I : STEREOISOMERISM

1.1 Definition-Classification into Optical and Geometrical isomerism.

1.2 Optical isomerism-Optical activity-Optical and Specific rotations-conditions for optical activity-asymmetric centre-chirality achiral molecules-meaning of (+) and (-) and D and L notations-Elements of symmetry.

1.3 Projection formulae-Fischer, Flying Wedge, Sawhorse and Newmann projection formulae-Notation of optical-isomers-Cahn-Ingold-Prelog rules-R-S notations for optical isomers with one and two asymmetric carbon atoms-erythro and threo representations.

1.4 Racemisation-methods of racemisation (by substitution and tautomerism) - Resolution methods of resolution (mechanical, seeding, biochemical and conversion to diastereoisomers)-Asymmetric synthesis (partial and absolute synthesis) Walden inversion.

1.5 Optical activity of allenes,spiranes and biphenyls. Geometrical isomerism-cis-trans, syn-anti and E-Z notations-geometrical isomerism in maleic and fumaric acids and unsymmetrical ketoximes-methods of distinguishing geometrical isomers using melting point, dipole moment, dehydration,cyclisation and heat of hydrogenation.

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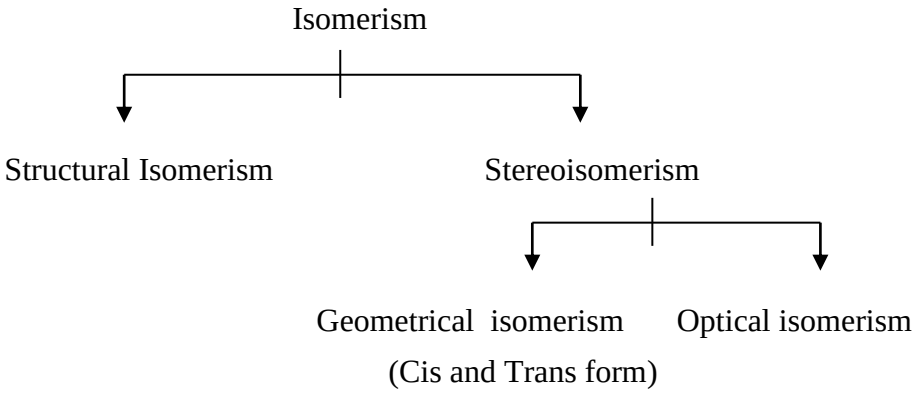
UNIT – I

1.1 STEREOISOMERISM

The molecular formula of a compound indicates the name and the number of elements present in the compound. The compounds having same molecular formula but different physical characteristics or chemical properties are known as isomers and the phenomenon is known as isomerism. Various organic compounds represented by the same molecular formula are called isomers. Obviously, this difference in properties must be due to some difference is the arrangement of atoms within the molecules of the isomers.



Depending upon the type of this difference in arrangement of atoms, there can be two types of isomerism.

i. Structural isomerism ii. Stereoisomerism

Structural isomerism:

This type of isomerism arises from the difference in the arrangement of atoms within the molecule resulting is two or more different structural formula and the isomers are known as structural isomers. Thus, the structural isomers have same molecular formula but different structures. This is further classified into the following different types.

1. Chain isomerism,
2. Position isomerism,
3. Functional isomerism,
4. Metamerism,
5. Tauto merism.

Stereoisomerism

The phenomenon exhibited by two or more compounds with the same molecular formulae, but different spatial arrangement of atoms or groups is termed stereoisomerism.

It is of two types:

1. Optical isomerism, 2. Geometrical isomerism.

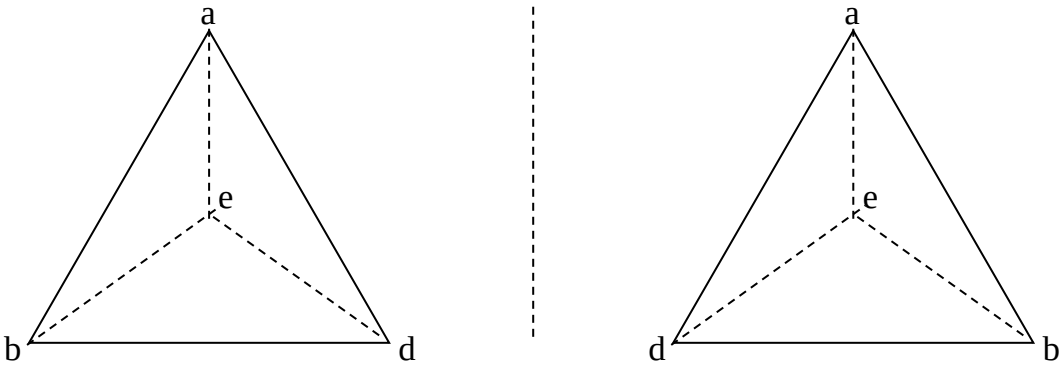
Optical isomerism:

The optical isomers have same chemical and physical properties except that they show a pronounced difference is their behaviour towards the plane polarized light. Due to the difference in the spatial arrangement of atoms or groups, optical isomers have object mirror image relationship and one cannot be superimposed on the other.

The optical activity of substance in solutions or in liquid state depends upon the asymmetry of the molecules.

A carbon atom is supposed to be situated at the centre of an imaginary regular tetrahedran and its four valences are directed towards its four corners. Now if four different atoms or groups are attached to a carbon atom, the molecule becomes asymmetric. Hence, it a substance has at least one asymmetric carbon atom, it will be optically active.

Let there be a carbon atom having four different atoms or groups a, b, d and e attached to its valencies at the four corners of the regular tetrahedron. Obviously two arrangements are possible which will be related to one another as an object to its mirror image. They will not be superimposable upon each other.



The above arrangements correspond to the two isomers rotating the plane polarized light is the opposite directions. Therefore only that molecule which has an asymmetric carbon atom or chiral centre will posses optical activity and will erist is two forms i.e. dextro (d or +) and laevo (l or-). This

isometric pair is known as enantiomeric pairs and the isomers as enantiomers. Few optically active compounds with the chiral centre are given below:

*

1. Lactic acid → CH_3CH (OH) COOH

*

2. glyceroldehyde → CH_2OH CH (OH) CHO

*

3. Phenylmethyldeuteromethane→ CH_3 CHD C_6H_5

*

4. α-phenylethylchloride → CH_3CHCl C_6H_5

*

5. Deutero ethanol → CH_3 CHD COH

*

6. malic acid → HOOC – CH (OH)CH_2 COOH

*

7. α-alanine → $CH_3CH(NH_2)$ COOH

*

8. α-butanol → CH_3CH_2 CH(OH) COOH

*

9. mandelic acid→ CH_6H_5 CH(OH) COOH

* *

10. Tartaric acid → HOOC CH (OH) – CH (OH) COOH

The enantiomers rotate the plane polarized light to the same extent but is opposite direction.

Before going into the details of optical isomerism, it is necessary to discuss briefly on symmetry elements.

Elements of symmetry:-

It has been found that is order to exhibit optical activity, a compound must be chiral. A chiral molecule may be defined as one that is not superimposable on its mirror reflection. However the presence of asymmetric carbon atoms or chiral may not make a compound necessarily optically active. What is essential in the asymmetry of the molecule as a whole. In order to examine the presence or absence of symmetry elements in a molecule, it becomes important to know them.

Symmetry elements are the following:

1. Place of symmetry,
2. Centre of symmetry,

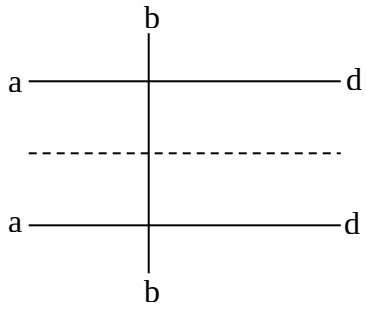
3. Rotation reflection symmetry or alternating axis of symmetry.

The molecules, which possess any one of these symmetry elements, are known as symmetric and they can superimpose and they cannot rotate the plane polarized light i.e. they cannot to optical isomers.

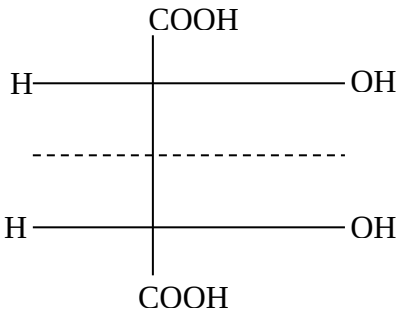
Plane of symmetry:

It is denoted by σ. A plane of symmetry is an imaginary plane which cuts the molecule into two parts, so that pair is the mirror image of the order.

The molecules possessing such a plane are always inactive and are said to be inactive due to internal compensation e.g.meso-tartaric acid.

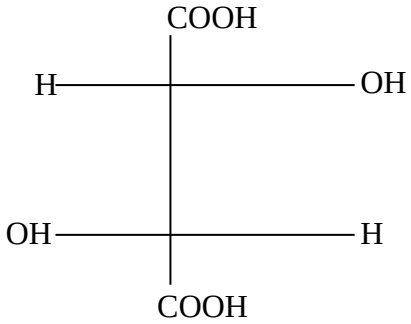


Meso form

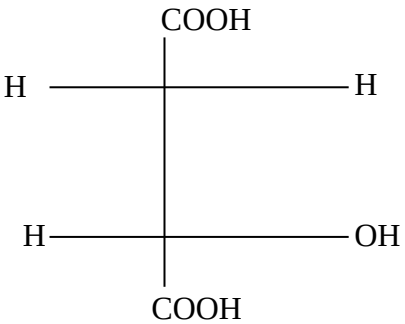


Meso tartaric acid

But the d and 1-forms of these compounds will not have plane of symmetry and they will be optically active.



d- tartaric acids



l- tartaric acids

Centre of symmetry or Inversion centre

It is designated by i A cetnre of symmetry is an imaginary point in the molecule such that, if a line is drawn from any group of the molecule to this

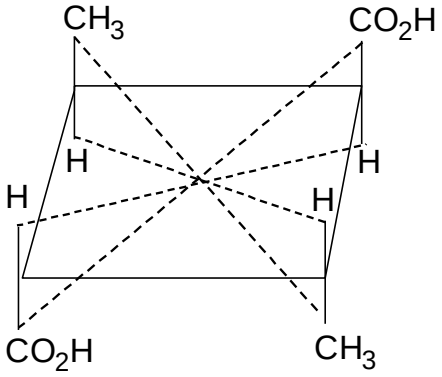
point and then extended to an equal distance beyond the point it meets the mirror image of the original group.

Examples:

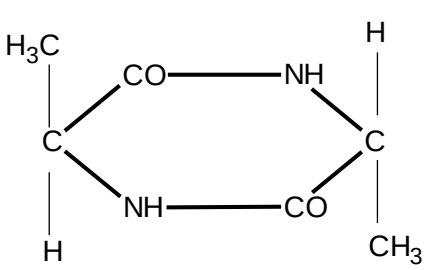
1. Trans-cyclobutance – 1, 3 – dicarboxylic acid.
2. Staggered form of ethane

Centre of symmetry is prevalent in cyclic compounds as given below.

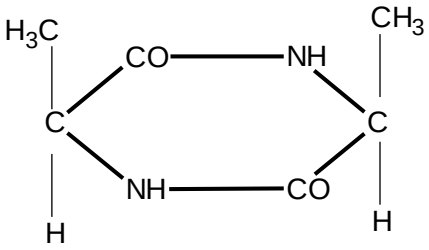
(1) 2.4 dimethylcyclobutane – 1,3 dicarboxylic acid.



(2) Dimethyl diketopiperazine:



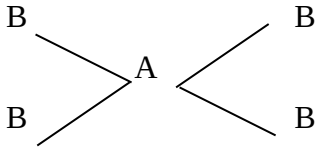
Trans



cis

Please note that trans compound has the centre of symmetry and cis compound does not have the centre of symmetry and is optically active.

One can expect centre of symmetry in a ring compound having even number of atoms that constitute the skeleton of the ring. Since inversion centre is a point, only one atom or no atom must be present at the centre. In the above examples, no atom lies at the centre and all other atoms occur in pairs. When the centre is occupied by an atom, which is unique, the order atoms must occur is pairs as follows:

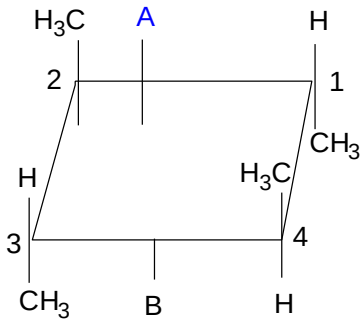


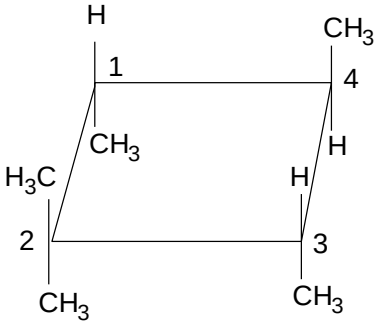
Alternating axis of symmetry or Rotation reflection axis (S_n):

A species is said to possess an improper rotation axis of order n if rotation of the species about the axis by $\frac{2\pi}{n}$ or $\frac{360°}{n}$ following by reflection through a plane perpendicular to this axis produces a structure indistinguishable from the original.

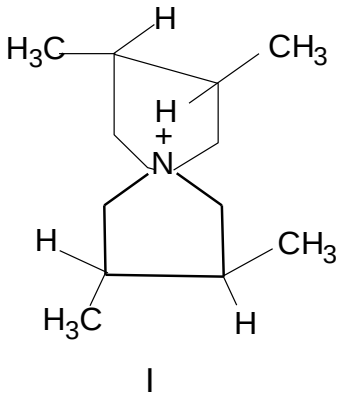
The improper rotation is denoted by the symbol Sn. Only a few compounds are optically inactive due to this elements of symmetry.

e.g: (1) 1,2,3,4 – tetra methylcyclobutane.





(2) Spiro compounds:



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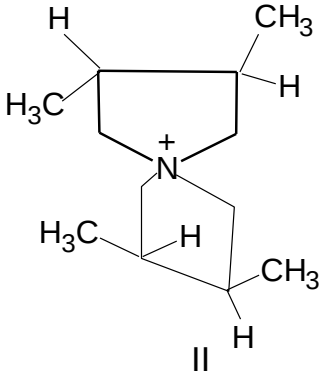
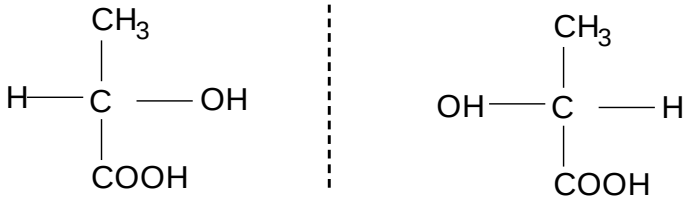


II

1.2 OPTICAL ISOMERISM IN LACTIC ACID:

The molecular formula of lactic acid is $C_3H_6O_3$ and the structural formula is $CH_3CH(OH)\ COOH$.

It contains one asymmetric carbon (C) atom. Hence, it will exist in $2' = 2^1 = 2$ forms which are shown in the figure.



dextro leavo

These two molecules are not superimposable and are related to each other like an object and its mirror image. One is called dextro, D or (+) lactic acid and other is laevo, l(or) (-) lactic acid.

The specific rotation of dextro acid is $+2.2^{o}$ and that of laevo latic acid is -2.2^{o}. Both these acids have the same physical properties like,

1. Melting point, 299k
2. relative density 1.24
3. specific rotation, 2.2^{o}.

But they rotate the plane polarized light in opposite direction. Both the compounds undergo chemical reactions with same rate.

Compounds which are mirror images of each other and are not superimposable are termed enantiomers [Enantio-oopposite: Meros – Part) and the phenomenon is described as enantiomerism. Enantiomers resemble each other in physical and chemical properties except that they rotate the plane polarized light in opposite direction.

Dextro-rotatory lactic acid may be obtained from meat extract and is also known as sarcolactic acid.

Laevo-rotatory lactic acid maybe otained by the fermentation of sucrose by Bacillus.

Acidic Laevolactic

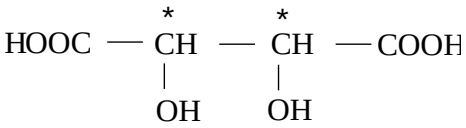
A third optically inactive variety emerges when the dextro and the laevo varieties are present in equal quantities. It is called racemic mixture or dl ± lactic acid. Ordinary lactic acid present in sour milk or manufactured by fermentation or synthetic methods is racemic mixture and therefore, in active.

The properties of a racemic modification in the liquid state are the same as that of the pure enantiomers because the mixture is essentially an ideal mixture. However, in the solid state the properties of a racemic mixture may be different from that of the enantiomers depending upon the relative affinity of the molecules of one enantiomer for that of the or there or for its own molecules. The physical properties of racemic mixture is different from that of

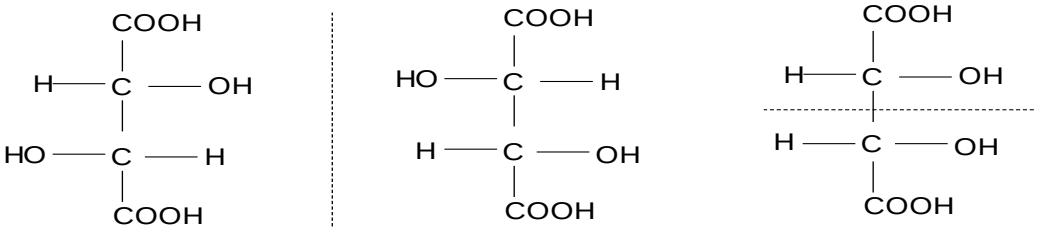
the enantiomers. By adopting suitable methods, it is possible to separate the dextro compound and leavo compound from the racemic mixture and the technique is called resolution. Racemeic mixture undergoes chemical reactions with the same rate as that of the enantiomers.

Optical isomerism in tartaric acid:

The molecular formula of tartic acid is $C_4H_6O_6$. The structural formula is.



It has two asymmetric carbon atoms (C) and these carbon atoms are joined by four similar atoms or groups (-H, OH, -COOH & -CHOH COOH). This type of compounds can exist in three forms as given below:



dextro leavo meso

Dextro (+) or (d -) tartaric acid:

It rotates the plane of polarization of light to the right. The rotation due to the upper half is strengthened by one due to the lower half. It has no plane of symmetry. Acid obtained from natural sources, e.g. tamarind or graps is of dextro- variety.

Laevo (- or l-) tartaric acid:

It is the mirror image of the above and rotates the plane of polarization of light to the left. This also has no plane of symmetry. It does not occur in nature and is prepared by resolving the racemic acid.

Meso - tartartic acid:

It has one dextro rotatory carbon atom and one laevo rotatory carbon atom. It has a plane of symmetry as shown in the figure. It is denoted as i-tortaric acid. Though the molecule contains two asymmetric carbon atoms. It is optically inactive. This is because the rotation if upper half is compensated by the rotation due to the lower half. It cannot be resolved into active constitutents. It is therefore, inactive by internal compensation. The physical and chemical

properties of meso tartaric acid are different from those of d(+) & l (-) tartaric acids. It does not occur in nature. It is however, obtained along with racemic mixture by different methods.

Racemic tartaric acid:

It is a 50-50 mixture of d- and l- tartaric acids. Hence, it is optically inactive. It can however, be resolved into the active, constituents namely dextro-and laevo varieties. It is therefore inactive by external compensation.

Synthetic acid is always inactive being either racemic or a mixture of racemic and the meso-varieties. Racemic tartaric acid does not occur in native.

Table

Physical properties of various tartaric acids

S.No	Name	Specific rotation	Density	Solubility at 293K	Melting Point	Crystal form
1.	Dextro	+12	1.76	139	443IK	Prisms
2.	Laevo	-12	1.76	139	44K	Prisms
3.	Meso	0^o	1.69	125	413K	Prisms
4.	Racemic	0^o	1.66	206	479K	Rhombic

Comparison of racemic tartaric acid with meso-tartaric acid:

S.No	Property	Racemic form	Meso form
1.	Symbol	dl or ±1	I
2.	Specific rotation	0^o	0^o
3.	Reason for in-activeness	External compensation	Internal compensation
4.	Plane of symmetry	Absent	Present
5.	Nature	50-50 mixture of d and l-forms	Single compound
6.	Resolution	Possible	Not possible.

Diastereo – isomers:

Tartartic acid exists in four forms as 1. dextro, 2. laevo, 3.meso, 4.racemic. Among the, dextro and laevo-tartaric acids are optically active and

they are enantiomers. Meso-tartaric acid is the dia-stereo-isomer of either dextro or laevo – tartaric acid. Thus, diastereo – isomers are two stereoisomers that are not mirror images of each other.

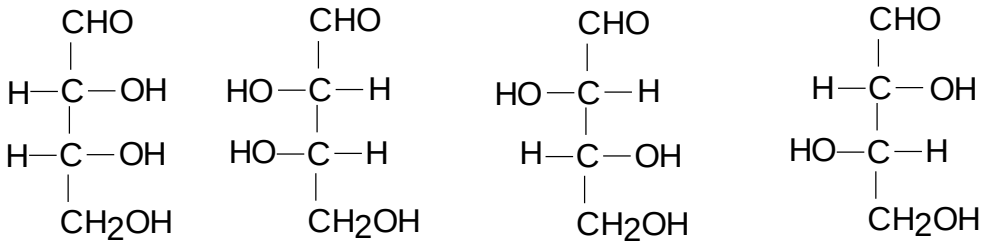
Diastereo-isomers differ from optically active (d- & l-) forms in specific rotation, physical properties & chemical reaction rates.

1.3 ERYTHIO AND THREO REPRESENTATIONS

Special nomenclature for molecules with two chiral carbon atoms has been employed. This nomenclature is derived from the names of the four Carbon Sugars (tetrose) erythrose and threose.

When an acylic molecule has in non-identical centres of chirality, it exists as 2^n steroisemers which are enantiomeric in pairs. Moreover, such a molecular exists as 2^{n-1} diastereomeric pairs of enantiomers. However, restrictions of molecular symmetry or geometry may prevent the existence of some of these eg. Meso compounds. In the case of a molecule with two chiral centres, there can be four such arrangements. This classic example is the four carbon sugars – the tetroses which have two chival carbon atoms and are shown in the following figure as Fischer projections.

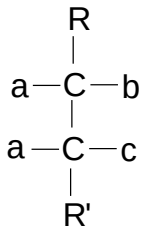
Inspection of these structures reveals that 1 and 2 are minor images of each other and are thus the optical isomers of a single substance and similar is the case with 3 and 4. A comparison of either of the threoses with either of the erythroses shows that although they are stereoisomers, they are not minor images. Such stereoisomers, which are not mirror images of each other, are termed diastereo isomers. When one considers two stereoisomers which are diastereo isomers these have one chiral centre with opposed configuration and one with an identical configuration and as a result, these cannot be mirror images.



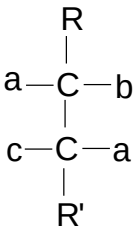
(-) Erythrose (+) Erythrose (-) Threose (+) Threose

1 2 3 4

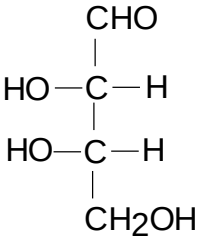
In all systems of the type R-Cab-Cac-R, when the two like groups in the projection formula are on the same side, the isomer is named erythroform (5) and if these are on the opposite sides (6), the isomer is called the threoform.



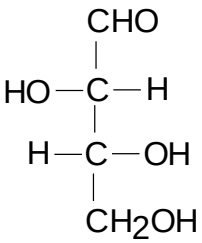
Erythro (5)



Threo (6)



(+) Erythrose



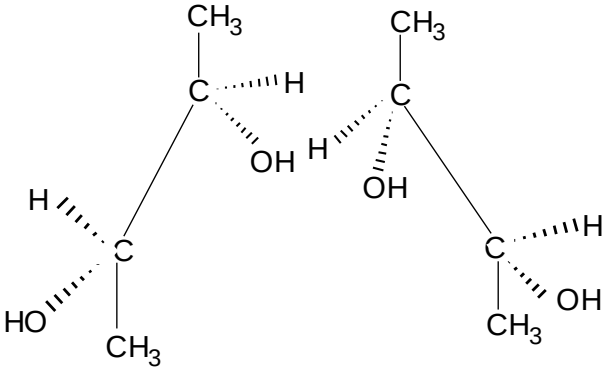
(-) Threose

The use of terms erythro and threo is a shorthand way of naming diastereoisomers with two adjacent stereocentres with configurations. Similar to erythrose and threose in a Fisher projection formulae. The erythro form is often described as “meso like” because its Orientation, there would be a plane of symmetry if the two dissimilar groups were equivalent.

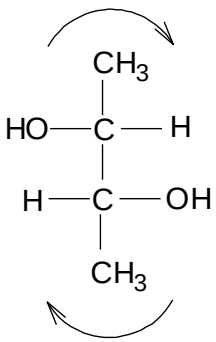
A use of the prefixes erythro and threo is done to name dissymmetric molecules, where the ends are different. The erythro diastereoisomer is one with similar groups on the same side of the Fischer projections, while the threo diastereoisomers has similar groups. On opposite sides of the Fischer projections. The use of terms meso and (±) are preferred when the molecules are symmetric.

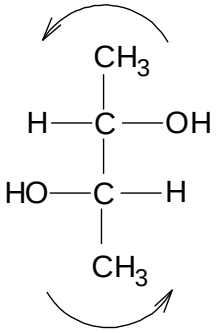
Projection of 2, 3 butanediol:

Sawhorse models: I



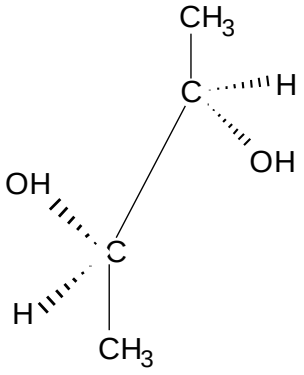
Fischer's projections I and II

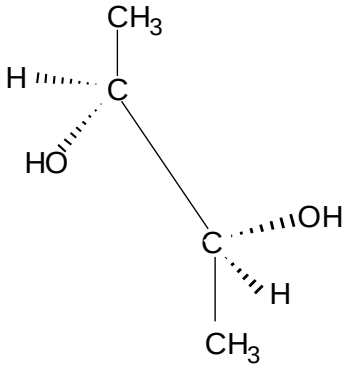




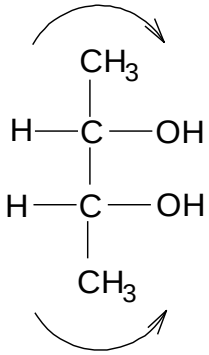
(+) 2, 3 butanediol (-) 2,3 butanediol

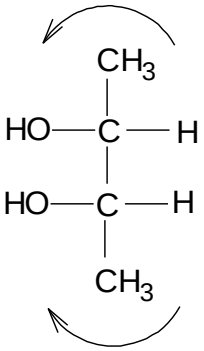
Sawhorse models III and IV





Sawhorse models III and IV



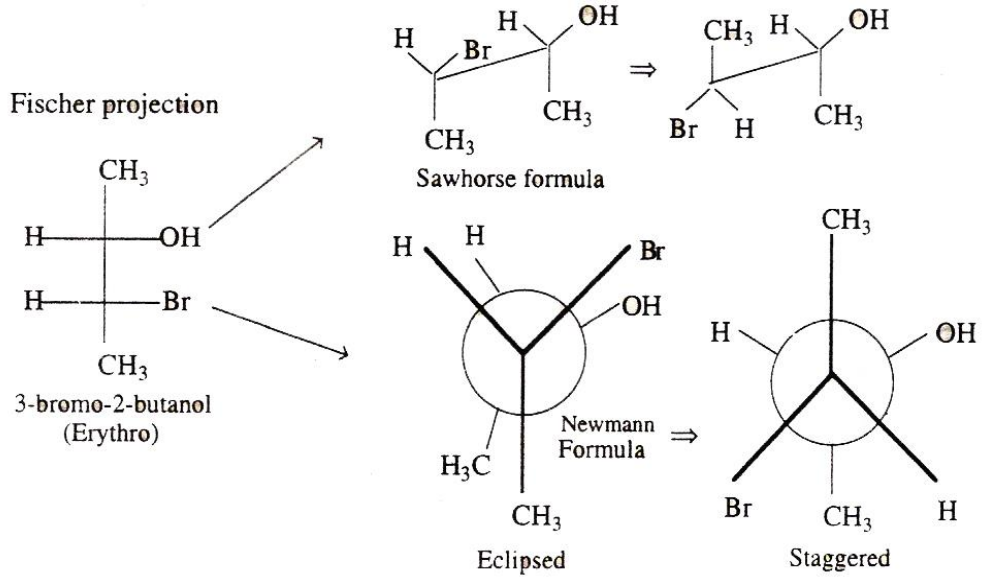


Structures I and II are enantiomers

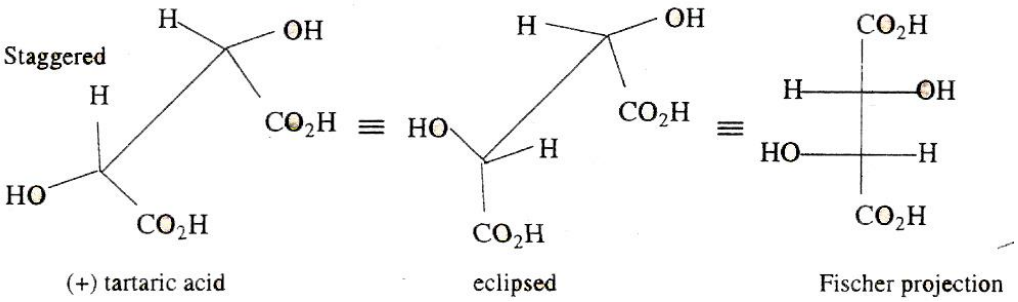
Structures III and IV are the meso-forms

While dealing with stereochemical problems it is necessary that one is able to translate one set of representation into other. A shift from the Fischer projection formula to either Sawhorse or Newmann projection formula is particularly necessary. In one of the ways a Fischer projection is drawn, its

rotation gives the staggered form and from it Sawhorse or Newmann projection is drawn. Another way which does not require the use of models is to translate the Fischer projection into eclipsed Sawhorse or Newmann projection which is then rotated through 180° around C-2 and C-3 bond to provide the actual Sawhorse or Newmann representation as shown in the example given below of erythro-3-bromo-2-butanol.



The Interconversion of Fischer projection (i.e., the all eclipsed conformation) of (+) tartaric acid to Sawhorse representation can be done in the following way,



1.4 RACEMISATION:

The process of producing a racemic modification starting with one of the pur enantiomers is termed racemisation.

For racemisation 1.heat, 2. light, 3. acid & 4. base are used. Depending on the nature of the reactants one or more of these are used.

1. Thermal racemisation:

This is carried out by applying heat.

e.g: o-substituted biphenyls, amyl alcohol.

2. Treating with reagents:

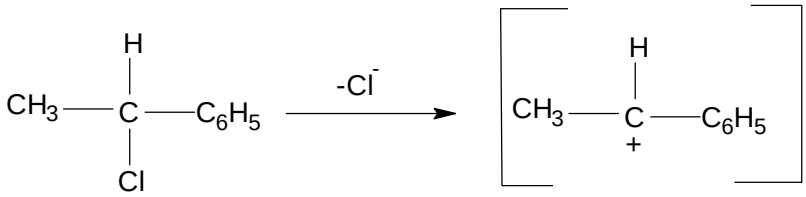
When the enantiomers are treated with suitable reagents, racemisation occurs, for example.

a. When laevo – lactic acid is treated with dilute sodium hydroxide, racemic – lactic acid is obtained. Mandelic acid also behaves in the same way.

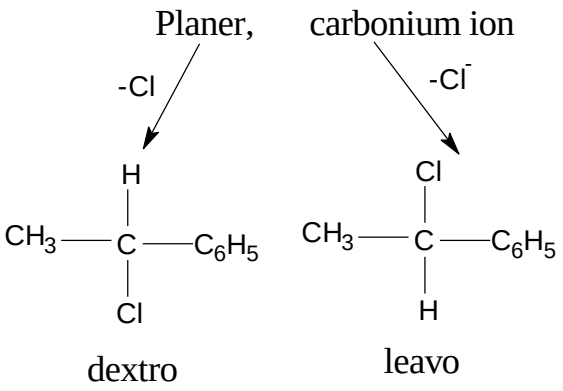
b. When (x) mandelic acid is reacted with hydrobromic acid, racemic mandelic acid is formed.

3. Substitution reaction

The SN^1 reactions taking place in step wise in the compounds and the changes in the configuration produce racemic modification. For example racemic form of α-chloro ethylbenzene using the following substitution reactions.



dextro



dextro leavo

Explanation:

A carbonium ion is generated by with drawing Cl ion form the asymmetric carbon atom. Being a Lewis base, an anion can be withdrawn, temporarily by Lewis acid like $SbCl_5$, $AlCl_3$, BF_3, SO_2, $HgCl_2$ etc.

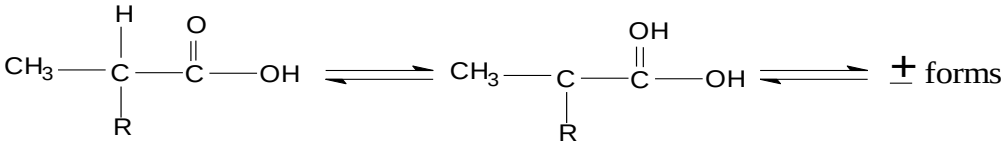
The SP^2 hybridised carbonium ion so formed has a planner structure and the anion then attacks the carbonium ion from either side which gives rise to the racemised product.

Auto – racemisation:

In some cases, racemisation occurs spontaneously at room temperature. For example, dimethyl bromosuccinate racemises on standing at room temperature. This type of racemisation is termed auto-racemisation.

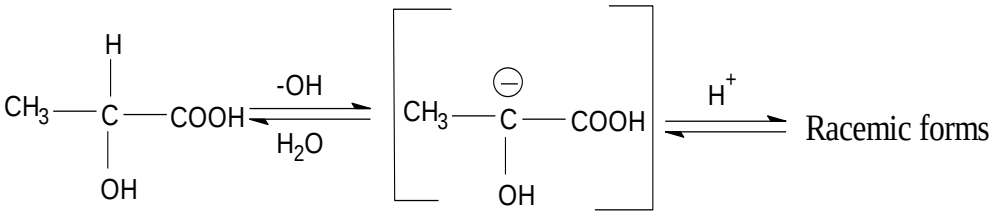
Mechanism of racemisation

One important set of compounds which readily racemise are those in which the chiral atom is jointed to a hydrogen atom and a negative group. This readily undergoes tautomeric change and racemisation occurs via enolisation. For example,



laevo acid Enol forms

When the intermediate enol form which is not chiral, reverts to the stable form, there are equal changes to produce the dextro and laevo forms. Hence, it gives a racemic mixture. For example laevo latic acid is converted into racemic lactic acid using a base as catalyst as follows:



laevo plamar

intermediate

In case of some other compounds which cannot undergo tautomeric change, e.g. limonene, this mechanism of racemisation is uncertain.

Resolution:

Whenever an optically active compounds is synthesized in the laboratory, the dextro and the laevo-varieties are obtained in equal amounts and a racemic mixture results. The two components called enantiomorphs can, however be obtained from the racemic mixture.

The separation of a racemic mixture into its enantiomorphs (d & l-forms) is termed resolution.

Due to identical properties of the optical isomers, their separation cannot be effected by simple methods like fractional crystallization or fractional distillation. Following methods have been used for resolving racemic compound.

1. Mechanical Separation

When the enantiomers (d & l) or their salts form well defined crystals showing hemihedral faces, they can be separated by simple hand picking. Pasteur in 1848 separated in this manner the crystals of sodium ammonium racemate. This method though simple in principle, always offers some experimental difficulties resulting in its limited application. It is therefore manily of historical interest at present.

2. Bio-chemical separation

This was introduced by Pasteur in 1858. This method is based on the fact that certain lower organisms such as moulds bacteria or fungi when allowed to grow in a solution of the racemic compounds, destroy one of the optical isomers at a much quicker rate than the other due to selective assimilation.

For example, when Penicillium Glaucum is allowed to grow in a solution of ammonium racemate, it destroys the (+) tartrate by assimilation leaving behind the (-) tartrate practically unaffected.

Though slow, method is of wide, application, since biological processes are highly specific, the method leads to a high extent of resolution.

Demerits of the method:

a. It is difficult to find the proper organism.

b. One gets one of the enantiomers at the expense of the other.

c. Dilute solutions must be used. If otherwise organisms may be and hence small amount of resolved product is obtained.

d. The separation, however is not always complete.

e. Some other side-products may also be formed and the sample maybe difficult to purify.

f. It the racemic mixture is poisonous, then suitable organisms maynot be available.

3. Selective adsorption method

Optically active substance, may be selectively adsorbed by certain optically active adsorbents. For example,

a. Henderson and Rule in 1939 separated the active constituents of racemic camphor using dextrolactose as an adsorbent.

b. Bradley et at in 1951 separated the dextro mandelic acid from the racemic mixture using wool and casein as adsorbent.

4. Chromatographic separation

Enantiomers react with an optically active reagent at different rates and produce diastereoisomers of different stabilities. This property is utilized in chromatographic separation of enantiomers.

The process consists in allowing a solution of the racemic form in a chosedn solvent to pass slowly down an optically active adsorbent like starch. Then the enantiomers are adsorbed by the active adsorbent at different rates of form diastexoisomers of different stabiloities. Now the column is eluted (washed) with the solvent.

The enantiomer forming loss stable dia-stereoisomer comes down the coloumn faster then the other ant the elution is collected in a separate versel. In this way separation of enantiomers may be possible. Racemic mandelic acid is resolved almost completely using starch as an adsorbent paper chromatrography can also be used for this purpose. Here cellulose acts as an optically active adsorbent.

5. Salt formation method

This was discovered by Pasteur in 1858. This method is the best of all methods of reduction. It consists in conversion of the active constituents of a racemic mixture into diastereoisomers (salt) with another optically active base or acid.

Racemic mixture Diastereo isomers

The two salts thus obtained often differ in their solubilities & can be separated by fractional crystallization. The salts can be hydrolysed with inorganic acids or alkalis to get the original active compounds.

For example, salts of racemic acid ± tartaric acid with + cinchonine are (+) – cinchonine (+) tartrate and (+) cinchonine (-) tartrate. On crystallization from a saturated solution, the latter being less soluble crystallizes out foist,

Dextro and laevo varieties of tartaric acid can be prepared by hydrolysis of these salts.

Bases used for the purpose are mainly alkaloids, e.g.quinine, brucine, cinchonine and morphine.

Asymmetric synthesis:

The production of an optically active compound from a symmetric molecule without resource of resolution is termed asymmetric synthesis.

This may be classified under two heads/

1. Partial asymmetric synthesis.
2. Absolute asymmetric synthesis.

Partial asymmetric synthesis:

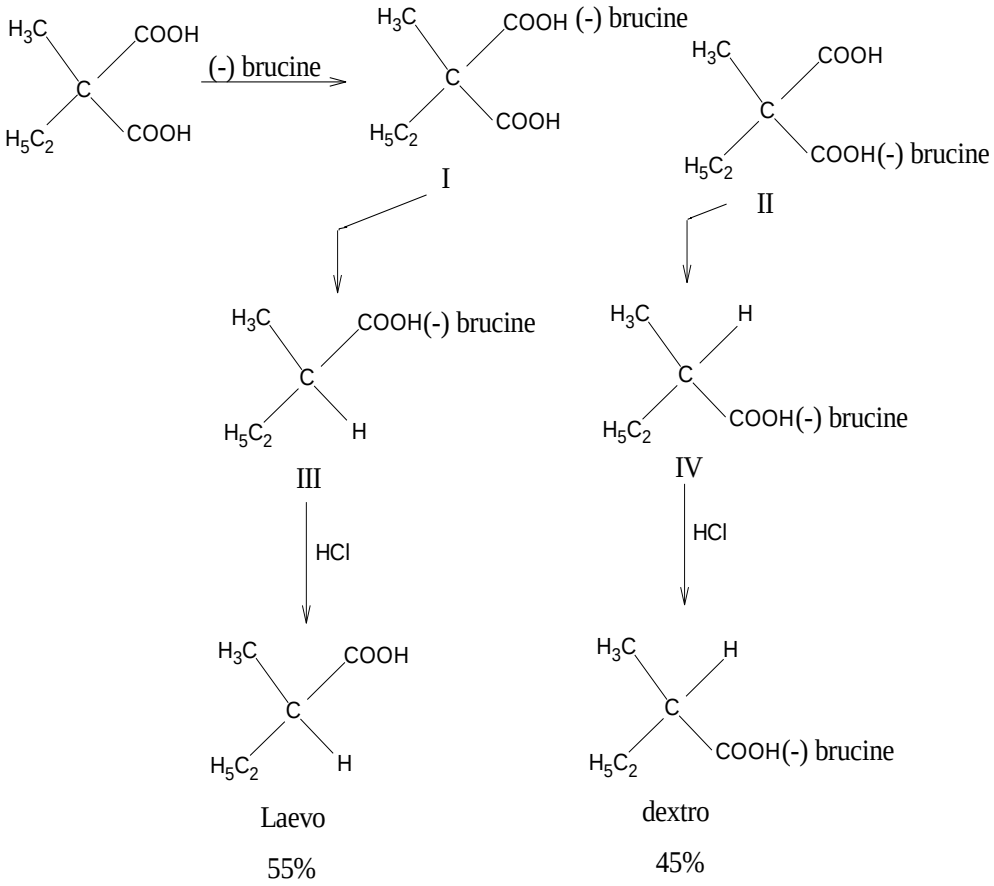
This is a process in which two stereoisomers of opposite configurations are formed under asymmetric condition in unequal amounts and this an optically active product is obtained without recourse to resolution.

1. The first asymmetric synthesis was that of leavo - isovaleric acid carried out by Marckwald in 1904 by heating the half brucine salt of ethylmethyl-malonic acid at 440K. (Reaction -I)

The laevo – variety was in excess to the extant of about 10%.

2. Mackenzie in 1905 reduced pyruvic esters in which alcohol was optically active (eg.1-menthol, 1-amy1 alcohol). The lactic ester produced gave on hydrolysis slightly excess l-lactic acid (Reaction – II)

Reaction : I



Reaction: II

$$CH_3\ CO\ COOR + 2[H] \longrightarrow CH_3\ CHOH\ COOR$$

Lactic ester

$\downarrow H_2O$

l - Lactic acid $CH_3\ CHOH\ COOH$

With enzymes:

(-) mandelic acid has also been synthesized by treating benzaldehyde with hydro cyanic acid in the presence of the enzyme emulsin with subsequent hydrolysis.

C_6H_5 CHO + 4CN ⟶ C_6H_5 CH (OH) CN $\xrightarrow{H_2O}$

Mandelonitrile

C_6H_5 CH (OH) COOH

Mandelic acid

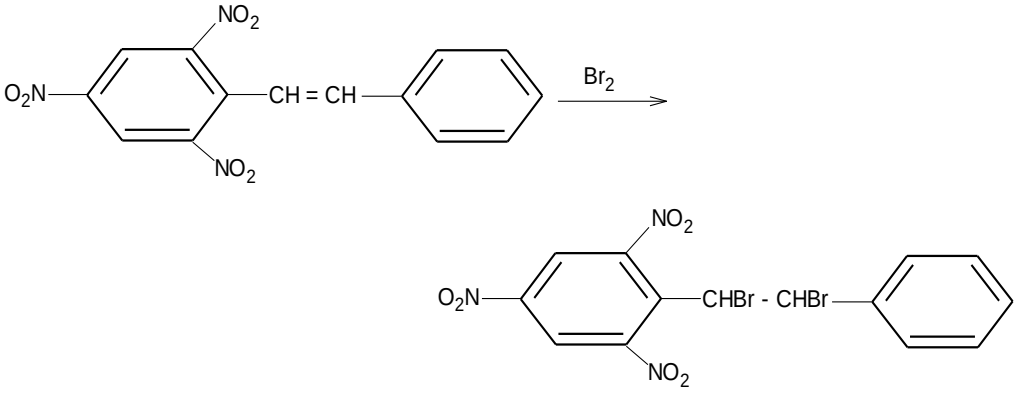
The laevo rotatory acid is obtained is large excess.

2. Absolute asymmetric synthesis:

A plane polarized light is composed of left circularly polarized light and right circularly polarized light the left circularly polarized light has a plane of polarization rotating continuously in the left direction around the axis of propagation of the wave. The plane of polarisation of the right circularly polarized light rotates continuously in the right direction. It is found that when left or right circularly polarised light is passed through a racemic modification, only one form of the enantiomers is obtained in pure state.

As the process gives rise to a 100% pure enantiomer from an optically inactive form, the asymmetric synthesis is said to be absolute asymmetric synthesis

When bromine is added to 2,4,6 trinitro-stilbene in a beam of right circularly polarized light, a dextro product is obtained.



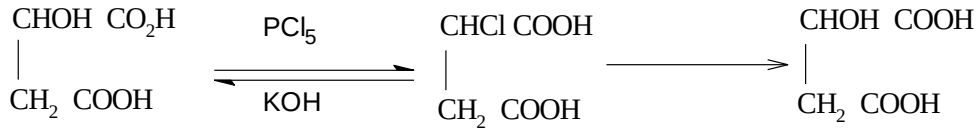
dextro

Walden Inversion:

In a reaction when a group or atom directly attached to an asymmetric carbon is replaced by other group or atom. The configuration of the new compound and usually the sign of rotation also may be opposite to that of the initial compound.

The term Walden inversion or optical inversion is applied to any step of a reaction in which the inversion of configuration occurs.

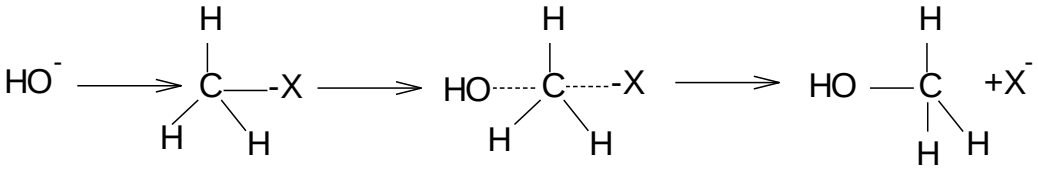
It is important to note that any change in the direction of rotation is purely coincidental and the term Walden inversion refers only to the change is configuration of the molecule. For example, in the conversion of l-malic acid to d-malic acid and vice versa as below:



L-Malic acid D-chlorosuccinic acid L-Malic acid

Here, Pcl5s and KO4 causes inversion and AgOH does not. In some cases the inversion is almost quantitative. Whereas in some cases partial inversion occurs. Factors like nature of the compound Reagent and the solvent etc. Play an important role in the Walden inversion. The mechanism of inversion is perhaps a pimolecular substitution.

SN^2 occurring by the attack of the reagent. From the opposite side of the leaving group resulting in inversion of configuration. The following mechanism has been proposed by Hughes & Ingold.



This can be readily understood by considering the molecule to have the shape of an Unbrella. The inversion of configuration may be compared to the upside down turning of umbrella on a particularly windy day.

1.5. OPTICAL ACTIVITY IN ALLENES, SPIRANS AND BIPHENYL COMPOUNDS:

The presence of a chiral carbon atom in an organic molecule is a sufficient condition for showing optical activity. The chirality ie dissymmetry or asymmetry of a molecule as a whole is the necessary condition for the same.

Meso tartaric acid is optically inactive, through it contains two asymmetric carbon atoms or chiral centres. This is because, it has a plane of symmetry and hence it is optically inactive by internal compensation. The dextro rotation of the plane polarized light made by one chiral carbon is

compensated by the laevo rotation made by the other chiral carbon atom. Thus an optical isomer containing more than one like chiral carbon atoms is found to be optically inactive. During to the presence of symmetry elements (Plane or centre of symmetry).

Now we are going to study some organic molecules which do not have asymmetric carbon atoms. Yet they are optically active because they are dissymmetry as a whole.

Allenens:

The general structural formula of allene is

abC = C = Cde abC = C = Cab

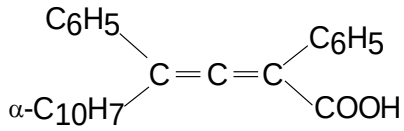
I II

Examination of the spital arrangement of compounds of this type shows that the molecule and its mirron invage or not super imposable. The σ-π way of writing (I) is shown in the figure.

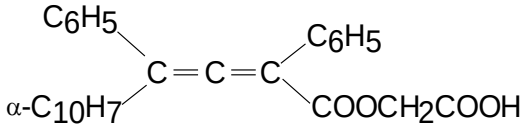
The two end carbon atoms are in a state of trigonal sp^2 hybridisation and the centre carbon atom is in the Sp-hybridised diagonal state. Thus, the centre carbon atom forms two π-bonds which are perpendicular to each other.

The π_x-bond is perpendicular to the plane of the paper and the π_y bond is in the plane of the paper. In the trigonal state, the π bond is perpendicular to the plane containing the 3σ bonds, consequently the groups a and b lie in the plane of the paper and the groups d and e in the plane perpendicular to the plane of the paper. This molecule does not possess a plane or centre of symmetry. This is also true for molecules (II). Thus (I) and (II) will be resolvable.

The first successful resolution of an allene derivative was prepared from 3-α-naphthyl-1,3-diphenyl allene-1- carboxylic acid (III), but failed to resolve it. They were unable to crystalllise the salts with active base and this acid into the glycolic acid ester (IV) and was then able to resolve it by means of brucine.

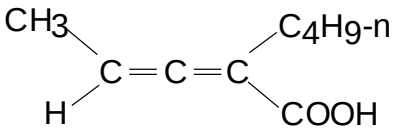


III



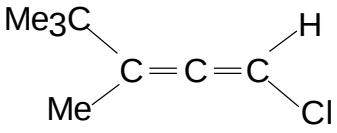
IV

The simpler allenic acid is (V) by means of strychmine.



V

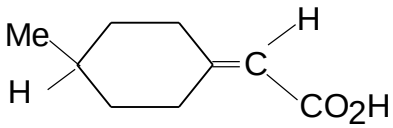
3-methyl-1-n-butylallene-1-carboxylic acid also deduced the absolute configuration of the following VI.



VI

It has been known that if the number of double bonds in the cumulene is odd, the molecule exhibits geometrical isomerism. But if even, then it exhibits optical isomerism. The allenes so far discussed contain two double bonds

Although allenes were not successfully resolved until 1935, compounds with a similar configuration were resolved as early as 1909. In this year, Pope et al resolved 4-methylcyclo hexylidene-1-acetic acid (VII).



In this compound one of the double bonds of allenes has been replaced by a 6 membered ring and the general shape of the allene molecule is retained.

Spirans:

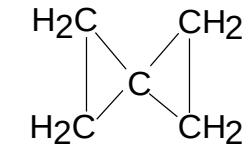
If both double bonds in allene are replaced by ring systems, the resulting molecules are spirans.

One method of naming spirans obtains the root name from the number of carbon atoms in the nucleus. This is then prefixed by the term “Spiro” and followed by numbers placed in square brackets which indicate the number of carbon atoms joined to the “Junction” Carbon atoms. The positions of substituents are indicated by numbers, the numbering beginning with the smaller wing and ending on the junction carbon atom.

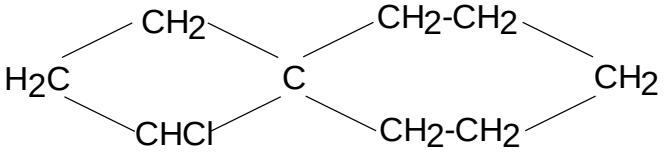
For example,

I is Spiro-(2,2)-pentane

II is 1-chlorospiro-(5,3)-nonane



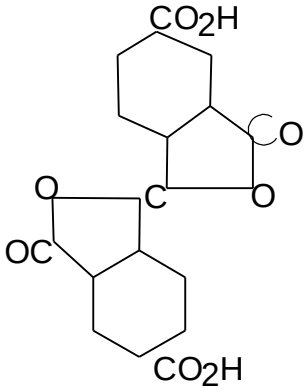
Spiro (2,2) Pentane



1-Chlorospiro (5,3) nonane

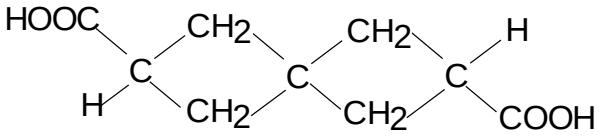
Examination of these formulae shows that the 2 rings are perpendicular to each other and hence suitable substitution will produce molecules with no elements of symmetry, thereby giving rise to optically active forms.

Mills and Nodder (1920,1921) resolved the dilactone of benzophenone 2.2', 4,4'-tetracarboxylic acid (III). In this molecule, the two shaded portions are perpendicular to each other and consequently there are no elements of symmetry.

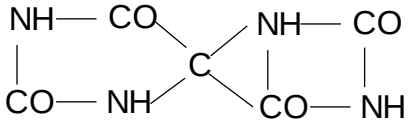


Some other Spiro compounds that have been resolved re the,

(i) Spiroheptane derivatives (IV) (Backeer et al 1928, 1929)

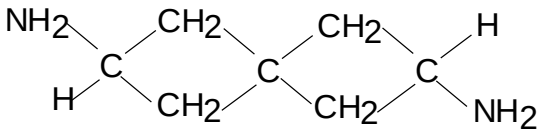


(ii) Spirohydantion (V) (Pope and Whitworth, 1931)



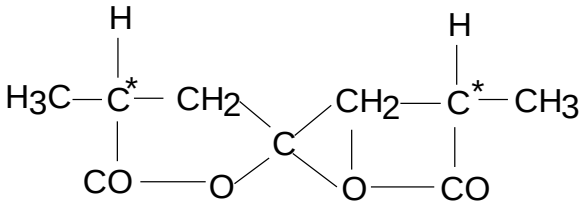
V

(iii) Spiroheptane derivatives (VI) by Jansen and Pope 1932



VI

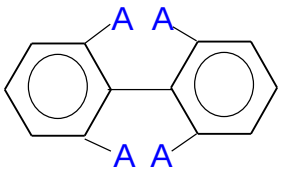
(iv) Sutter et al in 1935 prepared the Spiro compound VII which contains two similar asymmetric carbon atoms (*)



VII

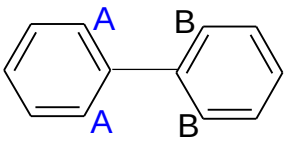
Biphenyl Compounds

The molecular formula of biphenyl is ($C_{12}H_{10}$) and its structural formula is,

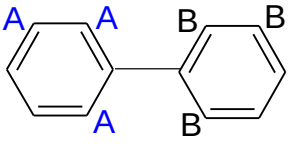


I

The benzene ring is planar, then the biphenyl molecule will consist of two planar rings and are coaxial. The possible four ortho positions are indicated by A. Biphenyl compounds in which at least three of the four ortho positions in biphenyl are occupied by certain groups could be resolved. It was then soon found that two conditions were necessary for biphenyl compounds to exhibit optical activity (I). Neither ring must have a vertical plane of symmetry. Thus (II) is not resolvable but (III) is,

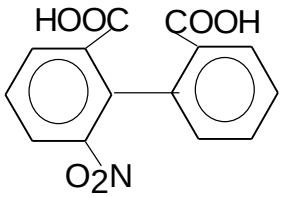


II

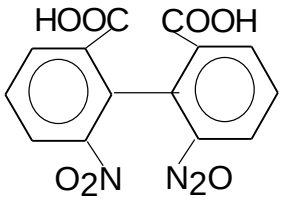


III

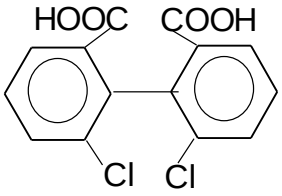
(ii) The substituents in the ortho positions must have a large size. Examples



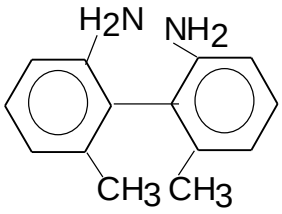
6-nitrodiphenic acid



6,6'-dinitro dipheric acid



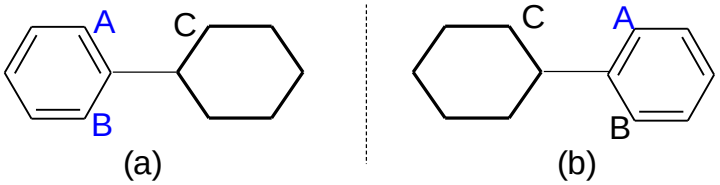
6,6'-dichloro dipheric acid



2,2' - di amino

6,6'-di methyl triphenyl

The earlier work showed that 3 groups have to be present in the ortho positions. This gives rise to the theory that the groups in these positions impinged on one another when free rotation was attempted, i.e. steric effect prevented free rotation.



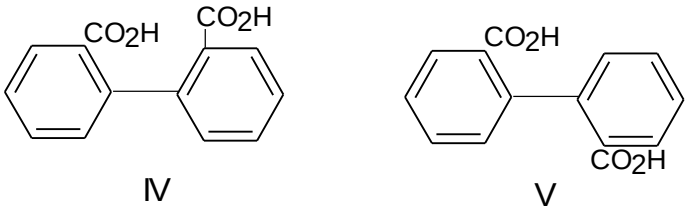
(a) (b)

Consider a molecule (a) and its minor image (b) provided that the groups A,B and C are large enough to interfere mechanically, then free rotation about the single bond restricted.

Thus, the two benzene rings cannot be coplanar and consequently (b) is not superimposable on (a) i.e. (a) and (b) are enantiomers. In molecule (a) there is no chiral centre. It is the molecule as a whole which is chival due to the restricted rotation.

In biphenyl the two benzene rings are co-axial and in optically active biphenyl derivatives the rings are inclined to each other due to the steric and repulsive effects of the groups in the ortho positions. The actual angle of inclination of the two rings depends on the nature of the substituent groups, but it appears to be usually in the vicinity of 90° i.e. the rings tend to the approximately perpendicular to each other. Thus in order to exhibit optical activity the substituent groups in the ortho positions must be large enough to

prevent the two rings from becoming coplanar in which case the molecule would possess a plane or a centre of symmetry. E.g. diphenic acid is not optically active.

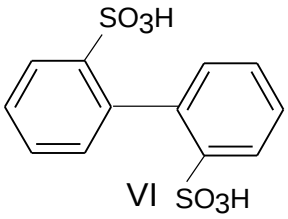


IV V

Diphenic acid

In configuration (IV) the molecule has a plane of symmetry and in configuration (V) a centre of symmetry; of these two, (V) is the more likely because of the repulsion between the two carboxyl groups.

If the substituent groups are large enough then only two in the O and O' positions will produce restricted rotation. Turner et al in 1932 resolved biphenyl-2,2'-disulphonic (VI).

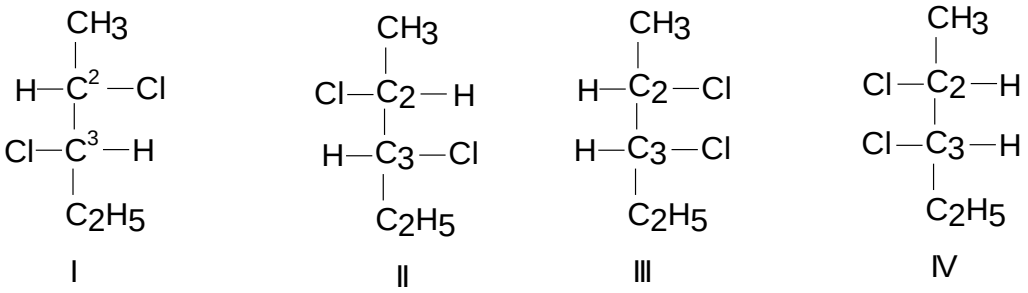


VI

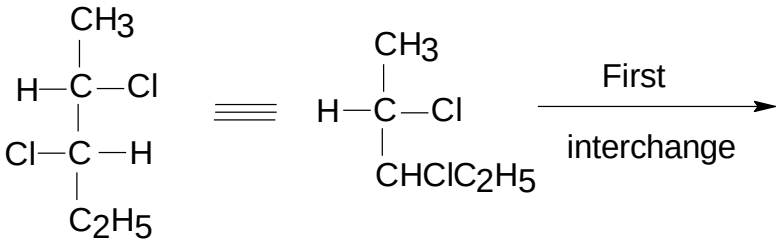
diphenic-2,2-disulphenic acid

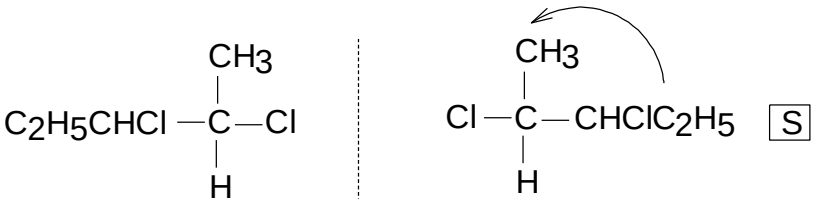
Since one phenyl group can rotate with respect to the other, the various positions would correspond to different conformations. In acyclic compounds, although there are preferred conformations the energy barriers are very low, and so the various conformations the energy barriers are very low, and so the various conformations are interconvertible.

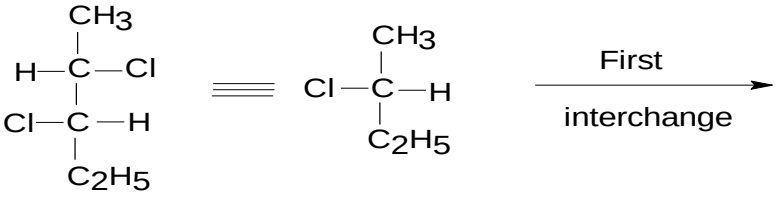
In the case of biphenyls, however, because of steric hindrance, the molecules have large energy barriers separating the two forms, and these barriers are large enough to produce separable rotational isomers. Such isomers are called atropisomers.

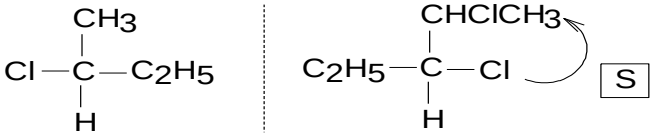


In the order of priority, the 4 groups attached to C_2 are C_1, CH_3CH_2CHCl; CH_3; H. These attached to C_3 are C_1; CH_3CHCl; C_2H_5; H. Proceeding as before in the case of tartaric acid, are specify the configuration about each of the two chiral carbon atoms in I, by making necessary double inter changes as follows:









Thus, we find that both C_2 and C_3 have S-configuration. Hence I has the configuration (2S, 3S) and it is named as (2S,3S)-2,3-dichloropentane.

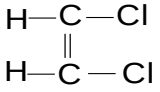
Similarly II has the configuration (2R,3R), III has the configuration (2S,3K), IV has the configuration (2R,3S).

Let us consider ethylene. The two carbon atoms are sp^2 hybridised.

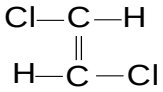
The unhybridised Pz orbitals overlap with each other to form a π bond. The molecule will have a double bond between two carbon atoms. The molecule is locked up and free rotation is restricted. If hydrogen atoms are substituted by different groups, two different spatial arrangements are possible.

These two forms are different, because they differ is their spatial arrangement of the different groups. All the four groups attached to the carbon atoms lie in the same plane. The molecule has a plane of symmetry and hence is optically inactive.

Four groups are different the molecule will be not be asymmetric. This type of isomerism is called by geometrical isomerism.



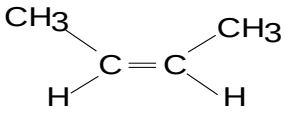
Cis



Trans

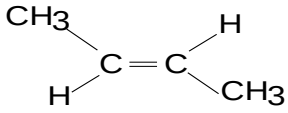
Other,

(i)



(2-Butene)

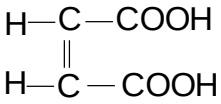
Cis



(2-Butene)

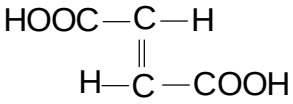
trans

(ii)



Maleic Acid

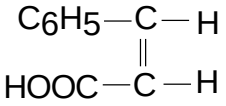
(Cis)



Fumeric Acid

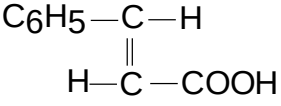
(trans)

(iii)



Cinnamic Acid

(Cis)

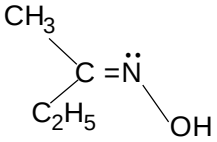


Cinnamic Acid

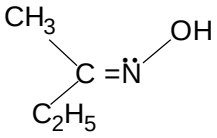
(trans)

In the case of aloloximes, the ‘syn’ isomer is one. Where hydrogen and hydroxyl groups lie on the same side of the double bond. Where as ‘anti’ isomer, these two groups are on the opposite side.

In the case of ketoximes, where two different alkyl groups R and R' exist the designation is arbitrary.

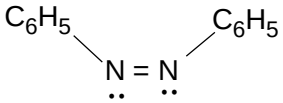


Syn-ethylene ketoxime

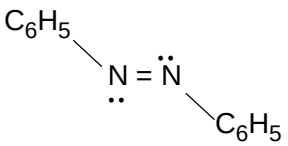


Anti-ethylene ketoxime

The azo compounds like azobenzene exhibit geometrical isomerism.



Syn azorbenzene

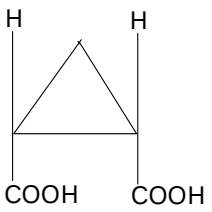


Anti azobenzene

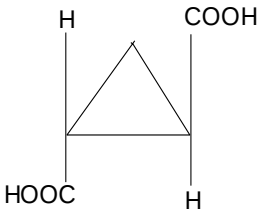
Just the double bond imposes restrictions on the free rotation. The geometrical isomerism, will therefore also arise in the cyclic compounds.

Ex:

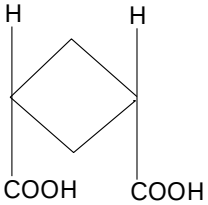
Cyclopropame dicarboxylic acids, cyclobutame dicarboxylic acid.



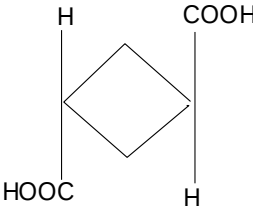
Cis



Trans



Cis



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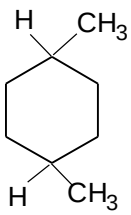
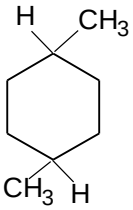


Cis



Trans

E-Z Nomenclature:

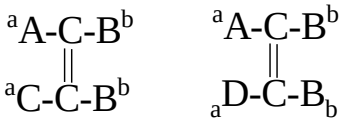
The type of nomenclature given above becomes very confusing. When its found that the groups altered to a particular carbon atom. The three or four different groups are attached in the molecule. This difficulty was later

overcome by a new nomenclature called the E-Z system. It's based upon the order up precedence of various group attached to the double bond.

Following Rules:

Rule 1:

Give the order of precedence a corl b to groups. A,B,C and D attached to double bond carbon atoms.



A > B> and C > D

Rule 2:

If the groups having higher precedence are on the same side of the double bond, the configuration of the isomer is called seqcis corl Z from the Zerman word, Zusammen, meaning together, and on the opposite side configuration of the compounds is called 'Seqtians' corl E from the German word.

Determination of configuration of the Geometrical isomers:

There is no general method for determining the configuration of geometrical isomers. In practice one uses a number of different method.

The method used depends on the nature of the compound in question. At the same time, the use of several methods, if applicable will give more reliable results.

The methods which may be used mainly for compounds that own their geometrical isomerism to the presence of a double bond.

(i) Physical Properties:

Comparison of the physical properties of geometrical isomers of known configurations.

S. No.	Physical Property	Cis	Tram
1	Melting Point	Low	High
2	Boiling Point	High	Low
3	Solubility	High	Low

4	Heat of combustion	High	Low
5	Heat of hychogenation	High	Low
6	Density	High	Low

(a) Melting Point:

The melting point of tram compound is higher than that of Cis isomer.

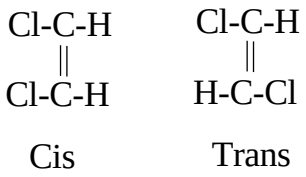
(i) Cinnamic acid pair melting point difference is 65°C.

(ii) Crotonic acid pair melting point difference is 57°C.

(iii) Ethylene 1,2 dicarboxylic acid pair difference is 170°C.

(b) Dipole moment:

Dipole moment is a vector property. Tram 1,2 –dichloroethylene is a centro symmetric molecule. The bond moments are opposed and consequently it has zero dipole moment.

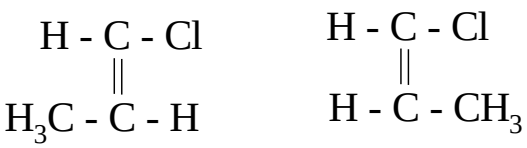


Cis Trans

The method is satisfactory so long as the groups attached to the organic carbon atoms have linear moments. When, the groups have non-linear moments, then the vector sum in the tram isomers will no longer be zero and the difference between the dipole moments of the cis and tram isomers.

The former is (diethyl maleate) with μ=2.540 and the later compound is tram (diethyl fumerate) with μ=2.38D.

If one substituent is electron donating and other is electron with drawing the individual bond moments are fully additive in the tram isomer.

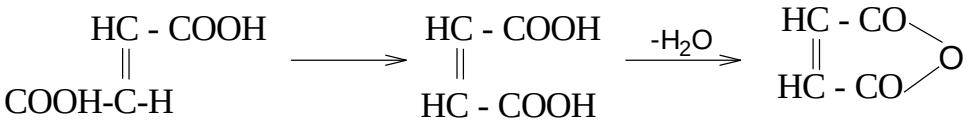


Trans μ=1.97D Cis μ=1.71D

Chemical Properties:

(i) Method of Cyclisation (Dehydration):

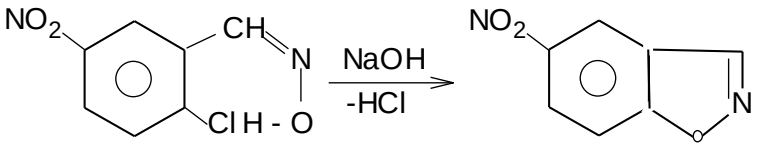
The two acids Maleic acid and fumuric acids only the former readily forms a cyclic anhydride when heated, the latter don't form an anhydride. But when strongly heated gives Maleic Anhydride.



fumaric Acid maleic Acid Maleic anhydride

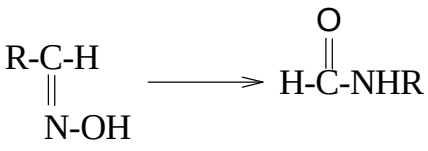
(ii) Maleic Acid on hydroxylation with either Bayer's reagent or O_sO_4 gives optically inactive, Meso tartaric acid.

(iii) Out of the two isomers of 2-chloro-5-nitro benzaldoximes one is readily cyclised on treatment with NaOH.

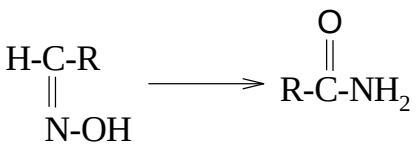


Anti-oxime Indoxarole

The configuration of Oximes is best determined by a rearrangement known as Beauman Rearrangement. When an oxime is treated with reagents like Acetic Anhydride, PCl_5. It's converted to an acid Amide (or) substituted Acid amide by a molecular rearrangement.



Syn N - Substituted Amide

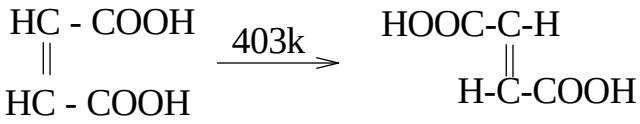


Anti Amide

(5) Inter conversion of Geometrical isomers:

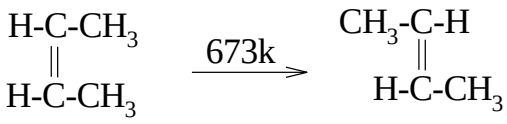
Geometrical isomers may be converted into each other. The isomerisation is brought about by rotation around the bond axis, which is only possible. When the double bond, becomes loose (or) breaks.

Maleic acid may be converted into Fumuric Acid on heating:



Malic Acid Fumuric Acid

The above inter-conversion can be brought out by adding little bromine to the reactane.



Cis -2-buteme Trans -2-buteme

1.6 CONFORMATIONAL ANALYSIS IS OF ACYLIC AND CYCLIC SYSTEMS

The term conformation, first used by W. N. Haworth in 1929, refers to various spatial arrangements of a molecule which differ in space by a rotation of two atoms about a single bond and are capable of finite existence. Less widely used terms are ‘constellation’ and ‘rotational isomers.’ Contrary to configurational isomers, the conformational isomers have energy barriers between them of the order of rotational energy barriers of single bonds (about l3 to 84 kJ mol^{-1}) and usually cannot be separated physically unless under some special circumstances the single-bond rotational barriers are dramatically increased by introducing bur-groups in suitable positions. The changes in molecular geometry which take place during rotation about the carbon-carbon bond of an alkane (e.g.,ethane) can be followed by projection formulas. Three types of conformations are possible taking into consideration the spatial relation that can be obtained by changing the dihedral angle (i.e., the angle observed between C – H bonds).

Staggered conformation (Transoid) - Here torsional energy is minimum. In this arrangement the carbon-hydrogen bonds of one methyl group (in ethane) are as far as possible away from those of the other. This

spatial relationship occurs when the dihedral angle between C - H bond (as viewed along the C - C bond axis) is 60°.

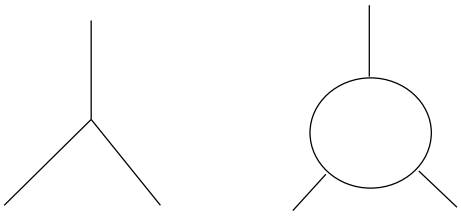
Eclipsed conformation (Cisoid) – When the dihedral angle is 0° or 120°, the eclipsed conformation is seen in which the hydrogen of the forward carbon are directly in front of those on the back carbon (i.e. the rear methyl group is completely eclipsed and only the front group is visible). In this form, the carbon-hydrogen bonds are at their closest approach in the spatial arrangement.

Skew or Gauche conformation – Several other forms are possible in between the eclipsed and the staggered form. Such an arrangement is called the skew conformation.

Planar representation of conformation – It is not very convenient to depict three dimensional formulae on paper. Two methods are used to depict these conformations they are,

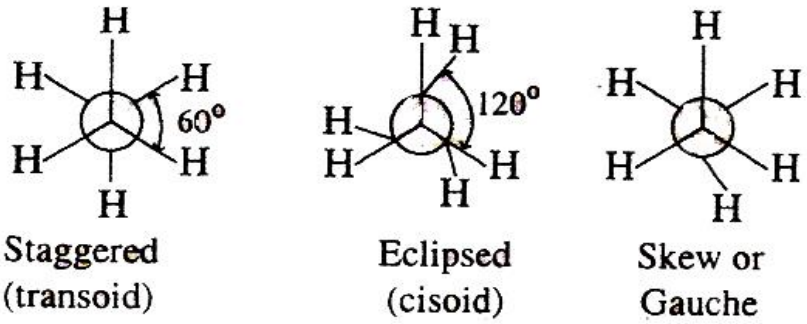
(1) Newmann Projections – Example taken is ethane.

The front carbon atom is represented as a point with the bonds intersecting at the point. The rear carbon appears as a circle.

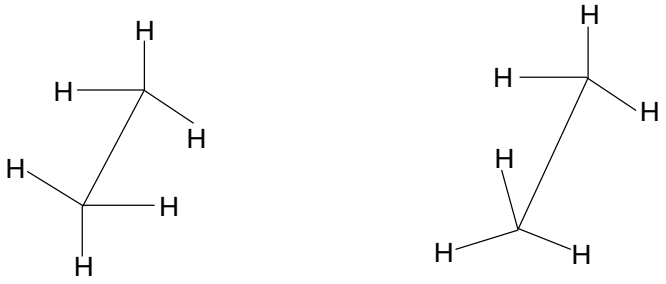


Front carbon Rear carbon

The three conformations may then be depicted as—

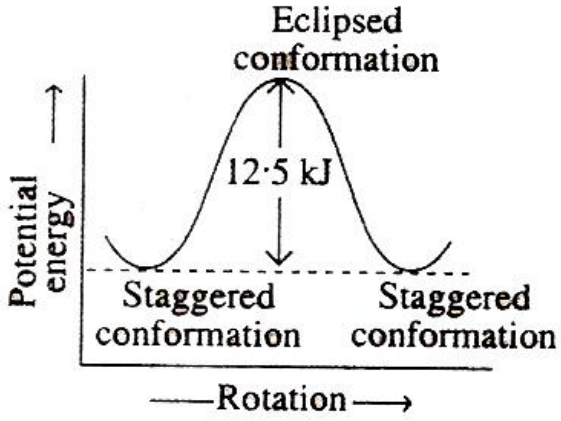


(2) Sawhorse representations—In 'Sawhorse' drawings, the lower left hand carbon is always taken to be towards the front. In this model, the molecule is viewed slightly from above and from the right.



Staggered Eclipsed

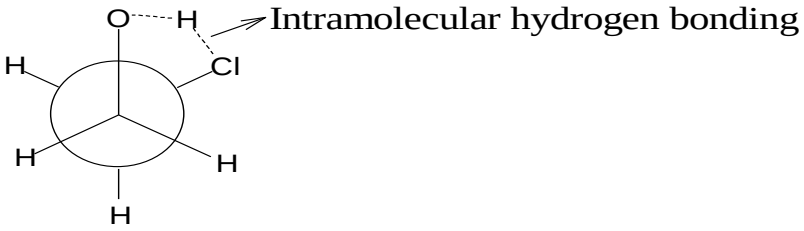
The repulsive interaction between the electron clouds which affects the stability of a conformation is known as torsional strain of all infinite number of possible conformations of ethane molecule, the staggered conformation is the most stable due to the least torsional strain. Due to torsional strain an energy barrier equivalent to torsional energy has to be overcome to permit rotation around the carbon-carbon single bond.



Energy changes during rotation about carbon-carbon single bond in ethane

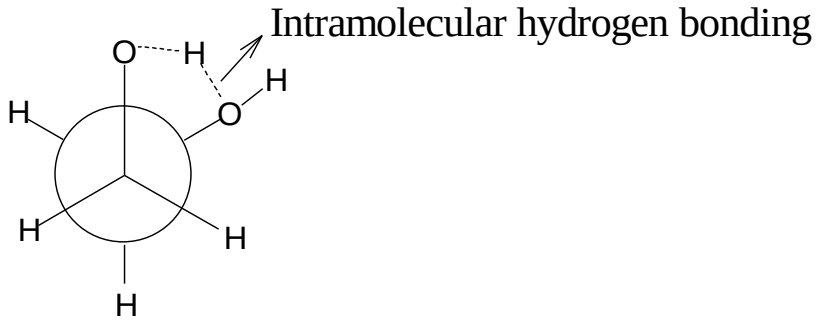
Conformation of Chlorohydrin

The stable conformation of ethylene chlorohydrin is Gauch form due to the presence of intramolecular hydrogen bonding.

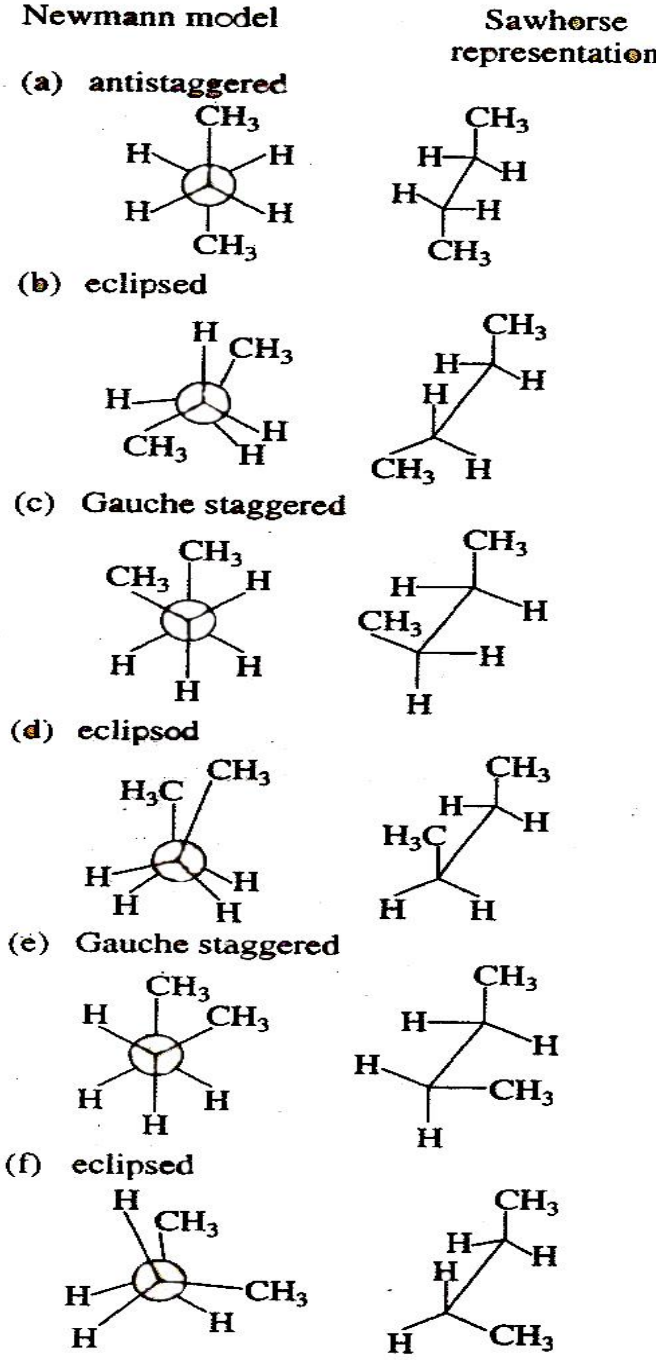


Conformation of Ethylene glycol

The stable conformation of ethylene glycol is Gauch form due to the presence of intra-molecular hydrogen bonding.



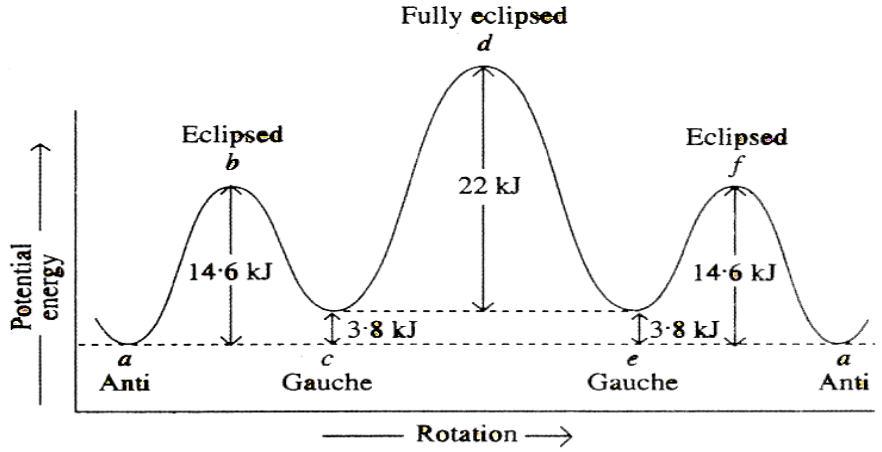
Projections of Butane—The different spatial arrangements of butane can be got from rotation around the central carbon-carbon bond CH_3CH_2— CH_2CH_3. It is possible to get 3 staggered and 3 eclipsed conformations by rotating one side of the molecule through 360° relative to the other.



The most stable conformation isomer is (a) This staggered rotamer in which the methyl groups are farthest apart is known as the 'anti' (or trans) form. The staggered rotamers (c) and (e) with adjacent methyl Groups at an angle of 60° to each other are the Gauche (or skew) conformations. The two gauche form: are equal in energy but they are not identical molecules, they are related to each other as mirror images. In two of the eclipsed forms [structures (b) and (f)] the methyl groups are eclipsed by hydrogens and in structure (d)

one methyl group eclipses the other. In this structure the repulsive forces will be greater and hence less stable than the other two eclipsed forms.

The energy change during rotation about C_2—C_3 bond in n-butane is shown in energy diagram.

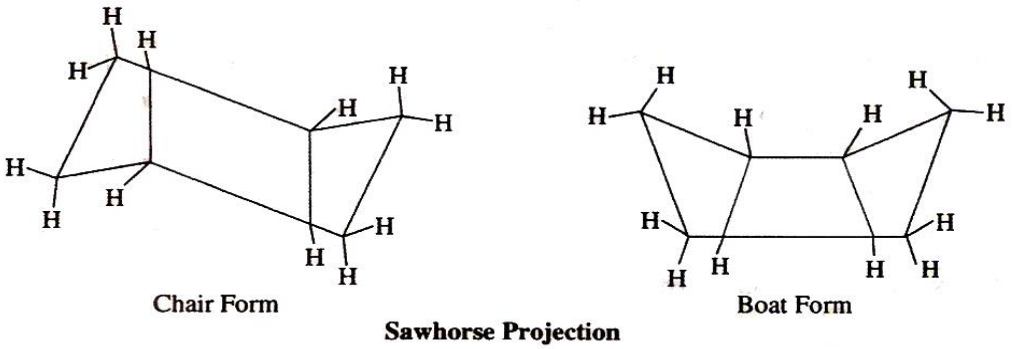


Energy changes during rotation around the central carbon bond in the *n*-butane

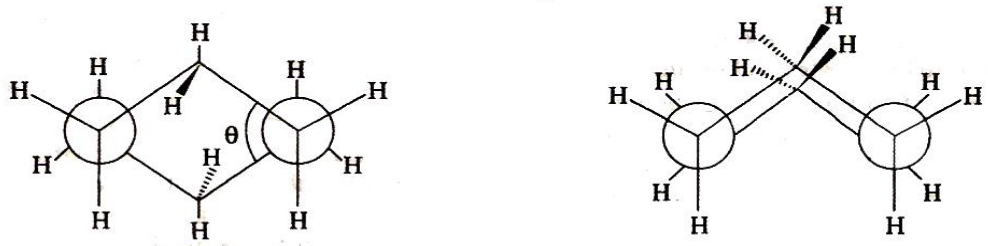
Fischer's configuration—It becomes rather difficult to draw three dimensional formulas as the number of chiral carbon atoms in a molecule increases. Fischer developed a two-dimensional projection formula particularly for carbohydrates and amino acids which can be applied to represent a chiral compound like the 2-3 diols, e.g., 2, 3 butanediol.

In the Sawhorse models the broken wedges represent vertical and solid wedges horizontal in the two dimensional surface. Fischer's projections may then be obtained by flattening the two dimensional surface.

Conformational Analysis of Cyclohexane—The importance of Baeyer strain was First appreciated in 1890 by Sasche, who pointed out that two non-planar models of cyclo-hexane could be constructed in which all the bond angles were 109'-28', so that the systems were free of Baeyer strain. One of these was a fairly rigid form, shaped roughly like a chair and the other was a flexible form whose most symmetrical form was shaped like a boat. Apparently, all the pairs of the carbon-carbon bonds in the chair form of cyclohexane are perfectly staggered bonds, whereas in the boat form these are eclipsed bonds.

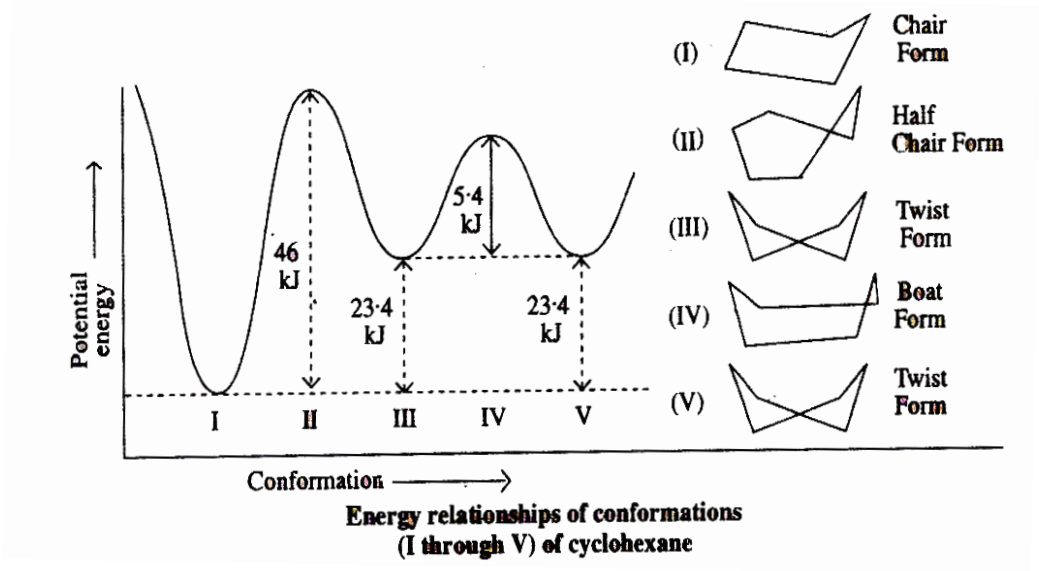


Sawhorse Projection



Newmann Projection

The chair form of cyclohexane is free from angle strain as well as torsional strain while boat form has considerable torsional strain and also steric strain due to the crowding of C_1 and C_4 hydrogens. Thus chair form contains 28-8 kJ mol^{-1} less energy (hence more stable) than the boat conformation. The above mentioned chair and boat forms are not the only conformations which cyclohexane can have. Actually several other conformations are also possible as shown in energy diagram.

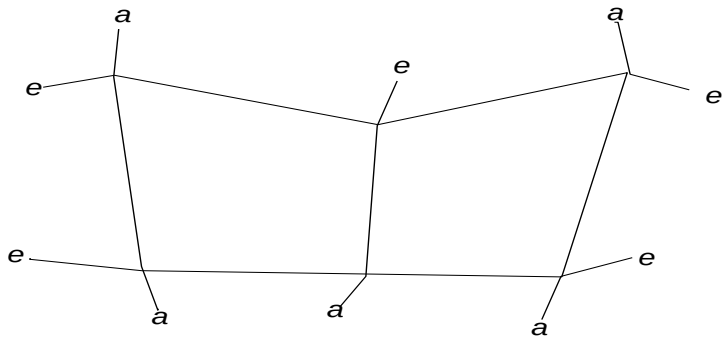


Energy relationships of conformations (I through V) of cyclohexane

The relative distribution of cyclohexane molecules with chair conformation and the two twist conformations is about 10,000 to 1 at room

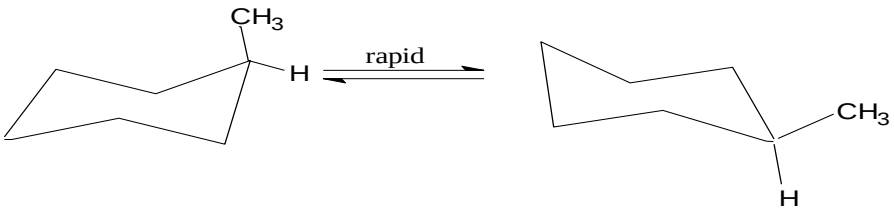
temperatures. For all practical purposes, cyclohexane exist almost exclusively in the chair conformation.

Axial and Equatorial Bonds in Cyclohexane—In chair conformation of cyclohexane all the carbon atoms lie roughly in a plane. Six hydrogen lie in a plane and six hydrogens lie above or below the plane. Hydrogens lying in the plane of the ring are called equatorial hydrogens because they are situated essentially along the equator of the ring. The bonds holding such hydrogens are called the equatorial bonds. The hydrogens lying above or below the plane of the ring are called the axial hydrogens because they are situated along an axis perpendicular to the plane of the ring. The bonds holding such hydrogens are referred to as axial bonds. Each carbon in the chair conformation has one equatorial and one axial bond. Axial bonds have been marked V and equatorial bonds 'e'.



a= Axial hydrogen *e* = Equitorial hydrogen

1, 3-Diaxial interactions in cyclohexane derivatives—When a hydrogen in cyclohexane is replaced by a larger atom (e.g., Br) or a bulky group (e.g., CH_3) it leads to crowding especially among atoms located on the three axial bonds on the same side of the molecule. The non-bonded interactions between such axial atoms or groups which results from this crowding are referred to as 1, 3-diaxial interactions. They account for the relative stabilities of various conformations of a cyclohexane derivative. For example, in methyl-cyclo-hexane.



Not favoured
Axially substituted

Favoured
Equatorial subsituted

The energy difference between equatorial and axial conformations is about 7-5 kJ.

To sum up—

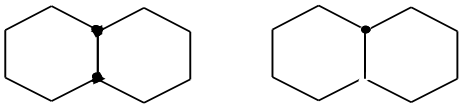
(a) chair conformations are more stable than twist conformations.

chair conformations in which the large atoms or groups occupy equatorial positions is the most stable and the preferred conformation.

Conformational analysis of Decalin:

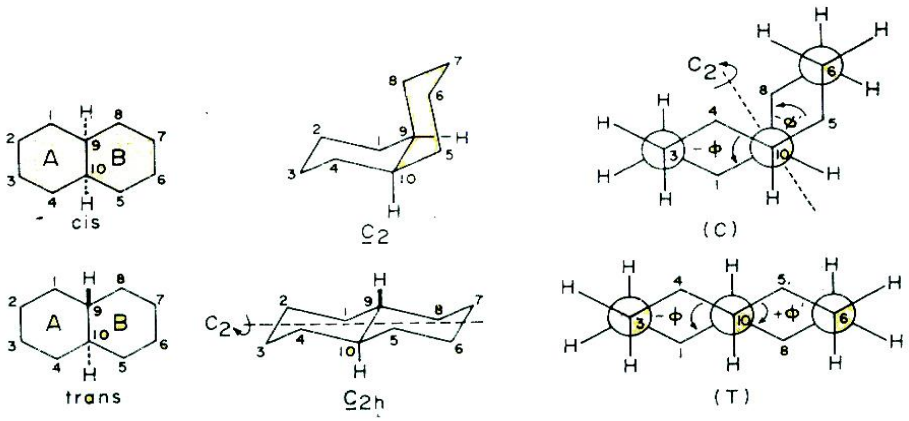
Decalin exists in two diastereomesic forms such as cis-form in which the two rings are cis fused and a trans form in which the two rings are trans fused. They are shown in Figure,

1,4 dimethyl cyclohexane



Cis Trans

Decalin



cis- Decalin and *trans*-decalin

The Newman projection formula shows the torsion angle (ϕ) in each ring across the common central bond. Known as torsion angle of junction.

The planar structures may be simplified by replacing the bridgehead. If atom above the plane of the rings (denoted by thick line) with a dot. If may be noted that the trans isomer cannot exist in planar form. Since it necessitates spanning of two 1,2 – trans bonds (torsion angle 180^o) by a tetramethylene chain.

NOTES

UNIT – II

CARBOHYDRATES

Carbohydrates are important biomolecules available in nature, the structure of vegetables and animal kingdoms are constructed by them.

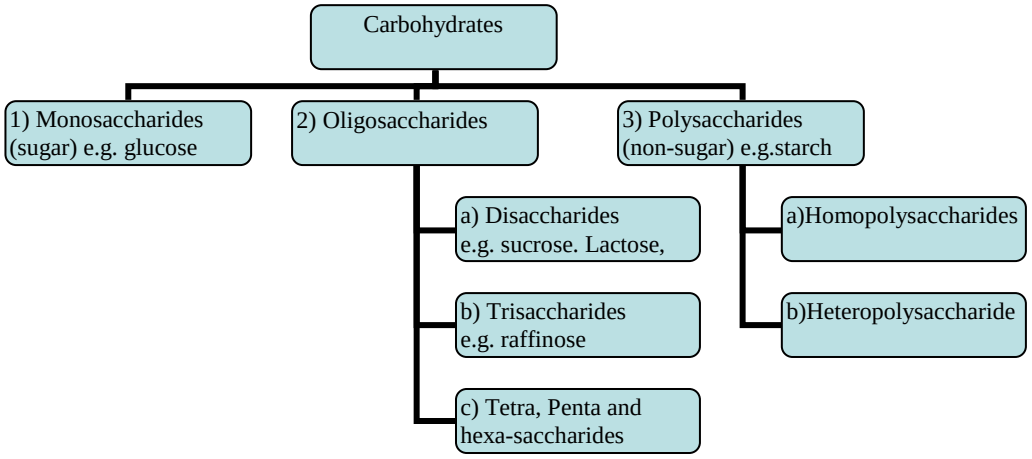
The term carbohydrates are all polyhydroxy aldehydes or ketones along with substances which yield these on hydrolysis.

The formula of carbohydrates is $Cx(H_2O)Y$. Hence, they are considered to be the hydrates of carbon and named as carbohydrates. Some carbohydrates cannot be represented as hydrates of carbon. E.g. rhamnose-$C_6H_{12}O_5$.

Some substances other than carbohydrates can be represented as hydrates of carbon. E.g. formaldehyde.

Classification :

They can be classified on the basis of acid hydrolysis



Monosaccharides

Non-hydralysable into simple carbohydrates. They are soluble in water, sweet in taste and building block of various sugar carbohydrate molecules. General formula is $C_6H_{12}O_6$.

Disaccharides

They yield two monosaccharides on hydrolysis. General formula is $C_{12}H_{22}O_{12}$. Crystalline solids, soluble in water and sweet in taste. E.g. Sucrose, Fructose, Maltose.

Trisaccharides

They yield three monosaccharides on hydrolysis. General formula is $C_{18}H_{32}O_{16}$

e.g. raffinose.

Polysaccharide :

They yield large number of monosaccharide molecules on hydrolysis. They are amorphous, tasteless and mostly insoluble in water. Non-sugar in nature

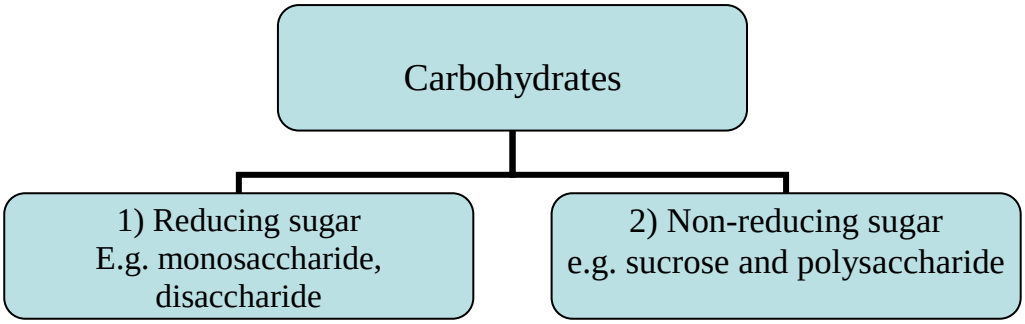
Homopolysaccharides

They yield one kind of monosaccharide units on hydrolysis.

Heteropolysaccharide

They yield more than one kind of monosaccharide units on hydrolysis.

Classification depends upon the reduction reaction



Reducing sugars

They reduces Tollen's reagent and Fehling's solution, e.g. monosaccharides, disaccharides (except sucrose)

Non-reducing sugars

They not reduces Tollen's reagent and Fehling's solution

Classification depends upon the number of carbon atoms. E.g. ribose is a pentose, glucose is a hexose.

Classification depends upon the presence of carbonyl group

If the presence of aldehyde group – aldoses – Glucose

If the presence of ketone group – ketoses – Fructose

GLUCOSE - $C_6H_{12}O_6$

Glucose serves as the source of energy for all living systems. It occurs in ripe grapes, honey and most sweet fruits. It is present in many disaccharides. It is the building blocks of starch, cellulose and glycogen. It is a normal constituent of blood and is present in urine of diabetic persons.

Preparation

From starch: Commercially pure glucose is prepared by the hydrosis of starch.

$$(C_6H_{10}O_5)n + n\,H_2O \xrightarrow{H^+} n\,C_6H_{12}O_6$$

Starch → Glucose

From sucrose : Glucose can be easily prepared from hydrolysis of sucrose.

$$C_{12}H_{22}O_{11} + H_2O \xrightarrow{H^+} C_6H_{12}O_6 + C_6H_{12}O_6$$

Sucrose → Glucose + Fructose

Properties

Physical :

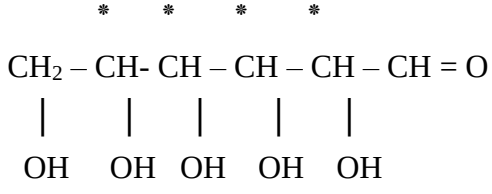
Glucose is a white crystalline solid (m.p. 419 K).

Readily soluble in water.

Sparingly soluble in alcohol.

Optically active and is dextro-rotatory, specific rotation is $+52.5^o$.

Chemical :



Structural formula of glucose indicates the presence of

(i) one aldehyde group (-CHO)

(ii) one primary alcoholic group ($-CH_2OH$)

(iii) four secondary alcoholic group (-CHOH)

Structural elucidation of glucose

1) Elemental analysis and molecular weight determination indicates the empirical formula as CH_2O**.**

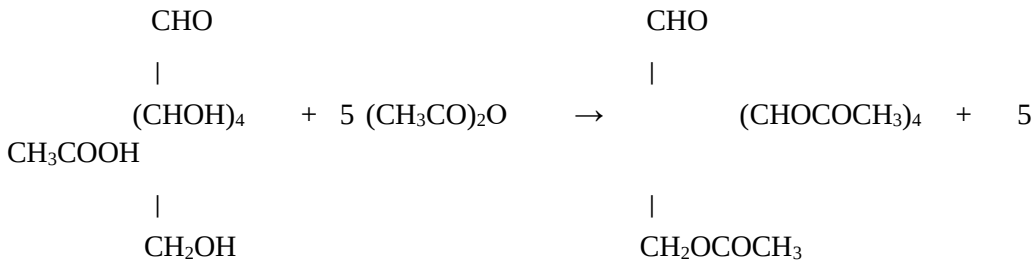
2) Molecular weight as 180 by depression of freezing point method. The molecular formula as $C_6H_{12}O_6$.

3) Reduction of glucose with conc.hydroiodic acid to give n-hexane.

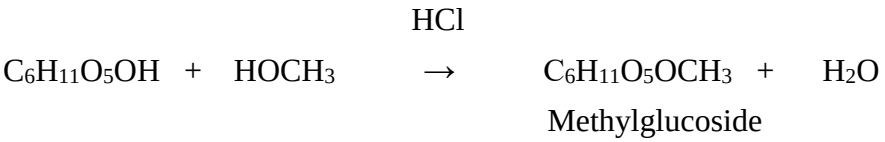
$$\text{Glucose} \xrightarrow{\text{Conc. HI}} \text{n- hexane}$$

This reaction indicates the presence of six carbon atoms.

4) Glucose reacts with acetyl chloride or acetic anhydride to give penta- acetyl derivates.

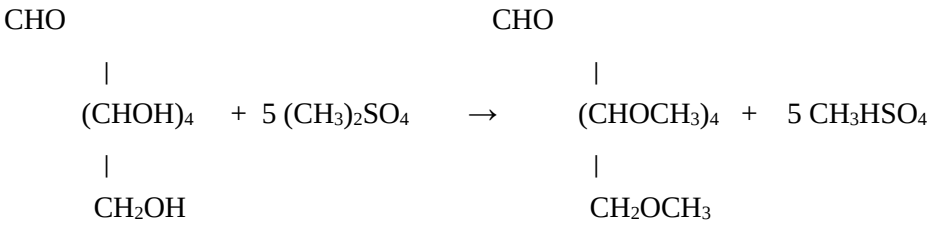


5) Glucose reacts with methanol in the presence of dry hydrochloric acid gas to form methyl glycoside, an ether.

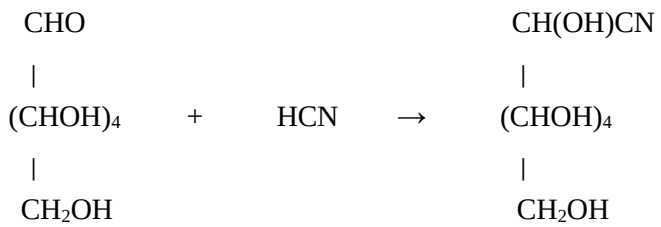


Methylglucoside

6) Glucose reacts with methyl sulphate to gives penta – O – methyl derivative, which indicates the presence of 5 alcoholic groups

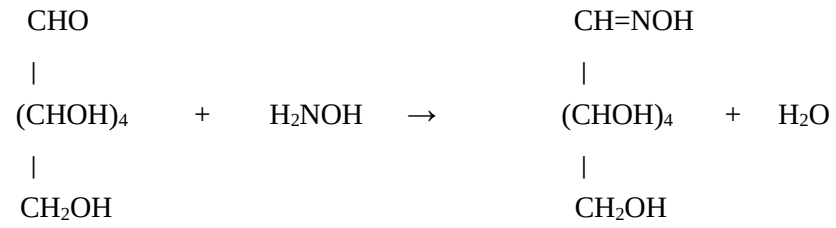


7) Glucose gives addition products, glucose cyanohydrin by the addition of a molecule of hydrogen cyanide.



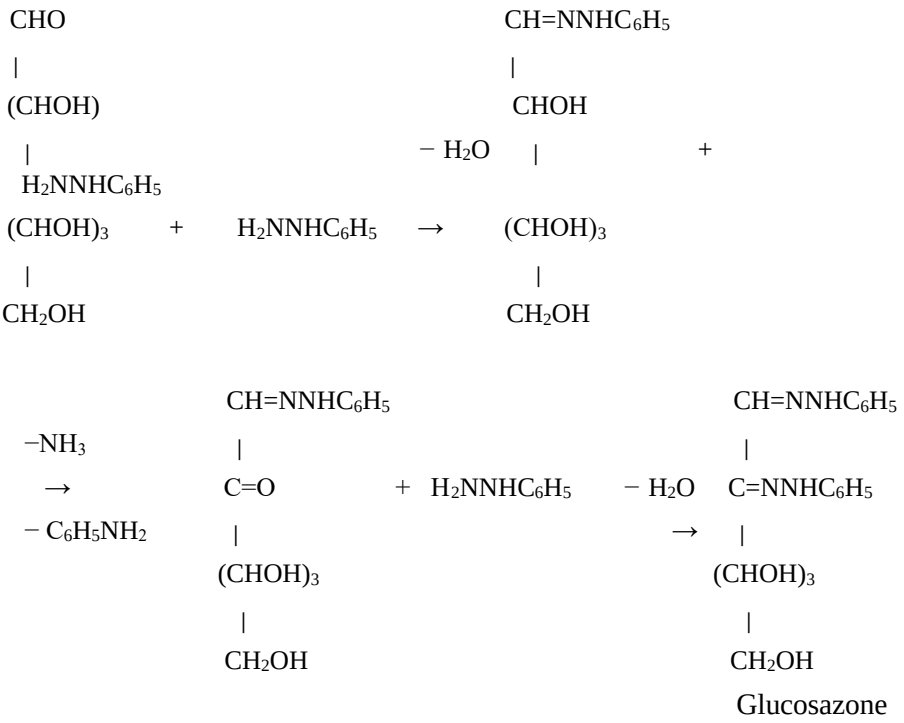
This reaction for carbonyl group.

8) Glucose condenses with hydroxylation with the elimination of water to yield the oxime.



9) Glucose on treatment with excess of phenylhydrazines in acetic acid gives glucosazone or osazone in short. The aldehyde group of

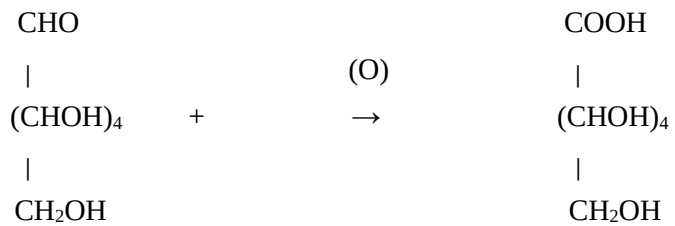
glucose condenses with one mole of phenylhydrazine to give phenylhydrone, then warmed with excess of phenyhdrazine the secondary alcoholic group adjacent to the aldehyde group is oxidized to ketonic group. With this ketonic group, the third mole of phenylhydrazine condenses to give glucosazone.



Glucosazone

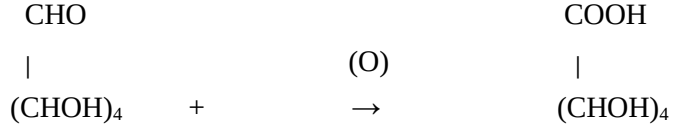
The participation of first two carbon atoms in the osazone formation is due to stable **chelate formation** of the first two carbon

10) Glucose is oxidized with mild oxidizing agent like Br_2/H_2O to gluconic acid.



Gluconic acid

11) With strong oxidizing agents like nitric acid, its terminal groups CHO as well as $–CH_2OH$ are oxidized to COOH group to give the dicarboxylic acid called saccharic acid or glucaric acid.



| |
CH₂OH COOH

Saccharic acid or glucaric acid

12) When reduced with sodium amalgam the aldehyde group is reduced to a primary alcoholic group to yield a hexahydric alcohol, **Sorbitol.**

CHO CH₂OH
| (H) |
(CHOH)₄ + → (CHOH)₄
| Na-Hg |
CH₂OH CH₂OH

Sorbitol

13) Glucose reduces Fehlig's solution (I) and ammonical silver nitrate (Tollen's reagent, II)

COOH CHO COOH
| II | I |
2 Ag ↓ + (CHOH)₄ ← (CHOH)₄ → (CHOH)₄ + Cu_2O↓
| | |
CH₂OH CH₂OH CH₂OH

From the above discussions it is clear that glucose is

(i) a straight carbon, linear compound with six carbon atoms.

(ii) Having five alcoholic groups on five different carbon atoms.

(iii) Having one aldehydic group.

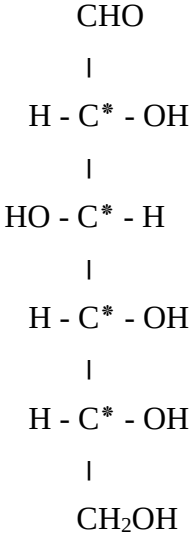
On the basis of these, the open structure of glucose is

* * * *

CH_2 – CH- CH – CH – CH – CH = O
| | | | |
OH OH OH OH OH

The structure reveal that there are four structrurally different chiral carbon atoms, shown as *

16 optically active forms ($2^4 = 16$). Glucose has the structure as given below.



This open chain formula assigned to glucose readily accounts for most of the reactions satisfactory but fails to explain the following—

(i) Even though an aldehyde group is present in glucose, it does not react with $NaHSO_3$ and NH_3.

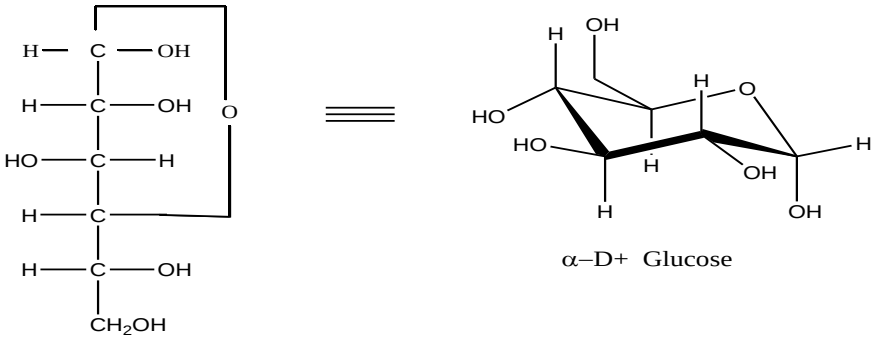
(ii) Two stereoisomeric forms of glucose (α – and β – glucose) exist. α – glucose with specific rotation + 110^0 is obtained by crystalling glucose from alcoholic or acetic acid solution whereas β – glucose with specific rotation +19.7^o is obtained by crystallizing glucose from pyridine solution.

(iii) An aqueous solution of glucose shows **mutarotation.**

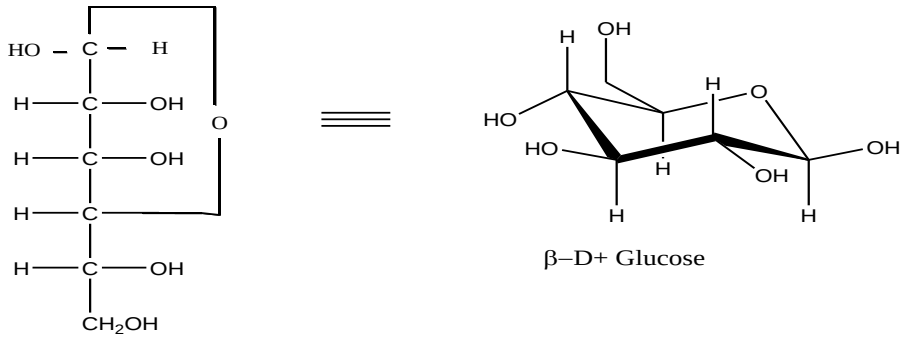
i.e. its specific rotation gradually falls from + 110^0 to + 52.5^0 in the case of α – glucose and increases from +19.7^0 to 52.5^0 in the case of β – glucose.

(iv) Two isomeric methyl glucosides (α – and β –) are obtained by heating glucose with methyl alcohol and dry HCl gas.

To account for the above facts a six membered **pyran** structure has been derived.



α–D+ Glucose



β–D+ Glucose

The ring structure explains all the reactions of glucose. The objections raised against the open chain structure of glucose have also been satisfactorily explained.

For e.g.

(i) The aldehyde carbon atom becomes chiral on ring formation and gives rise to two **anomers,** α – and β – glucose.

(ii) The glucose ring is not very stable. It is easily broken up by strong reagents like HCN, NH_2OH, $NH_2C_6H_5$ etc. Weak reagents like NH_3 and $NaHSO_3$ are unable to open the chain and cannot react with it.

(iii) It explains mutarotation.

Mutarotation

The change in specific rotation of an optically active solution without any change in other properties is known as mutarotation.

Explanation :

Glucose is dextro – rotatory. The specific rotation of freshly prepared aqueous solution of glucose crystallized from alcoholic or acetic acid solution decreases from gradually from $+110^0$ to $+52.5^0$ in about 24 hours. The change is accelerated by heat or the presence of an alkali. Similarly specific rotation of

a freshly prepared aqueous solution of glucose crystallized from pyridine solution increases from + 19.7º to + 52.5^0.

Mutarotation has been explained by assuming that glucose exists in two forms, anomeric α – and β – varieties. In an aqueous solution, the two varieties are present as an equilibrium mixture containing α – form into β – form and vice-versa.

Mechanism

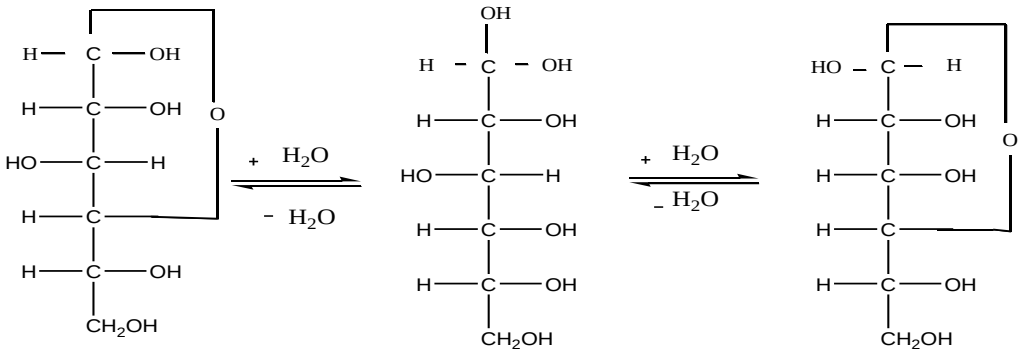
α – D- Glucose ⇌ Equilibrium mixture β – D-Glucose

[α] = + 110º [α] = + 52.5º [α] = + 19.7º

36% α – Glucose

64% β – Glucose

In water the transformation occurred through the intermediate product, **aldehydrol.**



α- D(+)Glucose Aldehydrol β – D-Glucose

[α] = + 110º intermediate [α] = + 19.7º

Uses

(i) As a sweeting agent in confectionery.

(ii) In medicine and as food for children and invalids.

(iii) In fruit preservation and in making jams and jellies.

(iv) As a cheap reducing agent in industry and in the manufacture of wines.

(v) As a starting material in the synthesis of vitamin C.

FRUCTOSE, $C_6H_{12}O_6$

Fructose is the most important ketohexose. It is called **fruit sugar** and **laevulose.**

Preparation

(i) From cane sugar : Fructose is prepared by the hydrolysis of a concentrated solution of cane sugar with dilute mineral acid.

$$C_{12}H_{22}0_{11} + H_20 \xrightarrow{H^+} C_6H_{12}O_6 + C_6H_{12}O_6$$

Cane sugar — Glucose — Fructose

(ii) From inulin : Fructose is manufactured by the hydrolysis of inulin, a polysaccharide, with sulphuric acid.

$$(C_6H_{10}0_5)n + nH_20 \xrightarrow{H^+} nC_6H_{12}O_6$$

Inulin — Fructose

Properties

Physical :

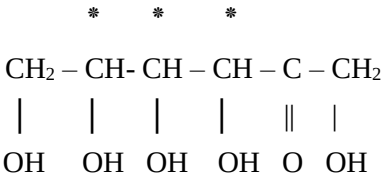
(i) It is a white crystalline solid (375 K).

(iii) It is the sweetest of all sugars.

(iv) It is readily soluble in water but is sparingly soluble in alcohol and insoluble in ether.

(v) It is laevorotatory and is called **laevulose.**

Chemical



Structural formula of fructose indicates the presence of

(i) One ketonic group (-CO-)

(ii) Two primary (-CH_2OH) alcoholic groups.

(iii) Three secondary (-CHOH-) alcoholic groups.

(iv) Three asymmetric carbon atoms (C*)

Chemical properties of fructose are, therefore, the properties of these groups.

Structural Elucidation of Fructose

1) Elemental analysis and molecular weight determination clearly indicate the molecular formula of fructose is $C_6H_{12}O_6$.

2) Reduction of Fructose with concentrated hydroiodic acid and red phosphorus at 370 K yields 2- iodohexane. Prolonged heating with conc. HI produces n-hexane.

$$CH_2OH - (CHOH)_3 - CO - CH_2OH \xrightarrow{HI} CH_3 - (CH_2)_4 - CH_3$$

n-hexane

This reaction clearly indicates that all six carbon atoms are present in a straight chain linearly.

3) Fructose reacts with acetyl chloride or acetic anhydride to give penta-acetyl derivates.

$$\begin{array}{l} CH_2OH \\ | \\ CO \\ | \\ (CHOH)_3 \\ | \\ CH_2OH \end{array} + 5\,(CH_3CO)_2O \rightarrow \begin{array}{l} CH_2OCOCH_3 \\ | \\ CO \\ | \\ (CHOCOCH_3)_3 \\ | \\ CH_2OCOCH_3 \end{array} + 5\,CH_3COOH$$

4) Fructose reacts with methanol in the presence of dry hydrochloric acid gas to form methyl glycoside, an ether.

$$C_6H_{11}O_5OH + HOCH_3 \xrightarrow{HCl} C_6H_{11}O_5OCH_3 + H_2O$$

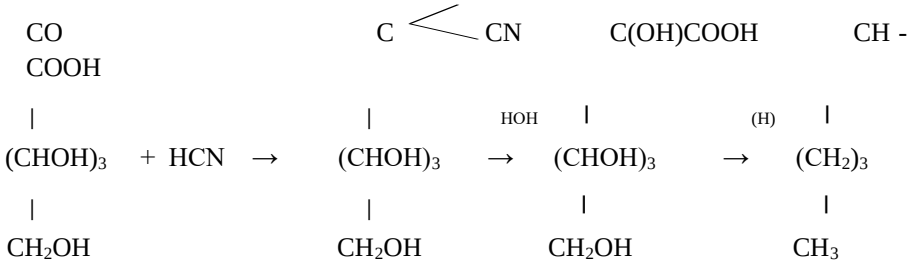
Methylglucoside

5) Fructose reacts with methyl sulphate to gives penta – O – methyl derivative, which indicates the presence of 5 alcoholic groups

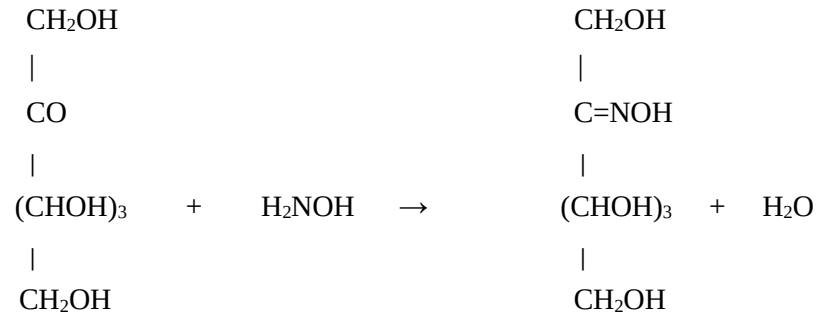
$$\begin{array}{l} CH_2OH \\ | \\ CO \\ | \\ (CHOH)_3 \\ | \\ CH_2OH \end{array} + 5\,(CH_3)_2SO_4 \rightarrow \begin{array}{l} CH_2OCH_3 \\ | \\ CO \\ | \\ (CHOCH_3)_3 \\ | \\ CH_2OCH_3 \end{array} + 5\,CH_3HSO_4$$

6) Fructose gives cyanohydrin by the addition of a molecule of hydrogen cyanide, which on hydrolysis gives 2-methyl hexanoic acid.

$$\begin{array}{llll} CH_2OH & CH_2OH & CH_2OH & CH_3 \\ | & | \quad OH & | & | \end{array}$$

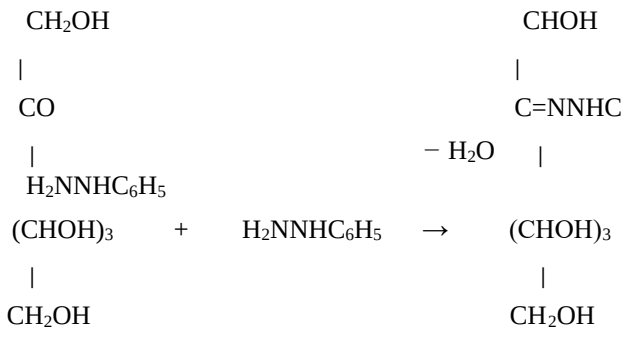


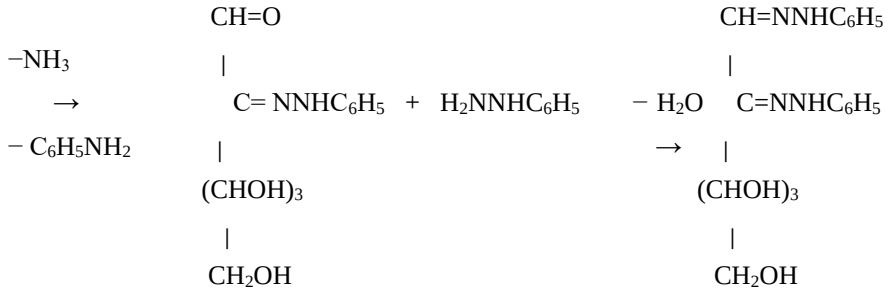
7) Fructose condenses with hydroxylation with the elimination of water to yield the oxime.



Reaction 5 and 6 are the reactions of a carbonyl group. Fructose does not react with ammonia and sodium bisulphate.

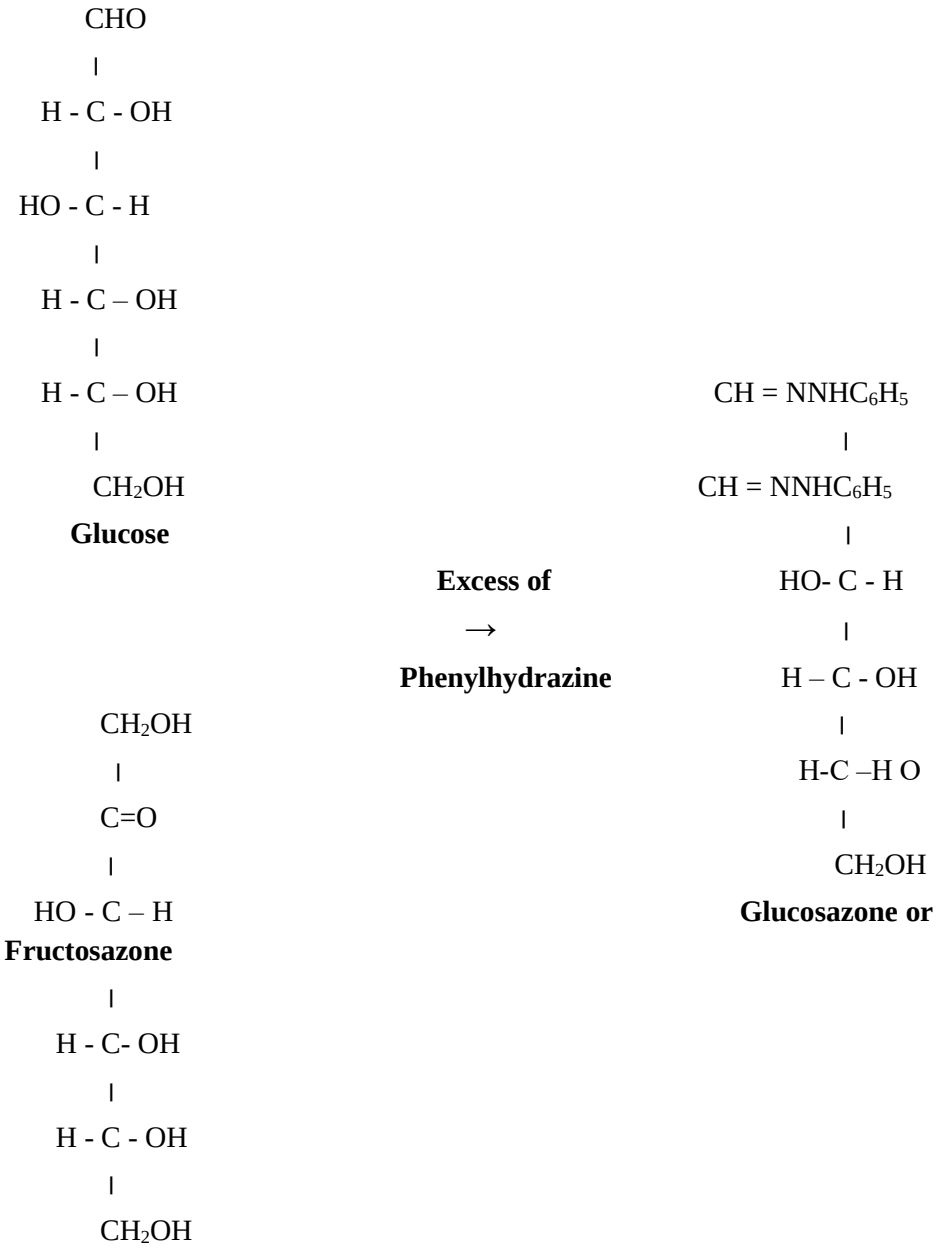
8) Fructose on treatment with excess of phenylhydrazines in acetic acid gives fructosazone.





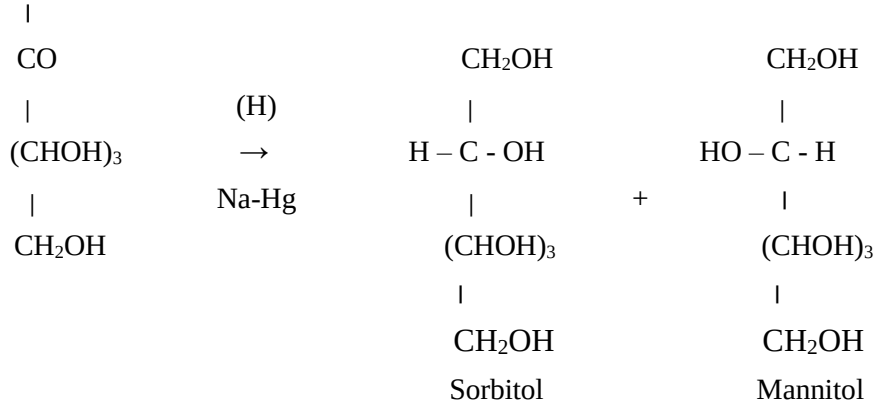
Fructosazone

Note : Close examination of fructosazone will reveal that it is similar to glucosazone. This is because glucose and fructose differ only in the configuration of first two carbon atoms and these carbon atoms only take part on the osazone formation yielding the same osazone. This is shown as follows –



9) When reduced with sodium amalgam the ketonic group is reduced to a secondary alcoholic group to yield a hexahydric alcohols, i.e. a mixture of **Sorbitol** and **mannitol.**

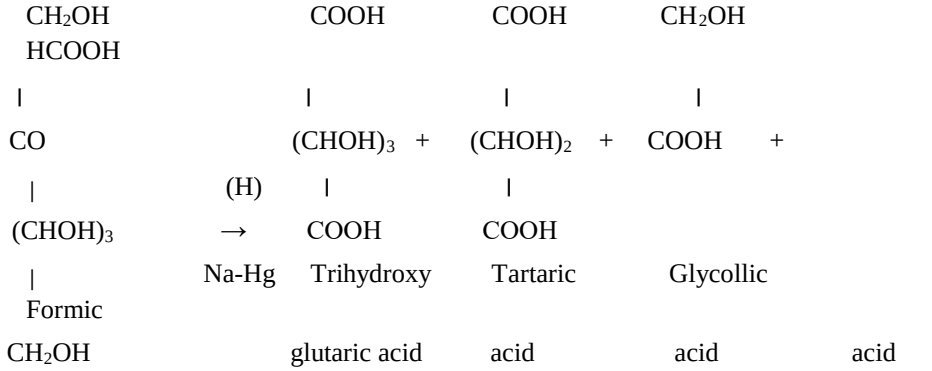
CH_2OH



This reaction shows the presence of a ketonic group in fructose.

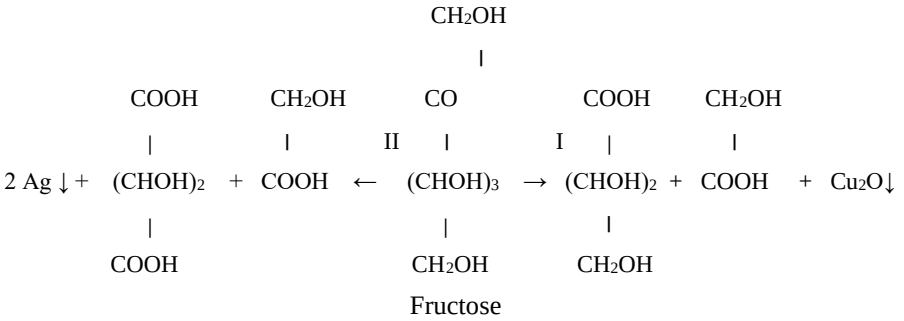
10) Fructose is not oxidized with Br_2/H_2O

11) When fructose is oxidized by strong oxidizing agent like conc. HNO_3, a mixture of acids having glycolic acid, tartaric acid, trihydroxyglutaric acid and formic acid. All these acids are having less than six carbon atoms.



This reaction clearly shows the presence of a ketone group in fructose.

12) Fructose reduces Fehlig's solution (I) and ammonical silver nitrate (Tollen's reagent.



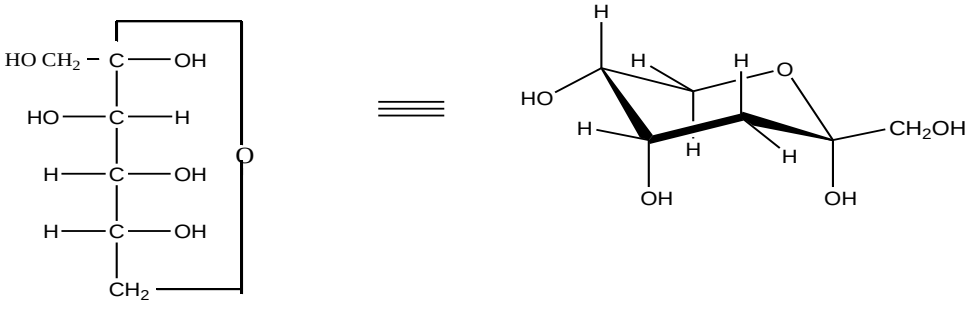
From the above discussions it is clear that glucose is

(iv) a straight carbon, linear compound with six carbon atoms.

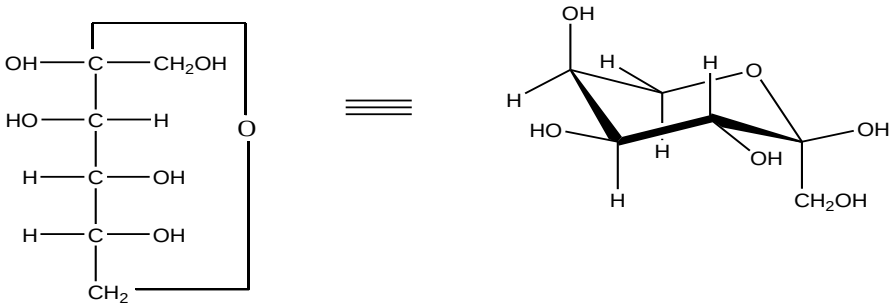
(v) Having five alcoholic groups on five different carbon atoms.

(vi) Having one ketonic group.

13) Like glucose, it shows mutarotation and the specific rotation of the equilibrium mixture obtained on standing is - 92^0. Hence, forms of fructose (α – and β – forms) are possible just like in glucose. These two forms have pyran structure as shown below.

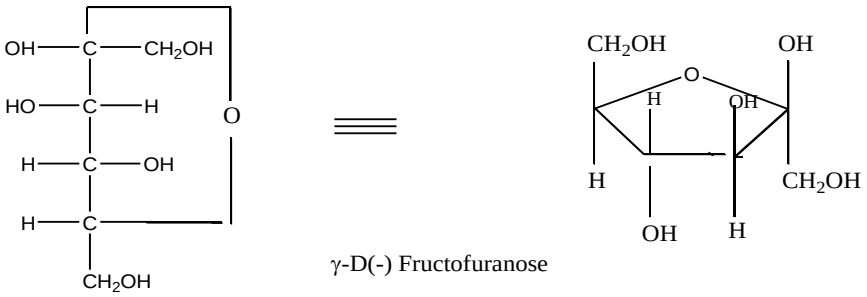


α–D(-) Fructose



β–D(-) Fructose

Yet another form (γ – form) is also possible for fructose. This is based on a five membered **furan** structure as follow.



γ-D(-) Fructofuranose

Uses

(i) Fructose finds use as sweetening agent.

(ii) It is used by diabatic patients in place of cane sugar.

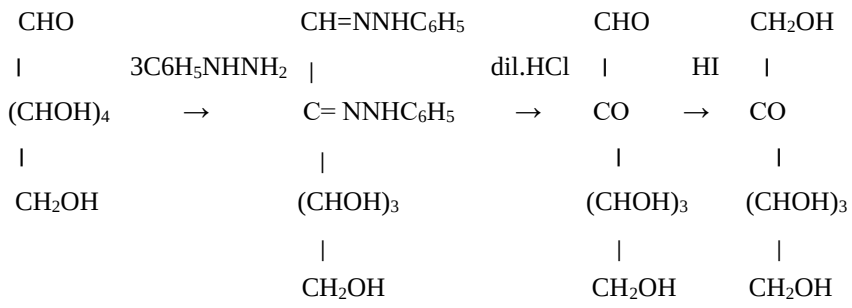
CONVERSIONS

Glucose to fructose :

(i) Glucose is warmed with excess phenylhydrazine when it gives glucosazone.

(ii) Glucosazone is treated with dil.HCl when it gives glucose by hydrolysis.

(iii) The later on reduction with Zinc dust and acetic acid gives fructose.



Glucose **Fructose**

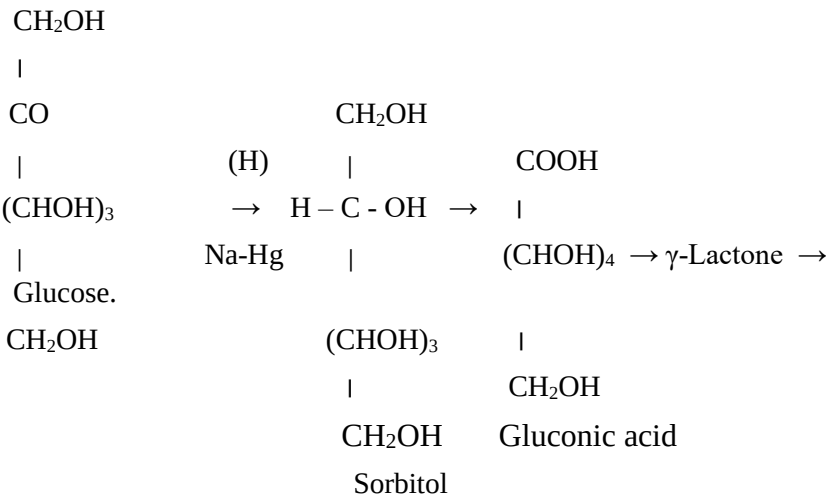
2) **Fructose into Glucose :**

(i) Fructose on catalysis reduction gives hexitol (a mixture of sorbitol and mannitol).

(ii) Sorbitol on oxidation gives gluconic acid.

(iii) Which on heating gives γ- lactone.

(iv) Lactone reduced with Na/Hg to glucose.

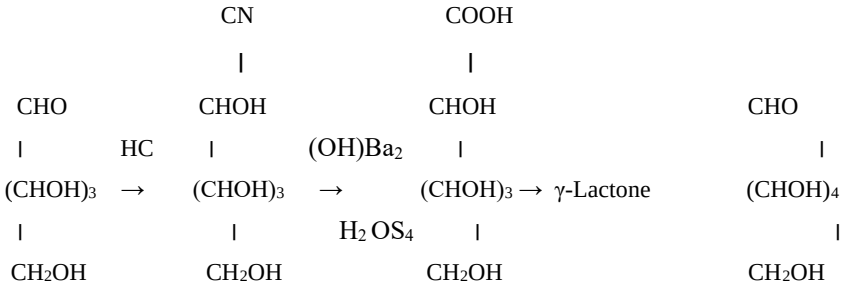


Arabinose to Glucose (or) Ascending (stepping up) the sugar series

Kiliani reaction (or) Aldopentose to aldohexose

(i) The aldopentose is dissolved in dil. HCN and the cyanohydrin obtained is hydrolysed with aqueous barium hydroxide. A polyhydroxy acid with six carbon atoms is obtained in aqueous solution.

(ii) The solution is evaporated to dryness when γ- lactone is obtained. This on reduction with sodium amalgam in fainly acid solution yields an aldohexose.

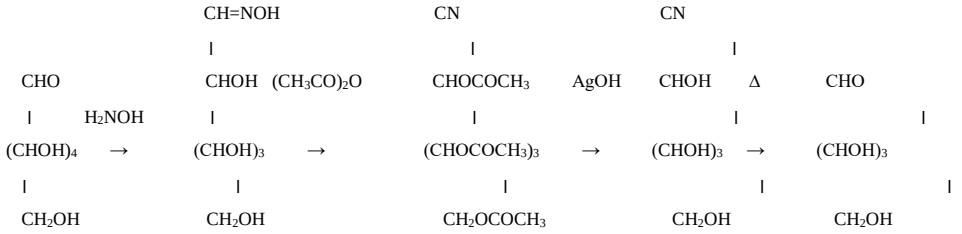


Aldopentose Cyanohydrin Polyhydroxy Aldohexose

Glucose to arabinosen or Descending (stepping down) the sugar series or Aldohexose to aldopentose (Wohl's method)

(i) The aldohexoses (Glucose) is treated with hydroxylamine and the oxime produced is heated with acetic acid anhydride. In this way the oxime is dehydrated to the cyano compound whereas the hydroxyl groups get acetylated.

(ii) The acetyl derivate is warmed with ammoniacal silver nitrate which removes the acetyl groups by hydrolysis and eliminates a molecule of HCN. An aldopentose (arabinose) is obtained as a result of these changes.



Aldohexose Oxime Cyanocompoud Alpentose

Disscharides- SUCROSE, $C_{12}H_{22}0_{12}$

Sucrose is an important disaccharide. It is one of the most important compounds commercially. It is available in plenty in many plants like sugar cane beet. They serves as raw materials for sucrose manufacture. It is also called **cane sugar**.

Properties

Physical : Sucrose is a colourless, crystalline substance (m.p. 461 K) sweet in taste and very soluble in water but only sparingly soluble in alcohol. It is optically active with specific rotation $+66.5^0$. It does not exhibit mutarotatio.

Chemical :

(i) Action of heat : When heated with a little water, it melts and given an amorphous glassy mass (barley sugar) on cooling.

(ii) Hydrolysis : On warming with dilute mineral acids, it gives glucose and fructose

By hydrolysis.

$$C_{12}H_{22}O_{11} + H_2O \rightarrow C_6H_{12}O_6 + C_6H_{12}O_6$$

Sucrose — Glucose — Fructose

$[\alpha] = 66.5^0$ — $+ 52.5^0$ — $- 92^o$

Invert sugar

The change is called inversion as dextro rotatory sucrose changes into laevo-rotatory mixture of glucose and fructose.

This reaction is brought out by invertase or sucrase enzyme.

(iii) Oxidation : With concentrated nitric acid, sucrose is oxidized to oxalic acid.

$$C_{12}H_{22}O_{11} + 18\,[O] \rightarrow 6\,(COOH)_2 + 5\,H_2O$$

(iv) Acetylation : With acetic anhydride sucrose gives octa-acetyl derivative.

(v) Fermentation : An aqueous solution of sucrose with yeast invertase and zymase gives ethanol by fermentation.

$$C_{12}H_{22}O_{11} + H_2O \xrightarrow{\text{invertase}} C_6H_{12}O_6 + C_6H_{12}O_6$$

$$C_6H_{12}O_{11} \rightarrow 2CO_2 + 2C_2H_5OH$$

(vi) Laevulic acid is produced by cane sugar is boiled with con. HCl

(vii) Conc.HCl

$$C_6H_{12}O_{11} \rightarrow CH_3COCH_2CH_2COOH$$

(viii) Sucrose solution reacts with lime to give calcium sucrose.

(ix) Dehydratio : With conc.H_2SO_4, it loses water to give sugar charcoal. A smell of sulphur dioxide is also notised due to reduction of the acid.

$$C_6H_{12}O_{11} \xrightarrow{H_2SO_4} 12C + 11H_2O$$

(x) Sucrose does not contain any aldehyde or ketone group.

Uses

Sucrose is used –

(i) as an article of food and as sweetening agent in sweets and drinks.

(ii) In fruit preservation.

(iii) In the preparation of oxalic acid in the laboratory

(iv) For the manufacture of octa-acetate which is used to denature the spirit.

(v) In the preparation of hydrophobic resins.

Structural Elucidation of Sucrose

(i) Molecular formula is $C_6H_{12}O_{11.}$

(ii) In the sucrose molecule glucose and fructose molecules are linked through an oxygen atom.

(iii) Sucrose is a non reducing sugar.

(iv) It does not give an oxime or an osazone. This shows clearly that neither the aldehydic group of glucose nor the ketonic group of fructose is free in sucrose.

(v) It gives octa-acetyl derivative showing the presence of eight hydroxyl groups.

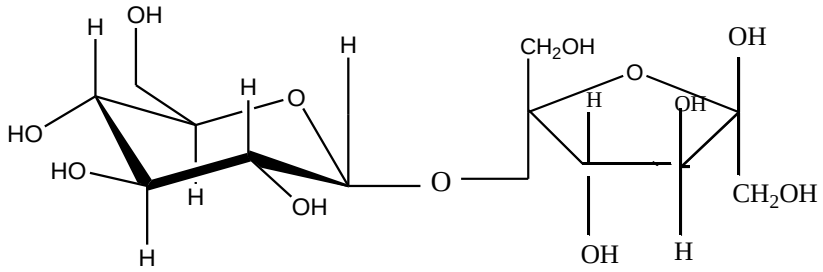
(vi) On complete methylation sucrose yields the octa-methyl derivative which on hydrolysis, yields-

(a) 2:3:4:6 – tetramethyl – δ – glucose and

(b) 1:3:4:6 – tetramethyl – γ – fructose.

This shows that fifth carbon (C_5) in both cases, has no OH group which could be methylated. Absence of –OH groups with these carbon atoms suggested that they must have participated in ring formation in their respective molecules.

Bearing in mind all the foregoing facts, the following structure was assigned to it by Haworth.



α- D –glucopyranosyl - β – D - fructofuranose

MALTOSE, $C_{12}H_{22}O_{11}$

It is known as malt sugar. It is obtained by the action of enzyme diastase present in malt or starch.

$$2(C_6H_{10}O_5)n + nH_2O \rightarrow nC_{12}H_{22}O_{11}$$

Starch Maltose

Properties

Physical :

(i) It is a white crystalline solid (m.p. 438 K)

(ii) It is very soluble in water and the solution is dextro rotatory.

(iii) It is sweet in taste.

Chemical :

(i) It forms an oxime and cyanohydrin.

(ii) It forms an osazone with phenylhydrazine.

(iii) It undergoes mutarotation. The specific rotation of α-form is $+168^o$; β-is $+112^o$; equilibrium mixture is $+136^o$

(iv) It is a reducing sugar e.g. It reduces Fehlings solution and tollens reagent.

(v) Oxidation with bromine water forms maltobionic acid.

These reactions (i) to (v) indicate that at least one aldehydic group of the two molecules of glucose is free in maltose.

(vi) On hydrolysis with dilute hydrochloric acid or the enzyme maltose, it gives two molecules of glucose.

$$C_{12}H_{22}O_{11} + H_2O \rightarrow C_6H_{12}O_6 + C_6H_{12}O_6$$

(vii) On acetylation gives octa-acetyl derivative and on methylation it forms octa-methyl derivate.

These reactions indicate the presence of eight hydroxyl groups in maltose.

Based on the above reactions the structure of maltose is given as follow.

Maltose finds use in the manufacture of malted milk and various types of food for the infants.

POLYSACCHARIDES

STARCH, $(C_6H_{10}0_5)n$

Starch is present in plenty in all green plants. Wheat, barley, potatoes and maize have large amount of starch. The general formula is **$(C_6H_{10}0_5)n$.** The value of n may range from 12 to 1000. Hence the structure of starch is complex. Starch can be regarded as complex, natural polymer or biomole formed using α-glucose units.

Properties

Physical :

(i) It is tasteless

(ii) It is odourless

(iii) It is amorphous powder, soluble in water

Chemical:

(i) Action of heat: When heated to 470-530^{0}K starch changes into dextrin a gummy substance. Charring occurs at higher temperature.

(ii) Hydrolysis : When boiled with dilute mineral acids, it is first converted into dextrin and firmly into glucose.

$$\underset{\text{Starch}}{(C_6H_{10}O_5)n} \rightarrow \underset{\text{Dextrin}}{(C_6H_{10}O_5)m} \rightarrow \underset{\text{Glucose}}{(C_6H_{12}O_6)}$$

Hydrolysis of starch with malt extract containing the enzyme diastase gives maltose.

$$\underset{\text{Starch}}{2(C_6H_{10}O_5)n} + nH_2O \xrightarrow{\text{Diastase}} \underset{\text{Maltose}}{n(C_{12}H_{22}O_{11})}$$

There are two components in starch. They are-

(A) Amylose (B) Amylopectin

These are discussed in detail.

Amylose :

It constitutes 17-34% of starch. It is soluble in water. It gives a blue colour with iodine. This is due to occlusion of iodine molecule in the helix of starch.

The aqueous solution of amylase tends to become insoluble, Hence, it forms precipitate slowly.

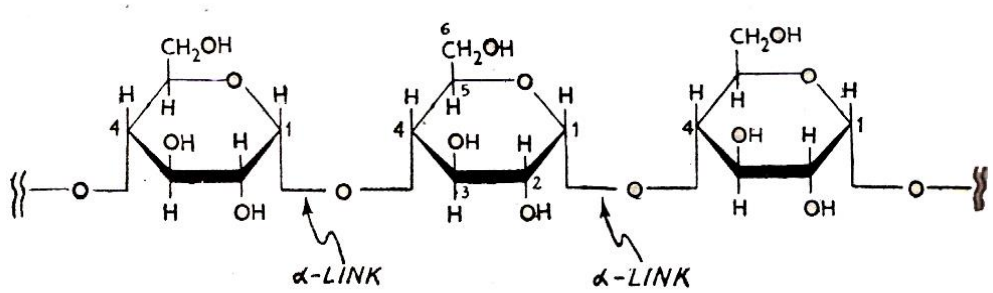
With diastase it gives maltose.

With nitration mixture, it forms nitrostarch.

On hydrolysis using mineral acids, it forms dextrin first and forms glucose finally.

The molecular weight of amylase is the order of $1x\ 10^6$. The molecular is linear with straight chain compound of approximately 300 glucose unit.

Structure



AMYLOSE

Amylose is a straight chain compound having many α-glucose units. One glucose unit is connected with another glucose unit through α-glucoside linkage. This linkage occurs using C1 of the first glucose unit and C4 of second glucose unit. Hence, there is no branching in amylase.

Amylopectin

It constitutes 66-87% of starch. It is insoluble in water. It gives violet colour with iodine. With diastase, it gives maltose.

It also gives nitrostarch with nitration mixture.

On hydrolyzing using mineral acids, dextrin is formed initially and glucose finally.

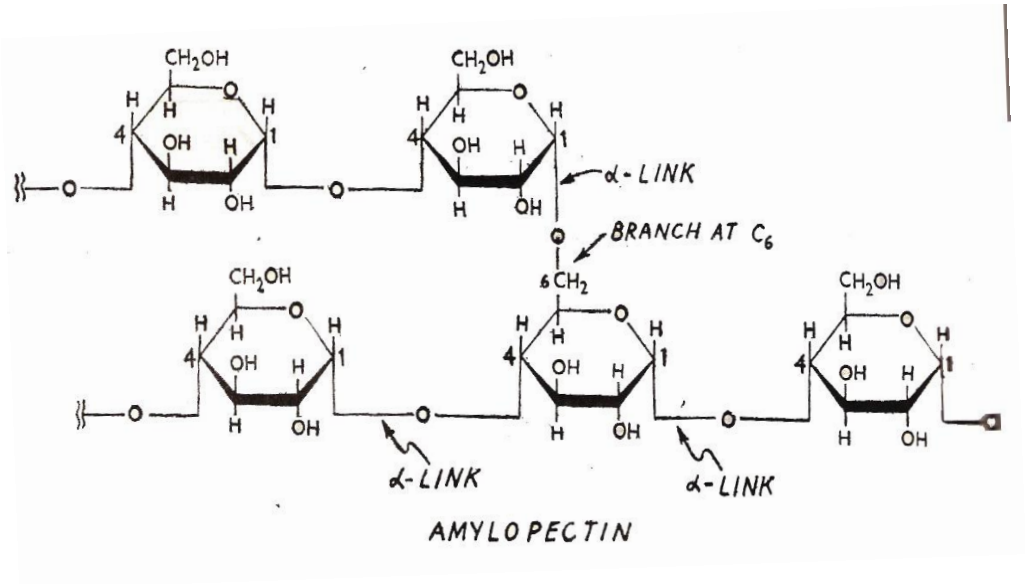
At higher temperature, amylopectin chars.

The molecular weight of amylopectin is of the order of 5×10^6.

It is composed of about 1000 glucose units.

Along with α-1,4-glucosidic linkages (as in amylase) it has few α-1,6-glucosidic linkages.

Hence amylopectin has branched structure as follow.



Uses

Starch is used –

(i) as food

(ii) in textiles

(iii) in laundering

(iv) in the manufacture of paper, glucose, ethanol,dextrin etc.

(v) as an indicator in volumetric analysis.

Table

Differences between amylase and amylopectin

S.No.	Amylose	Amylopectin
1.	Constitutes 17-34% of starch	Constitutes 66-83% of starch
2.	It is soluble in water	It is insoluble in water
3.	Gives blue colour with iodine	Imparts violet colour with iodine
4.	Has molecular weight about $1x10^6$	Has molecular weight about $5x10^6$
5.	Has about 300 glucose units	Has about 1000 glucose units
6.	Has linear structure	Has linear structure with few branched structures.

CELLULOSE, $(C_6H_{10}O_5)n$

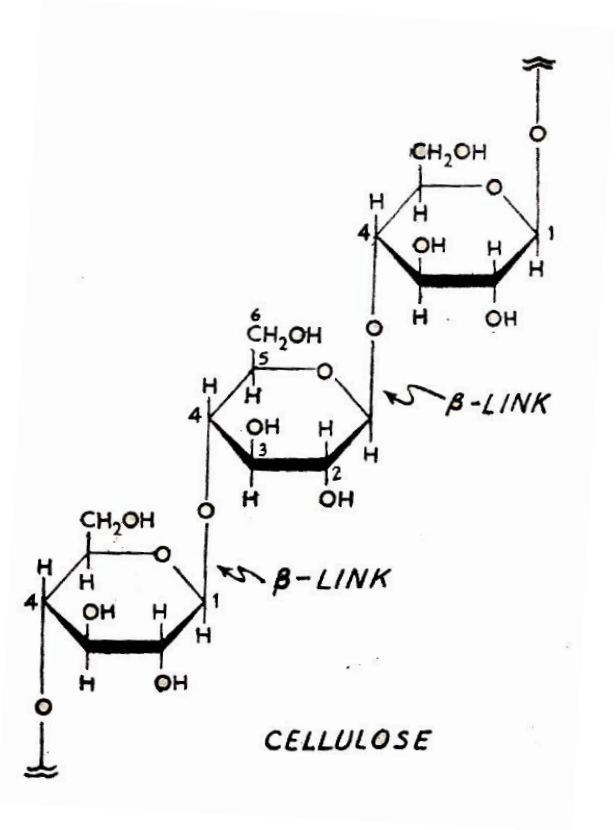
Cellulose is the main constituent of the cell walls of plants. It is present in the tissues of few animals. Cotton and wood constitute two main sources of cellulose. Cotton and filter paper are almost pure cellulose. The molecular formula is **$(C_6H_{10}O_5)n$.** The value of n ranges from 1000 to 10000. Hence, its molecular weight is higher than starch. Cellulose is the biopolymer containing β-glucose units.

Properties

Physical : Cellulose is a white amorphous solis, insoluble in water, but soluble in ammoniacal copper hydroxide solution called **Schewitzer's reagent.**

Chemical :

(i) On hydrolyzing cellulose carefully it gives cellulobiose first and gives β-glucose finally. Cellulose has linear without branching as given below.



(ii) Action of conc. H_2SO_4: Cellulose dissolves in cold, concentrated sulphuric acid but is precipitated as amyloid on dilution.

(iii) Action of alkali : Cellulose is unaffected by dilute alkali. It immersed in strong caustic soda solution, stretched cotton

(iv) With acetic anhydride : Cellulose is unaffected by dil.alkali. If immersed in caustic soda solution, stretched cotton fibres, swell and become rounded, stronger and more lustrous (silky appearance). This process is called mercerizing.

(v) Nitration : Cellulose is nitrated in a dilute mixture of nitric acid and

sulphuric acid when mono-and dinitrates are obtained and are known as pyroxylin in the solid state. Pyroxylin is dissolved in a mixture of alcohol and ether to get collodion. It has plastic property.

The transparent plastic material obtained when pyroxylin is heated with camphor under pressure is called celluloid. It can be moulded while hot.

With a mixture of conc.H_2SO_4 and HNO_3 it forms cellulose trinitrate called Gun cotton.

(vi) When cellulose is heated to 373 K with organic chloride in presence of alkalis, it forms cellulose ethers.

(vii) Like sucrose, cellulose does not reduce Fehlings solution and Tollens reagent. It does not form osazone.

(viii) Cellulose is not hydrolysed by enzymes.

Uses

1. Cellulose serves as raw material for the manufacture of clothes and rayons.
2. It finds use in the manufacture of paper, celluloid, collodion films, cinema films and explosives.
3. Celluloid is used in making toys and other articles of daily use.
4. Collodion is being used in medicine, photography and in the manufacture of rayons.
5. Gun cotton is used in the manufacture of smokeless powders.
6. Cellulose acetate is used in the manufacture of cinema films, varnishes, lacquers, safety glass.
7. Cellulose ether is used in the production of insulators and toilet fittings.

TABLE

COMPARISON OF STARCH WITH CELLOSE

S.No.	Starch	Cellulose
1.	It is the polymer of α-glucose	It is the polymer of β-glucose.
2.	It has low molecular weight	It has high molecular weight.
3.	It has linear structure with few branched structure.	It has linear structure.
4.	It has no tendency to become fibre.	It has tendency to form fibres.
5.	It serves as the food for human beings.	It serves as the food for cud chewing animals.
6.	It has limited industrial applications.	It has ample industrial applications.

NOTES

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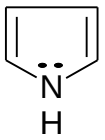
UNIT – III

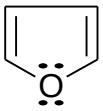
3.1 HETEROCYCLIC COMPOUNDS

Heterocyclic compounds, or heterocycles, are cyclic compounds in which one or more of the atoms are hetero atoms. A variety of atoms, such as N, O and S, can be incorporated into ring structures. Some of the important heterocyclic compounds are:

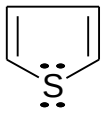
5-Membered Heterocyclic Compounds:



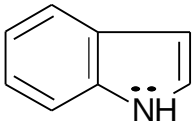
Pyrrole



Furan

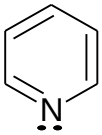


Thiophene

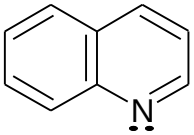


Indole

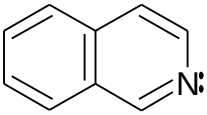
6-Membered Heterocyclic Compounds:



Pyridine

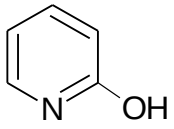


Quinoline

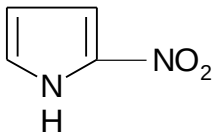


Isoquinoline

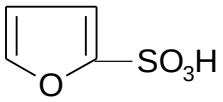
1. Heterocycles make up an exceedingly important class of organic compounds. Almost all compounds we know us drugs, most vitamins, and many other natural products are heterocyclic compounds.
2. Most of the heterocyclic compounds are known by their common names. For naming their derivatives, the hetero atom is always numbered as 1. 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.



2-Hydroxypyridine



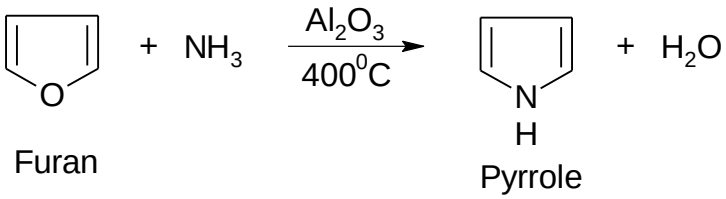
2-Nitropyrrole



2-Furansulphonic acid

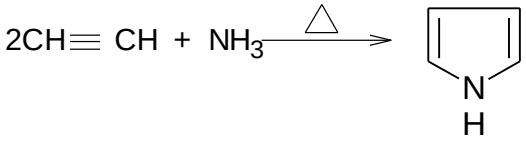
Synthesis of Pyrrole:

Pyrrole is obtained by passing a mixture of furan and ammonia over alumina at 400^0C.

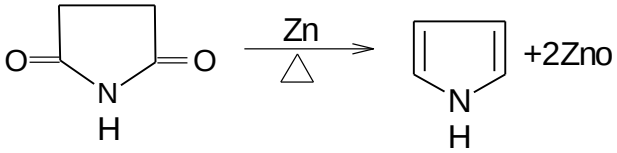


Furan Pyrrole

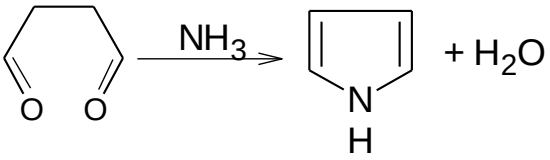
2. By passing a mixture of acetylene and ammonia through a red hot tube



3. By heating succinimide with Zinc dust.

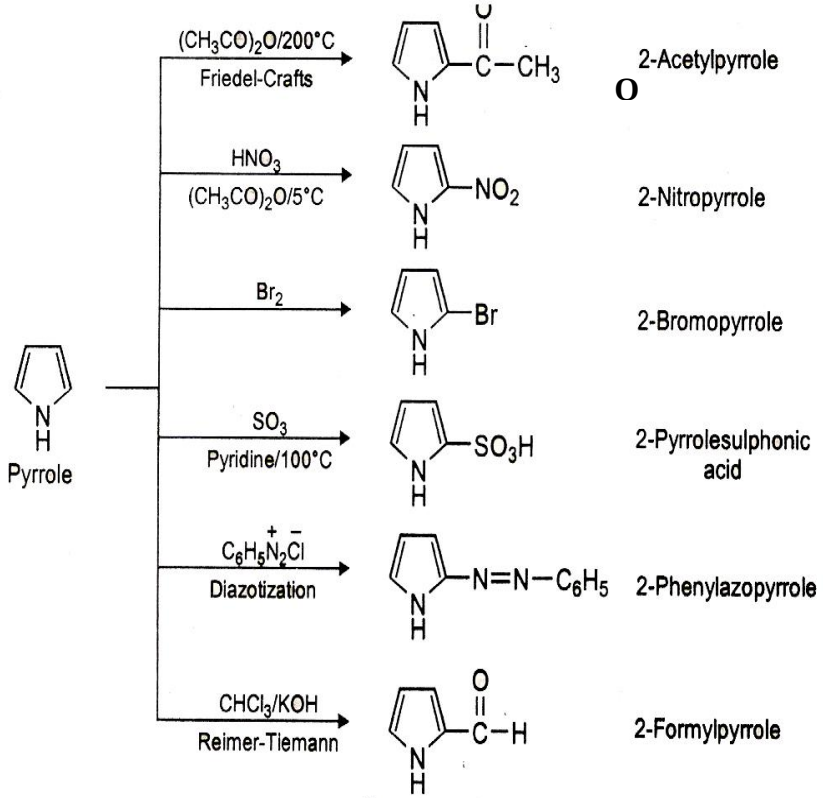


4. By warming succinic dialdehyde with NH_3.



Important Reactions of Pyrrole:

Pyrrole undergoes electrophilic substitution at 2-position.

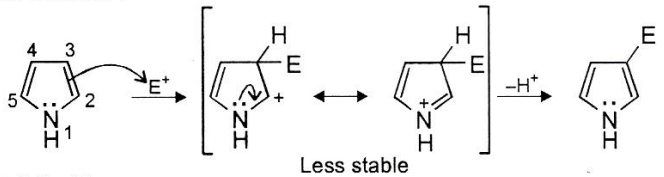


Reactions of pyrrole.

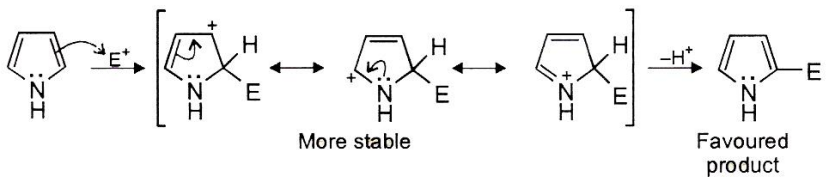
Pyrrole undergoes Electrophilic substitution at 2-position:

Attack of the electrophile at 3-position in pyrrole leads to an intermediate with only two resonance structures. Three resonance structures are possible for the intermediate produced by attack at 2-position. That is, the intermediate produced by attack at 2-position is more stable. This is the reason that electrophilic attack occurs at 2-position rather than at 3-position. E^+ in the following equations represents an electrophile.

Attack at 3-Position :

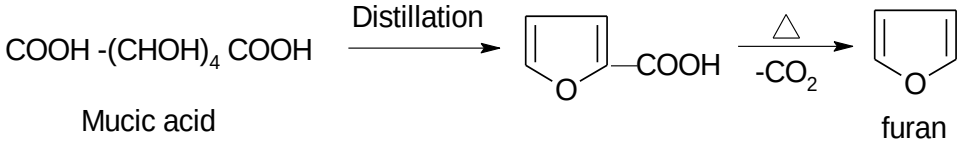


Attack at 2-Position :

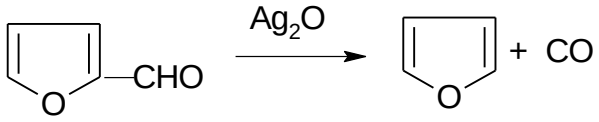


Synthesis of Furan

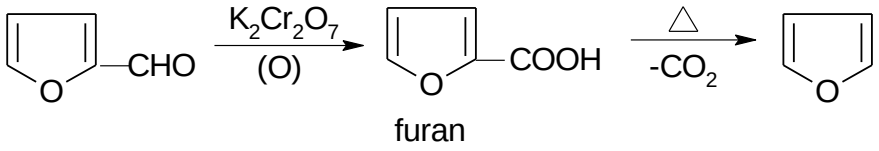
1) Dry distillation of mucic acid and heating the products, furoic acid at 200 – 300°C.



2) By decarnylation of furfural

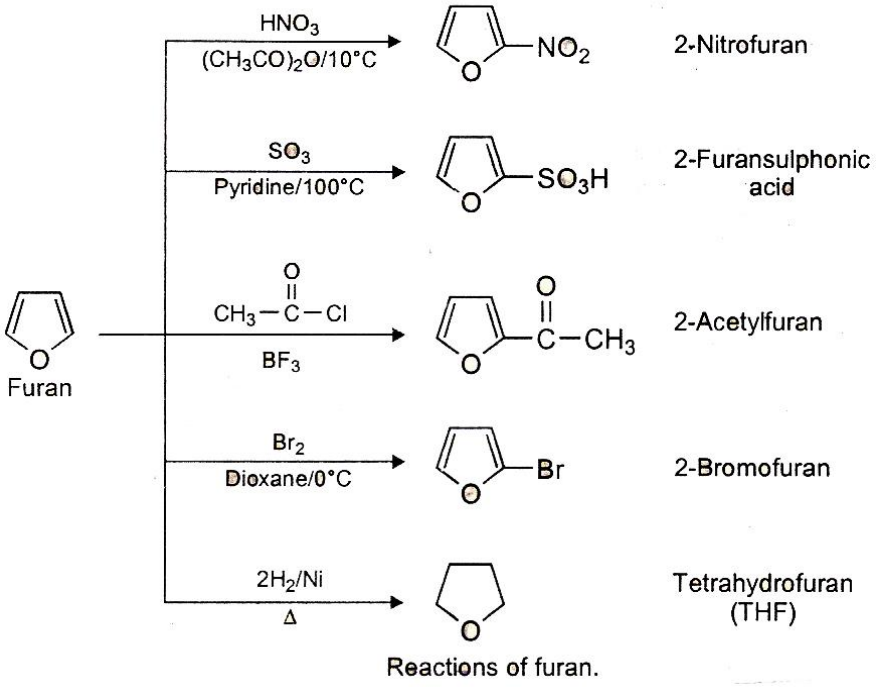


3) Oxidationof furfuraldehyde and decarboxylation.



Important Reactions of Furan:

Furan, like pyrrole, undergoes electrophilic substitution reactions at 2-position.

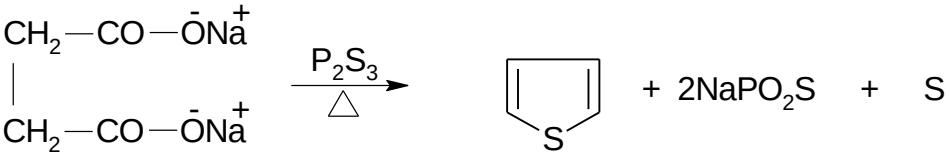


Reactions of furan.

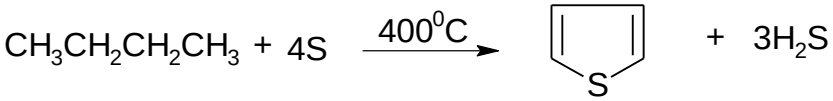
Synthesis of Thiophene:

Thiophene is obtained:

(1) By heating sodium succinate with phosphorus trisulphide.



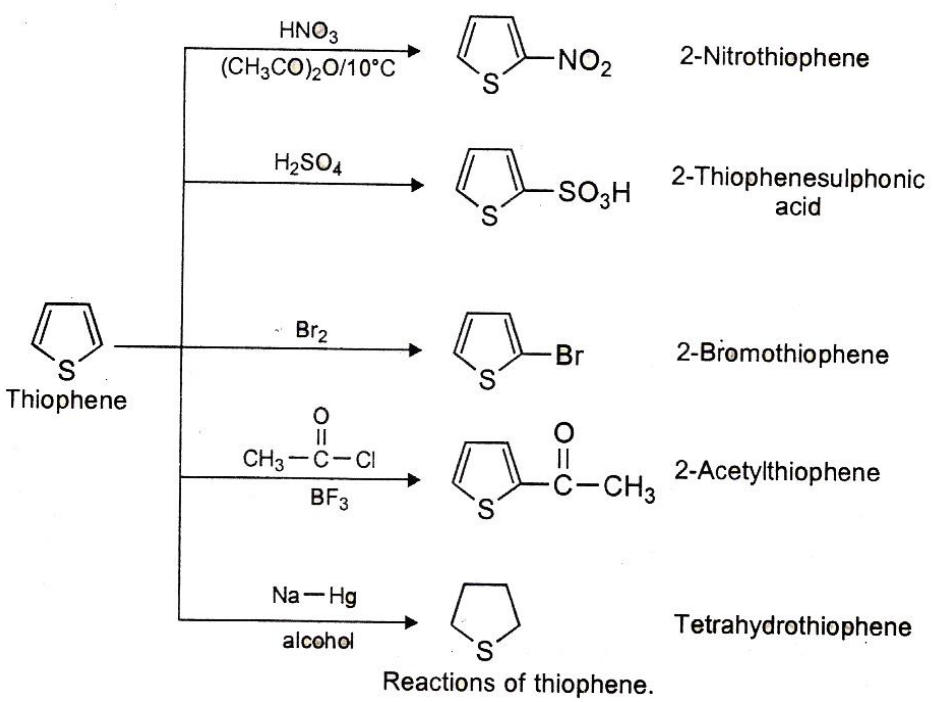
(2) By heating *n*-butane with sulphur at 600^0C.



n-Butane Thiophene

Important Reactions of Thiophene:

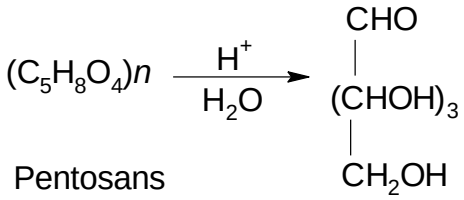
Thiophene, like furan and pyrrole, undergoes electrophilic substitution reactions at 2-position.



Reactions of thiophene.

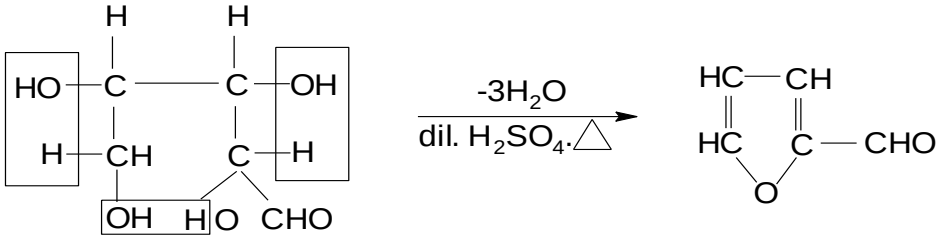
Preparation and Properties of Furfural:

Furfural is obtained from agricultural waste materials such as corncobs, oat hulls, rice hulls, and bagasse, which are rich in pentosans (C_5-polysaccharides). The pentosans on acid hydrolysis give pentoses (mainly xylose) that dehydrate to yield furfural on distillation.



Pentosans

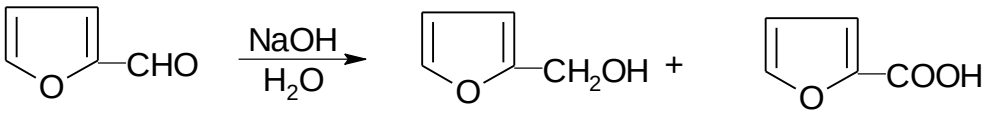
Aldopentose



Chemical Properties:

Furfural gives the following important reactions:

(1) Cannizzaro Reaction:

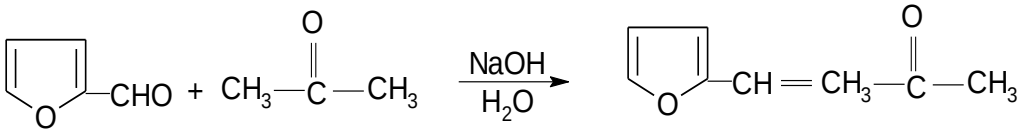


Furfural

Furyl alcohol

Furoic acid

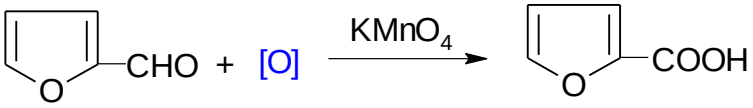
(2) Claisen-Schmidt Condensation:



Furfural

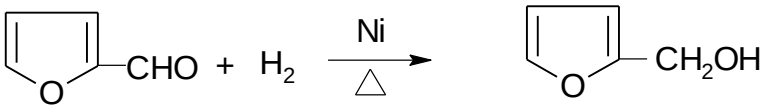
Furylidene acetone

(3) Oxidation:



Furfural Furoic acid

(4) Reduction:



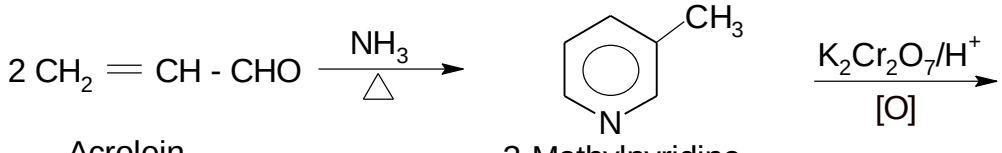
Furfural Tetrahydrofurfuryl alcohol

1. Pyridine is a colourless liquid, bp 115.5^0C. It is soluble in water and most organic solvents.
2. Pyrrole is a colourless liquid, bp 131^0C. It is only slightly soluble in water but totally soluble in ether and alcohol.
3. Furan is a colourless liquid, bp 31.4^0C. It is insoluble in ether but soluble in most organic solvents.
4. Furfural is a colourless liquid, bp 162^0C. It is soluble in water and most organic solvents.
5. Thiphene is a colourless liquid, bp 84^0C. It is insoluble in water but freely soluble in alcohol, ether, and acetone.

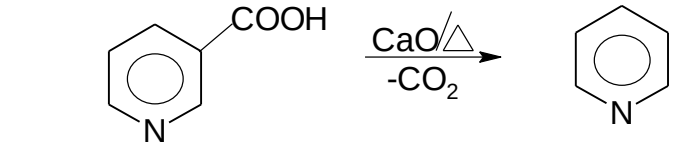
3.2 SYNTHESIS OF PYRIDINE:

Pyridine may be obtained:

(1) From acrolein by the following steps:

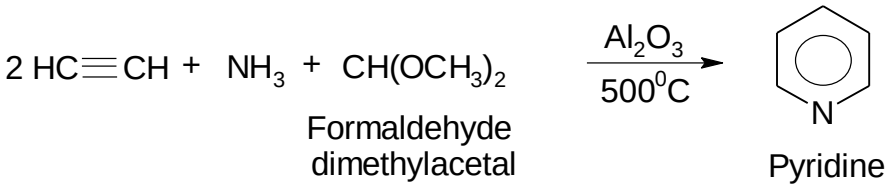


Acrolein 3-Methylpyridine



3-Pyridinecarboxylic acid Pyridine

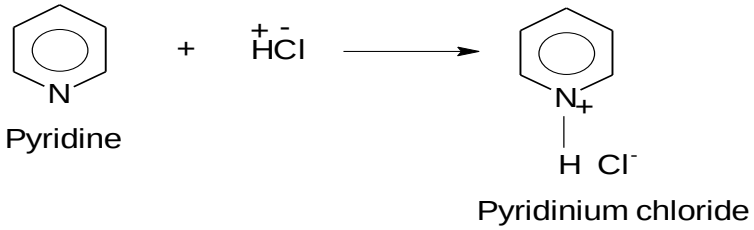
(2) By heating a mixture of acetylene, ammonia and formaldehyde dimethylacetal in the presence of Al_2O_3 at 500^0C. (Commercial method)



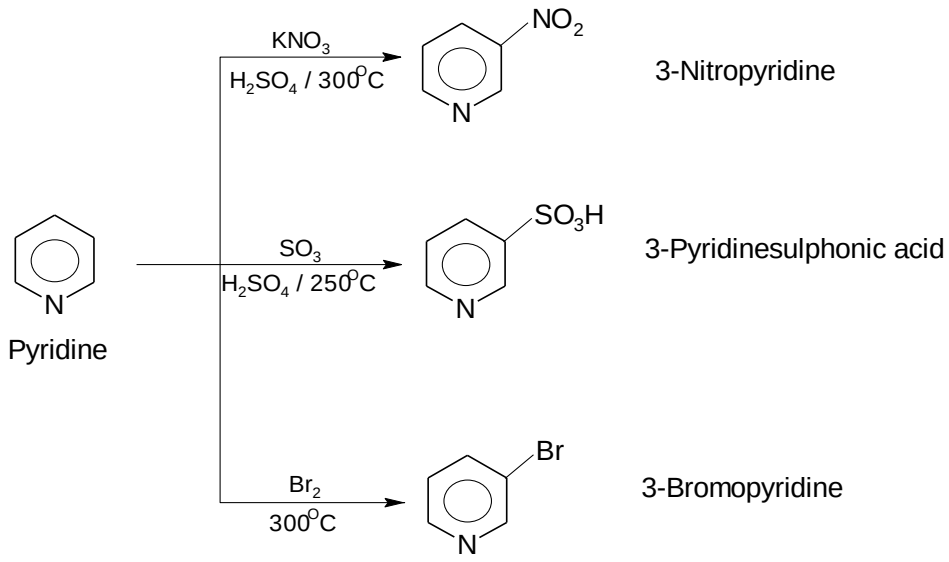
Important Reactions of Pyridine:

Some important reactions of pyridine are given below:

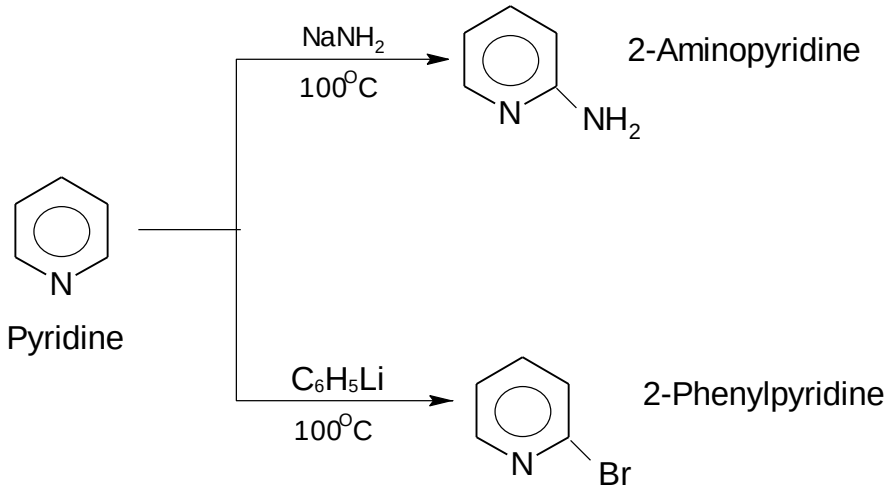
(1) Salt Formation: Pyridine is basic. It reacts with strong acids to form salts.



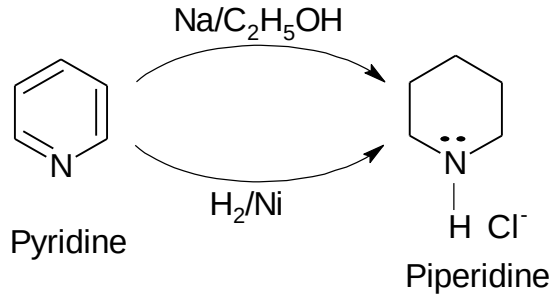
(2) Electrophilic Substitution Reactions: Pyridine undergoes electrophilic substitution reactions at 3-position only under vigorous conditions. Examples are,



(3) Nucleophilic Substitution Reaction: Pyridine undergoes nucleophilic substitution reactions at 2-position. Examples are:

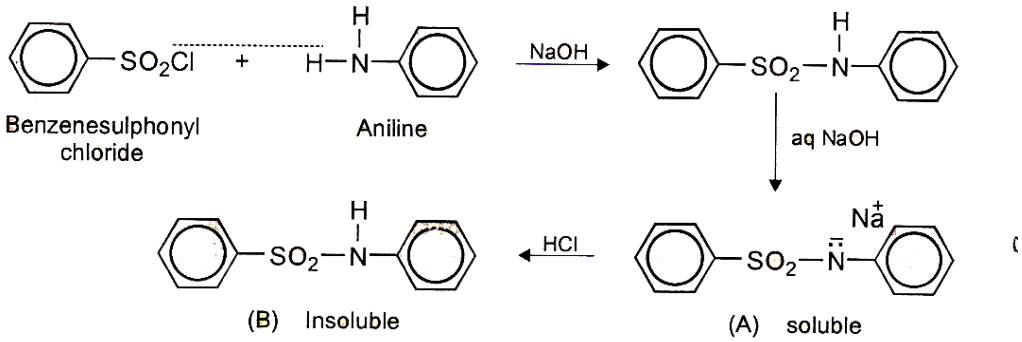


(4) Reduction: Pyridine undergoes reduction with Na/C_2H_5OH or H_2/Ni to form piperidine.

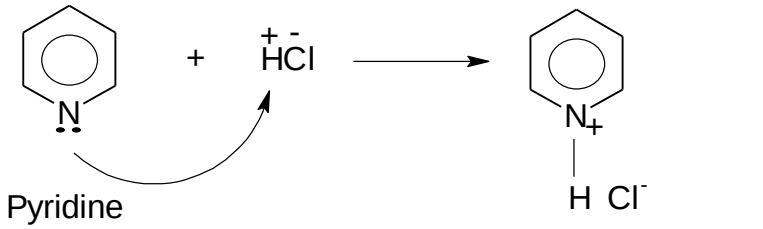


Distinction between Pyridine and Aniline:

Aniline (1^0 amine) gives Hinsberg test, pyridine does not. When aniline is shaken with benzenesulphonyl chloride in dilute aqueous sodium hydroxide solution, a clear solution is formed (Soluble salt A is formed). Acidification of this solution gives a precipitate (Insoluble sulphonamide B is formed).

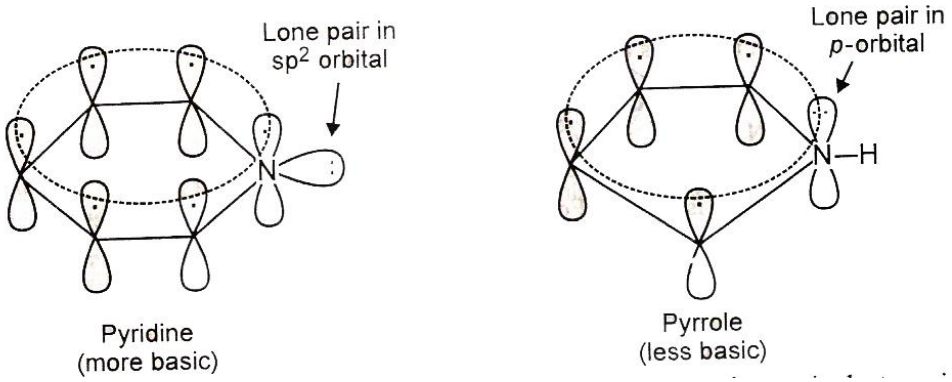


Pyridine is basic ($pK_b = 8.75$). It reacts with strong acids to form salts.



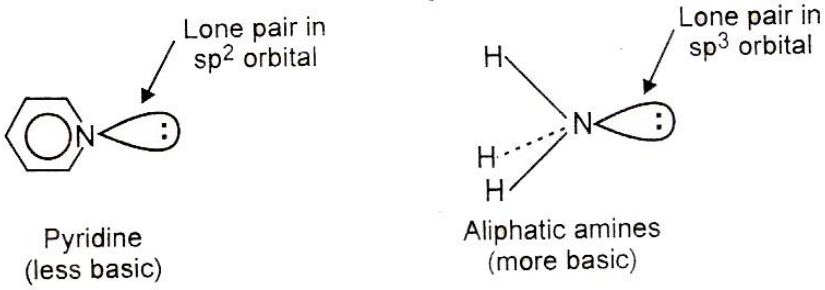
Pyridine is more basic than pyrrole. This is because the nitrogen lone pair electrons in pyrrole are in p orbital and form part of the delocalised π molecular orbital. They are not available for the formation of a new N-H bond with proton.

The reason for the basic character of pyridine is that the nitrogen lone pair electrons are in sp^2 hybrid orbital and are not involved in the formation of the delocalised π molecular orbital. It is readily available for the formation of a new N-H bond with proton.



Pyridine is less basic than aliphatic amines. (Pondicherry BSc,2000)

Pyridine is less basic (pK_b = 8.75) than aliphatic amines (pK_b = 4). This is due to the difference in the nature of hybrid orbitals containing the nitrogen lone pair electrons.



In pyridine it is in an sp^2 orbital; in aliphatic amines it is in an sp^3 orbital. We know that sp^2 orbital are smaller (due to more s character) than sp^3 orbitals. This means that the lone pair of electron; on nitrogen in pyridine is more closely associated with the nitrogen nucleus. It is, therefore, less available

for the formation of bond with proton and consequently the relative basicity is reduced.

Pyridine and pyrrole are aromatic.

There are three requirements (**Aromaticity Rules**) for a molecule to be aromatic:

1. An aromatic molecule is cyclic and planar.
2. Each atom in an aromatic ring has a p orbital. These p orbitals must be parallel so that a continuous overlap is possible around the ring.
3. The cyclic π molecular orbital formed by overlap of p orbitals must contain (4n + 2)pi electrons, where n = integer 0, 1, 2, 3, etc. This is known as **Huckel Rule**.

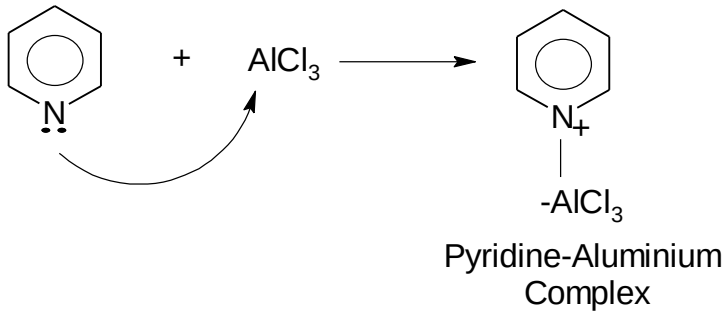
Pyridine and pyrrole are both aromatic. Both obey the above aromaticity rules: they are cyclic and planar; each has a p orbital on every ring atom; and each obeys the Huckel Rule (both have 6π electrons; n = 1).

Pyridine has low reactivity toward electrophilic substitution.

Pyridine contains an electronegative nitrogen and therefore is polar. Because the nitrogen is more electronegative than carbon, the rest of the pyridine ring is electron-deficient. An electron deficient ring means that the carbon atoms in the ring carry a partial positive charge. A pyridine ring therefore has low reactivity toward electrophilic substitution.

Pyridine undergoes Friedel-Crafts Alkylation:

This is because the Lewis acids ($FeCl_3$ or $AlCl_3$) which are used as catalysts in these reactions coordinate with the lone pair of of electrons on nitrogen to form a complex.



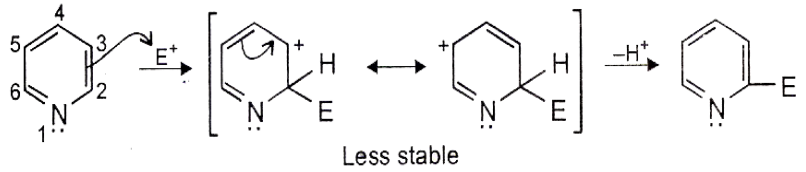
Pyridine-Aluminium Complex

Pyridine undergoes electrophilic substitution at 3-position:

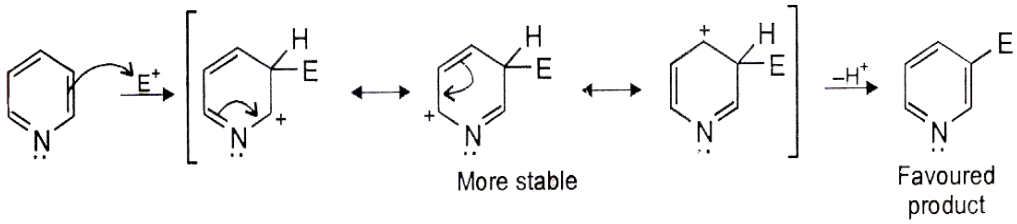
Attack of the electrophile at 2-position (or 4-position) in pyridine leads to an intermediate with only two important resonance contributing structures. Three resonance structures are possible for the intermediate produced by attack at 3-position. That is, the intermediate produced by the attack at 3-position is

more stable. This is the reason that electrophilic attack occurs at 3-position. E^+ in the following equations represents an electrophile.

Attack at 2-Position:



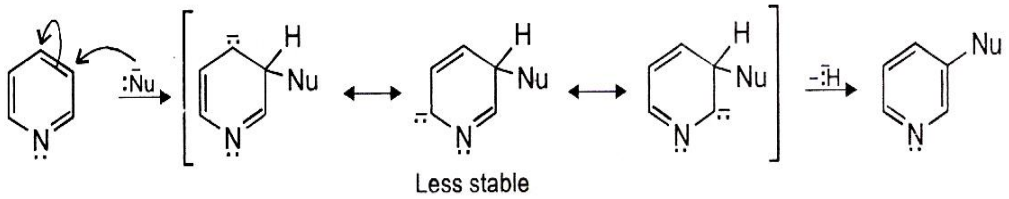
Attack at 3-Position :



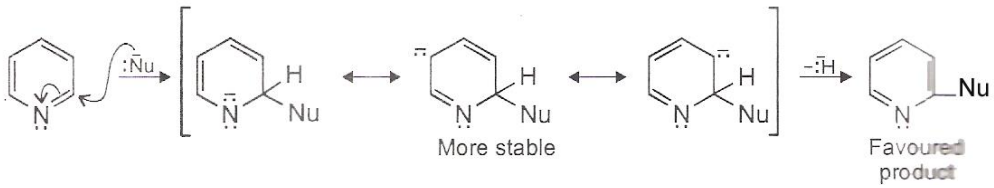
Pyridine undergoes nucleophilic substitution at 2-position:

Attack of the nucleophilic at 3-position in pyridine leads to an intermediate with three resonance contributing structures. Attack of the nucleophile at 2-position (or 4-position) also gives an intermediate with three resonance structures. (Attack at 4-position resembles attack at 2-position). This position is attacked only when 2-position is blocked). $Nu:^-$ in the following equations represents a nucleophile.

Attack at 3-Position :



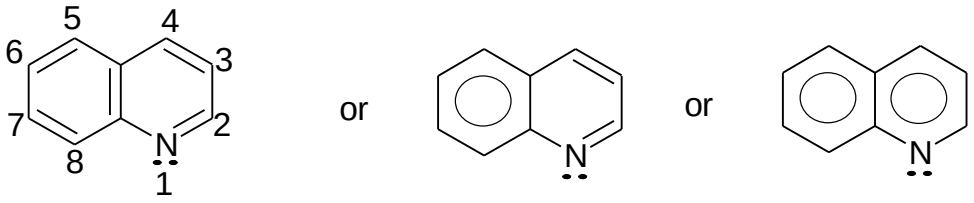
Attack at 2-Position :



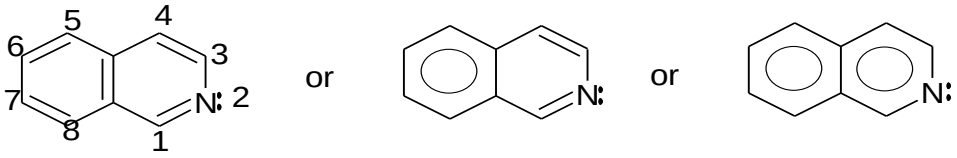
Notice that the attack at 2-position gives resonance structure in which the electronegative nitrogen carries a negative charge. This structure is especially stable and leads to greater stability of the intermediate. This is the reason that nucleophilic attack occurs at 2-position rather than at 3-position.

3.3 QUINOLINE AND ISOQUINOLINE:

Quinoline and Isoquinoline are represented as shown below. In these compounds, the numbering system is fixed by convention and does not change with the position of the hetero atom.



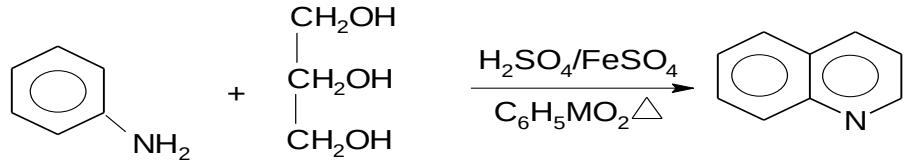
Quinoline



Isoquinoline

Synthesis of Quinoline:

Quinoline is obtained by Skraup Synthesis. In this method, a mixture of aniline and glycerol is heated in the presence of sulphuric acid and nitrobenzene (mild oxidising agent). The reaction is exothermic and tends to become violent. Ferrous sulphate is generally added to make the reaction less violent.

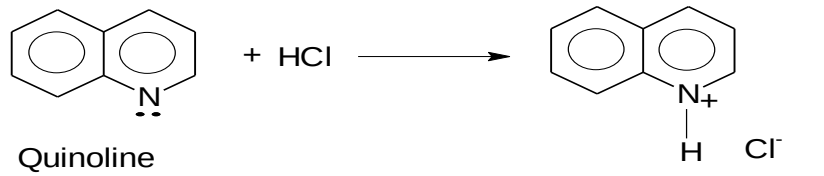


Aniline Glycerol Quinoline

Important Reactions of Quinoline:

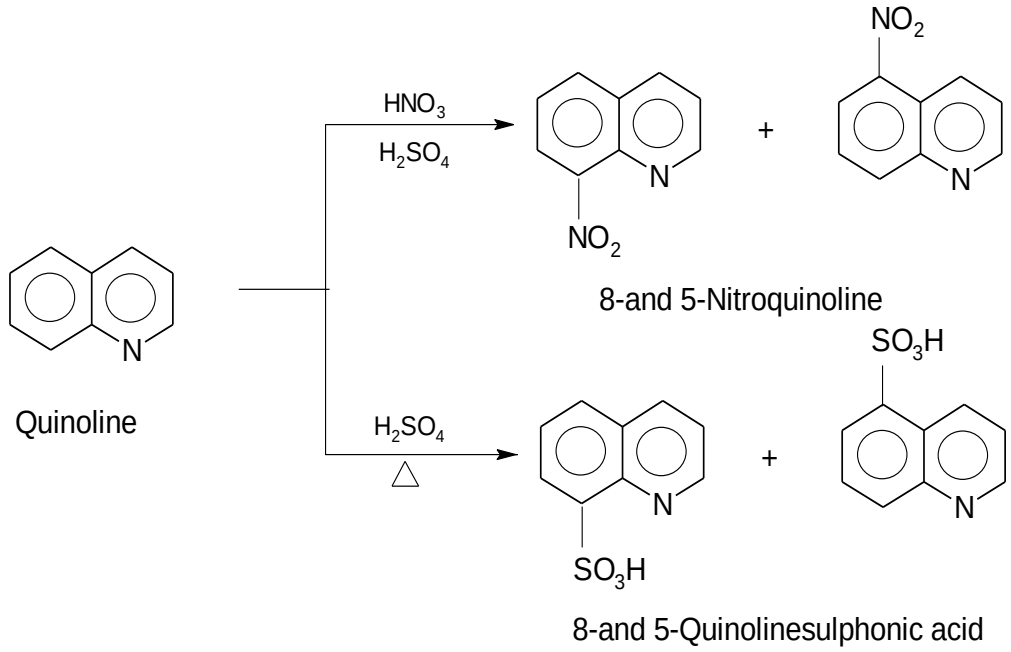
The important reactions of Quinoline are:

(1) Salt Formation : Quinoline is basic. It reacts with acids to form salts.

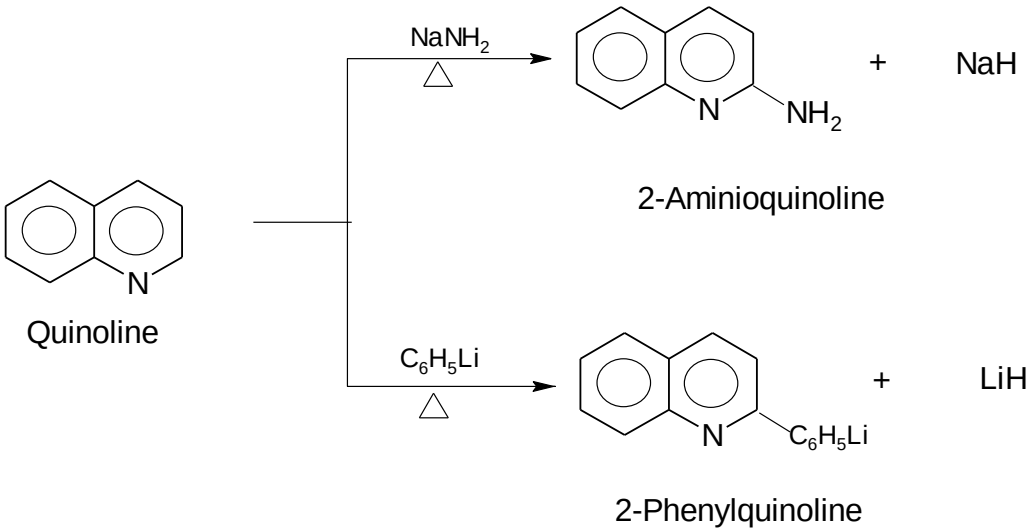


Quinoline Quinoline hydrochloride

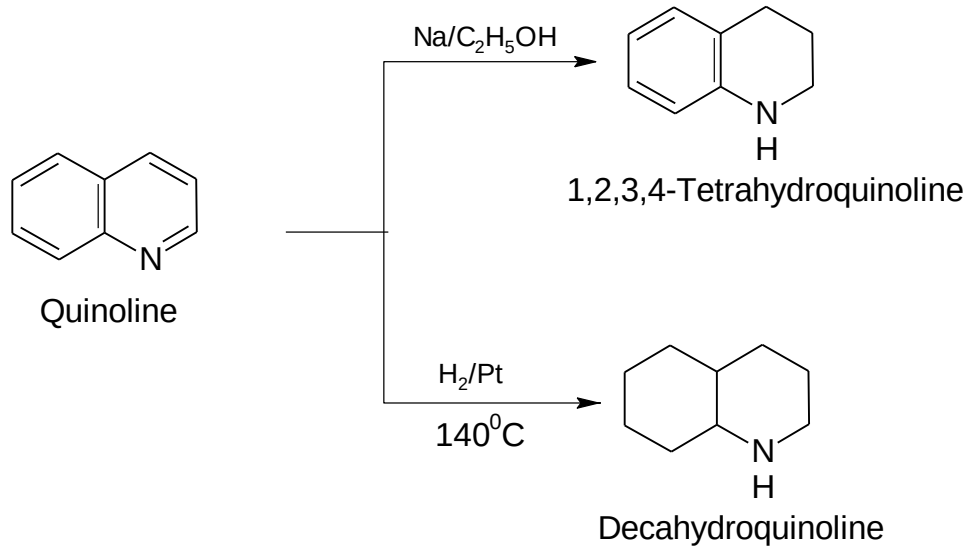
(2) Electrophilic Substitution Reactions: Quinoline undergoes electrophilic substitution reactions at 8-position and 5-position. For example,



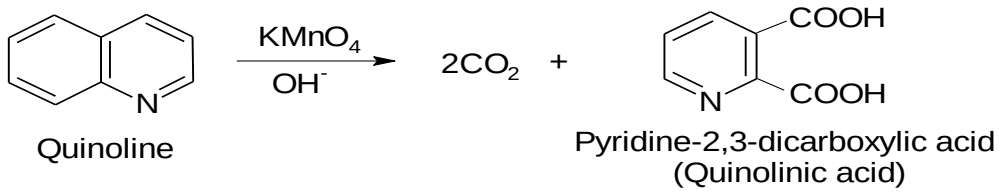
(3) Nucleophilic Substitution Reactions: Quinoline undergoes nucleophilic substitution reactions at 2-position. For example,



(4) Reduction: Mild reduction of quinoline with Na/C_2H_5OH gives 1,2,3,4-tetrahydroquinoline. Catalytic reduction gives decahydroquinoline.



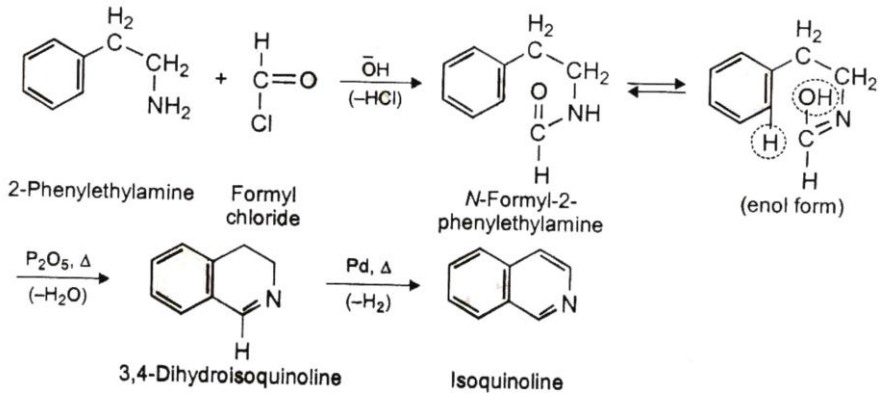
(5) Oxidation: Quinoline undergoes oxidation with alkaline $KMnO_4$ to give pyridine 2,3-dicarboxylic acid (Quinolinic acid).



When quinolinic acid is heated, it gives pyridine-3-carboxylic acid (Nicotinic acid).

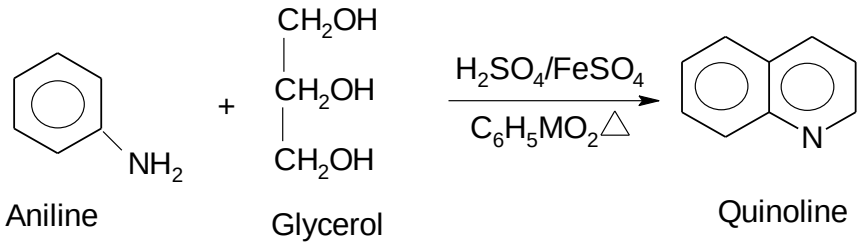
Synthesis of Isoquinoline:

Isoquinoline is prepared by Bischler-Napieralski synthesis. In this method, 2-phenylethylamine is used as a starting material.



Skraup Synthesis:

Skraup synthesis is used for the commercial preparation of quinoline. In this reaction, a mixture of aniline and glycerol is heated in the presence of sulphuric acid and nitrobenzene. The reaction is exothermic and tends to become violent. Ferrous sulphate is added to make the reaction less violent.



Mechanism:

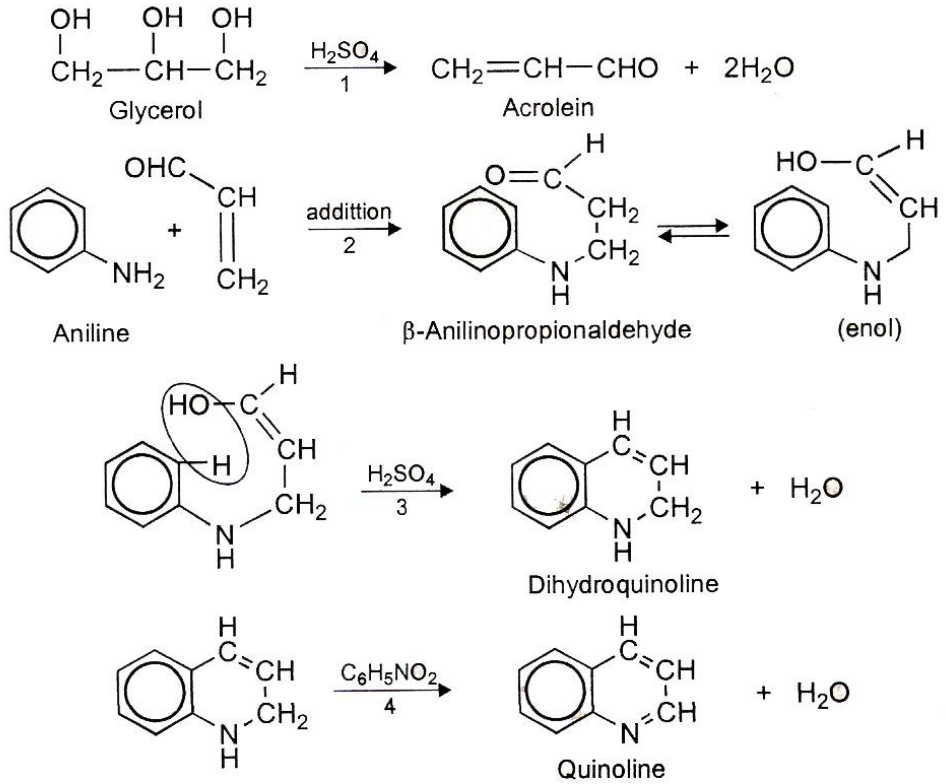
The Skraups reaction is believed to proceed by the following steps:

(1) Glycerol dehydrates with H_2SO_4 to form acrolein;

(2) Acrolein undergoes 1,4-addition with aniline;

(3) The resulting β–anilinopropionaldehyde cyclizes to dihydroquinoline;

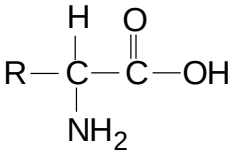
(4) Dihydroquinoline is oxidised to quinoline, while nitrobenzene is reduced to aniline which is reused.



The Skraup synthesis is also important because by starting with substituted anilines, substituted quinolines can be made.

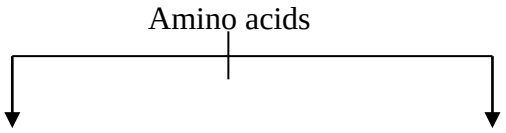
3.4 Amino Acids

- An amino acid is bifunctional organic molecule, that contains both a carboxylic group (COOH) as well as on amino group (NH_2).
- It is derived from proteins have the amino group on the alpha(α) carbon.
- α-amino acid may be represented as



a - amino acid

- The nature of R-group determines the properties of proteins.
- Nearly 25-amino acids from hydrolysis of proteins.
- Nearly 51-amino acids from insulin.

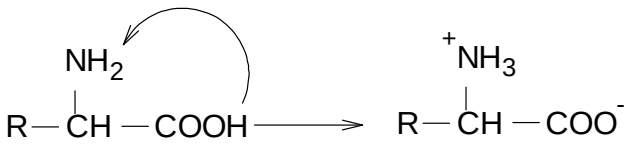


1. <u>Essential amino acids</u>	2. <u>Non-essential amino acids</u>
Cannot be synthesised by body and supplied in the diet	Syntheissed from others Compounds by the tissues of the body
eqs: as valine, leucine, Tryptophan phenyl analine, methionine	eqs: glycene, Alanine, proline, cystine, serine, cystein.

Glycine is optically inactive no asymmetric carbon, all other are optical isomers.

Due to the presence of both acidic and bosic group, amino acids exists in an ionic form called a zwitterion.

A proton is transffered from –COOH- gp to NH_2gp.



Zwitter ion

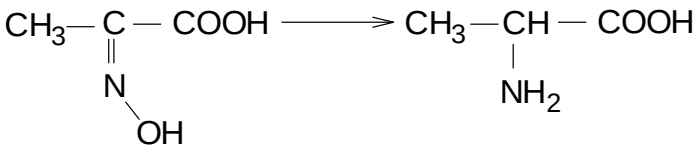
General methods of preparation:

1. Halogenated acid $+NH_3$ $\rightarrow$ Amino acid

   eg. $Cl\text{-}CH_2\text{-}COOH + NH_3 \rightarrow NH_2 - CH_2 - COOH + HCL$

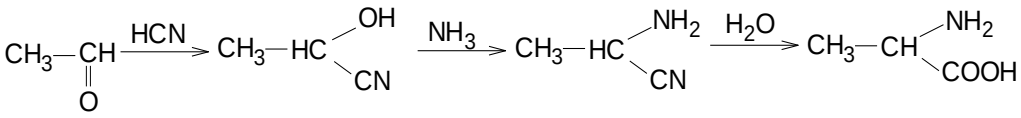
2. Reduction of oximes of aldehydic and ketonic acid.

   eg.



3. Stucker's syntheiss : - [starting material is aldehyde (or) ketones]

Aldehyde (or) Ketone + HCN + NH_3 + Hydrolysis $\longrightarrow$ Amino acid



Properties

- ✶ Reacts with both acid and base gives salt (amino & acid)
- ✶ Depending on the p^H of the solution the amino acid can donate (or) accept a proton.
- ✶ The p^H at which the amino acids show no tendency to migrate when placed in an electric field is know as Isoelectric point.

(or)

The point at which ionisation and solubility of an amino acids are at minimum.

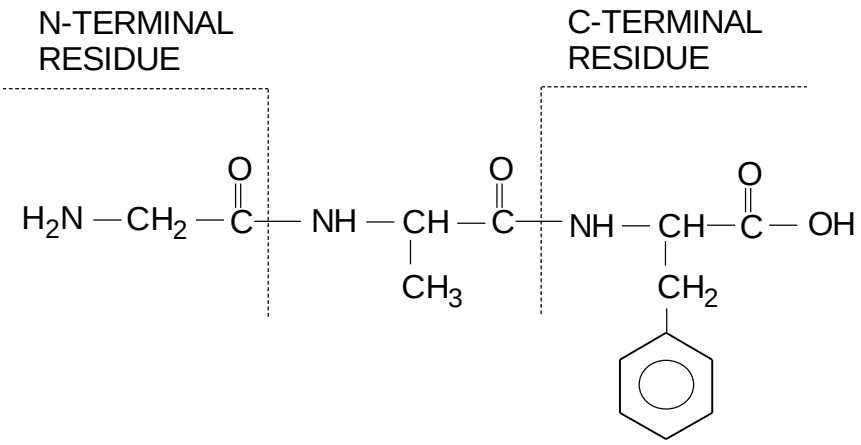
Two amino acids combined to form peptide linkage.

i.e – CO-NH – is-peptide.

3.5. PEPTIDES

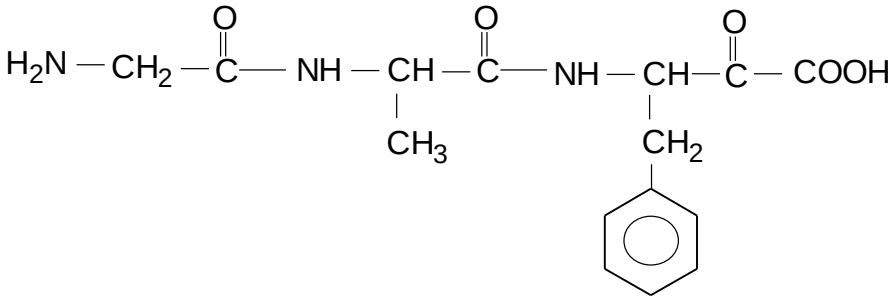
Proteins are made of may α-amino acids bonded together by a peptide linkage formed between the amino group of one amino acid and the carboxyl group of another. When two amino acids combine in this way, the resulting product is called a Dipeptide.

When three amino acids combine, the product is called a Tripeptide. When four amino acids combine the product is tetrapeptide. It is always written on the left-hand side of the polypeptide chain. Similarly, the amino acid that contains the free carboxyl group is called the C-terminal residue. It is always written on the right-hand side of the polypeptide chain. A tripeptide from glycine, alanine, and phenylalanine should thus be written as in the fig.



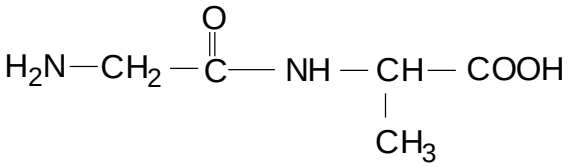
NOMENCLATURE OF PEPTIDES

Peptides are named by listing the amino acids present in the order they occur starting from the N-terminal amino acid. The typical amino acid suffix '-ine' is replaced by the suffix '-yl' for all amino acids except the C-terminal amino acid.



glycyclalanylphenylalanine

(Atripeptide from glycine, alanine, and phenyloalanine)



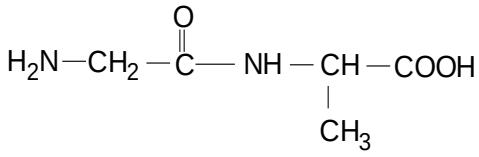
glycyclalanine

(A dipeptide from glycine and alanine)

Peptide names formed in this way are not used very often. Instead, the standard 3-letter abbreviations are used. Fro example, glycylalanylphenylalanine may be represented as Gly-Ala-Phe.

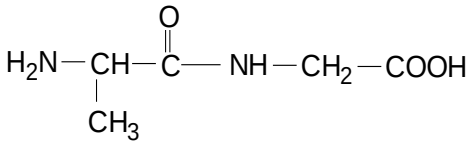
Variations in peptide and protein structures

They are two ways in which two amino acids can combine to form a dipeptide. For example, glycine and alanine may combine to give the dipeptide Gly-Ala or Ala-Gly. In the first, glycine is the N-terminal and alanine is the C-terminal. In the second, alanine is the N-terminal and glycine is the C=-terminal.



Gly-Ala

(glycylalanine)



Ala-Gly

(alanylglycine)

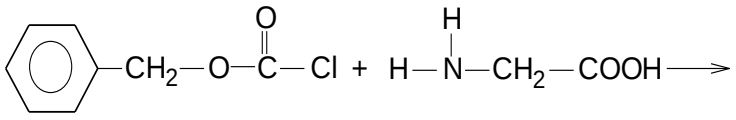
Three amino acids can combine in six different ways to form six tripeptides. For example, Glycine, alanine, and phenylalanine may combine to give the following tripeptides.

Gly-Ala-Phe	Ala-Gly-Phe	Ala-Phe-Gly
Phe-Ala-Gly	Phe-Gly-Ala	Gly-Phe-Ala

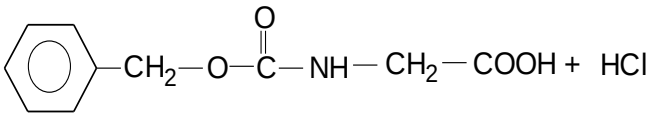
Synthesis of Peptides

Specific peptides can be obtained by the following steps. Glycylalanine (Gly-Ala) is taken as an example.

The amino group of glycine is protected by treatment with benzyl chloroformate.



benzyl chloroformate glycine



Carbobenzoxyglycine

3.6 PROTEINS

The name protein as introduced by Mulder (1839) who derived it from the Greek word, proteins (meaning first). Proteins are nitorgeneous, substances which occur in the proloplasm of all animal and plant cells. Their composition varies with the source. Proteins are predominantly constituted by five major elements in the following proportion.

(i) Carbon (50-53%), (ii) Hydrogen (6-7.3%)

(iii) Oxygen (19-24%), (iv) Nitrogen (13-19%)

(v) Sulphur (0-4%) Basides there elements, proteins may also contain other elements such as P, Fe, Cu, I, Mg, Mn, Zn etc.

Proteins be broken down into smaller and smaller fragments until the final products are the amino acids. This sequence may be written as,

Protein $\rightarrow$ polypeptides $\rightarrow$ peptides $\rightarrow$ amino acids

There is no sharp dividing line between peptides, polypeptides and proteins. One arbitrary convention designates proteins as those molecules with a molecular weight above 10,000 and peptides (poly peptides) as those molecules with a molecular weight below 10,000.

Classification of proteins:

Several arbitrary classifications of proteins are in use.

One method divides the proteins into two,

(i) Fibrous proteins (ii) globular proteins.

Fibrous proteins

They are insoluble in water. They are highly resistant to digestion by proteolyting enzymes. They are unbranched and are in the form of fibres. They are linear molecules. The long linear protein chains are held together by intermolecular hydrogen bonds. They are not folded into globular molecules. They serve as structural proteins. The common fibrous proteins are,

a) Collangen of tendons

b) Elastin of connective tissue

c) Fibroin of silk

d) Keratin of hair

e) Proteins of skeletal muscles such as actin and myosin.

Globular proteins:

These proteins are spherical in shape and are soluble in water and other solvents. They are highly branched. The polypeptide chains are cross linked by

the peptide bonds. The globular proteins may also be tightly folded into spherical or globular shape. The globular proteins include,

a) enzymes

b) protein hormons

c) antibodies

d) blood proteins such as haemoglobin, miaoglobin

e) Serum proteins.

A more common method of classification is the division of proteins into three main groups,

(i) simple proteins

(ii) Conjucated proteins

(iii) Derived proteins

Each group is subdivided into a number of classes designated by general names. Each class contains sub classes of proteins of similar but not identical physical and chemical properties.

1) Simple proteins

The proteins which yield amino acids or their derivatives on hydrolysis are called simple proteins. They are further calssifed into the following types on the basis of the decreasing solubility.

(i) Albumins: There are simple proteins and are soluable in water. They are coagulated by heat. They are precipitated by saturated ammonium sulphate salt solution. They are deficient in glycine.

Examples: Plasma albumin, Serum albumin, Ovalbumin of egg. white lactalbumin of milk.

(ii) Globulins: There are insoluble in water but are soluble in dilute salt solution and in dilute solutions for strong.

(iii) Globulins: There are insoluble in water but are soluble in dilute salt solution and in dilute solutions for strong inoganic acids and alkalis. They are coagulated by neat. They are precipitated by lower concentrations of salts. Such as ammonium sulphate or sodium sulphate. Globulins are precipitated by saturated sodium chloride solution. They contain glycine.

Examples: Plasma globulin, serum globulin, ovaglobulin in egg white, myosin in nuclues, edestin in hemp seed and vegatables globulins.

(iii) Prolamins: They are insoluble in water or salt solution but are soluble indilute acids and alkalis and in 70-90% ethand. Prolamins are deficient in lysine and contain large amounts of proline.

Some prolamins are,

Zein (from maize), Secalin (from rye), gliadin (from wheat), hordein (from barley).

(iv) Glutelins: There are insoluble in water or dilute salt solution but are soluble in dilute acids and alkalis. They are coagulated by heat. They are comparatively richin arginine, proline and glutamic acid.

Some glutelins are,

Glutenin (From wheat) and oxyrzenin (from rice).

(v) Histones: There are soluble in water or dilute acids but are insoluble in dilute ammonia. They are not coagulated by neat. They contain large amounts of histidine and arginine but contain no tryptophan and very little cysine and methoonine. They are hydrolysed by pepsin and trypsin. Histones are the proteins of the nucleic acids, hemoglobin etc.

(vi) Protamins: They are more basic than histones. They have a simpler structure. They are soluble in water, dilute acids and dilute ammonia. They are not coagulated by heat. They are precipitated from solution by ethanol. They contain large amounts of arginine and occur in various nucleic acids. They do not contain sulphur. They are hydrolysed by various enzymes e.g., trypsin, papain but not pepsin. Tyrosine and tryptophan are absent.

Example: Salmine from salmon sperum; clupeine from herring sturine from sturgeon.

II) Conjugated proteins:

There are the proteins which contain a non protein group (i.e., a compound not containing amino acid residues) attached to the protein part. The non protein group is known as the prosthetic group and it may be separated from the protein part by careful hydrolysis. The conjugated proteins are further classified on the basis of the prosthelic group as given in the table.

Table

Conjugated Proteins

S.No	Conjugated Protein	Prosthetic group	Examples
1.	Nucleo proteins	Nucleci acid	Yeast
2.	Chromoproteins	Fe, Cu, Mg	Chlorophil, heamoglobin, Phythalocynin.

3.	Glyco (ormuco) proteins	Carbohydrate	Mucin, egg albumin
4.	Phosphoproteins	Phosphoric acid	Casein, vitellin
5.	Haemoproteins	Heam	Haemoglobin in blood
6.	Lipoproteins	Lecithin, Kephalin	Lipproteins of blood serum.

III Derived proteins:

Derived proteins are the intermediate products formed from natural proteins when they are hydrolysed by heat, acids, alkalis or enzymes.

They are further classified into, denatured proteins, meta proteins, peoptons, polypetides and simple peptides.

a) Denatured or coagulated proteins:

There are insoluable proteins formed by the action of heat etc., on proteins. Coagulated egg white is an example of this type.

b) Meta proteins:-

They are insoluable in water or dilute salt solution but are soluble in acids or alkalis. They are precipitated by ammonium sulphate solution.

c) Peptones, polypeptides and simple peplides:

There are soluble in water, not coagulated by heat and are not precipitated by saturation with ammonium sulphate.

Classification based on biological function:

Proteins play crucial roles in all biological processes. We can classify proteins on the basis of their biological functions in the following way,

a) Almost all chemical reactions in the biological system are catalysed by enzymes. The enzymes exhibit enormous catalytic power. The increase the reaction rates at least a million times. Several thousand enzymes have been identified in the biological systems. The striking fact is that all the enzymes are nothing but proteins.

b) Proteins are used to transport ions and small molecules. Feco examples are,

i) Haemoglobin transports oxygen.

ii) Myoglobin transports oxygen in the muscle.

iii) Transferrin carries iron in the plasma of blood.

iv) Lipoproteins of plasma carry lipids from the liver to other organs.

v) Membrane proteins transport glucose, amino acids and other nutrients across the membrane into the cell.

c) Certain proteins function as a storage of molecules.

i) Ferritin, a protein stores iron in the liver.

ii) Seeds store nutrient proteins, eg., wheat, rice, corn.

d) Certain proteins function as nutrients

The egg contains ovalbumin.

The milk contains casein.

e) The contraction of muscle is brought about by two fibrous proteins called actin and myosin.

f) Many proteins serve as supporting filaments, cables or sheets to give biological structures, strength, support and protection.

i) Collagen is the major component of tendons, cartilage, and leather.

ii) Ligaments contain elastin, a structural protein.

(iii) Keratin, an insoluble protein is the main component of hair, finger nails and feathers.

(iv) Fibroin is the major component of silk fibres and spider web.

g) Many proteins defend organisms against invasion by other species. Invading bacteria, virus etc, elicit the production of antibodies by lymphocytes. Antibodies neutralise the foreign germs.

h) Bleeding is stopped by the formation of dot which is brought about by blood clotting proteins such as fibrinogen and thrombin.

i) Many hormones are proteins, e.g., insulin, growth hormone, parathyroid hormone etc.

j) Nucleoproteins are conjugated proteins composed of substances called nucleic acids. They are the main constituents of genes, the carriers of heredity.

Properties of protein:

Protein exhibits the following properties,

1. Most of the proteins are hydrophilic colloids. A few proteins are crystalline in nature e.g., insulin.
2. Proteins have no characteristic colour except chromoproteins.
3. A pure protein is tasteless and odourless.
4. Proteins are highly viscous in nature. Generally fibrous proteins are more viscous than globular protein.

5. The molecular weight of proteins varies from 30000 to a few millions. Their molecular weight is determined by ultra centrifuge. Typical protein many contain 135 to 635amino acids.

6. All proteins are laevo rotatory. This porperty is due to the presence of α-amino acids which are building blocks of proteins.

7. Protein undergo hydrolysis by means of dilute HCl or H_2SO_4, alkali or enzymes into their constituent amino acids.

8. When proteins are brought into contact with water they absorb water and swell up. The polar gruops like COOH – NH_2 and OH become hydrated. Electrolytes, alcohol, sugar will complete for the water of hydration, dehydrate the protein and precipitate it from solution.

9. Proteins are precipitated or coagulated in solutions alkaline to the isoelectric pH by positive ions such as

   Zn^{2+}, Cd^{2+}, Pb^{2+}, Hg^{2+}, Ca^{2+}, and Fe^{3+}. At this pH, the proteins have a negative charge.

The common precipitants are trichloro acidic acid, tungstic acid, phosphotyngstic acid, sulphosalicyhi acid and tannic acid.

10) The solubility of many proteins is increased in the presence of small concentrations of various, natural salts. This is referred to as salting in of proteins. Salting in of proteins is caused by forces of attraction between salt and protein at low salt concentrations leading to increased solubility.

As the concentration of the neutral salt is increased, the solubility increases to maximum and then starts decreasing and finally the protein is precipitated.

This is referred to as salting out. This is caused by the competition between protein and the salt at high concentrations. The salting out of proteins is an effective method of purification of proteins.

11) As each protein contains one free amino group, the protein has an ionising property. Due to the presence of these ionisable groups in the protein chains, the proteins also have some definite isoelectric pH at which they do not migrate in an electric field. At the isoelectric pH, the number of positive charges is equal to the negative charges giving a net charge of zero.

The isoelectric pH of the protein has been found to depend upon the relative number of acidic or basic groups which are rendered by amino acids.

Proteins are cations at pH values lower than the isoelectric pH and anions at pH vlaues higher than the isoelectric pH.

12) Denaturation:

Proteins undergo remarkable changes in their solubility, optical rotation and bilogical properties when they are treated with heat, x-rays, ultra violet rays, light, alcholol, acetone, KI solution, urea, detergents etc. These changes occuring in proteins are called denaturation. Denaturation has the following salient features,

i) Denatured proteins precipitate from their solutions. This process is called coagulation.

ii) Denaturation is the rersult of changes in conformations or unfolding of the protein molecules. The secondary and tertiary structures of proteins are completely lost in denaturation without any break in the primary structure.

iii) Indenatured proteins, the solubility is decreased or lost.

iv) Denaturation causes changes in the optical rotation property of proteins.

v) Denaturation makes the proteins inactive. Eg. Enzymes.

vi) Denaturation may be a reversible or irreversible process. The common example of irreversible denaluration is the familiar change which occurs during the boiling of an egg.

vii) The reversal of denaturation is called renaturation or refolding. In case denaturation is effected by heat, renaturation may be carried out by very slow cooling.

The process of this type of renaturation is called annealing. E.g. heamoglobin can be denatured in acid solution and the process is reversed by neutralisation under the correct conditions.

Denaturation property of proteins helps in the clinical laboratory. Theprotein free substances of the blood such as glucose, uric acid and drugs are analyserd by precipitating the protein of blood by the addition of certain acids.

13) Colour reactions:

Proteins give characteristic colours on treatment with specific reagents. These reactions help to identify proteins. Hence, they are called tests for proteins. They are the following,

a) Biuret Test: The protein solution is warmed gently with 10% solution of sodium hydroxide and then a drop of very dilute copper sulphate solution is added. The formation of raddish violet colour indicates the presence of peptide bonds. This is answered by all proteins, peptons and peptides excepts dipeptides.

b) **Millon's Test:** Million's reagent is a solution of mercuric nitrate and mercurous nitrate on nitric acid containing a little nitrous acid. Proteins on adding Million's reagent followed by heating the solution gives a red precipitate or red colour. This test is responded by the proteins having tyrosine.

c) **Ninhydrin Test:** When ninhydrin is added to protein solution and the mixture is heated to boil a blue to violet colour appears. It is a testy for amino acids also.

d) **Xanthoproteic test:** When a few drops of nitric acid is a added to the protein solution, yellow precipitate appears. The yellow precipitate is due to the formation of meta proteins insoluble in nitric acid.

e) **Hellex's test:** In a test tube containing concentrated nitric acid, small quantity of protein solution is slowly added. The two solutions are mixed slowly by rotating on the palm. A white ring appears at the junction of the two solutions.

Nitroprusside test: Proteins containing free SH groups (or cystene) give a reddish colour with sodium nitroprusside in ammoniacal solution.

3.7 VITAMINS

Vitamins are defined as potent organic compounds occurring and varying and minute proportion in food, which must be available to the organisms in order that physiological processes essential to life, may proceed normally.

They are low molecular weight organic compounds indispensable for the normal vital activity of the organisms. Their absence causes deficiency diseases. They either participate in the production of coenzymes (or) act as regulators of biological processes. Plants synthesis all vitamins. Vitamins are known as the "accessory dietary factors and are only necessary in vary small amounts.

The vitamins have been arbitrarily classified into the,

i) Fat soluble group e.g. vitamines A.D.E and K.

ii) Water soluble group e.g.vitamins B and C.

Vitamin B, Thiamine, Aneurin (C_{12} H_{18} Cl_2 N_4OS)

Sources : It is present in cereals. This vitamin is concentration in the outer germ and bran lagers. During milling and polishing, this vitamin is discarded. Hence, unpolished rice is the richest sources. Rice polishing and yeast have been the usual sourced of thiamine, eggs are also a rich source. Thiamine occurs in all cells as its pyrophosphate ester.

Biological Functions:

1) It undergoes reaction with ATP in which two terminal phosphates form ATP are tranferred to the thiamine molecule to form thiamine pyrophosphate (TPP). This acts as a coenzyme in glycolytic pathway as well as koubs cycle.

   Thiamine + ATP $\rightarrow$ Thiamine pyrophosphate

   (TPP)

   glycolytic pathway and Krubs cycle - TPP as coenzyme.

2) Thiamine activates carbxylase which is essential for the oxidative decarboxylation of pyruvic acid, ketoglotaric acid and other keto acids.

3) TPP acts as a coenzyme for certain trans ketolase rxns.

4) Thiamine helps the enzyme system which is responsible for the synthesis of fats from carbohydrates and proteins.

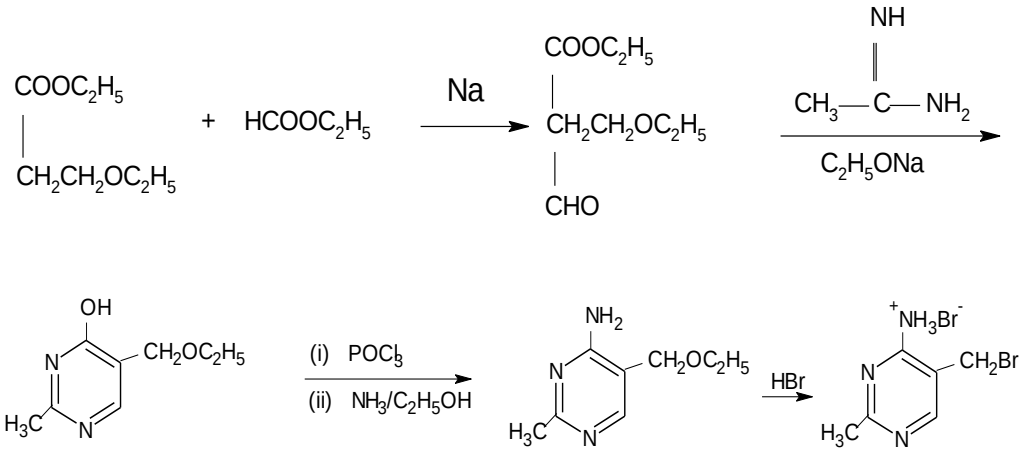
Deficiency symptoms:

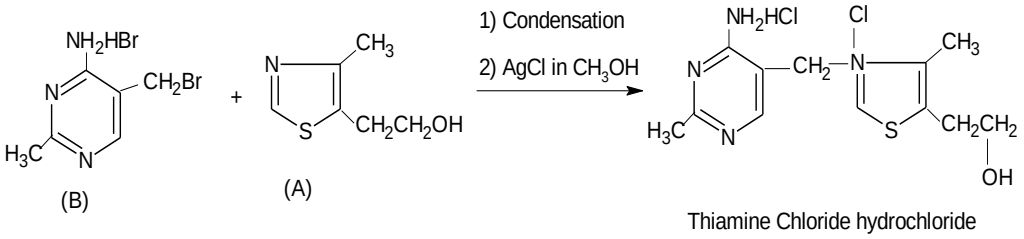
The deficiency of this vitamin causes beri-beri in man. Beri Beri is characterised by odema in the legs. Thus, this vitamin is the antineuritic factor and lence the name arevrin.

Isolation: Dilute acid is added to the source material, thiamine is formed in the solution. Fuller's earth is added, Quinine sulphate added to remove thiamine. On the addition of $AgNO_3$, thiamine is converted as its silver salt.

By adding HCl, thiamine hydrochloride is precipitated as crystals.

Synthesis of Thiamine





Vitamine B_2, riboflavin (Lactoflavin) C_{17} H_2O N_4O_6

Source:

It occurs in yeast, green vegetables, milk, meat etc.

Chemically vitamin B_2 is closely related to the yellow, water soluble pigments known as flavins isoalloxazines and since it was first isolated from milk, vitamine B_2 is also known as lactoflavin.

Biological Functions:

1) Riboflavin is a component of two important coenzymes namely flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD). They play major roles in various enzyme systems.

2) It is essential for the metabolism of growth.

3) It is an important component of acyl CoA dehydrogenase.

Deficiency systems:

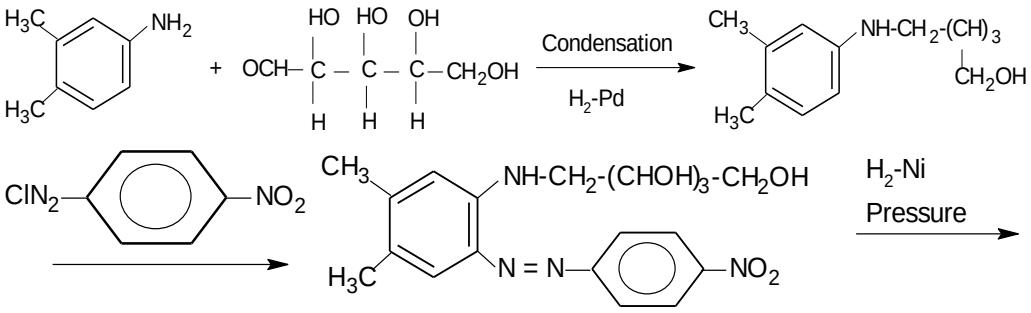
1. It is characterised by the development of fissures developing in the lips and the corners of the mouth.

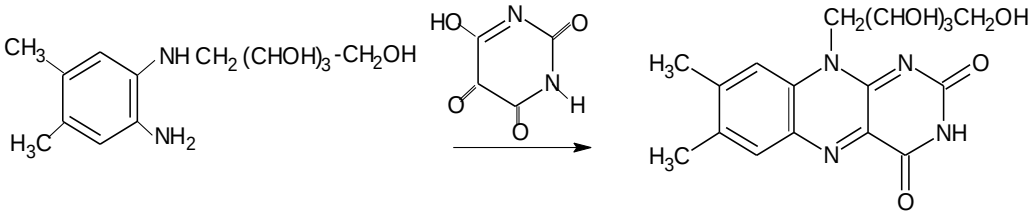
2. Sore tongue.

3. The skin loses hair, it becomes dry and scaly.

4. Growth is atrested.

Synthesis of Riboflavin





Riboflavin

Vitamin B_6, Pyridoxine, Adermin, $C_8H_{11}NO_3$

Source

The richest sources are yeast, rice polishing germs of grains and cereals. leafy vegetables, liver, eggs and meat etc.

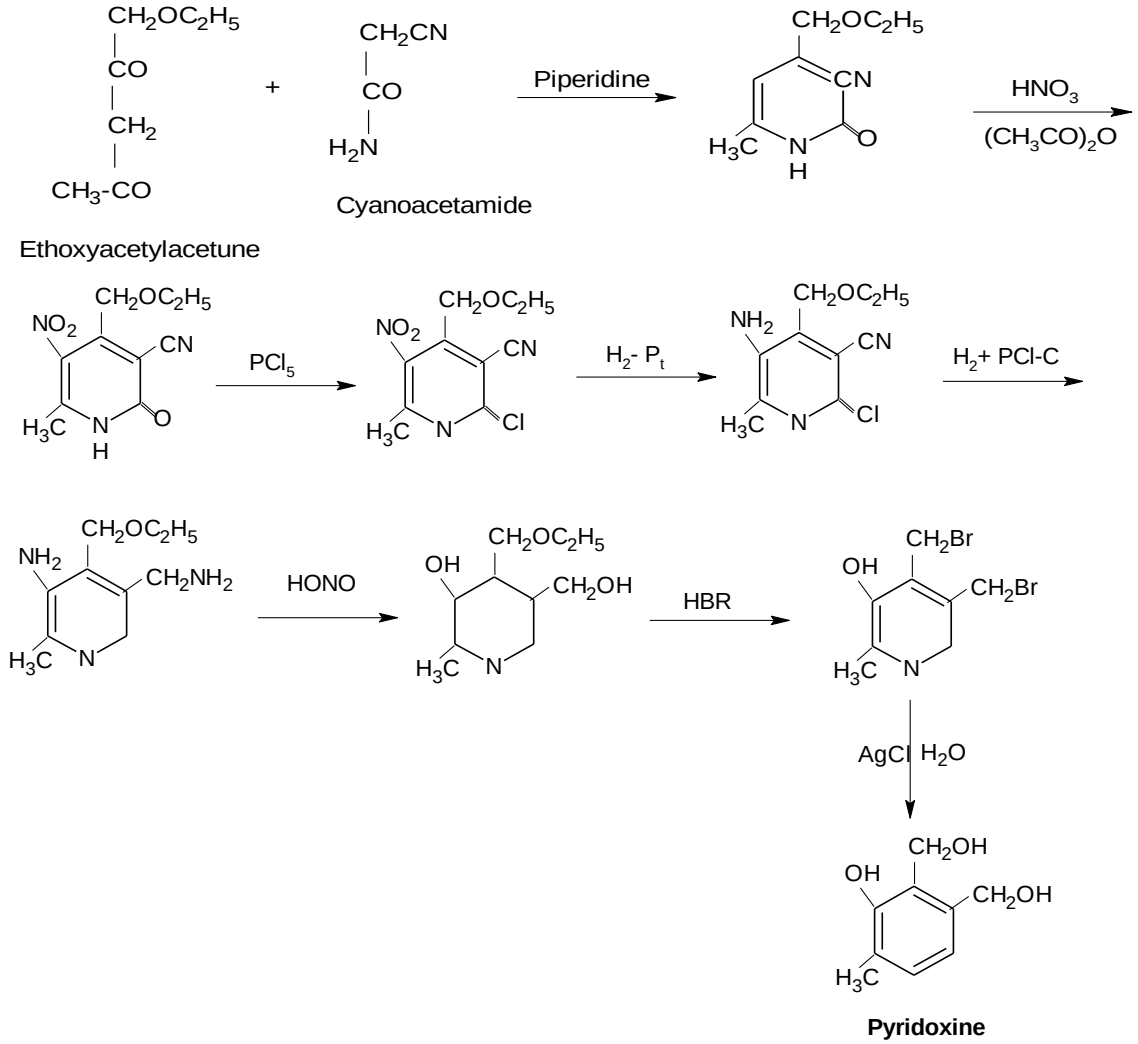
Biological Functions:

1) Pyridoxal phosphate acts as conenzyme
2) It helps in the synthesis of fat from carbohydrates and proteins.
3) It is involved in the active transport of amino acids and certain metalic ions across cell membranes.
4) It is linked with the metabolism of central nervous system.

Deficiency symptoms:

In rats deficiency of this vitamin causes a specific type of dermatitis called acrodynia anemia and convulsiuns. The deficiency disease produced in man is not known.

Synthesis of pyridoxine



Vitamin C Ascorbic acid, Hexuronic acid, $C_6H_8O_6$

Sources

The main sources of Ascorbic acid are Tomato, leafy vegetables, citrus fruits, cabbage, paprika etc.

Functions

1) It regulates oxidation - reduction potential inside the cell by acting as a hydrogen carrier.
2) It regulates carbohydrate metabolism.
3) It plays a major role in wound healing by producing connective tissue.
4) It helps in the absorption of iron from the intestine.

5) It provides resistance power against toxins, cold and stress conditions.

6) It involves in the maturation of RBC.

7) It is essential for the synthesis of adrenal hormones and gondal hormones.

Deficiency symptoms

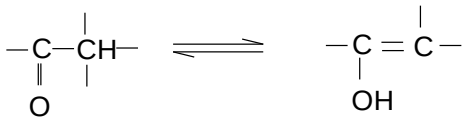
1. In man, deficiency of this vitamin causes scurvy. It is characterised by internal bleeding.
2. malfunctions of bones and teeth.
3. Increased brittleness of bones leading to fracture.
4. Anaemia
5. Delayed blood clotting.
6. Increased susceptibility to infections.
7. Wound healing is delayed.
8. Disturbances in carbohydrate metabolism.

Isolation

The sources like rose hips and pine needless are extracted with water, and neutral lead acetate solution is added to it. The imputities are precipitated, and ammonia is added to the filtrate, vitamic C is precipitated as its lead salt, and treated with sulphuric acid, lead is precipitate as lead sulphate. The solution is purified with acetone, ether and alcohol. The filtrateis distilled. Pure ascorbic acid is obtained with specific rotation is $+24^{o}$.

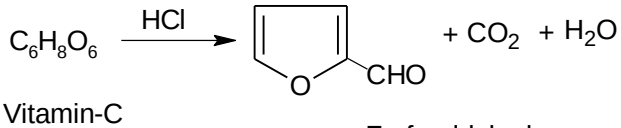
Structural determination

1. The molecular formula of vitamic C is $C_6H_8O_6$.
2. Since it formed a monosodium and monopotassium salt, it was thought that there was a carboxyl group present.
3. With ozone it forms mono ozonide, indicating the presence of on C=C structure in the molecule.
4. It behaves as an unsaturated compound and as a strong reducing agent.
5. It also forms a phenylhydrazone (test for ketene) and gives a violet colour with ($FeCl_3$ test for phenol)
6. All above suggests that a keto-enol system is present.



Keto Enol

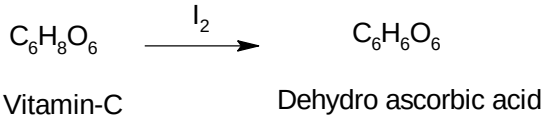
7. It does not react Schiff's base, hence there is no aldehyde group in the molecule.
8. When boiled with hydrochloric acid, it gives furfuralcehyde



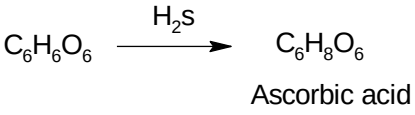
Vitamin-C Furfuraldehyde

This reaction indicates, at least 5 carbon atoms and no hydroxyl groups are present.

9. Aqueous iodine solution oxidises ascorbic acid to dehydroascorbic acid.
10. Dehydroascoribic acid reduces with H_2S, it is reconverted into ascorbic acid.

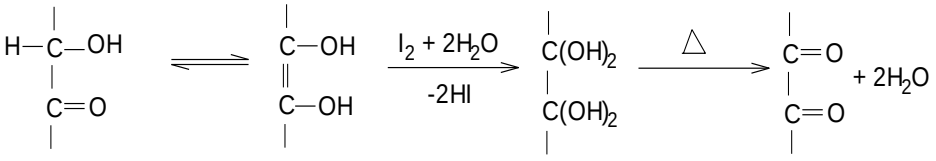


Vitamin-C Dehydro ascorbic acid



Ascorbic acid

11. It forms salt due to the presence of enol group.
12. Thus, all the precceding reactions can be explained by the presence of an α-hydroxy ketone grouping in ascorbic acid in the following way-



Reducing property

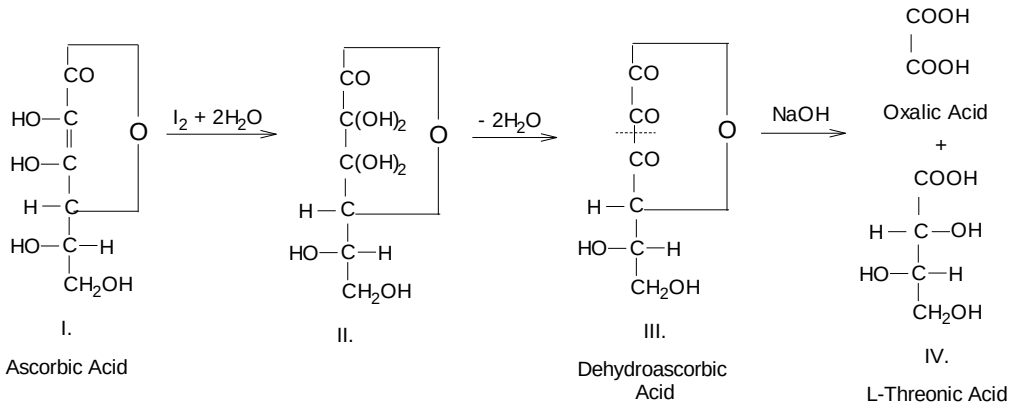
Neacts with $C_6H_5NHNH_2$

Unstaturated impats colour with F_eCl3_3

The final result is the removal of two hydrogen atoms to form dehydroascorbic acid.

$$C_6H_8O_6 + I_2 \longrightarrow C_6H_6O_6 + 2HI$$

13. When dehydroascorbic acid is oxidised with sodium hypoiodite, oxalic acid and L-Threonic acid are produced. This reaction indicates structure III is dehydroascorbic acid and I is ascorbic acid.



The structure of ascorbic acid as I has been confirmed by the following evidence.

(i) On treatment with diazomethane, it gives dimethyl ascorbic acid (v), in which the methoxy groups on C_2 and C_3.

(ii) When dissolves in NaOH to form a sodium salt without the elimination of methoxy group. Thus, there cannot be a carbomethoxy group.

(iii) When diemthyl ascorbic acid is methylated with CH_3I to a tetramethyl derivative (Vl), which indicates two more alcoholic groups on it.

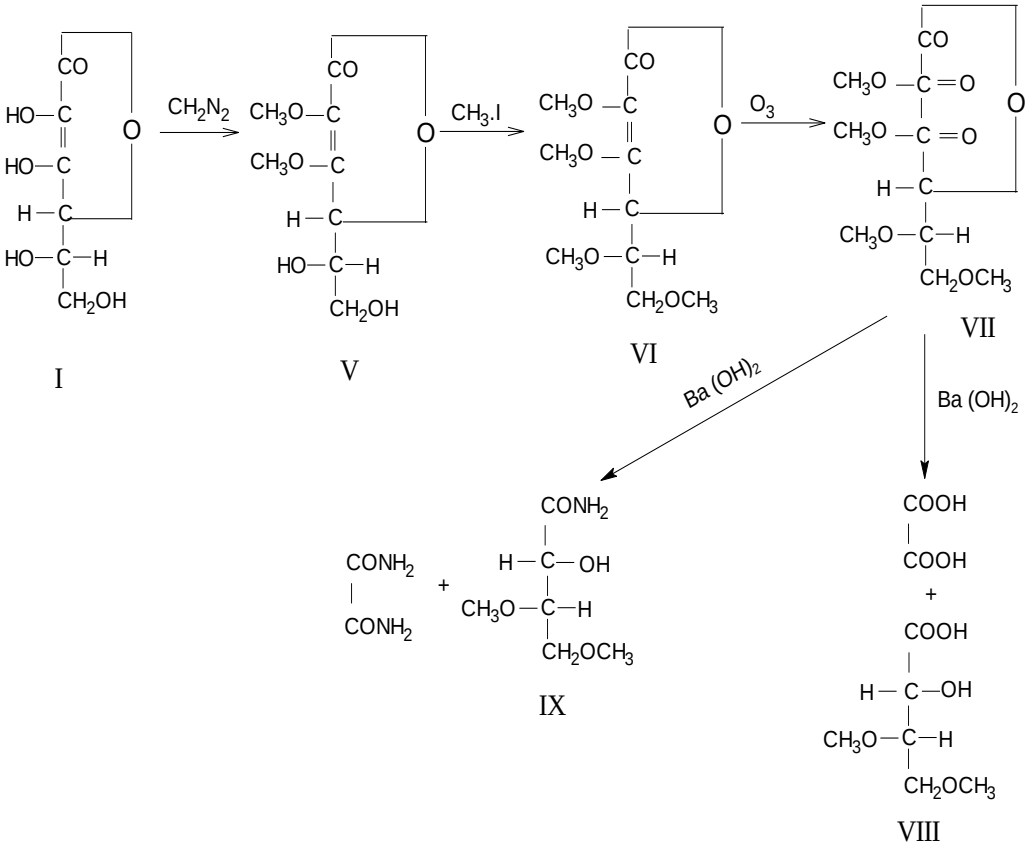
iv) Ozonolysis of tetramethyl compound produces a neutral compound with ring system.

v) The ozonised product (vii) on hydrolysis, with $Ba(OH)_2$ gives oxalic acid and dimethyl-L-threonic acid (viii)

vi) On methylation and followed by conversion of VII to the amide (ix).

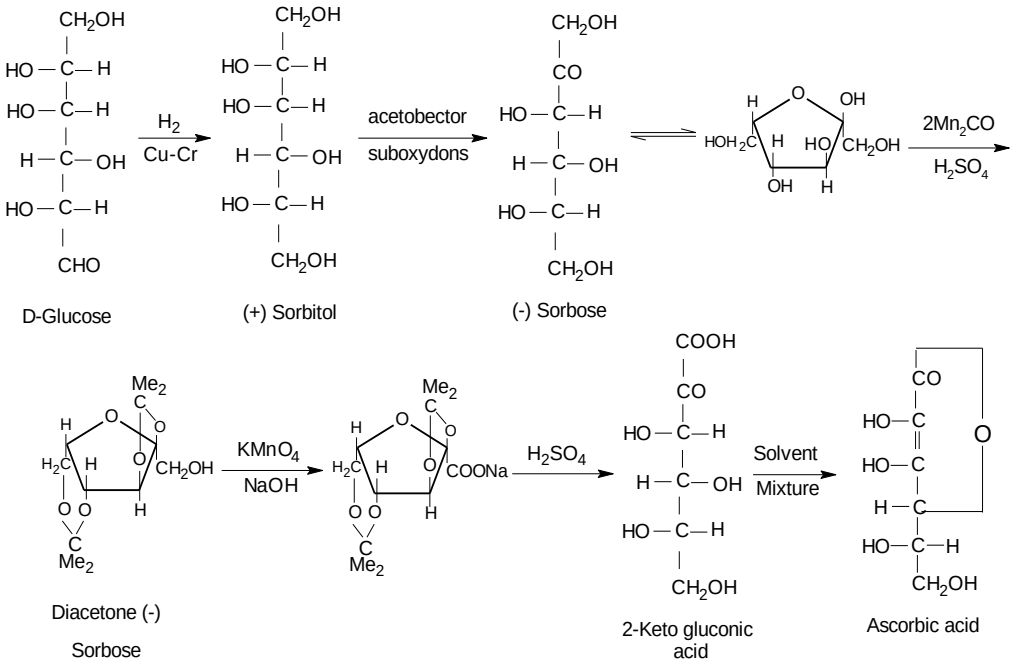
vii) The dimethyl - threonic acid (viii) is converted into its amide which is sutisted to Weerman's test. (viii) contains a free α-hydroxy group. Therefore, it must be 3,4-di-o-methyl-l-threonic acid (viii). Therefore the lactone ring in ascorbic acid must be v-lactone ie. as membered ring.

All the above facts can be represented by equations as,



Synthesis of Ascorbic acid from Glucose

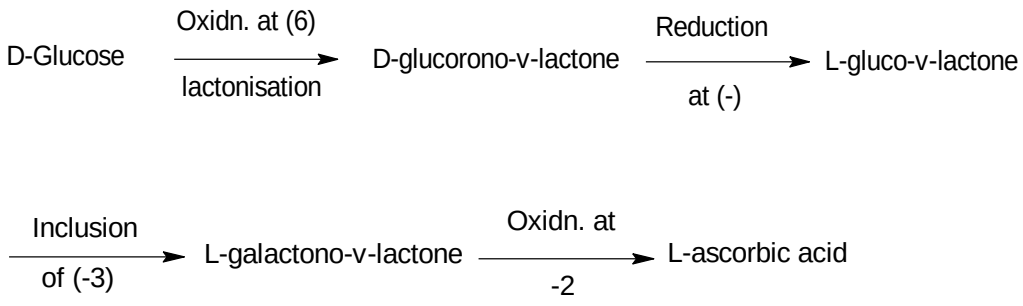
D-glucose is catalytically hydrogenated to (+) sorbitol which is then converted into (-) sorbose by microbiological oxidation using Aectobacter suboxydans. Sorbose can be oxidised directly to 2-keto(-) -gluconic acid with nitric acid. The gluconic acid is then discolved in mixed solvents and hydrogen chloride passed in. The product, L-ascorbic acid, is then finally purfied by charcoaling.



Biosynthesis of ascorbic acid

Rat and plant tissues can convert D-glucose into ascorbic acid. A very interesting observation is that glucose labelled at (with C^{14}) produces the vitamin labelled at C-6. The glucose melocule is turned upside down to form the glucose derivative.

One possible pathway for the biosynthesis of it is:



UNIT – IV

4.1. DYES

The dyeing of cloth is one of ancient arts. Natural colouring matters like indigo, alixarin etc., have been used by men since the advent of civilization. Now a days all dyes are synthetically prepared from aromatic compounds. At present the dye industry occupies an important place among the major chemical industries.

4.1.1. Theory of Colour and Constitution:

There are two theories of colour and its relation to organic structure.

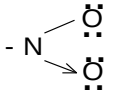
1. The Chromophone – Auxochrome Theory:

This theory completely based on the correlation between colour with molecular structure.

Postulates:

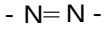
(i) The colour of organic compounds is due to the presence of certain multiple bonded groups called chromophore (Greek: Chroma-colour; phorein to bear).

Ex:

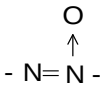


Nitro

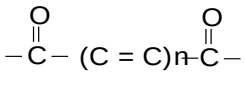
Nitroso



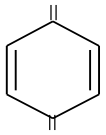
Azo



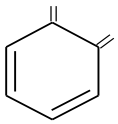
Azoxy



n=0 or more

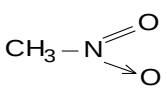


p - Quinoid



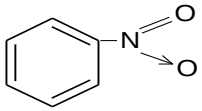
O-Quinoid

It has been noted that the presence of a chromophore is not necessarily sufficient for colour. To make a substance coloured, the chromophore has to be conjugated with an extensive system of alternate single and double bonds as exists in aromatic rings. Thus nitro methane is colourless, while nitrobenzene is yellow.



Nitromethane

(Colourless)



Nitrobenzene

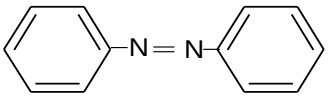
(Yellow)

(ii) Some groups are not producing colour themselves, when present along with an chromophore is an organic substances, intensify the colour. Such colour assisting groups are called Auxochromes (Greek: Auxanein = to increase; chroma=colour). The auxochromes are acidic or basic functions, of which the more important ones are listed below.

Acidic :	- OH	- SO_3H	- COOH
	Hydroxy	Sulphonic acid	Carboxyl
Basic :-	NH_2	- NHR	- NR_2
	Amino	Alkylamino	

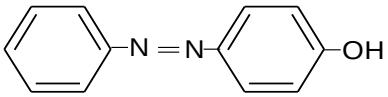
Dialkylamino

For illustration, azobenzene has red colour, while p-hydroxyazo benzene is brilliant red.



Azo benzene

(Red)

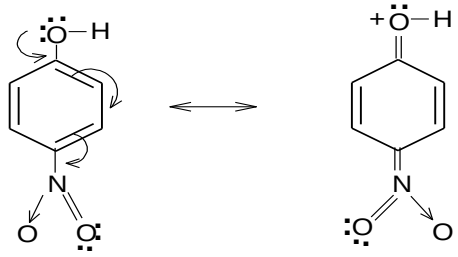


p-hydroxy Azo benzene

(Bright Red)

Similarly, nitrobenzene is a pale yellow substance but when the auxochrome – OH is present in ortho or para position, the product becomes deeply yellow.

The auxochrome – OH deepens the colour by extending the conjugated system between the chromophore and the auxochrome due to resonance.



P-Nitro phenol

p - Quinoid sturcture

(Extended conjugated system between NO_2 and OH)

II. Modern Theory of Colour and Delocalization:

When a molecule absorbs light, its bonding electrons are excited. In other words the bonding electrons absorb energy and are promoted to orbitals of higher energy. The energy absorbed by an electron in such a transition is equal to difference of the energy of MO in the ground state and the energy of

MO to which the electron is promoted. The relative energies of the MOs in the ground state are:

π Delocalized > π > σ

Therefore, to promote an electron to the same higher energy orbital, maximum energy will be required for a electron, less for π electron and still less for delocalized electron. Further the smaller the energy required for promotion, the longer will be the wavelength of light absorbed.

Dye definition:

A dye is a coloured compound, normally used in solution, which is capable of being fixed to a fabric.

The dye must be 'fast' or chemically stable so that the colour will not wash with soap and water, or fade on exposure to sunlight (ultraviolet light).

Classification of Dyes by Structure:

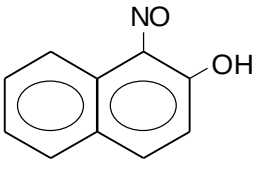
Dyes may be classified according to the parent 'colouring moiety' or the chrmophoric group present in their chemical structure. Thus chemical classification of dyes includes the following principal types.

Classes of dyes:

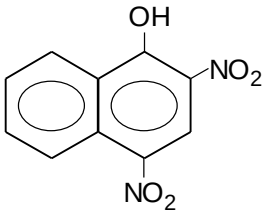
1. Nitro and Nitroso dyes.
2. Azo dyes
3. Triphenyl methane dyes
4. Phthalein dyes
5. Anthraquinone dyes
6. Indigo dyes (vat dyes)

1. Nitro and Nitroso dyes:

The NO_2 and NO groups are chromophores in this class of dyes. For example,



Naphtho-greeny



Martius yellow

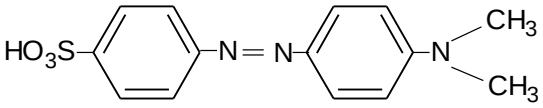
(A direct dye)

Marthius yellow can be used for wool and silk but the colour is not fast.

2. Azo Dyes:

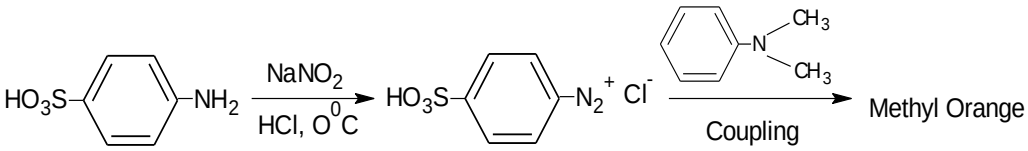
The azo dyes contain one or more azo gropus, - N = N -, as the primary chromophore. The common auxochromes are NH_2, NR_2, OH, SO_3H, etc. For example,

(i) Methyl orange (ii) Bismark brown



Preparation:

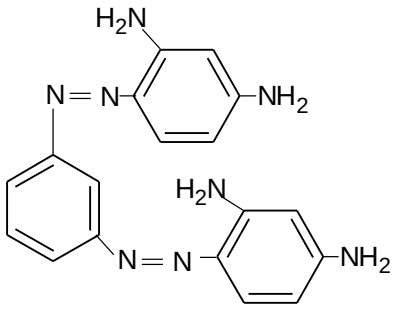
It is prepared by coupling N, N-dimethyl aniline with diazotized sulphanilic acid.



(i) Methyl orange imparts orange colour to wool and silk but the colour is not fast to sunlight or washing. (ii) It is a valuable indicator for Acid-Base titrations because it gives yellow colour in basic solution and pink in acid solution. The change in colour at the end-point is due to the change in the structure of the ion.

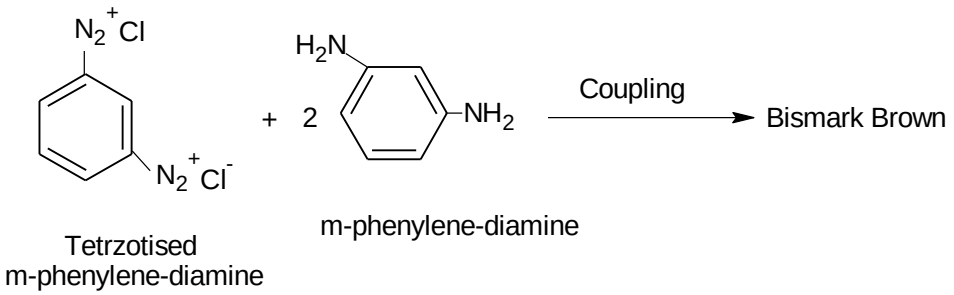
(ii) Bismark Brown

Structure:



Preparation:

It is made by coupling tetrazotised m-phenylenediamine with two molecules of m-phenylenediamine.

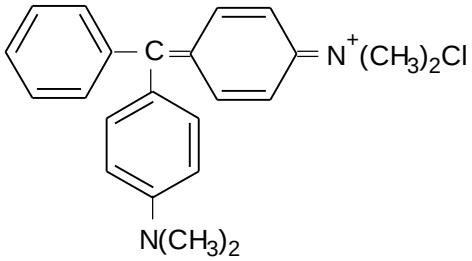


Bismark Brown is a brown dye used in boot polishes, and for dyeing wool and mordanted cotton.

3. Triphenyl Methane Dyes:

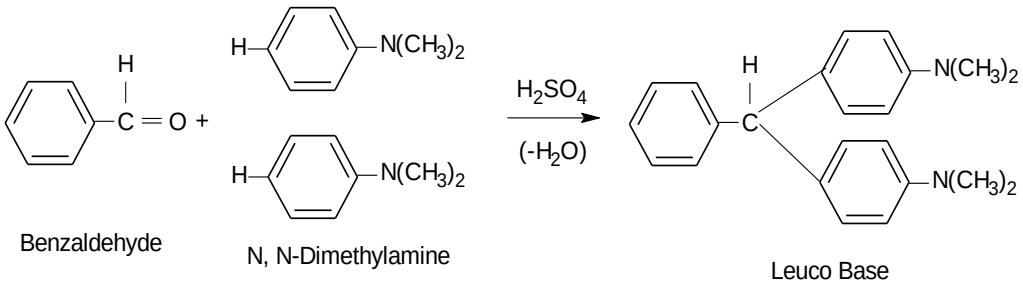
In triphenyl methane dyes, a central carbon atom is bonded to two benzene rings and one p-quinoid group (the chromophore). The auxochromes are, $-NH_2$, $-NR_2$, and –OH. Triphenyl methane dyes have brilliant colours but not very fast to light or washing.

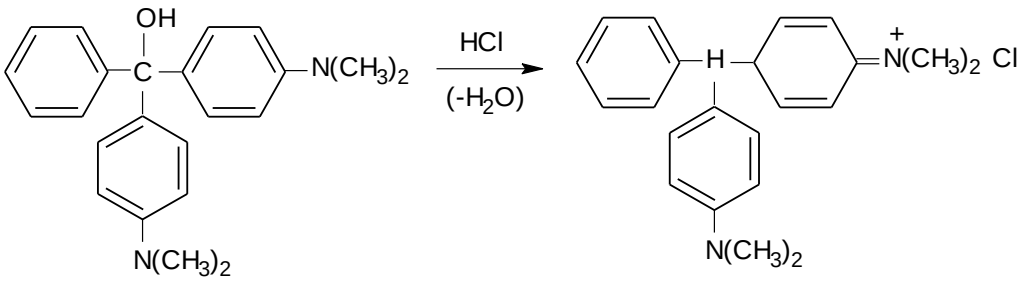
Example: Malachite Green (Basic Green 4):



Preparation:

Malachite green is prepared by condensing benzaldehyde (1 mole) with N, N-dimethyl aniline (2 moles) in the presence of Conc. H_2SO_4. The Leuco Base (G. leuco-colourless). So formed, is oxidized with lead oxide and then treated with hydrochloric acid to get the dye.





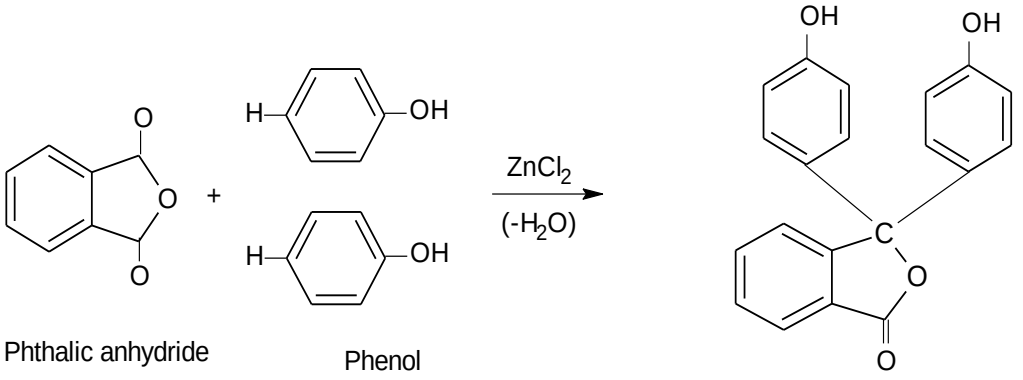
(Colourless) Malachite green

Malachite green has a deep-blue green colour which resembles that of the copper or malachite. Although the colour fades in light, malachite green is used for direct dyeing of wool and silk, and cotton after mordanting.

4. Phthaleien dyes:

Phenolphthalein:

Phenolphthalein is prepared by heating phthalic anhydride (1 mole) and phenol (2 mole) in the presence of anhydrous zinc chloride at 120°C.



Phthalic anhydride Phenol Phenolphthalein

It is a white crystalline substance. It is insoluble in water but dissolves in ethanol giving colourless solutions which turn pink on addition of alkali. The pink colour disappears when acid is added to it.

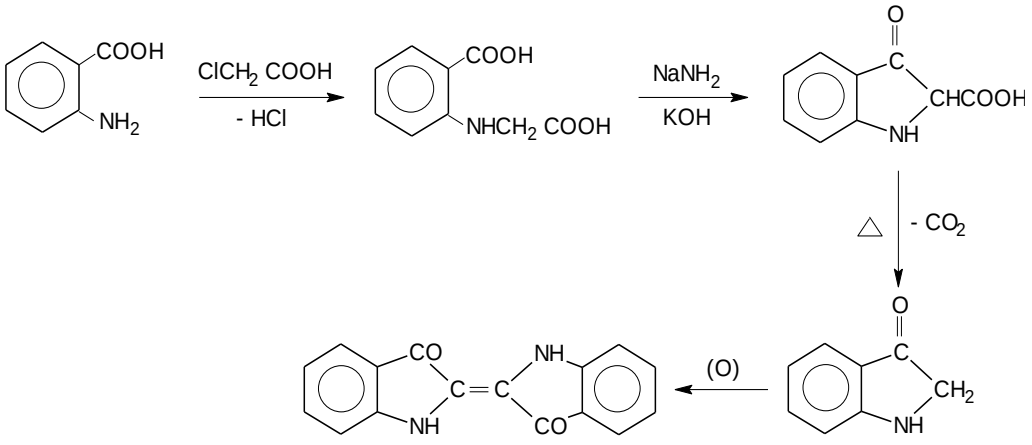
Phenolphthalein is acid from and on account of the above changes it is used as acid-base indicator rather than a dye.

5. Vat dyes:

Ex : Indigo dyes

Preparation:

It is prepared from anthoranilic acid.



Indigo

Properties:

Indigo is a deep blue coloured crystalline solid. It is soluble in water but soluble in many organic solvents. It sublimes at low pressures.

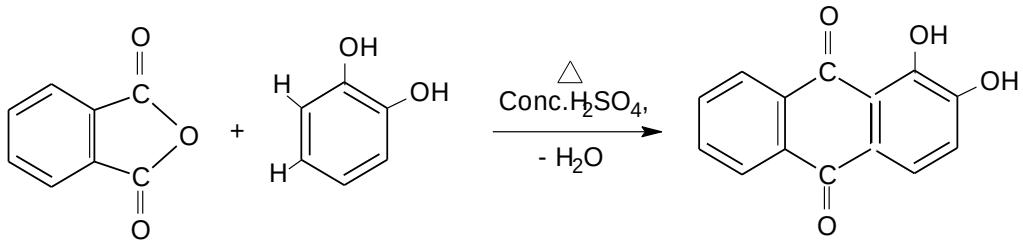
6. Anthraquinone dyes:

Ex : Alizarin

Alizarin is the best known member of this class of dyes. It forms ruby red crystals which dissolves in alkali to give purple solutions. It is used to dye wool and cotton.

Preparation:

It can be prepared heating phthalic anhydride and catechol in the presence of sulphuric acid (or anhydrous $ZnCl_2$) at 180°C.

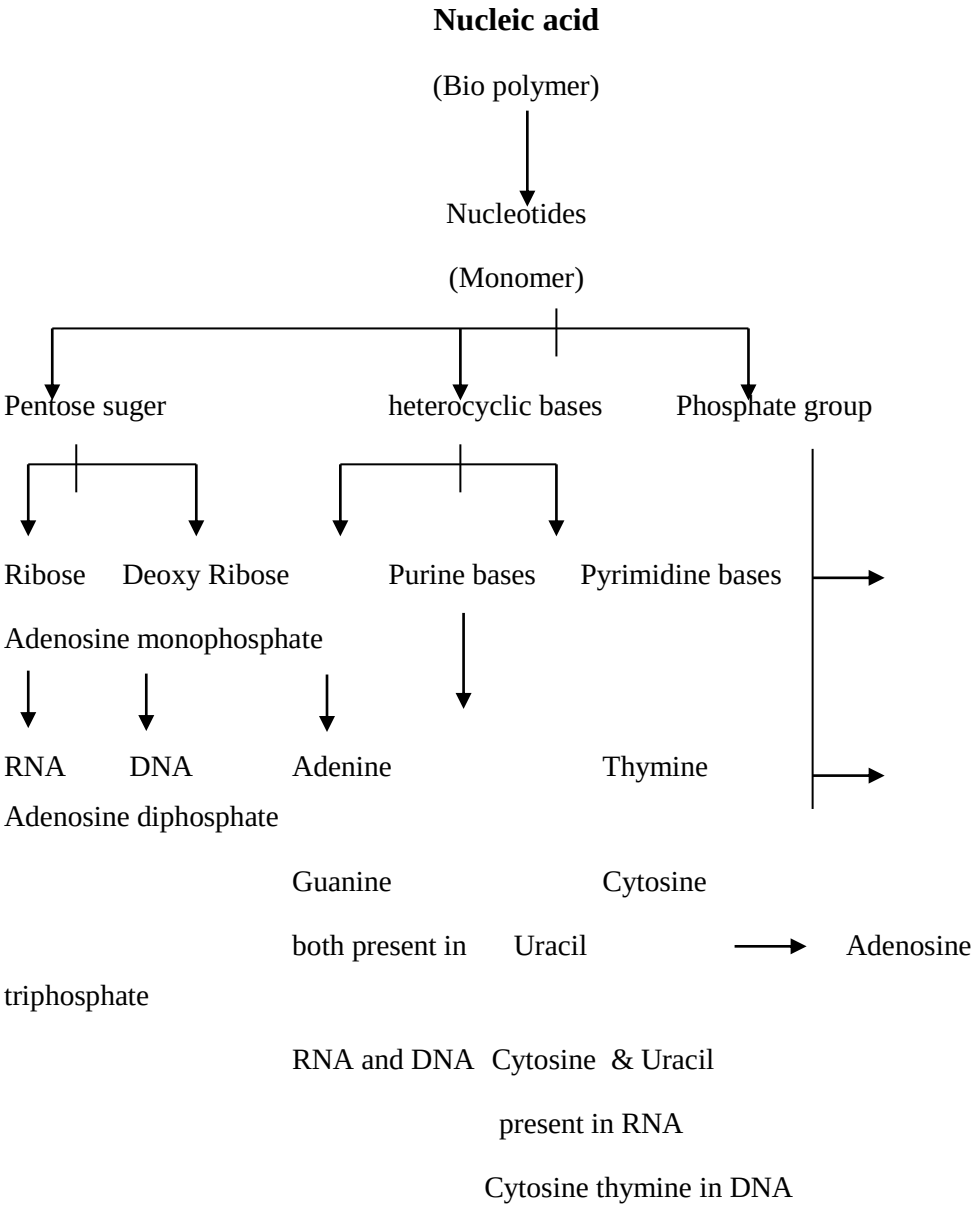


Alizarin

4.2. NUCLEIC ACIDS

Nucleic Acids occur in all livings cells as a major component of the nucleus and also as a component of cytoplasmic structures such as the ribosomes. Substances made up of proteins combined with natural polymers like carbohydrates are **Nucleic acids.** They are generally associated with proteins to form Nucleo proteins, in which the nucleic acid being the prosthetic group while the protein part consists of protamins and histones. In nucleo-

proteins, the nucleic acid is bound to the protein by salt like bonds which are cleared by adding electrolytes (or) chaging the pH of the solution.

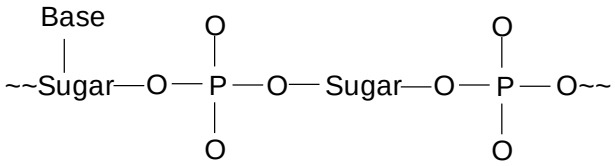


The function of nucleic acid is controlled the heredity. The backbone of the protein is a polyamide chain (a polypeptide chain). Whereas the backbone of the nucleic acid is a polyester chain (called a polynucleotide chain).

Nucleic acids are made up of three units:

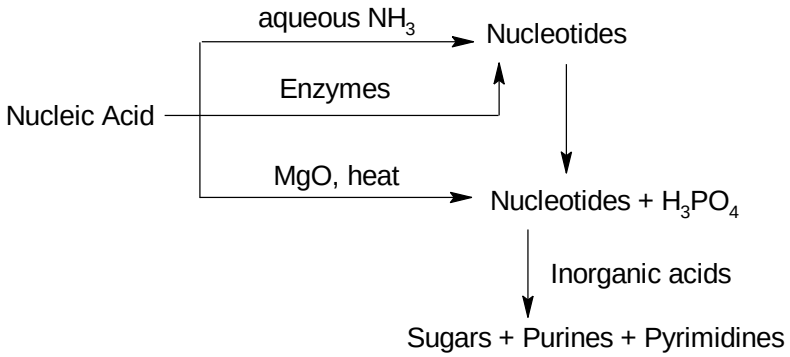
1) Bases (purise OH pyramidine)
2) Sugar (Ribose and Deoxyribose)
3) Phosphoric acid

The structure of the polynucleotide chain is,



A base sugar unit is a nucleoside and a base sugar phosphoric acid unit is nucleotide.

The hydrolysis of nucleic acids give the three units as,



Classification of Nucleic acids:

The two types of nucleic acids are Ribonucleic acids (RNA) and Deoxyribose nucleic acids. DNA is found predominantly in the nucleus while RNA is predominant in the cytoplasm. DNA synthesizes RNA and RNA is responsible for the synthesis of proteins.

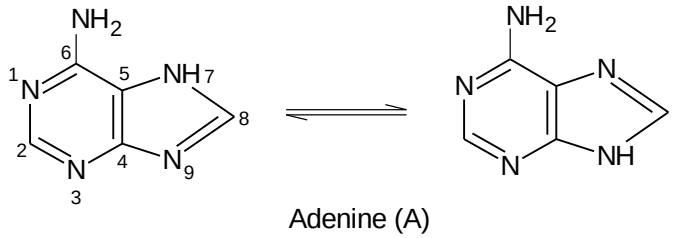
There are two types of heterocyclic bases found in nucleic acids. They are,

(i) Purine bases

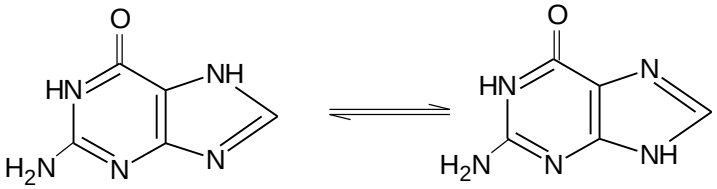
(ii) Pyrimidine bases

(i) Purine bases

Two purine bases are found in RNA and DNA. They are (i) Adenine (A), (ii) Guanine (G). These bases utilize their 9^{th} position to unite with sugar.



Adenine (A)

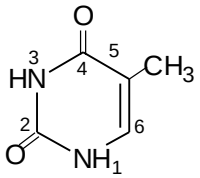


Guanine (G)

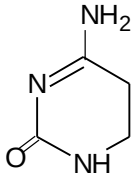
(ii) Pyrimidine bases

Three pyrimidine bases are found in RNA and DNA. They are (i) Thymine (T), (ii) Cytosine (C), (iii) Uracil (U).

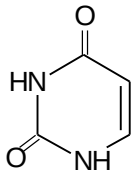
They use the nitrogen atom present at the first position to unite with sugar.



Thymine (T)



Cytosine (C)



Uracil (U)

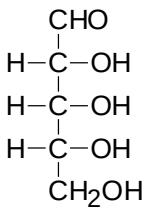
Cytosine and uracil are present in RNA.

Cytosine and thymine are present in DNA.

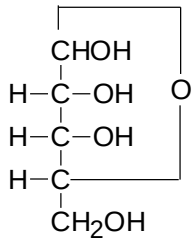
Apart from these three pyrimidine bases, 5-methyl cytosine and 5-hydroxymethyl cytoxine are found in few nucleic acids.

Structure of ribose and 2-deoxyribose

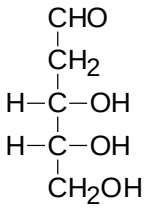
In the hydrolysates of nucleic acids (or nucleosides), only two sugars have been isolated. Both are pentoses, D(-) ribose and 2-deoxy-D(-) – ribose. The ribose is only present in the ribonucleic acids (RNA) while deoxyribose is present only in the deoxy-ribonucleic acids (DNA). The open-chain and cyclic structures of these sugars may represented as follows:



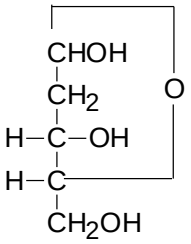
Open chain structure of (-) ribose



Ring structure of (-) ribose

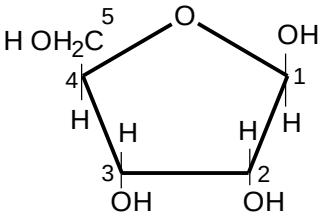


Open chain structure
of 2-deoxy-D(-) ribose

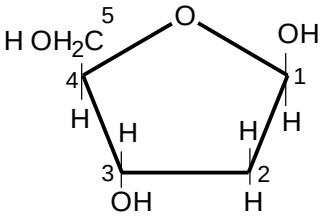


Ring structure of
2-deoxy-D(-) ribose

The five membered furan ring structures are:



D-β -Ribose



D-β -Deoxyribose

These sugars have D-configuration. The utilize C_1 Carbon atom to unite with base. β-form is found in nucleic acids. Deoxyribose differs from ribose at C_2 carbon atom. In the case of ribose, it is CHOH group and in the cse of deoxyribose, it is CH2 CnO oxygen atom is present at this position, hence the name deoxyribose.

The nucleosides (sugar and base unit) are stable in alkali solution but hydrolyzed with dilute acid solutions, this suggested that they are neither O-glycosides nor C-glycosides but are N-glycosides. Both ribose and deoxyribose are monosaccharides.

]Nucleoside:

A base combined with sugar molecule is nucleolide. If ribose sugar is involved, it is called ribonucleoside CoH riboside. For deoxyribose sugar, the nucleoside is called deoxyriboside (OH) deoxyribonucleoside.

These base sugar molecules are so named as to reflect the names of the base and sugar present. For eg.

i) Adenosine (ribose + odenine)

ii) Guanosine (ribose + guanine)

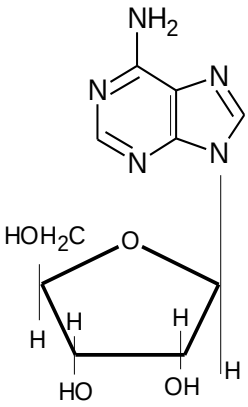
iii) Cytidine (ribose + cytosine)

iv) Uridine (ribose + uracil)

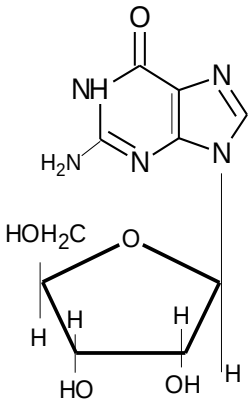
v) Deoxyadenosine (deoxyribose + adenine)

vi) Deoxyguanosine (deoxyribose + guanine)

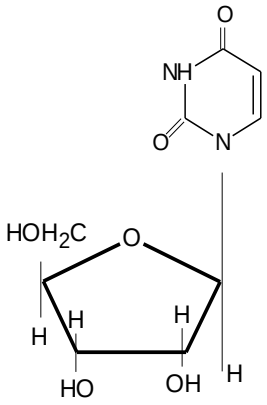
The structures of few nucleosides like uridine, adenosine, and guanosine are given.



Adenosine



Guanosine



Oridine

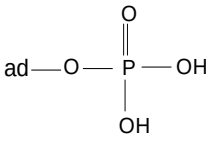
Nucleotides:

The nucleoside is combined with phosphate is nucleotides. The OH group present at C_2, C_3 and C_5 of the ribose in riboside is used to unite with phosphate. We may have mono, di and triphosphates. Example,

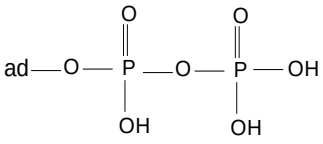
i) Adenosine monophosphate (AMP)

ii) Adenosine diphosphate (ADP)

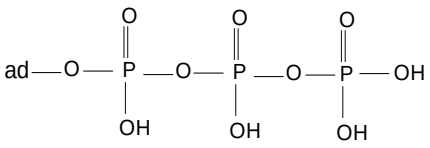
iii) Adenosine triphosphate (ATP)



AMP



ADP



ATP

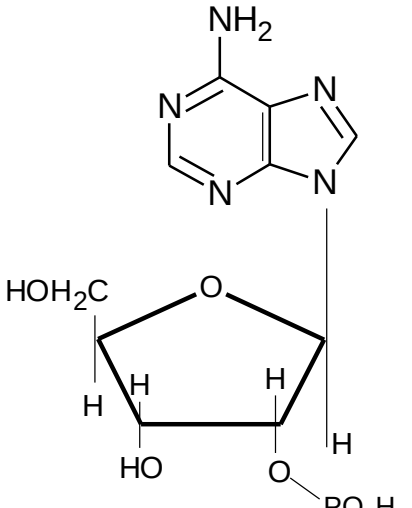
ad - adenosine (ribose + adenine)

The OH group present at C_3 and C_5 of deoxyribose in nucleoside is used to unite with phosphate.

Depending upon the pentose sugar present in nucleotides they are two types-

1. Ribonucleotice (or) ribotide
2. Deoxyribonucleotide (or) deoxyribotide

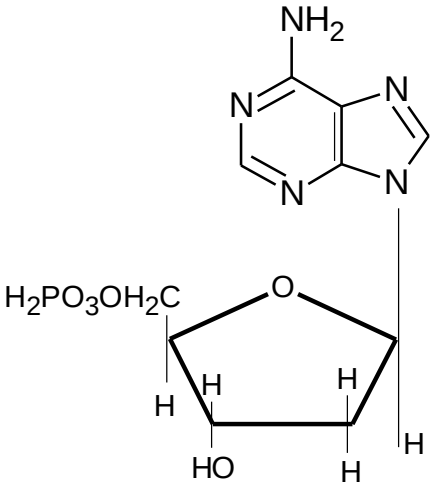
The structure of nucleotide is shown as:



Ribonucleotide

(or)

Ribotide



Deoxyribonucleotide

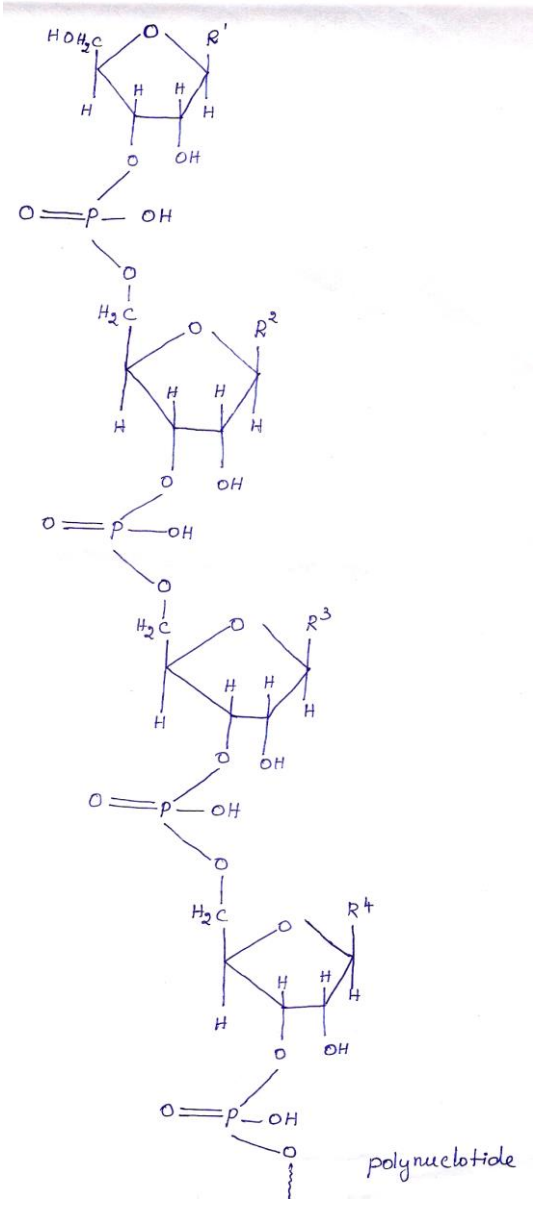
(or)

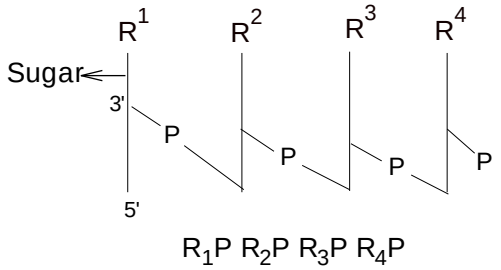
Deoxyribotide

Ribonucleic Acid (RNA)

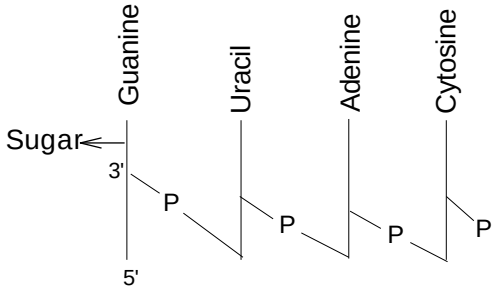
These are polymers of ribonucleotides, and hydrolysis by alkali (or) by certain enzymes to give a mixture of ribonucleotides. The ribonucleotides are linked together by phosphodiester bonds, the attachment of the phosphate is at the 3-position in the ribose molecule. The RNA is a long-chain polynucleotide which does not exist in a regular conformation like a double-chain DNA although some viruses (e.g. reo virus and wound tumour virus) have double stranded RNA. They single RNA stand is folded upon itself, here a majority of the bases are complementary and are joined by hydrogen bonds. This helps the stability of the molecule.

The common bases in RNAs are adenine, guanine, uracil and cytosine, the above bases present in equimolar proportions. The structure of polynucleotide is as follows:





$R_1P\ R_2P\ R_3P\ R_4P$



GP UP AP CP

(or)

G-U-A-CP

Types of RNA:

There are three distinct RNA species: (1) Messenger RNA (mRNA) (or) Template RNA, (2) Ribosomal RNA (rRNA) and (3) Soluble RNA (sRNA (or) transfer RNA (tRNA).

a) Ribosomal RNA (rRNA):

It occurs in combination with protein as ribonucleoprotein is called ribosomes which are attached to the surfaces of the intracellular membrane system called endoplasmic reticulum. It constitutes about 80% of the total RNA of the cell.

It is being synthesize on special regions of chromosomal DNA. It has been found to be stable for at least two generations. Depending upon the sedimentation and molecular weight, three types of ribosomal RNA are,

(i) High molecular weight σRNA.

(ii) Medium molecular weight σRNA.

(iii) Low molecular weight rRNA.

b) Messenger RNA (mRNA)

It carries information for protein synthesis from DNA (genes) to the sites of protein formation (ribosomes). Only about 5% of total cellular content of RNA is mRNA. The half-life of mRNA may vary from very short to very long. mRNa is always single stranded. The sequences of bases in mRNA constitute the genetic code, each gene transcribes its own mRNA.

c) Transfer RNA (tRNA)

It transfers the amino acids in the process of protein synthesis. This constitutes 10 to 15% of total RNA of the cell. It containing about 15 to 80 nucleotides. It has four recognition sites:

i) Amino acid attachment site

ii) Anticodon site – It consists of the middle three bases on the anticodon loop which forms the anticodon.

iii) Ribosome recognition site.

iv) Amino acid activating enzyme recognition site.

Deoxyrbonucleic Acid (DNA)

These are polymers of the deoxyribonucleotides and hydrolysis by certain enzymes results in a mixture of the deoxyribonucleotides. The alkaline hydrolysis of DNA is very slow is due to the absence of the 2'-hydroxyl group in deoxyribose, this difference is used to separate RNAs from DNAs.

The DNA molecule consists of two very long single polynucleotide strands wrapped around each other in the form of a double helix. The width of the double-stranded helix is 20A°, each turn of the helix is 34A°.

The common bases in DNAs are Adenine (A), Guanine(G), Thymine (T) and Cytosine (C).

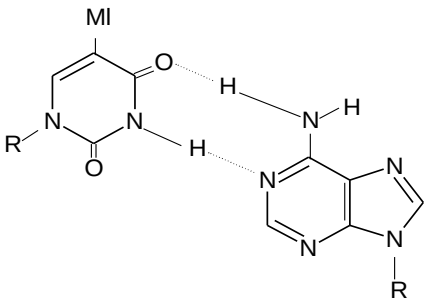
They are present as equimolar proportions. Some important differences between RNAs and DNAs are possible. The following regularities in the composition of DNAs have been observed.

a) A=T; b) G=C; c) A+G=T+C; d) A+C=G+T.

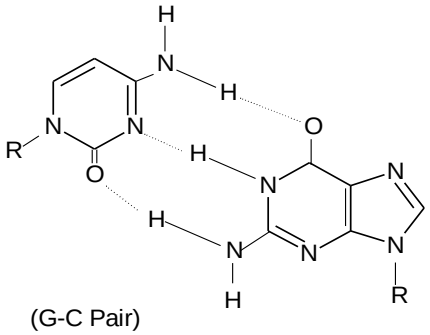
The sum of the keto-bases (G+T) is equal to the sum of the amino-bases (A+C).The equivalence of A and T and of G and C are of paramount importance in connection with the secondary structure of DNAs.

From 1959 onwards, it has been found that DNAs can exist as cyclic single strands, i.e., as rings. Double helical DNAs example is naturally occurring **Catananes.**

The pyrimidine base can pair with its complementary purine base. Such complementary pairs are A-T and G-C are shown below:

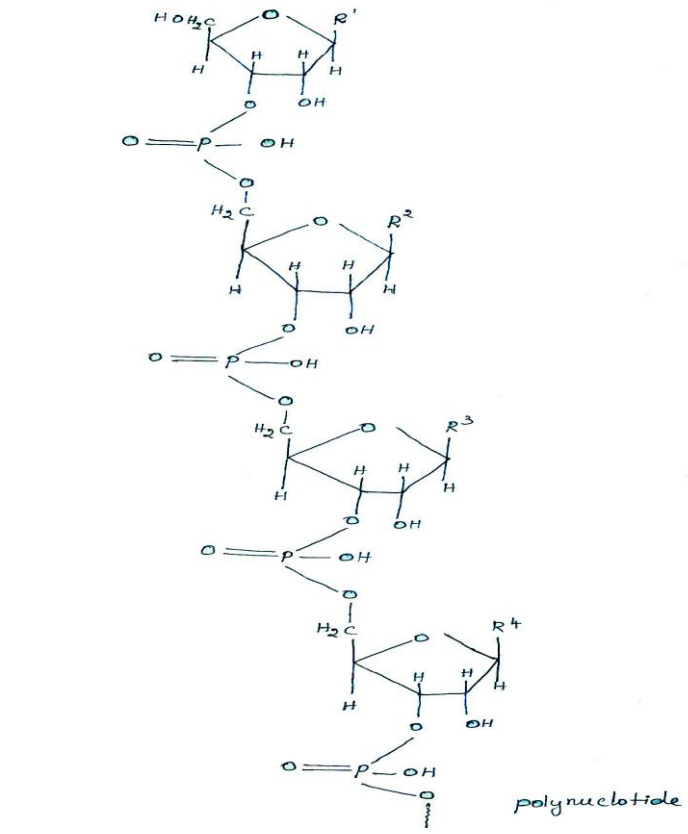


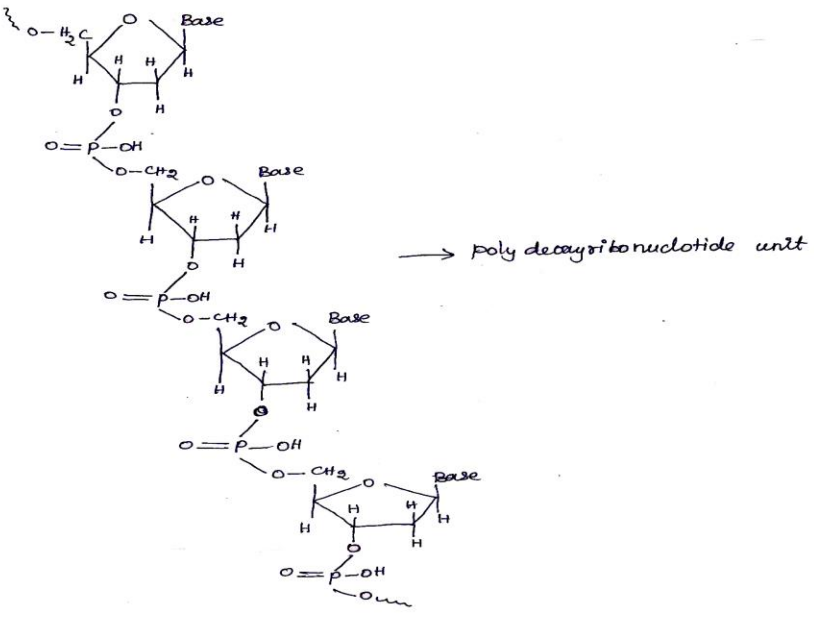
(A-T Pair)

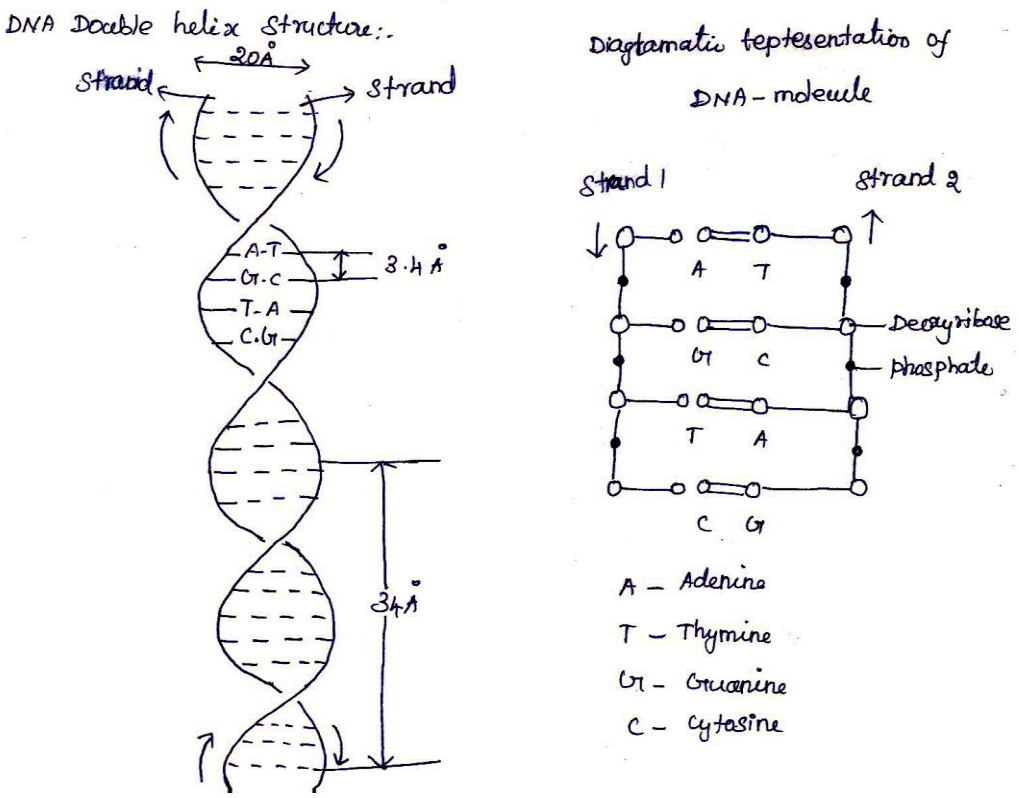


(G-C Pair)

The structure of polydeoxyribonucleotice is shown as follows:


polynucleotide


Base
poly decaxyribonuclotide unit



Biological functions of Nucleic Acids:

The main two biological functions of nucleic acids are,

1. DNA replication
2. Protein Synthesis

1. Replication of DNA:

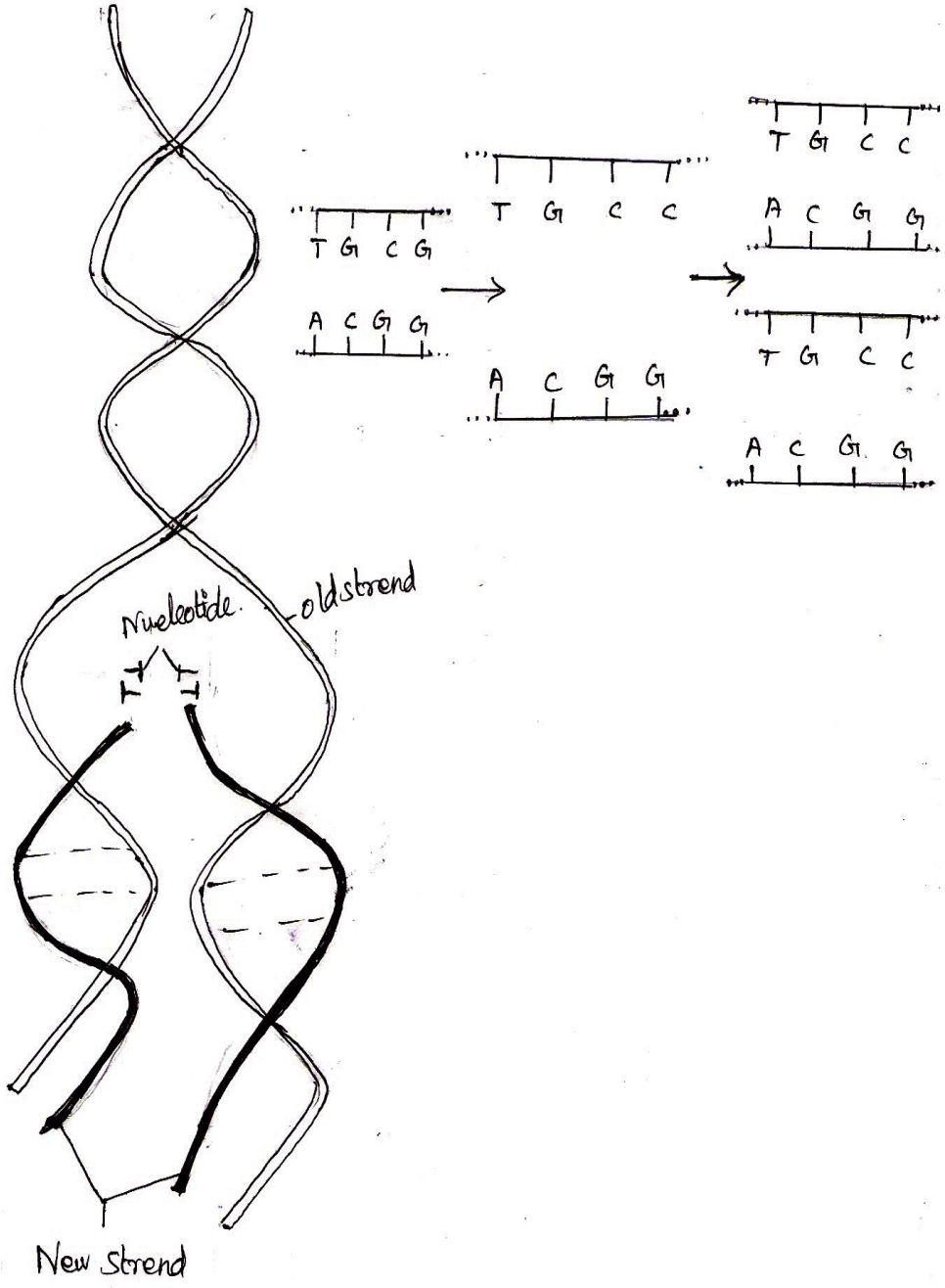
One of the most important properties of DNA is that it can make exact copies of itself. This process is called replication of DNA.

By using the original DNA as a model the newly created DNA structure is replica. The replication process is the very basis of life.

The replication of DNA can be explained by the two strands are separated by breaking the hydrogen bonds. Each single strand has an exposed row of bases (called Primer) that serves as a template. The bases of free deoxyribonucleotides form hydrogen bonds with these exposed bases. The template strand contains the sequence in which the free nucleotides are assembled, i.e., complementary base pairs (A-T, T-A, C-G, G-C). If a segment of the template has the arrangement TTGACCA the newly synthesized chain will be TAACTGGT, which is combine into a DNA molecule identical to the original.

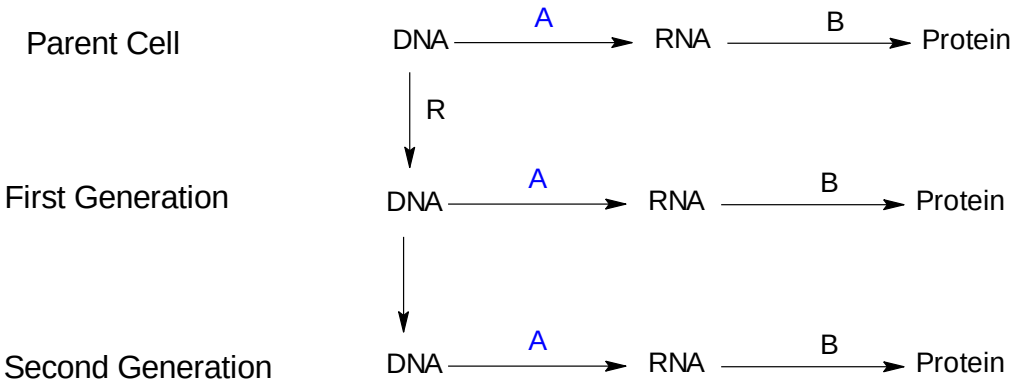
Replication ensures that the genes, which are segments of the DNA molecule.

Replication of DNA is shown diagrammatically:



2. Protein Synthesis:

Proteins are built from about 20 amino acids. The basic mechanism of protein synthesis is that DNA produces RNA, which is converted to protein as follows:



A – transcription

B – translation

R – Self Replication of DNA.

a) Transcription:

Transcription is the copying of a complementary messenger RNA (mRNA) from DNA strand. On replication DNA produces two new strands. One of which produces mRNA strand. In mRNA uracil (U) replaced thymine (T) of DNA. As a result A-U pair will be G-C. The mRNA combines with no. of ribosomes to form polyribosomes.

DNA $\xrightarrow{\text{Replication}}$ Two newly strand $\longrightarrow$ m RNA is transcription

b) Translation:

Here the genetic information present in mRNA direct the order of specific amino acids to form a polypeptide (or) protein. The translation process involves the following steps.

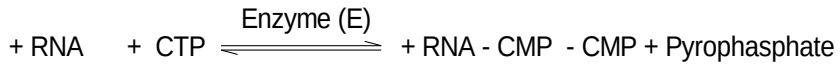
i) Activation of amino acids:

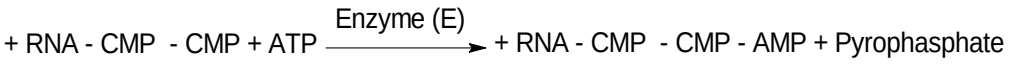
The amino acids are activated by ATP in the presence of specific activating enzyme (E) to form enzyme-amino acetyl adenylates.

Amino acid + ATP $\xrightarrow{\text{Enzyme (E)}}$ Enzyme - amino acyl adenylate (activated amino acid I)

ii) Addition of Nucleotides to transfer RNA:

The transfer RNA reacts with two molecules of cytidine triphosphate (CTP). The resulting compound react with ATP to add adenosine monophosphate to CMP group. The transfer RNA is ready to accept an amino acid.





iii) Transference of amino acid from enzyme-aminoacyl adenylate complex to transfer RNA:

The compound (II) reacts with (I) to form transfer complex tRNA-CMP-CMP-AMP-amino acid III.

tRNA-CMP-CMP-AMP + Enzyme-amino acetyl adenylate

II I

tRNA-CMP-CMP-AMP- amino acetyl adenylate + Enzyme (E)

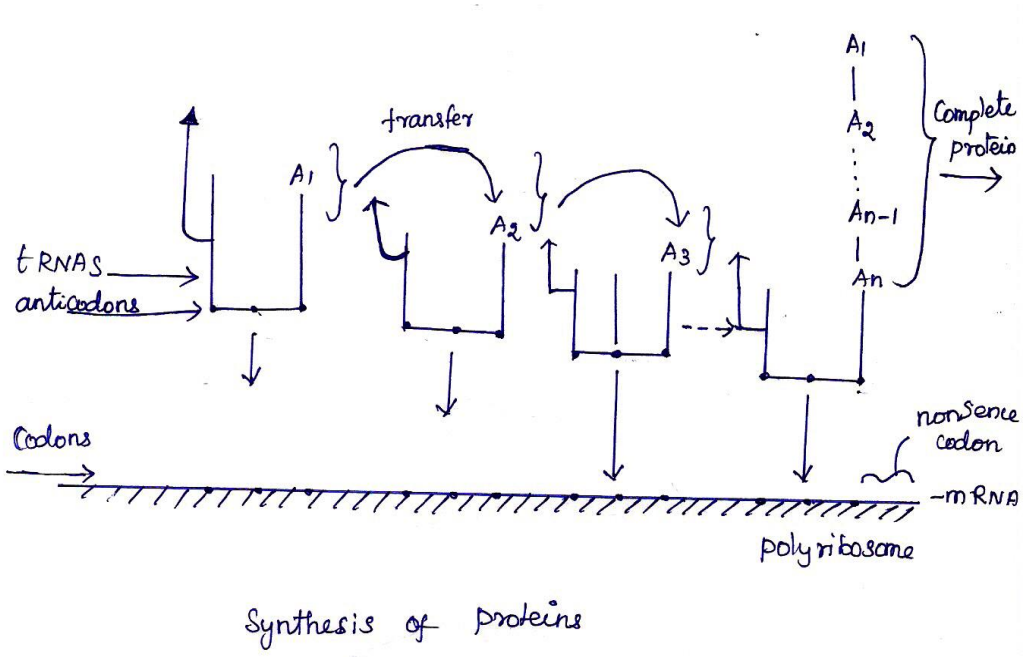
III

iv) Transference of amino acids from tRNA to ribosomes and formation of a Polypeptide chain:

The tRNA molecules will transfer their amino acids to ribosomal RNA. The amino acids are joined together in the specific sequence. This sequence depend upon base pairing between the triplet sequences (codone) on the mRNA, and complementary triplet sequences (anticodone) on the III. It is possible to transfer the amino acid attached form III to form polypeptide (protein).

c) Release of Protein from RNA molecule:

A polypeptide chain is synthesized at each ribosome. A large no. of ribosomes are attached to mRNA. Each of these ribosomes is synthesizing protein and moving towards the end of the mRNA, and protein chain is released to a cytoplasm.



Synthesis of proteins

4.3.1. ALKALOIDS

W.Meissner in 1819 has defined alkaloids (organic alkali like) as basic nitrogeneous compounds of vegetable origin usually having a marked physiological action and which may be regarded as derived from cyclic nitrogeneous nuclei like pyrrole, pyridine, quinoline etc.

Nomenclature and Classification:

Alkaloids have complex structure. Hence, it is not possible to name them systematically. However, they are named in the following way,

(i) Based on the name of the plant:

Eg. Papaverine as it is obtained from the plant papaver somniferum plant.

(ii) Based on the physiological action:

Eg. Morphine

(iii) Based on the name of the discoverer:

Eg. Pelletierin as it was discovered by Pelletier.

Based on the heterocyclic (nitrogen containing) base they are classified as:

(i) Pyrrolidine alkaloids : Eg. Hygrine

(ii) Pyridine and piperidine alkaloids. Eg. Coniine, Piperine, Recimine

(iii) Quinoline alkaloids: Eg. Quinine, Cinchonine

(iv) Isoquinoline alkaloids: Eg. Papaverine

(v) Indole alkialoids: Eg. Reserpine, Heptaphylline

(vi) Tropane alkaloids: Eg. Cocaine, Atropine.

Isolation:

The plant material is finely powdered and treated with water, acidified with hydrochloric acid or sulphuric acid when the alkaloids form salts and dissolve in water. The water extract contains the hydrochlorides or sulphates of alkaloids together with dye stuffs, carbohydrates and other products from the plant tissue. This is treated with alkali when the alkaloids which are sparingly soluble in water are precipitated. In the case of volatile alkaloids, the acidulated water extract is treated with alkali and steam distilled.

Purification of the crude product obtained above is carried out by special methods like chromatography or frequently by crystallization of the freed compounds or their salts.

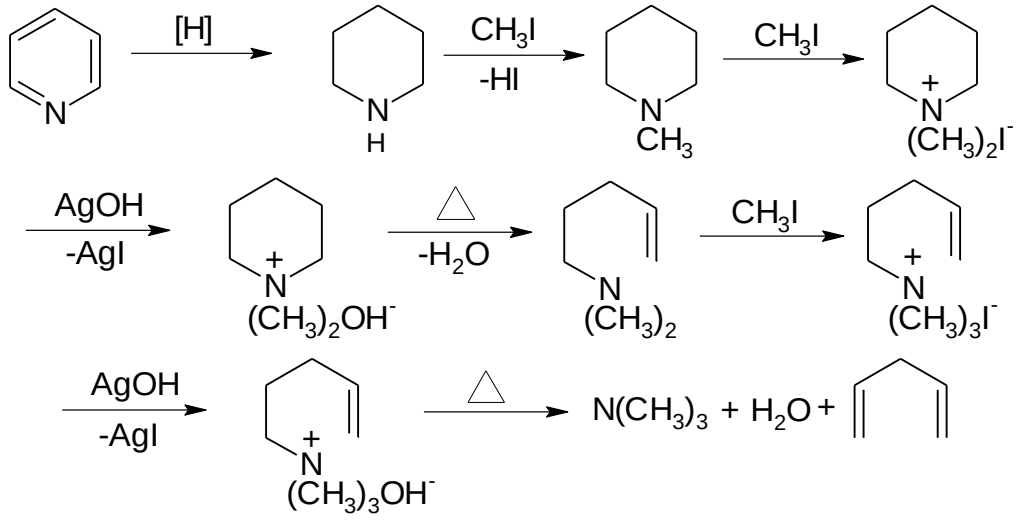
Heterocyclic ring size determination or Hofmann's Exhaustive Methylation:

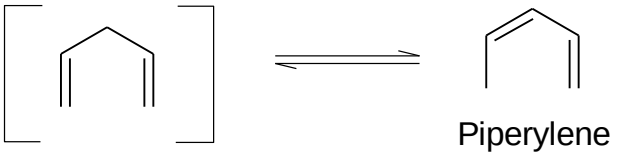
Heterocyclic rings containing nitrogen are opened with the elimination of nitrogen when subjected to exhaustive methylation. If thus helps us in knowing the nature of the carbon skeleton.

The heterocyclic compound is hydrogenated, if unsaturated and converted to the quaternary ammonium hydroxide. This on heating loses a molecule of water by the combination of –OH group with a hydrogen atom in β-position with respect to the nitrogen atom and the ring is opened at the nitrogen atom.

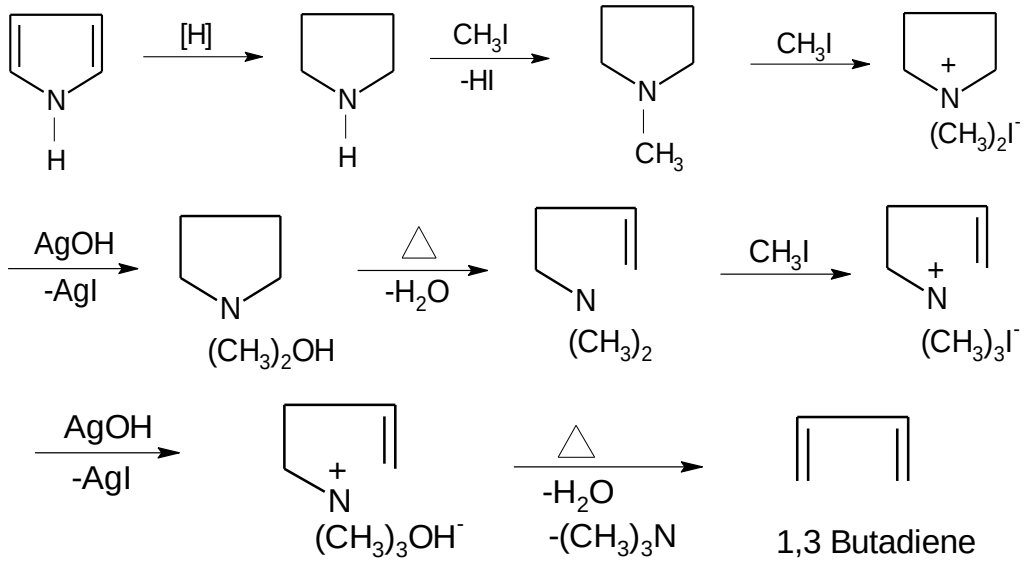
On repeating the process with the product, nitrogen atom is completely removed having an unsaturated hydrocarbon behind which generally isomerizes to a conjugated diene. For example, starting with

(a) Pyridine (Six membered ring)





(b) Pyrrole (Five membered ring)



Piperine ($C_{17}H_{19}O_3N$)

Piperine occurs in pepper, especially black pepper (piper nigrum) to the extent of about a percent. It was first prepared by Oersted in 1819 and crystallizes in monoclinic crystals. It is sparingly soluble in water. It is much less toxic than other alkaloids. It gives salts with strong mineral acids. It exhibits geometrical isomerism. Chavicine is the other geometrical isomer.

Structure Determination:

1) Molecular formula of piperine as deduced from its analytical data and molecular weight determination is $C_{17}H_{19}O_3N$.

2) Hydrolysis of piperine by boiling with aleoholic potash gives piperidine and piperic acid.

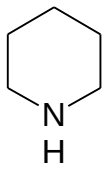
$C_{17}H_{19}O_3N + H2O \longrightarrow C_5H_{10}NH + C_{11}H_9O_2COOH$

Piperine Piperidine Piperic acid

This shows that piperine is piperidine amide of piperic acid. If the structure of piperidine and piperic acid could be elucidated, the constitution of the alkaloid, piperine will be known.

3) Structure of Piperidine:

Piperidine is the hexahydropyridine and this has been confirmed by Hofmann's exhaustive methylation. It formed piperylene in the above reaction indicating the presence of six membered ring. Thus, the structure of piperidine is



4) Structure of Piperic acid:

a) The molecular formula is $C_{12}H_{10}O_4$.

b) It gives brisk effervescence with $NaHCO_3$, indicating the presence of carboxylic group in the molecule.

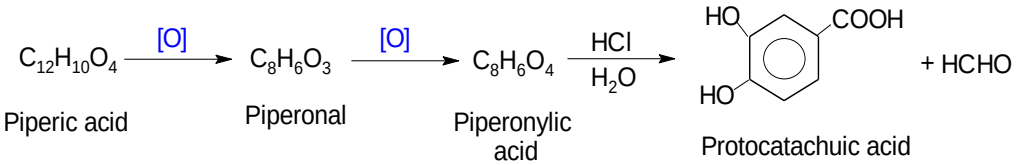
c) It forms tetrahydro derivative on hydrogenation and gives tetra bromo derivative with bromine water. The bromine water loses its colour during the reaction. These reactions clearly indicate the presence of two double bonds in piperic acid.

d) Piperic acid on oxidation with potassium permanganate gives first piperonal, tartaric acid and oxalic acid mixture. Piperonal on further oxidation gives piperonylic acid. Piperonylic acid has four carbon and four hydrogen atoms less than the parent acid. Change of piperonal to piperonylic acid involves the change of aldehydic group (-CHO) to carboxylic group (-COOH).

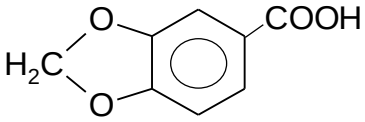
$$C_{11}H_9O_2COOH \xrightarrow{[O]} C_7H_5O_2.CHO \xrightarrow{[O]} C_7H_5O_2.COOH$$

Piperic acid — Piperonal — Piperonylic acid

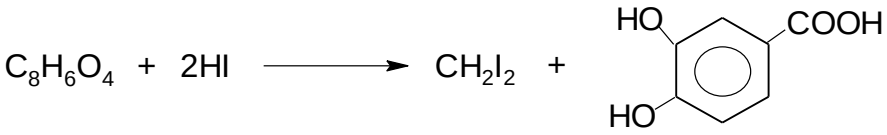
e) On heating with hydrochloric acid at 470K under pressure piperonylic acid forms protocatechuric acid (3,4-dihydroxy benzoic acid and formal dehyde).



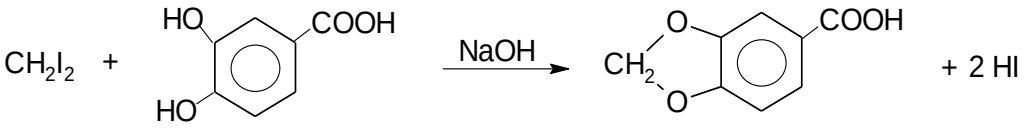
Since there are no free hydroxyl groups in piperonylic acid and in the above conversion it loses only one carbon atom, it suggests that piperonylic acid is possibly the methylene ether of protocatachuic acid i.e., it is 3,4-methylene dioxybenzoic acid.



f) This structure of piperonylic acid is further confirmed by the reaction of hydroiodic acid and its synthesis. When piperonylic acid is boiled with hydriodic acid, it gives methylene iodide and protocatachuic acid.



When protocatachuic acid is boiled with methylene iodide in presence of alkali, it forms piperonylic acid.



g) Further, since piperonal is an aldehyde which gives piperonylic acid on oxidation, it must be 3,4-methylenedioxy benzaldehyde.

From there reactions it becomes clear that piperic acid contains one benzene ring, one methylendioxy group and only one side chain. This side chain has –COOH group. The difference between piperic acid ($C_{12}H_{10}O_4$) and piperonylic acid ($C_8H_6O_4$) is C_4H_4 and this constitutes the side chain in piperic acid.

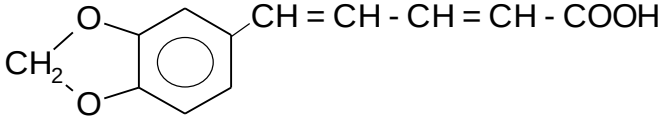
5) Structure of C_4H_4:

(i) It has two C=C moiety which is shown by the ready addition of four bromine atoms.

(ii) Ozonylsis of piperic acid gives glyoxal and glyoxalic acid. This proves beyond doubt that C_4H_4 must be a conjucated diene.

(iii) Further since piperic acid on careful oxidation yields tartaric acid, the side chain must be a straight chain.

6) Hence, the formula of piperic acid containing 3,4-methylene dioxybenzene ring, a side chain containing two double bonds, a carboxylic group with the carbon atoms arranged in straight chain can be written as,

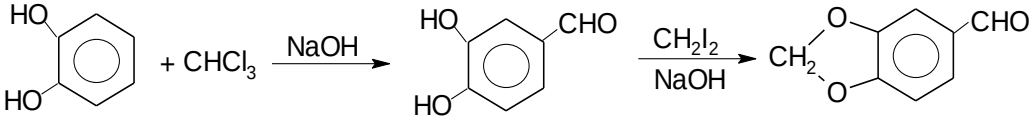


7) The structure of piperic acid has been confirmed by its synthesis by Ladenburg in 1894.

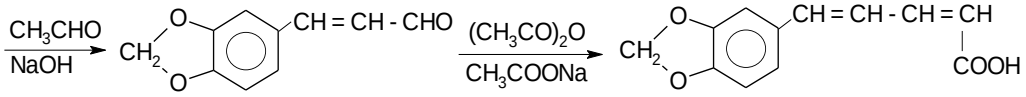
(i) Piperonal is prepared from catebol via Reimer Tiemann reaction.

(ii) This is condensed with acetaldehyde in presence of caurstic soda (Claisen reaction).

(iii) The condensation product, a cinnamaldehyde derivative, is then heated a mixture of acetic cenhydride and sodium acetate (Parkin reaction) when piperic acid is obtained.

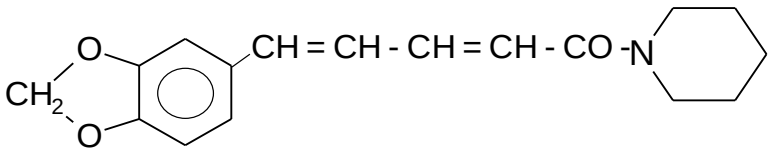


Catechol Piperonal

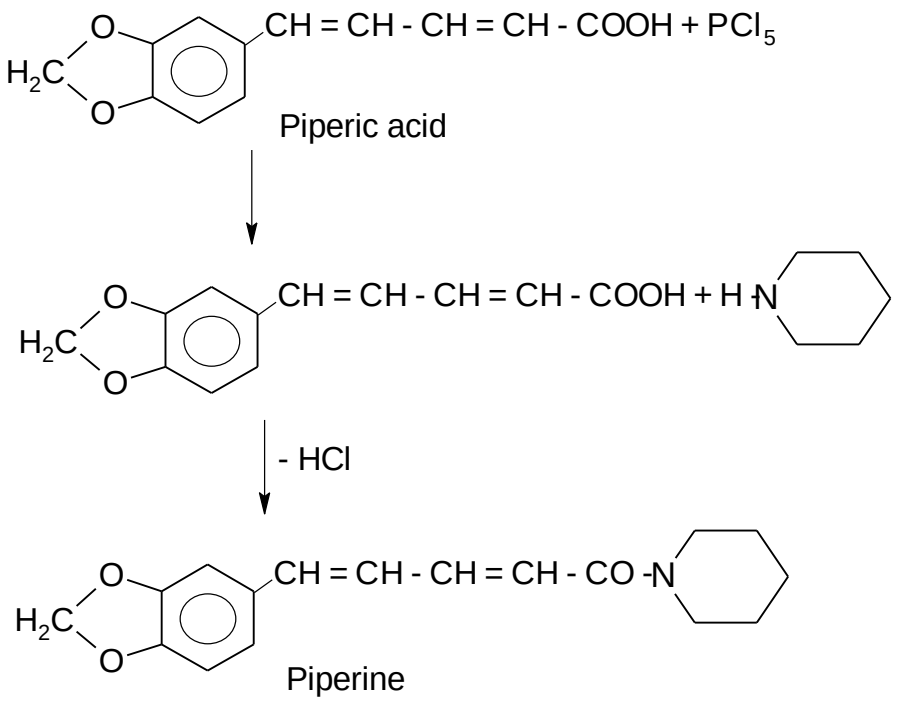


Cinnamaldehyde derivative Piperic acid

8) Structural formula of piperine as piperidine amide of piperic acid can be written as,



9) This structure is confirmed by its synthesis from the acid chloride of piperic acid (obtained by the action of PCl_5 on the acid). The acid chloride is heated with piperidine in benzene solution when piperine is obtained.



Uses:

(i) Piperine is used as a flavouring agent in beverages.

(ii) It is used in the preparation of exterminating agent for fly and other insect pests.

Coniine $C_8H_{17}N$:

Coniine is one of the simple alkaloids. It is found in the seeds and other parts of the spotted hemlock. It was the first alkaloid to be synthesized. This alkaloid which was responsible for causing the death of the wisest man Socrates which was the first to succumb to the synthetic skill of the organic chemist.

Isolation:

Coniine is isolated from the powdered hemlock seeds by distilling with caustic soda solution. The distillable contains coniine which is extracted with ether. The ethereal extract is evaporated when the alkaloid is left behind as an oily residue.

Properties:

(i) It is a colourless oil with boiling point 440k.

(ii) The natural product of coniine is dextro rotatory.

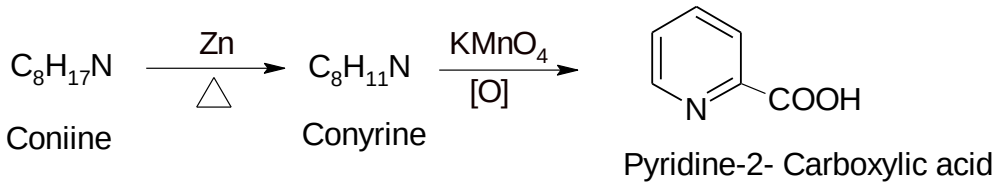
(iii) It has an unpleasant smell and turns brown on exposure to air.

(iv) It is soluble in water but more soluble in alcohol.

(v) Coniine as well as its salts are exceedingly poisonous and cause death by paralysis of the motor nerve endings and depression of the central nervous system.

Structure Determination:

1. The molecular formula of coniine as deduced from its analytical data and molecular weight determination is $C_8H_{17}N$.
2. Coniine in Hofmann's exhaustive methylation yields piperylene, indicating the presence of a six membered pyridine ring in the molecule.
3. When distilled with Zinc dust, coniine is converted into conyrine ($C_8H_{11}N$) which on oxidation with permanganate gave 2-pyridine-carboxylic acid, α-picolinic acid.

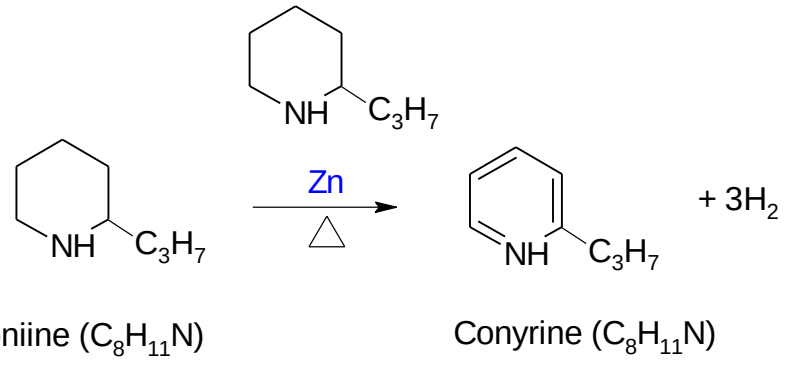


This shows that,

(i) In conyrine a pyridine nucleus is present with a side chain in the 2-position.

(ii) Conyrine is formed when coniine loses six hydrogen atoms on zinc dust distillation. Thus, coniine is probably a piperidine derivative with a side chain in 2-position.

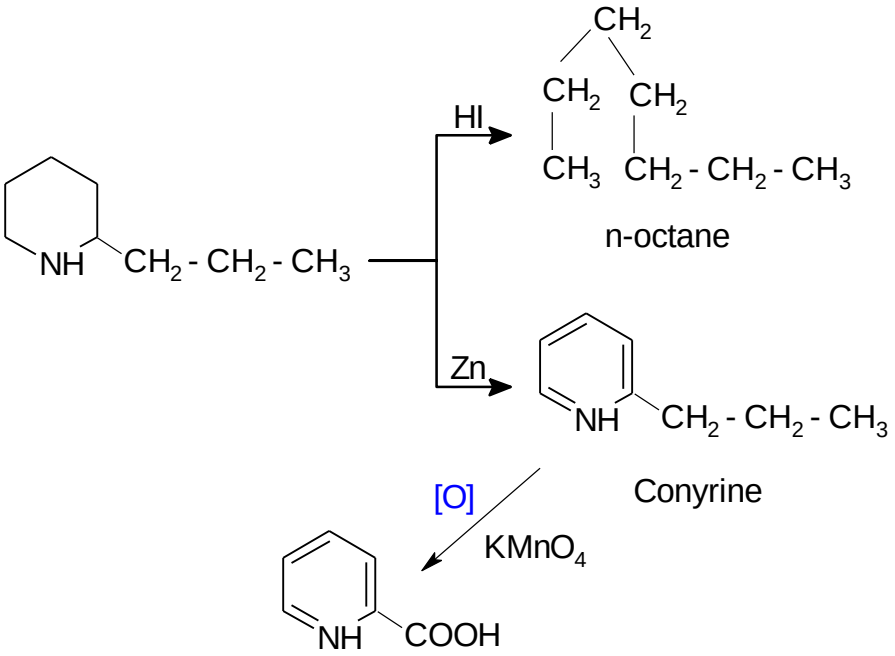
(iii) Coniine and piperidine being $C_8H_{17}N$ and $C_5H_{10}N$ respectively, the above side chain must be C_3H_7 (their difference) propyl radical.



Thus, the formulae of coniine and conyrine can be written as follows:

(iv) The propyl group constituting the side chain may be n-propyl or isopropyl. On heating with hydriodic acid at 570k under pressure, coniine gives n-octane. This shown that the side chain is n-propyl and

not isopropyl. Had it been isopropyl, the expected product would have been iso-octane.



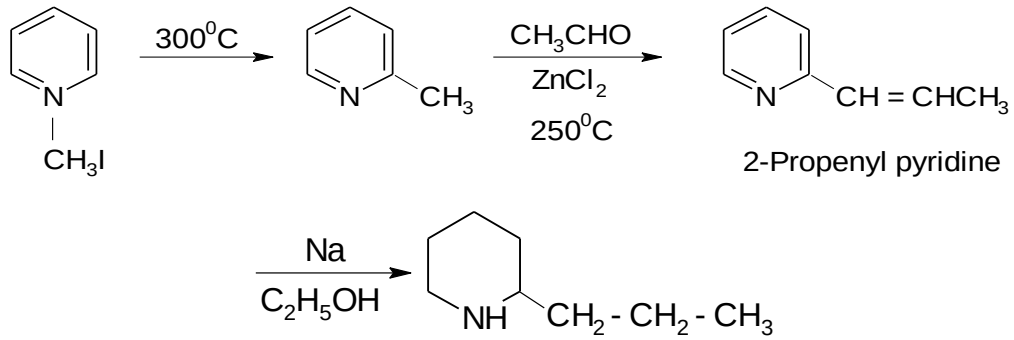
This shows that coniine is 2-n-propylpiperidine. The various reactions of coniine described can be formulated.

4) Synthesis:

The above structure has been confirmed by synthesis:

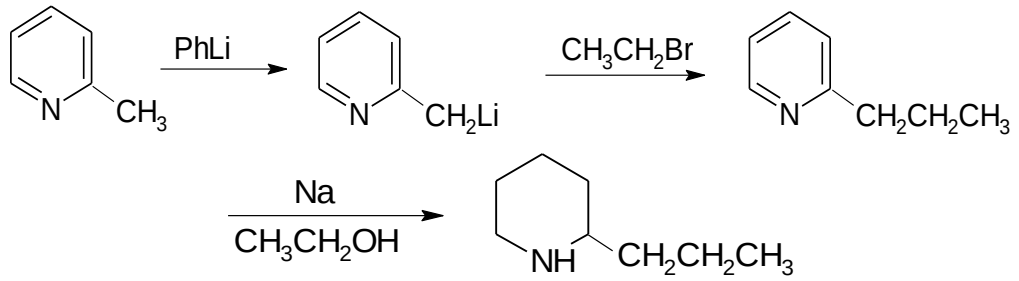
(i) Ladenburg (1885) synthesis:

N-methyl pyridinium iodide on heating to 570k gives 2- and 4-methyl pyridine 2-methyl pyridine condenses with acetaldehyde at 520k to form 2-propenylpyridine. This on reduction with sodium and alcohol gives coniine.



(ii) Bergmann (1932) synthesis:

Coniine has also been synthesized by Bergmann from 2-methyl pyridine and phenyl lithium as follows:



Nicotine ($C_{10}H_{14}N_2$)

Nicotine is the chief alkaloid of the tobacco plant (nicotiana tobaccum) where in it is present as a salt of malic or citric acid. In leaves of tobacco its concentration is the highest, 0.8%.

Isolation:

The alkaloid is conveniently prepared from tobacco leaves. Raw tobacco of high nicotine content is crushed and its soluble constituent is extracted with cold water. The hydrocarbons present in the extract are removed by acidifying the solution and extracting with ether. The residual solution is made alkaline and nicotine set free is extracted with ether.

Properties:

(i) Freshly prepared nicotine is a colourless, oily liquid with boiling point 520k.

(ii) It is readily soluble in water.

(iii) Pure nicotine has an unpleasant smell.

(iv) It has a burning task and is very poisonous (lethal does being about 50mg)

(v) In air it rapidly turns brown and refinifies.

(vi) It can be distilled without decomposition only in vaccum or in a current of hydrogen.

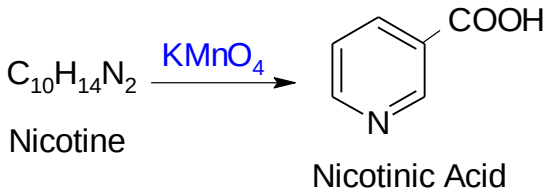
(vii) The natural alkaloid is laevo-rotatory with specific rotation – 169°.

(viii) Nicotine affects both respiratory and nervous system.

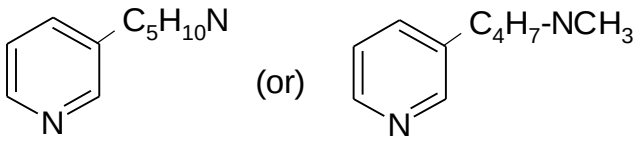
Structure Determination:

1. Molecular formula of nicotine as deduced from its analytical data and molecular mass determination is $C_{10}H_{14}N_2$.
2. Nicotine reacts with hydrochloric acid and forms a crystalline solid, nicotine dichloride. This reaction indicates the presence of two basic groups in nicotine.

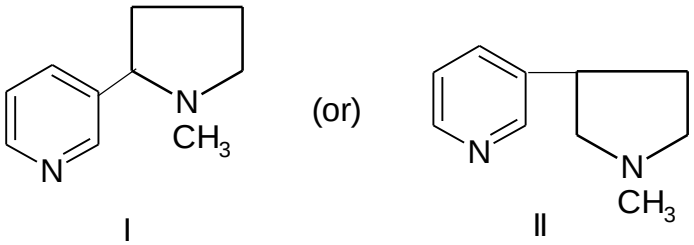
3. Nicotine reacts with methyl iodide to form dimethiodide and two monomethiodides but it does not form an acetyl or benzoyl derivative. This shows that the two nitrogen atoms in nicotine are tertiary.
4. Nicotine reacts with hydriodic acid at 500k to form methyl iodide which on treatment with silver nitrate gives silver iodide. From the weight of silver iodide, one N-CH_3 group is found to be present in nicotine (Cf.zeisel method).
5. Nicotine on oxidation with chromic acid or permanganate gives nicotine acid (C_5H_4NCOOH) which has one COOH group at the third position of pyridine ring. From this reaction we can conclude that nicotine is a derivative of pyridine having groups at third position.



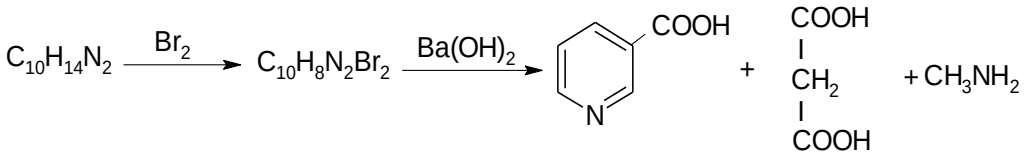
6. Subtracting the formula of mono substituted pyridine (C_5H_4N) from the molecular formula of nicotine ($C_{10}H_{14}N_2$) we have $C_5H_{10}N$ which is the group attached at the third position of pyridine. Based on this, the formula of nicotine will be,



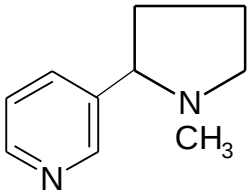
7. Nicotine reacts with zinc chloride to form an addition product which on treatment with lime water gives pyridine, pyrrole and methylamine. Hence, the group attached at the third position of pyridine must be a pyrrole derivative.
8. On reduction, nicotine consumes only three molecules of hydrogen and in this reaction, pyridine is hydrogenated to piperidine. Hence, the group attached at the third position of pyridine (C_4H_7-NCH_3) must be a saturated and cyclic in nature. Based on there we can the structural formula of nicotine as



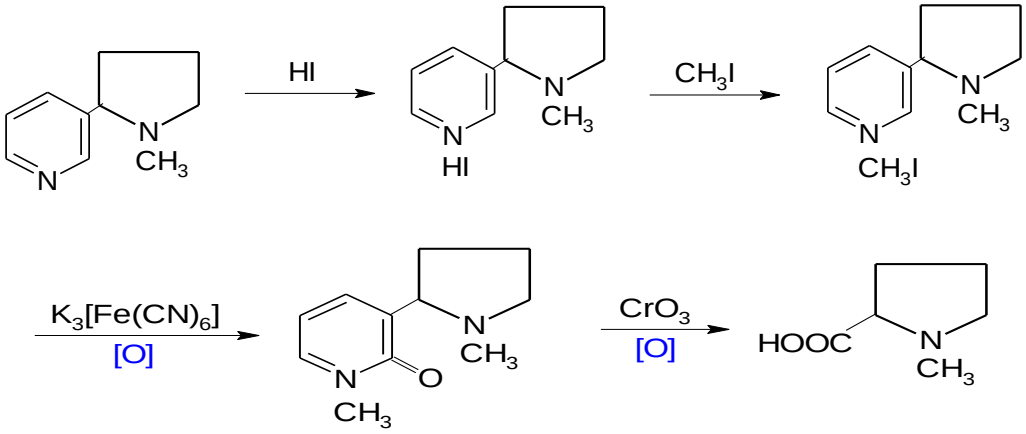
9. Nicotine reacts with bromine in hydrobromic acid to form nicotine dibromide. This on treatment with barium hydroxide gives nicotinic acid, malonic acid and methyl amine.



As malonic acid with three carbon atoms is formed in the reaction, it indicates clearly that a group with four carbon atoms must be attached at the third position of pyridine. Based on these reactions, the structure of nicotine must be I. In this N-methyl pyxrolidine using its second position unites with pyridine ring at its third position. Thus the structure of nicotine is -

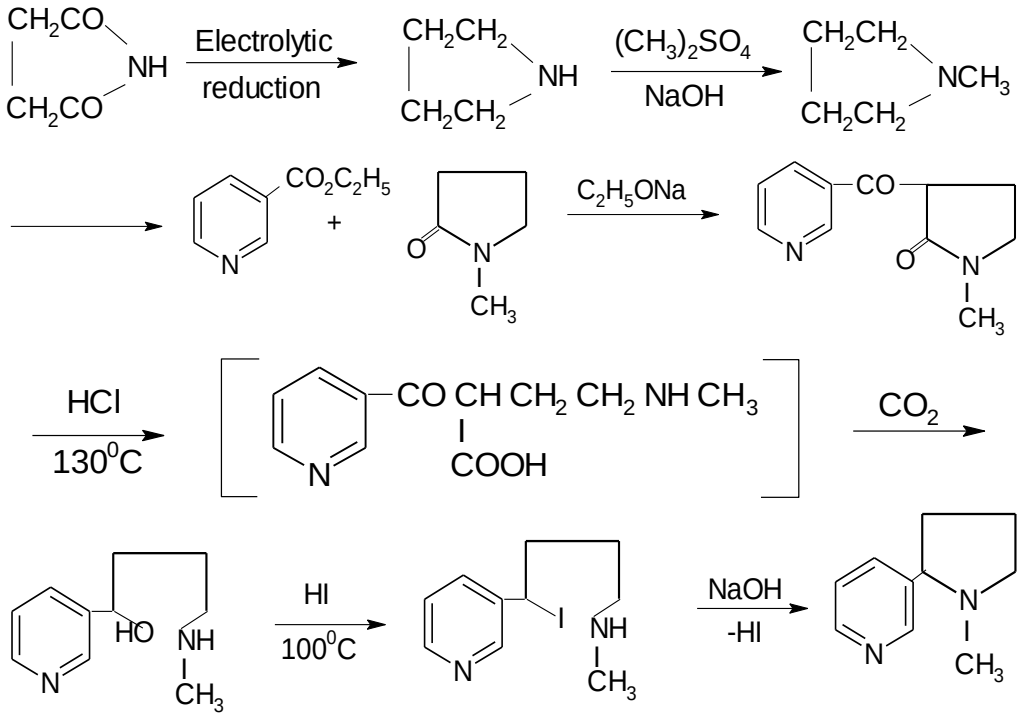


10. This structure is confirmed by the following reaction. Nicotine hydriodide on treatment with methyl iodide gives a methiodide. This on oxidation yields hygrinic acid (N-methyl pyroolidine-2-carboxylic acid). This indicates the presence of pyrrolidine ring with a methyl group attached to N-atom carrying some other group in 2-position.



This indicates that pyridine ring has been destroyed during the transformation and the group – $C_5H_{10}N$ attached to the pyridine ring in third position is N-methyl pyrrolidine.

The structural formula of nicotine has been further confirmed by its synthesis by Spath and Bretschneider (1928) as follows:



The (±) mixture was resolved by means Ol (±) fartaric acid and (-) nicotine thus obtained was found to be identical with the natural product.

Uses:

1) In admixture with soap solution, nicotine is one of the most effective exterminating agents for green fly and other insect pests.
2) It is used in the manufacture of nicotinamide and niacin.

4.3 TERPENES

The hydrocarbons with the general formula $(C_5H_8)n$ found in the essential oils of plants are called terpenes. Their oxidation products like alcohol, aldehycle, keton are known as terpenoids.

Essential oils and terpenoids are found in use in the preparation of cosmetics, flavouring agent in food stuffs and medicines.

Isolation of terpenoids

The isolation of terpenoids from plant tissues involves the following two steps,

(i) Isolation of essential oils from plant tissues.

(ii) Isolation of terpenoids from essential oils

We shall discuss them.

a) Isolation of essential oils from plant tissues:

The following methods are employed,

(i) **Steam distillation method:** This is the widely used method.

(ii) Solvent extraction using volatile solvents.

(iii) Enfleurage on pure fat.

Plant tissues (roots, stem, leaves, flowers or fruits) are macerated and steam distilled when the essential oil distill over. In case, constituents of the essential oil decompose on steam distillation, it is extracted with a solvent. e.g., light petrolat 320K. From the solution so obtained, the solvent is distilled away at reduced pressure.

To extract the essential oil present in the flower petals, there are spread over purified molten fat until the latter is saturated with the essential oil which may be extracted from the resultant fat with ethanol.

b) Isolation of terpenoids from essential oils:

Terpenoids are obtained from the essential oil by,

a) Fractional distillation

b) Chromatography.

Isoprene rule:

Products of thermal decomposition of terpenoids invariably contain isoprene (C_5H_8) as one of the constituents. Thisled Wallach (1887) to suggest that the skeleton structures of all naturally occurring terpenoids are built up isoprene units. This is known as the isoprene rule.

Explanation:

(i) The empirical formula of the most of the naturally occurring terpenoids is C_5H_8 which is the molecular formula of isoprene.

(ii) Products of thermal decomposition of terpenoids invariably contain isoprene.

(iii) Many terpenes are synthesised using isoprene units under sitable reaction conditions.

Citral, $C_{10}H_{16}O$

This is the most important acyclic terpenoid since the structures of most of the other monoterpenoids are based on the structure of citral. It occurs in the oil of lemon grass (upto 80%) and oils of lime, lemon, citronella etc.

Extraction:

It is obtained from lemon grass oil by fractional distillation under reduced pressure and purified by forming the bisulphite compound. The

crystalline bisulphite compound is decomposed with sodium carbonate to get free citral.

Properties:

Citral is a pale yellow oily liquid (bp about 500K). It has a pleasant odour of lemons. It is optically inactive.

Structure Determination

i) The molecular formula of citral as deduced from its analytical data is $C_{10}H_{16}O$.

ii) Presence of two double bonds

a. Citral on bromination forms citral tetrabromide

b. On reduction using hydrogen, citral gives tetrahyudrocitral.

$$\underset{\text{Tetrhydrocitral}}{C_{10}H_{20}O} \xleftarrow{Pd - H_2} \underset{\text{Citral}}{C_{10}H_{16}O} \xrightarrow{2Br_2} \underset{\text{Citral tetrabromide}}{C_{10}H_{16}OBr_4}$$

c. On ozoolysis it gives acetone, laevulaldehyde and glyoxal.

On ozonolysis the chain breaks at two points. This suggests the presence of two double bonds.

$$\underset{\text{Citral}}{C_{10}H_{16}O} \xrightarrow{O_3} \underset{\text{Acetone}}{(CH3)_2CO} + \underset{\text{Laevulaldehyde}}{CHO(CH_2)_2\ COCH_3} + \underset{\text{Glyoxal}}{CHO\text{-}CHO}$$

(iii) Presence of aldehyde group

Citral gives the typical reactions of an aldehyde. For Example,

a) If forms an oxime with hydroxylamine

b) It gives an addition compound with sodium bisulphite.

c) On oxidation with silver oxide, it gives geranic acid, an acid with the same number of carbon atoms as citral.

$$\underset{\text{Geranic acid}}{C_{10}H_{16}O_2} \xleftarrow[Ag_2O]{[O]} C_{10}H_{16}O \xrightarrow{NH_2OH} \underset{\text{Oxime}}{C_{10}H_{16}{=}NOH}$$

d) Citral reacts with Tollen's reagent and forms silver mirror.

e) Citral reduces Fehling's solution to form red cuprous oxide.

$$Cu_2O + C_{10}H_{16}O_2 \xleftarrow[\text{Solution}]{\text{Fehling's}} C_{10}H_{16}O \xrightarrow[\text{reagent}]{\text{Tollen's}} 2Ag\downarrow$$

Geranic acid

$+ C_{10}H_{16}O_2$

Geranic acid

f) Citral on reduction with sodium amalgam and water gives geraniol, a primary alcohol.

$$C_{10}H_{16}O \xrightarrow{[H]} C_{10}H_{18}O$$

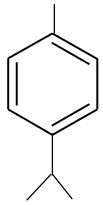
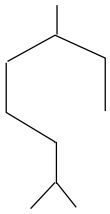
Geranic acid

All the above reactions indicate the presence of an aldehycle group in citral.

(iv) The corresponding saturated hydrocarbon of citral has the molecular formula, $C_{10}H_{22}$ which belongs to the general formula CnH_2n+2 Thus citral is a cyclic compound.

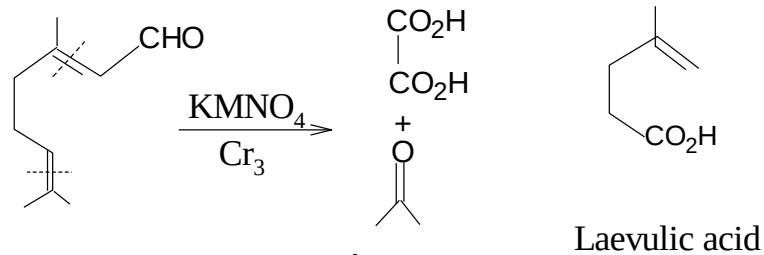
(v) Position of methyl and isopropyl groups

On heating with potassium hydrogen sulphate, citral forms P-cymene which is nothing but P-methyl isopropyl benzene from this semmler concluded that citral molecule was acyclic and assigned the following carbon skeleton for citral having two isoprene units joined head to tail.

$C_{10}H_{16}O \xrightarrow{KHSO4}$  (P-cymene) 

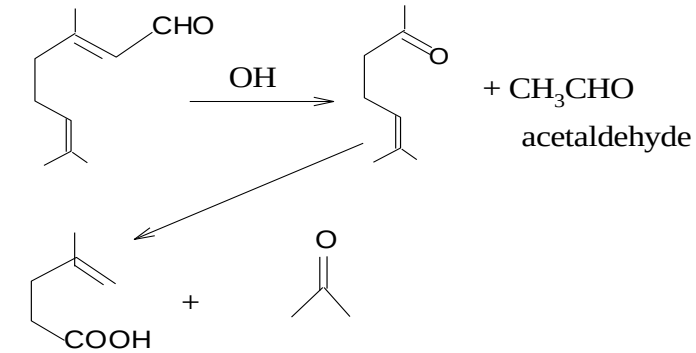
(vi) Location of double bonds

Oxidation of citral with alkaline potassium permanganate, followed by chromic acid gives acetone, oxalic acid laevulic acid. Formation of these oxidation product is in accordance with the assigned structural formula of citral.



Citral Acetone Laevulic acid

vii) Structure assigned to citral is further supported by its hydrolysis with aqueous potassium carbonate. Products of hydrolysis are acetaldehyde and 6-methyl-5hepten-2-one which itself on oxidation gives acetone and laevulic acid. This is in accordance with the assigned structural formula of citral.

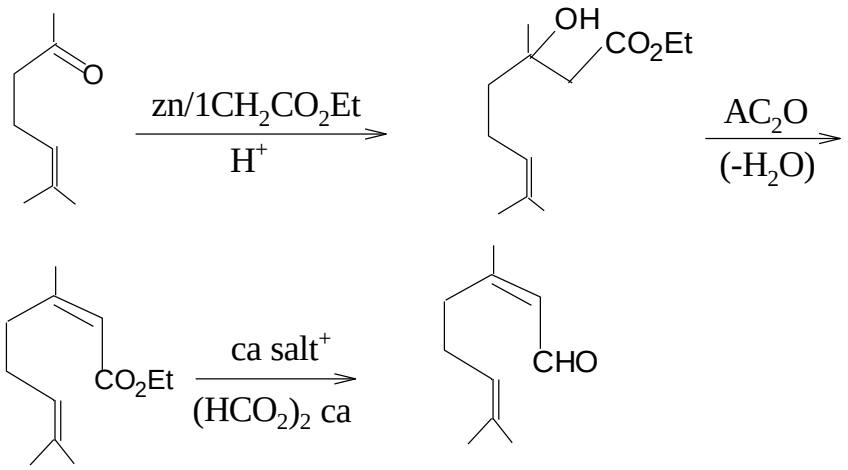


viii) Further, citral reacts with sodium bisulphite and forms mono and dibisulphite addition products. This is the characteristic reaction of α, β-unsaturated aldehydes. Thus, citral is an α, β- unsaturated aldehyde. This has been proved to be so by its absorption at 238 nm.

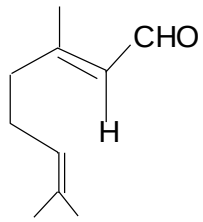
(ix) Synthesis

The structure of citral was finally concluded by the synthesis from 6-methyl -5- hepten -2- one by Reformatsky reaction using zinc and ethyl iodoacetate as follows

(Barbier, Bouveault and Tiemann, 1898)

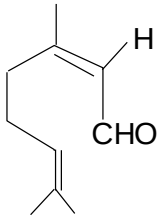


citral exhibits geometrical isomerism as below,



Trans (E-form)

citral-a; geranial



Cis (Z-form)

citral-b; neral

Uses

i) It is widely used as a flavouring agent and in preparing synthetic perfumes, e.g., α-and β- ionone.

ii) It is also employed for the manufacture of geraniol

Geranoil $C_{10}H_{18}O$

Geraniol occurs in rose, grass, geranium, lavender and citronella oils. It is obtained from the cheap oil of palmrosa by treating with anhydrous calcium chloride and decomposing the crystalline addition product thus obtained with water.

It may also be obtained by reduction of citral with aluminium amalgam. But some nerol is also formed at the same time.

Properties

Geraniol of a colourless liquid having pleasant rose like odour.

Structure Determination

i) Molecular formula of geraniol as deduced form its analytical data is $C_{10}H_{18}O$

ii) It gives the reaction of a diolefin.

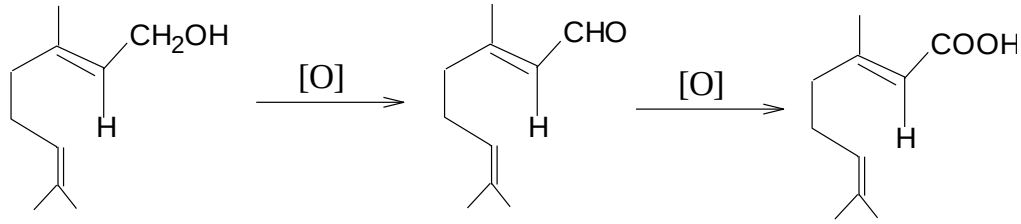
a. On bromination it gives a tetrabromide.

b. On reduction it gives tetrahydrogeraniol.

$$C_{10}H_{22}O \xleftarrow[[H]]{Ni} C_{10}H_{18}O \xrightarrow{2Br_2} C_{10}H_{18}O{:}Br_4$$

These show the presence of two double bonds.

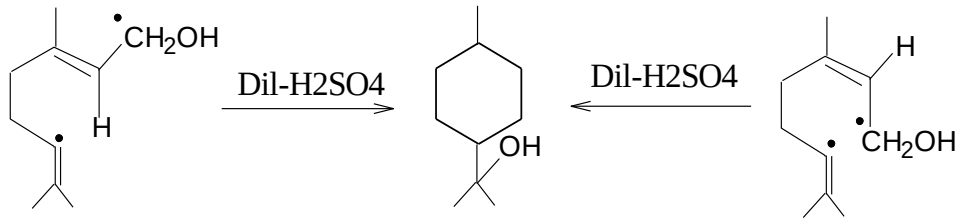
iii) It exhibits the reactions of a primary alcohol-on oxidation it given an aldehyde and on further oxidation gives an acid, geranic acid. They contain the same number of carbon atoms.



Geraniol Citral - a Geranic acid

iv) Geraniol on oxidation gives citral- a. Hence, geranid must have the structure skeceton of citral-a. The structure of citral was a well established one.

v) Geraniol and nerol are geometrical isomers. Hence the correct structure of geraniol is decided from their reaction with dilute sulphuric acid. Both the compounds from α-terpineol in the reaction with different rates. Nerol forms α-terpineol nine times faster than geraniol. This reaction is a ring closure reaction. When the participating groups are nearer, the reaction occurs faster. The ring closure reaction can be written as,

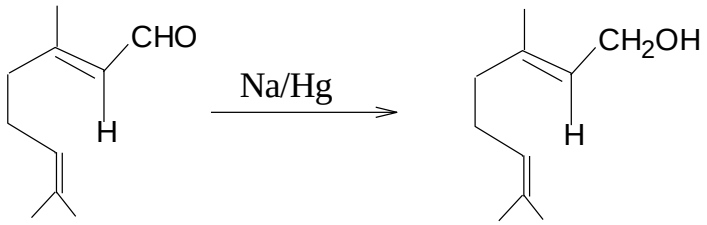


Geraniol (trans) α-terpineol Nerol (cis)

The carbon atoms participating in the ring closure reaction are shown by,

Thus geraniol is a trans compound,

vi) The structure of geraniol is confirmed by the following synthesis.



citral - a Geraniol

Uses

Geraniol and its esters are used in the preparation of flavouring agent and rose scent.

α-Terpineol $C_{10}H_{18}O$

α-Terpineol is an important monocyclic terpenoid. It is an optically active, crystalline solid alcohol. Dextro form is present in petitgrain and nerdi oil. Laevo form is present in camphor oil.

Racemic mixture is present in cajuput oil.

Structure Determination

i) Molecular formula of α-terpineol as deduced from its analytical data is $C_{10}H_{18}O$.

ii) α-terpineol decolourises bromine water and forms a dibromo derivative. It also adds withone molecule of nitrosyl chloride, NOCl

$$C_{10}H_{18}O.\ Br_2 \xleftarrow{Br_2} C_{10}H_{18}O \xrightarrow{NOCl} C_{10}H_{18}O.NOCl$$

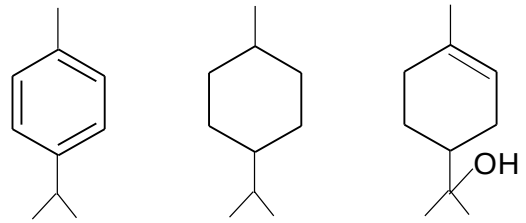
These reactions show the presence of one double bond in the molecule.

iii) The corresponding saturated hydrocarbon has the formula $C_{10}H_{20}$ which belongs to CnH2n category. Thus, α-terpineol is a monocyclic compound.

iv) The routine test indicate the alcoholic group is a tertiary alcohol.

v) When α-terpineol is treated with dilute sulphuric acid P-cymene is formed. Hence, α-terpineol possesses the carbon Skelton of P-cymene.

Thus, we may consider the α-terpineol as the menthane ($C_{10}H_{20}$) with one double bond and a tertiary alcoholic group as shown below.



P-cymene P-menthane α-terpineol

vi) Location of double bond and tertiary alcohol group (Wallach experiment)

When α-terpineol is oxidised stepwise, the following products are obtained. The fate of the carbon atoms alone is shown here,

$$\underset{C_{10}\ (I)}{\alpha\text{-terpineol}} \xrightarrow[KMnO_4]{1\%\ alk} \underset{C_{10}\ (II)}{\text{trihydroxy compound}} \xrightarrow[[O]]{CrO_3}$$

$$\underset{C_{10}\ (III)}{\text{Ketohydroxy acid}} \xrightarrow{-H_2O} \underset{C_{10}\ (IV)}{\text{Ketolactone}} \xrightarrow{\text{alk. kmno}_4}$$

Explanation of the degradation

i) The C=C present in α-terpineolis hydroxylated with 1% alkaline potassium permanganate (Bayer's reagent) to form trihydroxy compound (11).

ii) This compound is oxidised with chromium trioxide in acetic acid to form an unstable compound, ketohydroxy acid (III). This compound contains one keto group. This compound does not react with sodium bicarbonate. Hence it is a neutral compound. It is steam distilled with excess sodium hydroxide and then titrated with standard acid-Based on the volume of base used in the titration it is found that the compound III has one carboxylic group.

iii) Therefore, compound IV must be the lactone of the above acid. This lactone is obtained by the elimination of a water molecule form compound (III). The lactone is separable but not the corresponding hydroxy acid (III). Thus, the lactone formation takes places spontaneously.

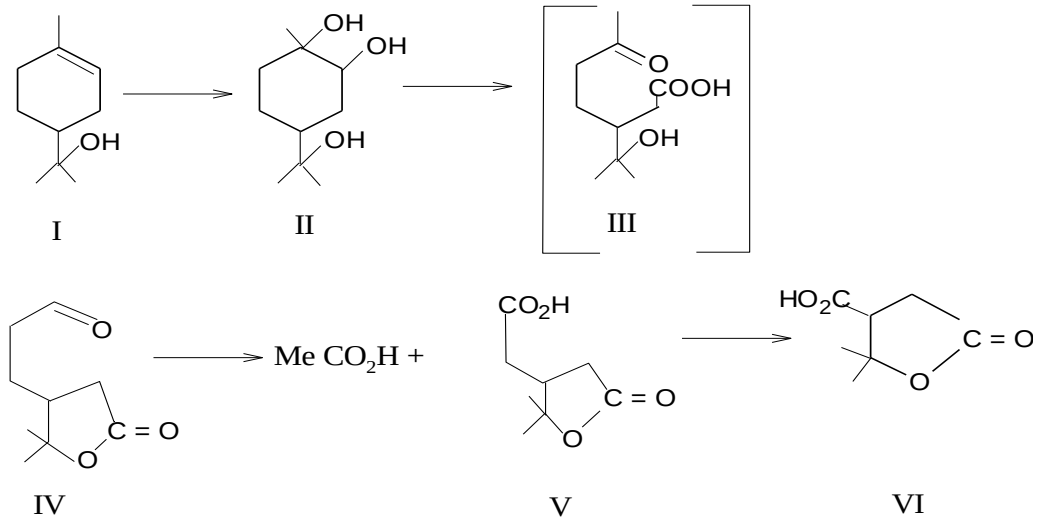
Based on these, we may infer that compound III may be r-or S-hydroxy acid and compound IV may be the lactone of r-or S-hydroxy acid.

iv) When the lactone is oxidised, terpenylic acid (V) and acetic acid are obtained. The formation of acetic acid in the reaction indicates the presence of methyl ketone group (CH_3CO) in compound (IV). Thus compound (IV) may be regarded as a lactone with one methyl ketone group. Terpenylic acid on analysis found to be a lactone of the monohydroxy dicarboxylic acid. Further it resembles the r-lactone obtained by synthesis. Thus compound (r) is the r-lactone of monohydroxy dicarboxylic acid.

v) Terpenylic acid on further oxidation yields terebic acid (VI). Terebic acid is also found to be the r-lactone of monohydroxy dicarboxylic acid.

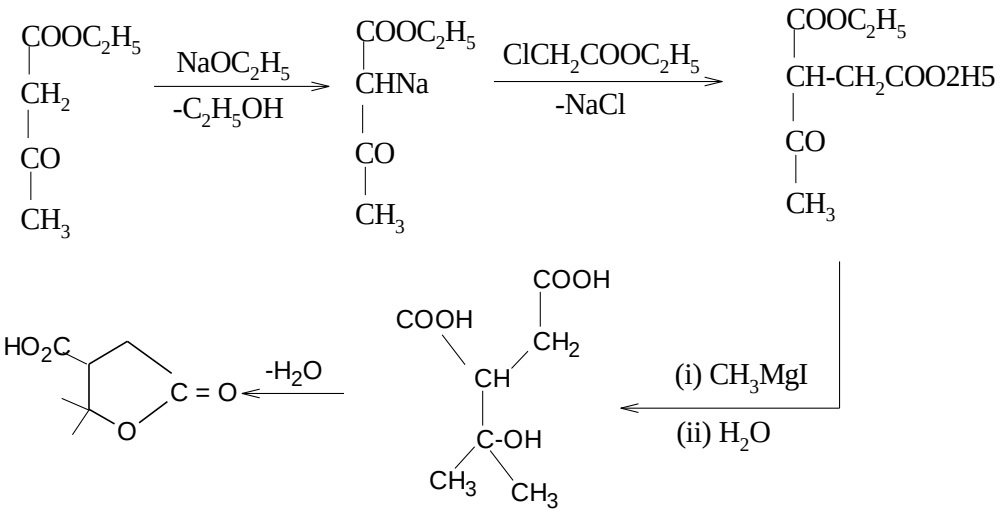
vi) The trihydroxy compound (II) formed during the reaction on oxidation gives compound (IV). During the oxidation, there is no loss of carbon atoms. This proves the presence of double bond in the ring of α-terpineol. Thus, we may conclude that α-terpineol is P-menth-1- ene-8-01.

The course of Wallach experiment is given below.

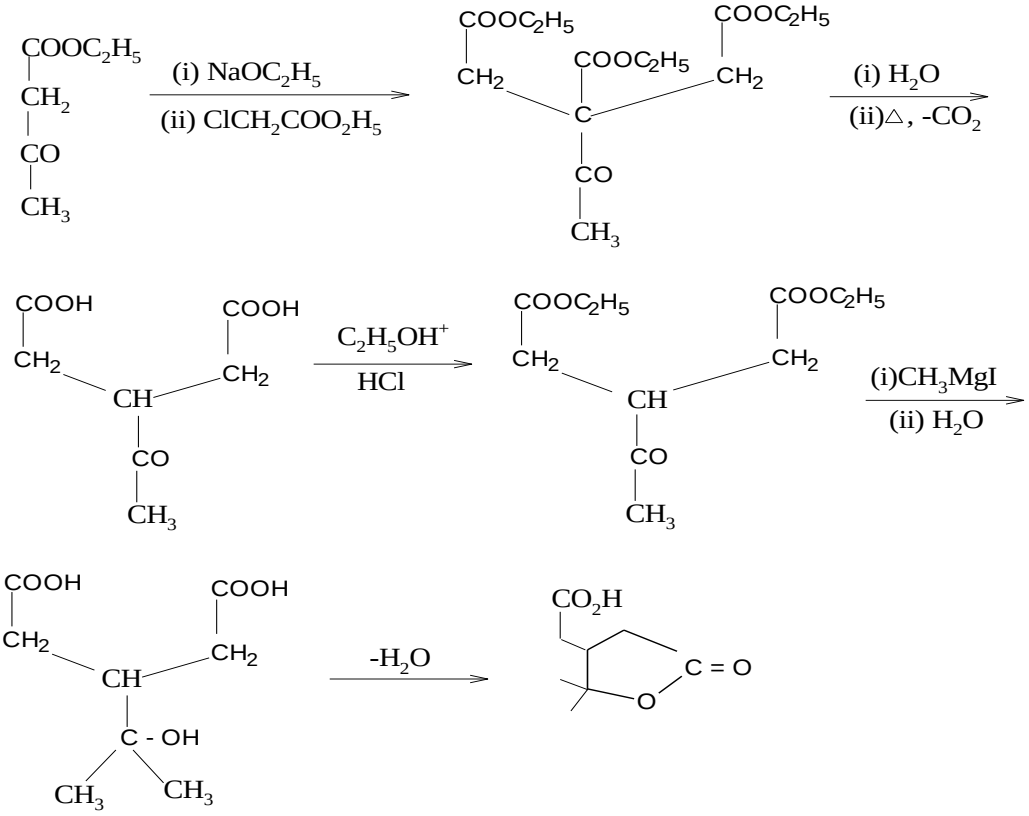


vii) The structures of terpenylic acid and terebic acid are confirmed by the following synthesis.

Synthesis of terebic acid

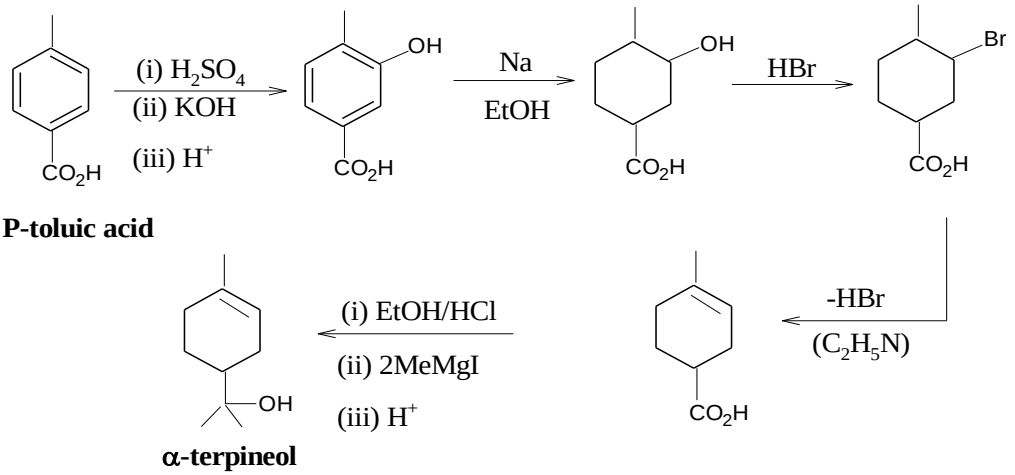


Synthesis of terpenylic acid



Synthesis of α-terpineol

i) Perkin and Fisher method (1908)

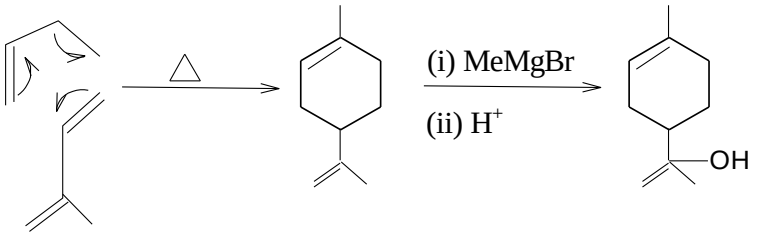


P-toluic acid

α-terpineol

(ii) Using Diels – Alder reaction

Isoprene



Methyl vinyl ketone **α-terpineol**

α-Pinene $C_{10}H_{16}$

α-pinene is present in all types of turpentine oils and makes the bulk of turpentine oil. It is the most widely distributed in all natural terpenodis. It is also found in eucalyptus oil.

It is obtained from turpentine oil by steam distillation or on treatment of trupentine oil with light petrol at 320K.

It is an optically active liquid with boiling point 429K/

Structure Determination

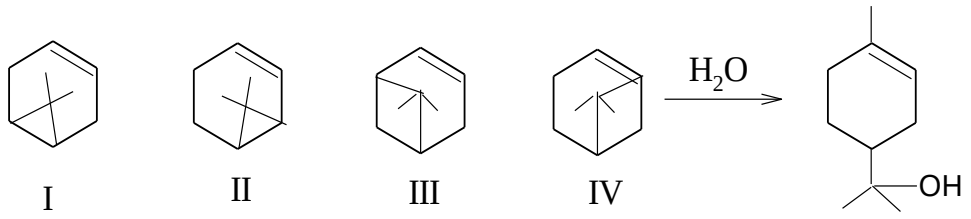
i) Molecular formula of α-pinene as deduced from its analytical data is $C_{10}H_{16}$.

ii) α-pinene decolourises bromine water and forms a dibromo derivative. It also adds with one molecule of NOCl. These reactions show the presence of one (C=C) double bond in the molecule.

$$C_{10}H_{16}.NOCl \xleftarrow{NOCl} C_{10}H_{16} \xrightarrow{Br_2} C_{10}H_{16}.Br_2$$

iii) The parent hydrocarbon of α-pinene has the formula $C_{10}H_{18}$ which is compatible with the general formula CnH_2n-2. Hence α-pinene is a bicyclic compound (Wallach 1891).

iv) α-pinene reacts with ethanolic sulphuric acid and is converted into α-terpineol. Therefore, α-pinene contains a six membered ring and another ring (Since it is bicyclic) the carbon skeleton being such as to give α-terpineol, when this second ring opens. Since in the fromation of α-terpineol one molecule of water is taken up and hydroxyl group is involved in forming the second ring in α-pinene. There are three possible points of union for this C6, resulting in two three membered (I and II) and two four membered ring (III and IV). At the same time the position of the double bond in α-pinene is also shown by the conversion into α–terpineol.

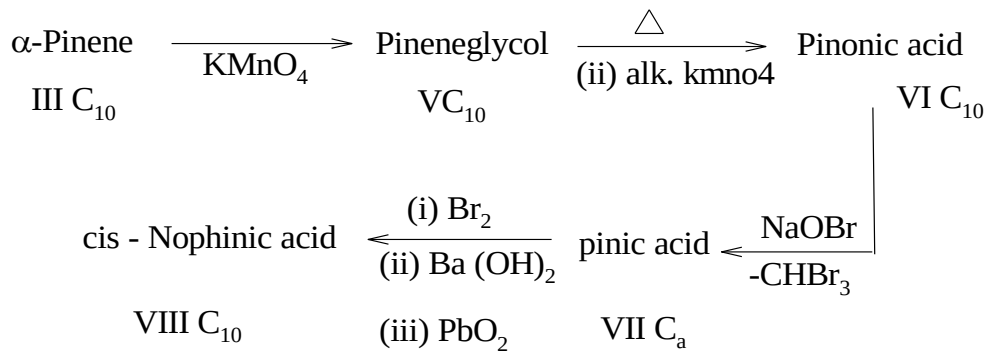


I II III IV

α-terpineol

v) The structure IV was rejected on the grounds of Bredt's rule (1924) which states that a double bond cannot be formed by a carbon atom occupying the bridge head of bicyclic system.

vi) The following reactions prove the presence of a four membered ring in α–pinene (Bayer, 1896).



Explanation:

i) On hydroxylation of α–pinene (III) pinene glycol (V) is obtained.

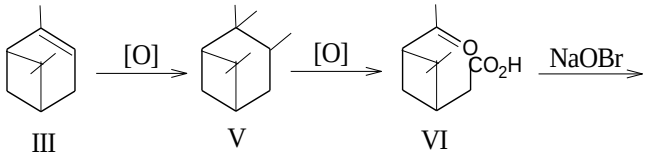
ii) The glycol on treatment with alkaline potassium permanganate cleaves the glycol linkage and forms pinonic acid (VI). From various studies, pinonic acid is found to be a saturated keto monocarboxylic acid.

iii) Pinonic acid reacts with sodium hypobromite and forms pinic acid (VII) and bromoform. Hence a methyl ketone group is present in pinonic acid.

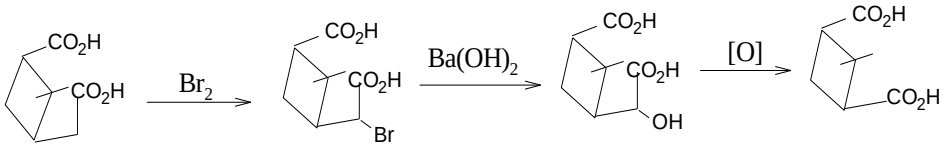
iv) Routine analysis of pinic acid shows that it is a saturated dicarboxylic acid. This on treatment with bromine first followed by barium hydroxide and lead dioxide produces cis-norpinic acid (VIII).

v) Norpinic acid is a saturated dicarboxylic acid which is based on various studies. Hence, we can write the formula of norpinic acid as $C_6H_{10}(COOH)_2$. Many studies prove the presence of two methyl groups in the second ring. In the Baeyer degradation only this second ring cleaved. Hence norpinic acid must have these two methyl groups. Hence we can write the formula of norpinic acid as $(CH_3)_2C_4H_4(COOH)_2$. The formula of basic hydrocarbon of second ring is C_4H_8 i.e., cyclobutane. Thus norpinic acid is the dimethyl cyclobutane dicarboxylic acid. Hence, the structure of α–pinene should be III.

Reactions:

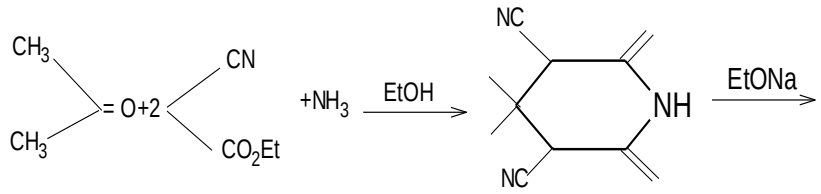


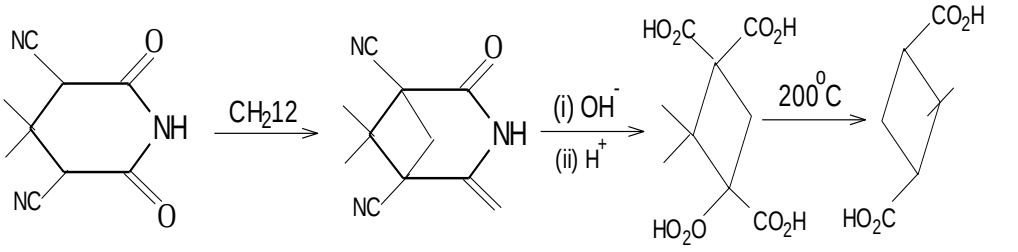
III V VI



VII Bromopinic acid Hydroxy pinic acid Pinic acid

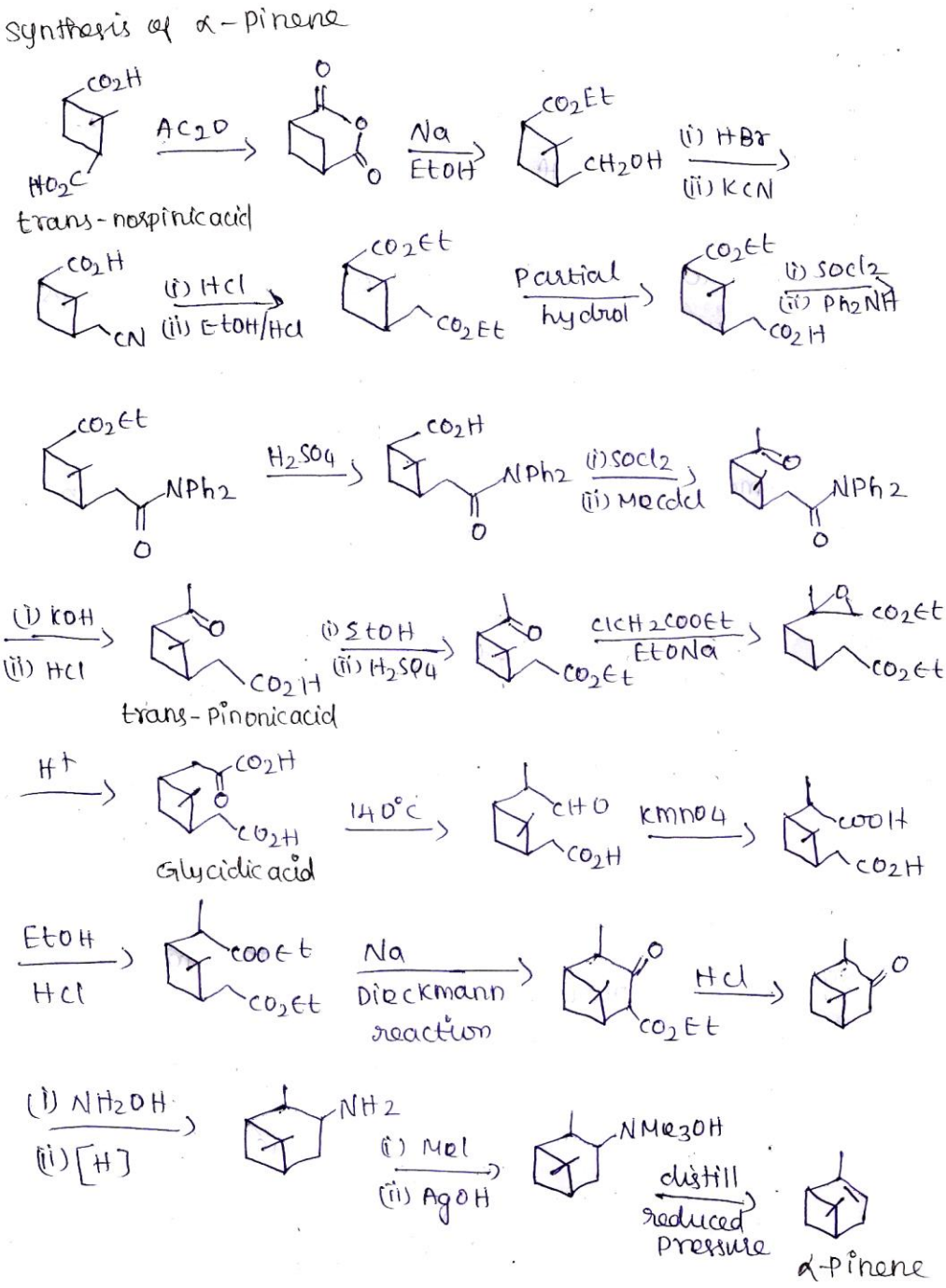
The structure of norpinic acid is confirmed by Kerr (1929) synthesis as follows:





transnorpinic acid

Synthesis of α-pinene



Uses:

i) It is used in the manufacture of camphor

ii) It is used as an oxidising agent.

NOTES

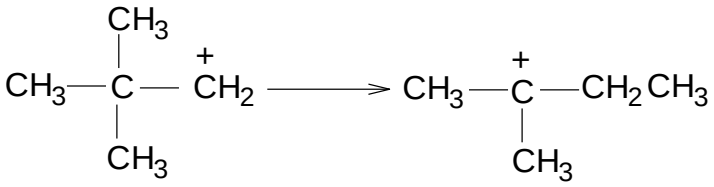
UNIT – V

5.1 MOLECULAR REARRANGEMENTS

Reactions involving reshuffling off the sequence of atoms to form a new structure.

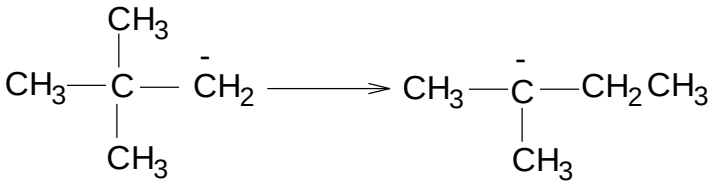
(1) Anionotropic Rearrangements

In which migrating group is nucleophilic and migrates to electron deficient centre.



2) Cationotropic rearrangements:

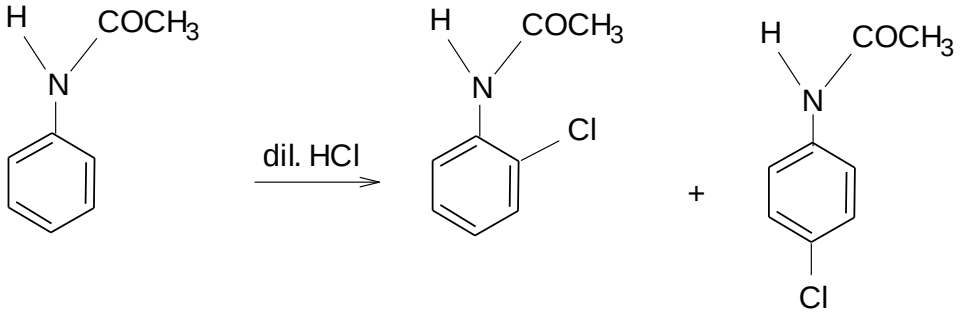
Migrating group is electrophilic and thus moves to electron rich centre. These rearrangements are initiated by those basic reagents which remove group or an atom. Two common examples are Stevens and Wittig rearrangements.



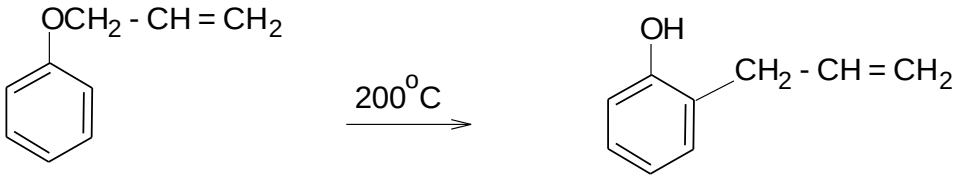
3) Aromatic rearrangements:

Migrating group migrates to armatic nucleus examples are,

(a) Intermolecular Aromatic rearrangements Migrating group from the outside the molecule.



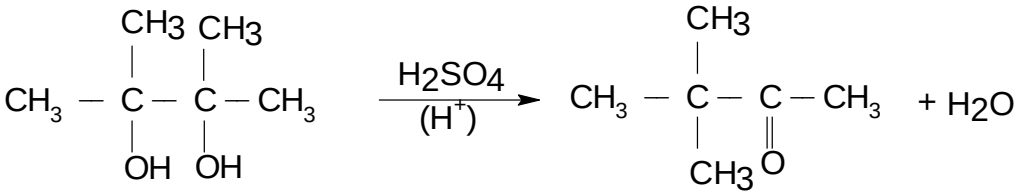
b) Intramolecular Aromatic rearrangements. Migrating group within the molecule.



5.2. MOLECULAR ARRANGEMENTS:

1. Pinacol – Pinacolone rearrangement:

Acid- catalyzed dehydration of 1,2-diols, to give rearranged ketones. Such rearrangement is called pinacol-pinacolone rearrangement. For eg. 2,3-dimenthybutane-2-3-diol (pinacol) is treated with H_2SO_4 to give 3,3-dimethyl-2-butanone (pinacolone).

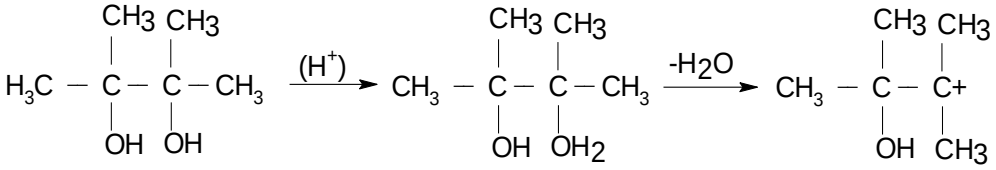


2,3- Dimethyly botane -2,3-diol (pinacol)

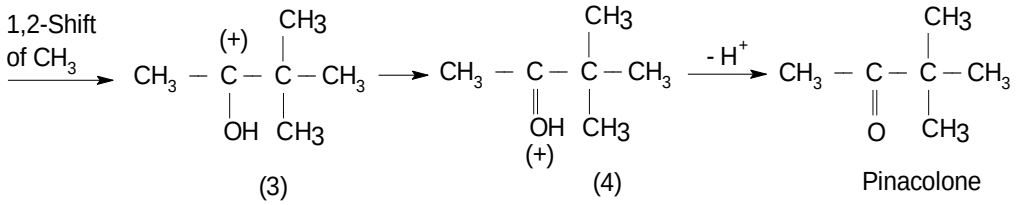
3,3 - Dimethylbotane 2-one (Pinacolone)

Mechanisms:

1. The first step is the addition of a proton to one of the hydroxyl groups to give oxonium ion (+).
2. The loss of water from oxonium ion to carboxation (2).
3. The 1, 2-shift of methyl group to carbocation to form another carbocation (3).
4. This carbocation is stabilized by shift of positive charge to oxygen atom.
5. The losses of proton to give pinacolone.



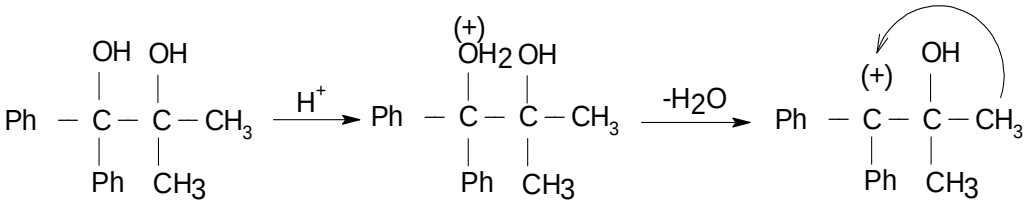
Pinacol (1) (2)

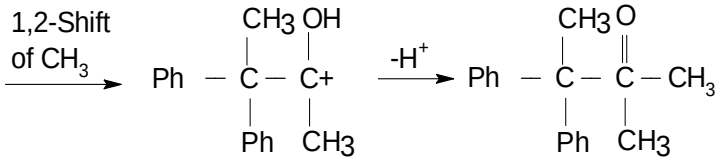


Note:

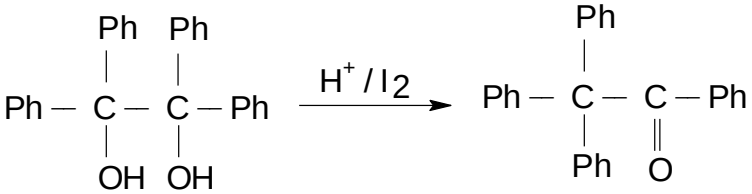
When unsymmetrical diol is rearranged, the removal of hydroxyl group take place with formation of stable carbocation. The 1,2-shift of group depends upon its migratory aptitude. The migratory aptitude is Ar > H > CH3.

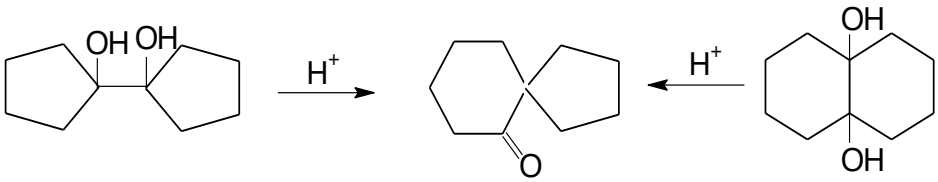
For eg. 2-methyl-1, 1-diphenylproparl-1,2-diol rearranged to 3,3,-diphenyl propane-2-one.

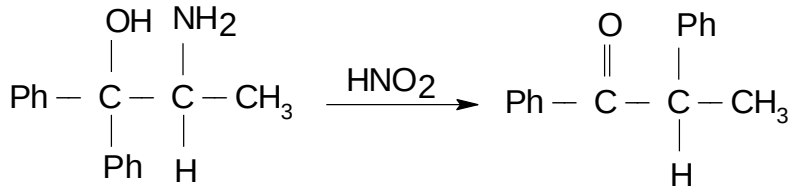




Applications:

1. 

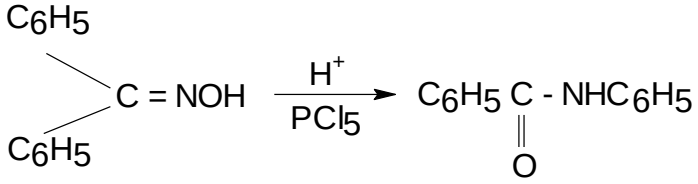
2. 

3. 

2. Beckmann Rearrangement:

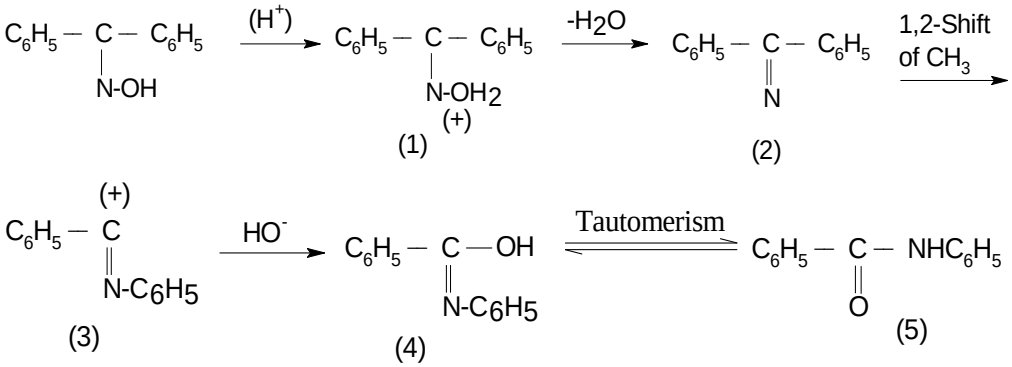
Ketoximes can be converted into N-substituted amides by a arrangement is known as Beckmann Rearrangement.

For eg. Benzophenone oxime gives benzanilide in the presence of an acid (or) PCl_5.

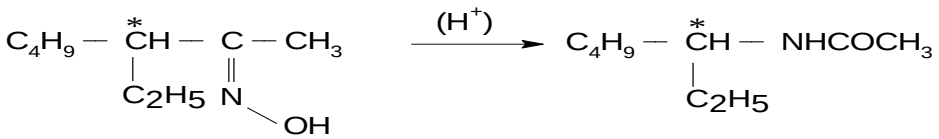


Mechanism:

1. Attack by an acid to give an oxonium ion (1)
2. Removal of water and 1,2-shift of phenyl group to give carbocation (3).
3. Attack by OH^- and tautomerism to give the amide as product.

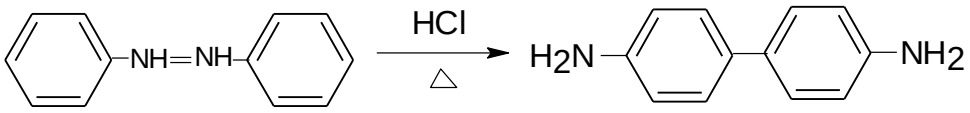


In the above mechanism, a group anti position to oxime hydroxyl group is migrated to N-atom. For eg. (+)-methyl-3-heptyl hetoxime is converted by rearrangement to 3-acetamidoheptane with retention of configuration.



3. Benzidine Rearrangement:

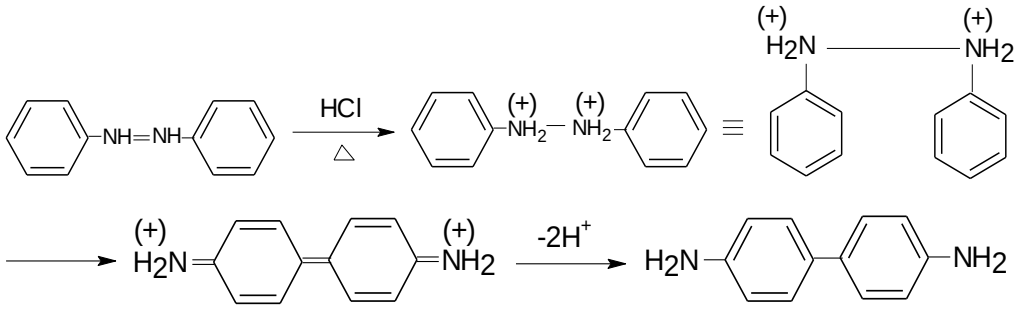
The acid catalysed rearrangement of hydrazobenene to 4,4'-diaminobiphenyl (p-benzidine) is known as Benzidien rearrangement.



Hydrozobenzene P-benzidines

Mechanism:

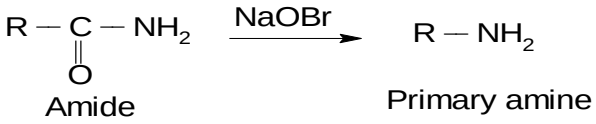
The mechanism involves the intramolecular rearrangement can be formulated as follows:



This mechanism support by when two different hydrozobenzenes are rearranged in same solution, only two benzidines are obtained and cross coupling product are not formed.

4. Hoffmann Rearrangement:

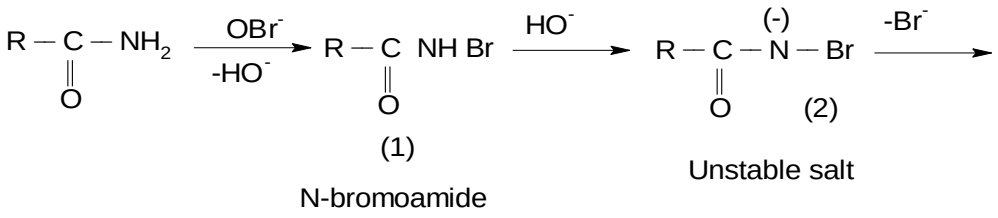
When an amide is treated with sodium hypobromite, it is converted to a primary amine that has one carbon atom less than the starting amide. This reaction is known as Hoffmann rearrangement. Here decarbonylation take place.

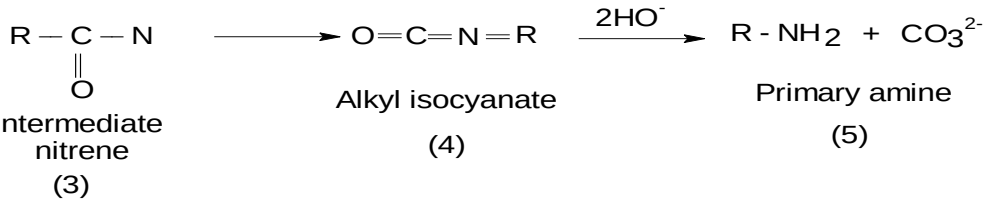


Amide Primary amine

Mechanism:

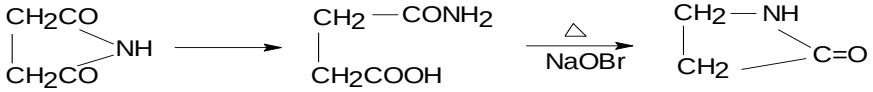
1. The first step is the attack by bromite ion on the substrate to give N-bromo amide (1).
2. Attack of HO^- ion on (1) to give unstable salt (2).
3. Removal of bromide ion (Br^-) from (2) to give intermediate nitrene (3).
4. The migration of alkyl group to N-atom forms iso cycanate (4) both the steps take place simultaneously.
5. Hydrolysis of (4) to give primary amine as product (5).





Applications:

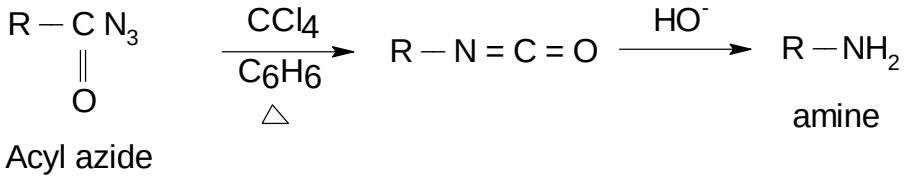
1. The Hoffmann rearrangement of β-camphoramic acid yields 1-aminodinhydro α-campholytic acid to Lactum.

2. 

Lactum

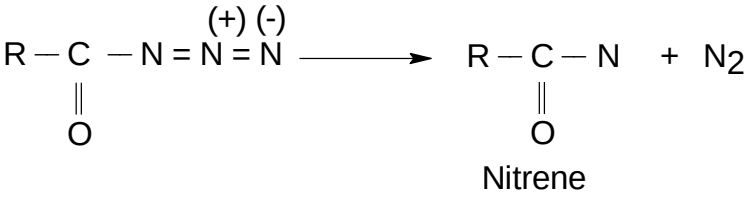
5. Curtius Rearrangement:

When azyl azides are heated in non-aqueous solvents such as chloroform, benzene (or) other to give alkylisocyanate. This reaction is known as curitus rearrangement. The hydrolysis of isocyanate gives primary amine.



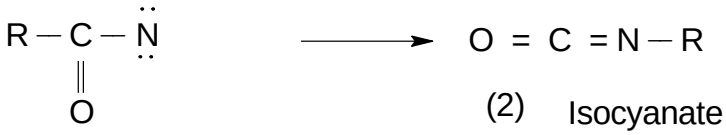
Mechanism:

1. When acyl azides are heated, lose of molecular nitrogen take place to give nitrene as an intermediate (1).
2. The migration of alkyl group to N-atom, isocyanate is formed (2), both steps take place simultaneous.
3. The hydrolysis of (2) to give amine as a product (3).

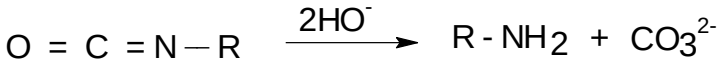


Nitrene

(1)

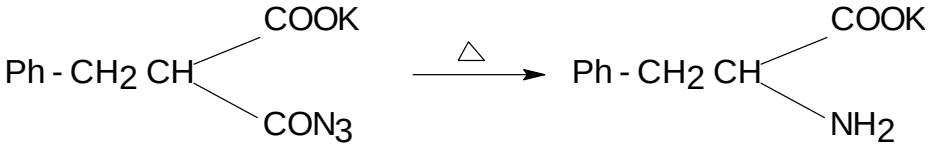


(2) Isocyanate



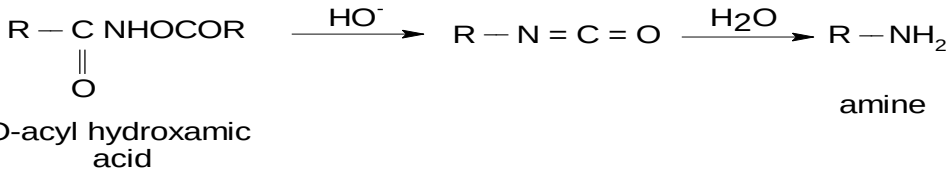
(3) amine

Application:



6. Lossen Rearrangement:

The rearrangement of 0-acyl derivative of hydroxamic acid in the presence of base to amine is Lossen rearrangement.

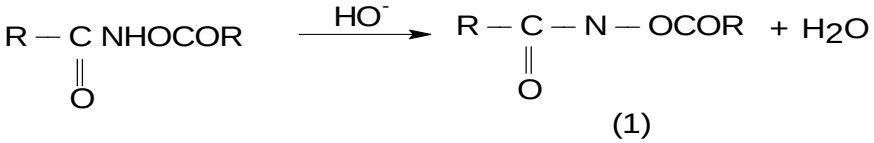


O-acyl hydroxamic acid

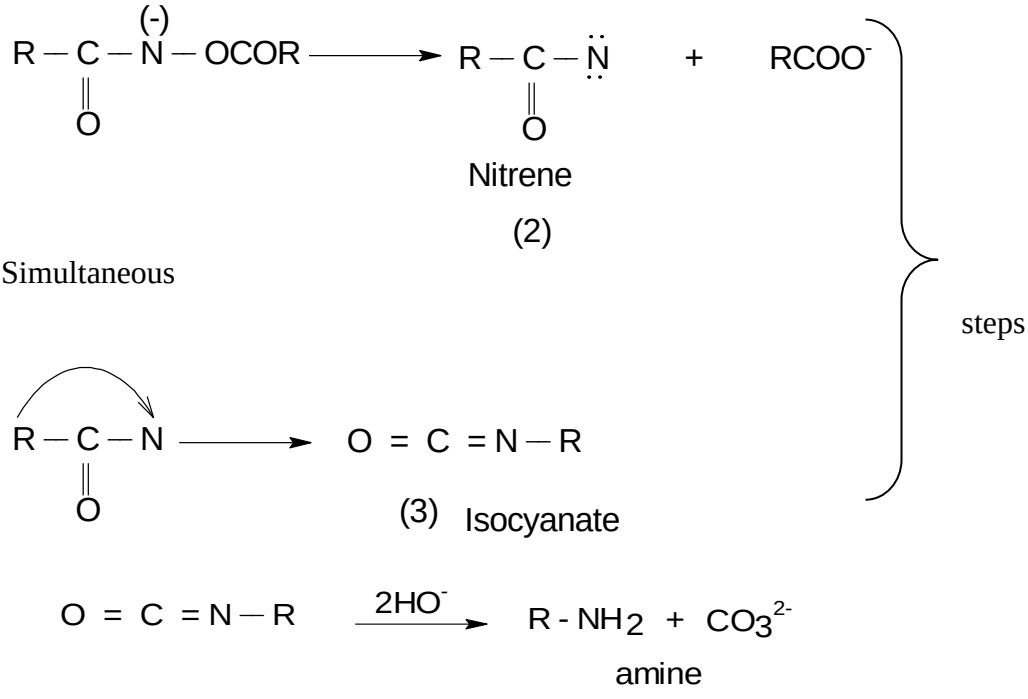
amine

Mechanism:

1. The first step is the abstraction of H^+ by HO^- to N-substituted keto ester (1).
2. The removal of ester group from (1) to Nitrene as an intermediate (2).
3. The migration of alkyl group to N-atom to give isocyanate (3) both steps are simultaneously take place.
4. The hydrolysis of (3) to amine as a product (4).



(1)



$$O = C = N - R \xrightarrow{2HO^-} R\text{-}NH_2 + CO_3^{2-}$$

amine

7. Schimdt Rearrangement:

The conversion of carboxylic acid to primary amine with hydrazoic acid in the presence of an acid is known as Schimdt Rearrangement.

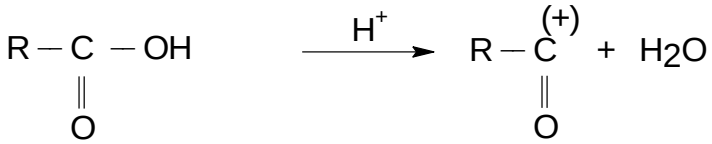
$$RCOOH + HN_3 \xrightarrow{H^+} R\text{-}NH_2 + CO_2 + N_2$$

Acid Amine

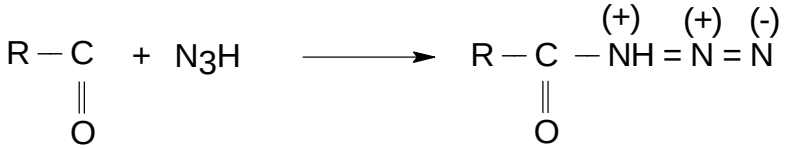
Mechanism:

1. When adding acid to the substrate, to give carbocation (1).
2. Removal of N_2 from (1) to give iminium salt (2).
3. The hydrolysis of (2) to give amine as a product (3).

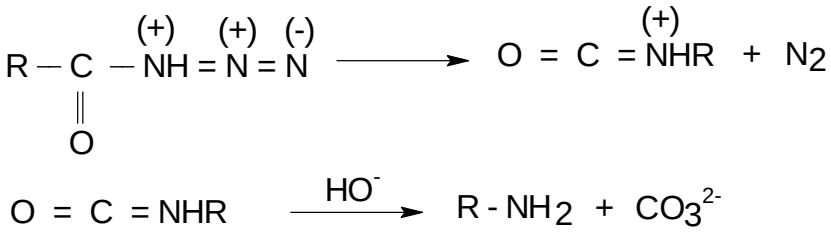
Step : 1



Step : 2

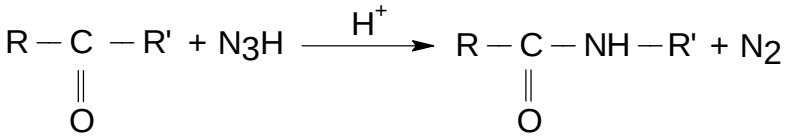


Step : 3

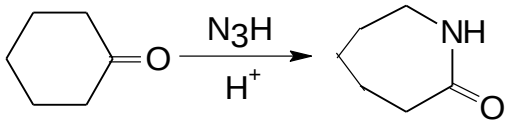


Application:

1. Ketone can be converted into amine by insertion of –NH group.

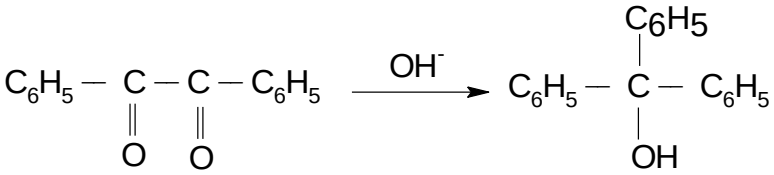


2. Ketone to Lactums.



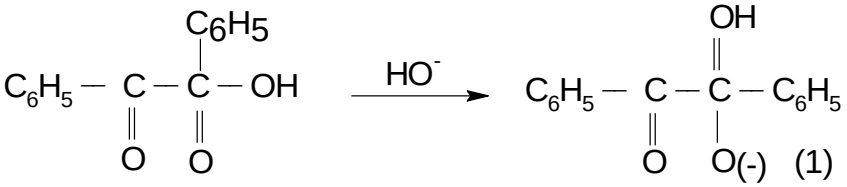
8. Benzilic acid Rearrangement:

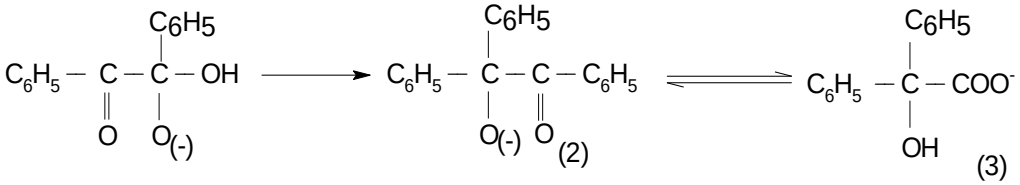
The base catalysed conversion of 1,2-diketones (benzyl) to a salt of 2-hydroxycarboxylic (benzilic acid) is known as the benzilic acid rearrangement.



Mechanism:

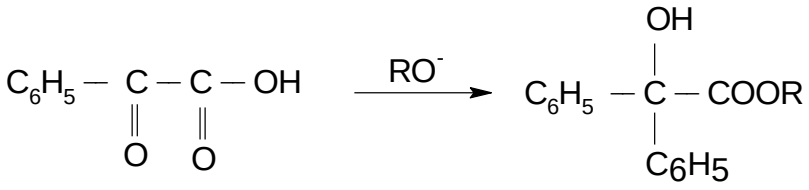
1. The hydroxyl group attacks any one bond to give (1).
2. The migration of phenyl group to neighbouring to give (2).
3. The proton shift to for benzilate ion (3).





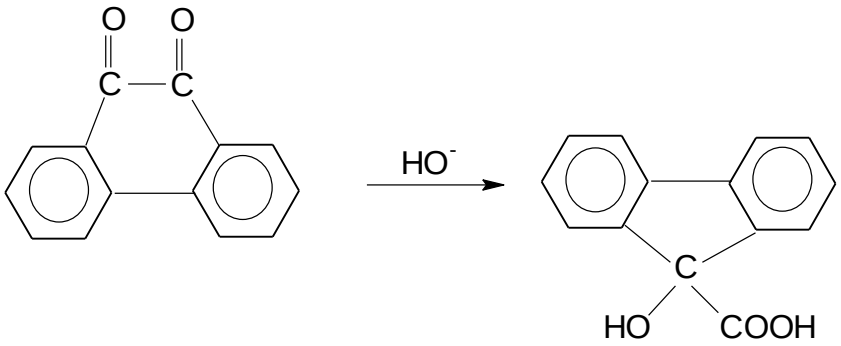
Applications:

1. When using alkoxide ion (RO^-) the product is 2-hydroxy ester.



α – hydroxy ester

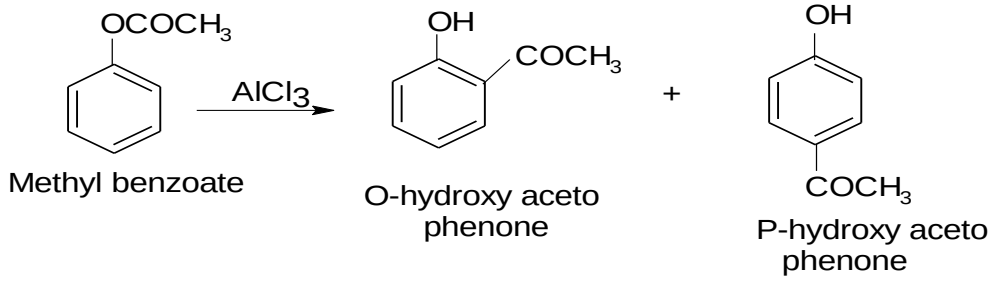
2.



9. Fries Rearrangement:

Phenolic esters can be converted into phenolic ketones (O-hydroxy ketones and p-hydroxy ketones) in the presence of Lewis acids is known Fries Rearrangement.

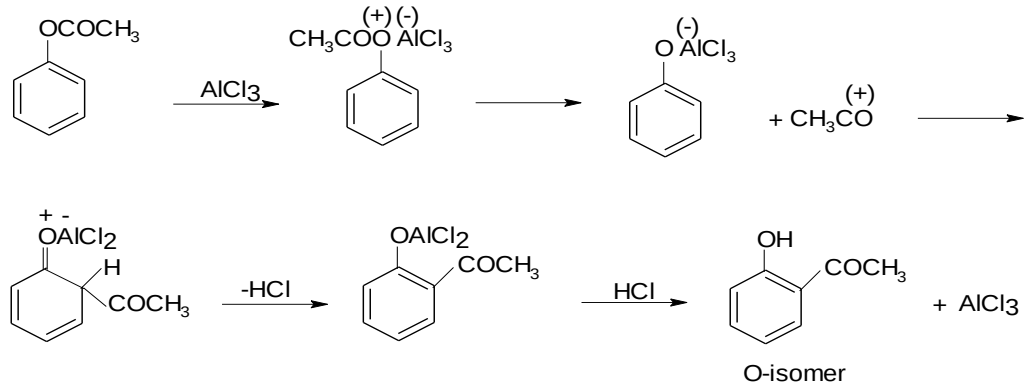
At low temperature (40°C) p-isomer is formed, while at 195°C O-isomer is predominant, it is stable in nature due to intramolecular hydrogen bond.



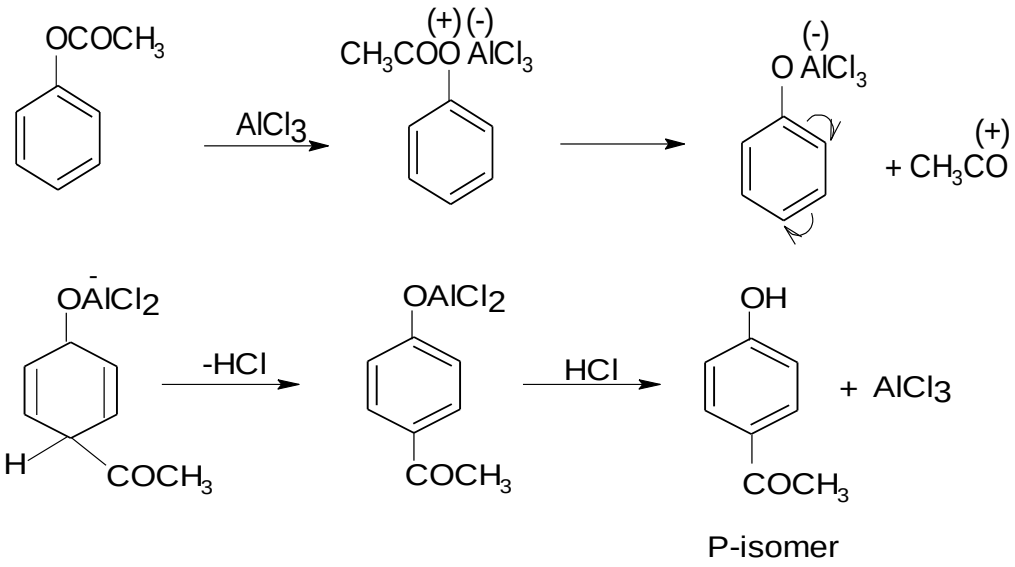
Mechanism:

Ortho Fires Rearrangement:

Intra-molecular rearrangement take place as follows:



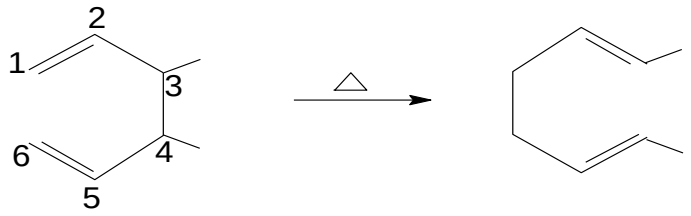
Para Fires Rearrangement:



10. Cope Rearrangement:

The thermal isomerization of 1,5-dienes by 3,3-sigmatropic shift is known as cope rearrangement.

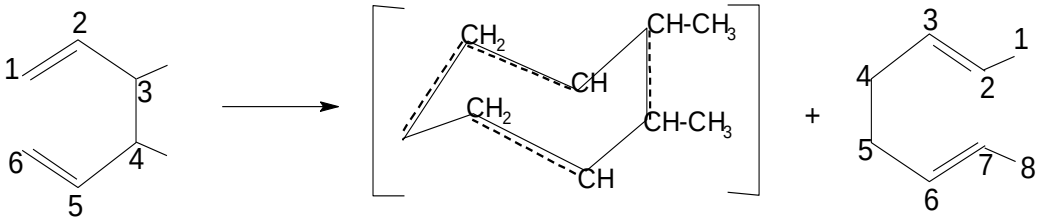
For eg. 3,4-dimethyl-1,5-hexadiene thermally isomerizes to 2,6-octadiene.



3,4-dimetyl - 1,5-hexadiene 2,6 -Octadiene

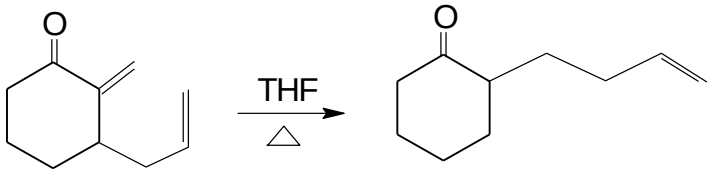
Mechanism:

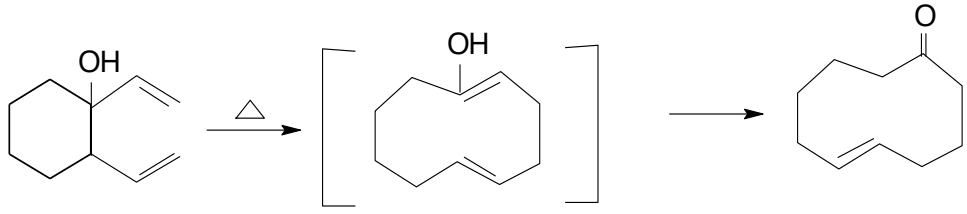
This mechanism take place by a single concerted step through a chair form of transition state as follows:



Chair form (Transition state)

Applications:

1. 

2. 

5.3. IMPORTANT REAGENTS AND THEIR APPLICATIONS IN ORGANIC CHEMISTRY:

1. Anhydrous Aluminium Chloride ($AlCl_3$)

Preparation:

i) By heating a mixture of alumina and coke in a current of chlorine gas.

$$Al_2O_3 + 3C + 3Cl_2 \rightarrow 2AlCl_3 + 3CO$$

ii) By passing chlorine gas (or) hydrochloric acid vapours over heated Aluminum powder.

$$2Al + 3Cl_2 \rightarrow 2AlCl_3$$

$$2Al + 6HCl \rightarrow 2AlCl_3 + 3H_2$$

Properties:

- It is white crystalline solid.
- It is hydroscopic and fumes in moist air.
- The molecular formula is Al_2Cl_6, but it present as monomer at higher temperatures.
- It undergoes hydrolysis by H_2O.

$$AlCl_3 + 3HOH \rightarrow Al(OH)_3 + 3HCl$$

Applications:

It is used a catalyst in various reactions.

2. Boron Trifluoride (BF3):

Preparation:

i) By passing fluorine gas over hot boron.

$$2B + 3F_2 \rightarrow 2BF_3$$

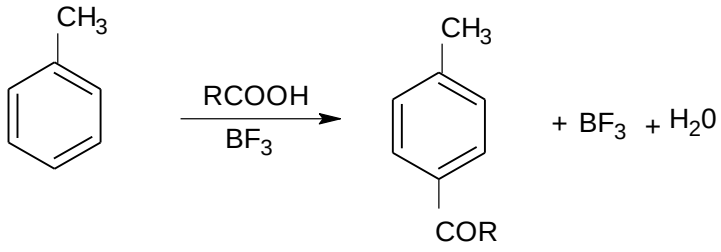
ii) By heating a mixture containing boron trioxides, calcium fluoride and conc. H_2SO_4.

$$B_2O_3 + 3CaF_2 + 3H_2SO_4 \rightarrow 3CaSO_4 + 3H_2O + 2BF_3.$$

Applications:

Many important organic compounds can be prepared by using it.

i) It is used as a catalyst in Friedel –crafts reactions.



ii) Esters can be prepared from various compounds using BF_3 as a catalyst.

a) From acid and alcohol

$$RCOOH + R'OH \xrightarrow{BF_3} RCOOR' + BF_3 + H_2O$$

b) From carboxylic acid and alkene

$$RCOOH + CH_2 = CH_2 \xrightarrow{BF_3} RCOOC_2H_5$$

c) From acid chloride and ether

$$RCOCl + R'OH \xrightarrow{BF_3} R'COOR + RCl$$

d) From alcohol and carbon monoxide.

$$ROR + CO \xrightarrow[398\ K]{BF_3} RCOOR$$

Carboxylic acid can be prepared from alcohol and co.

$$ROH + CO \xrightarrow[398\ K]{BF_3} RCOOH$$

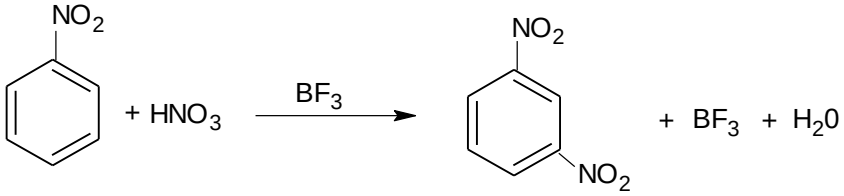
i)

ii) β-diketone can be prepared from ketone and unhydride.

$$CH_3COCH_3 + (CH_3CO)_2O \xrightarrow{BF_3} CH_3COCH_2COCH_3 + CH_3COOH + BF_3$$

β-diketone

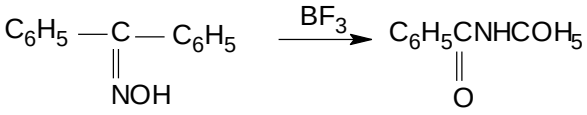
Nitration reaction:



Nitrobenzene m-dinitrobenzene

Beckmann Rearrangement:

Oximes can be converted into amides in the presence of BF_3.



Amide

4. Lithium Aluminum Hydride ($LiAlH_4$) (Reducing agent):

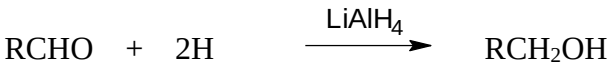
Preparation:

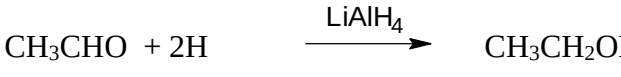
It is prepared by adding anhydrous aluminum chloride to a paste of Lithium hydride in ether.

$$4LiH + AlCl_3 \rightarrow LiAlH_4 + 3LiCl$$

Applications:

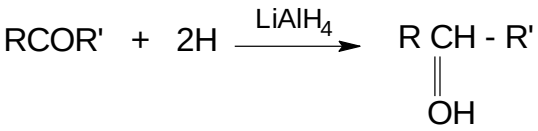
i) It reduces aldehydes to primary alcohols.

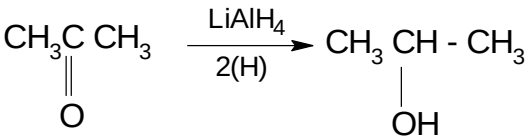




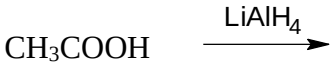
It does not reduces C = C and C ≡C bonds.

ii) It reduces ketones to secondary alcohols.

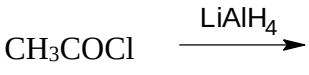




iii) Acids can be reduced to primary alocohols.



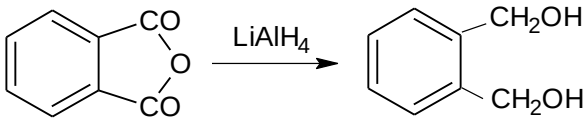
iv) Acid halides can be converted into primary alcohol.



v) Esters can be converted into primary alcohol.

$$C_6H_5COOC_2H_5 \xrightarrow{LiAlH_4} C_6H_5CH_2OH$$

vi) Anhydrides to primary alcohol.



vii) Amides are reduced to primary amines.

$$RCONH_2 \xrightarrow{LiAlH_4} RCH_2NH_2$$

Substituted amides to secondary amines and test amines.

$$C_6H_5NHCOCH_3 \xrightarrow{LiAlH_4} C_6H_5NHCH_2CH_3$$

2' Amine

$$C_6H_5N(CH_3)\text{-}COCH_3 \xrightarrow{LiAlH_4} C_6H_5N(CH_3)\text{-}CH_2CH_3$$

3' Amine

viii) Epoxides are reduced to alcohols.

$$RCH\text{-}CH_2 \xrightarrow{LiAlH_4} R\text{-}CH_2\text{-}CH_2OH + R\text{-}CH(OH)\text{-}CH_3$$

ix) Ozonides are reduced to alcohols.

$$CH_3\text{-}CH(O)\text{-}CH(O)\text{-}CH_3 \longrightarrow 2CH_3CH_2OH$$

Ozonides — Ethyl alcohol

x) Nitro compounds are reduced to primary amines.

$$CH_3\text{-}CH(NO_2)\text{-}CH_2\text{-}CH_3 \longrightarrow CH_3CH(NH_2)\text{-}CH_2\text{-}CH_3$$

xi) Alkyl azides are reduced to amines.

$$RN_3 \xrightarrow{LiAlH_4} RNH_2$$

xii) Oximes are reduced to amines.

$$R_2C = NOH \xrightarrow{LiAlH_4} R_2CHNH_2$$

$$C_6H_5\,C(NOH) - C_6H_5 - CH_3 \xrightarrow{LiAlH_4} C_6H_5\,CH\,NH\,CH_2\,C_6H_5$$

xiii) Nitrius can be converted into amines and aldehydes.

$$C_6H_5\,CN \xrightarrow{LiAlH_4} C_6H_5\,CHN\,NH_2$$

$$RCN \xrightarrow{/} RCHO$$

5. Sodiumboro Hydride ($NaBH_4$)

Preparation:

1. Sodium hydride reacts with methyl borate at higher temperature to produce $NaBH_4$.

$$4\,NaH + B(OCH_3)_3 \xrightarrow{523\ K} NaBH_4 + 3NaOCH_3$$

2. It is also prepared from sodium hydride and diborane.

$$2\,NaH + B_2H_6 \xrightarrow{LiAlH_4} 2\,NaBH_4$$

$NaBH_4$ is superior to $LiAlH_4$ due to

i) It is selectivity is high. It will reduce only the carbonyl group present in the aldehydes and ketones and not the other groups like (N, $-NO_2$, COOH etc.).

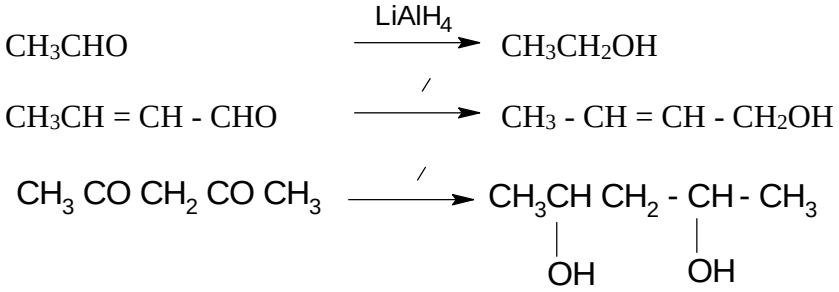
ii) It reduces particular functional only if the compounds contain more functional groups is known as chemoselective.

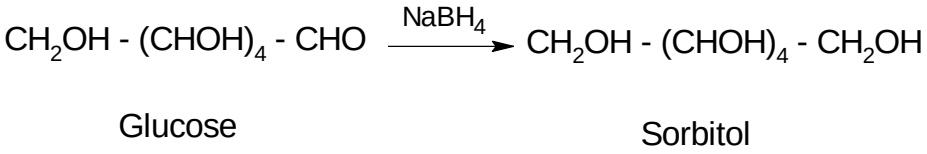
$$CH_3 - CH = CH\,CH(=O) \xrightarrow[NaBH_4]{} CH_3 - CH = CH - CH_2OH$$

iii) It is able to reduce lactones and acid chloride, but it does not reduce esters.

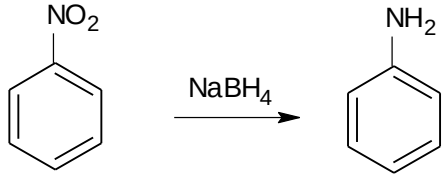
Applications:

i) Aldehydes are reduced to alcohols:

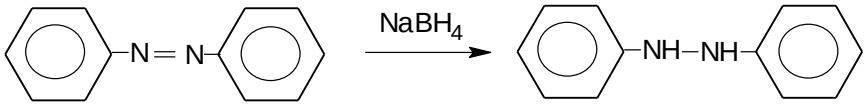




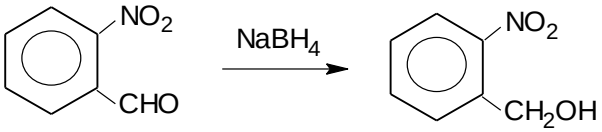
ii) Aromatic nitro compounds to amines



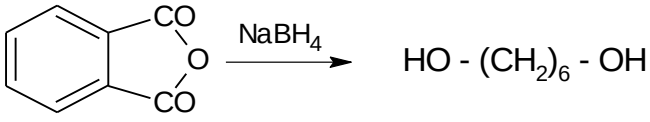
iii) Azobenzene is reduced to hydrozo benzene



iv) O-nitro benzaldehyde is reduced to O-nitrobenzyl alcohol.



v) It reduces ozonides to alcohols.



vi) Diborane can be prepared by using it.

$BF_3 + 3NaBH_4 \rightarrow 2B_2H_6 + 3NaH$

5. Phosphorous Pentachloride (PCl_5)

Preparation:

1) It is prepared by a passing excess chlorine gas over phosphorous.

$$2P + 5Cl_2 \rightarrow 2PCl_5$$

2) Dry chlorine gas is passed over phosphorous trichloride.

$$PCl_3 + Cl_2 \rightarrow PCl_5$$

Properties:

It is colourless crystalline solid, with pungent odour.

Uses:

It is good chlorinating agent in organic chemistry.

1. It converts alcohole into alkyl chloride.
2. It converts acids into acid chloride.

$$CH_3COOH + PCl_5 \rightarrow CH_3COCl + POCl_3 + HCl$$

3. It converts carbonyl group co into $-CCl_2$.

$$CH_3COOH + PCl_5 \rightarrow CH_3CCl_2CH_3 + POCl_3$$

$$CH_3CHO + PCl_5 \rightarrow CH_3CHCl_2 + POCl_3$$

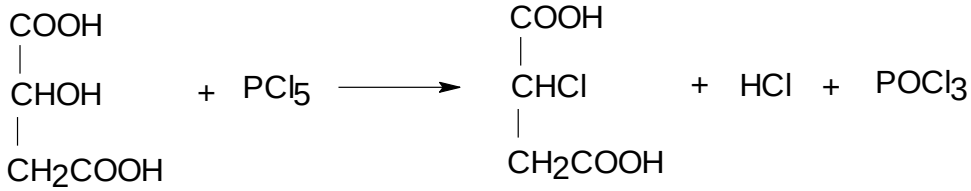
4. It converts amides into nitriles.

$$RCONH_2 + PCl_5 \rightarrow RCN + POCl_3 + 2HCl$$

5. It converts esters into acid chlorides.

$$RCOOR' + PCl_5 \rightarrow RCOCl + R'Cl + POCl_3$$

6. It takes part in Walden inversion and brings inversion in configuration.



DCH Malic acid

L (-) Chlorosuccinic acid

6. Phosphorous pentoxide, P_2O_5

Preparation:

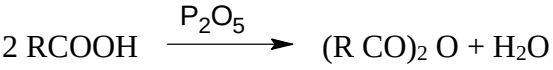
It is prepared by burning phosphorous in an excess of dried our (or) oxygen.

$$P_4 + 5O_2 \rightarrow 2P_2O_5$$

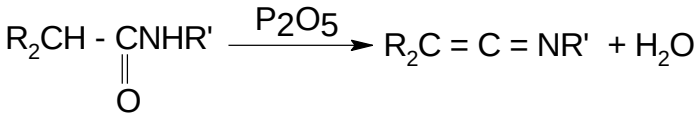
It is used as a dehydrating agent in organic chemistry.

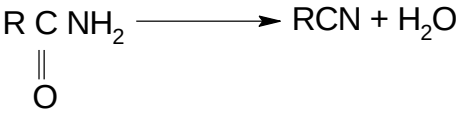
Uses:

1. It dehydrates acid into anhydride.

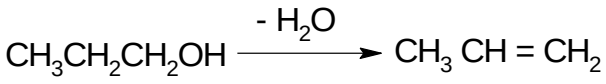


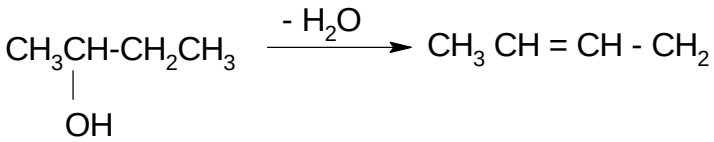
2. It converts amides into ketimines (or) nitriles on dehydration.





3. It dehydrates alcohols into alkenes.





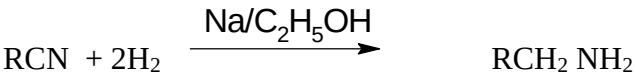
7. Sodium in alcohol (Na/C_2H_5OH)

Sodium reacts with alcohol to produce sodium ethoxide and hydrogen. Hence, it acts as a good reducing agents.

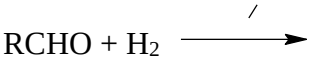
$2Na + 2C_2H_5OH \rightarrow 2C_2H_5ONa + H_2$

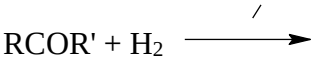
Uses:

1) It reduces alkyl cyanides to primary amines.



2) It reduces alchydes and ketones to primary alcohol and secondary alcohol respectively.





8. Alcoholic Potassium Hydroxide (AlC. KOH)

It is used in the dehydrohalogenation reaction.

$$CH_3CH_2X \rightarrow CH_2 = CH_2 + HX \qquad (X\text{-}F, Cl, Br, J)$$

9. Hydrogen in presence of Nickel (Hydrogenating agent)

By passing hydrogen gas over nickel at very high temperatures it is possible to reduce C = C and C ≡ C bonds. This reaction is called hydrogenation.

$$CH \equiv CH + H_2 \xrightarrow{Ni} CH_2 = CH_2 \xrightarrow{H_2} CH_3 - CH_3$$

$$R - CN \xrightarrow{H_2/Ni} ROH_2NH_2$$

$$RCHO \xrightarrow{/} RCH_2OH$$

$$RCOR' \xrightarrow{/} RCHOHR'$$

$$RNO_2 \xrightarrow{/} RNH_2$$

Raney nickel is more reactive than the supported nickel catalyst and is usually effective at lowest temperatures. By using Raney nickel, aromatic hydrocarbon is prepared from different compounds.

$$C_6H_5Cl \rightarrow C_6H_6 + HCl$$

$$C_6H_5OCH_3 \rightarrow C_6H_6 + CH_3OH$$

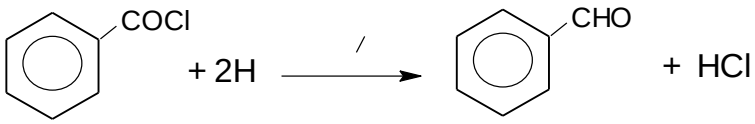
$$C_6H_5SO_3H \rightarrow C_6H_6 + H_2SO_3$$

10. Hydrogen, Palladium and Barium sulphate (Rosemund reduction)

Acid chlorides are reduced to aldehydes with hydrogen in Palladium and $BaSO_4$ is known as Rosemund reaction.

$$CH_3COCl + 2H \xrightarrow{Pd, BaSo_4} CH_3CHO + HCl$$

$$C_2H_5COCl + 2H \xrightarrow{/} CH_3CH_2CHO + HCl$$

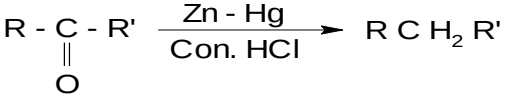


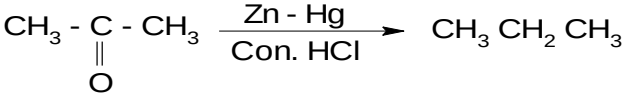
Formaldehyde cannot be prepared by this method as formyl chloride is very unstable at room temperature.

This reaction helps to convert acid to aldehyde.

11. Zinc amalgam and Conc. HCl (Clemmensen reduction)

The conversion of C = O group to CH_2 gp by Zn-Hgl HCl is called Clemmensen reaction.





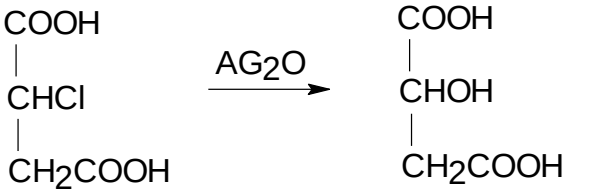
12. Silver Oxide (Ag_2O):

Moist silver oxide is used as a reagent for hydrolysis.

Silver oxide is used as a good reagent in many organic chemical reactions, for eg. Are-

1) It is used in Arndt –Eistert reaction to ascend organic chemical reactions, few examples are,

2) (+) Chlorosucanic acid is hydrolysed to (+) malic acid. It retains the configuration during the reaction.



D (+) - Chlorosoccinic acid D (+) Malic acid

3) It is used as Toller's reagent (ammonical silver nitrate) to oxidize aldehyde and carbohydrate.

$RCHO + Ag_2O \rightarrow RCOOH + 2Ag$

$CH_2OH – (CHOH)_4 – CHO + Ag_2O \rightarrow CH_2OH\ (CHOOH)\ COOH + 2Ag$

Glucose Glucoric acid

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