

Stereochemistry of Organic Compounds.

The molecular structure of compounds plays a very important role in the study of organic chemistry.

During this study one come across many instances where a given molecular formula represents two or more compounds having different properties.

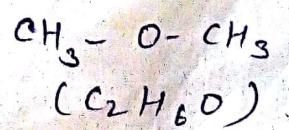
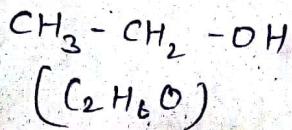
Such compounds which have the same molecular formula but different properties are known as isomers and the phenomenon is known as isomerism.

There are two types of isomerism:

- (i) Structural Isomerism
- (ii) Space or Stereo Isomerism

Structural Isomerism:- This is the type of isomerism which is due to the difference in the arrangement of atoms within the molecules having the same molecular formula. Structural isomers can involve the carbon skeleton or nature and position of functional groups.

Ex. simple example of structural isomers are the isomers ethanol and dimethyl ethers.

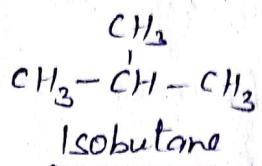
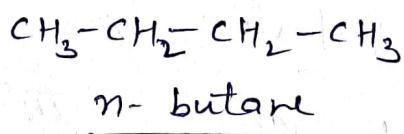


Types of Structural Isomerism.

(2)

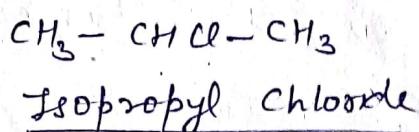
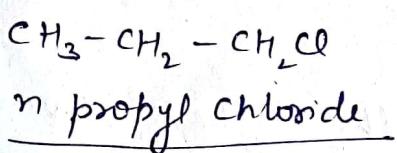
1) Chain Isomerism This is a kind of isomerism which arises when the compounds having the same molecular formula differ only in the arrangement of carbon atoms in a chain.

ex. Normal butane and iso-butane (C_4H_{10})

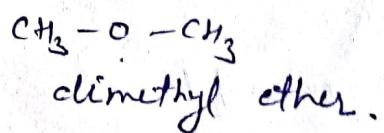
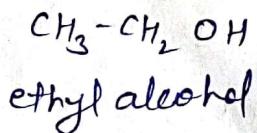


2) Position Isomerism. If the two or more compounds with same molecular formula have different positions occupied by a characteristic atom or group attached to carbon, position isomerism is said to exist.

ex. n-propyl chloride and isopropyl chloride



3) Functional Isomerism: This type of isomerism is due to the presence of different functional groups in compounds having the same molecular formula. For ex C_2H_6O represents two compounds

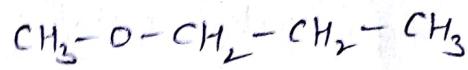


3) Metamerism: This type of isomerism is due to the difference in the distribution of carbon atom on either side of functional gp in compd having the same molecular formula.

Ex. $C_4H_{10}O$ -



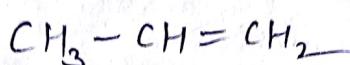
Diethyl ether



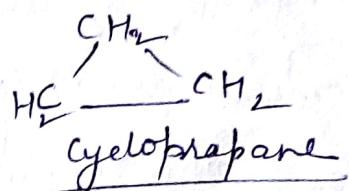
Methyl propyl ether

5) Ring-chain Isomerism: This type of isomerism in which two compounds having the same molecular formula have open chain and ring structures respectively.

Ex.



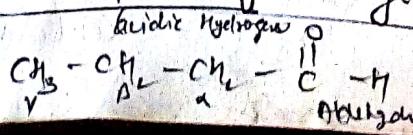
Propene



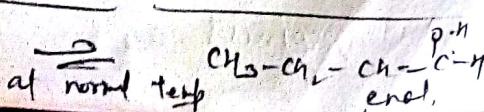
6) Tautomerism: This is a special type of functional isomerism where the isomers exist simultaneous in dynamic equilibrium with each other. The isomers which are involved in equilibrium are called tautomers.



Keto form of acetyl acetone
lactic hydrogen



Enolic form of acetyl acetone



(4)

Stereoisomerism - This is the type of isomerism which arises due to the difference in the arrangement of atoms in space. Its study is known as stereochemistry.

Stereoisomerism: The isomeric compounds which differ from each other only in the relative arrangement of atoms in space but resemble one another with respect to which atoms are linked to which other atoms are called stereoisomers and the phenomenon is known as ~~stereo~~ stereoisomerism.

Stereoisomers have 2 major classes

1. Configurational isomers.
2. Conformational isomers.

Configurational isomers in turn are of two types.

(i) Enantiomers

(ii) Diastereomers.

Isomers.

Structural
Isomers

Stereoisomers.

Conformational
Isomers

Configurational
Isomers

Diastereomers

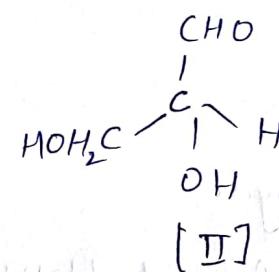
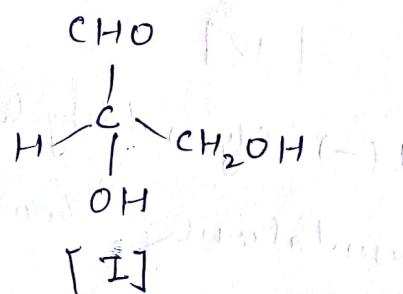
Enantiomers

Cis-trans
Isomers

Diastereomers containing
chiral centers.

Configuration and its specification

The arrangement in space of the atoms or groups constituting a stereoisomer is called its configuration. ex. The configurations of the two enantiomers of lactic acid are I and II shown below. One of these configurations represents dextro or (+) lactic acid while the other represents levo or (-) lactic acid.

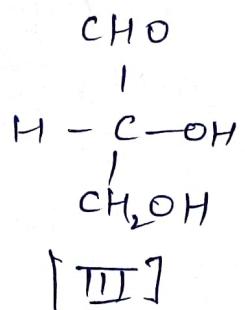


There are two possible configurations of the enantiomers of lactic acid. But we do not know the actual or absolute configuration of each of the two enantiomers.

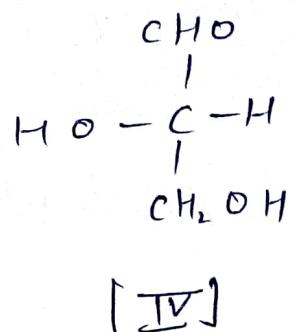
The compound chosen as the standard was glyceraldehyde ($\text{CH}_2\text{OHCHOHCHO}$) and its two enantiomers were designated by the symbols D and L. D and L refer to configurations and are quite different from the prefixes d and l (read as 'dextro' and 'levo') which refers to the direction of rotation.

(+) Glyceraldehyde was arbitrarily assigned the configuration III in which the OH group attached

to chiral carbon is towards right). And was given the symbol D. The (-) enantiomer was assigned the configuration IV (in which the $-OH$ attached to chiral carbon is towards left) and was given the symbol L.



D-(+)-Glyceraldehyde



L(-)-Glyceraldehyde

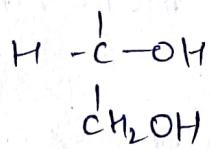
(Three dimensional and planar representations of two enantiomers of glyceraldehyde)

Absolute Configuration In 1951 that by using X-ray diffraction studies, Bijvoet was able to determine absolute configuration of a compound ie the actual arrangement in space of the atoms or groups constituting a particular stereoisomer. The first compound whose absolute configuration was determined was sodium rubidium salt of (+) tartaric acid. Bijvoet found that (+) tartaric acid actually have same configuration which it was previously assumed to have on the basis of configurational relationship between glyceraldehyde and tartaric acid.

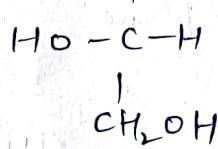
(+) ~~D~~

the assumed configuration of (+) tartaric acid was correct, the assumed configuration of the two enantiomers of glyceraldehyde must also be correct. Thus the relative configuration assigned to D(+) glyclic acid, L(-) lactic acid, carbohydrates and a large number of other compounds actually represent their absolute configuration.

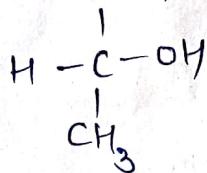
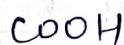
The absolute configurations of some simple but stereochemically important compounds given below in the planar form.



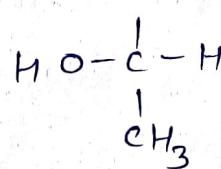
D(+) Glyceraldehyde



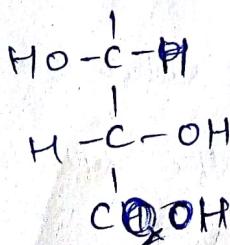
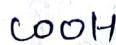
L(-) Glyceraldehyde



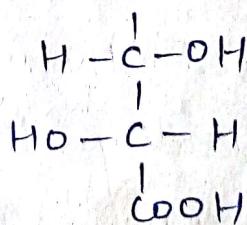
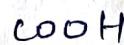
D(+) Lactic acid



L(+) Lactic acid

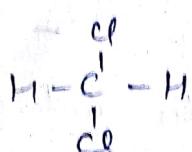


D(-) Tartaric acid

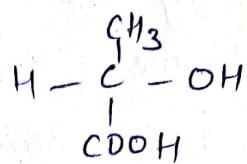


L(+) Tartaric acid

If C-atom has all the different group attached to it then it is said to be Asymmetric one or chiral-C-atom.



Symmetric
(Achiral)



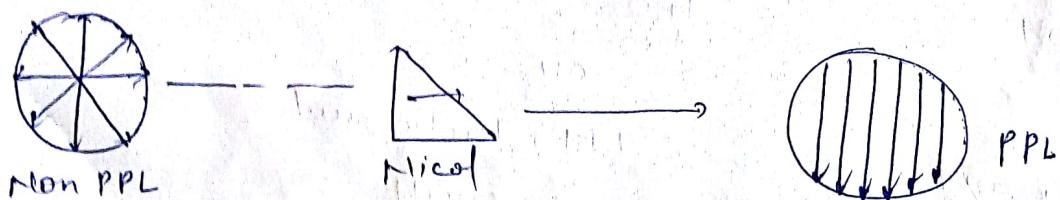
Asymmetric (Chiral)

Molecule having asymmetric C are ~~said to~~ said to Achirality.

OPTICAL ISOMERS

Monochromatic light (Rays of small wave length) has vibration in different plane. It is called NON-PLANE POLARISED LIGHT.

If this is passed through NICOL prism we have rays having vibrations in the plane at right angle to the incident path. This is called Plane Polarised Light.



If PPL is passed through the solution of the substance having achirality then it (PPL) is rotated either towards RHS or LHS. This property of the substance having achirality is called OPTICAL ACTIVITY.

- Some optical active substance rotated PPL towards RHS called d(+)-Dextro rotatory.

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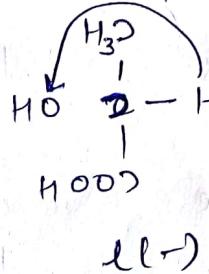
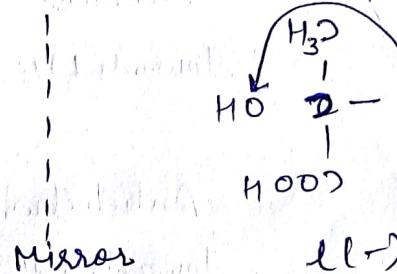
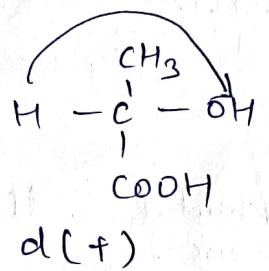
symmetric Some rotate PPL towards LHS l(-) . Lefto Rotatory.

If one form rotate PPL towards RHS then its mirror image with ~~rotate~~ is ENANTIOMER.

If one form rotate PPB towards LHS then its mirror image is also ENANTIOMER,

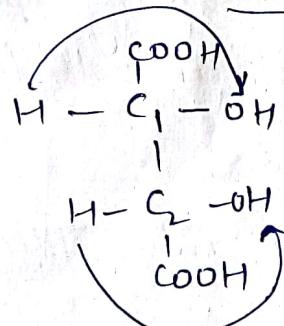
Normally no form is defined if one form is d(+)
its mirror image will be l(-)

Rotation is observed with respect to H form L to R

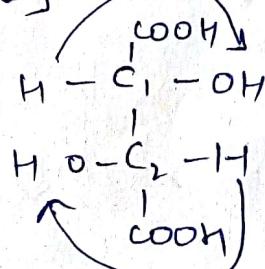


d(+) and l(-) form also called Enantiomers and
this isomorphism is called Enantiomerism. (Optical isomers)

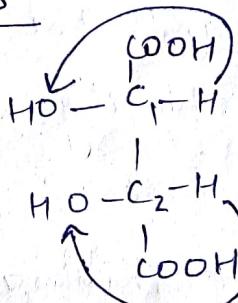
TARTARIC ACID



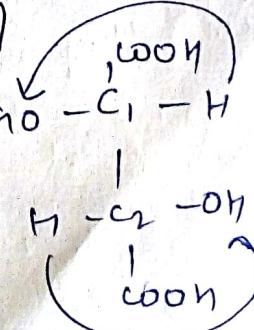
[I]



[II]



[II]



IV

Form	C_1	C_2	Net	(16) Result
[I]	Clockwise towards RHS	Anticlockwise, towards RHS	Zero	Optically inactive neither physical light is
[II]	Anticlockwise towards LHS	Clockwise towards LHS	Zero	"
[III]	Clockwise towards RHS	Clockwise towards LHS	Clockwise	d(+)
[IV]	Anticlockwise towards LHS	Anticlockwise towards RHS	Anticlockwise	l(-)

Mixture of (III) and (IV) in 1:1 mole ratio is optically inactive due to external cancellation. It is called Racemic mixture. and the process of converting optically active form into optically inactive forms is called Racemisation.

If optically inactive mixture is converted into optically active form is called Resolution.

Optically
inactive
internal
carbonyl

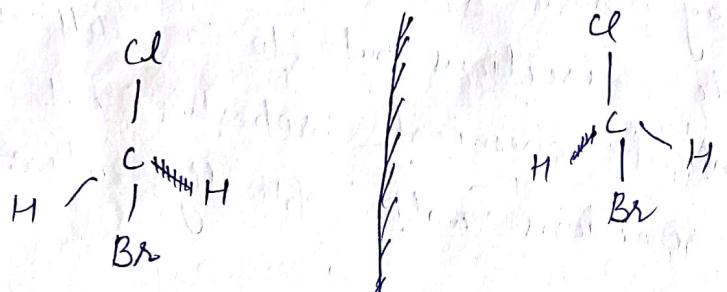
Enantiomers-

The isomers which resemble one another in their chemical reactions and most of the physical properties but differ in their effect on polarised light are called optical isomers and the phenomenon is known as optical isomerism.

There are two main types of optical isomerism.

- 1) Enantiomerism.
- 2) Diastereomerism.

Enantiomers are chiral molecules that are mirror images of one another, furthermore, the molecules of are non-superimposable on one another. This means that the molecules can not be placed on top of one another and give the same molecule.

Characteristics of enantiomers.

- 1) They have identical physical properties such as melting points, boiling points, densities, solubilities etc. The only difference lies in the direction of rotation of plane polarised light.
- 2) They have identical chemical properties except in

(12)

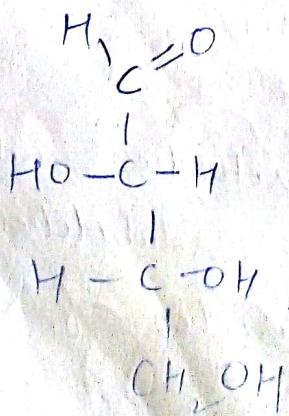
reactions with other optically active compounds
 ex. The ordinary chemical properties of (+) lactic acid are exactly like those of (-) lactic acid.

3) They have different biological properties.

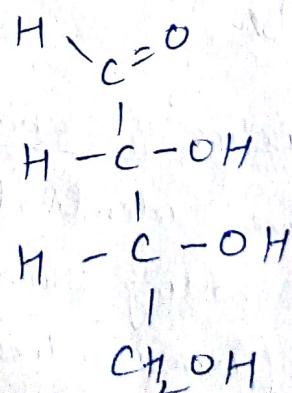
4) When equal quantities of enantiomers are mixed together it results in the formation of an optical inactive form called racemic modification or racemic mixture.

Diastereomers

These are stereoisomers which do not have a mirror image relationship. They have different physical properties such as melting point, boiling point, solubility in a given solvent and density. These may have optical rotation in the same or opposite directions but to a different extent. They have identical chemical properties but different in rate of reactions with optically active compounds.



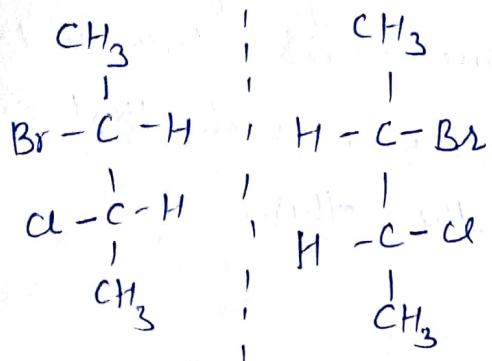
D-Threose



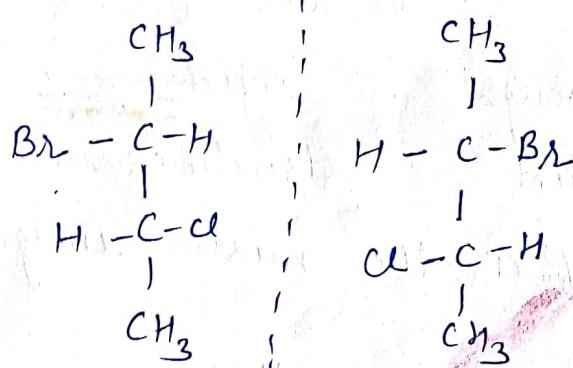
D-Erythrose

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are 2 bromo-3 chlorobutane which has stereocenters at C₂ and C₃. In general a molecule with n stereocenters has 2ⁿ stereoisomers, so there are a total of four possibilities for 2 bromo-3 chlorobutane



enantiomeric pair



enantiomeric pair)

diastereomers.

Four possible stereoisomers of 2-bromo-3-chlorobutane

Characteristics of diastereomers-

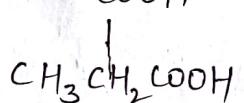
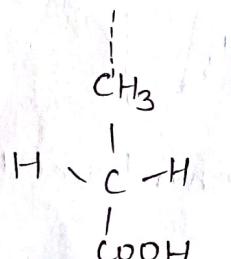
- * They show similar, but not identical, chemical properties.
- * They have different physical properties.
- * Their specific rotation are also different from each other.
- * On account of different physical properties can be rather easily separated from each other by physical methods such as fractional crystallisation, chromatography etc.

Symmetry: An element of symmetry may be defined as a plane, line or point with respect to which the structure possesses a definite symmetry.

There are three elements of symmetry

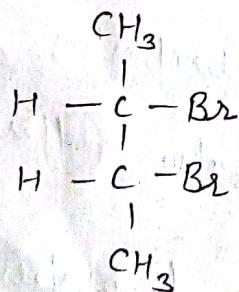
A) Plane of symmetry (Reflection (σ)).

It is an imaginary plane passing through an object or a structure which divides the object or structure into two halves such that one half is the mirror image of the other.



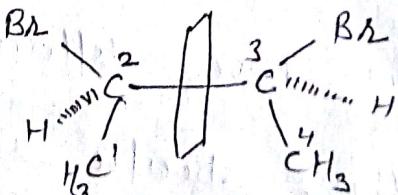
Plane of symmetry in propanoic acid.

In the study of optical isomerism, the plane of symmetry may be shown simply with the help of three dimensional formulae



Plane of symmetry

Planar representation



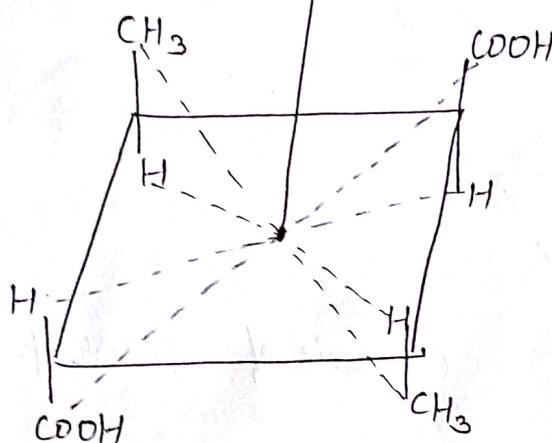
Plane of symmetry

Three dimensional representation

(Inversion - C)
Centre of Symmetry. It is an imaginary point within a molecule at which all the straight lines joining identical points in the ^{molecule} to cross each other.

Ex. The centre of symmetry in a molecule of 2,4-dimethylcyclobutane-1,3 dicarboxylic acid.

Centre of Symmetry



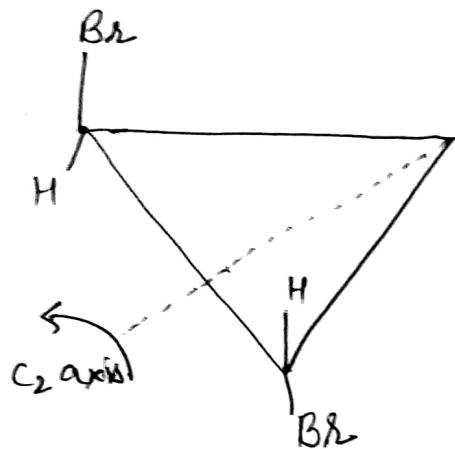
Centre of Symmetry in 2,4-dimethylcyclobutane-1,3 dicarboxylic acid.

It may be noted that a structure can have more than one plane of symmetry but no structure can have more than one centre of symmetry.

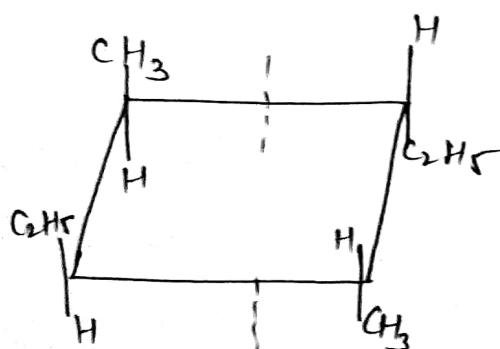
c) Axis of Symmetry. It is an imaginary line passing through the molecule so that when the molecule is rotated about this line, exactly similar geometrical arrangement appears more than once in one complete revolution (rotation through 360°). If it is identical arrangement appears twice in one complete revolution, the

axis is called two fold axis of symmetry^(b). If the similar arrangement appears thrice, it is three-fold axis of symmetry and so on.

e.g. trans-1,2-dibromocyclopropane possesses a C_2 axis of symmetry in the plane of the ring which bisects the bond between carbon atoms 1 and 2 and intersects the C atom 3 as shown in figure

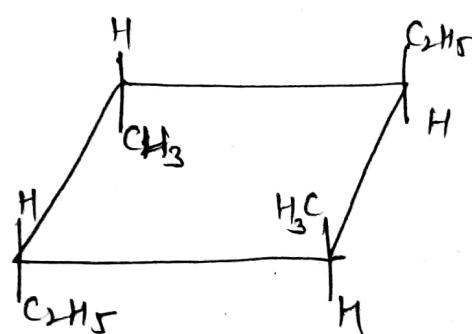


C_2 axis of symmetry.



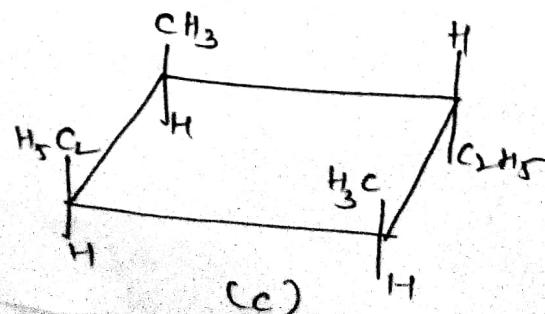
(a)

Rotation by 180°

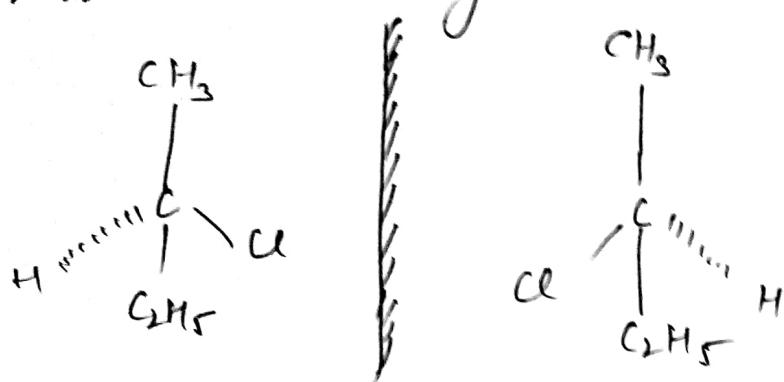


(b)

Reflection in plane



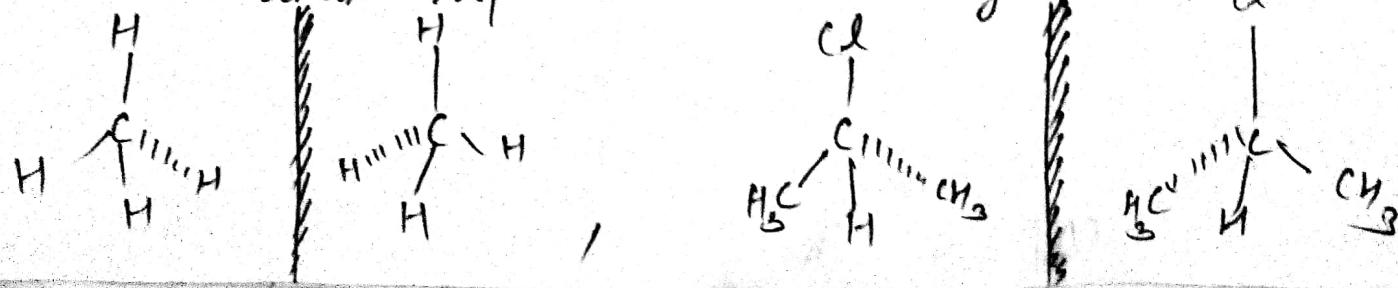
Chiral Structure. A structure or object is said to be chiral if it is superimposable on its mirror image. Such a structure does not have either a plane or a centre of symmetry. A very large number of organic molecules such as 2-chlorobutane and lactic acid are known to have chiral structure as they are not superimposable on their mirror images.



2-Chlorobutane

2. Achiral Structures - A structure or object which has a plane of symmetry and is superimposable on its mirror image is known as achiral. Such a structure always possesses a plane of symmetry or a centre of symmetry.

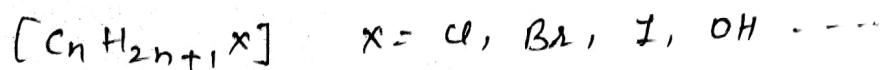
Ex. - Methane and carbon tetrachloride are perfect example of molecules having achiral structures as they are superimposable on their respective mirror images.



(18)

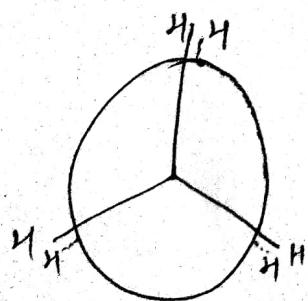
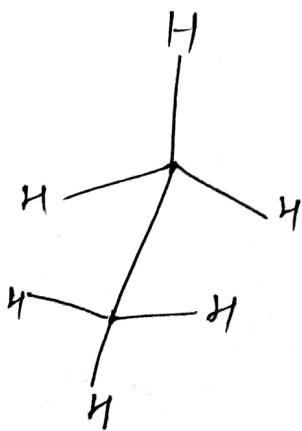
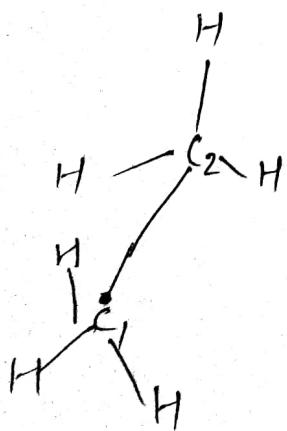
Conformation and conformers.

If there is free rotation about $C=C$ (σ bond) in alkanes. (C_nH_{2n+2}) or its compounds ($C_nH_{2n+1}X$), then we get various forms have $0^\circ - 360^\circ$. These various spatial (in space) forms obtained due to rotation about $C=C$ in alkanes or related compounds are called CONFORMERS and this process is called CONFORMATION.



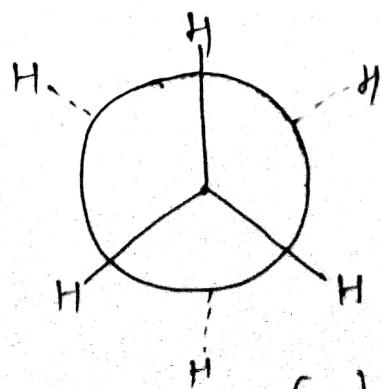
(I)* Consider CH_4 . In this case there is no [$C=C$] bond, hence conformation are not possible.

(II)* Consider the case - CH_3-CH_3 (ethane). There is one $C=C$ bond. There is free rotation. We can represent ethane as shown below.



(A)

[ECLIPSED]



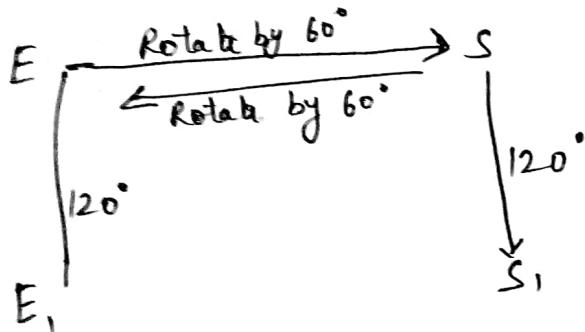
(B)

[STAGGERED]

Form (A) C-H bonds (C_1) are overlapping on C-H bonds (C_2). This form is called ECLIPSED form. It has less stability hence Maximum energy.

Stability $\propto \frac{1}{\text{Energy}}$

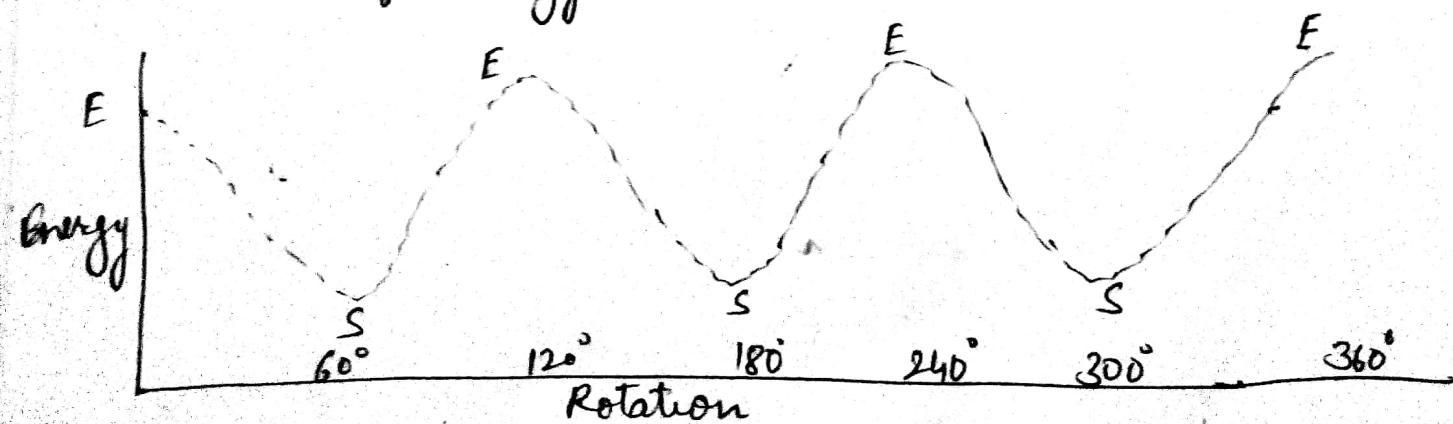
Form (B) C-H bond C_1 are opposite C-H bond at C_2 . This is called STAGGERED form. It has max. stability hence minimum energy. This form is obtained of E-form is rotated by 60° . If starm is further rotated by 60° (Total rotation 120°)



other forms which are obtained between 0° and 60° are called SKEW forms.

These conformers were first given by Newman, hence all three forms (E, S) are called NEWMAN is conformous.

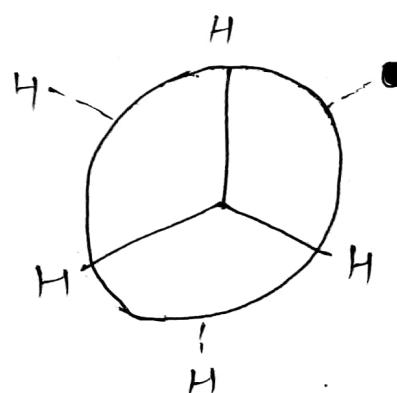
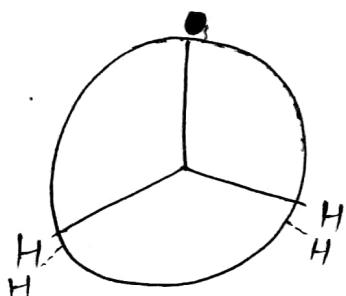
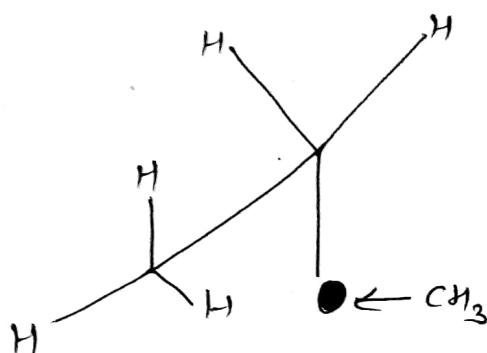
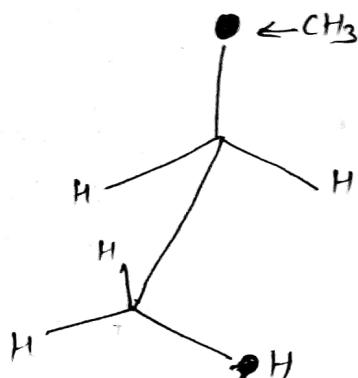
Variation of energy with rotation (0° to 360°)



Types of structural isomers

1) ★ We consider $[CH_3-CH_2-CH_3]$
Propane

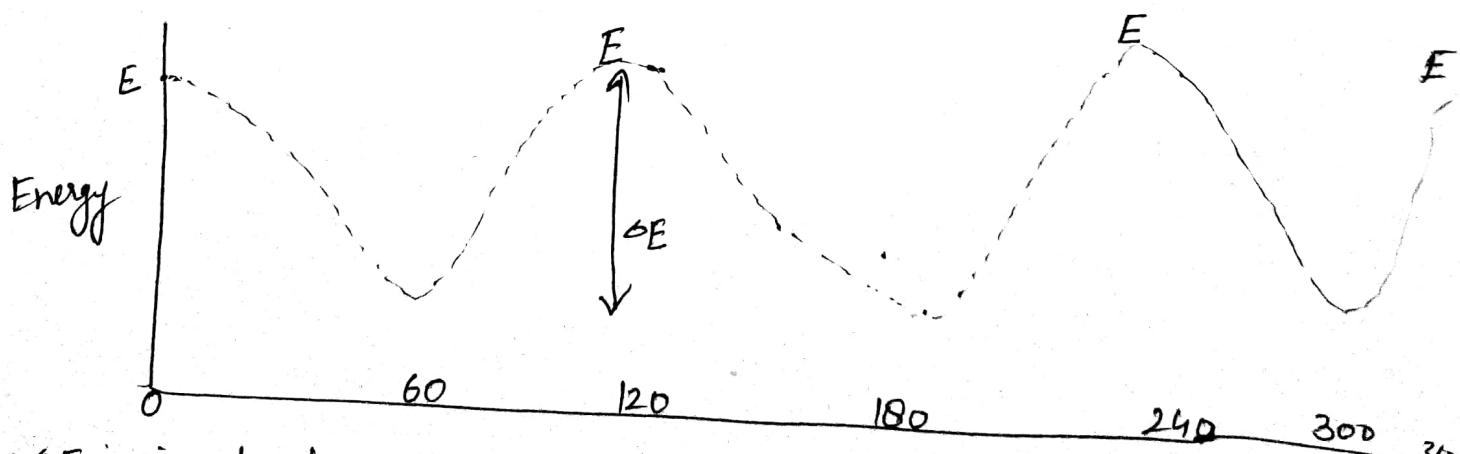
(H of ethane is replaced by $-CH_3$) we can make S and E conformers as shown below



Eclipsed

Staggered

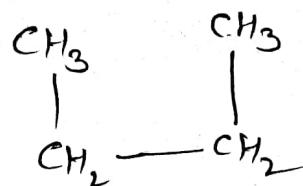
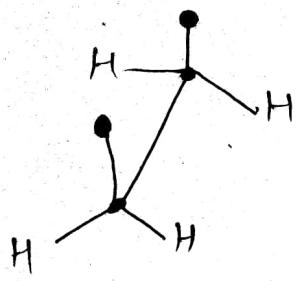
Energy and Rotation -



ΔE in propane $>$ ΔE in ethane. Hence E form of propane is less stable than E form of ethane.

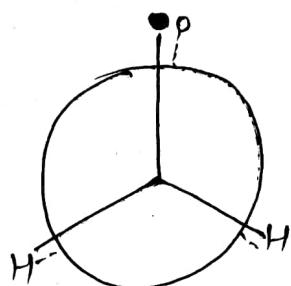
(2)

Butane [$\text{CH}_3 - \text{CH}_2 - \text{CH}_2 - \text{CH}_3$]

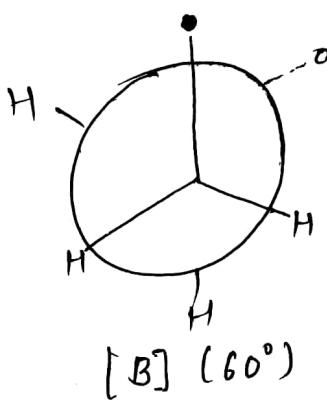


Butane

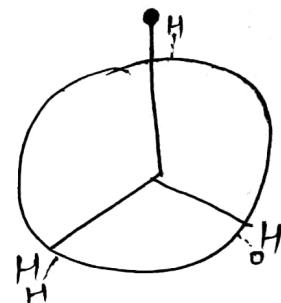
In case of butane we get so many staggered and eclipsed forms with different energy.



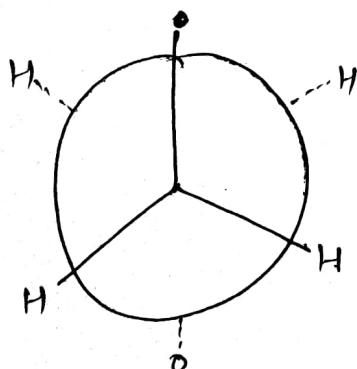
[A]



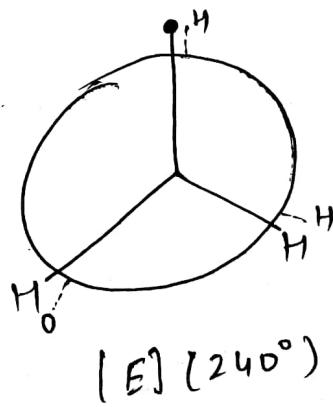
[B] (60°)



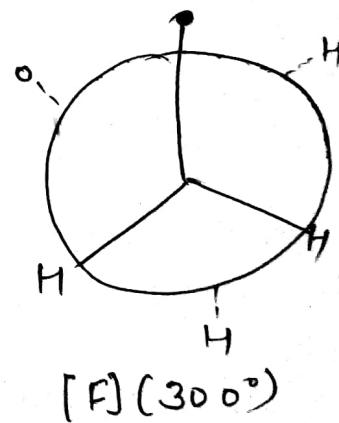
[C] (120°)



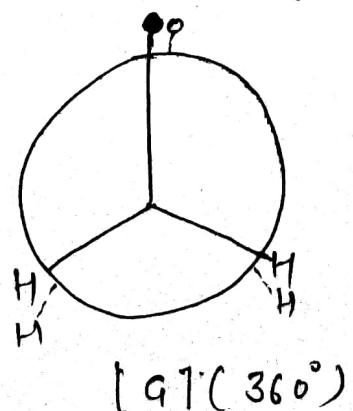
[D] (180°)



[E] (240°)



[F] (300°)



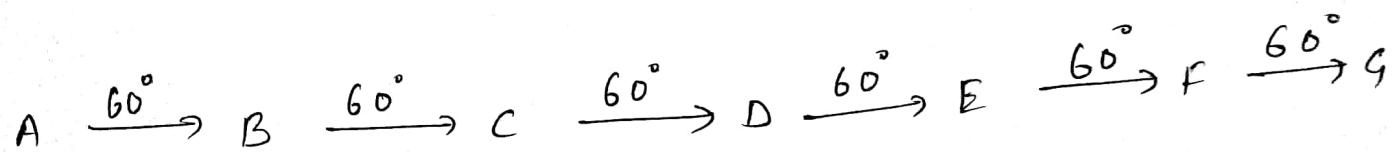
[G] (360°)

Structural Isomerism

(22)

Form A & Form G having maximum energy due to two $-CH_3$ group in overlapping position hence they are least stable.

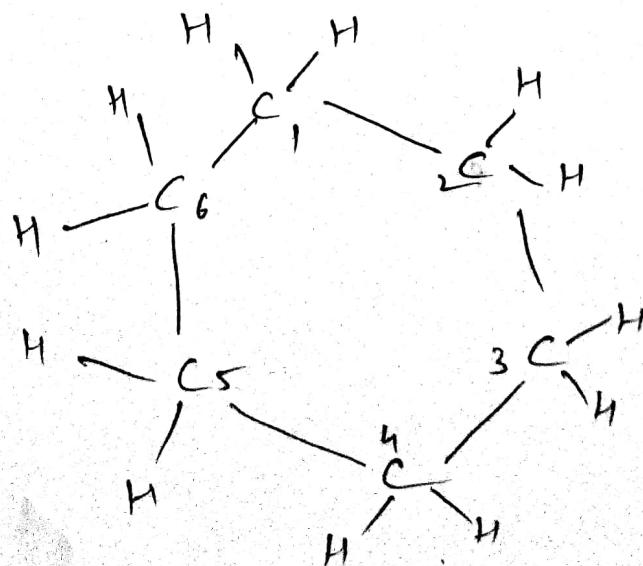
Form D - In which two $-CH_3$ groups are opposite to one each other has least energy and it has maximum stability.



Form A, C, E, G are Eclipsed forms

Form B, D, F are Staggered forms.

* Elementary idea about the conformers of cyclohexane C_6H_{12}

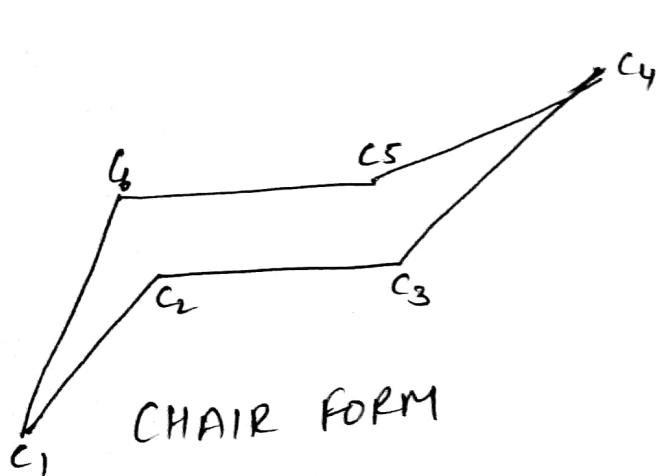


There are two main conformers.

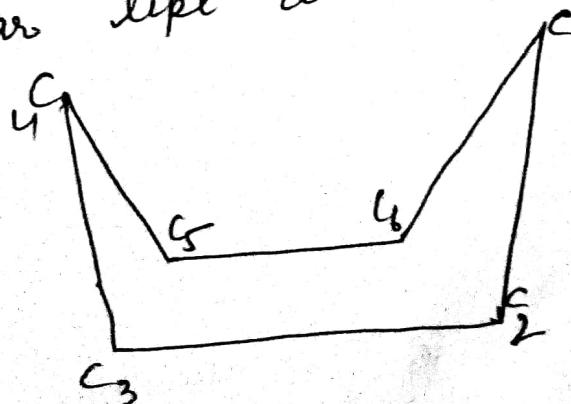
1) Chair form

2) Boat form

1) CHAIR FORM. In this conformer is such that C_1 and C_4 are opposite to one each other and C_2, C_3, C_5, H_6 plain. So that chair appears in this structure



2) Boat Form- In this form C_1 and C_4 are on the same side. C_2, C_3, C_5, H_6 are in plane. So that it appear like a boat in this structure



Intermediate forms are called (skew) forms