



University School of Automation and Robotics
GURU GOBIND SINGH INDRAPIRASTHA UNIVERSITY
East Delhi Campus, Surajmal Vihar
Delhi - 110092



BS-109 Engineering chemistry-I

Stereochemistry

Karan Chaudhary

STEREOCHEMISTRY

1. Classification →

molecules with same molecular formula

Homomers

Heteromers

Stereoisomers

Constitutional isomer

Enantiomers

Diastereomers

Chain

Group

Position

Mutamers

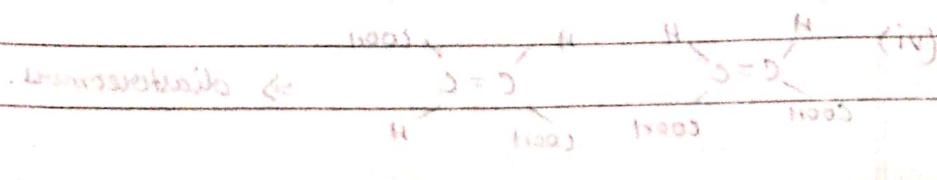
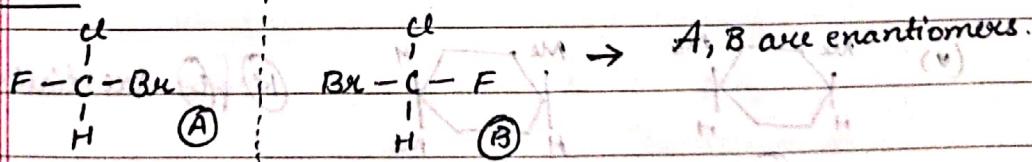
Tautomers.

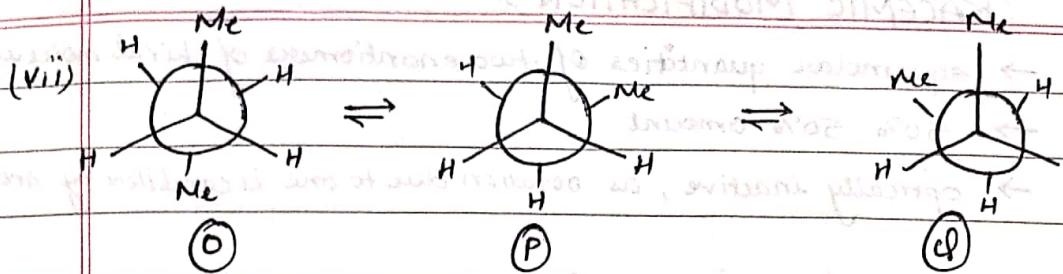
Enantiomers → two isomers which are mirror images of each other but are not superposable are called enantiomers & have enantioemic relationship.

enantiomers have same physical & chemical properties, except they turn the plane polarised light to equal degree but in opposite direction.

Diastereomers → isomers which are not mirror images of each other, and have diastereomeric relationship. diff chemical & phy property. Can be separated.

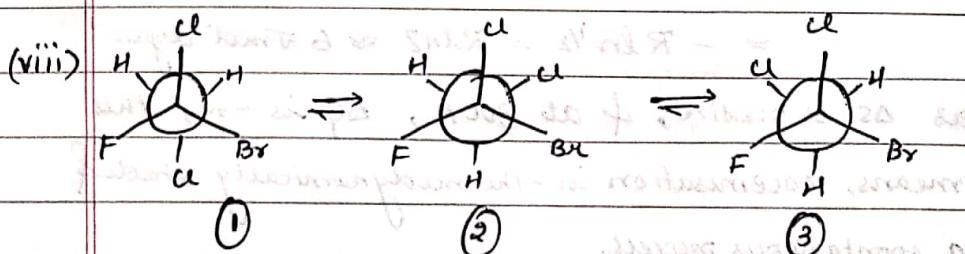
EXAMPLES



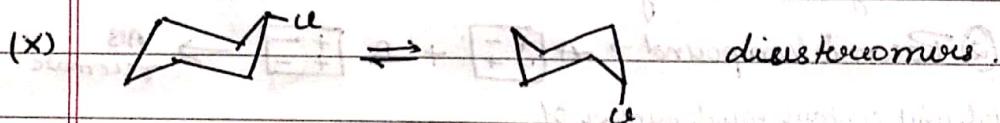
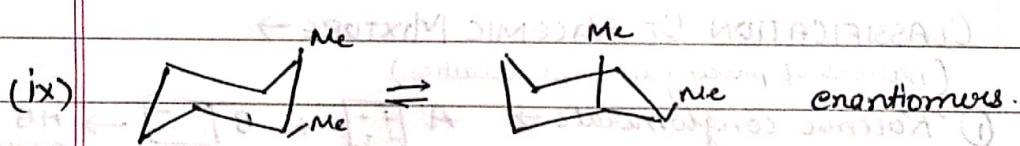


① & ②, ① & ③ are diastereomers.

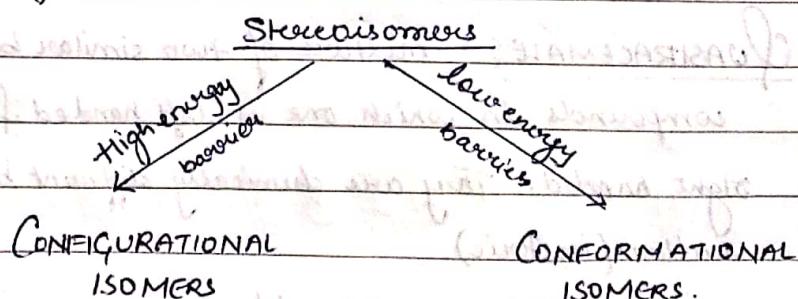
② & ③ are enantiomers.



①, ②, ③ are diastereomers.



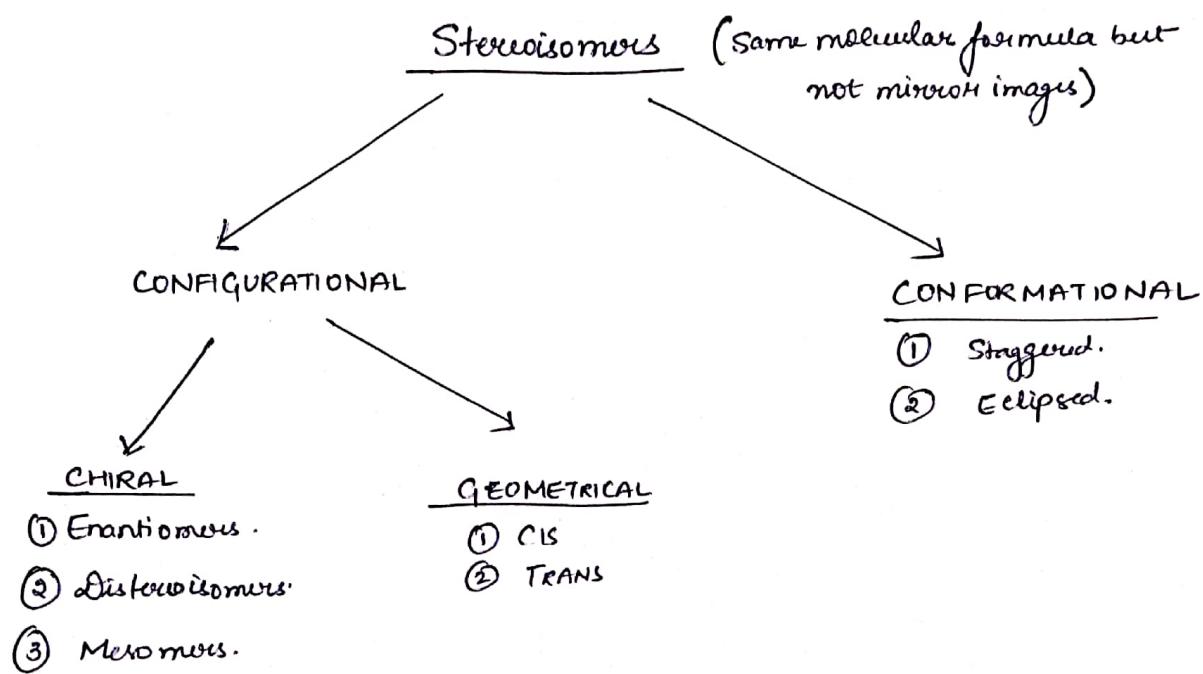
Stereoisomers are also classified on basis of energy barriers separating them.



Molecules that are superimposable with their mirror images are "ACHIRAL".

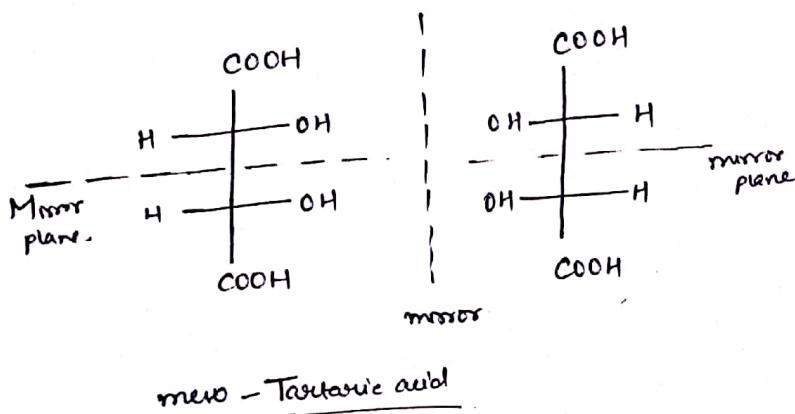
Whereas,

molecules that are not superimposable with their mirror images are "CHIRAL".



Mesomers or MESO COMPOUNDS

+ Have chiral centres but optically inactive because have plane of symmetry.



RACEMIC MODIFICATION →

- equimolar quantities of two enantiomers of chiral molecule.
- 50% : 50% amount
- optically inactive, as rotation due to one is cancelled by another

thermodynamic property →

when racemic acid is formed, there is ΔS of mixing.

$$\Delta S = -R X_1 \ln X_1 - R X_2 \ln X_2$$

$$= -R \ln^{1/2} = R \ln 2 \approx 6 \text{ J mol}^{-1} \text{ degre}^{-1}$$

as ΔS is positive, & at 300K, ΔG is -ve, this means, racemisation is thermodynamically stable & a spontaneous process.

CLASSIFICATION OF RACEMIC MIXTURE →

(nature of packing in crystal lattice)

① Racemic conglomerate $\rightarrow A \begin{smallmatrix} + \\ + \end{smallmatrix} + B \begin{smallmatrix} - \\ - \end{smallmatrix} \rightarrow AB$ racemate
crystal lattice is formed entirely from enantiomers of like chirality.

② Racemic compound $\rightarrow A \begin{smallmatrix} + \\ - \end{smallmatrix} + B \begin{smallmatrix} + \\ - \end{smallmatrix} \rightarrow AB$ racemate.
crystal unit contain equal number of (+) or (-) enantiomers.

③ Pseudo racemate $\rightarrow A \begin{smallmatrix} + \\ - \end{smallmatrix} + B \begin{smallmatrix} - \\ + \end{smallmatrix} \rightarrow AB$.
crystal unit is formed indiscriminately from both enantiomers.

CHIRAL RACEMATES \rightarrow mixture of two similar but distinct compounds in which one is left handed & another is right handed. They are chemically different but structurally similar (isosteric).

e.g. → (+) Chloro succinic acid

(-) Bromo succinic acid.

OPTICAL ROTATION →

- measurement of rotation of plane polarized light in degree
- depends upon T , λ , conc of length of tube.

$$[\alpha]_D^{20^\circ} = \frac{\text{observed rotation}}{c \times l}$$

$c \rightarrow \text{g/ml}$
 $l \rightarrow \text{dm.}$

e.g. enantiomers of 2-butanol

obs rotation = 4.05° anticlockwise

conc $\rightarrow 6 \text{ gml}/40 \text{ ml}$ $l = 200 \text{ mm.}$

$$[\alpha]_D = -\frac{4.05}{6/40 \times 2} = -13.5^\circ$$

$$\text{OPTICAL PURITY} \rightarrow O_p = \frac{[\alpha]_{\text{obs}}}{[\alpha]_{\text{max}}} \times 100$$

or ee = $\frac{R-S}{R+S} \times 100$

enantiomeric excess.

Q $[\alpha]_{\text{max}} = +23.1^\circ$ (S)

$[\alpha]_{\text{obs}} = +9.2^\circ$

$O_p \text{ or ee} = \frac{9.2}{23.1} \times 100 \approx 40\%$

$40\% \text{ (S) } 60\% \text{ R & S}$

$S = 70\%, R = 30\%$

Q $R:S = 95:5$

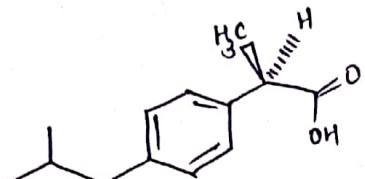
$O_p \text{ or ee} = \frac{95-5}{95+5} \times 100 = 90\%$

Separation of enantiomers

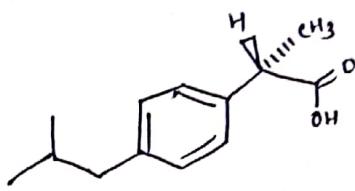
Most of the natural products, food stuffs, drugs, flavouring agents, perfumes and other biologically active materials usually show beneficial effects in one enantiomeric form only.

IBUPROFEN

e.g.



R form (non active) Side effects.



S form (active) anti inflammatory.

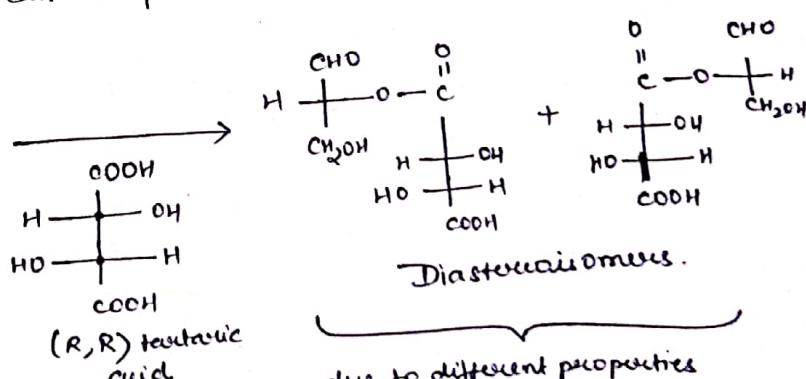
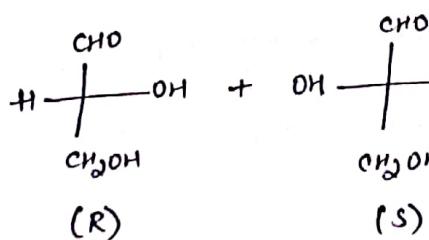
① Mechanical Separation: crystallisation method.

- applicable only to racemic conglomerates
- by normal crystallization can be separated as but require bigger crystal size to be picked from hand & check rotation by dissolving it.
- tedious method and not much practical applications.

② Resolution through formation of diastereomers:

- Since enantiomers have common physical properties they cannot be separated by methods like crystallization or any other like distillation or chromatography.
- Diastereomers have different physical properties; so they can be separated easily.
- This fact can be used to achieve resolution of racemates.
- Reaction of racemates with an enantiomerically pure chiral reagent gives a mixture of diastereomers, which can be separated.

e.g.



(R,R) tartaric acid

Diastereoisomers.

due to different properties can be crystallized & after separation on by dialysis can get (R) & (S) separately.

(3) Resolution through formation of molecular complexes:

- To separate enantiomers, we can make complexes of them by adding suitable complexing agent which can form easily & decompose easily.
- It would selectively complex only to one type of compound, so that both can be separated one by complexing & one left behind.
e.g. amide of (-)-malic acid and of tartaric acid.

(4) Resolution by Chromatography:

There are four conditions for resolution

- formation of diastereomeric mixtures by derivatization with optically active reagents and separation by classical chromatography using achiral adsorbents.
- direct resolution of racemic mixture using chiral adsorbent materials either as solid or liquid stationary phase.
- direct resolution on an achiral solid phase using a mobile chiral liquid phase.
- direct resolution using an achiral solid stationary phase modified by a chiral reagent.

(5) Resolution by biochemical transformation:

Resolution can also be done with help of micro-organisms or enzymes, which are often highly stereoselective in their reactions.

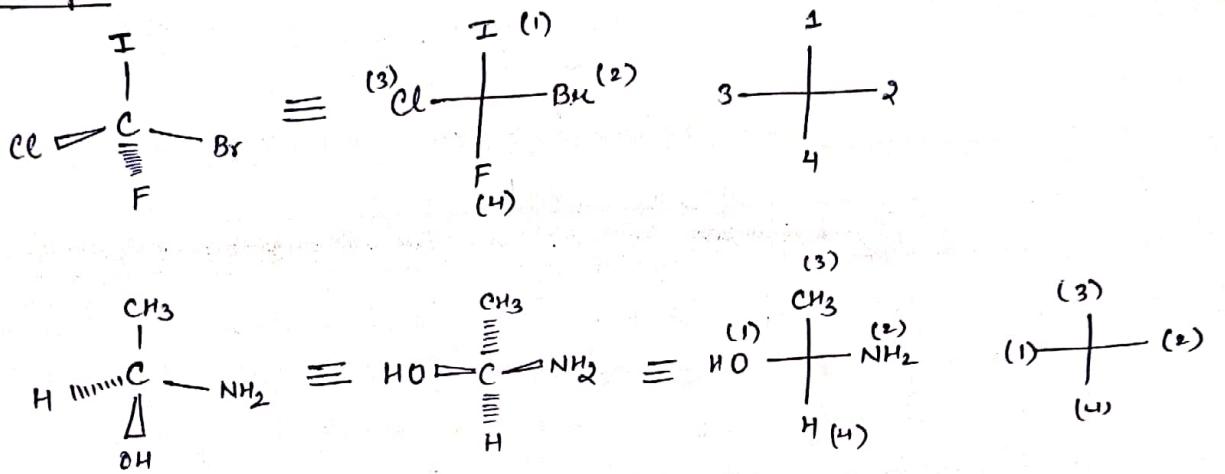
e.g. ammonium salt of (\pm)-tartaric acid is fermented by yeast or a mold (penicillium glaucum), the natural (+) form is completely consumed leaving behind the ammonium salt of (-)-tartaric acid.

ABSOLUTE CONFIGURATION (R AND S)

Sequence rules

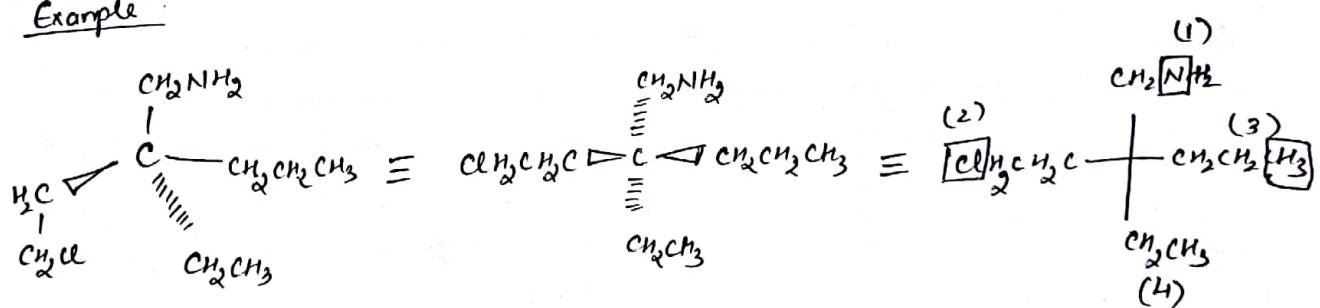
1. Write stereoisomer in terms of Fischer projection formula.
2. Identify the atoms or groups attached to chiral carbon (stereogenic centre). Now assign priority order in accordance with the atomic numbers.

Example



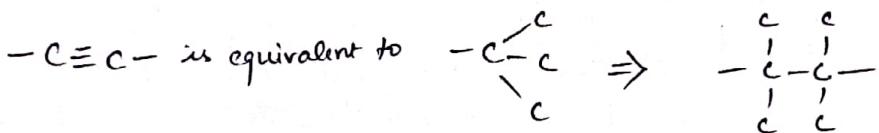
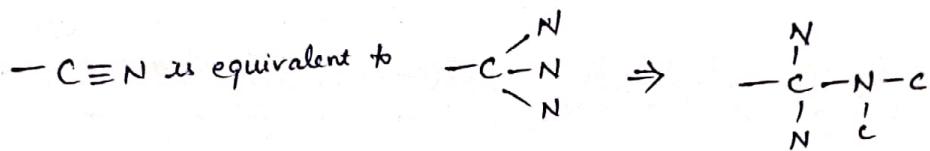
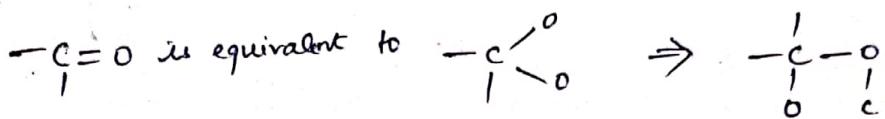
(3) If in a molecule different groups are attached to chiral centre through multiple atoms, priority order cannot be decided on basis of at. no. of atoms directly attached to chiral centre. In such case, we look at next set of atoms with higher atomic number present in group & priority is assigned at first point of difference in accordance of at. no.

Example

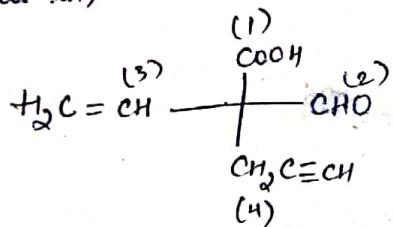


(4) In case groups having multiple bond, for assigning priority order a multiple bond is considered to be bonded to an equivalent number of similar atoms through single covalent bonds.

example



Thus in,

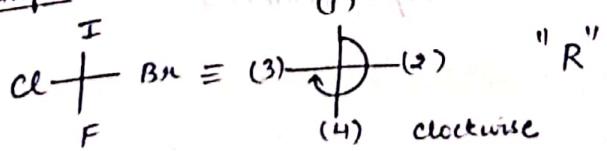


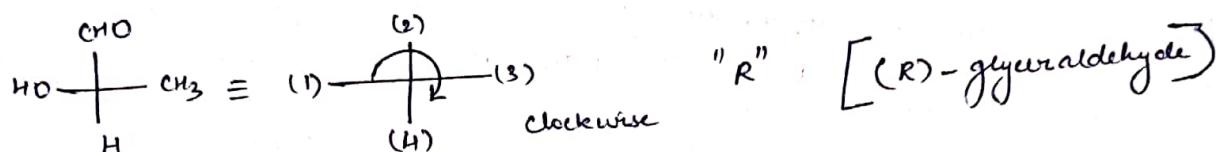
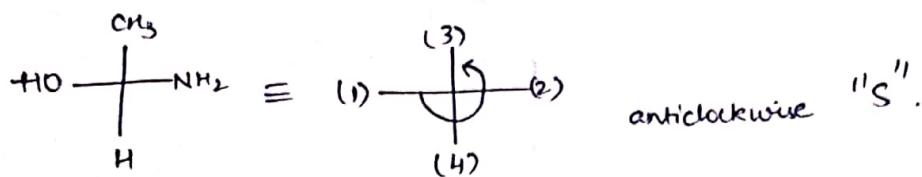
Now for assigning R and S, group or atom with least priority should be at position vertically down word in Fischer projection. Then arrangement of out three groups or atoms is considered to their decreasing priority order.

→ If groups or atoms are ordered in a clockwise manner \Rightarrow it is "R"

→ If groups or atoms are ordered in a anticlockwise manner \Rightarrow it is "S".

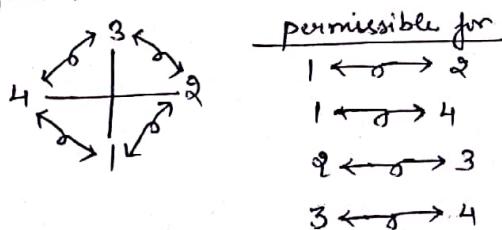
Example:



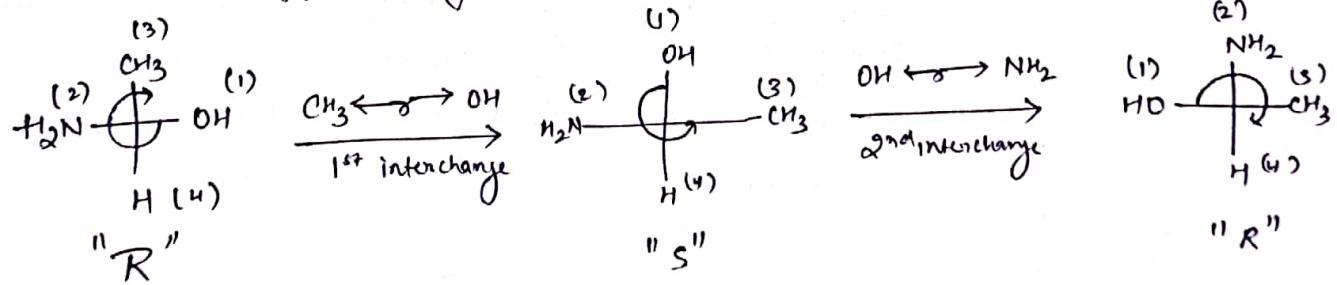


To assign R & S configuration to chiral molecule, the least priority group would be vertically downward in the Fischer projection. If not so, "interchange" in positions are carried out but care needs to be taken that interchanges do not change the actual configuration of molecule. This is done by following two rules:

(I) interchange is to be carried out only between adjacent positions in Fischer projection.

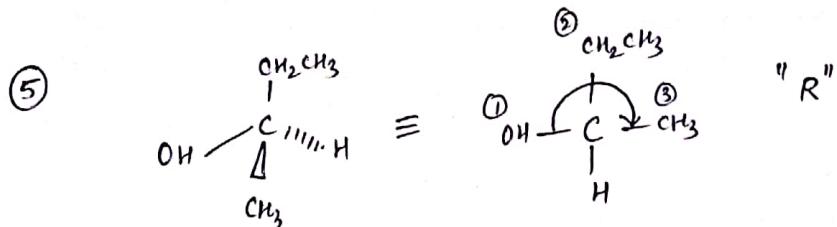
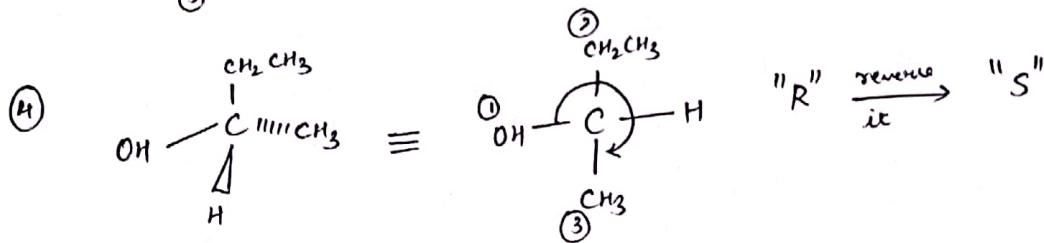
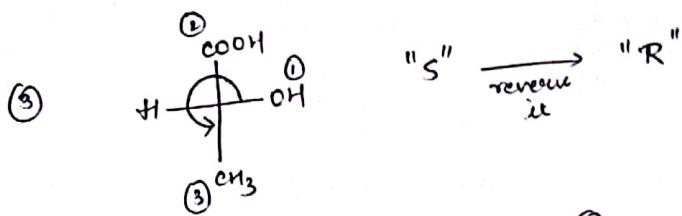
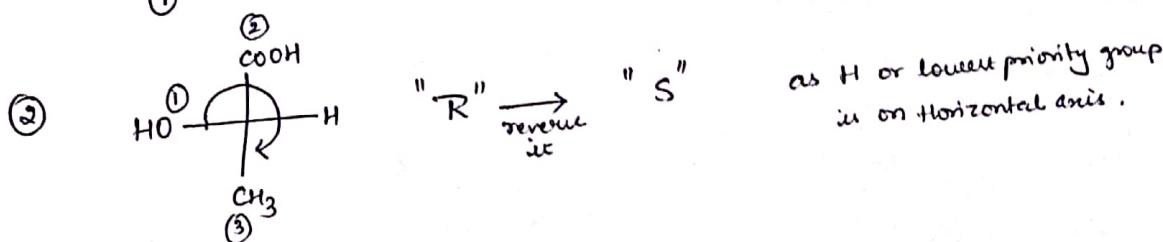
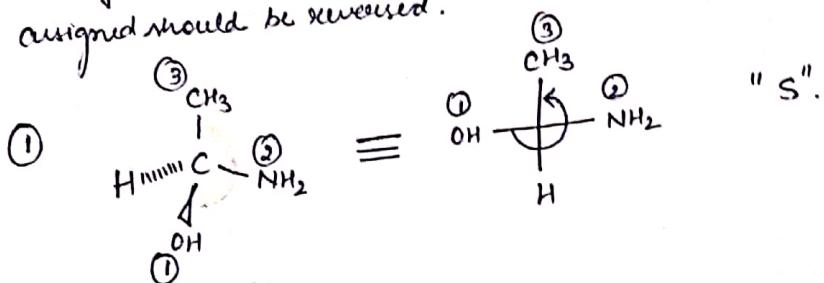


(II) even number of interchange must be carried out, as it does not change the actual configuration of molecule.



Alternative method for assigning R and S :

- Fix the priority order of ligands and tracing a semicircle joining $a \rightarrow b \rightarrow c$ ignoring 'd', the lowest priority group.
- If 'd' is on vertical line in Fischer projection (whether on top or bottom) sequence gives the correct descriptor.
 - Or if 'd' is on horizontal line, the sequence gives wrong answer, so descriptor assigned should be reversed.

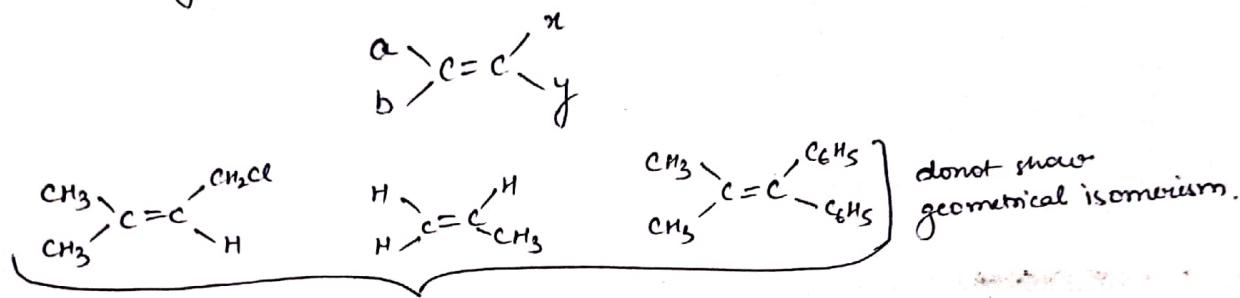


Geometrical isomers.

- compounds having similar molecular formulae but different arrangement of atoms or molecules (groups) around double bond are geometrical isomers.
& phenomenon is known as geometrical isomerism.
- restricted rotation about C-C double bond, as complete rotation around C=C causes breaking of π bond.

- Necessary & sufficient condition for geometrical isomerism:

an alkene of type $abC=Cb'$ may exhibit geometrical isomerism if $a \neq b$ & $a \neq y$.

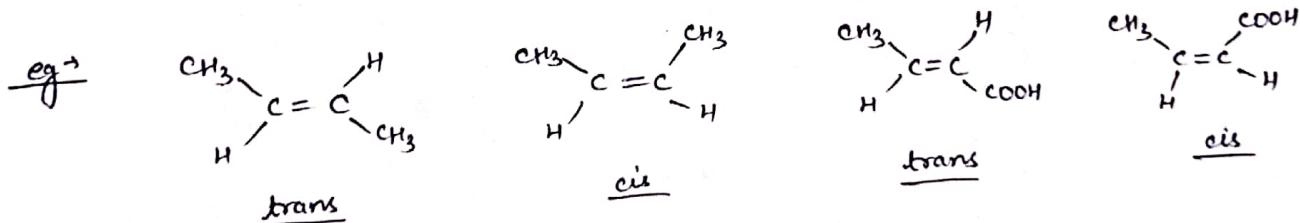


① Cis-trans system

used for the alkenes in which two olefinic carbons have at least one similar group on them. [$abC=Cab'$] or [$abC=Ca'b'$]

cis → when similar groups are on sides across the double bond.

trans → when similar groups are on opposite sides across the double bond.



- stability of trans isomer is more as compared to cis isomer, b'coz cis-isomers have groups on same side, experience van der waals repulsive forces due to steric factor.
- trans molecules have dipole moment "zero", whereas for cis it is not zero.

E-Z system:

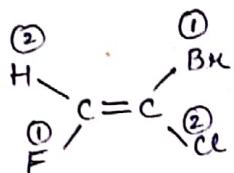
→ for alkenes of type $abc = \text{C}xy$ ($a \neq b \neq x \neq y$)

→ atoms or groups are given priority.

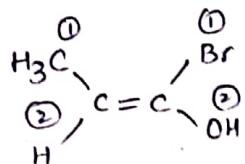
→ if higher priority groups are on same side across double bond $\Rightarrow Z$ isomer
[German: Zusammen = same side]

if higher priority groups are on opposite side across double bond $\Rightarrow E$ isomer
[German: Entgegen = opposite side]

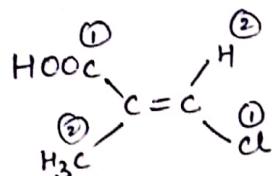
e.g.



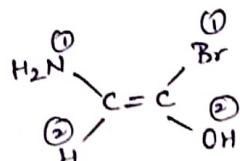
E-



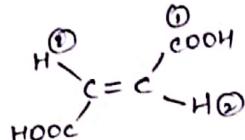
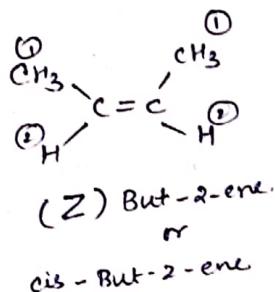
Z-



E-

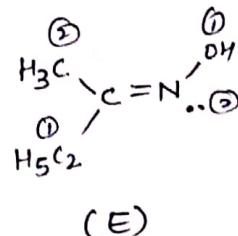
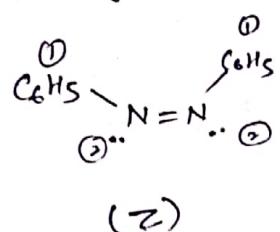
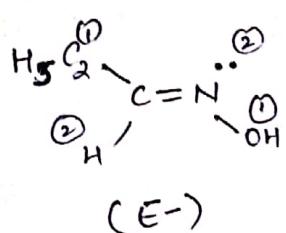


Z-



(E) But-2-ene diacid
or
trans-But-2-ene diacid.

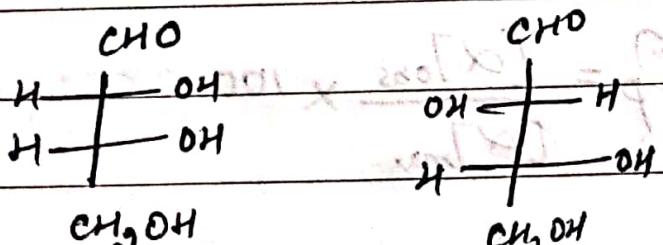
→ your lone pair gets the lowest priority.



SPECIAL NOMENCLATURE (THREO & ERYTHROS)

came from 4C sugar.

Erythro → substituents



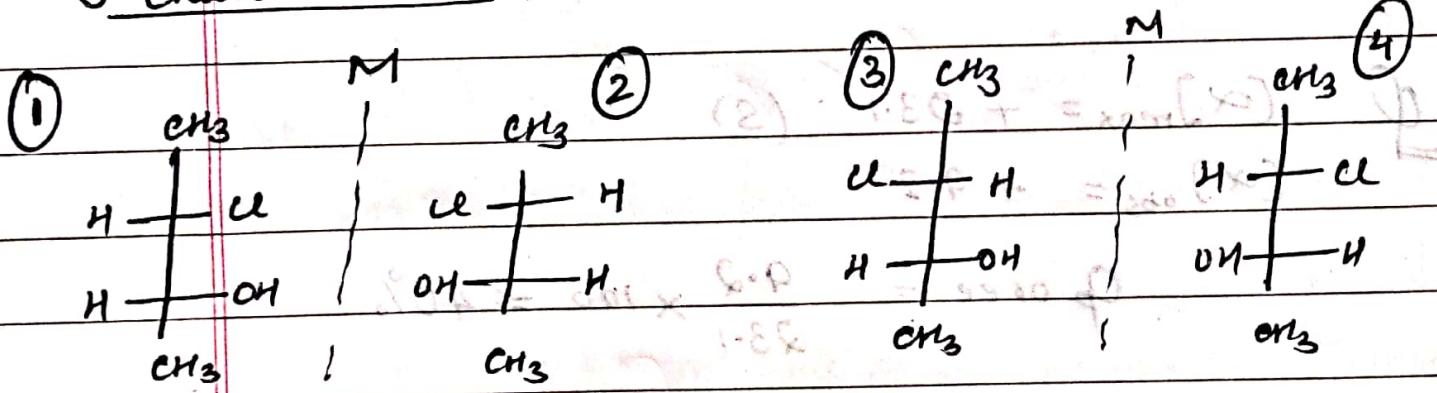
situated on same
side of chiral atom

Threo → substituents
situated on opposite
side of chiral atom.

D-erythrose

D-threose

3-chloro-2-butanol



(Erythro) enantiomer

(Threo) enantiomer.

①, ③ & ①, ④ & ②, ③ & ②, ④ are diastereomers.

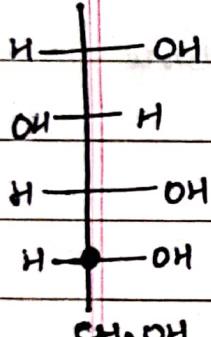
RELATIVE CONFIGURATION (D & L)

H O H

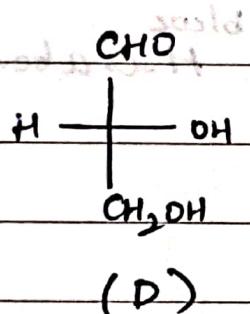
(S)

- for sugar & amino acids only.
- for this draw Fischer projection with all bonds solid lines.
 - horizontal line → toward observer
 - vertical line → away from observer
- longest carbon chain is on vertical of highly oxidised end group should be at top.
 - if -OH or -NH₂ of αC is on right its (D)
 - " " " " " " " left its (L)

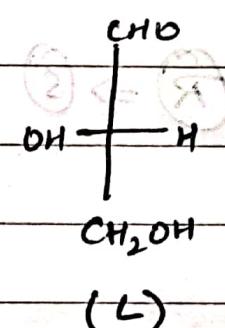
CHO



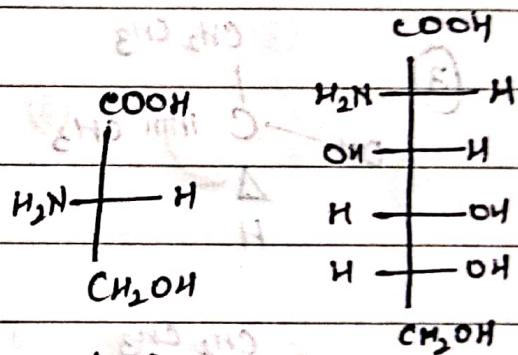
(D)



(L)



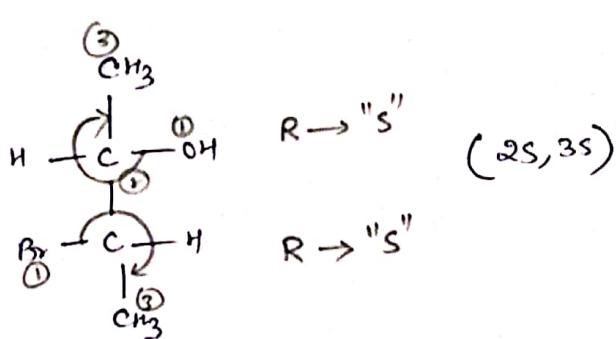
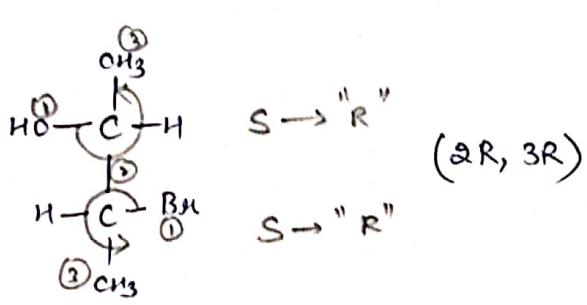
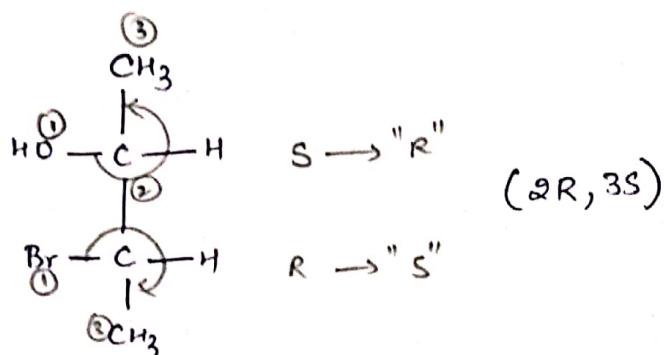
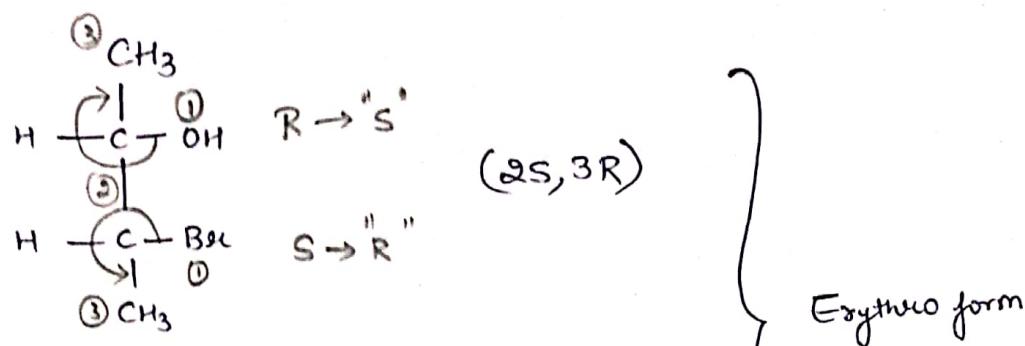
(L)



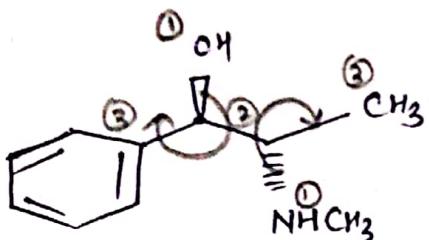
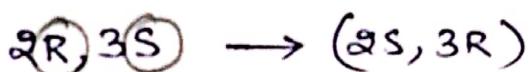
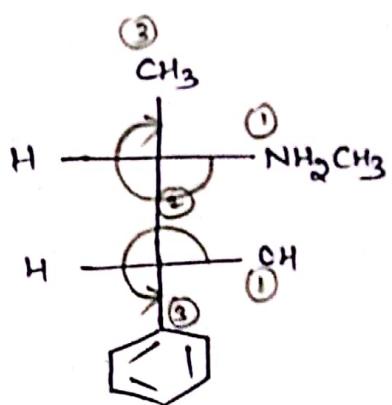
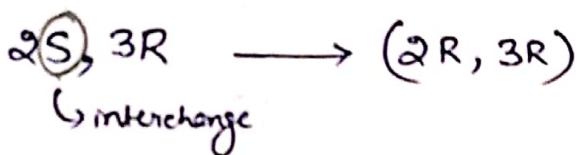
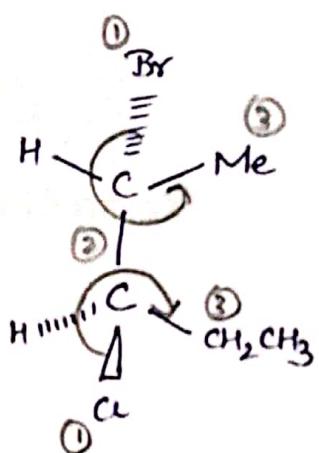
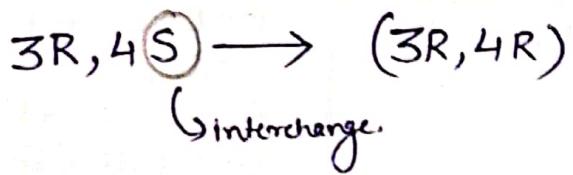
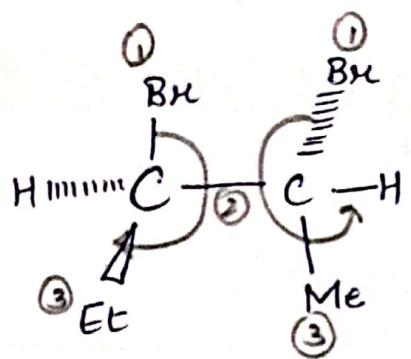
(L)

-OH reference (D_S)
-NH₂ reference (L_S)

Stereochemistry of compounds containing two asymmetric C atoms



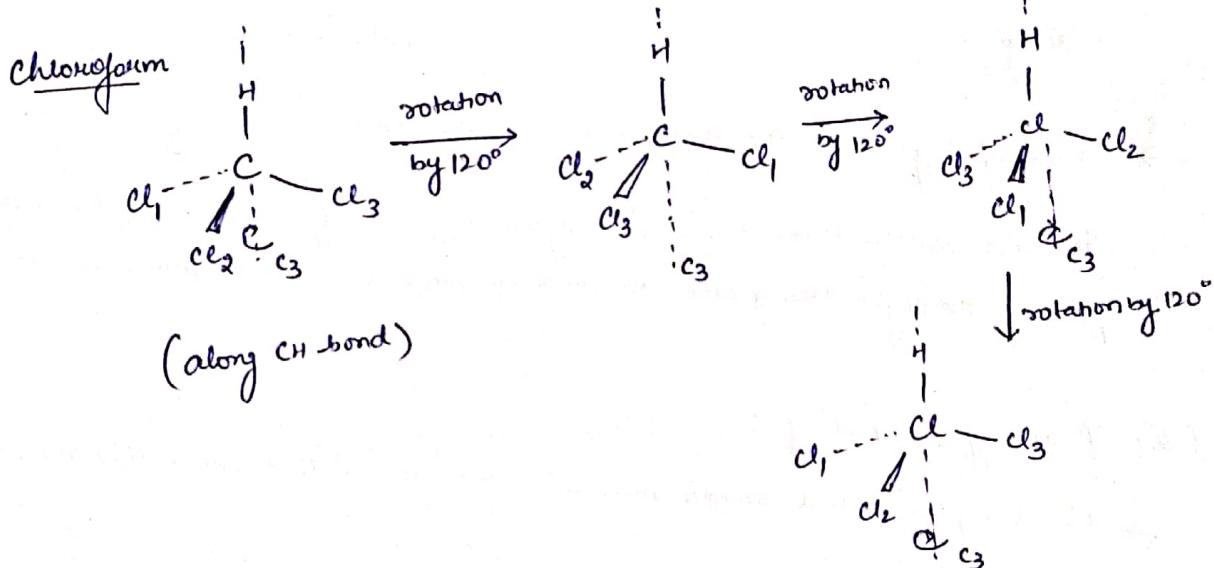
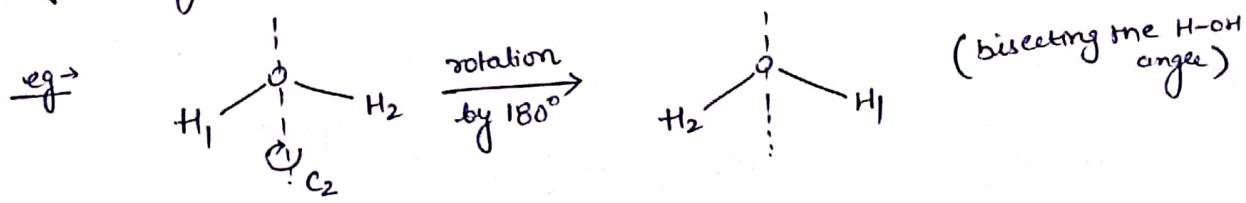
Each chiral centre is capable of existing in two configurations, R and S and the total number of stereoisomers is thus 2^n where n is no of chiral centres.



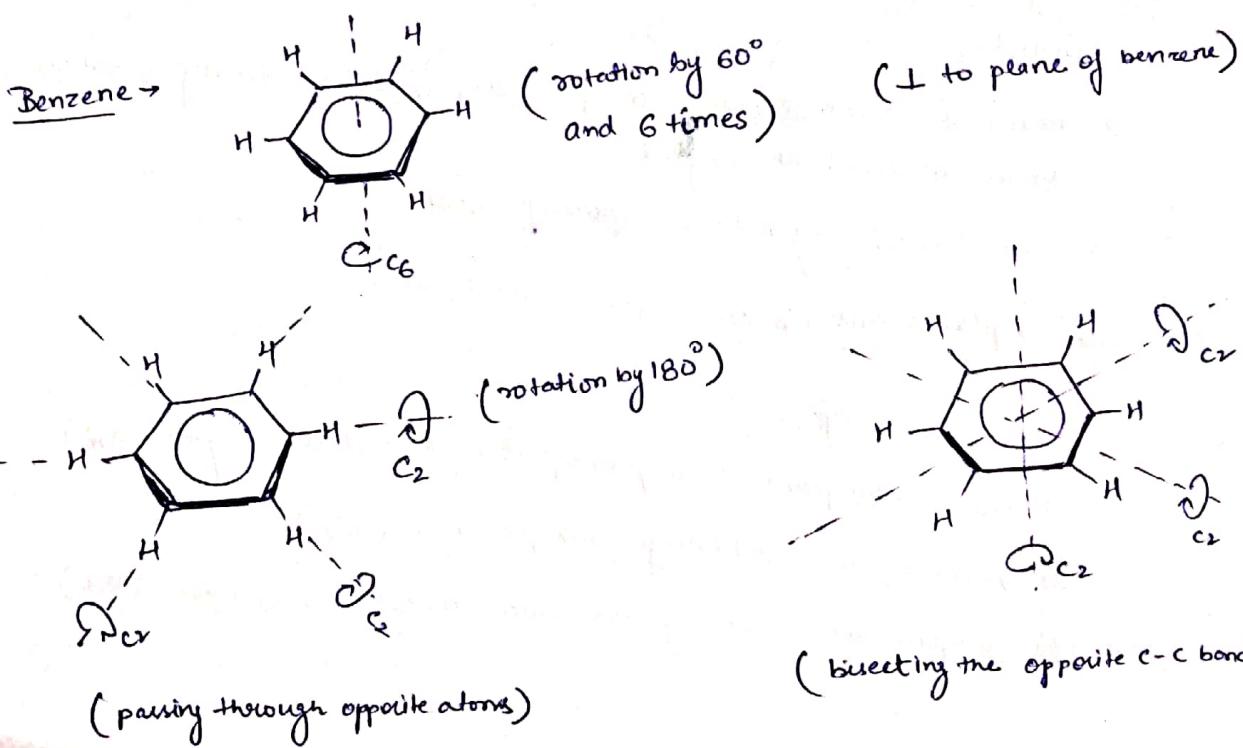
Elements of symmetry:

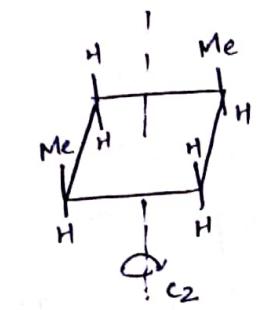
1. Axis of symmetry: (C_n)

When a molecule is rotated around appropriate imaginary axis by an angle of $\frac{360^\circ}{n}$ and arrive arrangement indistinguishable from original. This axis is called n -fold proper axis of symmetry.

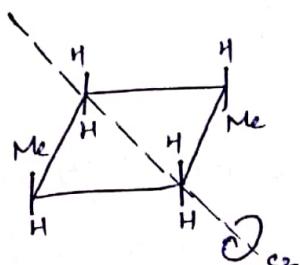


* NH_3 , RN_3 also have C_3 axis.

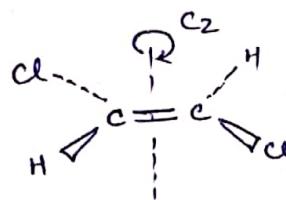




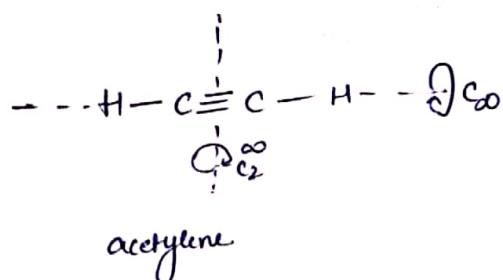
cis - 1,3-dimethyl
cyclobutane.



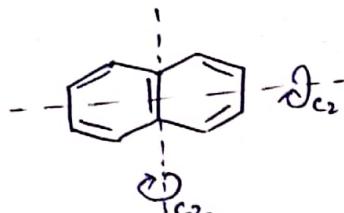
trans - 1,3-dimethyl
cyclobutane.



trans dichloroethylene



acetylene



naphthalene.

→ axis of higher order known as principal axis.

→ In case, where there are several symmetry axes of same order, then one passing through the greatest number of atoms is taken as principal axis.

(2) Plane of symmetry:

→ it is a plane that divides molecule into two halves which are mirror images of each other.

→ reflection of two halves of the molecule across the plane give a structure indistinguishable from original.

→ Plane is called σ plane, σ operation, called as identity operation since turns molecule into original.

→ two halves may not be superimposable.

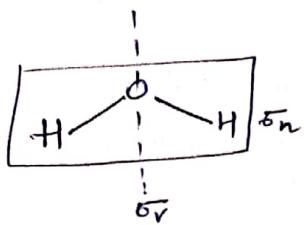
→ σ planes and C_n axes often occur together.

Planes of three types

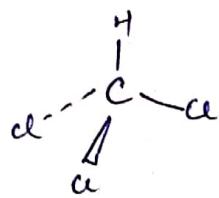
① Horizontal plane \perp to principal axis and is unique (σ_h)

② Vertical plane containing principal axis (σ_v)

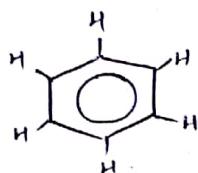
③ Diagonal plane bisecting the angle between two C_n axes. (σ_d)



two mutually \perp planes in H_2O molecule

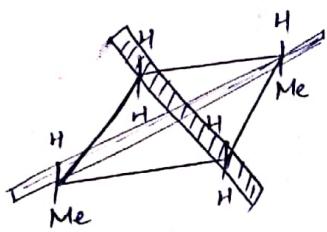


three planes each containing $\text{H}-\text{C}-\text{Cl}$ grouping.



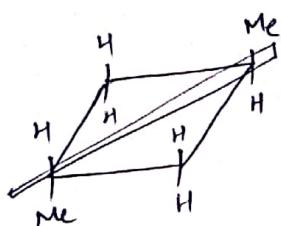
one molecular plane (σ_h)

6 vertical planes (3 along opposite atoms)
3 along opposite bonds)

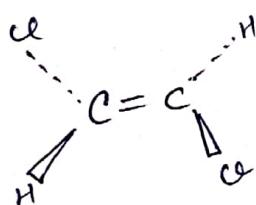


two vertical planes

- ① one along methyl bearing carbons.
- ② along other two carbons.



one vertical plane passing through methyl bearing carbons.



has one coincident with molecular plane. (σ_h)



one plane at center (σ_h)

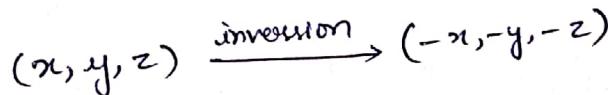
& ∞ plane passing through internuclear axis (σ_∞).

(3) Centre of symmetry OR inversion centre: (i)

a point within a molecule such that if an atom is joined to it and line is extrapolated to an equal distance beyond, it encounters an equivalent atom.

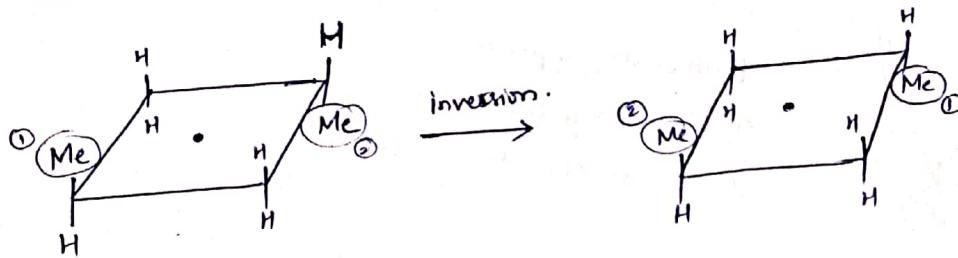
[Or]

inversion of all atoms in a molecule through the point gives an arrangement indistinguishable from the original.

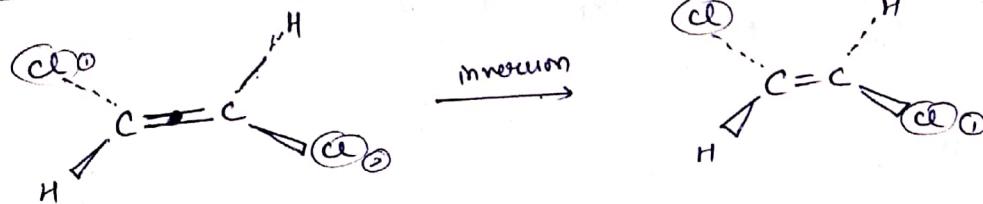


→ only one inversion center in a molecule.

e.g. trans-1,3-dimethylcyclobutane

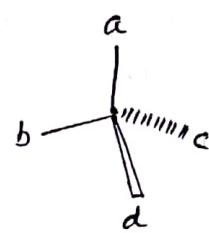


trans-dichloroethylene



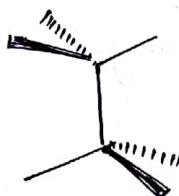
The flying-wedge projection:

- It is most common 3-D representation of a 3-D molecule on a 2-D surface.
- This is commonly done for molecules containing chiral centre/ asymmetric carbon atom.
- ordinary line represent bond in plane of paper (-)
- solid wedge (\rightarrow) represent bond above the plane of paper
- dashed wedge ($\cdots\cdots\cdots$) or broken line (---) represent bond below the plane of paper.



Projection formula

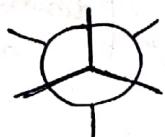
It is useful for compounds with two or more stereogenic/asymmetric centres and Fischer's projection developed 2-dimensional plane projection formula for 3-dimensional molecule.



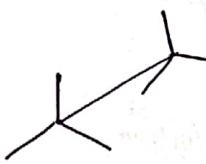
Flying wedge formula



Fischer Projection



Newman projection



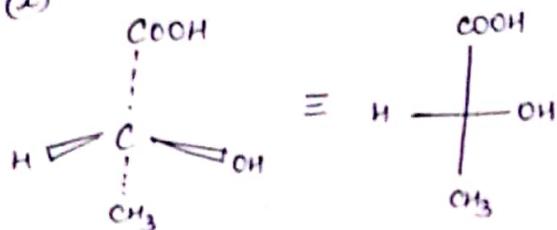
Sanhoeue projection

1. Fischer Projection:

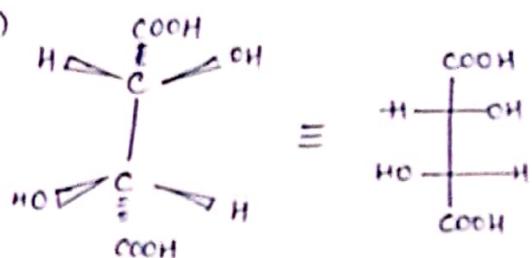
- (i) Hold the molecule in such a way that the central carbon lies in the plane
- (ii) Groups on carbon held at top and bottom must be inclined behind the plane (represented by dotted lines in wedge diagram).
- (iii) Groups on carbon at left and right must be inclined above the plane (represented by thick lines in wedge diagram).
- (iv) Most oxidised carbon be kept at top.

examples

(i)

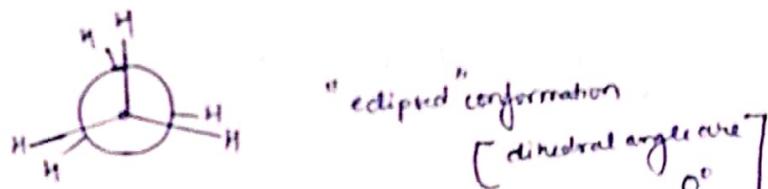
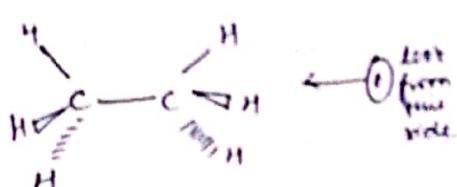
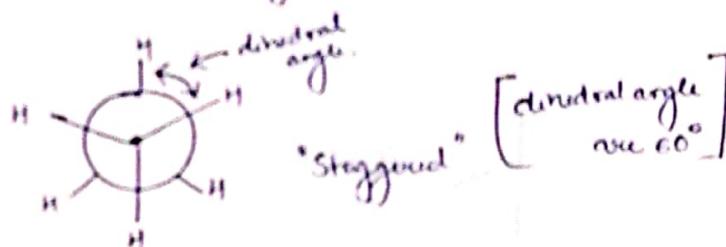
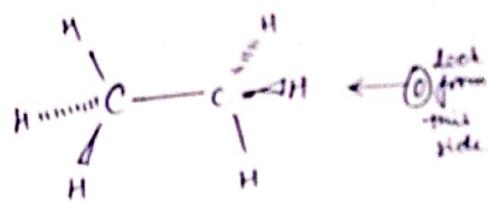


(ii)



2. Newman Projection:

- Obtained by looking at molecule/model exactly along the bond joining two carbon atoms.
- Front atom represented by dot and back carbon atom by circle.



→ Energy of eclipsed conformation is higher than staggered conformation.

→ In eclipsed conformation, another 60° rotation returns molecule to staggered conformation.

If we continue these rotations upto 360°,

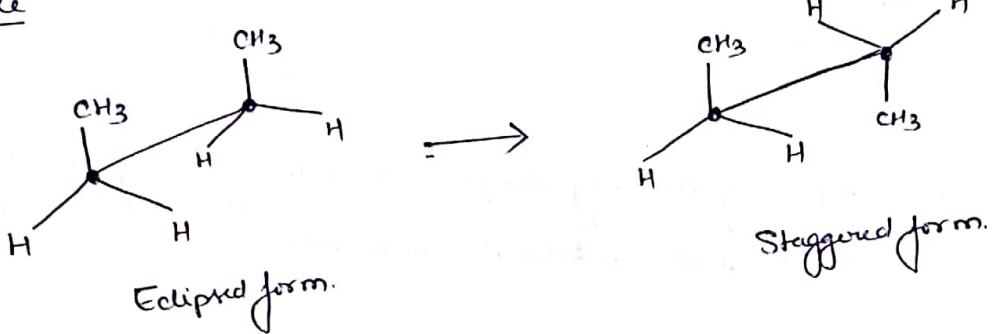
possible in three eclipsed conformations, & three staggered conformations.

also, infinite number of conformations in between two extremes.

(3) Sawhorse projection

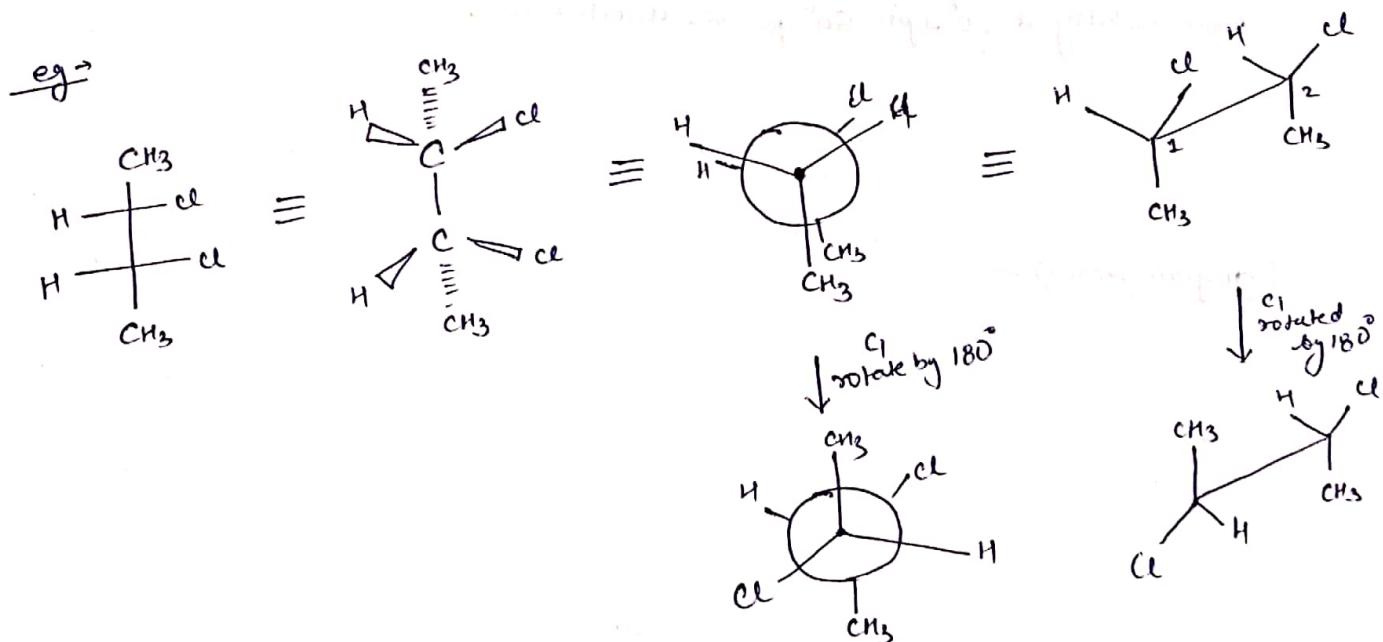
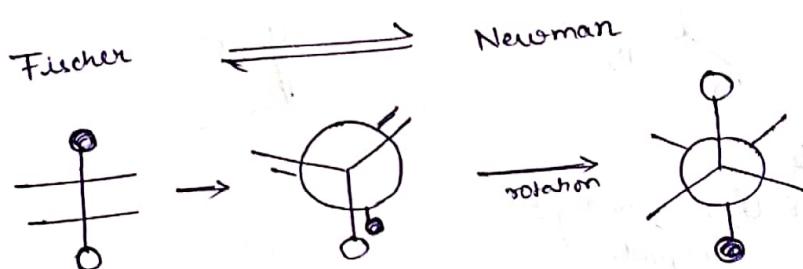
- obtained by looking at the molecule, at a small angle to bond joining the two carbon atoms.
- These bonds at each carbon are drawn in shape "Y" or inverted "Λ".

example



Projection formula interconversion

Note: Fischer projection refers to eclipsed conformation while converting to Newman.



Conformational isomerism:

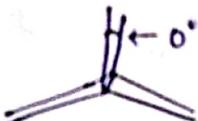
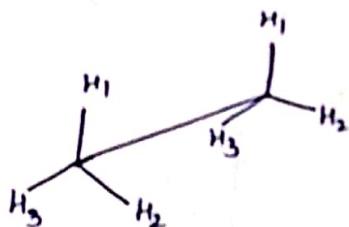
Conformation is one of the infinite number of momentary arrangements that are obtained by rotation of groups at a carbon, reference to a group at adjacent carbon joined through single bond.

Characteristics of conformers:

- (i) conformers are not separable or isolable, because they rapidly interconvert with slight change of temperature.
- (ii) but can be separated by lowering temperature to near freezing point of compound. as lower temperature will stop molecular movements.

Conformations of Ethane, stability and energy diagram:

Consider ethane molecule in sawhorse projection. & observe



at 0° dihedral angle
eclipsed.

now rotating at 60° upto 60° possible structures are,

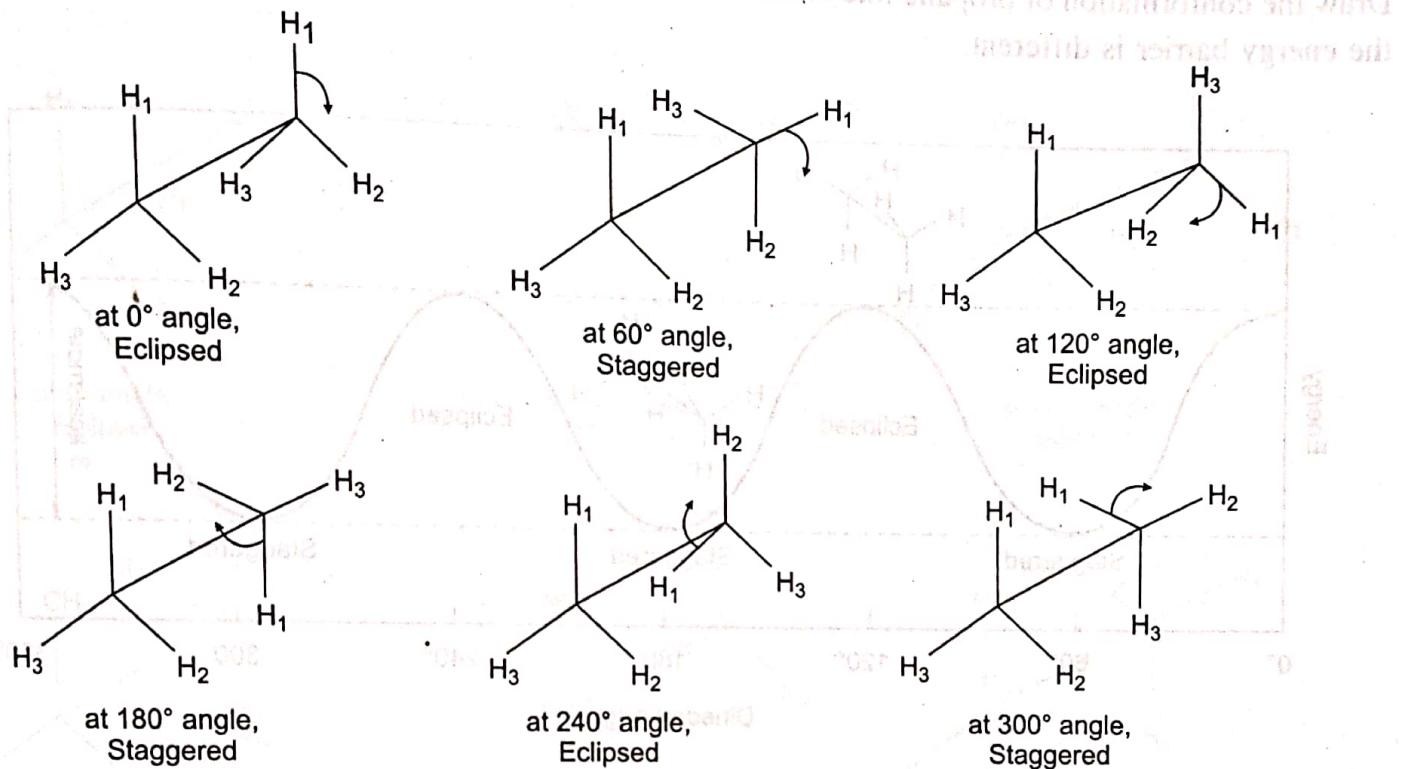


Fig. 7.9 Eclipsed and staggered conformation of ethane at different dihedral angles shown as Sawhorse projections.

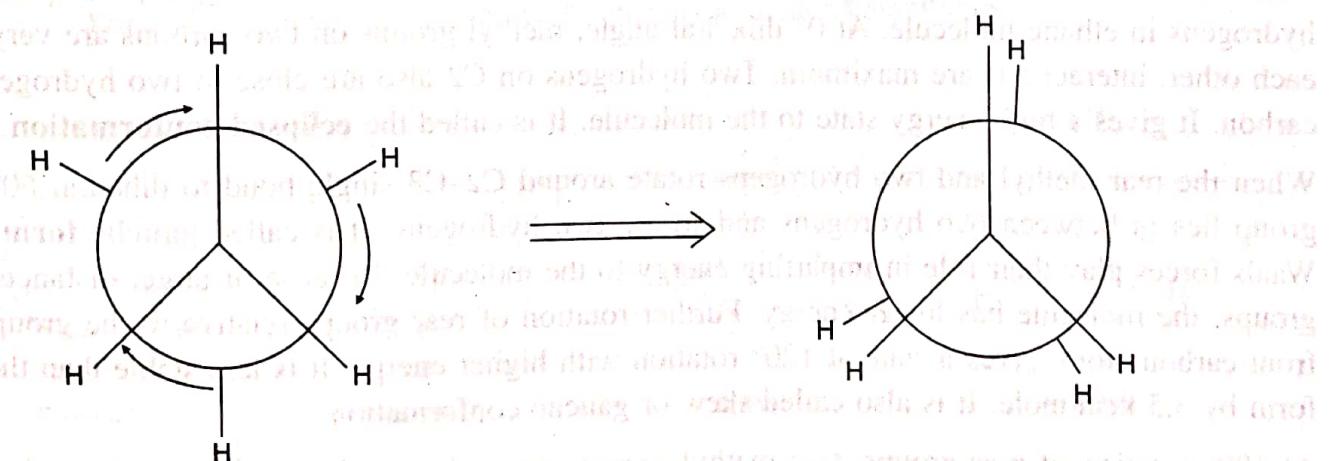


Fig. 7.10 Staggered and Eclipsed Newman's Projections of ethane.

there are only two different positions others are identical. The two differentiated conformations are called "eclipsed" at dihedral angles of 0° , 120° , 240° , and "staggered" at dihedral angles of 60° , 180° , 360° .

Let us now, examine energy diagram and analyse stability of all structures of ethane,
at 0° dihedral angle : front H atoms & rear H atoms, distance between them is smallest
(eclipsed) thus repulsive forces are maximum.
Same will be possible at 120° & 240° angle.

at 60° , 180° & 360° : distance b/w front and rear hydrogens is maximum. They
(staggered) have least interaction, consequently energy of molecule is minimum.

So band on this energy curve is as shown:

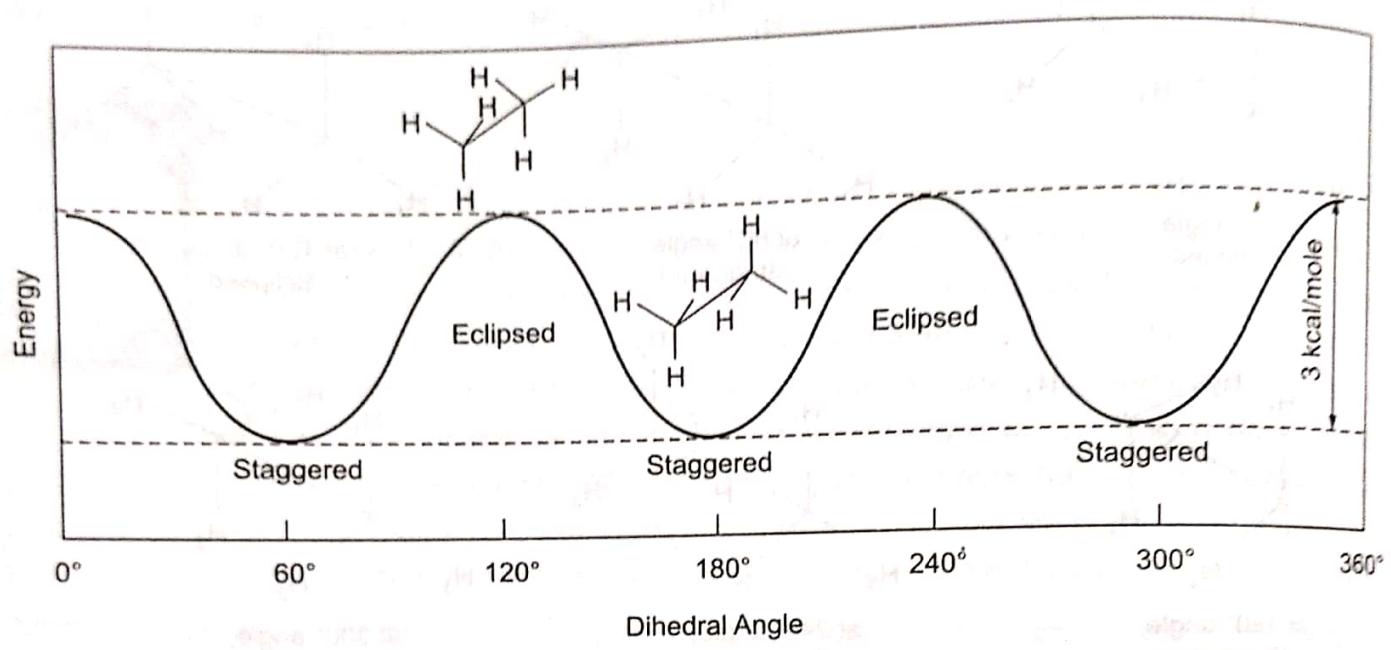


Fig. 7.11 Energy diagram of ethane conformations.

Conformation of Butane: ($\text{CH}_3 - \overset{1}{\text{CH}_2} - \overset{2}{\text{CH}_2} - \overset{3}{\text{CH}_2} - \overset{4}{\text{CH}_3}$)

- It has two methyl groups in place of two H-atoms in ethane molecule.
- At 0° dihedral angle, methyl groups on two carbons are very close to each other, interactions are maximum. Also αH on C_2 are close to αH on C_3 . So very high energy state. It is eclipsed conformation.
- Rear methyl and $\alpha\text{-H}$ rotates around C_2 & C_3 single bond to dihedral angle 60° , methyl group lies in b/w two H-atoms & no are αH atoms. It is called gauche form. Van der Waals forces play their role and imparts energy to molecule. Overall distance b/w groups is large, molecule has lower energy.
- Further rotation of rear groups relative to groups on front carbon, gives state at 120° rotation with higher energy. It is less stable than the gauche form by 3.5 Kcal/mole. It is called skew or gauche conformation.
- At 180° rotation of rear groups, two methyl groups are at maximum distance possible between them. It is called "staggered conformation". It is most stable state of butane. Thus there are 4 conformers in butane. And energy barrier of eclipsed & staggered forms is 4.5 to 6.1 Kcal/mole.

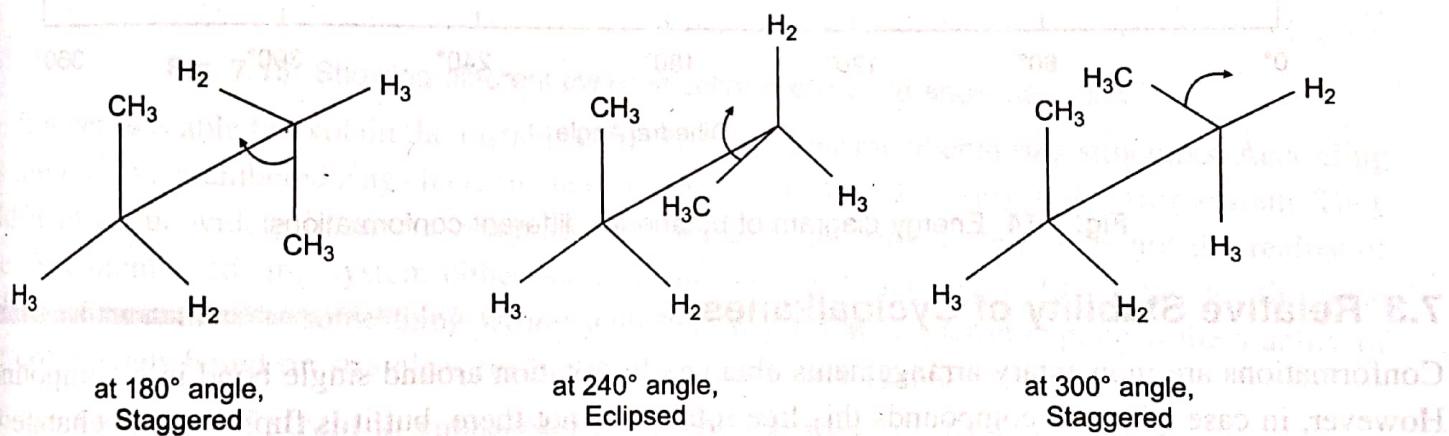
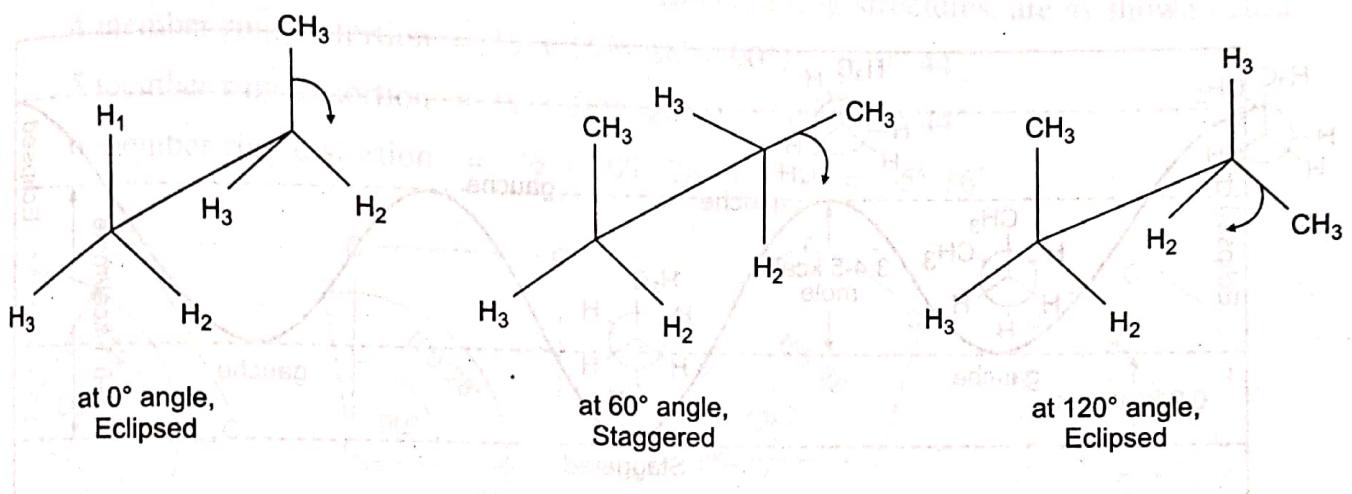


Fig 7.12 Conformations obtained by rotation through different angles.

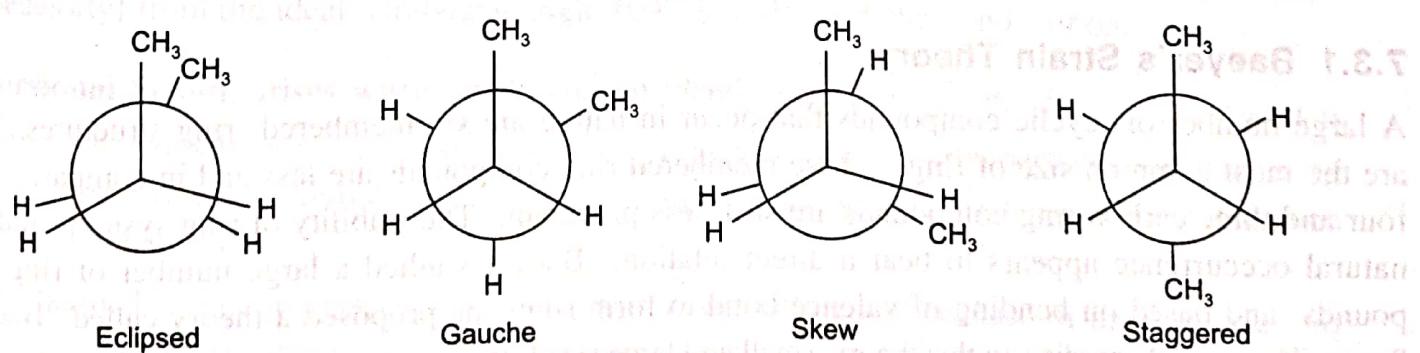


Fig 7.13 Different Conformations of butane.

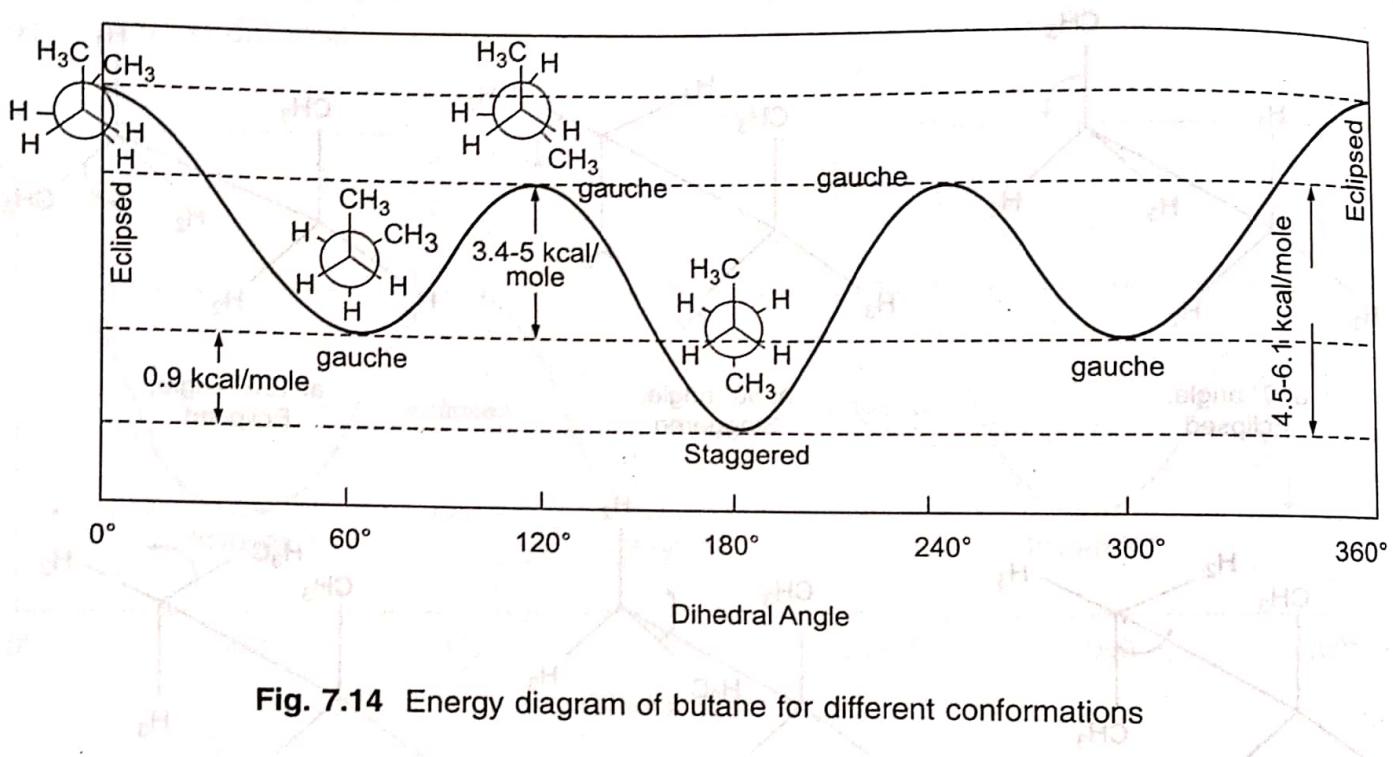


Fig. 7.14 Energy diagram of butane for different conformations

Conformers of cycloalkanes:

In case of cyclic compounds free rotation is not there, but it is flip over and change of orientation of groups that takes place. There are different theories to describe stability of cyclic compounds.

(i) Baeyer's strain theory:

- large number of cyclic compounds that occur in nature is 6-membered ring structures. It is that common size of rings.
- Five numbered ring compounds are less, and in comparison 4- and 3- carbon ring compounds are still less prevalent.
- So, stability of ring system and natural occurrence appears to bear direct relation.
- Baeyer studied large number of ring compounds and based on bending of valence bond to form rings, he proposed theory called "Baeyer's strain theory".

According to this theory:

- large and small sized rings compounds are not stable because they involve lot of angle strain or tension in C-C bonds of rings.
- The calculated tension of different sized ring compounds from distortion in bond angle from normal value of $109^\circ 28'$.

For example, In cyclopropane, the $\text{C}-\text{C}$ bond angle (triangle) is 60° . That is each bond has to come closer from normal angle to form 60° angle between two bonds. Hence distortion is

$$= \frac{1}{2} (109^\circ 28' - 60^\circ) = 24^\circ 44'$$

Similarly, for

$$4 \text{ numbered rings distortion} = \frac{1}{2} (109^\circ 28' - 90^\circ) = 9^\circ 44'$$

$$5 \text{ numbered rings distortion} = \frac{1}{2} (109^\circ 28' - 108^\circ) = 0^\circ 44'.$$

$$6 \text{ numbered rings distortion} = \frac{1}{2} (109^\circ 28' - 120^\circ) = -5^\circ 16'$$

As per this theory, 5-numbered should be most stable, but in nature more are 6-membered ring, so something wrong in this theory.

There are two kinds of strains in cyclic compounds:

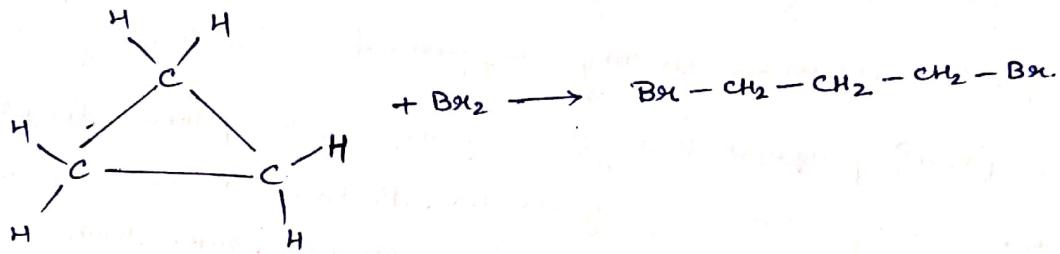
1. Ring strain

- (i) Bond angle strain: arises when the C-C-C bonds of ring depart from ideal tetrahedral angle of $109^{\circ}28'$.
- (ii) Torsional strain: arises when bonds are not ideally staggered. In most rings system, it is impossible to perfectly stagger all bonds. In cyclohexane, fortunately, perfect bond staggering occurs in chair conformation, but no conformation in any other ring allows for such perfect staggering.

2. Steric strain.

It is due to approach of atoms nearer to each other and because of their volume and repulsive force, steric strain become operative.

→ Strain (Ring) in cyclopropane.



It is the smallest cycloalkane & most reactive among ring compounds.

Instead of undergoing substitution reaction, it undergo addition type reaction with halogens. Its cyclic structure come from three points on plane, so is most strained ring. The ring strain has been estimated, from heat of combustion, to be 28 Kcal/mol. It thus weakens the C-C bond.

Other strain is angle strain (49.5°), there is angle change from 109.5° to 60°

It is best explained on the basis of overlap of atomic orbitals. There is very little overlap, so bonds are bent and weak.

Also, these bonds are not pure sigma bonds, there is partial pi bond character.

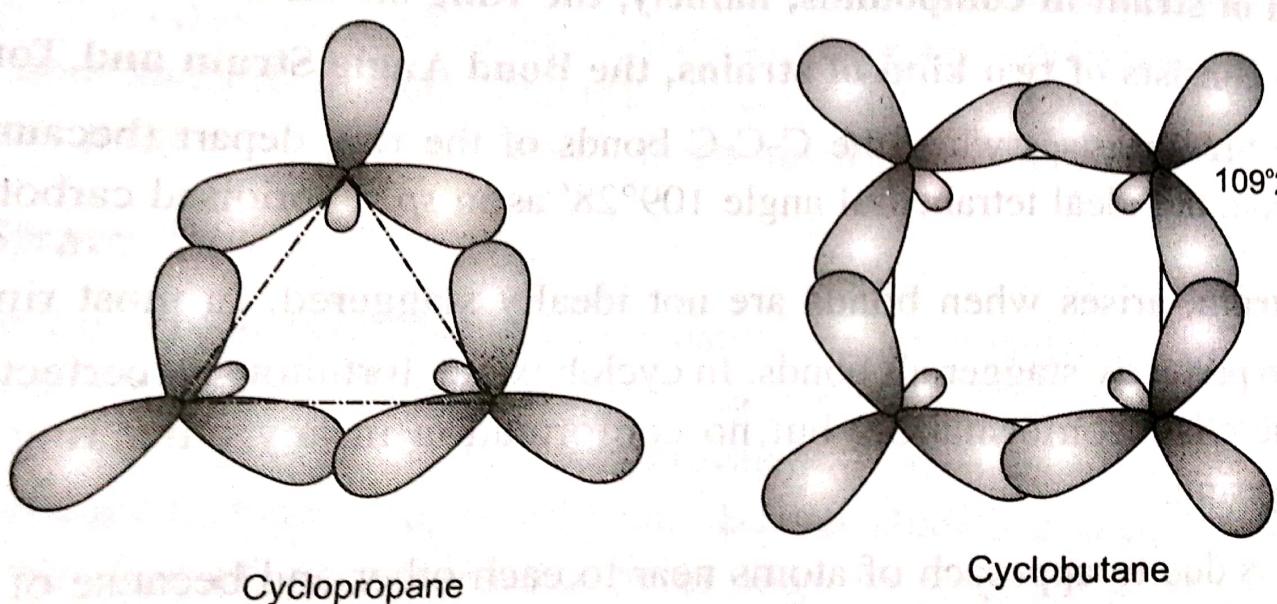


Fig.7.16 Cyclic structures formed by overlap of orbitals.

Ring strain in cyclobutane:

- Stability is slight more than cyclopropane.
- Ring strain per - CH₂ - of cyclobutane has been estimated to be 26 Kcal/mole.
- Four point in a plane form cyclobutane, that is planar structure, involves angle strain of (29.5°). It weakens C-C bond, but less than of cyclopropane.
- It can be explained on basis of A.O overlap. Overlap is not linear but angular. Thus cyclobutane also not have pure sigma bond, but partial π-bond.
- It goes addition reaction, but at higher temperature.
- It undergo substitution reactions also, that are carried out at -78°C via carbocation generation.

Sachse Explanation of stability of cyclic compounds (strainless rings)

- Baeyer had considered all rings are planar & ended with wrong conclusion.
- Sachse (1890) proposed that cyclic compounds are not planar. He proposed puckered rings structures of cyclohexane. Puckered means non planar & the C-C bond angles remain at 109°28'. It makes ring strainless & it offers stability to the cyclic compounds.

Conformations of Cyclohexane & their stability →

- Sachse proposed puckered structure for cyclohexane, so it acquires a completely strainless structure.
- Two forms known for cyclohexane structure are chair form & boat form. Shown using different models as shown.

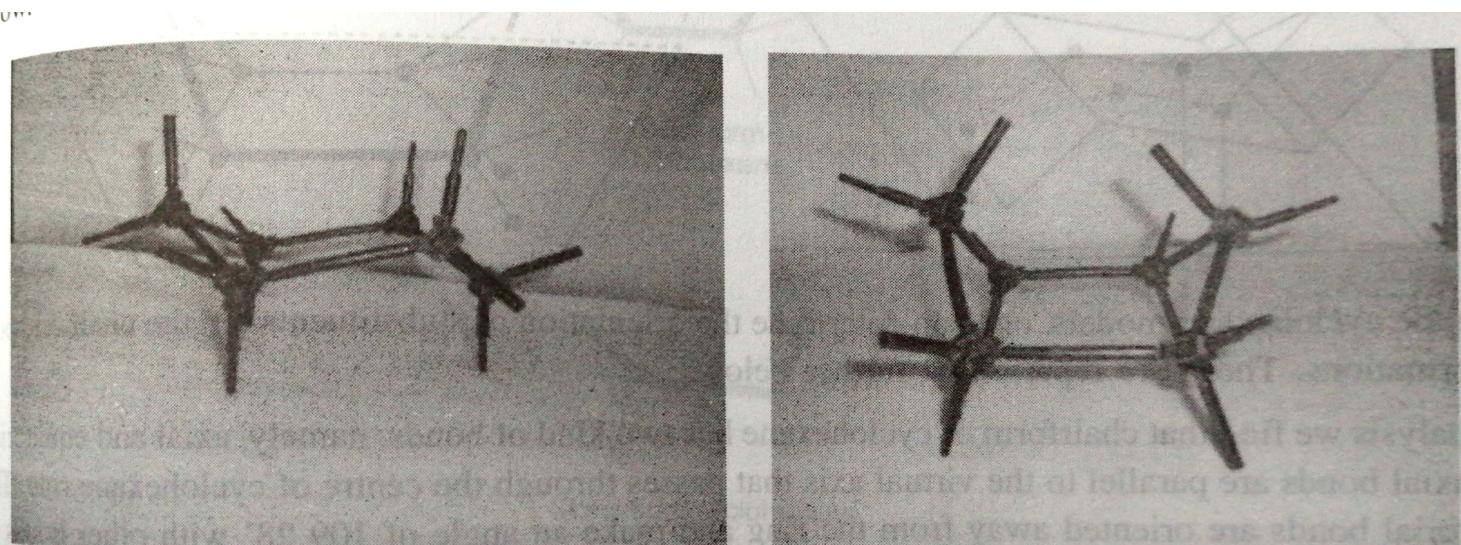


Fig. 7.17 Models of chair and boat forms of cyclohexane using flexible models.

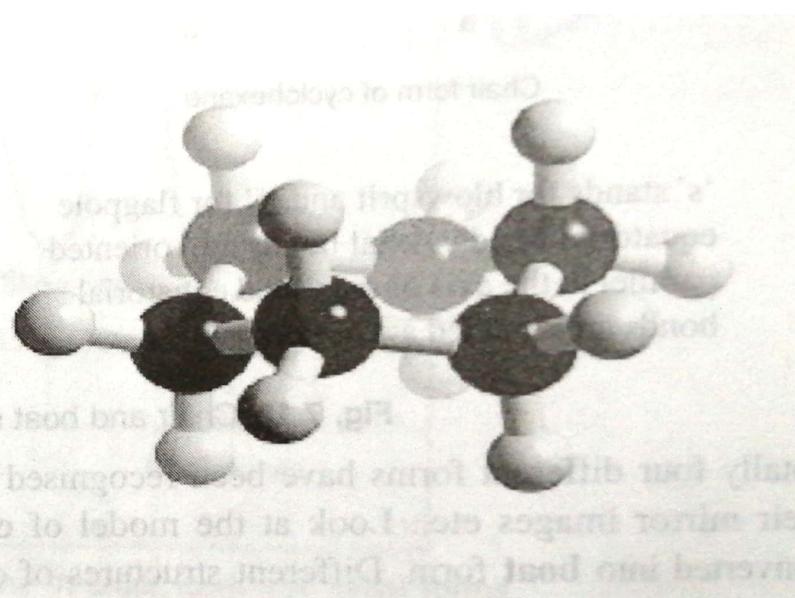
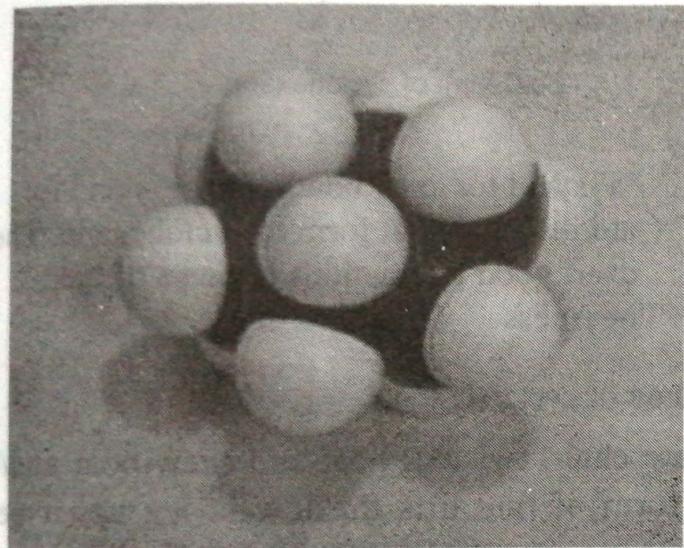


Fig. 7.18 Space filling and ball and stick model.

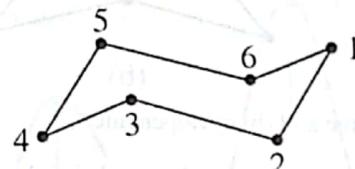
3.7.1 Conformations of Cyclohexane

Cyclohexane is as stable as its open chain counterpart hexane. Cyclohexane exists as a puckered or non-planar ring. The twisting about carbon–carbon bond results in the formation of different conformations of cyclohexane. The four main conformations of cyclohexane are:

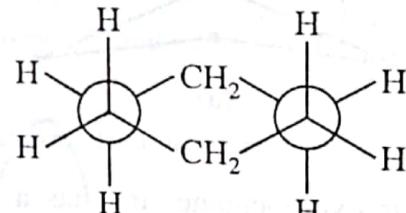
- (a) Chair conformation
- (b) Boat conformation
- (c) Twist boat conformation
- (d) Half chair conformation

Chair conformation

This is the most stable conformation of cyclohexane as it is free from torsional strain. All the twelve hydrogens are in staggered state as evident from Newman projection. The bond angle is nearly 109.5° and thus, it is free from angle strain also.



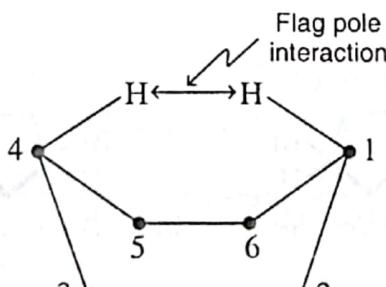
Chair conformation



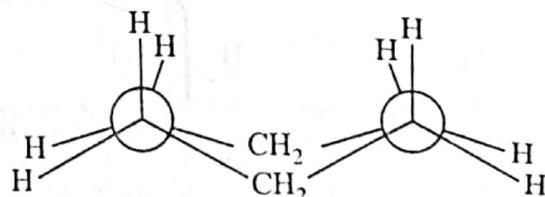
Newman projection of chair conformation

Boat conformation

Twisting about carbon–carbon single bond of the chair form results in the formation of boat conformation. Boat conformer is free from angle strain. However, in boat conformation the hydrogens are in eclipsed state, which causes torsional strain in the molecule. Along with this the *flagpole interaction*. The torsional strain and flagpole interaction make boat conformation less stable compared to chair conformation.



Boat conformation



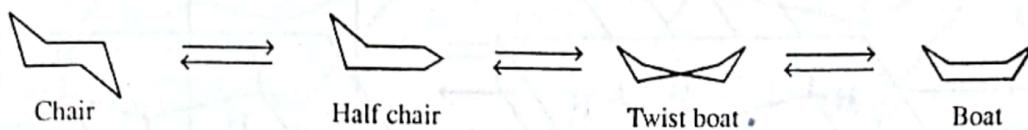
Newman projection of boat conformation

Twist boat conformation

The boat conformation is flexible and a slight twist about the bond reduces the torsional as well as flagpole interactions which makes the twist boat conformation a little more stable than the boat conformation.

Half chair conformation

This is the least stable conformation of cyclohexane because carbon atoms at one end of the ring are planar.



Interconversion of different conformations of cyclohexane

The stability order of different conformations of cyclohexane is:

Chair conformation >> twist boat conformation > boat conformation > half chair conformation

The conformational analysis of cyclohexane is given in Fig. 3.16 that follows.

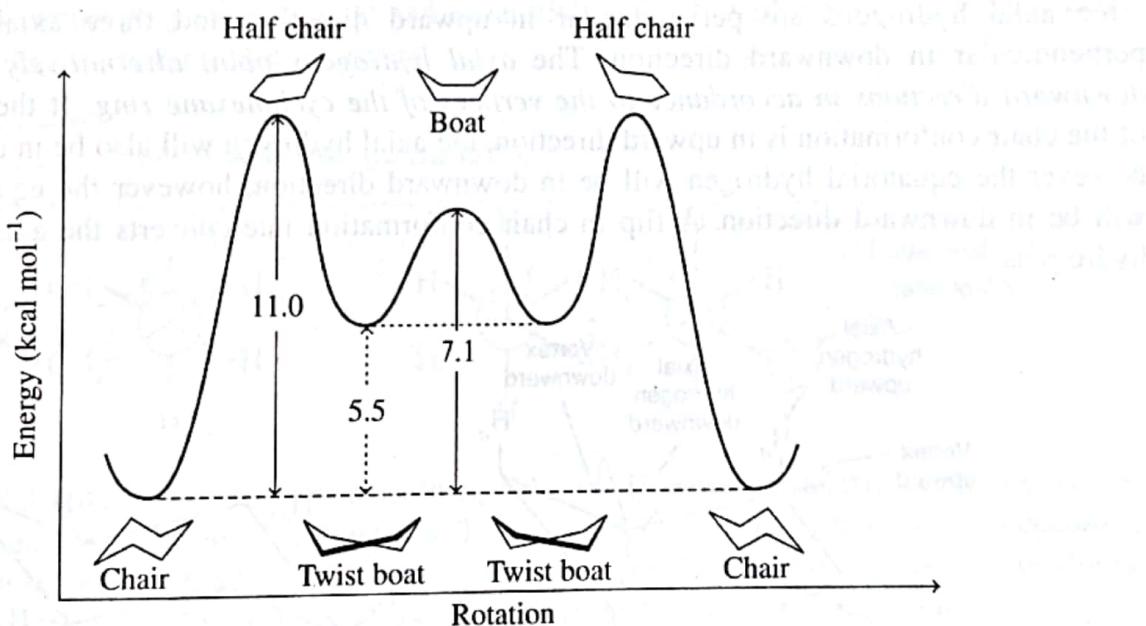
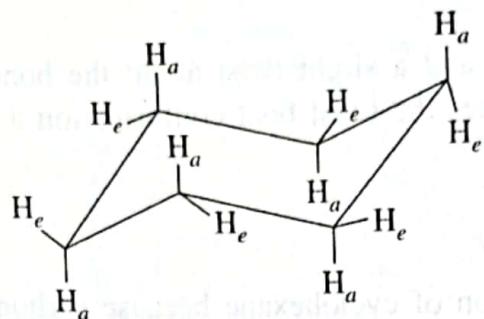


Fig. 3.16 Conformational analysis of cyclohexane.

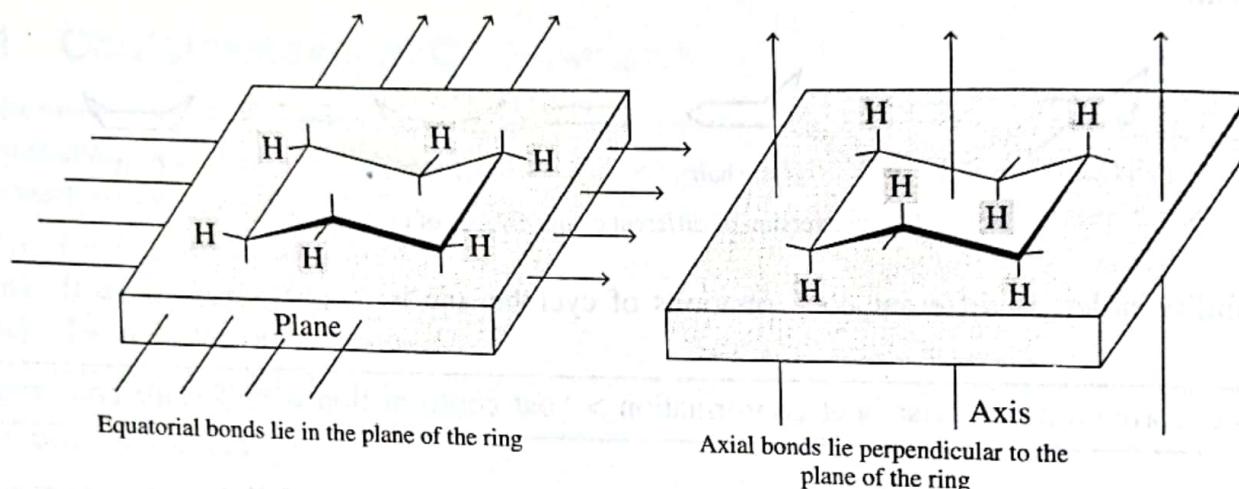
Axial and equatorial hydrogens in chair conformation

In the chair conformation of cyclohexane, all the twelve hydrogens are not equivalent. The chair conformation has two types of hydrogens, axial (*a*) and equatorial (*e*).

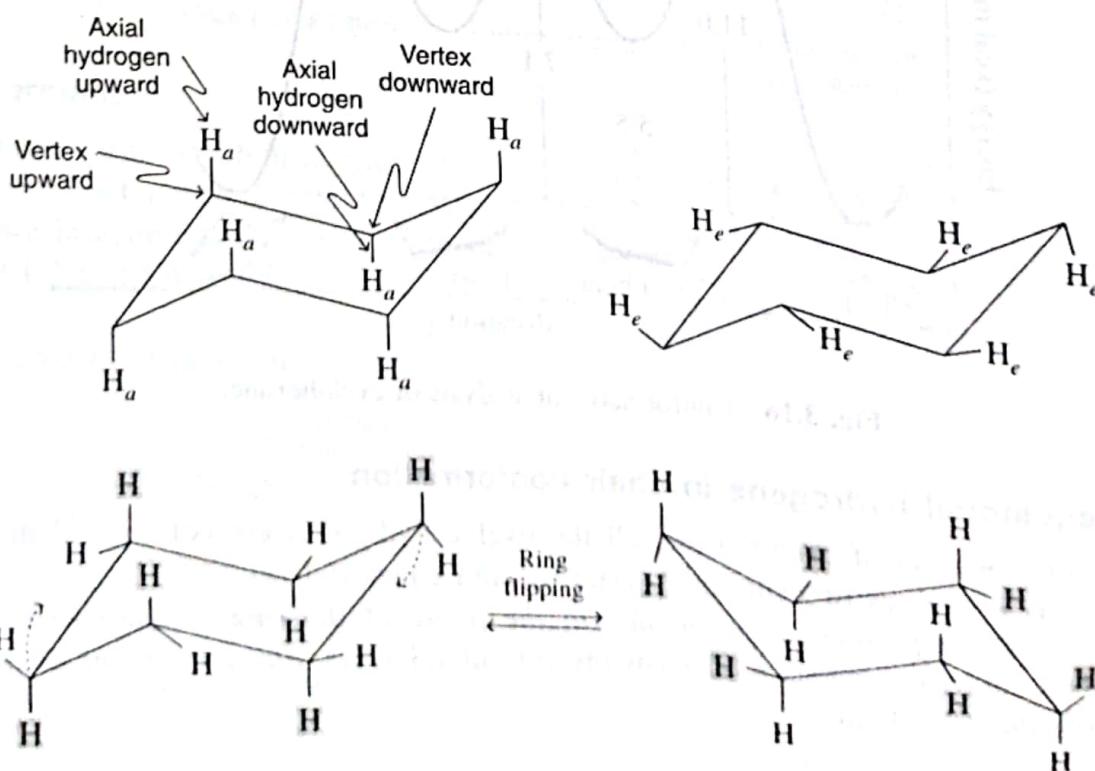
Six hydrogens are present *perpendicular to the plane* of the ring and are termed as *axial* hydrogens while the remaining six hydrogens project out sideways, *along the plane* of the ring and are termed as *equatorial* hydrogens.



H_a = axial hydrogen
 H_e = equatorial hydrogen

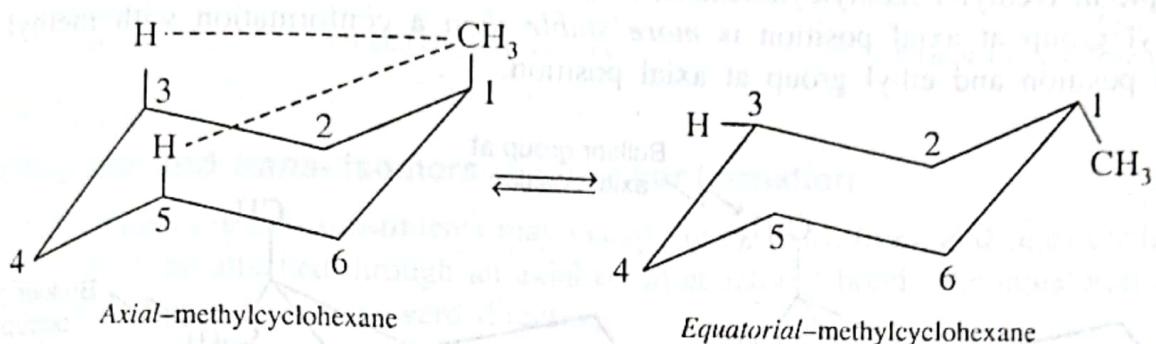


Each carbon has one axial and one equatorial hydrogen which point in opposite directions. The three axial hydrogens are perpendicular in upward direction and three axial hydrogens are perpendicular in downward direction. The *axial hydrogens point alternatively in upward and downward directions in accordance to the vertices of the cyclohexane ring*. If the carbon (vertex) of the chair conformation is in upward direction, the axial hydrogen will also be in upward direction, however the equatorial hydrogen will be in downward direction, however the equatorial hydrogen will be in downward direction. A flip in chair conformation interconverts the axial and equatorial hydrogens.

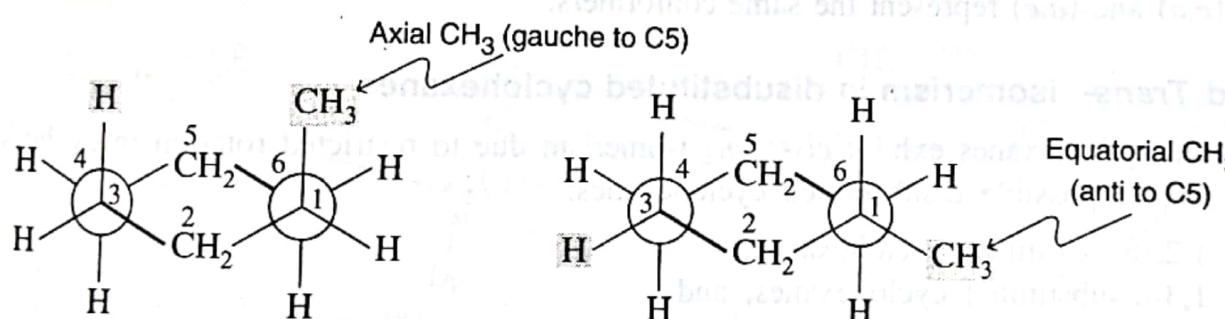


3.7.2 Conformations of Monosubstituted Cyclohexane

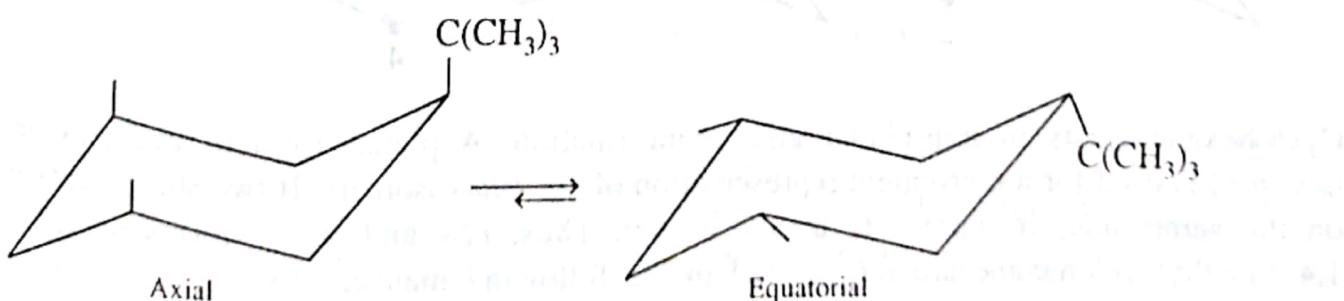
In the replacement of hydrogen of a cyclohexane ring by a substituent, the substituent can occupy either an axial or an equatorial position. For example, methylcyclohexane can be represented by following two chair conformations:



If methyl group occupies an axial position, it is close to axial hydrogens at C3 and C5 (as C5 and C3 are equidistant from C1, these positions are also referred to as 3 and 3'). The van der Waals repulsion occurs due to steric crowding of methyl group and two hydrogens. This causes transannular strain. The *transannular strain* is the strain produced in a ring due to steric repulsions. This effect occurs due to axial substituents and is known as *1,3-diaxial interaction*. A substituent at equatorial position does not experience any such repulsion as equatorial bonds project out sideways. The Newman projection of axial and equatorial conformers of methylcyclohexane clearly depicts the stability of equatorial conformers.



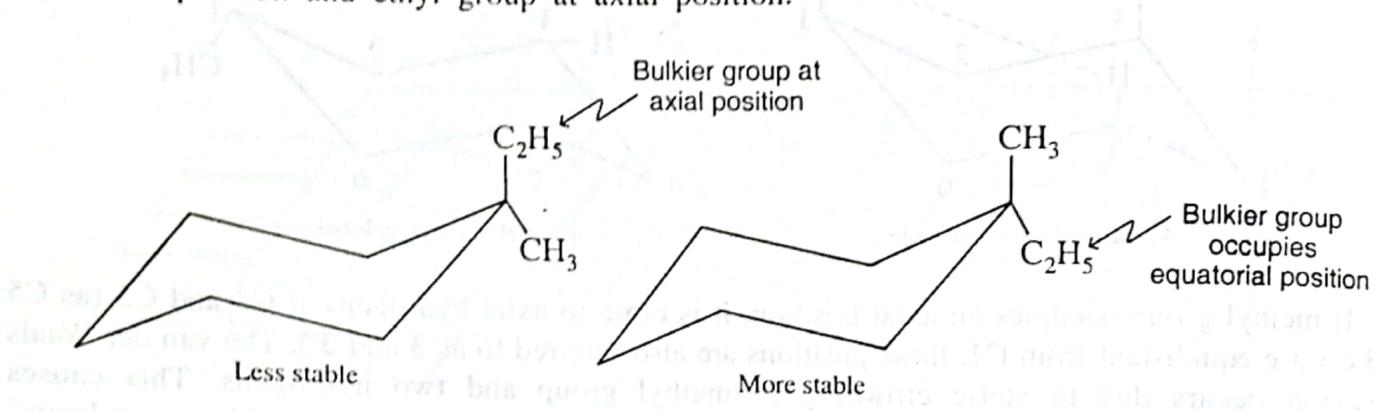
The equatorial and axial conformers exist in equilibrium. However, equatorial conformer is more stable due to absence of 1,3-diaxial interactions. Thus, a substituent prefers to occupy an equatorial position. With an increase in the bulkier substituent (bigger group), the ratio of equatorial conformer increases considerably and a very little of axial conformer is present at equilibrium.



3.7.3 Conformations of Disubstituted Cyclohexane

Two substituents present on same carbon

The substituent present in a cyclohexane ring prefers to occupy an equatorial position. In case two different substituents are present on same carbon, a bulkier substituent occupies equatorial position. For example in 1-ethyl-1-methylcyclohexane, a conformation with ethyl group at equatorial position and methyl group at axial position is *more stable* than a conformation with methyl group at equatorial position and ethyl group at axial position.



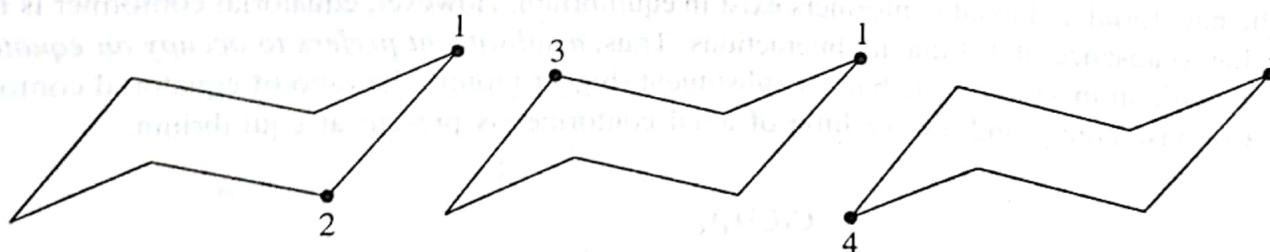
Two substituents present on different carbons

However, if two substituents are present at two different carbons then depending upon the position occupied by each substituent, the different conformers are designated as: equatorial-equatorial(e,e); equatorial–axial(e,a); axial–equatorial(a,e); and axial–axial(a,a). If two similar substituents are present, (e,a) and (a,e) represent the same conformers.

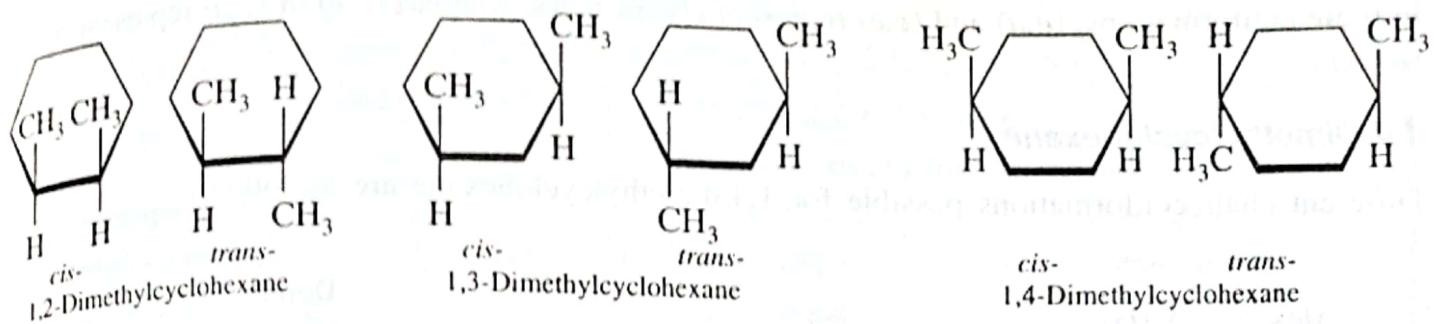
Cis- and Trans- isomerism in disubstituted cyclohexanes

Disubstituted cyclohexanes exhibit *cis-trans* isomerism due to restricted rotation in cyclic system. There are three possible disubstituted cyclohexanes:

- 1,2-disubstituted cyclohexanes,
- 1,3-disubstituted cyclohexanes, and
- 1,4-disubstituted cyclohexanes.



Cyclohexane exists in non-planar chair conformation. A planar form of cyclohexane (that is, hexagon) is used for a convenient representation of *cis-trans* isomers. If two substituents are present on the same side, it represents a *cis*- isomer. Thus, *cis*- and *trans*- forms of 1,2-, 1,3- and 1,4-dimethylcyclohexane are represented in the following manner:



Representing *cis*- and *trans*- isomers in chair conformation

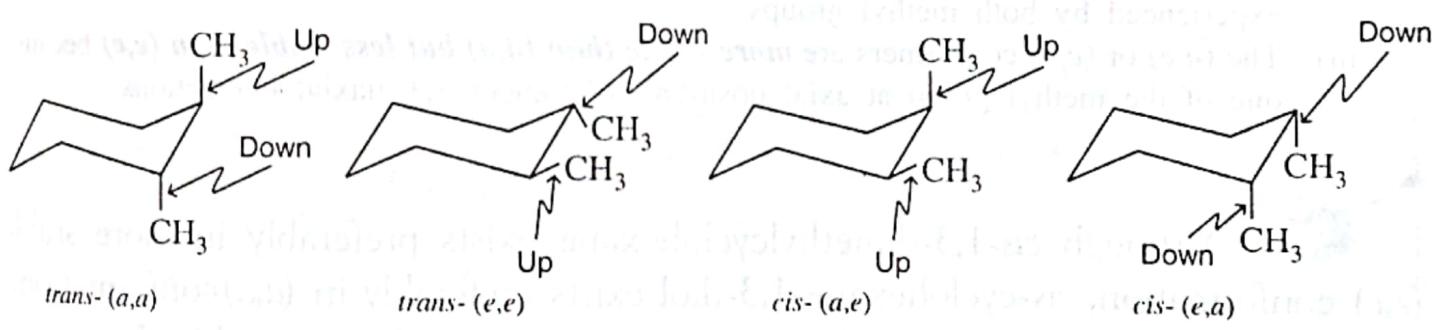
In chair conformations, the two substituents may occupy (*e,e*), (*e,a*), (*a,e*), and (*a,a*) conformation. The substituents may be attached through an axial or an equatorial bond. The equatorial and axial bonds may point in upward or downward direction.

- If both the bonds, through which substituents are attached, point in *same direction*, that is, both upward or both downward, the conformation represents a *cis*- isomer.
- If both the bonds, through which substituents are attached, point in *opposite directions*, that is, one upward and one downward, the conformation represents a *trans*- isomer.

The *cis-trans* isomerism and the stability of conformers in disubstituted cyclohexanes is explained by considering the examples of 1,2-, 1,3- and 1,4-dimethylcyclohexane as follows:

1,2-Dimethylcyclohexane

Different chair conformations possible for 1,2-dimethylcyclohexane are:

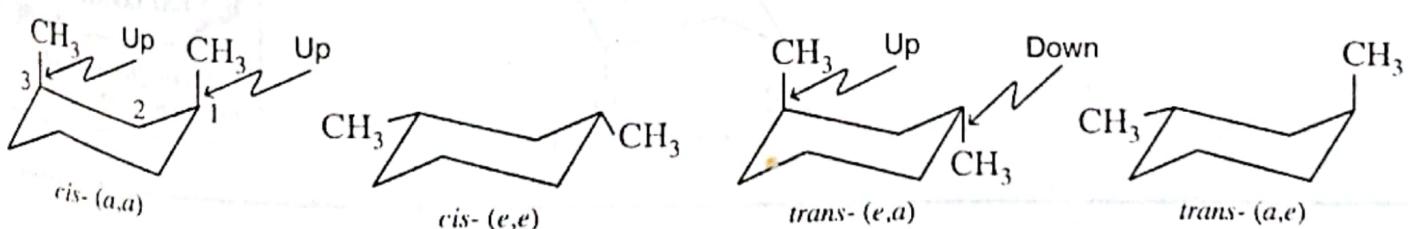


Key: up-down = *trans*-; up-up/down-down = *cis*-

In the above conformations, (*a,a*) and (*e,e*) represent *trans*- isomers, whereas (*a,e*) or (*e,a*) represent *cis*- isomers.

1,3-Dimethylcyclohexane

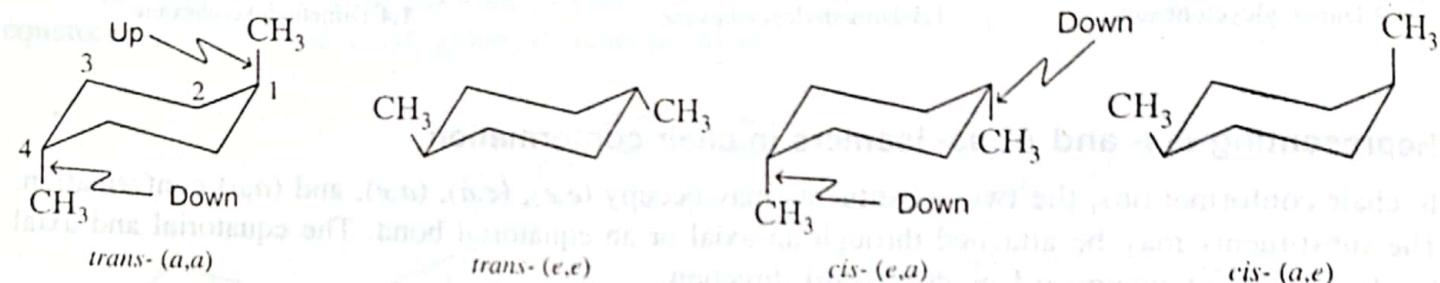
Different chair conformations possible for 1,3-dimethylcyclohexane are:



In these conformations, (a,a) and (e,e) represent *cis*- isomers, whereas (a,e) or (e,a) represent *trans*- isomers.

1,4-Dimethylcyclohexane

Different chair conformations possible for 1,4-dimethylcyclohexane are as follows:



In the conformations above, (a,a) and (e,e) represent *trans*-isomer whereas (a,e) or (e,a) represent *cis*-isomers.

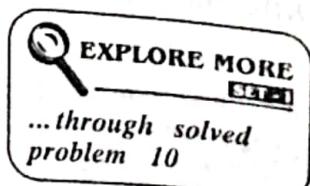
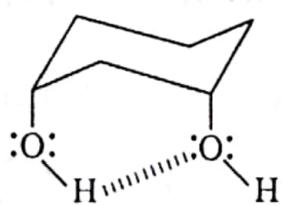
Stability of conformers in dimethylcyclohexanes

In 1,2-, 1,3- and 1,4-dimethylcyclohexane, the stability of conformers is decided on the basis of the following:

- The (e,e) conformer is the *most stable* and the most preferred conformation because of the absence of 1,3-diaxial interactions.
- The (a,a) conformer is the *least stable* because of 1,3-diaxial interactions that are experienced by both methyl groups.
- The (a,e) or (e,a) conformers are *more stable than (a,a) but less stable than (e,e)* because one of the methyl group at axial position experiences 1,3-diaxial interactions.



Although *cis*-1,3-dimethylcyclohexane exists preferably in more stable (e,e) conformation, *cis*-cyclohexane-1,3-diol exists preferably in (a,a) conformation. As already explained, in general, (e,e) conformations are more stable. In case of the strong intramolecular hydrogen bonding present in the molecule which is strong enough to overcome the 1,3-diaxial interactions. Hydrogen bonding is not possible in case of (e,e) conformation.



AT A GLANCE

THE CONFORMATIONS OF SUBSTITUTED CYCLOHEXANES

MONOSUBSTITUTED CYCLOHEXANE

Compound

Methylcyclohexane

Tert-butylcyclohexane

A substituent (**s**) prefers to occupy an equatorial position

Position occupied by substituent

Axial (*a*)

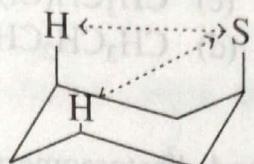
Less stable

Less stable

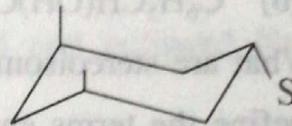
Equatorial (*e*)

More stable

More stable



1,3-diaxial interactions
(repulsive interactions)



Less repulsive interaction
at equatorial position

DISUBSTITUTED CYCLOHEXANE

Position occupied by two substituents

- If both substituents are upward or downward, call it **cis**- isomer.
- If one substituent is upward and other downward, call it **trans**- isomer.

(*a,a*)

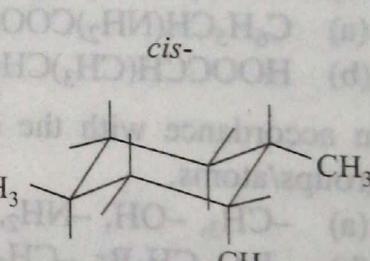
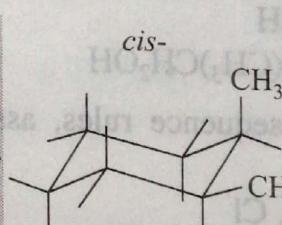
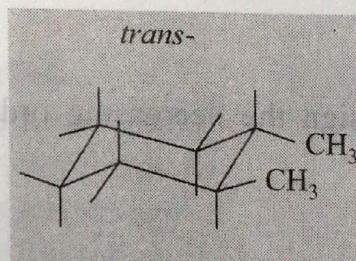
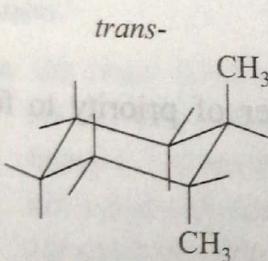
(*e,e*)

(Most stable)

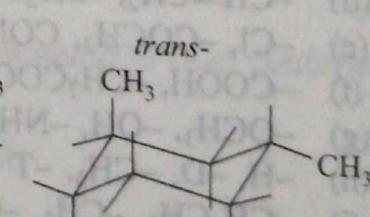
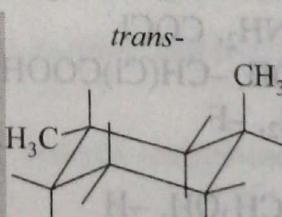
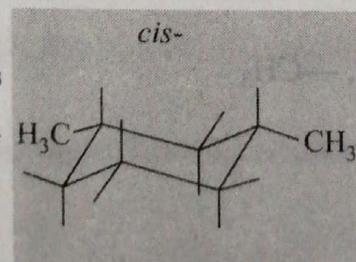
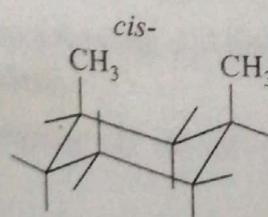
(*a,e*)

(*e,a*)

1,2-Dimethylcyclohexane



1,3-Dimethylcyclohexane



1,4-Dimethylcyclohexane

