STEREOCHEMISTRY

Compounds with the same molecular formula and of identical constitution but differing only in the spatial arrangement of the constituent atoms/ groups are called stereoisomers and the phenomenon of their existence is known as stereoisomerism. The study of the structure and chemistry of stereoisomers is known as stereochemistry.

Stereoisomerism may be subdivided under two heads:

1) Configurational isomerism and

2) Conformational isomerism.

Configurational isomerism:

The stereoisomers that convert with difficulty under normal conditions and thus can be isolated are known as configurational isomers. This type of isomerism exists either due to the introduction of rigidity in a molecule (Geometrical isomers) or due to the right- or left-handed arrangement of atoms or groups around carbon atom (Optical isomers).

Conformational isomerism:

Stereoisomers which interconvert easily at room temperature through rotation about single bonds are known as conformational isomers.

Representation of organic molecules in 2D and 3D:

In the study of stereochemistry, drawing a three-dimensional molecule in a two-dimensional plane like that of a paper is often required. A two-dimensional representation of the three-dimensional structure of a molecule is defined as a projection formula.

Fischer projection formula:

It is a simplified two-dimensional (2D) structure of three-dimensional(3D) structure on the plane of a paper introduced by E. Fischer in 1891.

In Fischer projection formula, all the bonds are drawn as solid lines which are either horizontal or vertical. The horizontal bonds point towards the viewer

while the vertical bonds points away from the viewer. The central tetrahedral carbon atom (usually not drawn) lies at the point of intersection of the two lines.
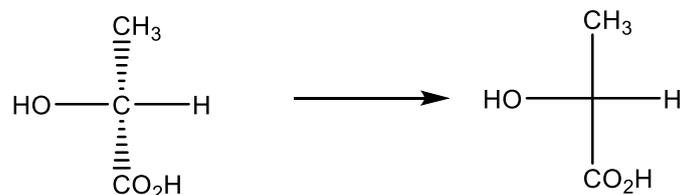

Figure: Fischer projection of lactic acid

Newman projection formula:

Newman projection formula is used in the study of conformation i.e. the spatial relationship of the bonds attached to adjacent carbon atoms. In this projection, the molecule is viewed along the carbon- carbon bond. The carbon atom closure to the viewer i.e. at the front, is represented by a dot while the distant one or the one at the rear side represented by drawing a circle. The other bonds attached to the two carbon atoms are shown as lines joined to the dot or circle.
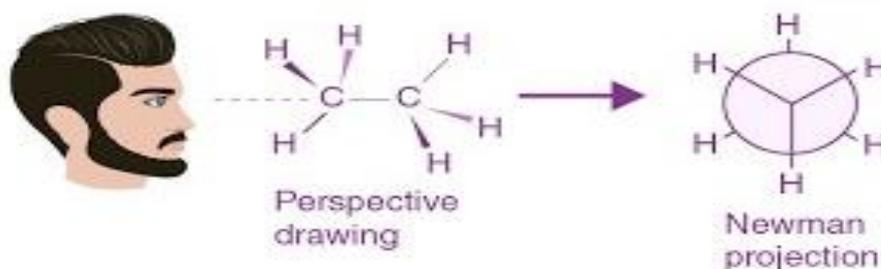
Sawhorse projection formula:

In the sawhorse projection, the molecule is viewed from an angle. So, the C-C bond is drawn backward obliquely. In this drawing, the left-hand carbon is nearer to and the right-hand carbon is farther from the viewer.

In this method, the eclipsed groups are drawn parallel to each other on the same side of the oblique line; the staggered groups are also drawn parallel to each other, but on the opposite sides of the oblique line. An eclipsed form gets converted into the staggered form when a C atom is rotated by 180^0 angle around C-C bond.
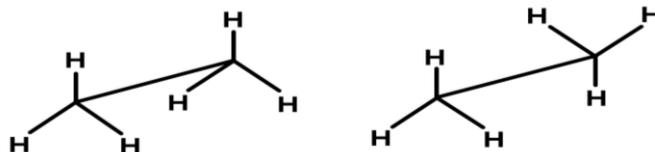
Figure: Sawhorse projection of ethane.
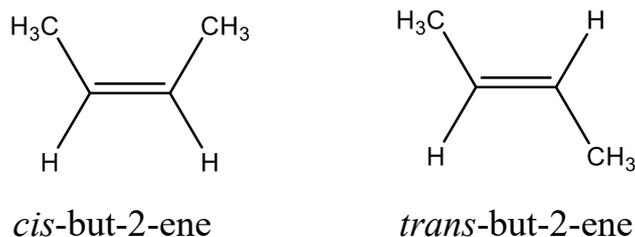
GEOMETRICAL ISOMERISM:

A C=C bond consists of a sigma and a pi bond. A pi bond prevents the free rotation of the carbon atoms of the double bond. Due to this restricted rotation, the relative positions of atoms or groups attached to the carbon atoms of the double bond get fixed in space. This results in the phenomenon of geometrical isomerism.

Geometrical isomerism arises when the molecule contains a double bond and two atoms or groups attached to each of the double bonded carbon atoms are different. Molecules of the type abC=Cab, abC=Cae, abC=Cde etc. exhibit geometrical isomerism.

Cis-trans notation:

The isomer which has similar groups on the same side of the double bond is called cis isomer and the isomer in which similar groups on the opposite side of the double bond is called trans.

Some examples of geometrical isomers are but-2-ene, 3,4-dimethyl hex-3-ene etc.
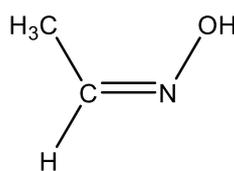

cis-but-2-ene   *trans*-but-2-ene

Syn-anti notation:

Oximes exhibit geometric isomerism due to restricted rotation about >C=N bond. In aldoxime, when H atom and the OH group lie on the same side of the double bond, the isomer is known as syn- isomer and when H atom and OH group lie on the opposite sides of the double bond, the isomer is known as anti- isomer.
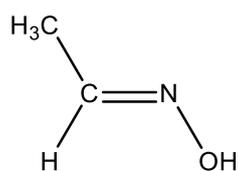
Syn- isomer   Anti- isomer

E / Z notation:

If there are three or four different atoms or groups are attached to the carbon atoms of a double bond then E/Z notation, devoloped by Cahn, Ingold and Prelog, is being used. In this system, the two atoms/groups attached to each of the double bonded carbon atoms are put priority on the basis of Sequence rule. The symbol E is assigned to the isomer in which atoms/groups of higher priority are on the opposite side, while the symbol Z is assigned to the isomer in which the atoms/groups of higher priority are on the same side.

Sequence rule:

1) Higher priority is assigned to the atoms of higher atomic number. Eg. I> Br> Cl> I.
2) In the groups, the priority is decided on the on the basis of atomic number of first atom of the group. Thus -Cl> -OH> -NH2 > -COOH.
3) If the first atom of the group is same, then priority is decided by the atomic number of the next atoms. Thus -COOH> -CH2-CH3> -CH3.
4) When a double bond or triple bond is present in a group, the atom is regarded as duplicated or triplicated. For example, in -CHO group, the carbon atom is considered to be linked with O, O and H.
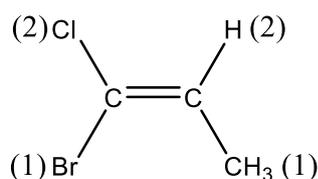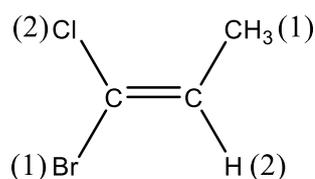
Some examples of E/Z notation:
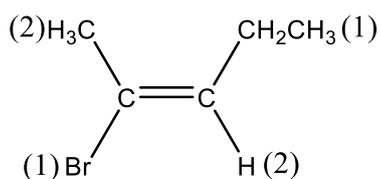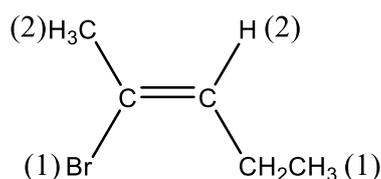
E- Isomer   Z- Isomer

Z- Isomer   E- Isomer

OPTICAL ISOMERISM:

The stereoisomers which have similar chemical reactions and most physical properties but differ in their behaviour towards plane polarized light are called optical isomers and the phenomenon is called optical isomerism.

Optical activity:

When ordinary light vibrating in all directions is passed through a nicol prism, it starts vibrating in one plane only. It is called plane polarized light. Certain substances in solution when placed in the path of a plane polarized light can rotate the plane of polarized light either to the right or to the left. Such substances are called optically active substances and the property is termed as optical activity.

The optical isomer which rotates the plane of polarized light to the right (clockwise) is known as dextrorotatory (+ sign), while the isomer which rotates the light to the left (anticlockwise) is known as laevorotatory (- sign). An equimolar mixture of the two form is optically inactive and is termed as racemic mixture (+_) mixture.
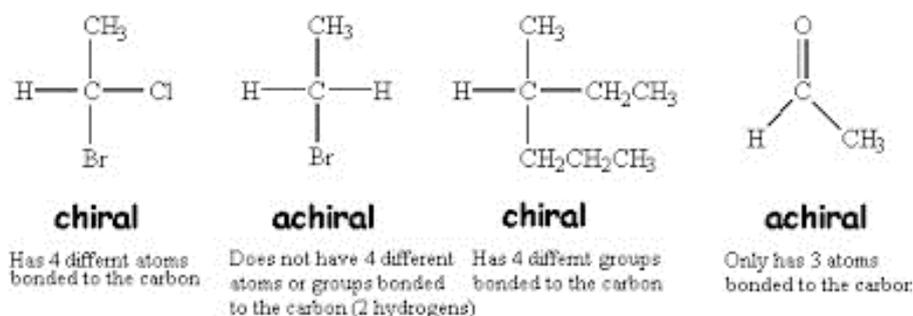
The degree of rotation observed when the plane polarized light is passed through a solution of a length of one decimeter and a concentration of 1 g ml^{-1} of the optically active compound at a specified temperature and wavelength is known as specific rotation.

$$[\text{ Specific rotation}]^t_{wavelength} = \frac{\text{Observed rotation}}{\text{Length x Conc}}$$

Chirality and Assymetric Carbon atom:

A plane which divides an object into halves that are mirror images of each other is called a plane of symmetry. An object lacking a plane of symmetry is termed as dissymetric or chiral while a symmetrical object is termed achiral. A chiral object is one which is not superimposable on its mirror image. Thus, hand is chiral but ball is achiral. Chirality is an essential condition for showing optical activity. A carbon atom bonded to four different atoms/groups is termed assymetric carbon atom or chiral centre designated as C^*.

A few molecules having one or more chiral centre(s) are shown below.

chiral	achiral	chiral	achiral
Has 4 diffent atoms bonded to the carbon	Does not have 4 different atoms or groups bonded to the carbon (2 hydrogens)	Has 4 diffent groups bonded to the carbon	Only has 3 atoms bonded to the carbon

Enantiomers

Compounds which are mirror images of each other but are not superimposable are termed enantiomers and the phenomenon of their existance is known as enantiomerism. Enantiomers of lactic acid is shown below.

$$(+) \textit{d}\text{-lactic acid} \qquad (-) \textit{l}\text{-lactic acid}$$
$$(I) \qquad\qquad\qquad (II)$$
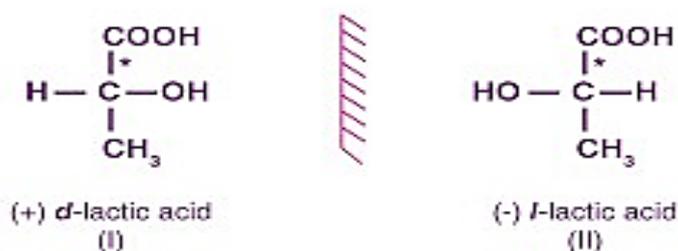
Enantiomers have similar physical properties such as melting point, boiling point, density, solubility in given solvent. They have identical chemical properties.

Diastereoisomers:

A pair of optical isomers of a compound which are not mirror images of one another are called diastereoisomers. Compounds containing more than one chiral centre can have more than one pair of diastereoisomers.

2,3-dibromobutyric acid has two chiral centres and the compound has four spatial arrangements.

| COOH	COOH	COOH	COOH
H——Br	Br——H	H——Br	Br——H
Br——H	H——Br	H——Br	Br——H
CH₃	CH₃	CH₃	CH₃
I	II	III	IV
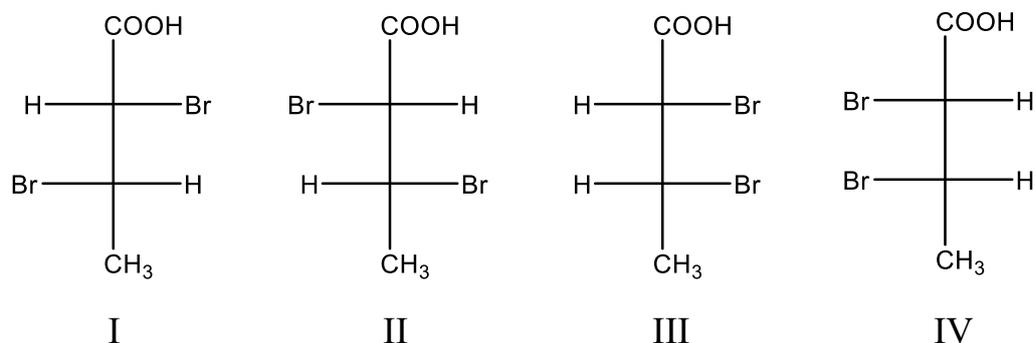
In this case the pairs I and II or III and IV are enantiomers. The pairs I and III, II and IV, I and IV, and II and III are diastereoisomers.

Diastereoisomers have different physical properties and can be separated by fractional crystallization, fractional distillation etc. Chemically they are similar, but their rates of reaction with other optically active compounds are different.

Meso compounds:

Certain compounds which contain two or more chiral carbon atoms are incapable of showing optical activity as the molecule as a whole is not chiral due to presence of a plane of symmetry in the molecule. In such compounds, the rotation due to one half of the molecule is cancelled by the rotation due to other half of the molecule in opposite direction because of the presence of the plane of symmetry. Such compounds are called meso compounds. For example, meso 2,3-dichloro butane, meso tartaric acid etc.

| CH₃	COOH
H——Cl	H——OH
- - - - - - - Plane of symmetry - - - - - - -	
H——Cl	H——OH
CH₃	COOH
Meso-2,3-dichlorobutane	Meso-tartaric acid
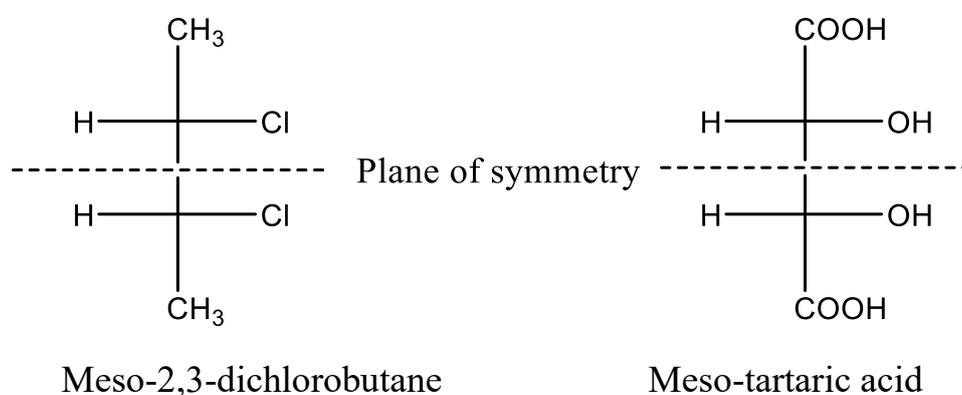
CONFORMATIONAL ISOMERISM:

The different arrangement of atoms in space that results from the free rotation of groups about C-C bond axis are called conformational isomers and the phenomenon is known as conformational isomerism.
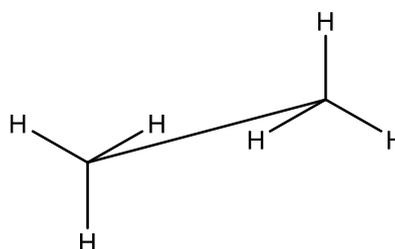
Conformation of Ethane:

In ethane molecule (CH_3-CH_3) molecule, the two carbon atoms are connected by single covalent bond while the remaining three valencies of each carbon are satisfied by hydrogen atoms. If one of the methyl groups in ethane molecule is kept fixed and other is rotated about C-C bond, a large number arrangements are obtained.

Out of infinite number of conformations, only two extreme conformations i.e., eclipsed conformation(I) and staggered conformation (II) are important.

In the Sawhorse projection, the bond between the two carbon atoms is drawn diagonally. In the case of eclipsed conformation, the hydrogens of one carbon atom are directly behind the other, while in the staggered conformation, the hydrogens of the two carbons are staggered with respect to one another.
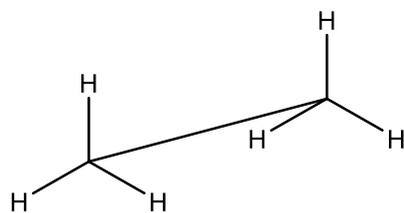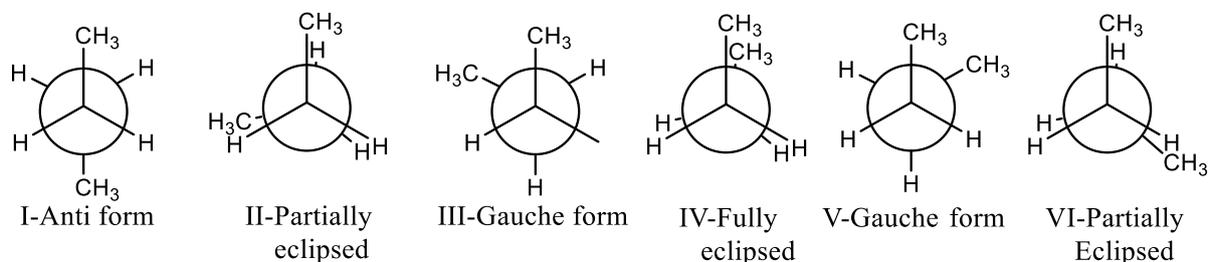

Eclipsed form (I)   Staggered form (II)

## Relative stability of conformations of ethane:

In the staggered conformation, the two hydrogen atoms on the adjacent carbon atoms are as far as possible. As a result, the repulsion between the electron cloud is the minimum. On the other hand, in eclipsed conformation, the hydrogen atoms on the adjacent carbon atoms are close to one another and have maximum repulsion. Thus, it possesses more energy and has lesser stability.

Conformation of Butane:

In n-Butane (CH_3-CH_2-CH_2-CH_3), two methyl groups are attached to two adjacent carbon atoms. By fixing rear carbon atom and rotating the front one, different conformations of n-butane are possible. These are illustrated by Newmann projection formula as shown below:

| I-Anti form | II-Partially eclipsed | III-Gauche form | IV-Fully eclipsed | V-Gauche form | VI-Partially Eclipsed |

Because of the presence of a methyl group at each carbon atom, the electron density will be unequal in case of C-H and C-CH_3 bonds. Therefore, form IV will be fully eclipsed as C-CH_3 bonds come closer whereas form II and VI will be partially eclipsed. On the other hand, form I will be completely staggered (anti form) because the -CH_3 groups of the two central carbon atoms are far apart. The forms III and V are not completely staggered and are named skew or gauche forms.

Fig. 8. Energy changes during rotation around the central carbon-carbon bond in *n*-butane.
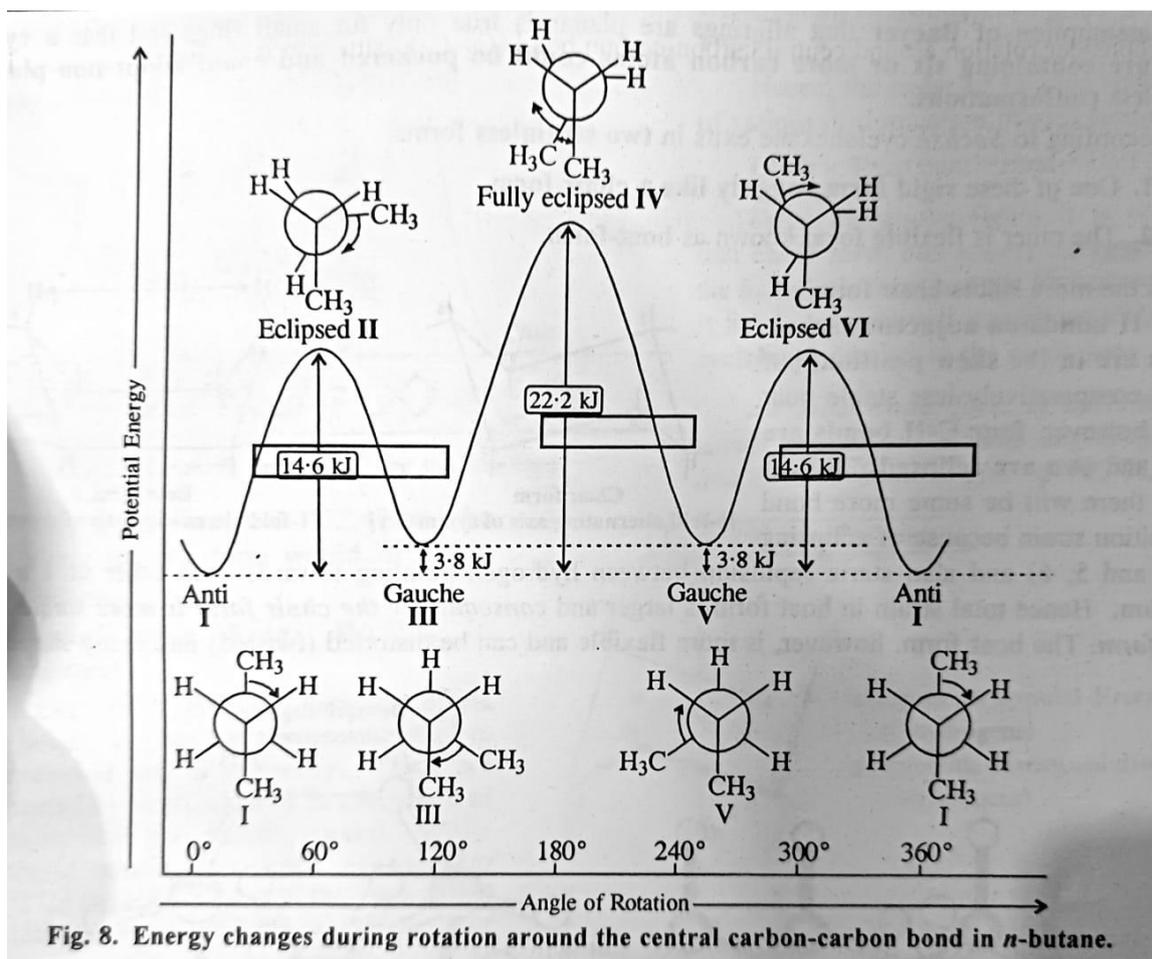
The order of stability of different conformations of n- butane is:

Staggered (anti) > Skew > partially eclipsed > Fully eclipsed.

Conformations of Cyclohexane:

Two important conformations of cyclohexane are: 1) Chair conformation and 2) Boat conformation.

1) Chair conformation: It is the most stable and hence most preferred conformation of cyclohexane. In this conformation, the electron pairs forming carbon carbon bonds are perfectly staggered. The bond angles are tetrahedral and there are no steric interactions between the non-bonded atoms. Hence this conformation has minimum energy

2) Boat conformation: In the boat conformation, the hydrogen atoms on four carbons (C-1 and C-3, C-5 and C-6) are eclipsed. Due to this, there is considerable strain. In addition, the two hydrogen atoms at C-1 and C-4 are very close to each other (Flag pole hydrogens).

Thus, it makes this form less stable than chair conformation by 28.84 kJ mol^{-1}.
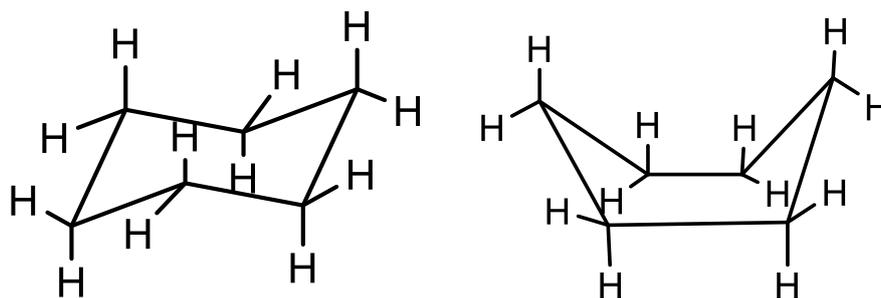
Other Conformations: In addition to chair and boat conformations, cyclohexane also exists in several conformations, viz., half chair, twist form etc.

Chair Form

Boat Form
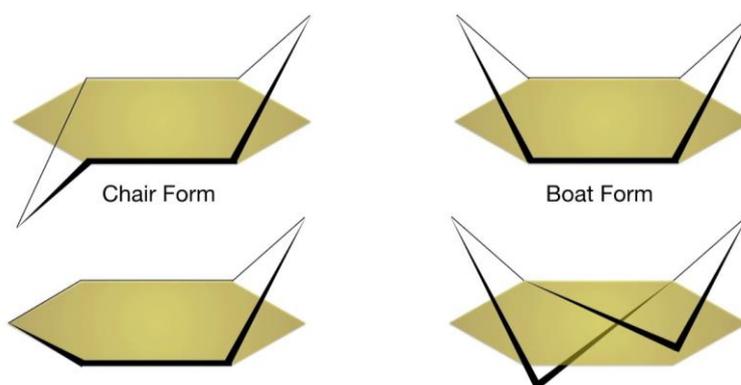
Axial and Equatorial bonds in cyclohexane:

On examining the various hydrogen atoms in the chair conformation, it is seen that there are two kinds of hydrogen atoms. Six hydrogen atoms (e) point sidewise along the general plane of the ring and are called **equatorial hydrogens**. The remaining six hydrogens (a) lie above or below the general plane and lie along the axis perpendicular to the plane. These are called **axial hydrogens**. Each carbon atom in the chair conformation of cyclohexane carries one axial and one bonds.