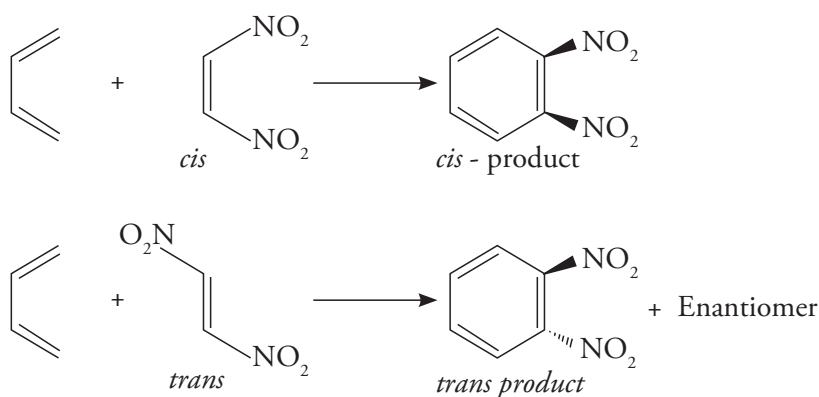


Trans dienes where transformation to *cis* form is not possible do not undergo the reaction.



- (ii) The Diels Alder reaction is also *cis* with respect to the dienophile, that is, groups lying *cis* to each other in the dienophile also lie *cis* to each other in the adduct. If they are *trans* on the dienophile, they form the *trans* product.



## 19.11 Stereochemistry

Stereochemistry is defined as the part of chemistry which deals with the study of **three dimensional arrangement of atoms in space**. It also studies the influence of this arrangement on the physical and chemical properties of these compounds.

Compounds having similar structure and connectivity but differing in their **three dimensional arrangement in space** are called **stereoisomers** and the phenomenon is called stereoisomerism. There are three types of stereoisomerism.

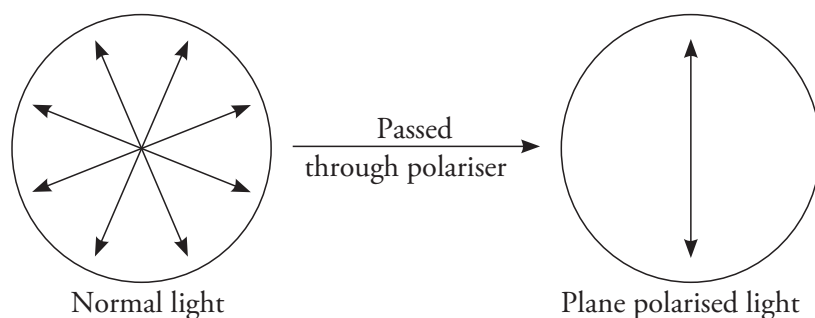
- (i) Optical isomerism
- (ii) Geometrical isomerism
- (iii) Conformational isomerism

### Optical Isomerism

It is a kind of stereoisomerism in which the isomers differ in the spatial arrangement of atoms or groups of atoms. Optical isomers have same physical properties but differ in their behaviour towards **plane polarised light**. Let us see what is plane polarised light?

### Plane polarised light

A beam of ordinary light has waves vibrating in all planes at right angles to the line of propagation. When this light is passed through a nicol prism (a special type of prism made of crystalline calcium carbonate), the vibrations in all but one plane are cut off (Fig. 19.7). Hence, the nicol prism converts an ordinary light into a plane polarised light.



**Figure 19.7** Normal and plane polarised light

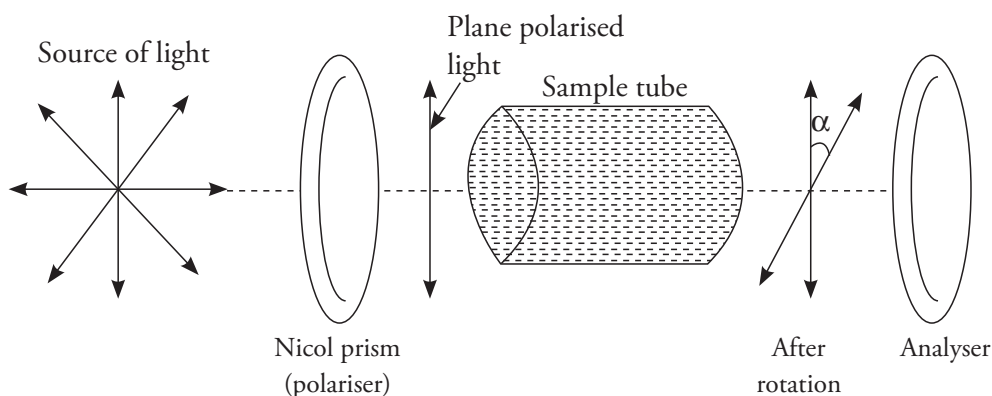
When the solutions of certain organic compounds are placed in the path of plane polarised light they rotate the plane polarised light either to the left or to the right. Such substances which rotate the plane of polarised light either to the left or to the right are called optically active substances. Common examples of such substances are lactic acid, tartartic acid, glucose, fructose, etc.

*This property of a substance by virtue of which it rotates the plane of polarised light is called optical activity.*

All optically active substances do not rotate the plane of polarised light in the same direction. Some rotate the plane polarised light to the right (clockwise) while some compounds rotate the plane polarised light to the left (anticlockwise).

A substance which rotates the plane polarised light to the right is called dextro-rotatory. Such compounds are designated as *d* or by the sign(+) (latin dexter = right). Those compounds which rotate the plane of polarised light to the left are called laevo-rotatory (latin laevous-left). They are designated as *l* or by the sign(−). The angle through which the plane polarised light is rotated is called the angle of rotation. It is expressed as  $\alpha$  (alpha).

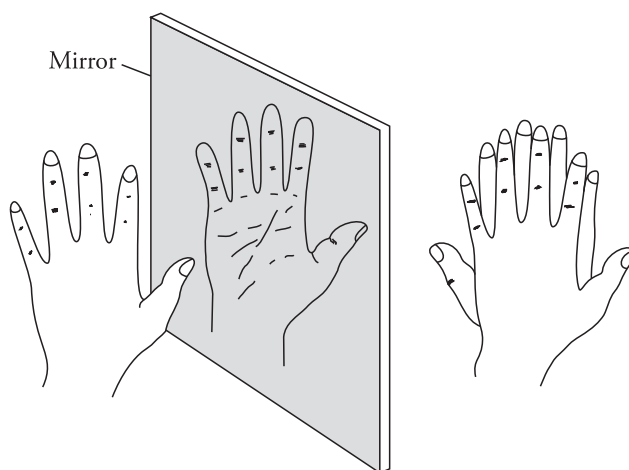
The direction and magnitude of the rotation of plane polarised light by a substance is measured with the help of an instrument called polarimeter. It consists of a light source, two nicol prisms and a sample tube to hold the substance. The sample tube is placed between these two prisms as shown in Figure 19.8. The prism placed near the source of light is called polariser while the other placed near the eye is called the **analyser**. The aqueous solution is placed in a sample tube between the polariser and analyser and the rotation of the plane polarised light is observed.



**Figure 19.8** Rotation of path of plane polarised light

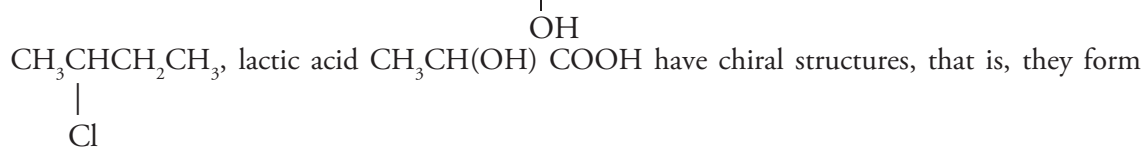
### Optical Activity and Chirality

Let us now see what are the conditions that lead to optical activity. A study of the structure of optically active compounds reveals that all of them have non-superimposable mirror images. The molecules which are not superimposable on their mirror images are called **chiral** or **dissymmetric** molecules. The property of non-superimposability of a structure on its mirror image is called **chirality** or **dissymmetry**. The word chiral comes from Cheiros-Greek-hand. If we hold our right hand in front of a mirror the image looks like left hand. If we try to superimpose left and right hands (both palms down), we observe that the hands cannot be superimposed (Fig. 19.9). Therefore, hands are chiral. Other examples of chiral objects are gloves, shoes, etc. On the other hand, cup, fork, spoon and socks are identical with their mirror images. Such compounds or molecules which are superimposable on their mirror image are called achiral molecules.



**Figure 19.9** Non superimposable mirror image of a hand

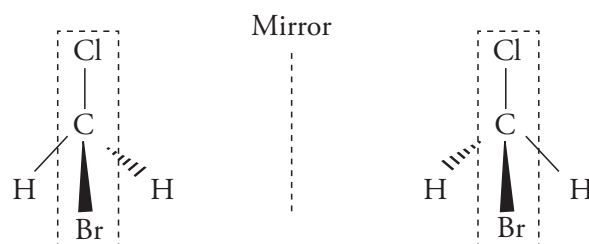
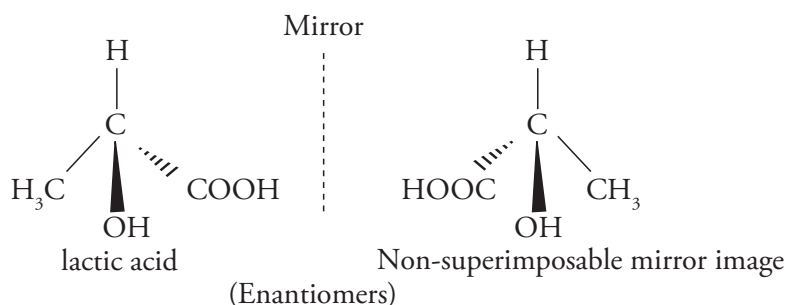
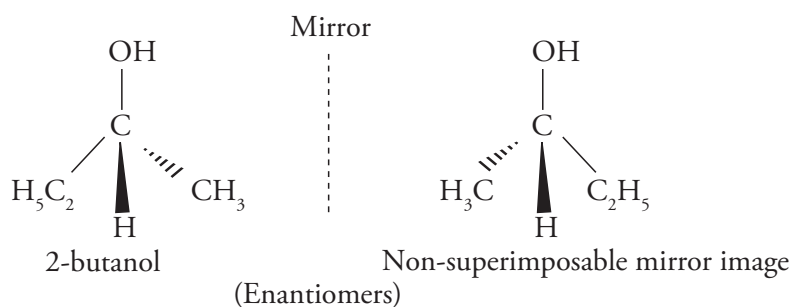
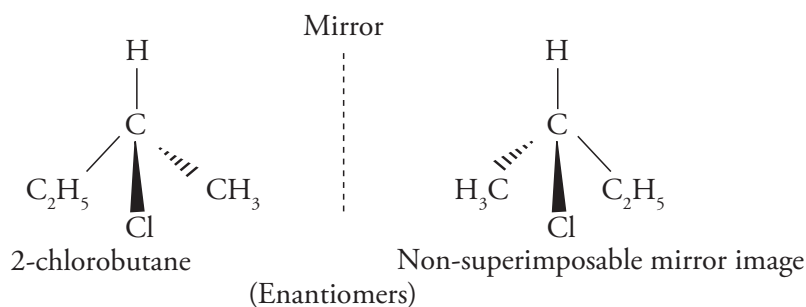
Many organic molecules such as 2-butanol  $\text{CH}_3\text{CHCH}_2\text{CH}_3$ , 2-chlorobutane



non-superimposable mirror images.

### Dissymmetry and Plane of Symmetry

A plane of symmetry is an imaginary plane which bisects the molecule in such a way that the two halves are mirror images of each other. The plane may pass through atoms or between them. Chiral molecules do not have plane of symmetry and therefore they are called dissymmetric. On the other hand, achiral molecules have a plane of symmetry and are called symmetric.

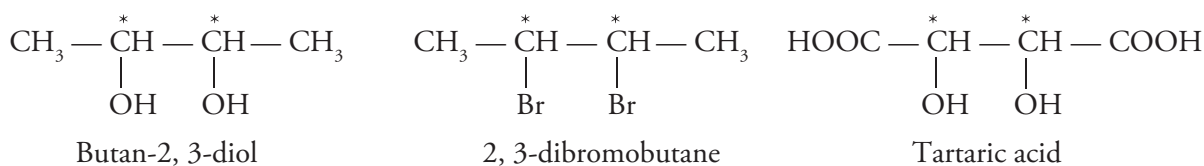


Mirror images: Superimposable

(Not enantiomers) The molecule possess plane of symmetry passing through Cl, C and Br.

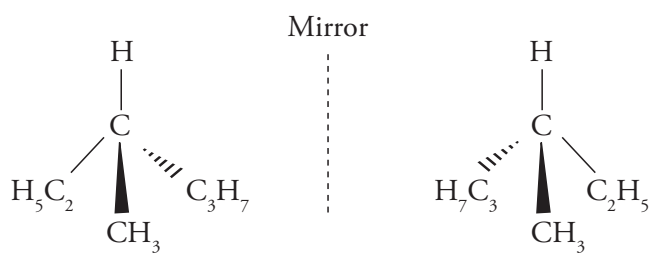
Thus dissymmetry is an essential condition for optical activity. A carbon atom bonded to four different atoms or groups of atoms is called a chiral carbon atom or asymmetric carbon atom. It is generally indicated as C\*.

Some other molecules having asymmetric carbon atom are



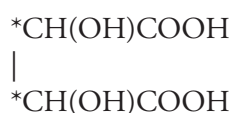
### Enantiomers and their characteristics

Enantiomers or enantiomorphs are non-superimposable mirror images of each other. They have identical physical properties like melting points, boiling points, density, solubility, etc. Their chemical properties are also similar. **They rotate the plane polarised light to exactly the same extent but in opposite directions.** In other words they have the same specific rotation but of opposite sign. Enantiomers may be dextrorotatory (denoted by *d* or +) or laevorotatory (denoted by *l* or –) depending upon whether they rotate the plane polarised light to the right or to the left. For example, 3-methylhexane has asymmetric carbon atom and forms non-superimposable mirror images.

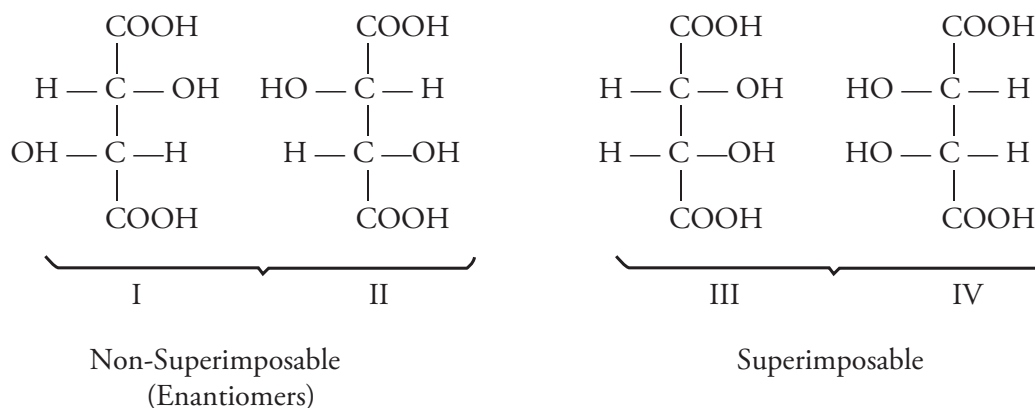


Enantiomers of 3 - methylhexane

Consider the example of tartaric acid having two asymmetric carbon atoms.



Since there are two asymmetric carbon atoms, four stereoisomers are possible (number stereoisomers =  $2^n$  where  $n$  is the number asymmetric carbon atoms. Where *meso* compounds exist, the number of stereoisomers will be lesser than this maximum (discussed later). The stereoisomers of tartaric acid are

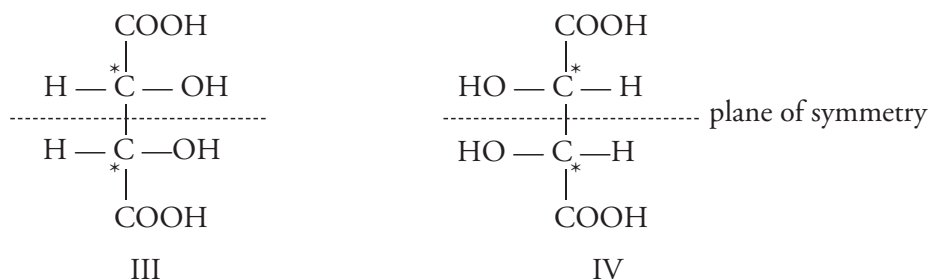


Structures I and II are enantiomers as they are non-superimposable mirror images. Similarly structures III and IV are also enantiomers. But how do structures I and II relate to structures III and IV? Structures I and II are stereoisomers of III and IV, but stereomer I is not the mirror image of either III or IV and so it is not an enantiomer of either one. A pair of stereoisomers that are not mirror images of each other are called diastereomers. Hence, the structures I and II are diastereomers of III and IV.

Diastereomers have different physical and chemical properties. Their physical properties like boiling points, solubilities, densities, refractive index, etc differ from each other. Their specific rotations are also different. They may have same or opposite signs of rotations or may be optically inactive also.

### Meso compounds

Consider the following structures of tartaric acid.



Structures III and IV of tartaric acid are mirror images but they are not dissymmetric because the molecule has a plane of symmetry; one half of the molecule is mirror image of the other half. Hence in spite of having two chiral centres (denoted by \*) the molecule is not chiral. It cannot exist in two enantiomeric forms and is optically inactive. It is called a meso compound.

*A meso compound is one where molecules are superimposable on their mirror image even though they have chiral centres.* The optical inactivity of a meso compound is due to **internal compensation**. One half of the molecule rotates the plane polarised light in one direction and the other half rotates it in the other direction. As a result the molecule is optically inactive.

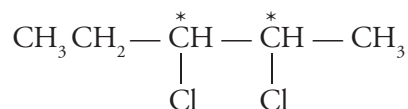
### Racemic Mixture

Racemic mixture is an equimolar mixture of the laevo and dextro rotatory enantiomers. It is represented as *dl* or  $\pm$  and will be optically inactive. The process of obtaining an optically inactive mixture from optically active *d* or *l* form is called racemisation. Racemic mixture is optically inactive due to **external compensation**. The (+) rotation caused by one enantiomer is cancelled by the rotation due to other enantiomer in the opposite direction (–).

### Total number of Optical Isomers

The number of optical isomers for a compound containing more than one asymmetrical carbon atoms can be calculated by the formulae given below

- (i) **Unsymmetrical molecules**     $\text{Cab}d \cdot \text{Cabe}$
- Number of *d* and *l* optical isomers =  $2^n$
- (where *n* is the number of chiral carbon atoms)
- Number of meso isomers = zero

**Example - 2, 3 dichloropentane**

$$n = 2 \quad \text{Hence total of optical isomers} = 2^n = 4$$

(ii) **Symmetric molecules**  $\text{Cabc} \cdot \text{Cabc}$   $n = \text{even} (2, 4, 6, 8)$

$$d + l \text{ forms} = 2^{(n-1)}$$

$$\text{meso} = 2^{n/2-1}$$

$$\text{Total} = 2^{(n-1)} + 2^{(n/2-1)}$$

**Example** Tartaric acid  $\text{CH}(\text{OH})\text{COOH} \cdot \text{CH}(\text{OH})\text{COOH}$

$$n = 2$$

$$d + l = 2^{(2-1)} = 2^1 = 2$$

$$\text{meso} = 2^{2/2-1} = 2^0 = 1$$

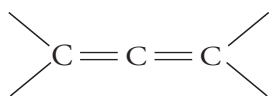
$$\text{Total} = 2 + 1 = 3 \text{ optical isomers (2 enantiomers + 1 meso compound)}$$

**Optical isomerism in compounds containing no asymmetric carbon atom**

As studied earlier the primary requirement for a compound to be optically active is its non-superimposable mirror image. Most of the compounds are optically active due to the presence of an asymmetric or chiral carbon atom. However, there are some compounds which do not have a chiral carbon atom but the molecule as a whole is asymmetric (such molecules are better called dissymmetric) and hence optically active. Some compounds belonging to this category are

(i) **Allenes**

Allenes are compounds having the general formula

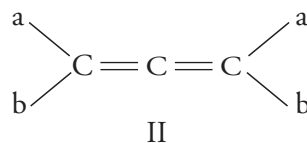
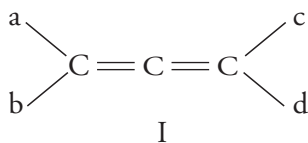


Allenes exhibit optical isomerism when the two groups attached to each terminal carbon atom are different.



Optically inactive

(groups on terminal carbon atom are the same)



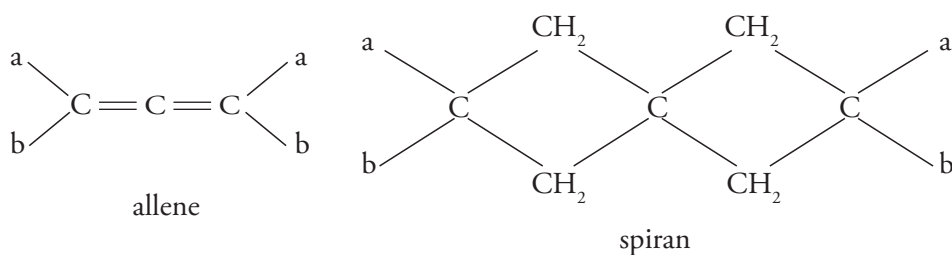
Optically active

(groups attached to terminal carbon atom are different)

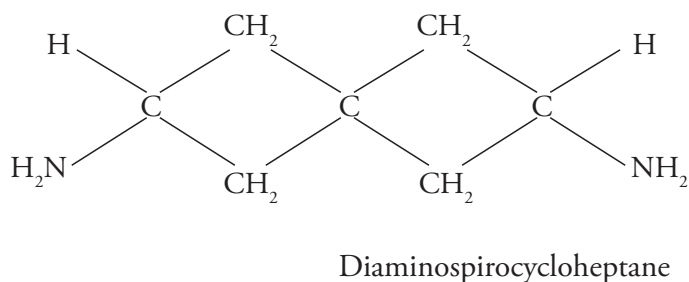
The above molecules I and II possess neither plane nor centre of symmetry and form non superimposable mirror image; hence, the allene molecule on the whole is asymmetric and optically active.

## (ii) Spiro Compounds (Spirans)

A spiro compound (spiran) is formed by the replacement of both the bonds of allenes by rings.



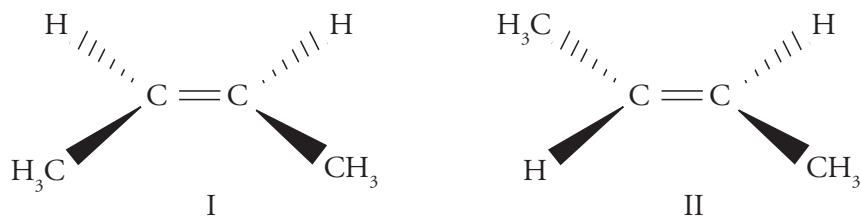
The two rings of spirans are perpendicular to each other and the molecule is dissymmetric, that is, it forms a non-superimposable mirror image and hence exhibits optical activity.



## Geometrical Isomerism

The compounds that have the same structural formula but differ in the spatial arrangement of atom or group of atoms about the double bond are called geometrical isomers and the phenomenon is called geometrical isomerism.

Consider the example of 2-butene. We find that the atoms can be arranged in two different ways around the double bond.



The connectivity of atoms in the two isomers is the same and they differ only in the way the atoms are oriented in space. In structure I, both the methyl groups lie on the same side, whereas they lie on opposite sides in structure II. These structures cannot be converted into one another by simple bond rotation. They can be converted only by breaking the  $\pi$  bond, which requires extra energy of about 70 kcal/mol. This energy is not available at room temperature. Because of this energy barrier



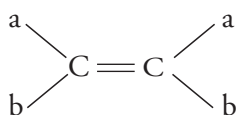
there is hindered rotation around the carbon carbon double bond. As a result of this hindered rotation, the structures I and II exist separately and have been isolated.

Structures I and II are stereoisomers, but as the two are not mirror images, they are called diastereomers.

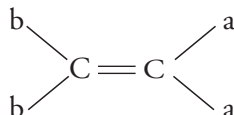
Structure I in which both the methyl groups lie on the same side is called *cis* (latin: on this side) and structure II in which both the methyl groups are on opposite sides is called *trans* (latin: across). Geometrical isomers differ in their physical properties. *Cis* isomers where bulky groups are on the same side are less stable than *trans* isomers where the groups are well separated.

The essential condition for geometrical isomerism is that

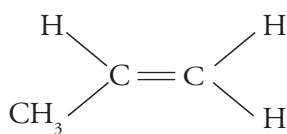
- The molecule must have a double bond
- Different atoms or groups must be attached to the same carbon atom.



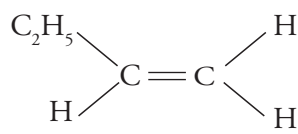
Different groups attached to same carbon atom  
(shows geometrical isomerism)



Similar groups attached to same carbon atom  
(Does not show geometrical isomerism)



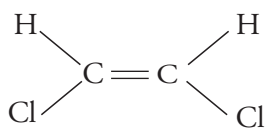
Propene



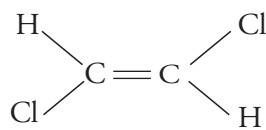
1 – butene

No geometrical isomerism

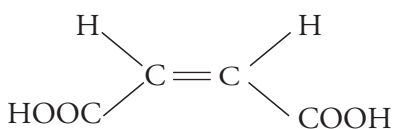
### Other examples of geometrical isomerism are



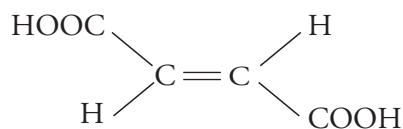
cis –1, 2 dichloroethene



trans –1, 2 dichloroethene

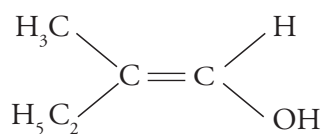
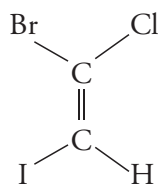


Maleic acid



Fumaric acid

This system using *cis* and *trans* prefixes works well for disubstituted alkenes, but what if all the groups are different?



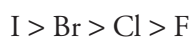
The *cis*, *trans* system cannot be applied to the above compounds. Such compounds are specified using the E – Z system.

### E – Z nomenclature

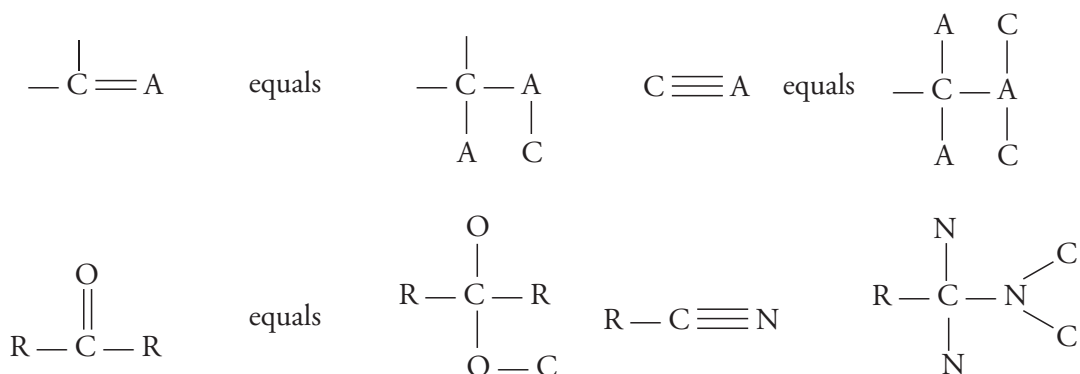
When three or four different groups are attached to the carbon atom of a double bond, then the E–Z system is used. Z means on the same side (German: Zusammen together) and E means on opposite side (German: entgegen-opposite).

The E–Z system is based on the assignment of priorities to the atoms or groups attached to each carbon atom of the double bond. The priority is assigned according to Cahn–Ingold–Prelog (CIP) sequence rules which are discussed below.

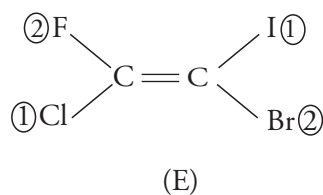
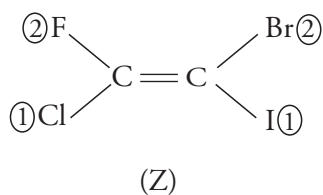
1. The atom with higher atomic number gets the highest priority. For example, if the four atoms attached are F, Cl, Br and I, then the priority becomes



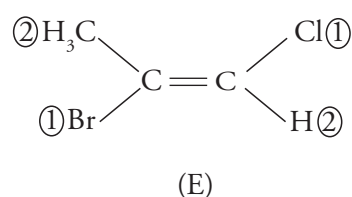
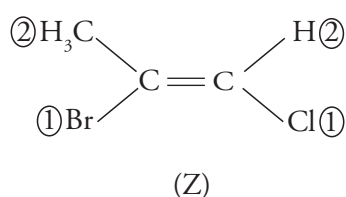
2. If two isotopes of the same element are present, the isotope of higher mass gets the higher priority. For example, deuterium (D) gets priority over hydrogen (H).
3. If the first atom of the two substituents is identical, then the next atom is considered for priority assignment. For example, ethyl group gets priority over methyl group. Similarly, –COOH gets priority over –CHO.
4. If double, or triple-bonded groups are present as substituents, both atoms are considered to be duplicated or triplicated. For example



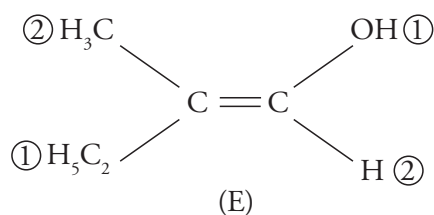
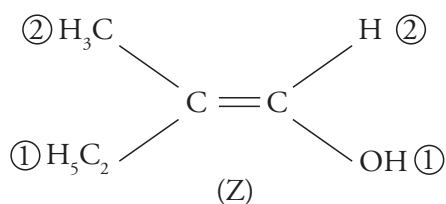
According to E–Z system, priorities are assigned to the groups attached to the double bonds. If the two groups of higher priority are on the same side of the double bond, the isomer is a Z isomer and if the two higher priority groups are on the opposite sides of the double bond, the isomer is called E isomer.

**For example**

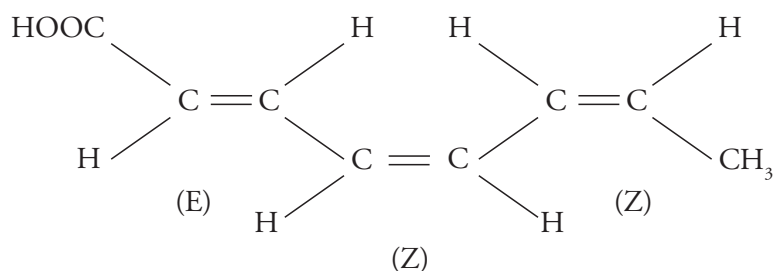
Priority  $\text{Cl} > \text{F} : \text{I} > \text{Br}$



Priority  $\text{Br} > \text{CH}_3 : \text{Cl} > \text{H}$

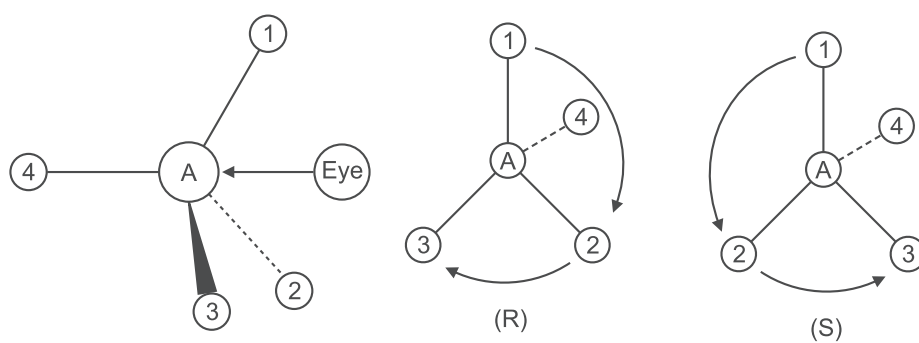


Priority  $\text{C}_2\text{H}_5 > \text{CH}_3 : \text{OH} > \text{H}$

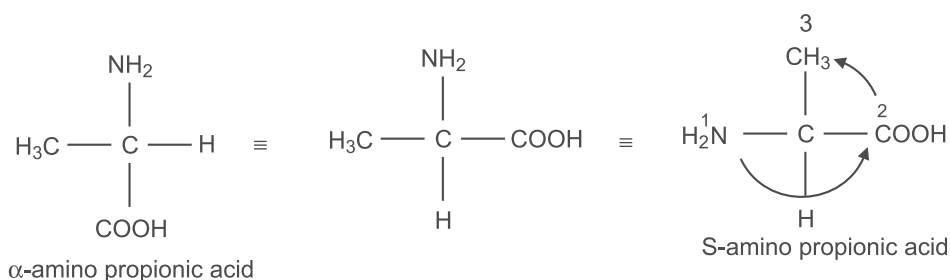
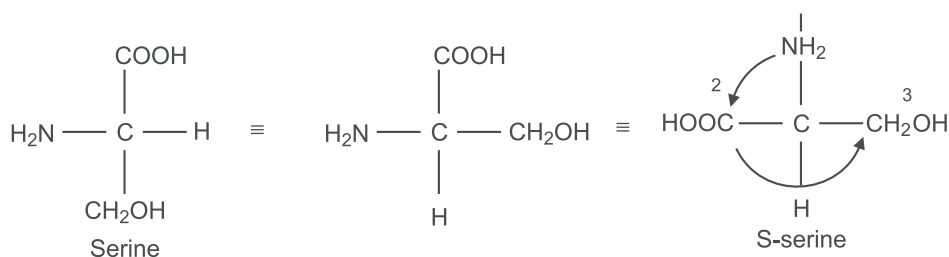
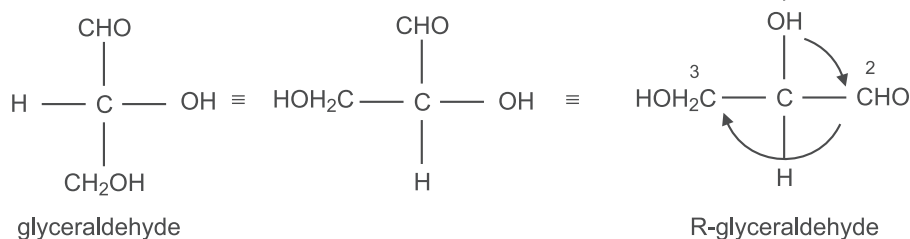
**Absolute configuration**

Absolute configuration defines the arrangement of atoms around the chiral centre. It makes use of the sequence rules given by Cahn–Ingold–Prelog. To decide the configuration of the molecule the ligands are sequenced according to the rules mentioned above. They are arranged in the order of decreasing precedence, that is,  $1 > 2 > 3 > 4$ .

- The molecule is viewed from the side farthest away from the ligand of lowest priority (i.e., ligand 4) and the directions of decreasing precedence of ligands 1, 2 and 3 are determined.
- If the order of precedence  $1 \rightarrow 2 \rightarrow 3$  is clockwise then the molecule is assigned the configuration R (from the latin word *rectus* = right) and if it is anticlockwise then the configuration assigned to the molecule is S (*sinister* = left).
- If the molecule is represented by the Fischer projection formula then the group of least priority should be written at the bottom of the projection formula but it may not always be the case. In case the group of least priority is not at the bottom, then it is brought at the bottom by two (or even) number of exchanges of groups around the asymmetric atom. If odd number of exchanges are made, then the enantiomer is formed.
- The above explanation are illustrated by the examples given below:



A molecule with  
chiral center

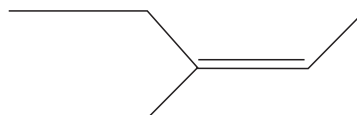
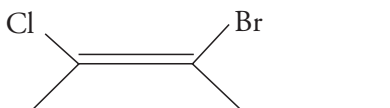
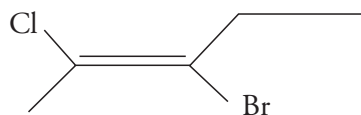
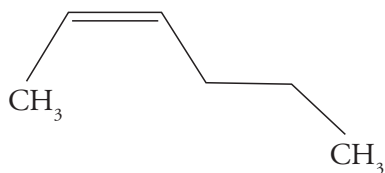
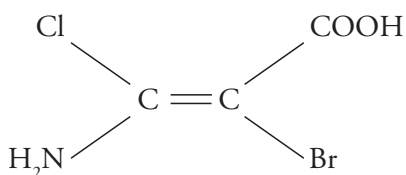
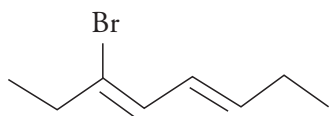
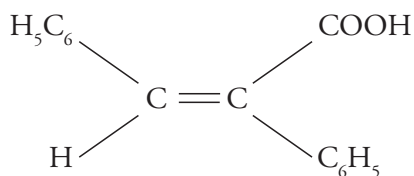
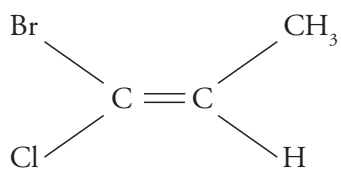




## Practice Problems

### Give reasons why

- 2-butene exists in two isomeric forms, but not 1-butene.
- Butan-2-ol is optically active, whereas butan-1-ol is optically inactive.
- Assign E and Z to the following compounds



4. Which of the following compounds will show optical isomerism



### Conformational Isomerism in Hydrocarbons

This type of isomerism arises due to rotation about carbon–carbon single bond. The carbon–carbon single bond in alkanes is a sigma bond and has cylindrical symmetry. As a result, the rotation about the carbon–carbon single bond is quite free. Therefore, a large number of spatial arrangements of the atoms or groups of atoms attached to the carbon atoms are possible. These different spatial arrangements are called conformations. Thus, the different arrangement of atoms in a molecule which can be obtained due to rotation about carbon–carbon single bond are called conformations.

#### Conformations of ethane

In the ethane molecule ( $\text{CH}_3\text{--CH}_3$ ), the two carbon atoms are bonded by single covalent bond. If one of the methyl groups is kept fixed and the other is rotated about the C–C bond an infinite number of arrangements of the hydrogen atoms attached to one carbon with respect to the other carbon atom are possible. These infinite number of different arrangements are called conformations. However, two conformations are important. These are

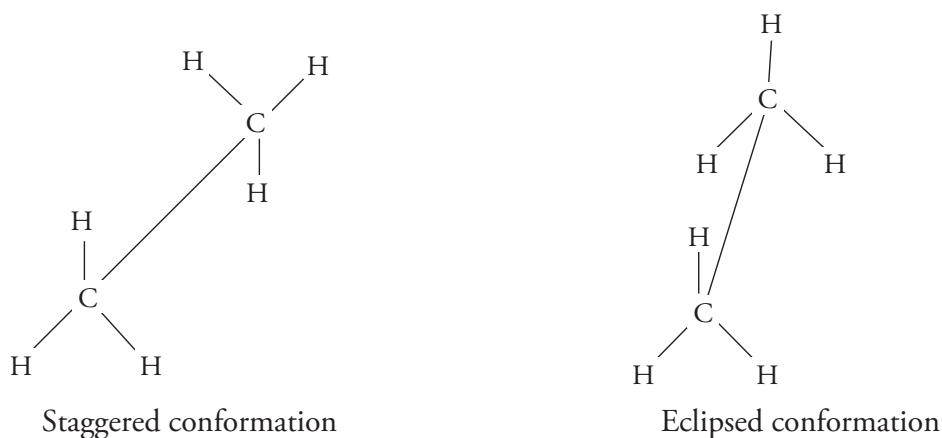
(i) Staggered conformation

(ii) Eclipsed conformation

(i) **Staggered conformation** In this type of arrangement, the hydrogens on the two carbon atoms are staggered with respect to each other. They are at maximum distance from each other and the repulsion between them is minimum. Hence the stability is maximum.

(ii) **Eclipsed conformation** In this type of conformation the hydrogen of the second carbon atom are right behind the hydrogen atoms of the first carbon atom. Consequently the repulsion between them is maximum. The conformations can be represented by two kinds of formulae.

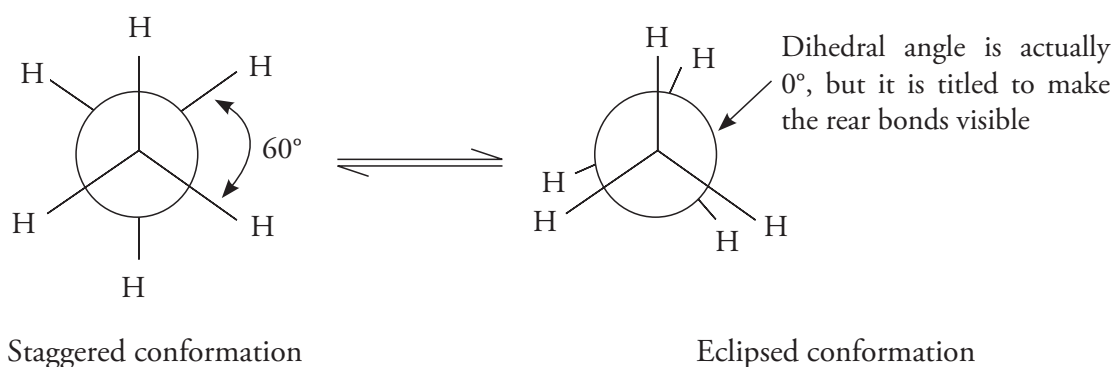
#### Saw horse projections



**Figure 19.10** Saw horse projection formulae of ethane

**Newman projections**

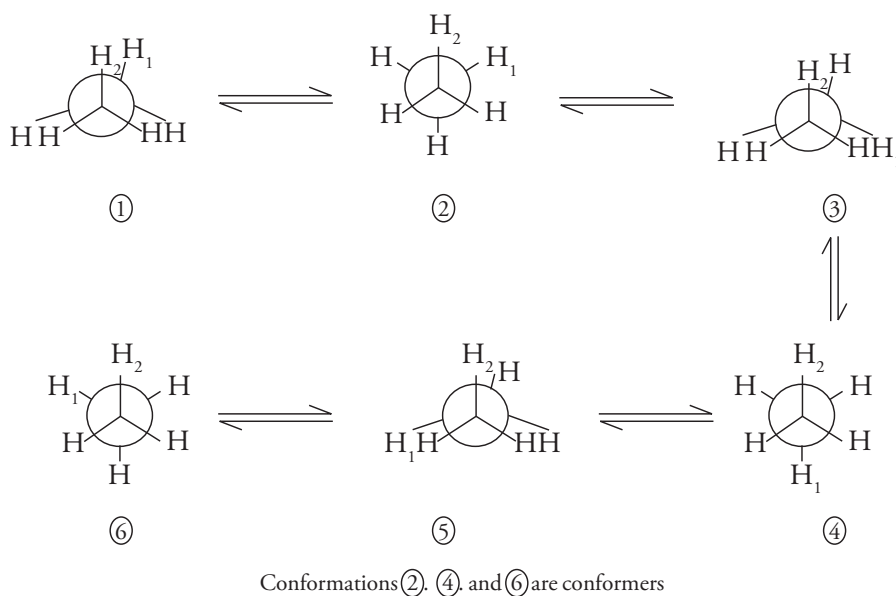
In these projections, the two carbon atoms forming the  $\sigma$  bond are represented by two circles, one behind the other so that only the front carbon is seen. The C–H bonds of the front carbon are depicted from the centre of the circle. The C–H bonds of the rear carbon atom are drawn from the circumference of the circle (Fig. 19.11).



**Figure 19.11** *Newman projection formulae of ethane*

When a staggered conformation is rotated through an angle of  $60^\circ$  it changes to eclipsed conformation and when the eclipsed conformation is rotated by  $60^\circ$  it again changes to staggered conformation.

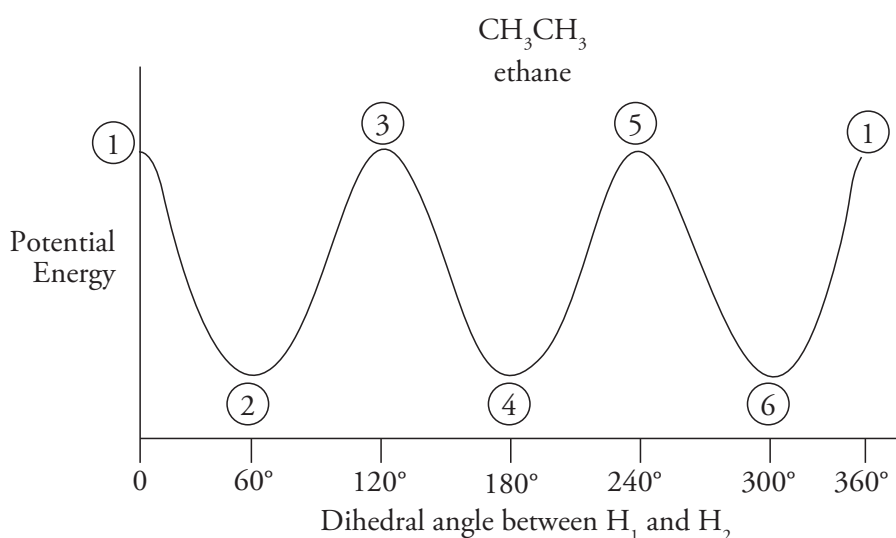
Apart from staggered and eclipsed conformations infinite number of intermediate conformations are the possible. These conformations are called skew conformations.



**Figure 19.12(a)** *Conformations of ethane*

### Relative Stabilities of Conformations of Ethane

The different conformations of ethane differ in their relative stabilities. In staggered conformation the hydrogen atoms are at a maximum distance apart (dihedral angle is  $60^\circ$ ) and hence the force of repulsion is minimum making it energetically stable. In eclipsed conformation there is maximum repulsion between the hydrogen atoms (dihedral angle  $0^\circ$ ) and hence its energy is more and hence stability is less. The difference in energy contents of staggered and eclipsed conformation is  $3 \text{ kcal mol}^{-1}$ . However, this energy difference is not large enough to prevent rotation. Even at ordinary temperatures, the two forms keep converting into each other and it is not possible to isolate them.



**Figure 19.12(b)** Potential energy of various conformers of ethane

### Conformations for butane

In butane the rotation about  $C_2$  and  $C_3$  bond is of interest because of the relative positions of the two methyl groups. Focussing attention on  $C_2$  and  $C_3$  due to the presence of methyl groups the following positions are observed (Fig. 19.13 a).

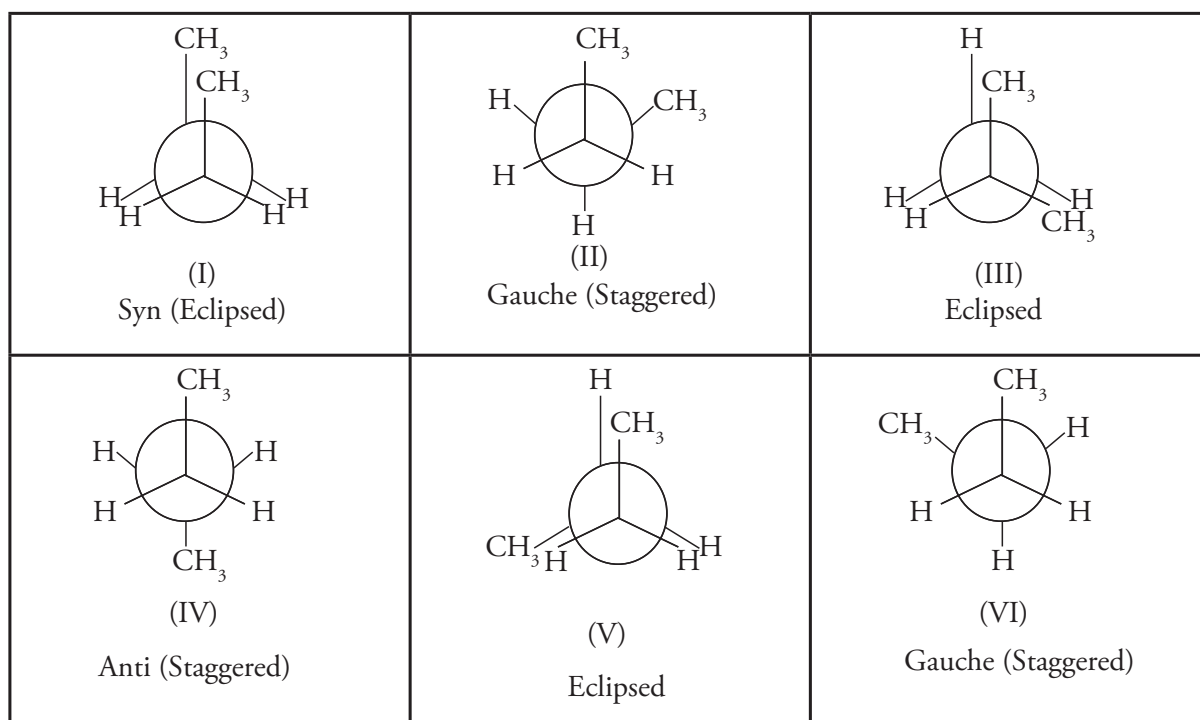
Structure I which is a fully eclipsed conformation. All the methyl groups and hydrogen atoms are aligned completely. There is maximum steric or van der Waals repulsion between the groups and hence its potential is maximum and it is unstable. This is the **syn** conformation.

On rotating the front carbon atom by  $60^\circ$  we get another conformation in which the two methyl groups are separated by  $60^\circ$ . The dihedral angle between the two methyl groups is  $60^\circ$ . It is a staggered conformation called **gauche** conformation and the potential energy is lesser than the **syn** conformation (conformations II and VI are gauche conformation).

On further rotating the front carbon atom by  $60^\circ$ , as eclipsed conformation (III) is obtained in which the  $CH_3$  group is aligned with H atom.

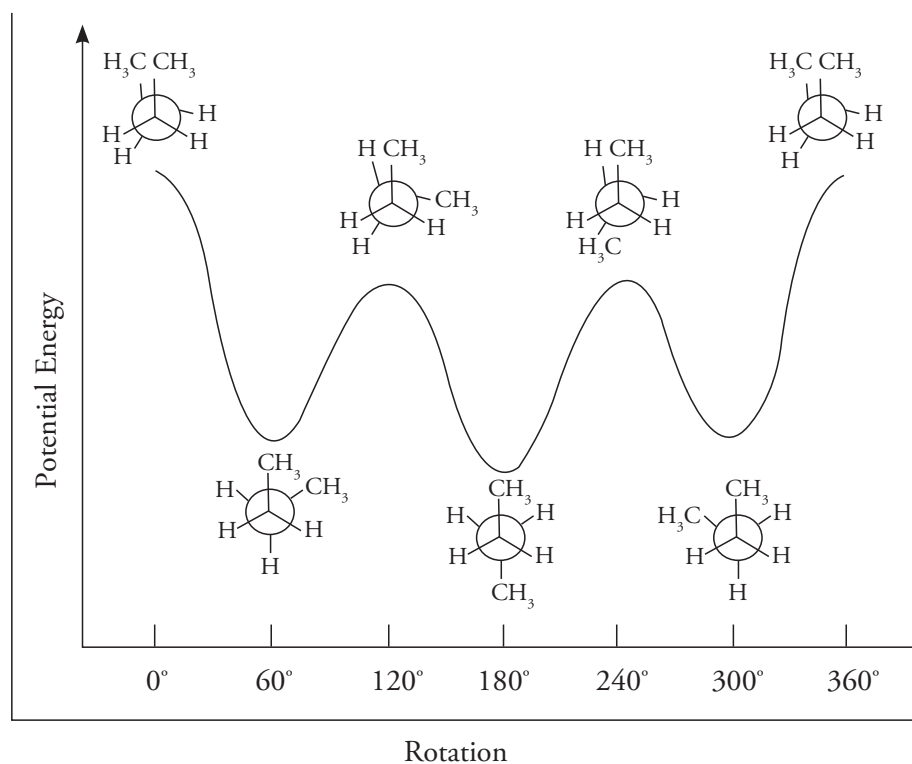
A further rotation of  $60^\circ$  gives the most stable conformation called **anti** conformation (IV). It is a staggered conformation in which the dihedral angle between the two methyl groups is  $180^\circ$ . The steric repulsion is minimum and hence the stability is maximum. The anti-conformation is more stable than gauche conformation by  $0.8 \text{ kcal/mol}$ .





**Figure 19.13(a)** Conformations of butane

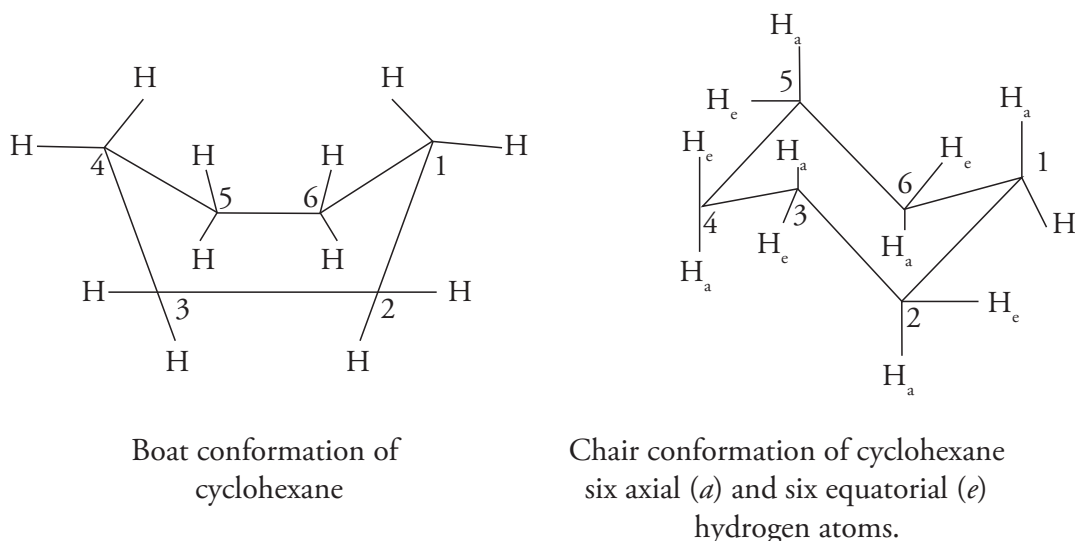
The potential energy curve for the various conformations of butane is given below.



**Figure 19.13(b)** Potential energy of various conformers of butane

### Conformations of cyclohexane

The cyclohexane molecule is quite stable. It avoids strain by assuming a conformation in which all the bond angles between carbon atoms are close to the tetrahedral angle of  $109^\circ 28'$ . Therefore it adopts a non-planar structure. Moher in 1918 postulated the **puckered ring conformations** for cyclohexane having all the angles as tetrahedral. These two puckered conformations are **chair conformation** or **Z form** and **boat conformation of C form**.



**Figure 19.14** Boat and chair conformations of cyclohexane

### Stabilities of conformations of cyclohexane

The chair **conformation** of cyclohexane is more stable than the boat conformation due to the following reasons.

- (i) In chair conformation the adjacent hydrogen atoms on all the neighbouring carbon atoms are quite staggered and the force of repulsion between them is minimum. However, in boat conformation, the adjacent hydrogen atoms on  $C_2-C_3$  and  $C_5-C_6$  atoms are eclipsed.
- (ii) The two hydrogen atoms marked as  $H_f$  bonded to the  $C_1$  and  $C_4$  atoms in boat conformation are quite close and they repel each other.

Therefore the energy of boat conformation is more than that of chair conformation.

**Therefore, cyclohexane exists mainly in the chair form.**

## 19.12 Drugs

Drugs are chemicals that interact with the macromolecular targets to produce a biological response. When the biological response is therapeutic assisting in the diagnosis, treatment or prevention of a disease it is termed as a medicine. However, some drugs are also used as a stimulant arising a state of euphoria and can be habit forming leading to addiction.