

The background of the page features a large, faint watermark of the University of Delhi logo. The logo is circular and contains the text 'UNIVERSITY OF DELHI' at the top and 'विद्या ऽ मृतमश्नुते' at the bottom. In the center of the logo is a shield with a book and a lamp, symbolizing knowledge and enlightenment.

Discipline Course-1 (DC-1)

Semester-1

Section A: Organic: Basic Concepts and Stereochemistry

Unit-II Stereochemistry

Lesson: Stereochemistry

Lesson Developer: Vimal Rarh

College/Department: SGTB Khalsa College, University of Delhi

6.1 Introduction

The world of molecules is amazing. But if you think they are static, you are wrong! In fact, molecules are anything but static. They move about, vibrate, rotate, spin, etc. All of this all can be visualized and understood by the study of the spatial arrangement of atoms in molecules in 3-D space. This is done in **Stereochemistry!**

Stereochemistry is the study of spatial arrangements of atoms or group of atoms in molecules, i.e., the arrangement of these atoms in relation to one another in three-dimensional space.

Isomers are those molecules that have the same molecular formula, but have at least one different physical and/or chemical property. This difference can arise either due to their different structural arrangement which gives rise to **structural isomerism** or due to different arrangement of the atoms in space which gives rise to **stereoisomerism** or **spatial isomerism**. In stereoisomerism, the atoms making up the isomers are joined up in the same order i.e., have same structural arrangement, but still have a different spatial arrangement.

Stereoisomerism can be studied under two main headings namely conformations and configurations.

A. Conformations:

Conformations are the different 3-D orientations achieved by the molecule formed due to rotation about sigma bonds. These are *freely inter-convertible* at room temperature into each other. The inter-conversion of these isomers does not require any breaking or forming of bonds.

B. Configurations:

Configurations are stereoisomers, which arise due to certain types of *rigidity* within the molecule. They can get converted into one another only if some bonds are broken and then re-established after rearrangement. They *cannot be inter-converted* into each other freely. There are two types of configurational isomers -geometrical and optical. Before studying them, one must be familiar with the different formulae used to represent them.

6.2 Projection Formulae and Their Interconversion

The molecules can be visualized and represented on a paper by several projection formulae as follows.

Wedge-Dash Representation

In this type of representation, **wedges** (or dark thick lines) () are used to represent bonds that are and **dashes** () are used to represent bonds that are going *into the plane* of the page (i.e., away from the viewer). The simple lines () represent bonds lying in the plane. This notation is frequently used to represent the tetrahedral geometry of sp^3 -hybridized carbons. The conversion of tetrahedral structure **into Wedge formula** is shown in Figure 6.1.

Figure 6.2 and 6.3 represent the wedge-dash formula for methane and ethane, respectively.

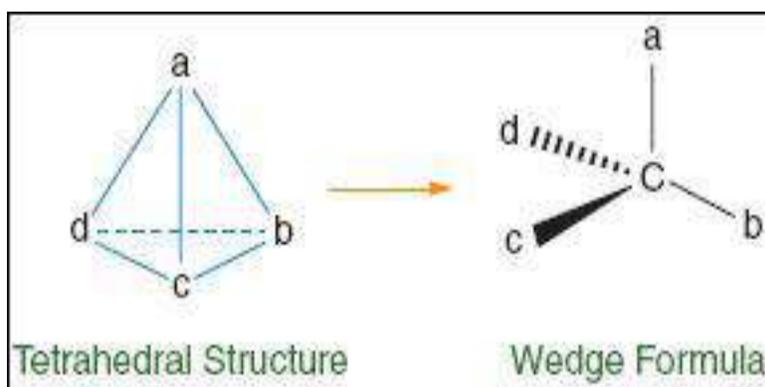
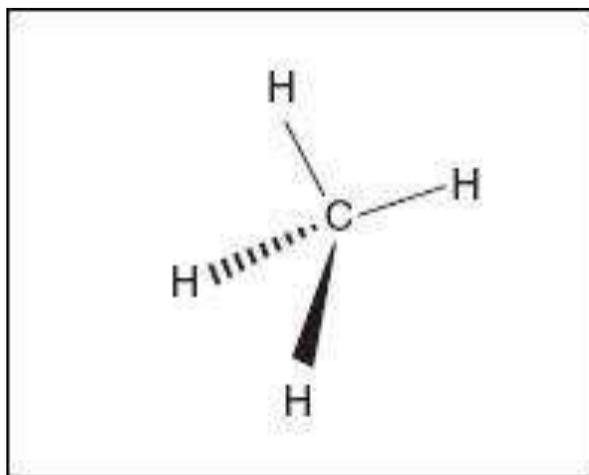


Figure 6.1:
Tetrahedral
structure and
wedge formula

Figure 6.2: Wedge-dash formula of methane



Newman Projection

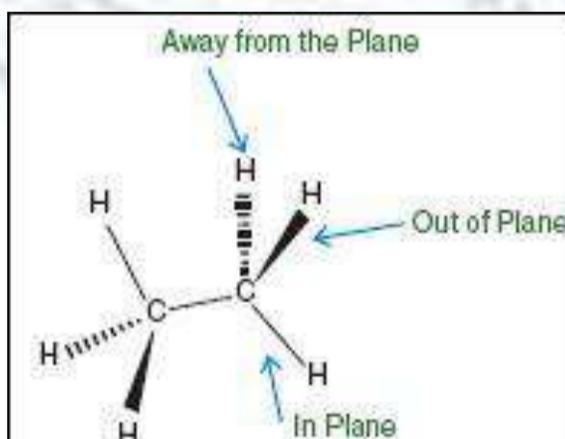
A Newman projection represents the head-on look down the bond of interest [Figure 6.4. (a)]. For example, in case of ethane, a point represents the front carbon atom and three lines emerging from it are the three bonds attached to three hydrogen atoms. The circle in the Newman projection represents the rear atom, and the lines radiating from the circle are the bonds of the rear carbon atom [Figure 6.4. (b)].

In general, the front carbon atom i.e., carbon nearer to the eye and its bonds is

represented as  and the rear carbon atom and its bonds as .

Newman projections are characterized by the angles formed between bonds on the front atom and bonds on the rear atom. Such angles are called **dihedral angles** (θ).

 a) Conversion of Wedgedash to Newman's formula of ethane (b) Newman's formula of ethane showing front and rear hydrogen atoms " onclick="MM_openBrWindow('BSCPI_PCH103_U6_SC_P_figure_6_4.html','width=640,height=518')" border="0" /> Figure 6.4: (a) Conversion of Wedge.dash to Newman's formula of ethane (b) Newman's formula of ethane showing front and rear hydrogen atoms



Sawhorse Projection Formulae

They are also used to represent the 3-D view of the molecule. But, it is a side view of the molecule unlike Newman's view. For example, in case of ethane, the two carbon atoms are drawn as points and the bond joining the two carbons is drawn as a line, which is considered to be in the plane of paper. The three lines originating from each point represent the rest of the three bonds on each carbon.

The lines pointing upwards are considered to be coming out of the plane and the lines pointing downwards are considered to be below the plane. For example, the two important sawhorse projection formulae for ethane are shown in Figure 6.5.

Figure 6.5: Two important sawhorse formulae of ethane

Fischer's Representation

For the compounds with one chiral carbon as centre, Fischer projection formula is drawn as intersecting horizontal and vertical lines. The chiral carbon is considered to lie on the point of intersection and the lines originating from this point are considered as four bonds joined to that chiral carbon (chiral C atom is the one which is attached to four different groups). The horizontal lines depict the bonds projecting out of the plane of paper and the vertical lines depict the bonds

projecting away (or behind) the plane of paper as shown in Fig 6.6.

For compounds with more than one chiral carbon as central atoms, Fischer projection formula is drawn as shown in Figure. 6.7.

Figure 6.6: Fischer's formula

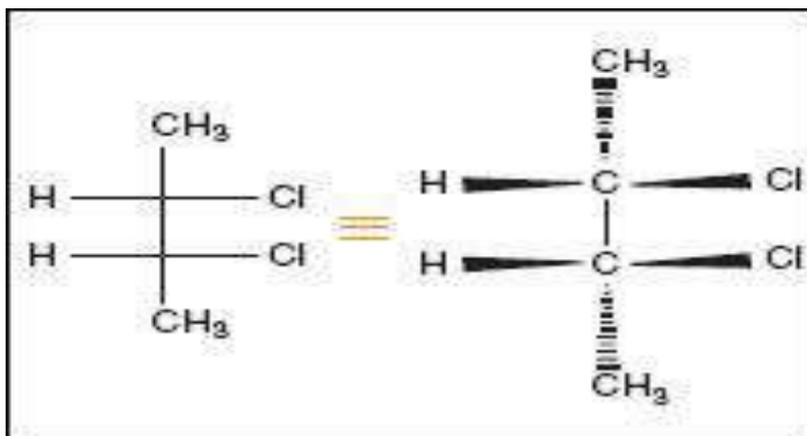


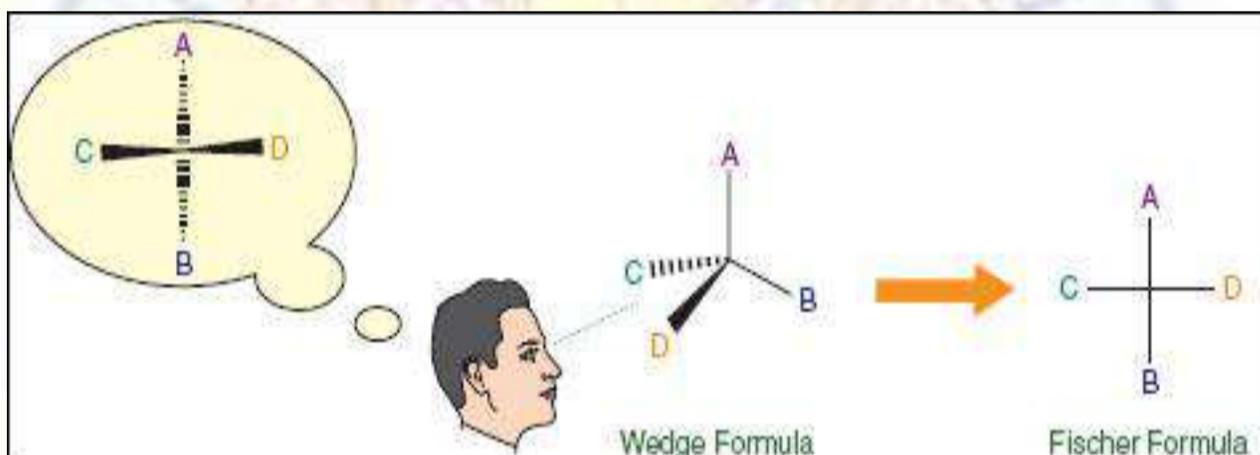
Figure 6.7: Fischer's formula for more than one central atom

6.2.1 Inter Conversion of Projection Formulas

A. For Compounds with one Chiral Carbon as Centre

(i) Conversion of Wedge formula to Fischer's formula

The molecule should be visualized in such a way that two horizontally placed groups are projected towards the viewer and two vertically placed groups are projected away from the viewer. Then simply write them on a plane around four perpendicular lines originating from a point depicting the chiral C atom as shown in Figure 6.8 {the group on the top (A), left (C), right (D) and bottom (B)}. The so obtained formula is the



Fischer's formula!

Figure 6.8: Conversion of Wedge formula to Fischer formula

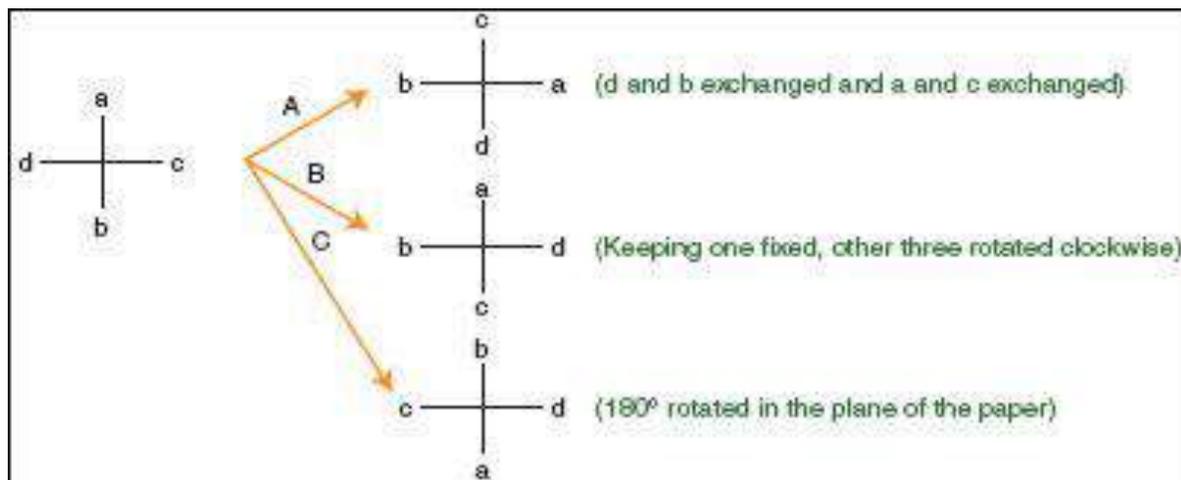
Animation

<http://www.illdu.edu.in/mod/resource/view.php?id=5661>

(ii) Conversion of one Fischer projection into an equivalent Fischer structure

It is possible to convert one Fischer projection to another without changing the identity of the molecule. This can be done by:

- Exchanging two pairs of substituents, or
- By rotating the substituents in a group of three keeping the fourth one fixed, or
- By rotating the whole molecule through 180° in the plane of the paper (either clockwise or anticlockwise).



This is illustrated in Figure. 6.9.

Figure 6.9: Rules for conversion of one Fischer projection into another Fischer projection

B. For the Compounds with more than One Chiral Carbon as Centre Atoms

(i) Conversion of sawhorse formula to Fischer's formula and vice-versa

To convert sawhorse into Fischer's formula, the viewer must visualize viewing the eclipsed conformation (section 6.3.1) of the molecule (sawhorse formula) in such a way that four horizontally placed groups are projected towards the viewer and two vertically placed groups are projected away from the viewer. Then simply write them on a plane across perpendicular lines originating from two points depicting the two chiral C atoms, as shown in Figure. 6.10., to get the Fischer's formula!

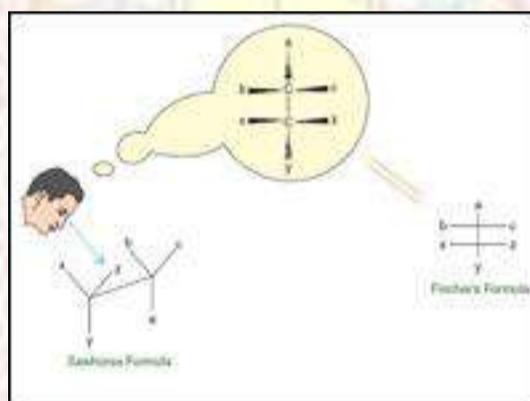


Figure 6.10: Conversion of sawhorse into Fischer's formula

Animation

<http://www.illdu.edu.in/mod/resource/view.php?id=5661>

To get Sawhorse from Fischer's formula, the reverse may be carried out.

(ii) Conversion of Newman or wedge-dash formula to Fischer's formula and vice versa

To convert Newman or wedge-dash formula to Fischer's formula, the molecule is first rotated to get an eclipsed (Sec. 6.3.1) stereoisomer (Figure. 6.11). It is then converted to an equivalent sawhorse projection by representing the hidden bond (bond between the front and the rear carbon atoms) in the Newman projection as a line in the plane of paper and showing rest of the bonds originating from the two ends of this line as shown in Figure. 6.11. Finally, the sawhorse formula is converted to Fischer's formula as described earlier in this section.

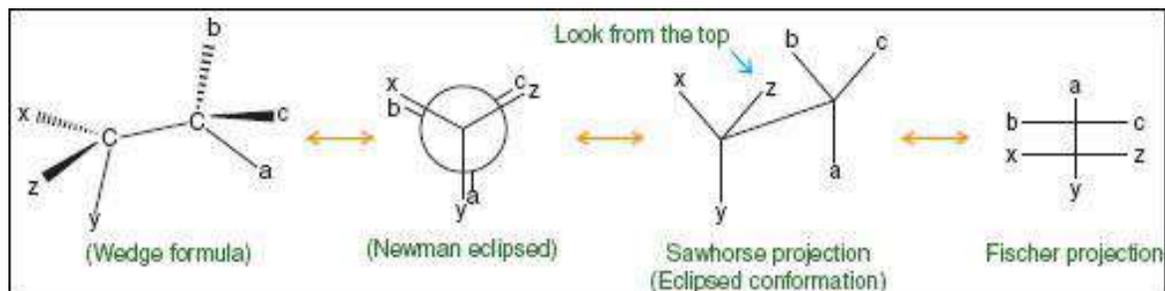


Figure 6.11: Conversion of Newman or wedge formula to Fischer's projection

The reverse may be carried out to obtain Newman or wedge-dash formula from Fischer's formula.

6.3 Conformations

Consider a simple hydrocarbon ethane, the free rotation of one carbon with respect to

another gives rise to various arrangements of the atoms differing in relative positions of hydrogen atoms attached to these carbon atoms. These different spatial arrangements of atoms in space resulting due to free rotation around a single bond are called **conformations** or **conformers** or **rotamers**.

The simplest molecule to show conformations is ethane.

6.3.1 Conformations of Ethane

While there are an infinite number of conformations about any sigma bond, in ethane two particular conformers are noteworthy and have special names. These are eclipsed and staggered conformations.

In eclipsed conformation, the C-H bonds on the front and back carbons are aligned with each other with dihedral angles as 0° . The following are the sawhorse (I), Newman's (II) and wedge-dash (III) formulas for the eclipsed conformation of ethane (Figure 6.12).

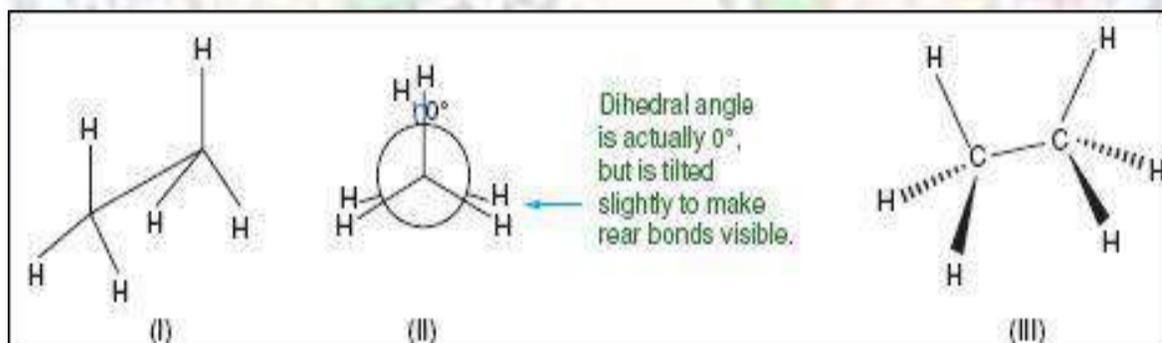


Figure 6.12: Eclipsed conformation of ethane

In staggered conformation, the C-H bonds on the rear carbon lie between those on the front carbon with dihedral angles of 60° . The following are the sawhorse (IV), Newman's (V) and wedgedash (VI) formulas for the staggered conformation of ethane (Figure. 6.13).

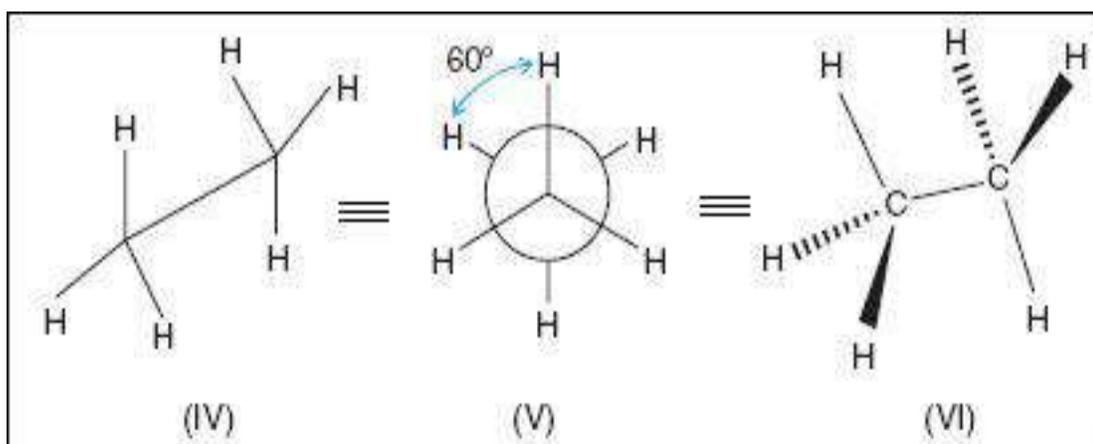


Figure 6.13: Staggered conformation of ethane

For ethane, the eclipsed and staggered are freely inter-convertible (Figure 6.14) and in between these two extreme conformations lie infinite number of conformations where the dihedral angle may be 1° or 2° or 10° or 15° or 50° or 58° or 59.1° or 59.9° etc. Thus, a slight change in the overall 3-D orientation in space results in a new conformer. Hence, the number of conformations for ethane are infinite. These in between conformations are called gauche or skew conformations.

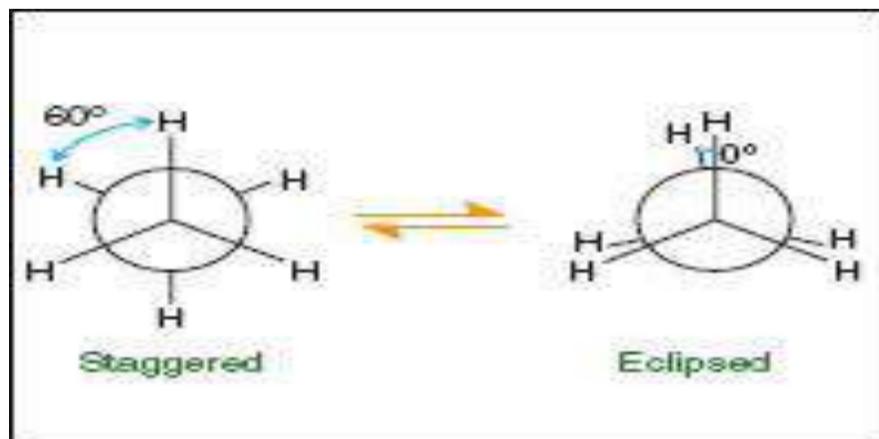


Figure 6.14: The eclipsed and staggered conformations of ethane

Energetically, not all conformations are equally favored. The eclipsed conformation of ethane is less stable than the staggered conformation by 12.6 kJ mol^{-1} (3 kcal/mol). The staggered conformation is the most stable of all possible conformations of ethane, since the angles between C-H bonds on the front and rear carbons are maximized at 60° . In the eclipsed form, the electron densities on the C-H bonds are closer together than they are in the staggered form. When two C-H bonds are brought into a dihedral angle of zero degrees, their electron clouds experience repulsion, which raises the energy of the molecule.

The eclipsed conformation of ethane has three such C-H eclipsing interactions (Figure 6.15), so one can infer that each eclipsed C-H 'costs' roughly 4.2 kJ mol^{-1} (1 kcal/mol). Eclipsing interactions are an example of a general phenomenon called steric hindrance, which occurs whenever bulky portions of a molecule repel other parts of the same molecule. Because such hindrance causes resistance to rotation, it is also called **torsional** (or **Pitzer**) **strain**.

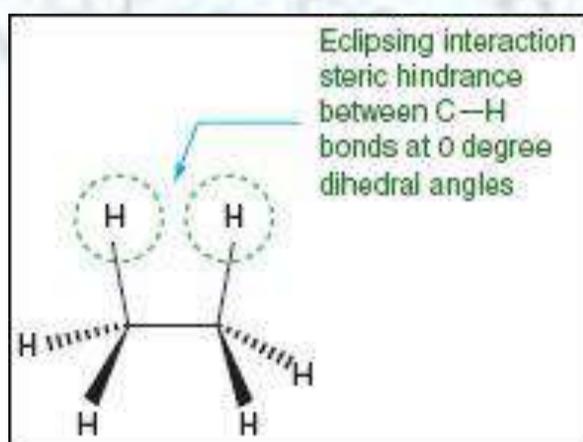


Figure 6.15: Eclipsing interactions in ethane

An energy of 12 kJ mol^{-1} (or 3 kcal/mol) is needed to overcome this strain in ethane. The energy diagram for rotation about the C-C bond in ethane is given in Figure 6.16. Note that this value is very small compared to the energy required to rotate C=C in ethene, which is 240 kJ mol^{-1} .

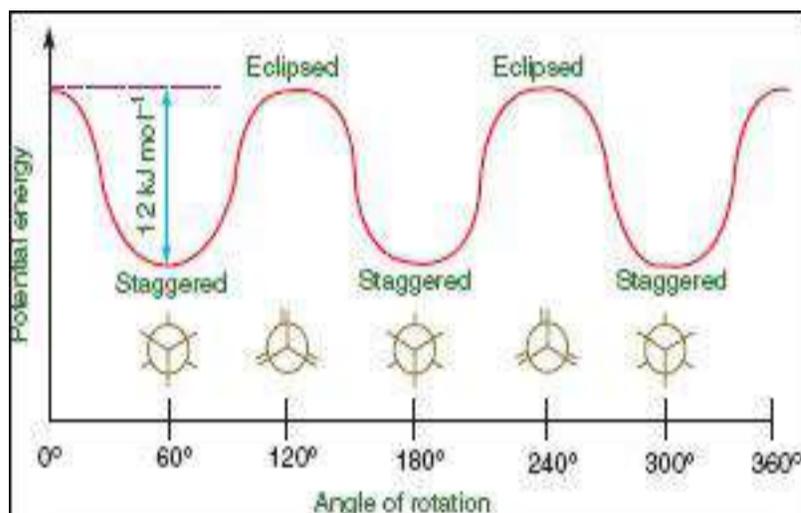


Figure 6.16: Energy diagram for rotation about the C-C bond in ethane

(or 60 kcal/mol) (the bond energy of a C=C, i.e. for π bond).

In the staggered conformation, there is maximum separation of the bonded electron pair while in eclipsed conformation the electron pair repulsions are maximum. A small contribution of identical C-H **dipole-dipole repulsion** on adjacent carbon atoms makes the eclipsed form less stable. Hence the staggered form is more stable than eclipsed form. Any other conformation, i.e. gauche conformations must have the energy content and stability, between these two extremes.

In a given sample of ethane, most molecules exist in staggered conformation and few in the gauche form and practically none in the eclipsed form at room temperature. However, the energy required for conversion of staggered to eclipsed conformation being small, the rotation about the carbon-carbon bond increases with increase in temperature increasing the contribution of gauche conformation and may be of the eclipsed form as well.

How do they get this energy to rotate and inter convert to one another? At room temperature, ethane molecules have enough energy to be in a constant state of rotation. These molecules constantly collide with each other, and in this process of collision, there is transfer of energy in between the molecules. A particular ethane molecule moving in eclipsed form when hits another one moving in staggered form, the former gets converted to staggered form and later to the eclipsed form and so on.

Because of this rapid rotation, it is impossible to isolate any particular conformation at room temperature. However, it is possible to isolate certain conformations at low temperature, when the energy of collision is not enough to overcome the energy barrier between the two conformations. Due to their rapid interconversion, conformations of a molecule are not considered as true isomers. Recall that isomers are the compounds having same molecular formula but at least one different physical or chemical property. Since the conformations, say eclipsed and staggered for ethane, cannot be bottled as pure eclipsed and pure staggered, they have no physical or chemical property different from each other. Any sample of ethane has these conformations rapidly interconverting into each other. So the property of the bulk is decided by the most stable one.

6.3.2 Conformations of n-Butane

We fix one C and rotate the other to get various conformations. In butane, as in ethane, there are infinite conformations due to the rotation of carbon-carbon single bonds, but the important ones can be visualized by considering the rotation between C2 – C3. Four of these are as shown in Figure 6.17.

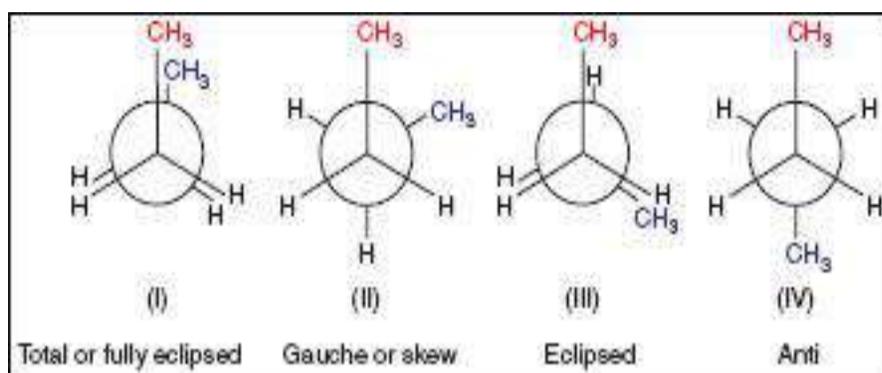


Figure 6.17: Four important conformations of n-butane

There are two kinds of eclipsed conformations. One having methyl-methyl eclipsing, called **total or fully eclipsed** (I) and is likely to be the conformation of highest energy (least stable) and the other having methyl-hydrogen eclipsing, called eclipsed conformation (III) having slightly lower energy than (I).

Similarly, there are two kinds of staggered conformations. One, where the two-methyl groups are 'anti' to each other (IV), called **anti-conformer**. It is the conformation of least energy (most stable) while the other one, called **gauche or skew conformation** (II), which is also staggered but has higher energy than (IV).

The overall stability order is thus: (IV) > (II) > (III) > (I) In addition, there will be thousands of gauche or skew conformations between them.

Note that on rotation of the C2-C3 bond, (I) gets converted to (II), which in turn gets converted to (III) and then to (IV), but (IV) gets converted to (III) and not (I). Hence, the rotation leads to (I) → (II) → (III) → (IV) → (III) → (II) → (I) → (II) → (III) → and so on. Using these, and the stability order, the energy diagram of n-butane is as shown in Figure 6.18.

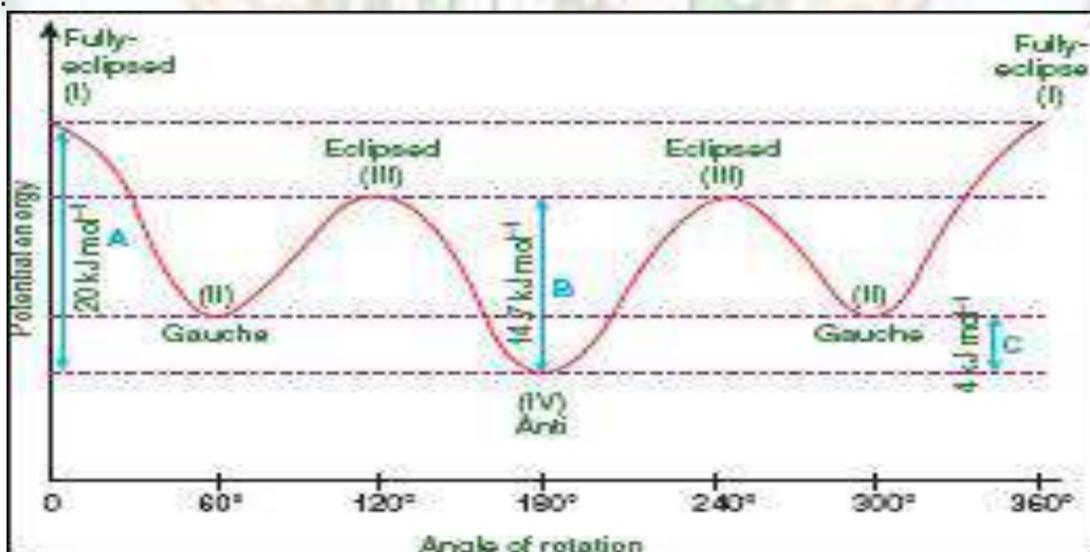


Figure 6.18: Potential energy diagram of n-butane showing correlation with C2-C3 rotation.

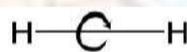
In the Figure 6.18, the high-energy barrier 'A' estimated at about 20 kJ mol^{-1} corresponds to eclipsing of two bulky methyl groups. Another barrier 'B' due to eclipsing of two methyl groups with hydrogen atoms is about 14.7 kJ mol^{-1} , which is slightly greater than the energy barrier in ethane. The three low energy troughs in the diagram are also not of equal energy. Compared to fully eclipsed (methyl-methyl) conformation a rotation of 180° gives fully staggered conformation, with methyl groups as far apart as they can be, which is the most stable one and trough of lowest energy in the diagram. A rotation of 60° and 300° also gives other staggered conformations somewhat less stable than first one but still corresponds to other potential energy minima.

Similarly the four maxima in curve are not of same energy. The two equal highest energy points at 0° and 360° correspond to fully eclipsed form (having methyl-methyl eclipsing) while two slightly lower maxima at 120° and 240° correspond to eclipsed form having two methyl-hydrogen eclipsing. In between the staggered minima and eclipsed maxima thousands of gauche or skew conformations exist along the curves differing slightly in angles and consequently in energy. In a sample of n-butane most molecules exist in staggered conformation and few in gauche or skew form, at room temperature. As the energy barrier between fully eclipsed and anti-form is small, the rotation about the carbon-carbon bond increases with the increase in temperature, increasing contribution of gauche or skew conformations. Here again the energy difference between various conformations is not sufficient to allow their separation as the anti-form is in dynamic equilibrium with other forms at room temperature.

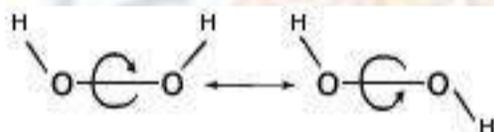
The physical and chemical properties of n-butane as a bulk is decided by the most stable 'anti-form' as most of the molecules prefer to be in this form. Thus n-butane (and similarly all alkanes) have zero dipole moment, as the net vector addition for the dipoles due to two methyl groups cancel each other. If the most stable form of n-butane had been the total eclipsed conformer, then the n-butane would have some dipole moment!

Common Misconception

1. Every single bond rotation leads to conformations.



No, not always. Consider hydrogen molecule.



The single bond rotates but there are no conformations, as there are no different stereo-orientations possible (not even two!). Whatever number of times, the single bond may rotate, the molecule always be linear.

2. Only C-C single bond rotation leads to conformations. No, not always. Consider the case of hydrogen peroxide, it also shows conformations.

The better requirement is: Conformations are the freely interconvertible 3D orientations in space.

6.3.3 Conformations of Cyclohexane

Cyclohexane has infinite conformations. In order to understand how, let us first understand why the stability of the cyclic rings is as follows:



Cycloalkanes are cyclic hydrocarbons, which form a homologous series with general formula C_nH_{2n} , whose first member is cyclopropane (with $n = 3$), next cyclobutane and so on. Let us first consider cyclopropane, cyclobutane and cyclopentane as shown in Figure 6.19.

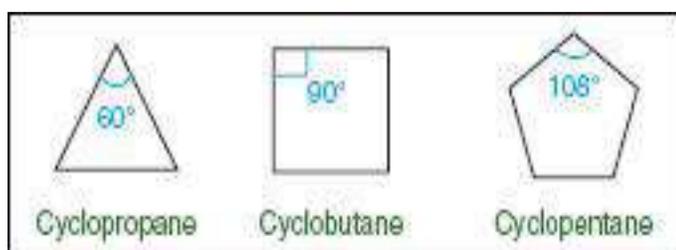


Figure 6.19: Members of cycloalkanes family

Stability order of the above three cycloalkanes can be explained in terms of '**Baeyer's strain theory**', which states that *the higher the angular strain, the lesser is the stability of the cyclic ring*.

Angular strain can be understood as follows: Although all the carbon atoms of these cyclic rings are sp^3 hybridised and thus normally the angles tend to be around $109^\circ 28'$. But the cyclopropane and cyclobutane have bond angles of 60° and 90° respectively. This deviation results in angular or torsional strain.

The greater the deviation from the normal tetrahedral angle, the greater will be the strain on the molecule. This leads to greater reactivity and lesser stability.

Magnitude of angular strain is given as,

$$\text{Angular Strain} = \left| \frac{1}{2} (109^\circ 28' - x) \right|$$

where, x = bond angle in the cyclic ring.

Cyclopropane (Bond angle, $x = 60^\circ$) is the most strained among all cycloalkanes. Cyclobutane has a bond angle of 90° while cyclopentane has a bond angle of 108° . Thus, out of these three, cyclopentane has least angular strain and should be most stable. According to the above calculation, the order of stability should be:

Cyclopentane > Cyclobutane > Cyclopropane

In fact, the same is observed experimentally. But this theory cannot be extended to **cyclohexane**.

Baeyer concluded that cyclopropane would be the most strained followed by cyclobutane. Cyclopentane would be strain free while cyclohexane would show a substantial amount of strain energy. Rings larger than cyclohexane would be highly strained and not capable of existing. Assuming cyclohexane to be a regular

hexagon, the bond angle in it would be 120° and there would be angular strain, greater than that in cyclopentane. Thus, the cyclopentane should be more stable than cyclohexane! But in fact cyclohexane is more stable than cyclopentane.

Heats of combustion can be used to measure the total amount of energy strain in a compound. Higher the value of heat of combustion, lesser is the stability of the compound. Table 6.1 gives heats of combustion per methylene group for a series of

Table 6.1 Heats of combustion ($\Delta_c H^\circ$)	
Molecule	$\Delta_c H^\circ$ in kJ per Methylene Group
Cyclopropane	697
Cyclobutane	685
Cyclopentane	664
Cyclohexane	659
Cycloheptane	662
Cyclooctane	664
Cyclodecane	664
Cyclododecane	660

cycloalkanes. Heat of combustion data indicate that Baeyer's theory was not fully correct. Cyclopropane and cyclobutane are quite strained but cyclopentane is more strained than cyclohexane. For larger rings, there is no regular increase in strain and rings of more than 14 carbons are strain free.

The higher stability of cyclohexane than cyclopentane was explained by **Herman Sachse**. According to him, these cyclic molecules (cyclohexane and onwards) try to

become non-planar, i.e., acquire puckered structure and thus relieve their angular strain.

Limitations of Baeyer's Strain Theory

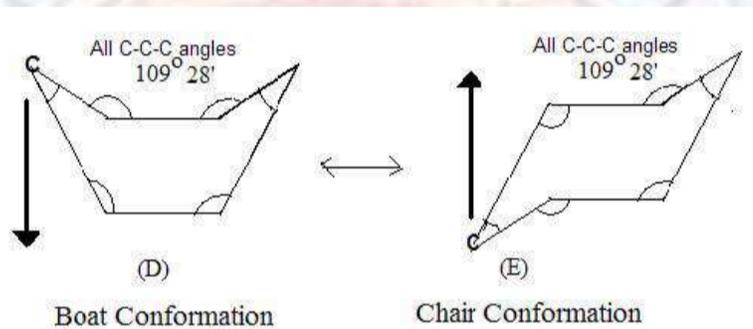
The Baeyer's strain theory could not be extended to cyclohexane and higher members of cycloalkanes.

Why was Baeyer's theory incorrect?

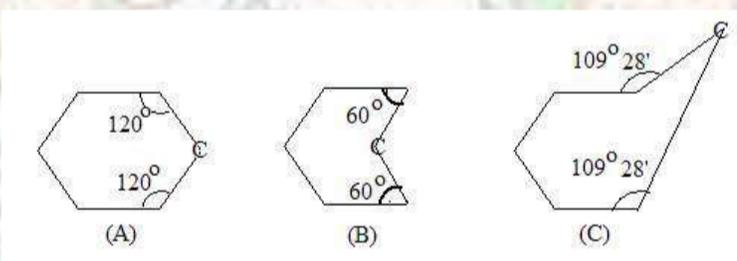
Baeyer assumed that all cycloalkanes are flat when in fact most adopt a puckered 3-D conformation. Furthermore, he did not consider the contribution of torsional strain to the overall strain energy of a molecule. In fact, rings larger than 3 atoms are not flat. Cyclic molecules can assume non-planar conformations to minimize angle strain and torsional strain by ring-puckering.

Visualize Them!

Let us start by visualizing cyclohexane as a regular hexagon lying on a plane where the bond angles are 120° . Let us look at the right half of the molecule and the carbon marked as 'C' in the fig (A) below. If we pick this carbon up and then bring it down inside, again in the plane, then the angles become 60° as shown in the fig. (B). But if we pick the carbon and stop somewhere mid-way, as shown in fig (C), the angles become $109^\circ 28'$, and that is what a regular tetrahedral angle is. And thus, there is no angular strain in this part of the molecule.



Similar treatment, when done on the left half of the molecule will give rise to two possibilities: either this carbon marked 'C' is lifted above to get the fig (D) or pushed down to get the fig. (E).



Thus the entire molecule has no angular strain (as all angles are $109^\circ 28'$) and hence the cyclohexane is more stable than cyclopentane.

Also as clearly evident, these carbons push up or down (i.e., ring flipping) easily and thus are freely inter-convertible into each other. Hence they are conformations.

There are two important conformations of cyclohexane called boat conformation and chair conformation. They are represented by sawhorse (Figure 6.20) and Newman's formulae (Figure 6.21). They are freely interconvertible and in between these two are infinite gauche or skew conformations. Out of these, the most stable conformation of cyclohexane is 'chair' conformation.

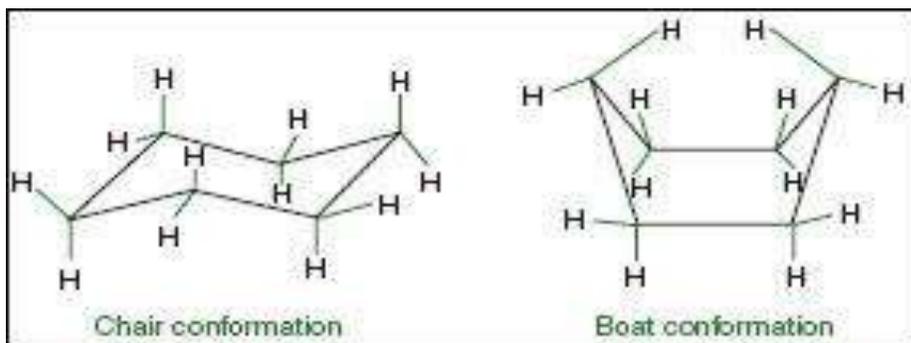


Figure 6.20: Sawhorse representation of chair and boat cyclohexane

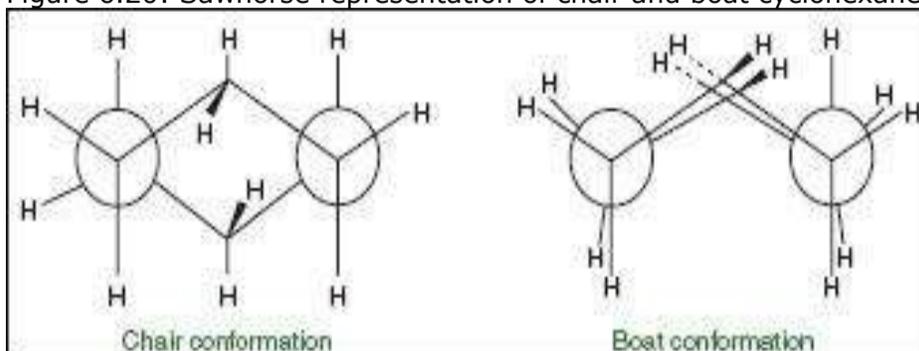


Figure 6.21: Newman's representation of chair and boat cyclohexane

Axial and Equatorial Hydrogen Atoms

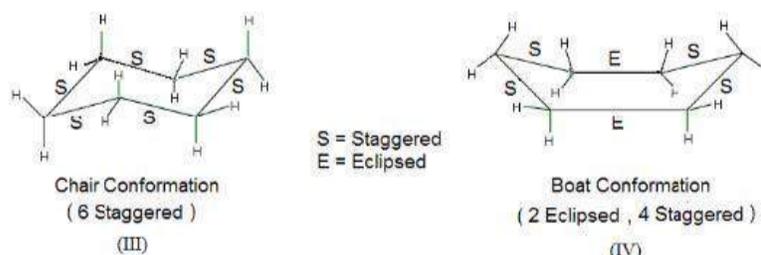
In *chair cyclohexane*, there are two different types of C-H bonds, and thus two different types of hydrogen atoms as substituents.

Think

Visualise the chair and boat conformations, along the C-C bonds as marked below (I and II) and compare with the n-butane case.

In the chair conformer, this C-C view can be compared with the anti form of n-butane where the atoms attached to these two carbon atoms are in staggered conformation. On the other hand, the boat form when viewed through the marked C-C bond gives the eclipsed view and is comparable with the total eclipsed form of n-butane.

Similar view on all the six C-C bonds in chair conformation give all staggered orientation, but in the boat conformations, four are staggered but two are eclipsed (see III and IV below). Hence the chair is overall more staggered and thus more stable than boat.



The C-H bonds, which point vertically upward or downward, are called **axial** hydrogen atoms (H_{ax}) (Figure 6.22). There are six of these, three upward and three downward bonds, and they alternate up/down/up, etc., around the ring.

The other six bonds, which radiate away from the "equator" of the ring, are called **equatorial** hydrogen atoms (H_{eq}) (Figure 6.22). There are six of them, three of which are "slant up" and three of which are "slant down", again alternating around the ring.

Stereochemistry

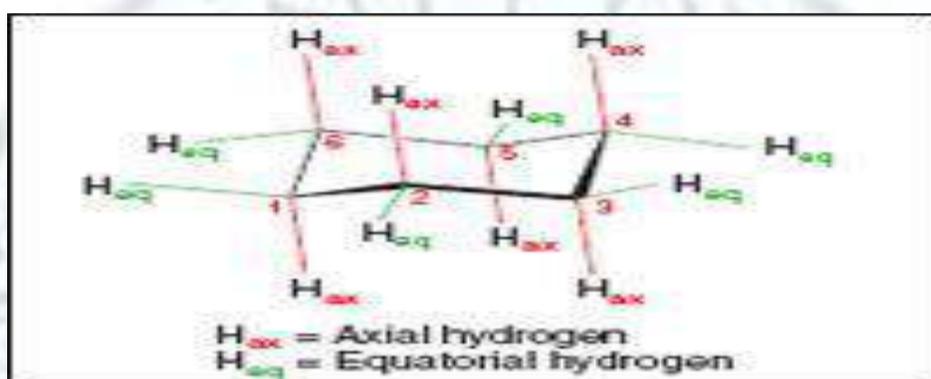
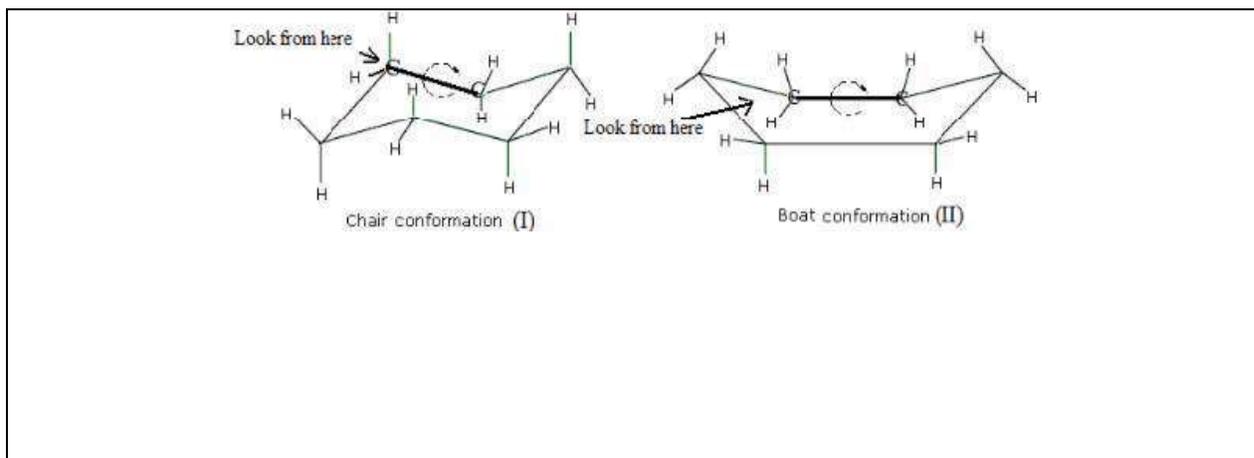


Figure 6.22: Chair conformation of cyclohexane showing axial and equatorial H-atoms

Flagpole Hydrogen Atoms

The C1 and C4 axial hydrogen atoms of the chair form are known as **flagpole hydrogen atoms** in the boat form (Figure.6.23). The steric interaction of these two H atoms, known as the **flagpole interaction** also destabilizes the boat conformation. Torsional strain and flagpole interactions cause boat conformation to have considerably higher energy than chair conformation. The chair form is more stable than the boat form by 44 kJ mol^{-1} .

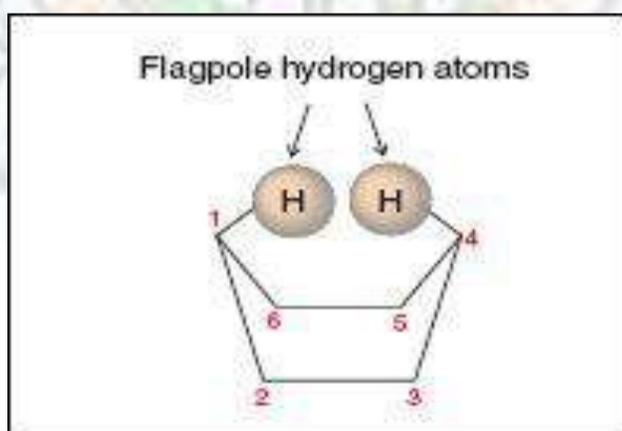


Figure 6.23: Boat conformation of cyclohexane

Check your Progress

What do you understand by 'torsional strain'? Why the chair conformation of cyclohexane is more stable than the boat conformation?

6.4 Configurations

Unlike conformations, configurations (or configurational stereoisomers) are rigid or fixed molecules, i.e. they cannot be interconverted into each other freely. They are of two types: Geometrical isomers and Optical isomers.

6.4.1 Geometrical Isomerism

If due to the presence of a double bond (or ring), the free rotation between the carbon atoms is prevented and the two groups attached to each carbon are different, then it results in two different relative arrangements of atoms or groups in space called **configurations**.

Geometrical Isomerism in Alkenes

Consider the two orientations of 2-butene in space (Figure 6.24).

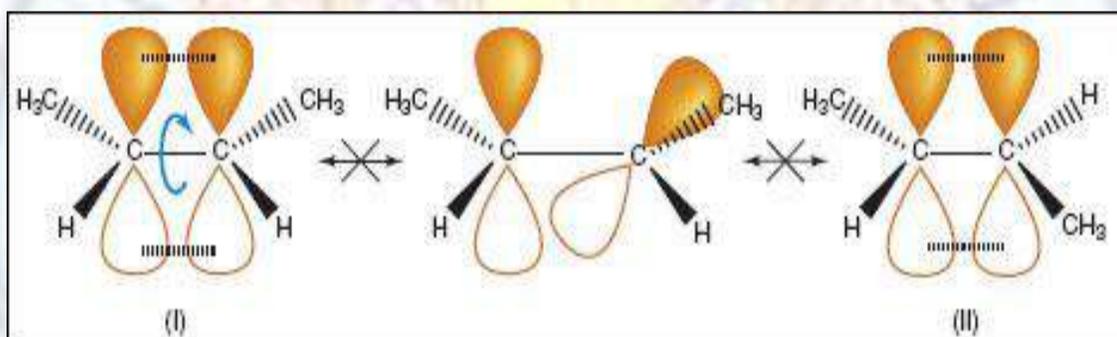


Figure 6.24: Two 3-D structures of 2-butene

The molecule (I), if rotated around the C=C double bond will get converted to (II), but this does not happen on its own. Although, this may happen at temperatures higher than 200°C , double bond does not remain a double bond (but that's a reaction and cannot happen on its own!). This is because more energy is required to break a π -bond. It is due to this restricted rotation around

the C=C double bond that 2-butene gets trapped in two different stereoisomers at room temperature: (I) and (II), called configurations. If (I) and (II) would have been freely convertible, then they would have been conformations. When conformations get trapped and become non-convertible or rigid, they become configurations.

(I) and (II) have same molecular formula and same structural formula, but they differ in their geometries. Both are planar molecules and their geometries are such that two groups (say methyls) are on the same side (or nearer) in (I) and are on the opposite sides (or farther) in (II). (same is true for hydrogen atoms). These types of stereoisomers are called as

geometrical isomers.

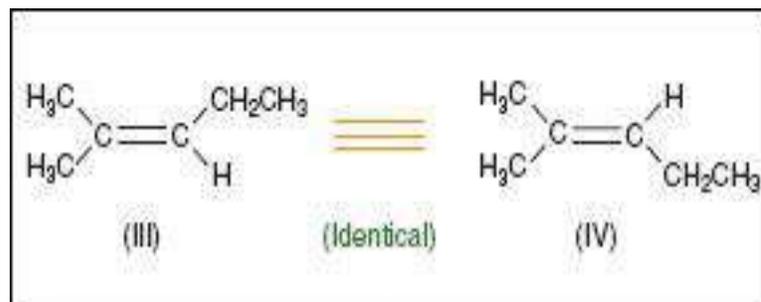


Figure 6.25: 2-methyl-pent-2-ene

Next, consider the molecule (III) (Figure 6.25), which does not exhibit geometrical isomerism. On carrying out the restricted rotation around the C=C double bond as earlier, the molecule (IV) is obtained. (III) and (IV) are not geometrical isomers. This is because they are superimposable and thus are same or identical. Thus (III) has no geometrical isomer.

Checking the superimposition tells us whether the two molecules are same or not. If the two molecules are same, they can't be isomers. This is true whenever, any or both of the doubly bonded carbon atoms are joined to identical groups. Hence, the condition required for exhibiting geometrical isomerism in molecules having C=C double bond may be given as follows:

In the given framework around the C=C double bond (Figure 6.26), a and b must be different, as well as a' and b' must be different (i.e., $a \neq b$ and $a' \neq b'$); but a and a' may be same or different. Similarly, b and b' may be same or different.

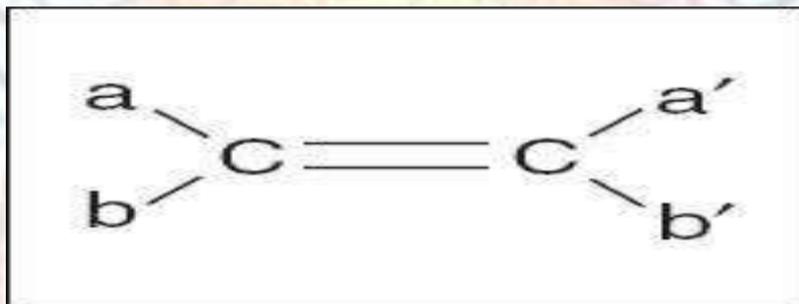


Figure 6.26: Framework required for geometrical isomerism around C=C double bond

In cases, where $a=a'$ and $b=b'$ (or at least one out of these is true), the two possible relative arrangements (Figure 6.27) are named as *cis* and *trans*.

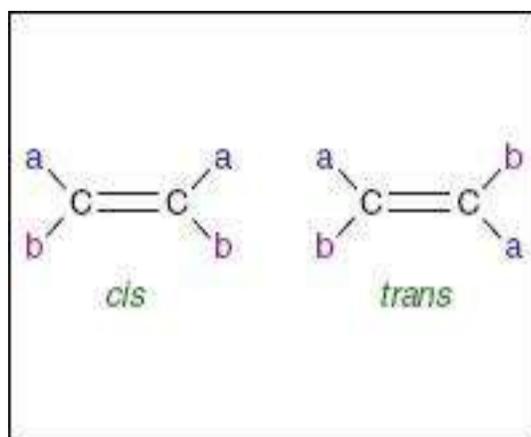


Figure 6.27: *cis* and *trans* alkenes

The isomers with identical groups on the same side of the double bond are called ***cis-isomers***, while those having identical groups on the opposite side of the double bond are called ***trans-isomers***. This is why geometrical isomerism is also sometimes called *cis-trans* isomerism.

Note that IUPAC names of both the compounds are the same. They are thus, not structural isomers, but stereoisomers.

In cases, where $a \neq a'$ and $b \neq b'$, i.e., all the four groups are different, they also show geometrical isomerism, but are not named as *cis* and *trans*, rather they are named as E and Z. E and Z nomenclature has been discussed later. For example, the following (Figure 6.28) are geometrical isomers.

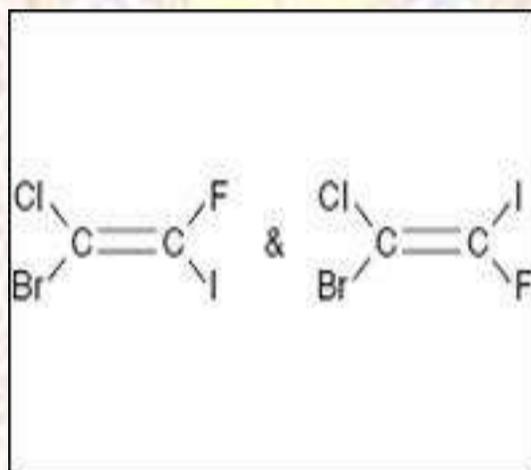
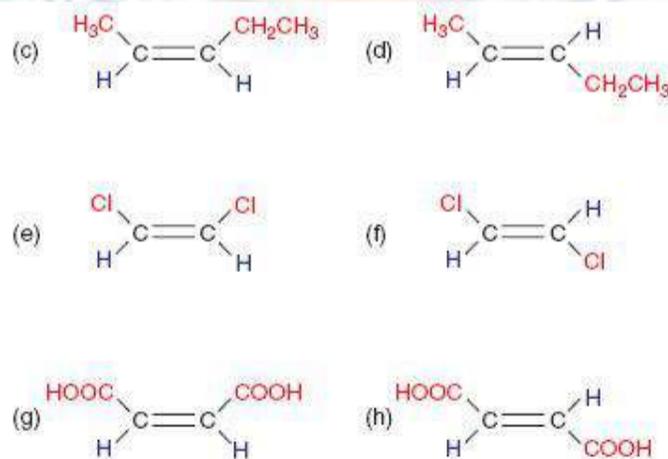


Figure 6.28: Geometrical isomers

Assign *cis* or *trans* designation to the following geometrical isomers.



Solution

- | | |
|--|---|
| (a) <i>cis</i> -2-Butene | (b) <i>trans</i> -2-Butene |
| (c) <i>cis</i> -2-Pentene | (d) <i>trans</i> -2-Pentene |
| (e) <i>cis</i> -1,2-Dichloro-ethane | (f) <i>trans</i> -1,2-Dichloro-ethane |
| (g) <i>cis</i> -But-2-en-1,4-dioic acid
(Maleic acid) | (h) <i>trans</i> -But-2-en-1,4-dioic acid
(Fumaric acid) |

Geometrical Isomerism in Cyclic Compounds

Cyclic compounds also exhibit geometrical isomerism. In these compounds although there is no double bond, the cyclic ring provides the restricted rotation. Figure 6.29 represents cyclic geometrical isomers.

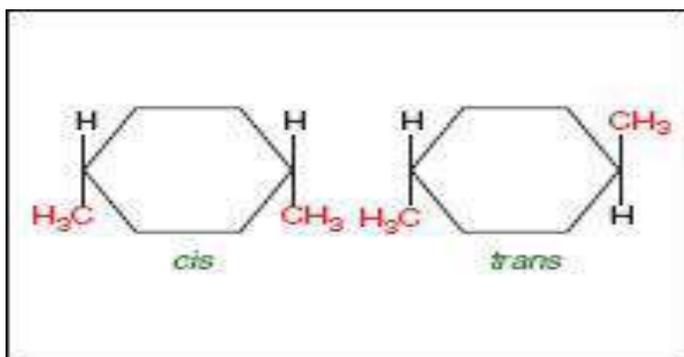


Figure 6.29: Geometrical isomers of 1,4-dimethylcyclohexane

Effect of Geometrical isomerism on Physical and Chemical properties

Geometrical isomers are true isomers. They differ in one or more physical or chemical properties (recall that isomers are the compounds having same molecular formula but at least one different physical or chemical property).

Difference in Physical properties:

The *cis*-isomers have generally lesser stability, higher dipole moment, etc. while *trans*-isomers have higher stability and lower dipole moments. The *trans* isomer usually has the higher melting point while the *cis* isomer has the higher boiling point.

Example 1: The Table 6.2 shows the melting point and boiling point of the *cis* and *trans* isomers of 1,2-dichloroethene.

Table 6.2 Melting Point and Boiling Point of the Isomeric <i>cis</i> and <i>trans</i> - 1,2-dichloroethene		
Isomer	Melting Point (°C)	Boiling Point (°C)
<i>cis</i> -1,2-dichloroethene	-80	60
<i>trans</i> -1,2-dichloroethene	-50	48

Example 2: *cis* and *trans* isomers of but-2-ene (Table 6.3)

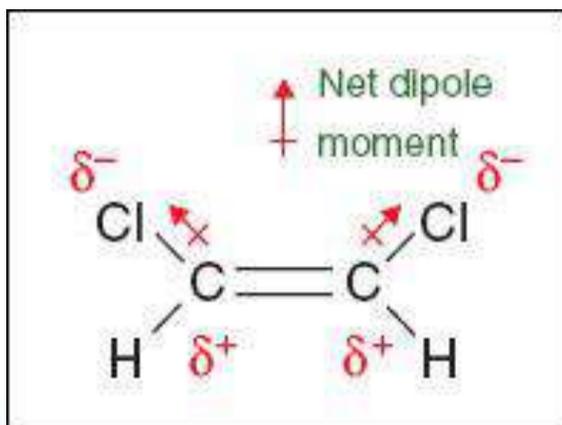
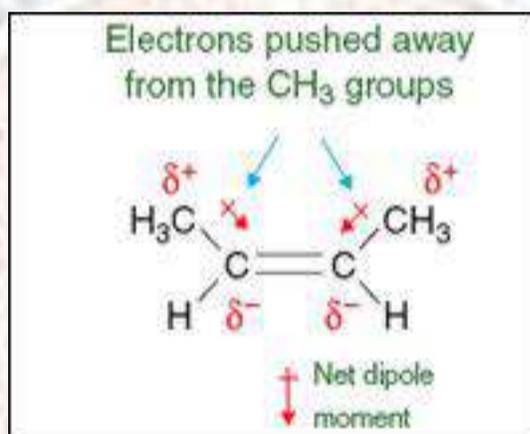
Table 6.3 Melting Point and Boiling Point of the Isomeric <i>cis</i> and <i>trans</i> -but-2-ene		
Isomer	Melting Point (°C)	Boiling Point (°C)
<i>cis</i> -but-2-ene	-139	4
<i>trans</i> -but-2-ene	-106	1

Why is the boiling point of the cis isomers higher?

There must be stronger intermolecular forces between the molecules of the *cis* isomers than between *trans* isomers. Consider the examples of 1,2-dichloroethene and 2-butene. Both of the isomers (*cis* and *trans*) have exactly the same atoms joined up in exactly the same order. That means that the van der Waals dispersion forces between the molecules will be identical in both cases. The difference between the two is that the *cis* isomer is a polar molecule whereas the *trans* isomer is non-polar.

cis-case

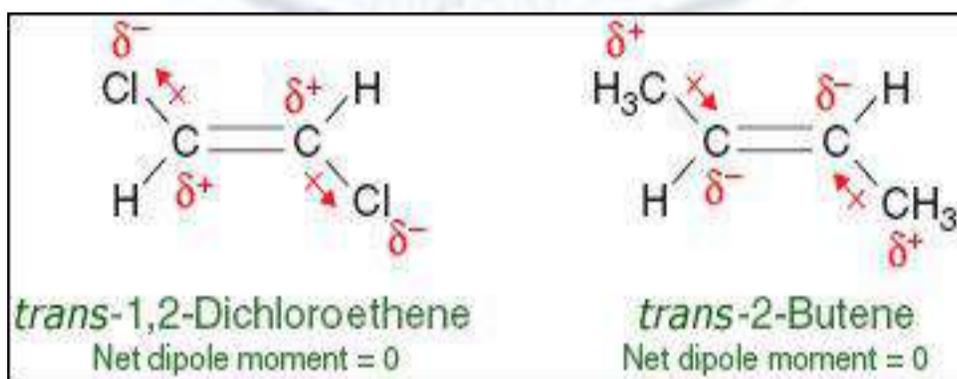
In the *cis* isomer of 1,2-dichloroethene (Figure 6.30), both chlorine atoms are on the same side of the molecule. That means that one side of the molecule will have a slight negative charge while the other will be slightly positive (by the $-I$ effect). Therefore, the molecule will be polar.

Figure 6.30: Polar *cis*-1,2-dichloroetheneFigure 6.31: Polar *cis*-2-butene

Because of polarity in *cis*-isomers, there will be dipole-dipole interactions as well as dispersion forces, which require extra energy to break. This raises the boiling point.

trans-case

By contrast, although there will still be polar bonds in the *trans* isomer, the overall molecule is non-polar. The slight charge on the top of the molecule (Figure 6.32) is exactly balanced by an equivalent charge on the bottom. The slight charge on the left of the molecule is exactly balanced by the same charge on the right.

Figure 6.32: Nonpolar *trans* alkenes

This lack of overall polarity means that the only intermolecular attractions these molecules experience are van der Waals dispersion forces. Less energy is needed to separate them, and so their boiling points are lower.

Why is the melting point of the cis isomers lower?

For intermolecular forces to work well, the molecules must be able to pack together

efficiently in the solid (crystal lattice). *Trans* isomers pack better than *cis* isomers. The "U" shaped *cis* isomers don't pack well as compared to the straight shaped *trans* isomers. The poorer packing in the *cis* isomers means that the intermolecular forces aren't as effective as they should be and so less energy is needed to melt the molecule. Hence, they have a lower melting point.

Difference in Chemical properties

Chemical properties usually are same for geometrical isomers but sometimes they may differ. For example, maleic acid undergoes dehydration to give maleic anhydride on heating (Fig 6.33) but its *trans* isomer, fumaric acid, does not show such reaction under the same reaction conditions. This is because the later has two -COOH groups farther away and hence, does not react and undergo dehydration.

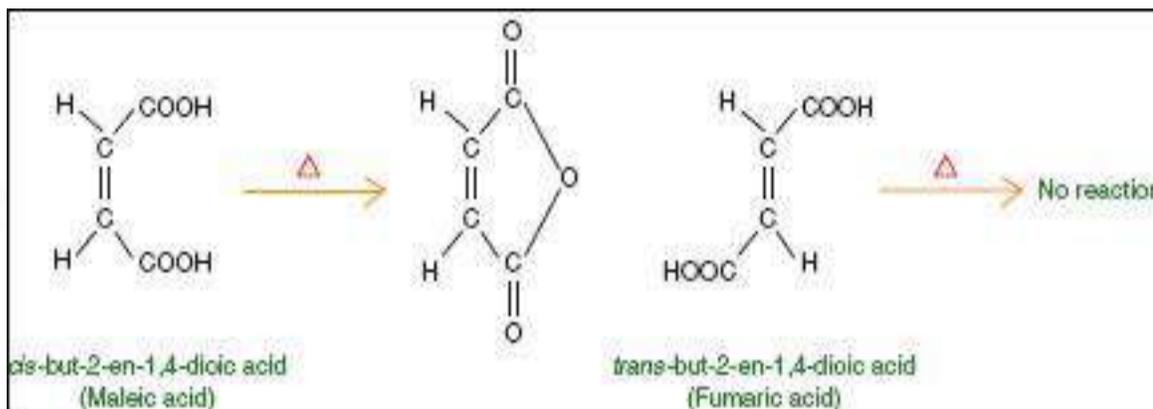


Figure 6.33: Effect of heating on maleic acid and fumaric acid Check your progress How will you differentiate between conformations and configurations?

Geometrical Isomers with Two Double Bonds

Consider the following two cases. **Case 1: Asymmetrical diene:** Total number of geometrical isomers is four.

Example: Hept-2,4-diene.(Figure. 6.34). None of the geometrical isomerism Figure 6.34 are same (or super-imposable).

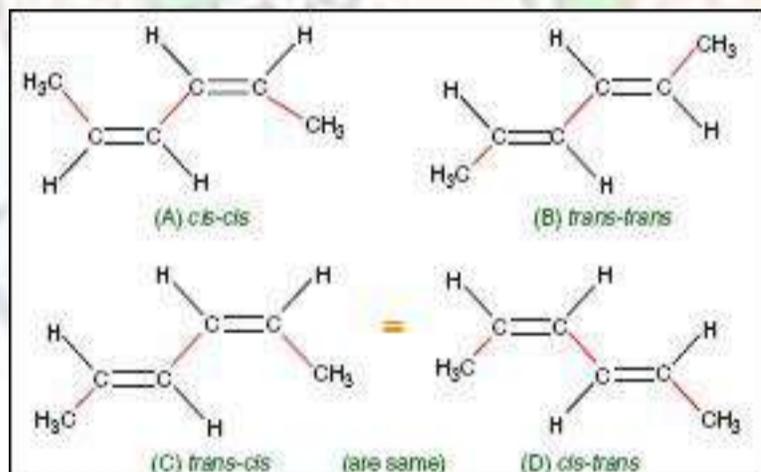


Figure 6.34: Four geometrical isomers of Hept-2,4-diene

Case 2: Symmetrical diene: Total number of geometrical isomers is three.

Example: Hex-2,4-diene (Figure. 6.35).

(C) and (D) are superimposable on each other and hence are same or identical (Figure 6.35.). Thus, there are only three stereoisomers and not four as in the earlier case.

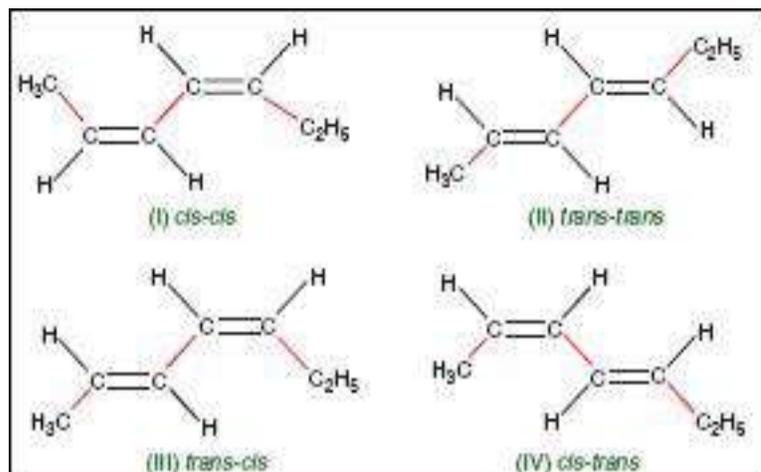


Figure 6.35: Three geometrical isomers of Hex-2,4-diene

6.4.2 Optical Isomerism

Optical isomerism is a type of stereoisomerism, where the compounds with same molecular and structural formula differ in the spatial distribution of the atoms or group of atoms that changes their behaviour towards the plane-polarized light. Optical activity is the ability of the molecule to rotate the plane of plane-polarized light. Before studying optical isomerism, one must know about plane-polarized light and its different behaviour towards different substances. Plane-Polarized Light Ordinary light can be considered as an electromagnetic wave, which has electric and magnetic vibrations in all the directions perpendicular to the path of propagation. Ordinary light is made of light waves of different wavelengths. By using prism or diffraction grating, light of a single wavelength, known as **monochromatic light** is obtained. If the light waves pass through a polarizer, which is made of Nicol prism, then only electric vibrations emerge in one plane. Such a beam of light is called **plane-polarised light**. Plane polarised light is produced in an instrument called polarimeter (Figure. 6.36).

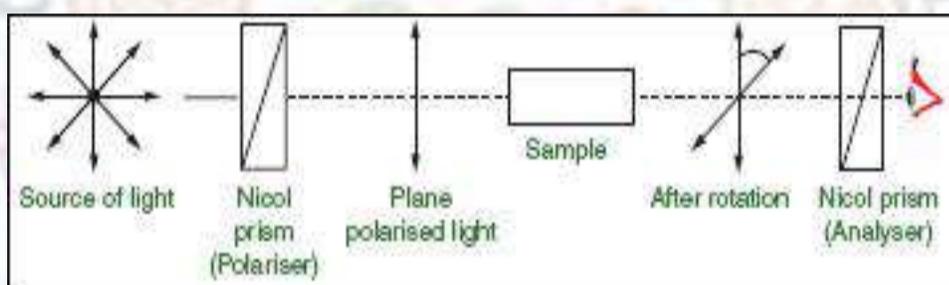


Figure 6.36: Schematic representation of a polarimeter

When monochromatic, plane-polarised light passes through certain organic compounds, the plane of polarisation is changed. These compounds are referred to as optically active compounds.

Polarimeter

The angle of rotation by which the plane polarised light is rotated, can be measured by an analyzer in a polarimeter. A diagram of the polarimeter is shown in Figure 6.36.

A polarimeter consists of a light source, two nicol prisms and a sample table to hold the substance. The sample tube is placed between two nicol prisms. The prism placed near the source of light is called **polarizer** while the other placed near the eye is called **analyzer**. The aqueous solution of the substance is placed between the polarizer and analyzer. The analyzer can be rotated by certain angle to compensate for the rotation of the plane-polarized light by the optically active sample. The observed rotation (α_{observed}) is expressed in degrees.

If the substance rotates plane polarised light *to the right (clock wise)*, it is called **dextro rotatory** (Greek for right rotation) or the *d*-form and it is indicated by placing a (+) sign before the degrees of rotation. If light is rotated *towards left (anti clock wise)*, the substance is said to be **laevo rotatory** (Greek for left rotating) or the *l*-form and a negative (-) sign is placed before the degrees of rotation. The dextro rotatory and laevo rotatory compounds are called **optically active compounds**.

If light is not-rotated towards any side, i.e., comes out undeviated, then the substance is said to be **optically inactive**. Since the rotation of the polarized light is caused by interaction of the photon of light with the 3D molecule, *the extent of rotation depends on,*

- i. Spatial structure.
- ii. The number of molecules in the path of light beam, which in turn is a function of concentration and length of the tube containing optically active compound.
- iii. Solvent used (if any)
- iv. Temperature.
- v. Wavelength of the light used.

To make optical rotation independent of all these factors, it is defined in terms of initial physical constant, "specific rotation".

Specific Rotation

It is the number of degrees of rotation observed if a 1 dm (10 cm) long tube is used, and the compound being examined is present to the extent of 1 g/mL. This is usually calculated from observations with tubes of other lengths and at different concentrations by means of

Observed rotation (α) = $+134^\circ$

$$c = \frac{2 \text{ g}}{10 \text{ mL}} = 0.2 \text{ g mL}^{-1}$$

$$l = 25 \text{ cm} = \frac{25}{10} \text{ dm} = 2.5 \text{ dm}$$

Therefore,

$$[\alpha]_D^T = \frac{\alpha_{\text{obs}}}{l \cdot c} = \frac{+134^\circ}{0.2 \cdot 2.5} = +268^\circ$$

Hence, the specific rotation of the compound is $+268^\circ$.

Check your Progress

What is a plane-polarized light? How is it produced?

the equation,

$$\text{Specific rotation} = \frac{\text{observed rotation}}{\text{length} \times \text{concentration}}$$

$$[\alpha]_D^T = \frac{\alpha_{\text{obs}}}{l \times c}$$

or

where l represents length of the polarimeter tube (in dm) and c represents concentration of a solution or density for a pure liquid in g/mL (or g/cm³). T is the temperature and D is the wavelength of the light used.

The specific rotation is as much a property of a compound as its melting point, boiling point, density, or refractive index. For example, the specific rotation of the 2

methyl-1-butanol is $[\alpha]_D^{20} = -5.90^\circ$. Here '20' is the temperature (in $^\circ\text{C}$) and 'D' is the wavelength of the light used in the measurement (D line of sodium 5893Å).

Example

The observed rotation of 10 mL of a solution containing 2.0 g of a compound when placed in 25 cm long polarimeter tube is $+134^\circ$. What is the specific rotation of the compound?

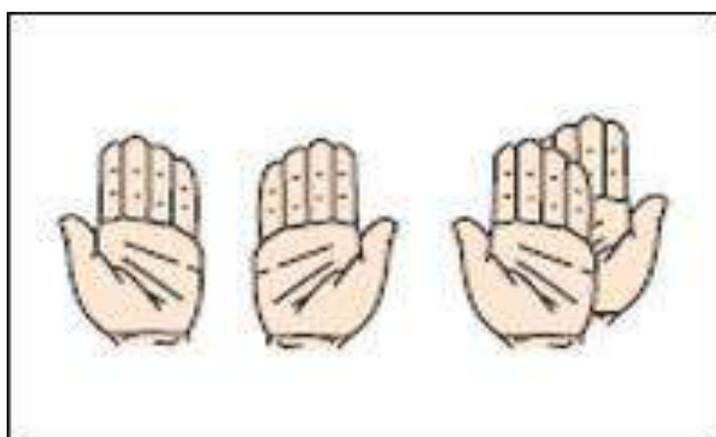
Solution

Molecular Asymmetry and Chirality

Stereochemistry

The foundation for modern stereochemistry was laid when Louis Pasteur in 1848 observed that crystals with mirror images of each other exist just like our left and right hands (Figure 6.37).

Figure 6.37: Non-superimposable left and right hands



Stereochemistry

An object, which is non-superimposable on its mirror image, is said to be chiral. Chiral means asymmetrical.

A molecule that lacks all the elements of symmetry (i.e., plane of symmetry, centre of symmetry and alternating axis of symmetry, discussed later in this section) is called **asymmetric**. Due to lack of symmetry, such molecules are not superimposable on their mirror images. For example, our left hand and right hand are non-superimposable mirror images of one another.

Molecules, having one or more elements of symmetry have an identical mirror image and are called **symmetric** molecules. The projection of object and its mirror image are superimposable for such molecules. For example, a sphere, a cone, and a tetrahedron are all identical to their mirror images and can, thus, be superimposed.

It was found that many organic compounds, which were optically active, had one thing in common: the presence of a chiral carbon atom. The word chiral is derived from the Greek word "*kheir*" which means, "hand" and property of being chiral is called **chirality** or **handedness**. Chirality results from an asymmetry in the molecule. When four different groups are present around a carbon atom then that carbon atom is called chiral carbon or asymmetric carbon (Figure 6.38). Presence of a chiral carbon atom generally leads to asymmetry in a molecule.

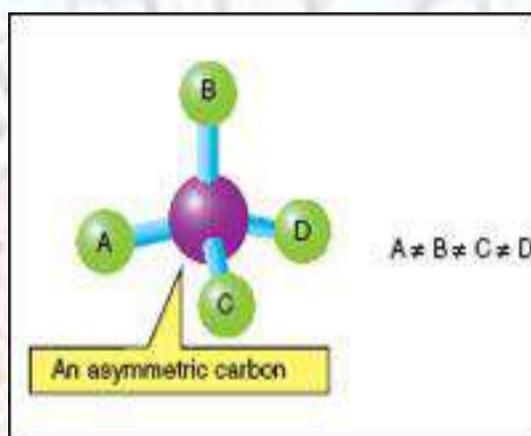


Figure 6.38: Chiral carbon atom

For example, lactic acid, $\text{CH}_3\text{CH}(\text{OH})\text{COOH}$ (Figure 6.39).

However, the presence of chiral carbon atoms is not a guarantee that the molecule will be optically active, and many molecules even if do not contain any chiral carbon, can still be optically active.

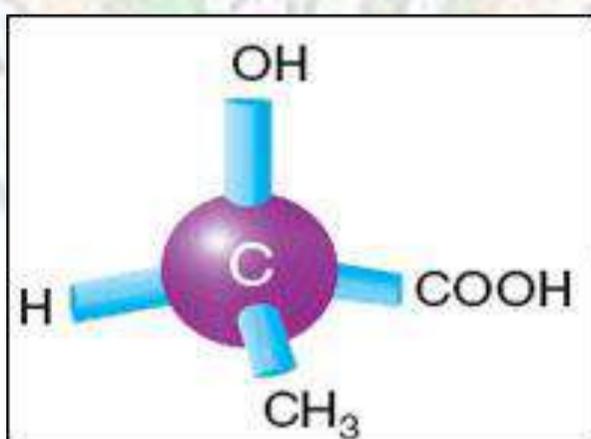


Figure 6.39: Lactic acid having chiral carbon

When a molecule contains only one asymmetric carbon, it is always chiral and hence, shows chirality. But with molecules having more than one chiral or stereogenic centre, the necessary condition for chirality is not just the presence of asymmetric carbon atoms but the asymmetry of the molecule as a whole.

A molecule as a whole is asymmetric or dissymmetric if it does not possess any element of symmetry such as,

(i) plane of symmetry

(ii) centre of symmetry

(iii) alternating axis of symmetry.

(1) **Plane of symmetry (mirror plane):** It represents the plane bisecting the molecule such that each half of the molecules is the mirror image of the other half. For example, tetrafluoroethane and tartaric acid (Figure 6.40.).

(2) **Centre of symmetry (Ci):** A molecule is said to have a centre of symmetry if any line drawn from the centre of the molecule meets identical atoms at equal distances from the centre. This is also called centre of inversion. For example, ethane (Figure 6.41).

(3) **Alternating axis of symmetry:** It represents an n-fold axis of symmetry such that when molecule possessing such an axis is rotated through an angle of $360^\circ/n$ about this axis and then reflected across a plane perpendicular to this axis, an identical structure results. The detailed discussion of this element of symmetry is beyond the scope of the syllabus.

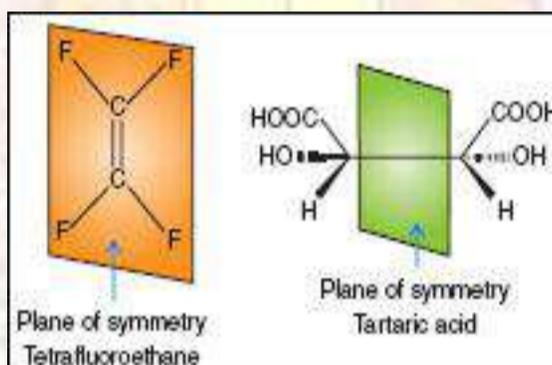


Figure 6.40: Plane of symmetry

Enantiomers

A pair of stereoisomers, which are related to one another as an object and its non-superimposable mirror image are called **enantiomers**. A chiral molecule is always non-superimposable on its mirror image and such non-superimposable mirror image molecules are called as enantiomers or enantiomorphs [Figure 6.42 and Figure 6.43 (a)].

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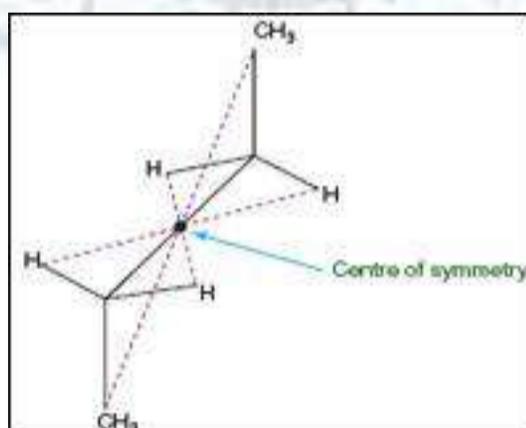


Figure 6.42: Enantiomers

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Enantiomers

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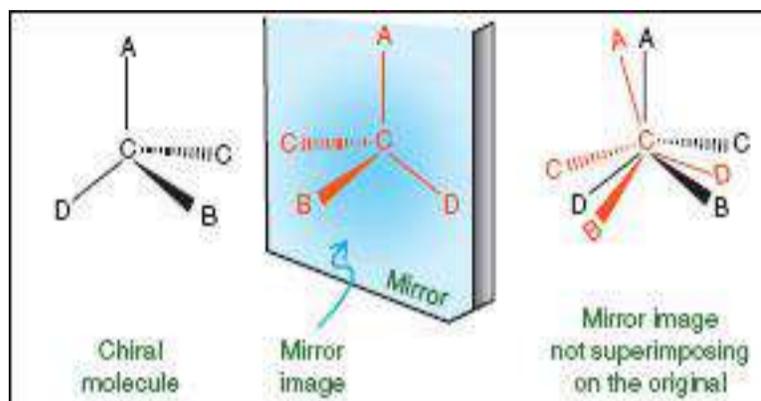


Figure 6.42: Enantiomers

Characteristics of Enantiomers

The important properties of the enantiomers are as follows:

- (i) Enantiomers are always non-superimposable on their mirror images.
- (ii) Enantiomers are optically active in nature and they rotate the path of plane polarised light to the same extent but in opposite directions.
- (iii) The physical properties of enantiomers such as melting points, boiling points, density, refractive index, solubility etc. are same.
- (iv) The enantiomers have identical chemical properties. However, they differ in the rates of reactions towards the optically active substances, but not towards optically inactive substances. For example, (+) lactic acid and (-) lactic acid, esterify with ethanol at the same rate but they react at different rates with (+) and (-) 2-butanol, $\text{CH}_3\text{CH}(\text{OH})\text{C}_2\text{H}_5$, which is optically active.
- (v) Enantiomers have different biological properties. For example, the carbohydrate (+) glucose plays an important part in animal metabolism and also in the fermentation industry. But (-) glucose has no such role.

Conditions for Optical Activity or Optical Isomerism

Molecules that are not superimposable on their mirror images are chiral. They may or may not have chiral carbon atoms in them! Chirality is the necessary and sufficient condition for the existence of enantiomers. That is to say, a compound whose molecules are chiral can exist as enantiomers, while a compound whose molecules are achiral (without chirality) cannot exist as enantiomers. The necessary condition for chirality is not just the presence of asymmetric carbon atoms but also the asymmetry of the molecule as a whole.

Racemic Modification

The mixture containing enantiomers (dextro and leavo) in equal proportion will have zero optical rotation as the rotation due to one enantiomer cancels the rotation due to the other. Such a mixture is known as **racemic mixture or racemic modification**. A **racemic mixture** is optically inactive due to external compensation (i.e. one stereoisomer cancels the optical activity of the other stereoisomer). The prefix \pm is used to specify the racemic nature of the particular sample, as, for example (\pm)-lactic acid or (\pm)-2-methyl-1-butanol.

It is possible to separate a racemic mixture into (+) and (-) enantiomers by suitable methods. This process of separation is known as **resolution** that shall be discussed later.

Stereochemistry of Compounds with two or more symmetric or Chiral Carbon Atoms

There are certain molecules, which contain more than one asymmetric carbon atoms but may still be optically inactive! Let us extend our study to the molecules with more than one chiral carbon atoms in them.

If a compound has n chiral carbon atoms (or chiral centres) then **the maximum number of stereoisomers = 2^n** . Note that it is the maximum number and not actual number of stereoisomers. Further they may or may not be all optically active.

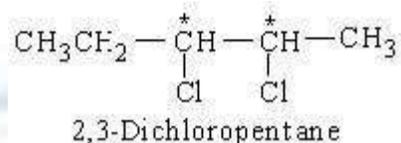
The next question that arises is how can one know the total number of stereoisomers and how many of them will be optically active? For deriving a general formula, one must study in detail the case of $n=2$.

Consider the following two cases:

Case I: Non-symmetrical molecule of the type: $Cabc.Cxyz$ (or $Cabc.Cabd$)

Case II: Symmetrical Molecule of the type: $Cabc.Cabc$

Case I: Unsymmetrical molecule: As an example, consider the case of 2,3-dichloropentane. This compound contains two chiral centers, C-2 and C-3 as each of them is joined to four different groups.



Using the 2^n formula there should be maximum of $2^2 = 4$ stereoisomers. Using Fischer's projection formula, the four stereoisomers can be represented as I, II, III and IV (Figure 6.45). Out of these, structure I and II are mirror image, and as they are not superimposable hence they are enantiomers. Their wedge-dash formulas and sawhorse formula are also shown in Figure 6.45, which provide their 3-D views. Similarly, III and IV are also non-superimposable mirror images and hence are also enantiomers.

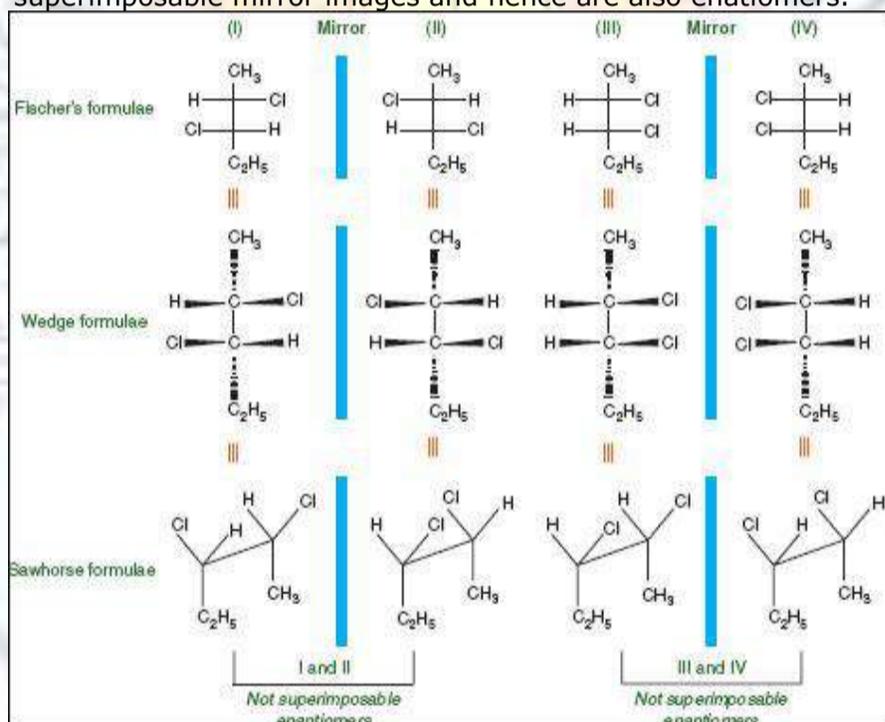


Figure 6.45: Four stereoisomers of 2,3-dichloropentane

As stated earlier, the maximum number of stereoisomers for a compound having two chiral carbon atoms is four.

Let's check out why not more than four? Consider another Fischer projection (A) as shown below in Fig 6.46. Is this really the fifth stereoisomer or is identical to one of the above four? To get the answer, one must convert this in sawhorse projection as shown in Fig 6.46.

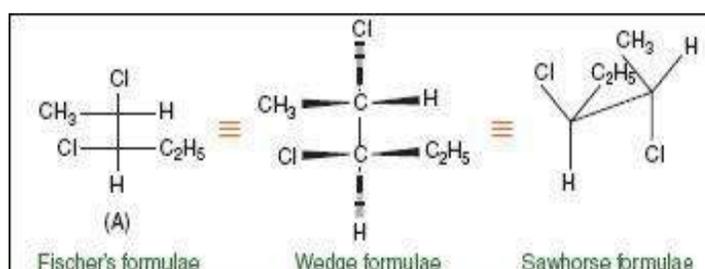


Figure 6.46: Interconversion of Fischer's formula into sawhorse formula

Stereochemistry

All the other four stereoisomers (I, II, III and IV) have the format as shown in Fig 6.47 for the Fischer or sawhorse projection.

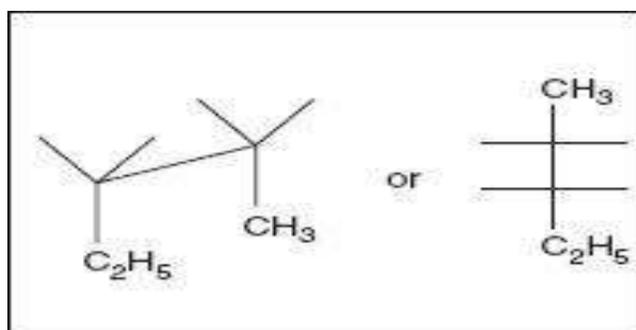


Figure 6.47: Format of sawhorse or Fischer's formula for I, II, III, and IV stereoisomers



Hence, convert the molecule (A) also in this format as shown in Fig. 6.48, by rotating the C-C single bond (recall that C-C single bond rotation leads to the formation of conformations, and thus, are same). The result is the stereoisomer (III).

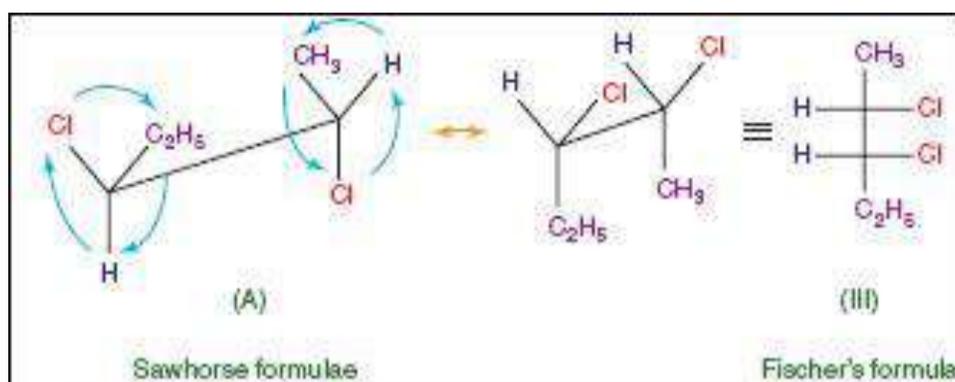


Figure 6.48: Interconversion of sawhorse formula into Fischer's formula

A short-cut, that can be directly applied to the Fischer's projection to get the other Fischer projection of the same molecule is as shown in Fig 6.49, i.e., move the three substituents across the chiral carbon in a cyclic manner (clockwise or anti-clockwise).

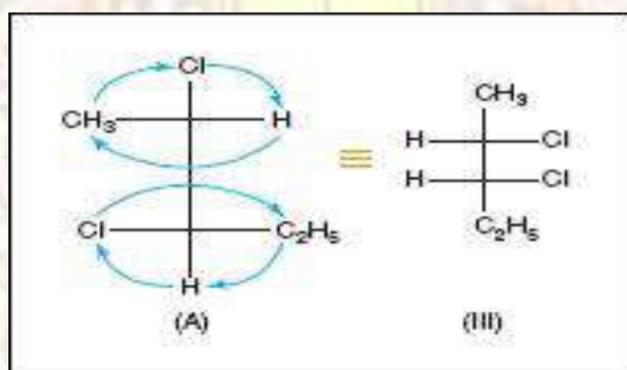


Figure 6.49: Conversion of one Fischer into another Fischer

Hence, (A) and (III) are the different conformation of same molecule. So should not be counted again and again. Similarly, try making any other structure that will be the conformation of either I, or II, or III, or IV. Actually, each one of the four (I, II, III, and IV) will have infinite conformations, but none of the infinite conformations of one is identical to any of the infinite conformations of the other and so on.

Thus, the maximum number of stereoisomers for $n=2$, is 4. Similarly, **2^n is the maximum number of stereoisomers for a molecule with n chiral carbon atoms.**

Now, if we try to interconvert I and II by rotations about the carbon-carbon bonds, we would find that they are not interconvertible. Thus, each of them is capable of retaining its identity and if separated from its mirror image, will show optical activity— one being dextrorotatory and the other laevorotatory.

Similarly, III and IV are also not interconvertible into each other. Structures III and IV thus represent a second pair of enantiomers.

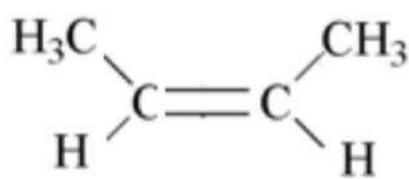
Diastereoisomers

What is the relationship between I and III; between II and III; between I and IV between II and IV? They are stereoisomers but not enantiomers as they are not mirror images. **Stereoisomers that are non-superimposable and not mirror images of each other are called diastereoisomers.** The pairs of diastereomers in this case are: I and III; II and III; I and IV; II and IV.

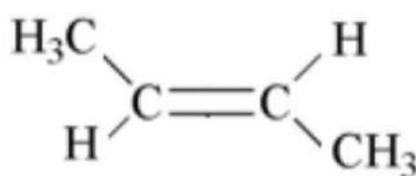
Hence, for the molecule 2,3-dichloropentane, there are four ($= 2^2$) stereoisomers in total and all of them are optically active. There are two pairs of enantiomers (I & II; III & IV).

Did you know?

Yes, as they are also non-superimposable and not mirror image molecules with same structural formula. *Diastereoisomers* is thus a broad term and is applicable to both the geometrical and optical isomers unlike enantiomers.



cis-2-butene



trans-2-butene

Properties of diastereoisomers

Diastereoisomers have similar chemical properties, since they have same structural formula. However, their chemical properties are *not identical*. In the reaction of two diastereoisomers with a given reagent, neither the two sets of reactants nor the two transition states are mirror images, and hence except by mere coincidence – will not be of equal energies. The *Eact* values will be different and so will be the rates of reaction.

Diastereoisomers have different physical properties, they have different melting points, boiling points, solubilities in a given solvent, densities, refractive indexes, and so on. Diastereoisomers differ in specific rotation; they may have the same or opposite signs of rotation, or some may be inactive.

For the above four cases we may say that I and II will have $+x^\circ$ and $-x^\circ$ specific rotation and for III and IV it will be any other value that is, $-y^\circ$ and $+y^\circ$.

As a result of differences in boiling point and solubility, diastereoisomers can in principle, be separated from each other by fractional distillation or fractional crystallization. Also because they differ in their molecular shapes and polarity, they differ in adsorption, and can be separated by chromatography.

Case II: Symmetrical Molecule (Meso Compounds): Let us consider 2,3-dichlorobutane, which also has two chiral centres. But, does this compound, too, exist in four stereoisomeric forms or lesser? And whether all of them are optically active or not?

The maximum number of stereoisomers are $2^2 = 4$. These are shown in Fig 6.50.

Using wedge-dash and sawhorse formulae as before, it is clear that the two structures V and VI are mirror images that are not superimposable and interconvertible; they are therefore enantiomers, and each should be capable of showing optical activity.

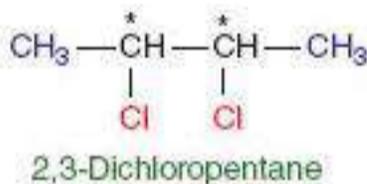


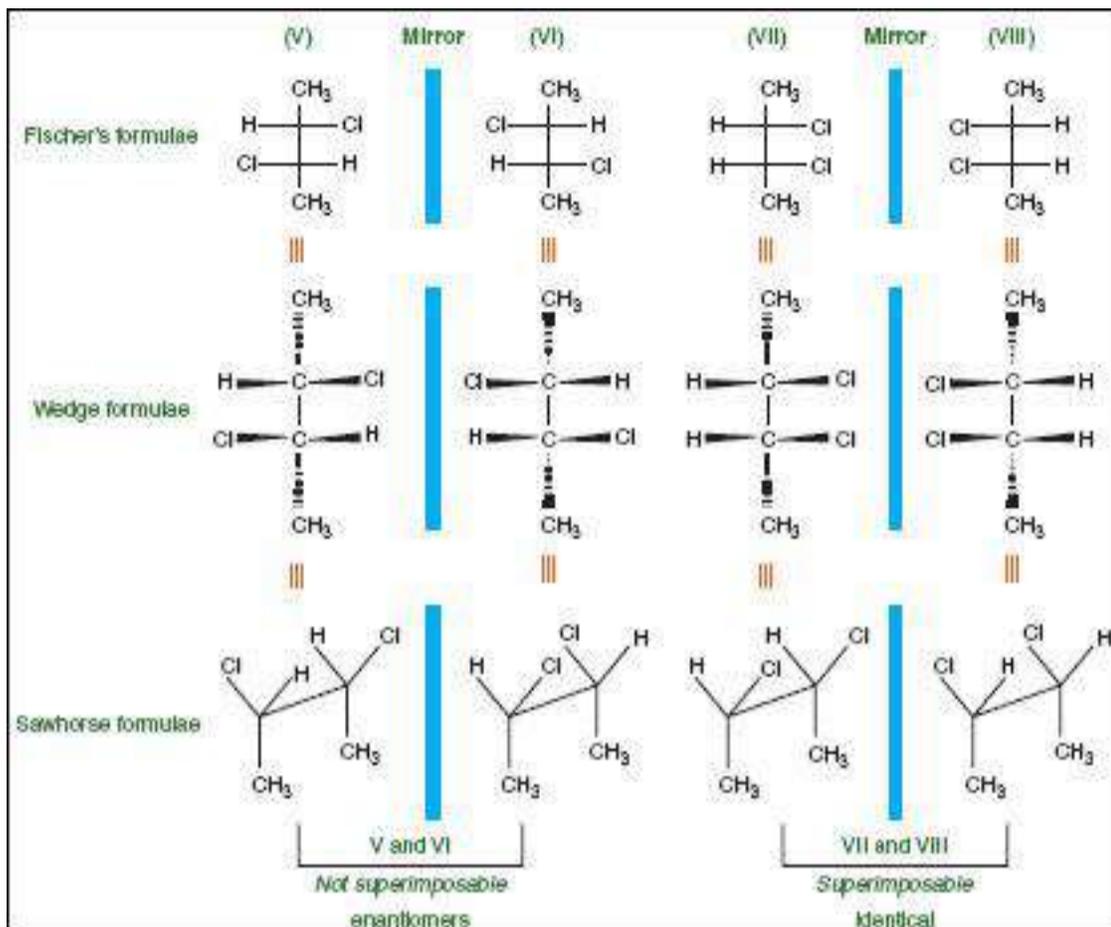
Figure 6.50: Stereoisomers of 2,3-dichlorobutane

But similar treatment when done on VII and VIII, one finds that they are superimposable (rotate by 180° in plane). Thus, VII coincides in every respect with VIII. Hence, they are identical or same. One molecule is standing straight, the other is upside down!

In spite of its two chiral centers, VII on the whole is not chiral as it is super-imposable on its mirror image molecule (VIII). It cannot exist in two enantiomeric forms, and it cannot be optically active. It is called a *meso* compound.

A **meso compound** is one whose molecules are superimposable on their mirror images even though they contain chiral centers.

A *meso* structure can be recognised by the fact that (in at least one of its conformations) one half of the molecule is the mirror image of the other half. This can be seen for *meso*-2,3-dichlorobutane by imagining the molecule to be cut by a plane lying where the dotted line is drawn (Fig 6.51). The molecule has a *plane of symmetry*, and thus cannot be chiral.

Figure 6.51: Plane of symmetry in *meso*-2,3-dichlorobutane

Thus, a *meso* compound is optically inactive. Its optical inactivity is due to **internal compensation**, i.e., optical activity contributed by one half of the molecule is compensated (or cancelled) by the other half of the molecule.

A *meso* compound, is the one whose molecules although possesses two or more than two chiral centres, but are optically inactive due to the presence of a plane of symmetry. Note that a *meso* compound will always contain even number of chiral centres.

Also structure VII is found to be a diastereoisomer of V and of VI as they are not superimposable and not mirror images. Thus, the diastereomeric pairs are: VII & V; VII & VI.

Thus, in total there are only three ($=2^2 - 1$) stereoisomers for 2,3-dichloro-butane. Out of these one is optically inactive (i.e., *meso*) and rest of the two are optically active.

Let us consider another example, tartaric acid. There, being two chiral carbon atoms, four stereoisomers of tartaric acid may be written as shown in Fig 6.52.

Stereoisomers of tartaric acid

Of these, A and B are optically active and are related to each other as object and image and are enantiomers. But, C and D are identical as they are super-imposable on each other and hence, are not isomers. C (or D) is the *meso*-tartaric acid and possess a plane of symmetry as shown in Fig 6.53.

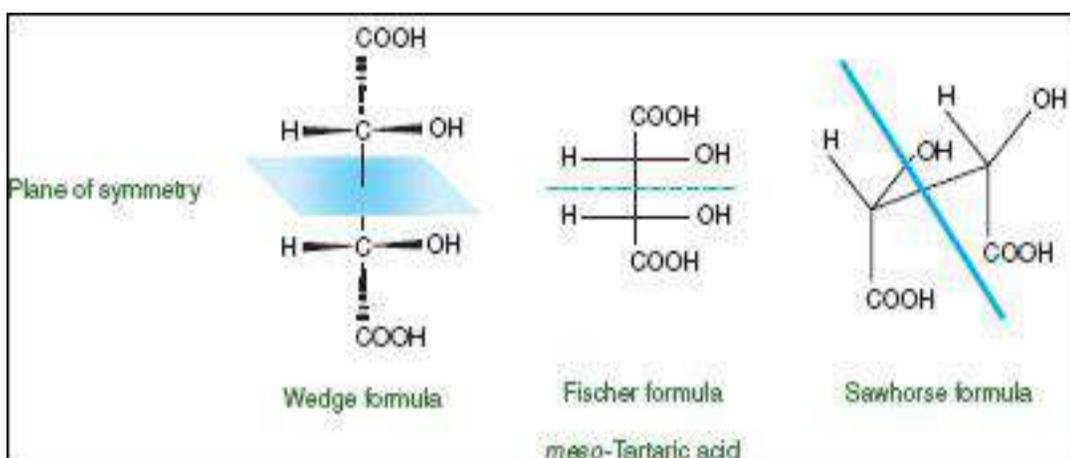


Figure 6.53: Plane of symmetry in *meso*-Tartaric acid

Therefore, tartaric acid exists only in three isomeric forms out of which one is *meso* (optically inactive) and the other two are optically active i.e., *d* or (+) and *l* or (-).

Some physical properties of the isomers of tartaric acid are given in Table 6.4.

Table 6.4 Specific Rotation and Melting Points of Stereoisomers of Tartaric Acid		
(+)-tartaric acid	$[\alpha]_D = +13^\circ$	m.p. 172 °C
(-)-tartaric acid	$[\alpha]_D = -13^\circ$	m.p. 172 °C
<i>meso</i> -tartaric acid	$[\alpha]_D = 0^\circ$	m.p. 140 °C

As is evident from the above cases, the presence of **two chiral centers** can lead to the existence of as many as four stereoisomers. Extending this further, for compounds containing **three chiral centers**, there could be as many as eight stereoisomers ($2^3 = 8$); for compounds containing **four chiral centers**, there could be as many as sixteen stereoisomers ($2^4 = 16$).

Formula to calculate number of stereoisomers of a compound having n chiral centres.

For the unsymmetrical molecules with n chiral centres, the number of possible stereoisomers are 2^n . (All of these will be optically active and exist as enantiomeric pairs).

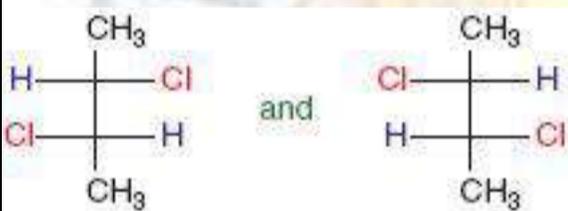
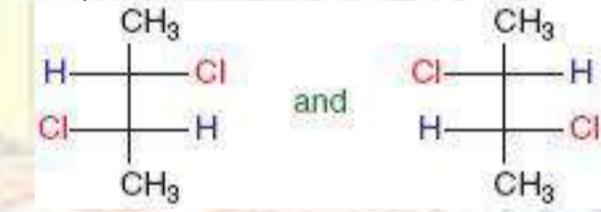
For symmetrical molecules, there are $2^n - 1$ stereoisomers. (Every symmetrical



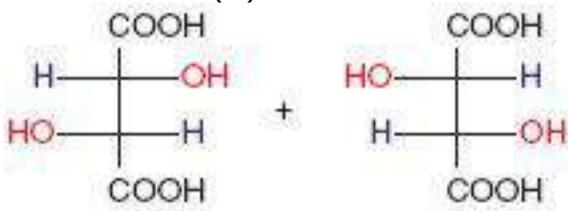
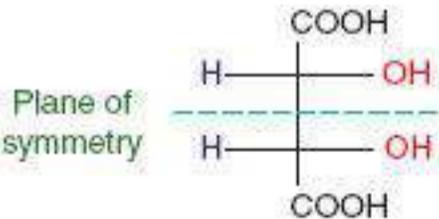
molecule will have only one *meso* stereoisomer which will be optically inactive, rest all will be optically active, as enantiomeric pairs).

Note that these formulae are also valid for geometrical isomers. Recall the case of compounds having one double bond and fitting into criteria for showing geometrical isomerism, ($n=1$) have 2 geometrical isomers. For non-symmetrical dienes ($n=2$), it is $2^n = 2^2 = 4$. For symmetrical dienes, it is $2^{n-1} = 2^{2-1} = 2$.

Comparative Study of the Enantiomers and Diastereoisomers

Enantiomers	Diastereoisomers
They form non-superimposable mirror images.	They do not form non-superimposable mirror images.
They have identical physical properties.	They have different physical properties.
They have identical chemical properties.	They have similar but not identical chemical properties.
They rotate the path of plane polarized light to the same extent but in opposite direction.	They may or may not rotate the path of plane polarized light in the same direction but to different extent.
They cannot be separated from each other by physical methods.	They can be separated by physical methods like fractional crystallization, distillation etc.
They are optically active.	They may or may not be optically active.
Example: 	Example: 

Comparative Study of the Racemic Mixture and Meso Compounds

Racemic Mixture	Meso Compound
An equimolar mixture of two enantiomers, both optically active {one (+) and the other (-)}	A single compound which is optically inactive although it has two or more chiral carbon atoms (or stereocentres)
Can be separated into two pure optically active components by the process called resolution.	Cannot be separated into two pure optically active components as it is a single compound
No element of symmetry in any of the two molecules.	It possesses a plane of symmetry .
Has external compensation of optical activity. Optical activity of one stereoisomer ($+x^\circ$) is cancelled by optical activity of another ($-x^\circ$) stereoisomer.	Has internal compensation of optical activity. Optical activity of one half of the molecule is cancelled by the other half of the molecule.
Example: equimolar mixture of (+) and (-) tartaric acid. 	Example: <i>meso</i> -tartaric acid 

Resolution of Racemic Modification

The process of separation of a racemic mixture into the enantiomers is called **resolution**. Many optically active pure compounds are obtained from natural sources, since living organisms usually produce only one enantiomer of a pair. For example, only (-)-2-methyl-1-butanol is formed in the yeast fermentation of starches, and only (+)lactic acid ($\text{CH}_3\text{CHOHCOOH}$) in the contraction of muscles etc. Indeed, we are composed of these optically active substances; we eat them, wear clothes, and read books made of optically active cellulose. The proteins that make up for muscles and other tissues, the glycogen in our liver and glucose in our blood, the enzymes and hormones that enable us to grow and that regulate our bodily processes – all these are optically active. Most of naturally occurring compounds are optically active because the enzymes that bring about their formation and often the raw materials from which they are made are themselves optically active.

But most of the synthetic organic reactions result in the formation of the **racemic mixture**. Since, the enantiomers present in the racemic mixture have identical physical properties (like melting points, boiling points, refractive indices, reactivities, and solubilities etc.), except for direction of rotation of polarized light, hence they cannot be separated by the usual simple methods like fractional crystallization or fractional distillation, etc. There are many methods for their separation, but the most widely used is by the chemical method in which racemic mixture is converted to diastereomeric mixture.

Chemical method (conversion into diastereomeric mixture)

This is the best method available for resolution. The majority of resolutions that have been carried out depend upon the reaction of organic bases with organic acids to yield salts (or of organic acids with alcohols to yield esters).

A. Resolution by Salt formation I. Resolution of organic acids: Consider a racemic mixture of enantiomeric organic acids, $(\pm)\text{-HA}$. It can be separated into pure enantiomeric acids by reaction with an optically active base, say a levorotatory base, $(-)\text{-B}$. The mixture of enantiomeric acids on reaction with an optically active base results in the formation of two diastereomeric salts as shown in Fig. 6.54. These diastereoisomeric salts have, of course, different physical properties, including solubility in a given solvent. They can, therefore, be separated by a simple technique, i.e., fractional crystallization.

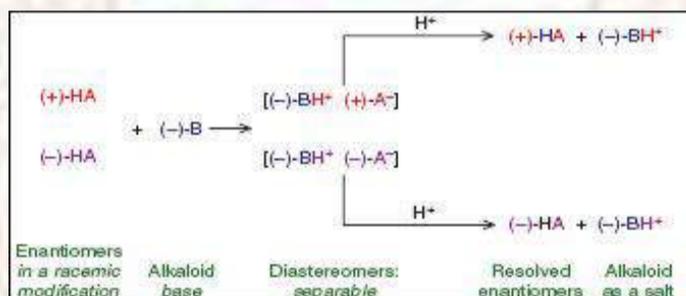


Figure 6.54: Separation of enantiomers of organic acid from their racemic mixture by salt formation

The optically active acid can then be recovered from each salt by the addition of a strong mineral acid. The most commonly used optically active organic bases for this purpose are (-)-brucine, (-)-quinine, (-)-strychnine, and (+)-cinchonine. For example, resolution of a racemic mixture of 2-chloro-propanoic acid by salt formation with (+) 1-phenylethylamine as shown in Fig. 6.55.

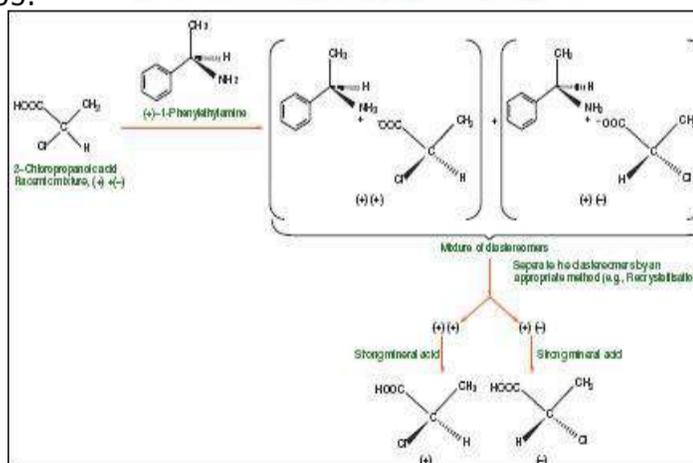


Figure 6.55: Separation of enantiomers of 2-chloro-propanoic acid from their racemic mixture by salt formation with (+)1-phenylethylamine

Stereochemistry

II. Resolution of organic bases: This is carried out by reversing the process just described, i.e., using naturally occurring optically active acids, like (-)-malic acid and reacting with the racemic mixture of organic bases.

B. Resolution of alcohols: Since alcohols are neither appreciably basic nor acidic, they cannot be resolved by direct formation of salts. Yet, they can be resolved by a rather ingenious adaptation of the method we have just described. One attaches to them an acidic 'handle', which permits the formation of salts (diastereomers) and then after resolution, can be removed from pure enantiomeric alcohols under mild reaction conditions.



Compounds other than organic bases, acids or alcohols can also be resolved. Although the particular chemistry may differ from the salt formation just described, the principle remains the same— a racemic modification is converted by an optically active reagent into a mixture of diastereoisomers, which can then be separated by simple techniques like fractional distillation or fractional crystallization.

The solution of the racemic mixture is prepared in a suitable solvent and is passed through a column packed with a suitable chiral absorbent. One of the enantiomers is selectively

Some other Methods of Resolution of a Racemic Mixture

1. Mechanical Method

This was the first method of separation of racemic mixture used by Louis Pasteur, and it is mainly of historical interest. This involved mechanical separation of the crystals of one enantiomer from the other in a racemic mixture based on differences in their shapes. Louis Pasteur did so by growing the crystals of tartaric acid. And they looked like mirror images! He then used a microscope and tweezers to separate the crystals from each other.

But this method has limitations as it is very time consuming and also not every compound can be crystallized into crystals at room temperature!

2. Biological Method

In this method, certain bacteria, yeast or mould are allowed to grow in a dilute solution of the racemic mixture. It reacts with or consumes only one of the enantiomers for its growth and give other small products while the other is left behind pure. For example, *penicillium glaucum* when allowed to grow in racemic mixture of ammonium tartarate, it consumes (+) ammonium tartarate while pure (-) ammonium tartarate is obtained as the product. This method also has some limitations as only one isomer can be obtained. Also the yield of that isomer is also very poor because only dilute solution can be used.

3. Chromatographic Method

A racemic mixture can also be resolved with the help of column chromatography. The solution of the racemic mixture is prepared in a suitable solvent and is passed through a column packed with a suitable chiral absorbent. One of the enantiomers is selectively absorbed on the surface of absorbent. It is then eluted with a suitable solvent and the solution is collected at the bottom of the column, which contains pure enantiomer.

Biographic



In 1848 Pasteur resolved (separated) an optically inactive substance (tartaric acid) into two optically active components. Each of the optically active components had properties identical to tartaric acid (density, melting point, solubility, etc.) except that one of the components rotated the polarized light clockwise (+) while the other component rotated the polarized light by the same amount counterclockwise (-). Pasteur made a proposal that still stands as the foundation of stereochemistry: The twin molecules of tartaric acid were mirror images of each other!

Additional research by Pasteur revealed that one component of tartaric acid could be utilized for nutrition by micro-organisms but the other could not. On the basis of these experiments, Pasteur concluded that biological properties of chemical substances depend not only on the nature of the atoms comprising the molecules but also on the manner in which these atoms are arranged in space.

Check your Progress

What is the significance of resolution of a racemic mixture?

absorbed on the surface of absorbent. It is then eluted with a suitable solvent and the solution is collected at the bottom of the column, which contains pure enantiomer.

6.4.3 Relative and Absolute Configurations

There are mainly two types of nomenclature used to identify configurational isomers: relative configuration and absolute configuration.

Relative Configuration: Fischer's D and L Nomenclature

This is a system of assigning relative configuration to a molecule by establishing configurational relationship among the members of a family of compounds (i.e. carbohydrates and amino acids). Glyceraldehyde (Fig 6.56) is arbitrarily chosen as standard. Most of the sugars are genetically related to either D or L glyceraldehyde and thus their configurations are defined by D or L.

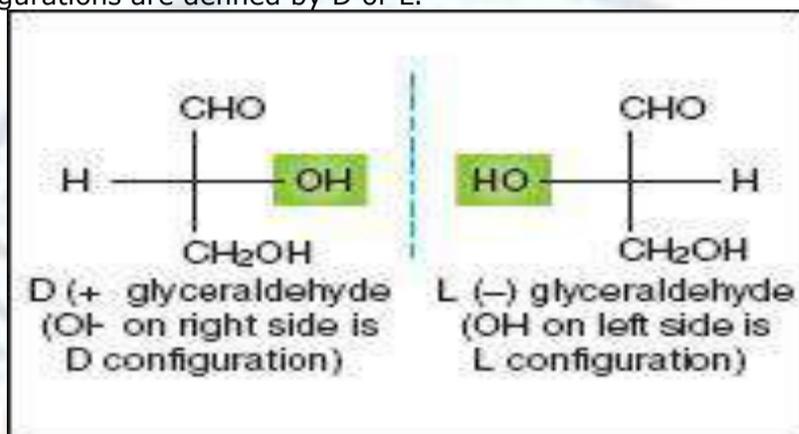


Figure 6.56: D-(+)-glyceraldehyde and L-(-)-glyceraldehyde

D- or L-glyceraldehydes) accepted as a standard.

Note that D and L have nothing to do with optical rotation of a molecule. The **D**-notation may be given to both a dextrorotatory [*d* or (+)] or laevorotatory molecule [*l* or (-)]. Same is true for **L**-notation. Hence, in the carbohydrate chemistry, to avoid the confusion (in the spoken language) between D- and *d*-, and L- and *l*-; the more commonly used term to denote dextrorotatory compounds is **(+)** and not *d*. Similarly, more commonly used term to denote laevorotatory compounds is **(-)** and not *l*.

Rules to assign D and L nomenclature to carbohydrates

- i. As in Fischer system, molecule is written with longest carbon chain placed vertically.
- ii. Most highly oxidized end of the chain is placed at the top (as CHO in aldehyde containing carbohydrates, for example, glucose and keto in ketone containing carbohydrates, for example, fructose). If the molecule is not given in this format, rotate the molecule by 180° in the plane of the paper.
- iii. If in the projected structure, the OH group (or any other negative group X) at the bottom most chiral centre is on the right hand side the molecule is assigned **D-configuration** and if on the left, it is assigned **L-configuration** (as in D and L glyceraldehyde respectively).

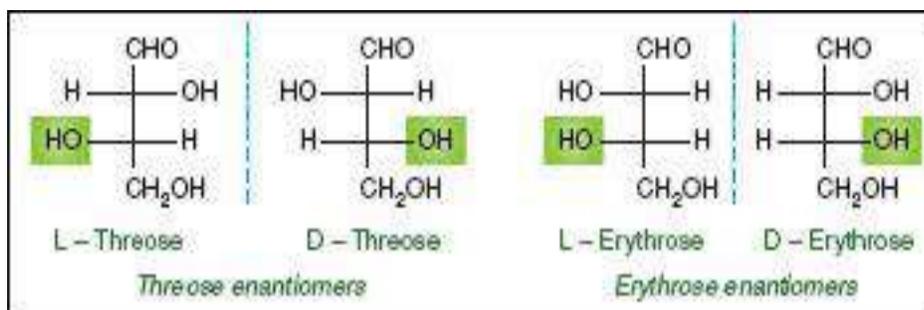


Figure 6.57: *threose* and *erythrose* enantiomers

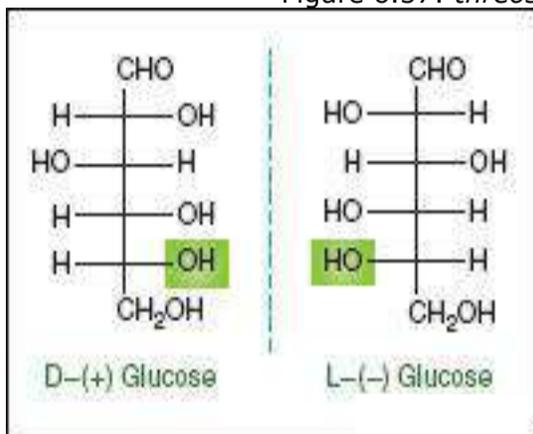
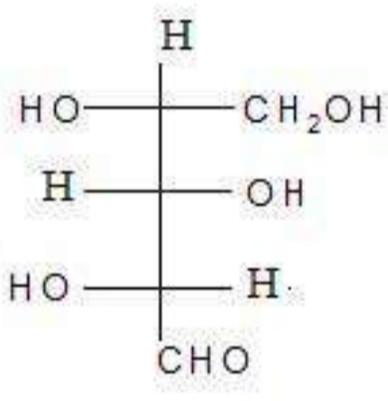


Figure 6.58: Glucose

3. Fructose (Fig 6.59):



enantiomers

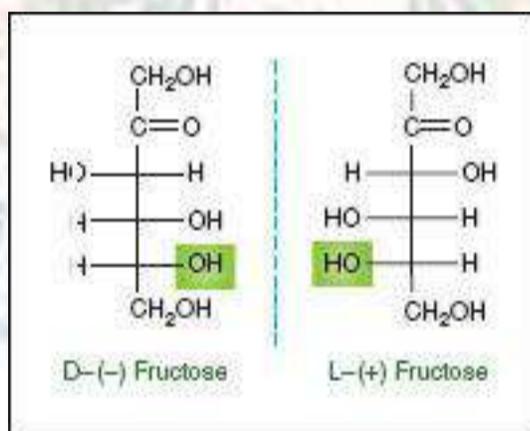


Figure 6.59: Fructose enantiomers

Example

Assign D or L to the following molecule:

Solution

The molecule given is not given in the required format to assign D-or L-. So the first step is to bring it in the required Fischer's format .The longest carbon chain is not in vertical position as required (A) . So, it is done so, by carrying out C-C single bond rotation as shown (B) below:

In the so obtained Fischer's projection, out of $-\text{CHO}$ and $-\text{CH}_2\text{OH}$, the more oxidised group i.e. $-\text{CHO}$ is not at the top position as required. So, it is done so, by rotating the molecule by 180° in-plane as shown in Fig.(C). Now the molecule is in the required Fischer's format. We may assign D-or L-. On the bottom-most chiral carbon, as it contains $-\text{OH}$ on the left (see Fig-D), it is assigned **L-notation**.

6.4.4 Absolute Configurations

Chiral carbon atoms are assigned R and S notations while the geometrical isomers are assigned E and Z notations. Both these notations are absolute configurations, as the molecule to be assigned these notations is not being compared to any other reference molecule (unlike D-and L-notations).

R, S Designation

Following are the steps to assign R or S designation to the molecule, which are based on set of rules known as **CIP Sequence rules** as proposed by R. S. Cahn, C. K. Ingold and V. Prelog.

Step I: Assign the priorities to the groups attached around the chiral centre using CIP priority rules (discussed later in this section). Assign priorities in order of decreasing atomic number, the atom with highest priority as 1, the next 2, next 3, and the atom or group with lowest priority as 4.

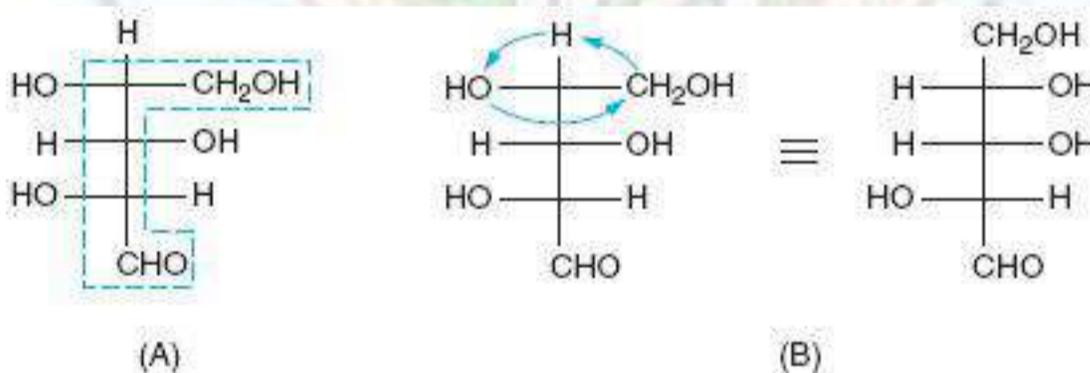
Step II: Rotate the molecule so as to visualise it in such a manner that the **lowest priority group (i.e., 4)** points towards back or away from you (i.e., it lies on the vertical line of the Fischer projection at the bottom position).

Step III: Examine the remaining group priorities and determine that on moving from the higher priority to lower priority if we are moving,

Biographic

- i. in a clockwise manner, then it is given (right for Greek word and **R notation** *Rectus*)
- ii. if in an anticlockwise manner, then it is given **S notation** (left for Greek word *Sinister*).

In other words, view the molecule so that the least priority group 4 is away from you, and the other three projected towards you. Then, move your eyes from the highest priority towards lower, i.e., from $1 \rightarrow 2 \rightarrow 3$. If this movement is clockwise, assign R and if anti-clockwise, assign S as shown in Fig. 6.60.



Stereochemistry

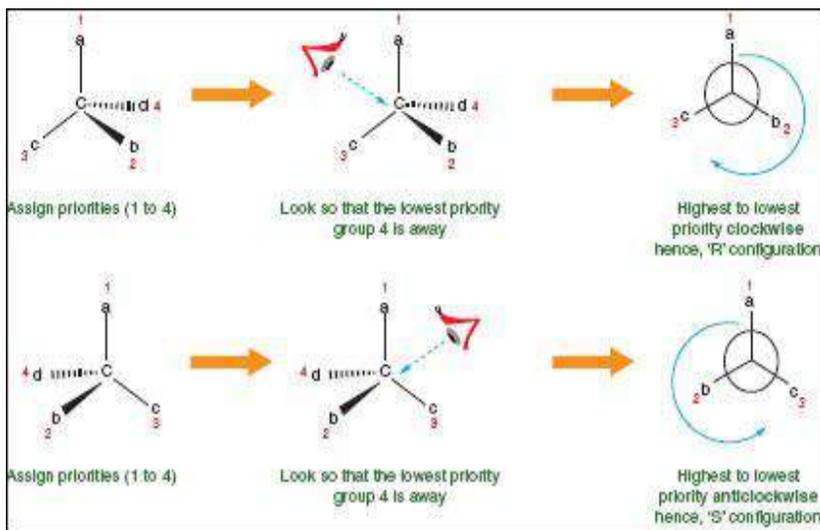


Figure 6.60: Assigning R and S configuration

CIP Sequence Rules

Rule 1: This rule tells how the **atoms** are to be compared. Atoms are compared on the basis of atomic numbers. Higher the atomic number, higher is the priority. Thus, the priority of the following atoms is as follows:



In case of isotopes of the same element, the isotope with higher mass number is given a higher priority. For example, D (deuterium) will be given higher priority than H (protium).

Rule 2: This rule tells how the **groups** are to be compared. If decision regarding priority cannot be reached by using rule 1, then compare the second atoms in each substituent (called as first chain), then third atom (second chain), etc. until the difference is found. Examples:

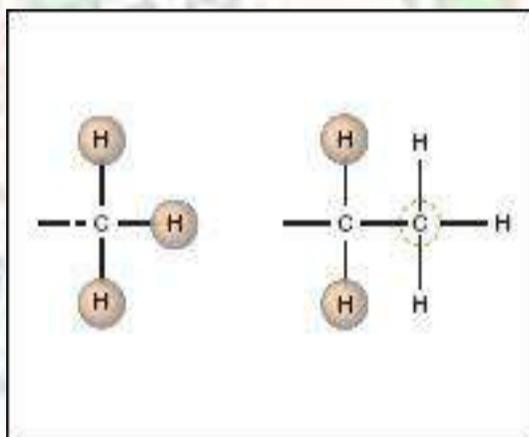


Figure 6.61: Comparison of first chain.

Take the sum of the atomic numbers of these atoms in each of the first chain and compare. In $-CH_3$, the first chain has 3 H atoms (sum of atomic numbers = $1+1+1=3$). In $-CH_2CH_3$, the first chain has 1 C and 2 H atoms (sum of atomic numbers = $6+1+1=8$). Thus, the later has higher priority.

Rule 3: This rule tells how the **groups containing multiple bonds** are to be compared. Multiple bonds are considered twice (for double bond) or three times (for triple bond) when examining substituents.

For example, in case of a double bond, the doubly bonded atom is considered as equivalent to two singly bonded atoms. Let us consider the group $-\text{CHO}$. Here, the $\text{C}=\text{O}$ is treated as if C has been joined to two oxygen atoms by two single bonds; and one of the O is also joined with two C atoms with two single bonds as shown in Fig 6.62.

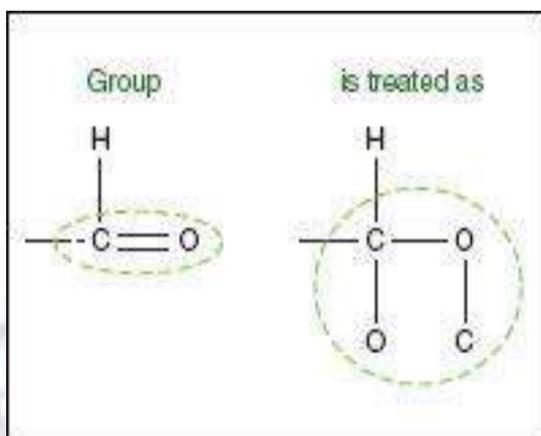


Figure 6.62: Opening up of $-\text{CHO}$ group.

In case of a triple bond, the triply bonded atom is considered as equivalent to three singly bonded atoms. Let us consider the group $-\text{C}\equiv\text{N}$. Here, $\text{C}\equiv\text{N}$ is treated as if the C has been joined to three nitrogen atoms by three single bonds; and one of the N is also joined with three C atoms with three single bonds as shown as shown in Fig 6.63.

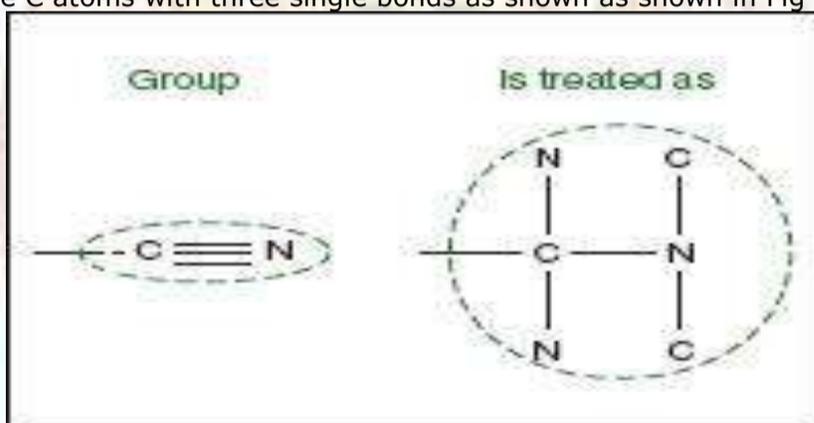


Figure 6.63: Opening up of $-\text{CN}$ group After this treatment, the comparison between the groups is done by using rule 2. Example: Comparison of $-\text{CHO}$ with $-\text{C}\equiv\text{N}$ (Fig 6.64).

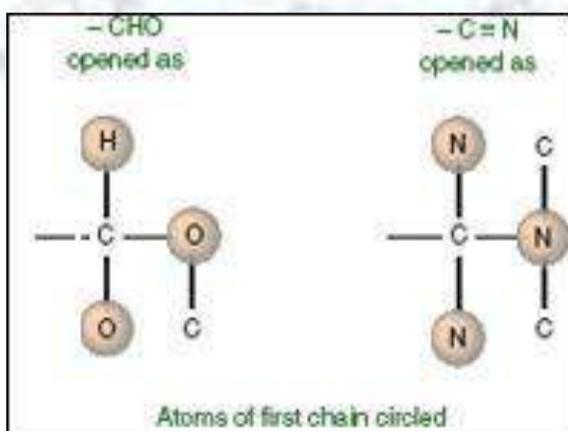


Figure 6.64: Comparison of $-\text{CHO}$ with $\text{C}\equiv\text{N}$

The sum of atomic number of atoms of first chain in $-\text{CHO}$ are $(\text{H}+\text{O}+\text{O})$ is 17 $(=1+8+8)$. The sum of atomic number of atoms of first chain in $-\text{CN}$ are $(\text{N}+\text{N}+\text{N})$ is 21 $(=7+7+7)$. **Thus, $-\text{CN}$ has higher priority than $-\text{CHO}$.**

R and S Notations for the Optical Isomers Represented by Wedge Formula

Consider for example, lactic acid, i.e., 2-hydroxy-propanoic acid. The four groups attached to the chiral carbon atom are -H, -CH₃, -OH and -COOH.

To give them priority, we first compare the atomic numbers of their first atoms, i.e., H (=1), C(=6) and O(=8). Thus H is given lowest **priority 4**, while -OH is given highest **priority 1**. To decide between -COOH and -CH₃, the first chain is compared.

In -COOH has the sum of atomic number of first chain atoms (O+O+O) as 24 (= 8+8+8), while -CH₃ has the sum of atomic number of first chain atoms (H+H+H) as 3 (= 1+1+1). Thus, -COOH has higher priority than -CH₃. -COOH is assigned **priority 2** and -CH₃ is assigned **priority 3**.

Then visualize the molecules as shown (Fig 6.65) to assign the R and S-notations.

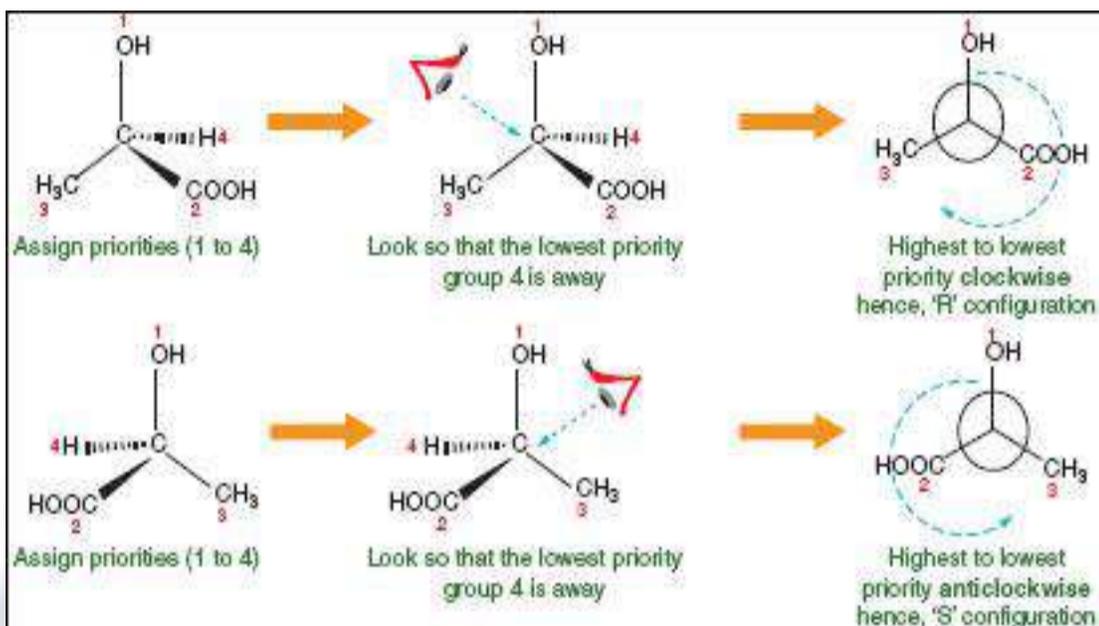


Figure 6.65: Assigning R and S configuration to lactic acid

Animation

<http://www.illdu.edu.in/mod/resource/view.php?id=5661>

Assigning R and S Notations to the Optical Isomers Represented by Fischer Projections

Case I : When the atom or group of lowest priority is at the bottom or top (i.e. *at vertical position*). Simply rotate the eye in decreasing order of priority and find the configuration of chiral carbon (Fig 6.66). (Actually this is the front view of the molecule as required to assign R or S).

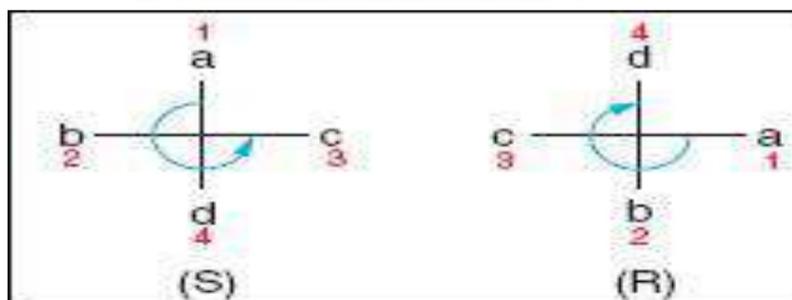


Figure 6.66: Assigning R or S when lowest group is at vertical position in a Fischer formula

Examples

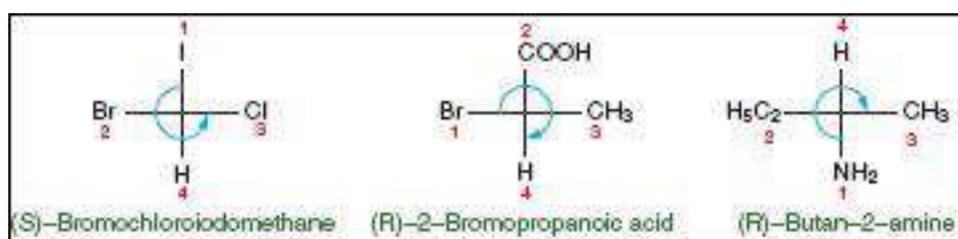


Figure 6.67: Assigning R and S configuration

Case II: When the atom or group of lowest priority is on the left hand side or right hand side (*i.e.* at horizontal position). Actually this is the back view of the molecule as required to assign R or S.

(a) Without changing the position at the top, rotate the molecule in the anticlockwise (or clockwise) direction so that the atom or group of lowest priority comes to bottom or top (*i.e.* at the vertical position). It is then assigned R or S configuration for example,

1, 2-Amino-propanoic acid

Keeping the group, assigned priority 1 fixed, the remaining three groups are rotated anti-clockwise such that the group with priority 4, comes to bottom. Now, it can be assigned R or S notation (Fig. 6.68)

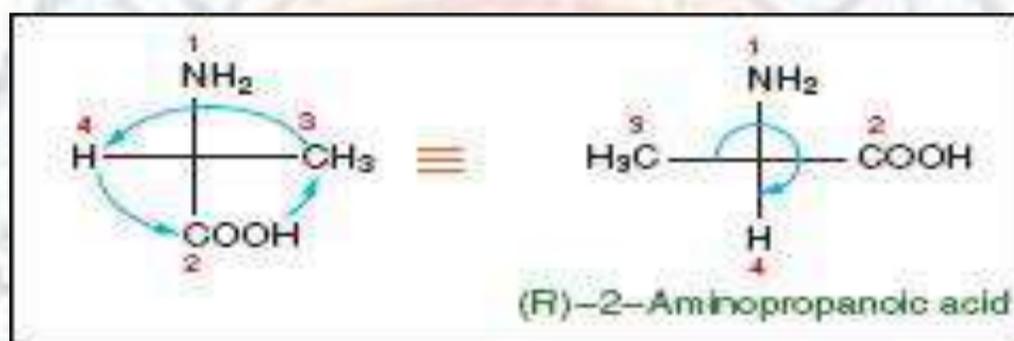


Figure 6.68: Assigning R or S when the lowest priority group is at horizontal position by rotation of three groups keeping one fixed

2. 2-hydroxy-propanoic acid (Lactic acid)

Keeping the group assigned priority 1 fixed, the remaining three groups are rotated clockwise in order to bring the group with priority 4 at the bottom. It is now assigned R or S notation (Fig. 6.69).

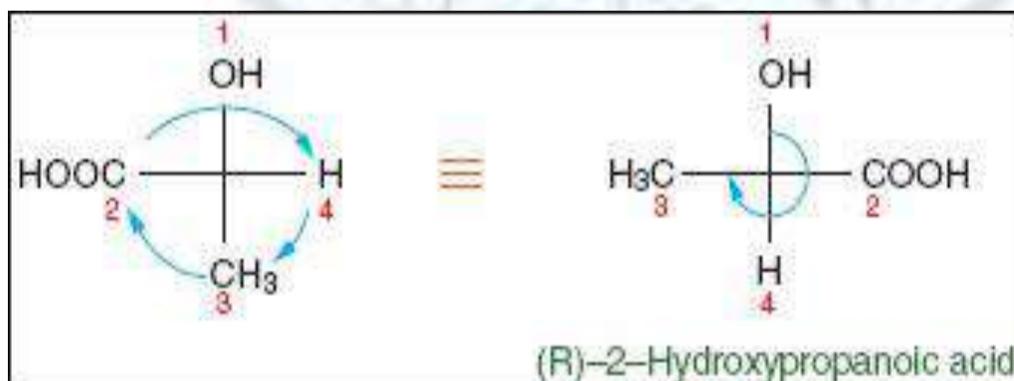


Figure 6.69: Assigning R or S when the lowest priority group is at horizontal position by rotation of three groups keeping one fixed

(b) Equivalent Fischer projection can be obtained by any two interchanges across the chiral carbon atom. These interchange are done to get the group with priority 4 at the bottom. R or S notation can then be assigned. For example, Assigning R or S when the lowest priority group is at horizontal position by inverting the direction of rotation

Important Rules

(i) Even number of interchanges across a chiral carbon generates equivalent Fischer projection with same configuration (Fig 6.72).

(ii) Odd number of interchanges across a chiral carbon generates Fischer projection of opposite configuration, i.e., its enantiomer (Fig 6.72).

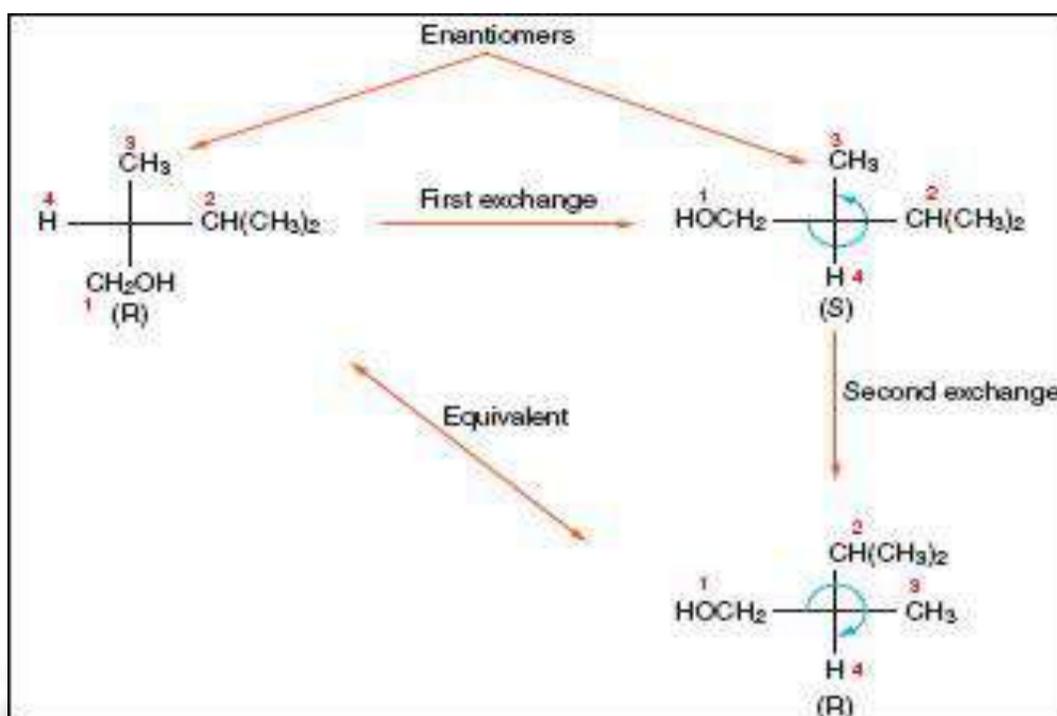


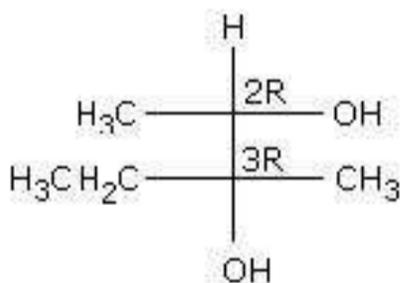
Figure 6.72: Even and odd number of interchanges across a chiral carbon atom

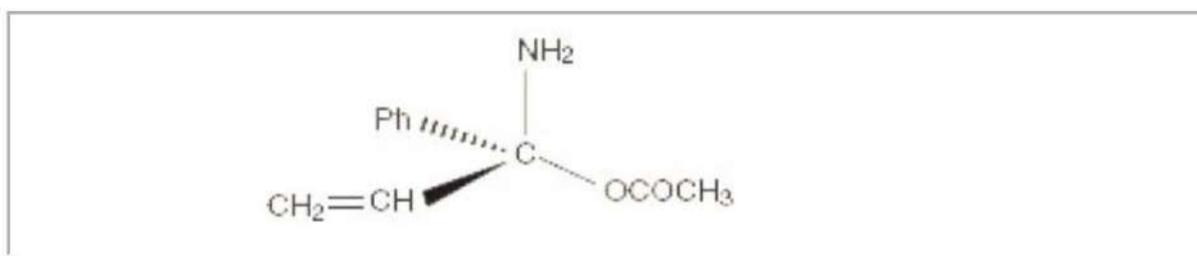
While assigning R or S to compounds with multiple chiral centers (2 or more), each chiral carbon is considered one by one and its R/S configuration is determined. If their sawhorse or wedge formula is given, it is first converted to Fischer's formula and then each chiral carbon is assigned R/S. For example, Notice that 2 and 3 are the IUPAC numbering. For **C2**

Therefore, the complete configuration is 2R, 3R.

Hence, the name of this stereoisomer is 3-methyl-pentan-2R, 3R-diol.

Example Assign R/S to the following:





E and Z Notation

When all four substituents across the C=C are different, they are geometrical isomers, but they cannot be named as *cis* or *trans*. They are denoted by E or Z notation. This is also used for all the geometrical isomers even if they can be named as *cis* or *trans*.

This system is based on the priorities of groups. The priorities are assigned for the two groups on each of the doubly bonded carbon atoms. The priorities are decided by using the same sequence rules (as discussed earlier), given by Cahn-Ingold-Prelog.

The group of higher priority on one doubly bonded carbon atom is compared with group of higher priority on other doubly bonded carbon atom.

If these two groups of higher priority are on **same side** of double bond, the alkene is **designated as Z** (*Zusammen* meaning together). If they are on **opposite sides**, the alkene is **designated as E** (*Entgegen* meaning opposite) (Fig 6.73).

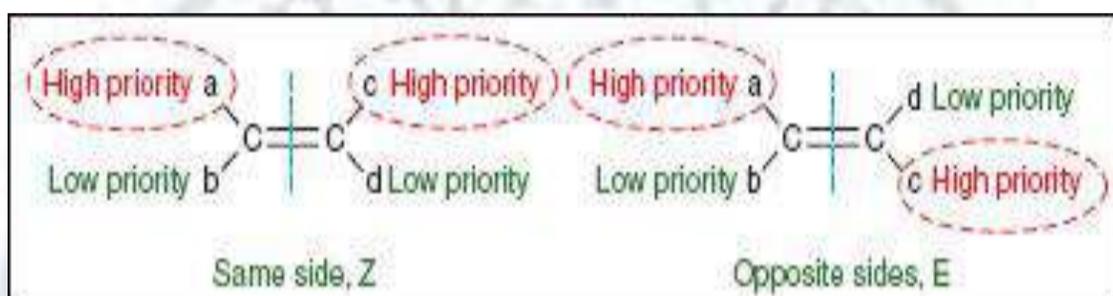
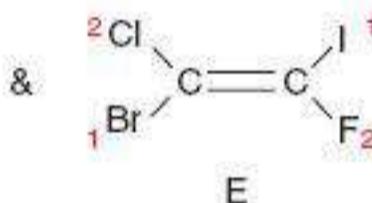
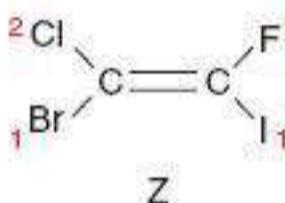
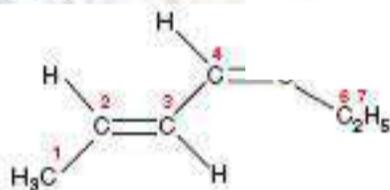


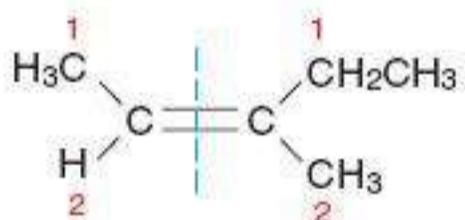
Figure 6.73: Assigning E or Z notation to alkenes One may assign 1 for higher priority and 2 for lower priority.

For example,

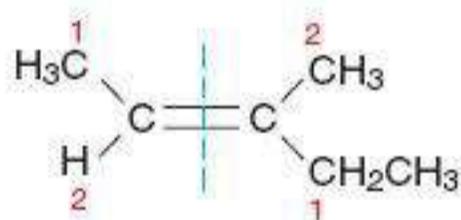
- 1-bromo-1-chloro-2-fluoro-2-iodoethene



3-methyl-pent-2-ene



(Z)-3-Methylpent-2-ene

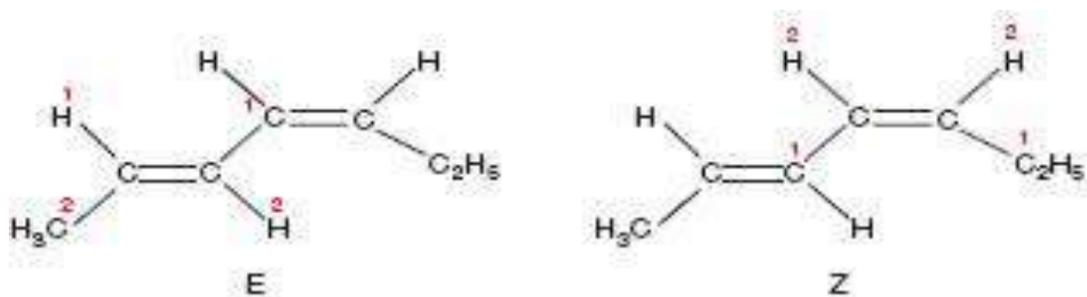


(E)-3-Methylpent-2-ene

While assigning E and Z to compounds with multiple double bonds (2 or more), each double bond is considered one by one and its E/Z is determined. For example,

Stereochemistry

The IUPAC numbering is shown here, so the two double bonds to be assigned E/Z
It is hence **2E, 4Z**.



The IUPAC name of this stereoisomer is thus, hept-2E,4Z-diene. Recall that hept-2,4-diene has 4 stereoisomers: they would be named as:hept-2Z,4Zdiene;

.....

hept-2E,4E-diene; hept-2Z,4E-diene and hept-2E,4Z-diene.

Erythro and Threo Isomers

Another commonly used notation (mostly in carbohydrate chemistry) is the *erythro* and *threo* notation.

The use of CIP nomenclature requires assignment of R,S descriptors for every center. The quicker way (older and a more ambiguous one) is by using ***threo/erythro*** nomenclature.

In general, *threo*-compounds are defined as those that have two ligands of higher precedence (say X) on each carbon atom on the opposite sides of the chain and *erythro*-compounds are defined as those that have two ligands of higher precedence (X) are on the same side of the chain (Figure 6.74).

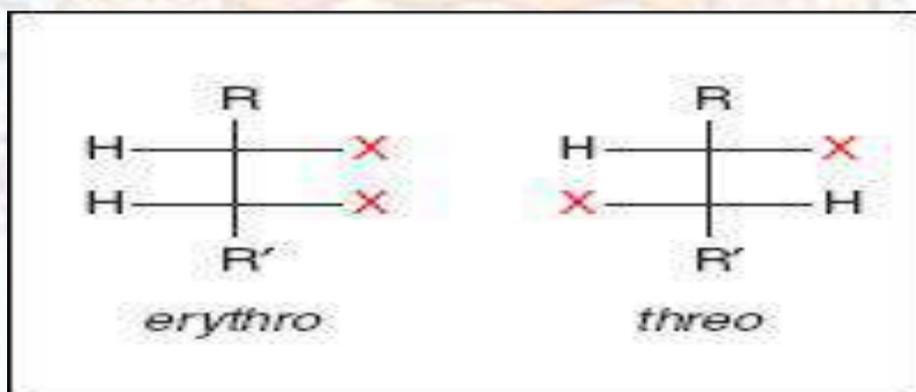
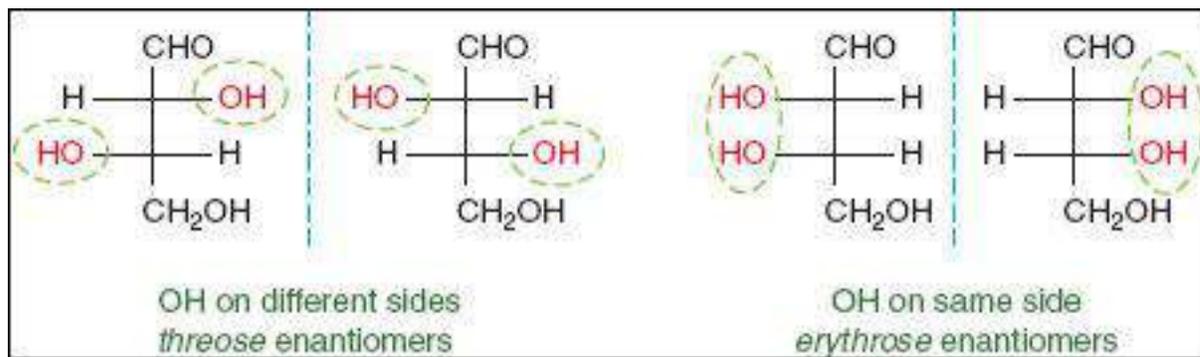


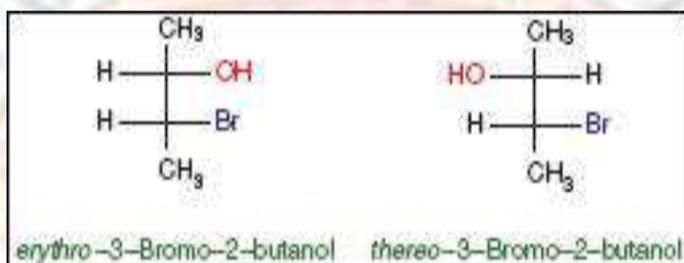
Figure 6.74: *erythro* and *threo* notations This notation is based on the four-carbon sugars

Threose and **Erythrose** (Figure 6.75).

Figure 6.75: *threose* and *Erythrose* pairs of enantiomers

The prefixes, *erythro* and *threo*, are used to distinguish between enantiomers containing two chiral carbon atoms when two pairs of atoms or groups attached to each chiral carbon are the same while the third is different. The stereoisomer in which these same groups are present on the same side of the Fischer projection formula is called **erythro isomer**. While the stereoisomer in which these are present on the opposite sides is called **threo isomer**. For example,

1. 2,3-Dichloro-pentane (Figure 6.76).
3. 3-Bromobutan-2-ol , $\text{CH}_3\text{CH}(\text{OH})\text{CH}(\text{Br})\text{CH}_3$ (Figure 6.78).

Figure 6.78: *erythro* and *threo* 3-Bromobutan-2-ol

Summary

Stereochemistry is the study of spatial arrangements of group of atoms in molecules, i.e. how these atoms are arranged relative to one another in three-dimensional space.

Conformations are the different 3-D orientations achieved by the molecule formed due to rotation about sigma bonds. These are *freely inter-convertible* at room temperature into each other. The inter-conversion of these isomers does not require any breaking or forming of bonds.

Configurations: They cannot be inter-converted into each other freely. There are two types of configurational isomers: geometrical and optical.

Ethane has an infinite number of conformations, the two extreme being eclipsed and staggered conformations. In between the staggered and eclipsed conformations, there are **Gauche or Skew conformations**.

The four important conformations of n-butane are: Total or fully eclipsed, Gauche staggered, Gauche eclipsed and Anti-conformer. Of these, the anti conformer is most stable.

Stability of the cyclic rings is as follows: Cyclopropane < Cyclobutane < Cyclopentane < Cyclohexane

According to **Baeyer's strain theory**, *higher is the angular strain, less is the stability of the cyclic ring*.

The two important conformations of cyclohexane are boat conformation and chair conformation. They are freely interconvertible and in between these two are infinite gauche or skew conformations.

The geometrical isomers with identical groups on the same side of the double bond are called **cis-isomers**, while those having identical groups on the opposite side of the double bond are called **trans-isomers**. For **Non-Symmetrical dienes**, the total number of geometrical isomers is 4. For **Symmetrical dienes**, the total number of geometrical isomers is 3. **Polarimeter** is the instrument used to measure optical rotation. If the substance rotates plane polarised light to *the right (clockwise)*, it is called **dextro rotatory** or the *d-form* and it is indicated by placing a (+) sign before the degrees of rotation. If light is rotated *towards left (anti clockwise)*, the substance is said to be **laevo rotatory** or the *l-form* and a negative (-) sign is placed before the degrees of rotation. The dextro rotatory and laevo rotatory compounds are collectively called as **optically active compounds**. If light is not-rotated towards any side, i.e. comes out undeviated, then the substance is said to be **optically inactive**. An object which is nonsuperimposable on its mirror image is said to be **chiral**.

Chiral means asymmetrical. A molecule which lacks element of symmetry, is called **Asymmetric**.

Specific rotation is the number of degrees of rotation observed if a 1 dm (10 cm) tube is used, and the compound being examined is present to the extent of 1 g/mL.

where l represents length of the polarimeter tube (in dm) and c represents concentration of a solution or density for a pure liquid in g/mL (or g/cm³). T is the temperature and λ is the wavelength of the light used. Pair of stereoisomers which are related to one another as an object and its nonsuperimposable mirror image are called **enantiomers**. **Enantiomers** possess identical physical properties but differ in the direction (sign) of rotation of the plane polarized light. Magnitude of rotation is, however, same for the two isomers. The mixture containing enantiomers (dextro and leavo) in equal proportion will

$$[\alpha]_{\lambda}^T = \frac{\alpha_{\text{obs}}}{l \times c}$$

have zero optical rotation and is hence optically inactive. Such a

mixture is known as **racemic mixture or racemic modification**. If a compound has n chiral carbon atoms (or chiral centres) then, **the maximum**

number of stereoisomers = 2^n . Stereoisomers that are non-superimposable and not mirror images of each other

are called **diastereoisomers**. Diastereoisomers have similar chemical properties but different physical properties.

A **meso compound**, is the one whose molecules although possesses two or more than two chiral centres, but are optically inactive due to the presence of a plane of symmetry. For the unsymmetrical molecules with n chiral centres, the number of possible stereoisomers are

2^n . All of these will be optically active and exist as enantiomeric pairs. For symmetrical molecules, there are $2^n - 1$ stereoisomers.

The *meso* stereoisomer will be optically inactive, rest all will be optically active, as enantiomeric pairs. The process of separation of a racemic mixture into the enantiomers is called **resolution**. Out of many methods available for their separation, the most widely used is the chemical method in which racemic mixture is converted to diastereomeric mixture. **Even number of interchanges across a chiral carbon** generates equivalent Fischer projection with same configuration. **Odd number of interchanges across a chiral carbon** generates Fischer projection of opposite configuration, i.e., its enantiomer.

Glossary

- **Axial hydrogen atoms** -The C-H bonds which point vertically upward or downward are called **axial**. Hax are known as axial hydrogen atoms. There are 6 of these, 3 upward and 3 downward bonds, and they alternate up/down/up, etc., around the ring.
- **Asymmetrical molecules**-Lacks all the elements of symmetry (i.e., plane of symmetry, centre of symmetry and axis of symmetry) and are not superimposable on their mirror images.
- **Axis of symmetry**-Represents the line around which the molecule has identical atoms at equal distances from this line.
- **Absolute Configuration**-Chiral carbon atoms are assigned R and S notations while the geometrical isomers are assigned E and Z notations. Both these notations are absolute configurations as the molecule to be assigned these notations is not being compared to any other reference molecule (unlike D- and L-notations).
- **Baeyer's strain theory**-Greater is the deviation from the normal tetrahedral angle, greater strained will be the molecule which lead to its greater reactivity and less stability.
- **Conformations**-Are the different 3-D orientations achieved by the molecule formed due to rotation about sigma bonds. These are freely inter-convertible into each other.
- **Configurations**-Arise due to certain types of rigidity within the molecule. They can get converted into another only if some bonds are broken and then reestablished after rearrangement. They cannot be inter-converted into each other freely.
- **Chiral** -When four different groups are present around a carbon atom then that carbon atom is called chiral carbon or asymmetric carbon.
- **Centre of symmetry** -If any line drawn from the centre of the molecule meets identical atoms at equal distances from the centre.
- **Dihedral angles**-The angles formed between bonds on the front atom and bonds on the rear atom.
- **Dextro rotatory** -If the substance rotates plane polarised light to the right (clockwise), it is called dextro or the *d*-form and it is indicated by placing a (+) sign.
- **Eclipsed conformation**-The C-H bonds on the front and back carbons are aligned with each other with dihedral angles as 0° .
- **Equatorial hydrogen atoms** -The other six bonds, which radiate away from the "equator" of the ring, are called equatorial. Heq are known as equatorial hydrogen atoms. There are six of them, 3 of which are "slant up" and 3 of which are "slant down", again alternating around the ring.
- **Enantiomers**-Pair of stereoisomers, which are non-superimposable on their mirror image and possess identical physical and chemical properties but differ in the direction (sign) of rotation of the plane polarized light.
- **E and Z Notation** -When all four substituents across the C=C are different, they are denoted by E or Z notation.
- **E designated** -If two groups of higher priority are on opposite sides, the alkene is designated as E.
- **Fischer projection-(2-D view)**, is drawn as intersecting horizontal and vertical lines. The chiral carbon is considered to lie on the point of intersection and the lines originating from this point are considered as four bonds joined to that chiral carbon.
- **Fischer's D and L nomenclature**-Fischer arbitrarily assigned D-configuration to (+) glyceraldehyde with OH group on stereocenter on the right of projection and L-configuration to (-) glyceraldehyde with OH group on the left.
- **Geometrical isomerism** -Due to the presence of a double bond (or ring), the free rotation between the carbon atoms is prevented and the two groups attached to each carbon are different, then it may result in, two different relative arrangements of atoms or groups, in space. i.e. **cis and trans** isomerism.
- **Isomers**-Are the molecules that have the same molecular formula, but have at least one different physical and/or chemical property.
- **Laevo rotatory** -If the substance rotates plane polarised light to the left (anti-clockwise), it is called laevo rotatory or the *l*-form and a negative (-) sign is placed before the degrees of rotation.
- **Meso compound**-Whose molecules are superimposable on their mirror images even though they contain chiral centers.
- **Newman projection**-(3-D view), represents the head-on look down the bond of

interest. A point represents the front carbon atom i.e., carbon nearer to the eye and its bonds is represented as bonds as .

- **Optical Isomerism** -The compounds with same molecular and structural formula differ in the spatial distribution of the atoms or group of atoms which changes their behavior towards the plane polarised light. Optical activity is the ability of the molecule to rotate the plane polarised light.
- **Plane polarised light** -Ordinary light is mixture of different wavelengths. By using prism or diffraction grating, light of a single wavelength is obtained. Such a beam of light is called plane-polarised light.
- **Polarimeter**-It can measure the angle of rotation of the substance by which the plane polarised light is rotated.
- **Plane of symmetry (mirror plane)**-When plane bisecting the molecule in such that each half of the molecules is the mirror image of the other half.
- **Racemic modification**-The mixture containing enantiomers (dextro and leavo) in equal proportion. Such a mixture will have zero optical rotation as the rotation due to one enantiomer cancels the rotation due to the other.
- **Resolution**-The process of separating a racemic mixture into (+) and (-) enantiomers by suitable methods.
- **Relative Configuration**-Is assigning configuration to a molecule by arbitrarily Chosen family of carbohydrates and amino acids as standard.
- **R, S Designation**-This system of assigning absolute configuration to the molecule, designed by **Cahn, C.K. Ingold and V. Prelog** is based on set of rules known as CIP Sequence rules.
- **Stereochemistry** -The study of spatial arrangements of atoms or group of atoms in molecules, i.e. the arrangement of these atoms in relation to one another in three-dimensional space.
- **Structural isomerism** - Arises due to their different structural arrangement of the same molecular formula.
- **Stereoisomerism**-Due to different arrangement of the atoms in space.
- **Sawhorse projection** -(3-D view) But, it is a side view, and the two carbon atoms are drawn as points and the bond joining the two carbons is drawn as a line. the two important sawhorse projection formula are:
 - Staggered Eclipsed
 - **Staggered conformation**-The C-H bonds  on the rear carbon lie between those on the front carbon with dihedral angles of 60° .
- **Super-imposability**-To check whether the two molecules are same or not. If the two molecules are same, they can't be isomers.
- **Specific rotation**-Is defined as the angle of rotation produced by decimeter length of solution having 1gm of sample per 1mL of the solution at a specific temperature and wavelength. It is as much a property of a compound as its melting point, boiling point, density, or refractive index.
- **Symmetric molecules**-Molecules having one or more elements of symmetry and have an identical mirror image are called symmetric molecules.
- **Torsional / Pitzer strain**-Whenever bulky portions of a molecule repel other parts of the same molecule such hindrance causes resistance to rotation, called torsional strain.
- **Threose and Erythrose nomenclature**-The erythrose and threo are used with dissymmetric compounds where the ends are different. A diastereomers is called erythro when the similar groups are on same side of the fischer projection. When the similar groups are on the opposite sides of the fischer projection, the diastereomer is called threose.
- **Wedge-dash** are used to represent bonds that are extending outfrom the plane of the page towards the reader and **dashes** () are used to represent bonds that are going into the plane of the page (i.e., away from the viewer). The simple lines (_ _) represent bonds lying in the plane
- Wedge-dash formula of methane
- **Z designated** -If two groups of higher priority are on same side of double bond, the alkene is designated as Z .

Exercises

- 1 i) What are enantiomers? Compare the chemical and physical properties of
- 2 (a) enantiomers
- 3 (b) enantiomers and its racemic form.
- 4 ii) What are diastereoisomers?
- 5 What do the prefixes (+), (-) and (\pm) before an organic compound mean?
- 6 What is optical rotation (α obs)? What are the factors on which it depends?

Stereochemistry

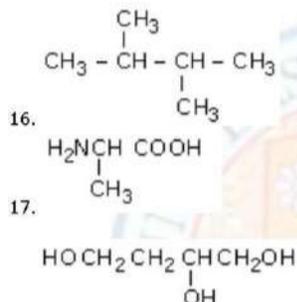
- 7 What would be obs if concentration of the sample and length of the polarimeter tube were doubled? Will specific rotation also change by the following changes?
- 8 Describe the following terms:
- 9 Diastereoisomers, Resolution, Racemisation, Chiral centre, Conformation



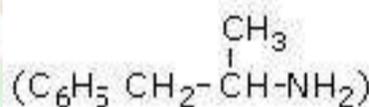
Stereochemistry

10. Define the following terms:
 11. Fischer projection, Enantiomers, Relative configuration, Absolute configuration, Gauche conformation, Anti conformation
 12. Calculate the specific rotation of the sample, if solution of the sample containing 0.75 g/10 mL is placed in 10 m polarimeter tube and its observed rotation at 25°C (D-line) is +1.2°. What would be the specific rotation of its enantiomer?
 13. A compound has an optical rotation of +15°. What will be the optical rotation of its enantiomer?
 14. What will be the effect on the observed rotation if the concentration is doubled and length of the tube is doubled? What is observed rotation of a solution of a compound containing 0.35 g/mL as measured in 5.0 cm tube. (specific rotation = +16°) The 25 mL of 0.5 M solution of (+) Lactic acid is mixed with 25 mL solution of 0.05 M (-) Lactic acid. What is the nature of resultant solution? Why is racemic mixture, optically inactive? A carboxylic acid of the formula C₃H₅O₂Br is optically active. What is its structure. Which of the following are optically active compounds.

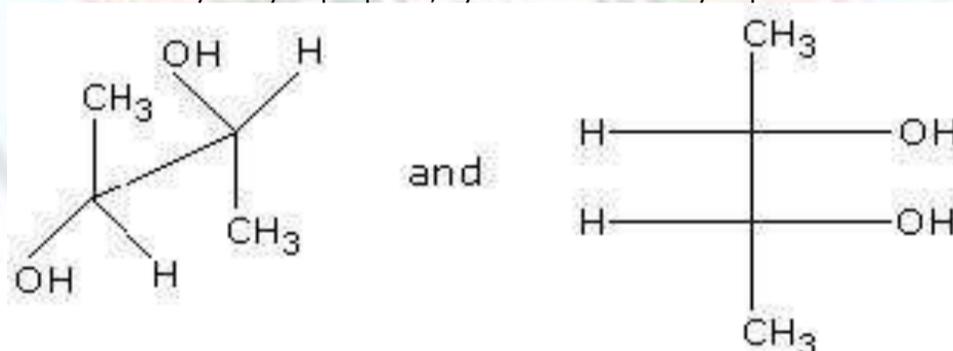
H₂NCH₂COOH



18. What is meant by *threo* and *erythro* isomers. Explain with the help of an example. What is a *meso* compound? Why is it optically inactive? What is a special feature that *meso* compound must have? What is the difference between a *meso* compound and a racemic mixture considering the fact that both are optically inactive? Write equation to show the chemical resolution of racemic mixture of lactic acid (2-hydroxy propanoic acid) using an optically pure reagent (R) - amphetamine



19. What are the maximum number of stereoisomerism for a given compound having *n* chiral carbon atoms? What is meant by Baeyer's Strain theory and using it compare the stability of cyclopropane, cyclobutane and cyclopentane.



20. What is meant by Baeyer's Strain theory and using it compare the stability of cyclopropane, cyclobutane and cyclopentane.

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