

CHAPTER

7

STEREOCHEMISTRY OF ORGANIC COMPOUNDS

1.1. INTRODUCTION

The molecular structure of compounds plays a very important role in the study of organic chemistry. During this study one comes across many instances where a given molecular formula represents two or more compounds having different properties. This is evidently due to some difference in the molecular structures of these compounds. Such compounds which have the same molecular formula but different properties are known as **isomers** and the phenomenon is known as **isomerism**.

1.2. ISOMERISM

The concept of isomerism is an important feature of the study of organic compounds. It relates to the existence of different compounds which have the same molecular formula but different properties. Such compounds are called **isomers** (*iso* = same; *mers* = parts). The difference in the properties of isomers is due to the difference in the relative arrangements of atoms in their molecules.

There are two types of isomerism :

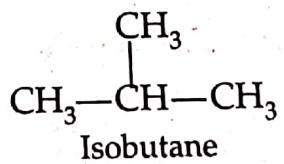
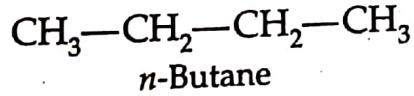
- (i) **Structural Isomerism**
- (ii) **Space or Stereo Isomerism.**

1.3. STRUCTURAL ISOMERISM

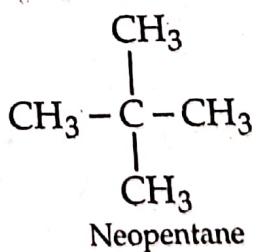
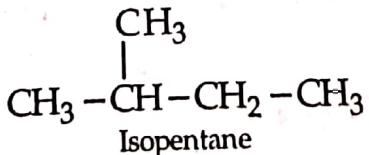
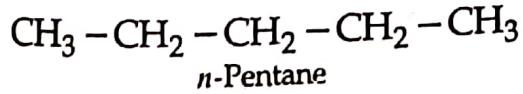
This is the type of isomerism which is due to the difference in the arrangement of atoms within the molecules having the same molecular formula.

The student is already familiar with the various types of structural isomerism. However, we shall present here a brief review for the sake of recapitulation.

1. **Chain or Nuclear Isomerism.** This is a kind of isomerism which arises when the compounds having the same molecular formula differ only in the arrangement of carbon atoms in a chain. Thus normal butane and iso-butane having the same molecular formula, C_4H_{10} , represent two chain isomers.

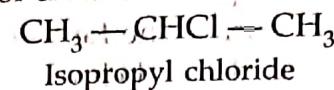
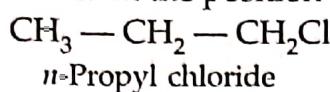


Similarly there are three chain isomers having the molecular formula C_5H_{12} .

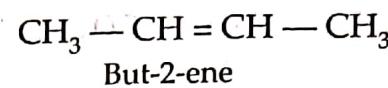
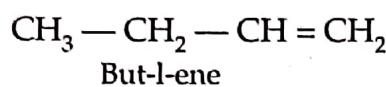


2. **Position Isomerism.** If two or more compounds with the same molecular formula have different positions occupied by a characteristic atom or group attached to carbon, position isomerism is said to exist. *n*-Propyl chloride and isopropyl chloride afford an outstanding example of this type of isomerism.

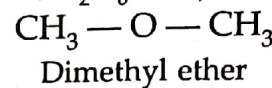
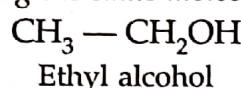
Both these compounds have the same molecular formula (C_3H_7Cl), the same carbon skeleton but differ from each other in the position of attachment of chlorine atom.



Similarly, there are two butenes (C_4H_8) which differ in the position of double bond in the molecule.

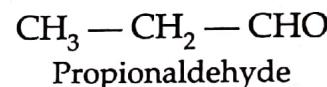
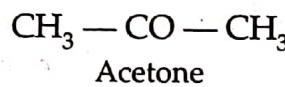


3. Functional Isomerism. This type of isomerism is due to the presence of different functional groups in compounds having the same molecular formula. For instance, C_2H_6O , represents two compounds.

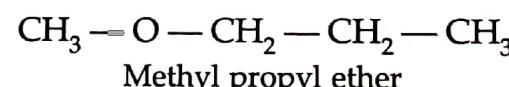
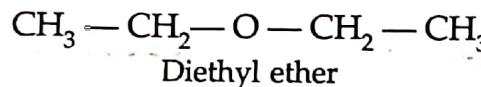


These two compounds have entirely different physical and chemical properties because of the presence of different characteristic groups.

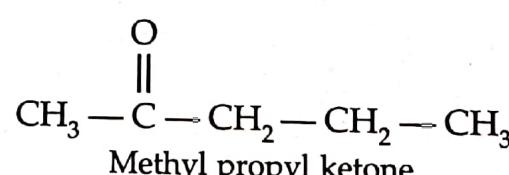
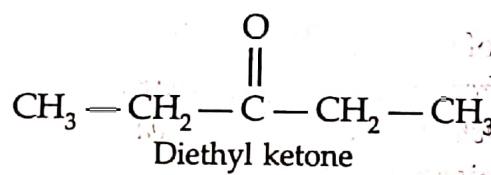
Acetone and propionaldehyde (C_3H_6O) represent another pair of compounds exhibiting functional isomerism.



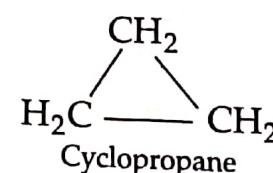
4. Metamerism. This type of isomerism is due to the difference in the distribution of carbon atoms on either side of functional group in compounds having the same molecular formula. For instance, diethyl ether and methyl propyl ether represent a pair of metamers having the molecular formula $C_4H_{10}O$.



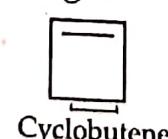
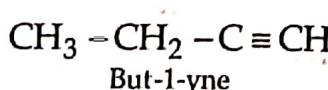
Diethyl ketone and methyl propyl ketone, having the molecular formula $C_5H_{10}O$, furnish another case of metamers.



5. Ring-chain isomerism. This is a type of isomerism in which two compounds having the same molecular formula have open chain and ring structures respectively. For example, propene and cyclopropane having the molecular formula C_3H_6 , afford a simple example of ring-chain isomerism.

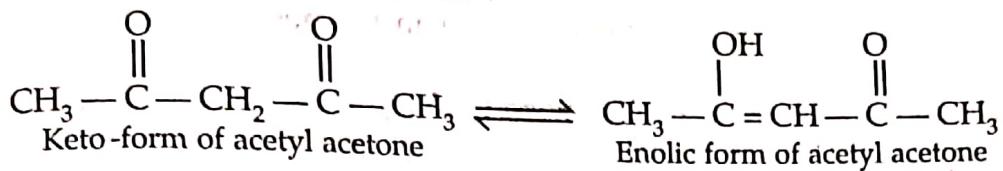


Similarly but-1-yne and cyclobutene are also ring-chain isomers of each other.

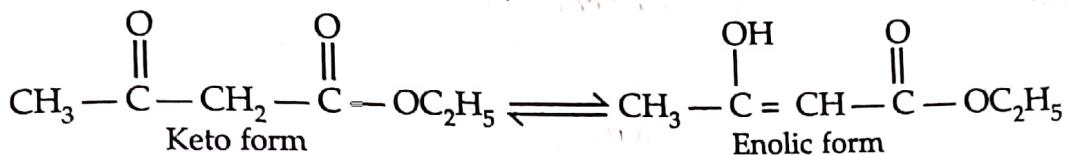


6. Tautomerism. This is a special type of functional isomerism where the isomers exist simultaneously in dynamic equilibrium with each other. The isomers which are involved in equilibrium are called tautomers. The structures of tautomers generally differ from each other in the point of attachment of one of the atoms in the molecule.

In keto-enol tautomerism, which is the most important type of tautomerism, the tautomers differ from each other in the point of attachment of a hydrogen. Thus acetyl acetone exists as a tautomeric mixture of two forms, the **keto form** and the **enol form**, which differ in the point of attachment of a hydrogen as shown below :



Similarly ethyl acetoacetate exists as a mixture of keto and enolic forms :



Tautomerism versus Resonance. It will be quite appropriate at this stage to distinguish between the phenomenon of tautomerism and resonance. It may be noted that :

(i) Tautomerism is marked by the existence of distinct structures which differ mainly in the point of attachment of one atom in the molecule.

On the other hand, in case of resonance the different contributing structures have the same arrangement of atoms.

(ii) The tautomers are distinct compounds which are actually known to exist and which may even be isolated in certain cases.

On the other hand, in resonance contributing structures do not exist as such. They are written only to have an idea of the structure of resonance hybrid as this structure cannot be represented in terms of the valence bond method of representation.

7.4. STEREOISOMERISM

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

In this unit, we shall discuss the important aspects of stereoisomerism.

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

There are three types of stereoisomerism :

(i) **Optical isomerism.**

(ii) **Geometrical isomerism.**

(iii) **Conformational isomerism.**

Before proceeding further, it may be pointed out that the different structures of conformational isomers of a substance are non-superimposable on one another but are easily interconverted into each other by rotation around single bonds. In contrast to this, the different structures of optical or geometrical isomers are non-superimposable on one another and at the same time they cannot be inter-converted except by breaking and making of bonds. For this reason optical and geometrical isomers are also collectively known as **configurational isomers**. While conformational isomers of a substance exist only as a mixture of different forms, the configurational isomers can be prepared as distinct individual substances. (For difference between conformation and configuration, please refer to sec. 7.20).

We shall now discuss the different types of stereoisomerism starting with optical isomerism.

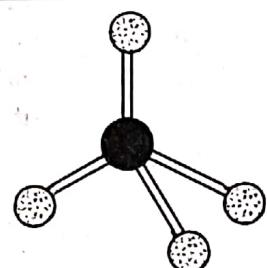
7.5. OPTICAL ISOMERISM

This is a type of stereoisomerism in which the isomeric compounds resemble one another in their chemical reactions and most of the physical properties but differ in their effect on polarised light. We shall now first review some fundamental terms concerning optical isomerism and then discuss other features of optical isomerism.

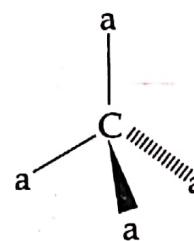
7.5.1. Tetrahedral concept of carbon

It is well-known that in methane and all other compounds having a carbon bonded to four other atoms or groups by single bonds, the four bonds of carbon are directed towards the four corners of a tetrahedron. The tetrahedral concept of carbon (put forward by Le Bel and van't Hoff) is very helpful in understanding the phenomenon of optical isomers.

A representation of the tetrahedral carbon atom is shown in Fig. 7.1 (a) by molecular model and in Fig. 7.1 (b) by wedged formulae.



(a) Molecular model.



(b) Wedge projection.

Fig. 7.1. Representation of tetrahedral carbon.

It should be noted that, by convention, the wedge represents the bond pointing towards the observer out of the plane of the paper, the hatched line (or dashed line) represents the bond behind the plane of the paper. The normal lines show the bonds in the plane of the paper.

7.5.2. Polarised light

An ordinary ray of light consists of electromagnetic waves of various wavelengths and its vibrations take place in all planes at right angles to the direction in which it travels. A ray of light which consists of waves having only one wavelength is known as monochromatic light. Even such a ray has its vibrations in all planes. However, if a ray of monochromatic light (such as yellow light from a sodium flame) is passed through a Nicol prism (a special prism made from calcite which is a particular crystalline form of calcium carbonate), the wave motion of emergent light is restricted to only one plane. Light whose vibrations take place in only one plane is known as plane polarised light or just polarised light. The plane along which vibrations take place is known as plane of polarisation and the Nicol prism used for polarising the light is known as polariser (Fig. 7.2).

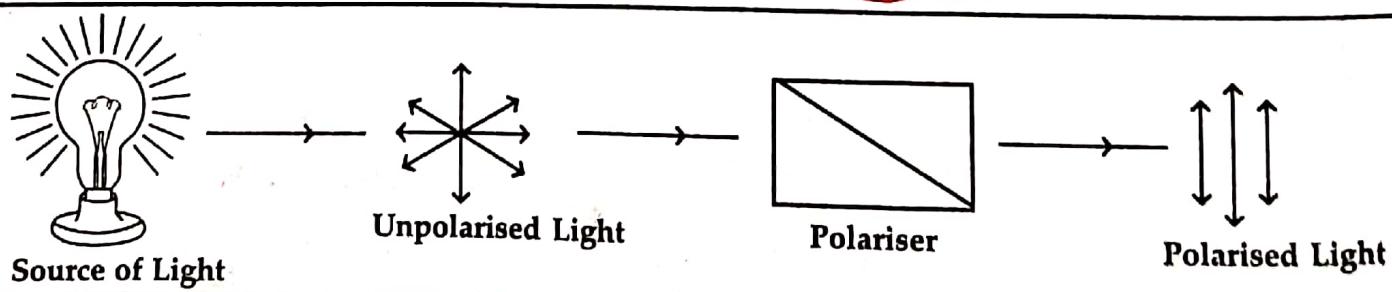


Fig. 7.2. Vibrations in ordinary and polarised forms of light.

7.5.3. Optical Activity

There are certain substances which can rotate the plane of polarised light. For instance, when polarised light vibrating in a certain plane is passed through cane-sugar solution, the light which emerges out vibrates in a different plane. Such substances which can rotate the plane of polarised light are said to be optically active and the property is called optical activity.

The substances which rotate the plane of polarised light towards the right are termed **dextrorotatory (+)** while those which rotate towards the left are called **laevorotatory (-)**. The instrument used for measuring the angle of rotation (denoted as α) of the plane of polarised light is known as a **polarimeter**.

The angle of rotation through which plane of polarised light is rotated by an optically active substance depends upon many factors which are :

- (i) Nature of the compound.
- (ii) Length of the liquid column through which the light passes.
- (iii) Concentration of the solution and nature of the solvent (in case of solid substances only).
- (iv) Temperature.
- (v) Wavelength of light used.

7.5.4. Specific Rotation

In order to compare the rotatory powers of different substances, optical activity is expressed as **specific rotation**, $[\alpha]_D^t$. It is the angle of rotation of the plane of polarised light produced by a tube one decimetre (10 cm) in length filled with a solution having one gram of the substance per ml of the solution at a temperature t using light of wavelength 5893 Å from sodium vapour lamp. (This light is called D-line of sodium).

Specific rotation is generally calculated from the equation :

$$[\alpha]_D^t = \frac{\text{Observed angle of rotation}}{l \times d}$$

where d represents the weight in grams of solute in 1 ml of solution or density of the substance if it is a liquid and l is the length in decimetres of the tube filled with the sample. For instance the specific rotation of cane-sugar solution at 293 K is $[+66.5^\circ]_D^{293}$.

7.5.5. Elements of Symmetry

The phenomenon of optical activity is essentially related to lack of symmetry in molecular structure. A simple method to decide whether a molecule is symmetrical or not involves three criteria of symmetry known as elements of symmetry. An element of symmetry may be defined as a plane, line or point with respect to which the structure possesses a definite symmetry.

There are three elements of symmetry as discussed below :

1. Plane of symmetry. It is an imaginary plane passing through an object or a structure which divides the object or structure into two halves such that one half is the mirror image of the other. For example, a beaker has a plane of symmetry as shown below in Fig. 1.3 (a). Similarly, the molecule of propanoic acid has a plane of symmetry as shown in Fig. 1.3 (b).

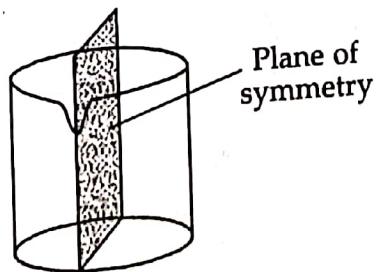


Fig. 7.3. (a) Plane of symmetry in a beaker.

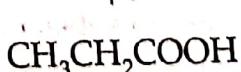
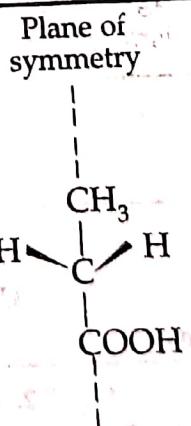


Fig. 7.3. (b) Plane of symmetry in propanoic acid.

In the study of optical isomerism, the plane of symmetry may be shown simply with the help of three dimensional formulae or more conveniently by using planar formulae as shown in Fig. 7.4 (a) and 7.4 (b) for the molecule of 2, 2-dibromobutane.

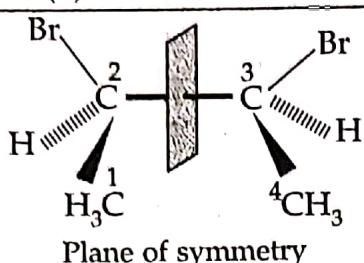


Fig. 7.4. (a) Three dimensional representation.

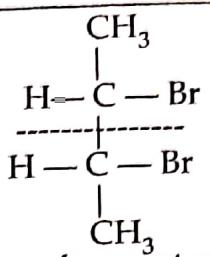


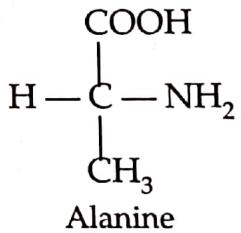
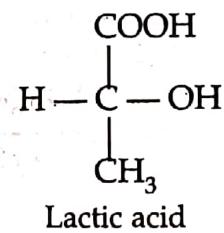
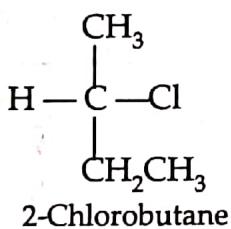
Fig. 7.4. (b) Planar representation.

Human hand is the most perfect example of an object having no plane of symmetry.



No plane of symmetry

2-Chlorobutane, lactic acid and alanine are some examples of molecules which do not have any plane of symmetry.



2. **Centre of symmetry.** It is an imaginary point within a molecule at which all the straight lines joining identical points in the molecule cross each other. For example, the centre of symmetry in a molecule of 2, 4-dimethylcyclobutane-1, 3-dicarboxylic acid is shown below in Fig. 7.5.

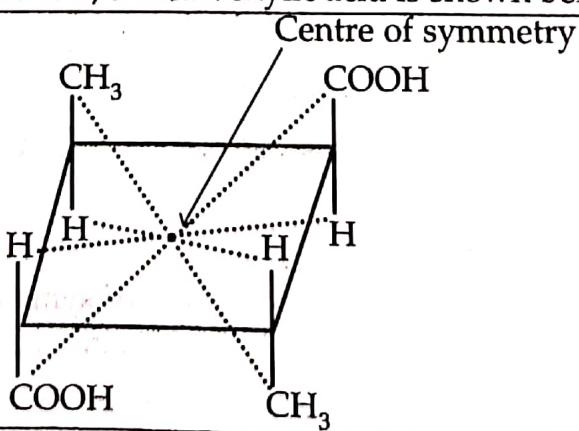
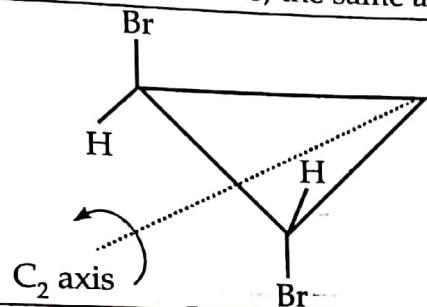


Fig. 7.5. Centre of symmetry in 2, 4-dimethylcyclobutane-1, 3-dicarboxylic acid.

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

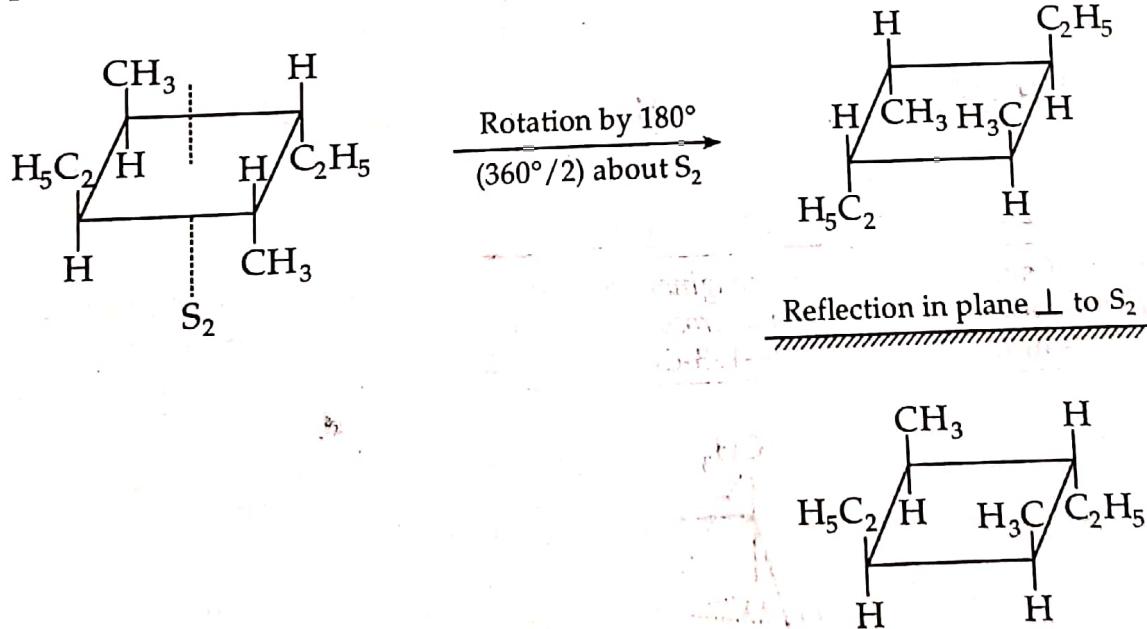
3. **Axis of symmetry.** It is an imaginary line passing through the molecule so that when the molecule is rotated about this line, exactly similar geometrical arrangement appears more than once in one complete revolution (i.e. in a rotation through 360°). If the identical arrangement appears twice in

one complete revolution (i.e. after every 180°), the axis is called **two fold axis of symmetry** (denoted as C_2 axis). If the similar arrangement appears thrice, it is **three-fold axis of symmetry** and so on. For example, trans - 1, 2-dibromocyclopropane possesses a C_2 axis of symmetry in the plane of the ring which bisects the bond between carbon atoms 1 and 2 and intersects the carbon atom 3 as shown in Fig. 1.6. When rotated around this axis, the same arrangement appears after every 180° .

Fig. 7.6. C_2 axis of symmetry.

Alternating axis of symmetry or rotation reflection axis. This is another element of symmetry which is rarely used. A molecule is said to have an n -fold alternating axis of symmetry if rotation by an angle of $360/n$ about the axis followed by reflection in a plane perpendicular to that axis gives a molecule which cannot be distinguished from the original molecule. For example, 1, 3 - diethyl - 2, 4 - dimethyl cyclobutane possesses a two-fold axis of symmetry as

shown below. If the molecule (a) is rotated by an angle of 180° . (i.e. $\frac{360^\circ}{2}$) about the axis S_2 which passes through the centre of the ring, it gives a molecule (b). The reflection of (b) in a plane perpendicular to the axis gives the original molecule (a).



It may be noted that a one-fold alternating axis of symmetry corresponds to a plane of symmetry while a two-fold alternating axis of symmetry corresponds to centre of symmetry.

Problem 7.1. Which of the following molecules have a plane of symmetry ?

- (i) Propanoic acid (ii) 2-Methylbutan-1-ol (iii) 2-Methyl cyclohexanone (iv) Aminoethanoic acid
[Ans. (i) and (iv)]

7.5.6. Molecular chirality : Chiral and Achiral Structures

1. Chiral structures. A structure or object is said to be chiral (or dissymmetric) if it is not superimposable on its mirror image. Such a structure does not have either a plane or a centre of symmetry.

The most perfect example of a chiral object is human hand. It does not have any plane of symmetry and cannot be superimposed on its mirror image. If you hold your left hand upto a mirror, the image looks like a right hand but if you try to superimpose one hand over the other (both palms down), you cannot do it (Fig. 7.7). Similarly a right handed glove and a left handed glove are chiral objects.

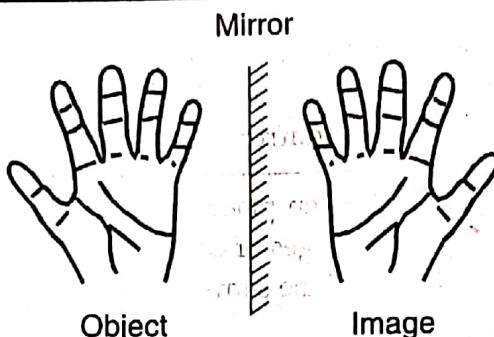
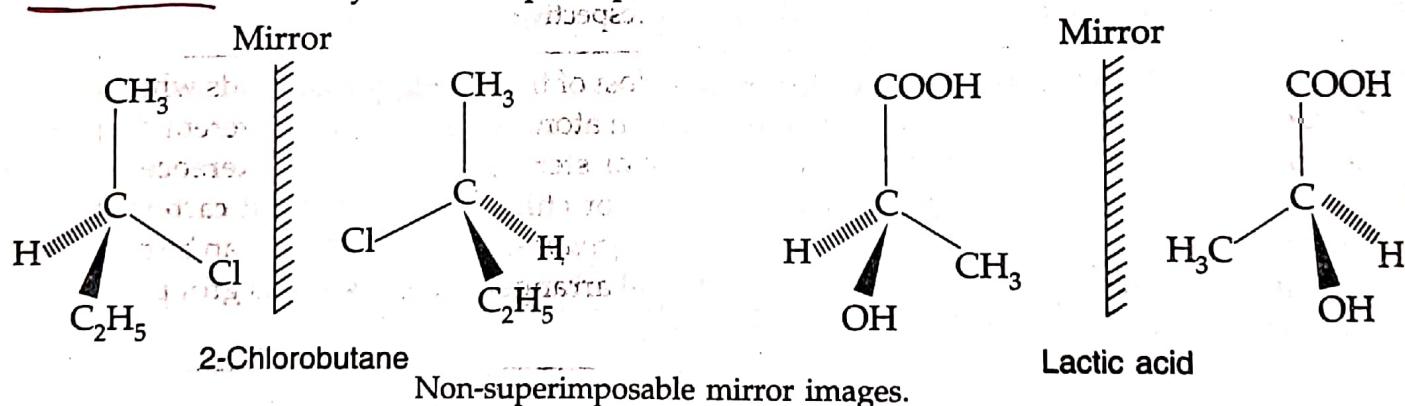


Fig. 7.7. Non-superimposable mirror images.

A very large number of organic molecules such as 2-chlorobutane and lactic acid are known to have chiral structures as they are not superimposable on their mirror images.



The substances having chiral structures are said to possess the property of **chirality**. It should be noted that chirality is the property of complete object or structure and not of its parts.

It may also be noted that even though there are three kinds of elements of symmetry, chirality is primarily related to lack of plane of symmetry and the centre of symmetry.

2. Achiral structures. A structure or object which has a plane of symmetry and is superimposable on its mirror image is known as **achiral** (or symmetrical). Such a structure always possesses a plane of symmetry or a centre of symmetry. For example, the letter A and the button on your shirt represent achiral structures or objects. It can be easily seen that each of these has a plane of symmetry and is superimposable on its mirror image (Fig. 7.8).

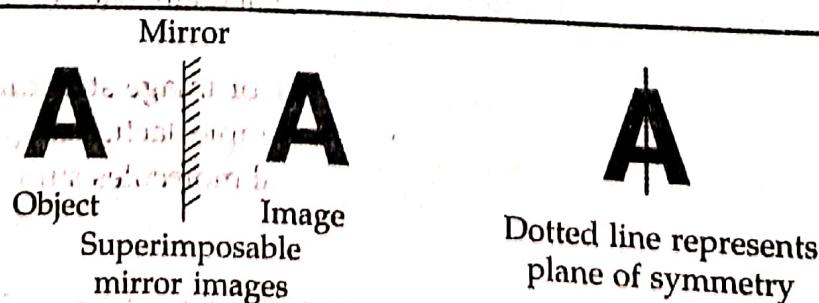
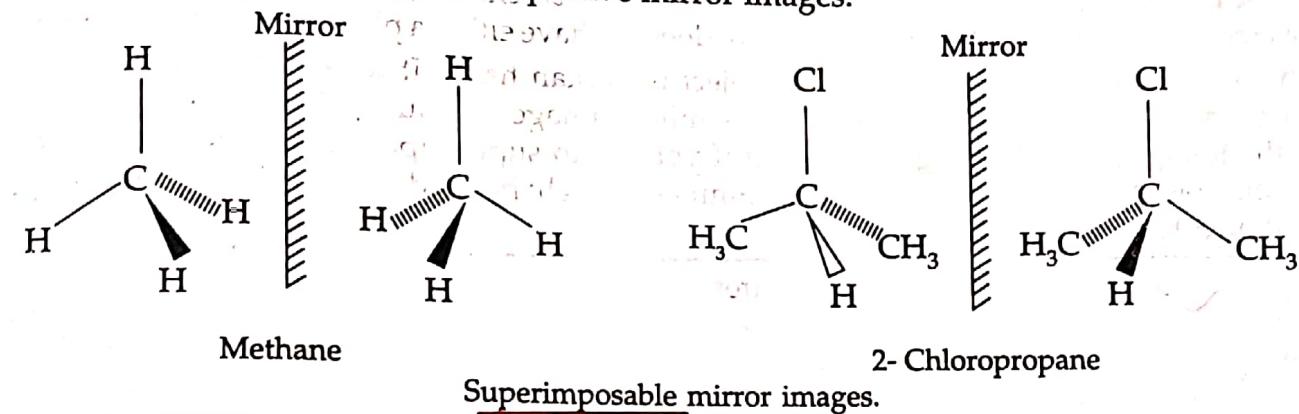


Fig. 7.8. Achiral structure.

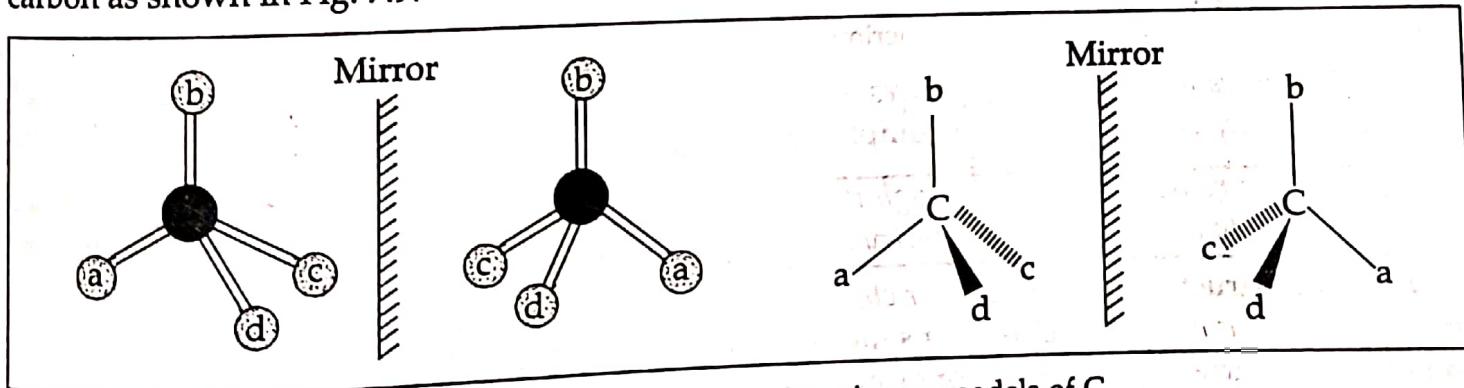
Methane and carbon tetrachloride are perfect examples of molecules having achiral structures as they are superimposable on their respective mirror images.



*Two objects are said to be *superimposable* if when placed one upon the other, their corresponding parts lie together. Two objects that are like mirror images of each other may be either superimposable or non-superimposable. For example, two note books of the same size having mirror image relationship are superimposable.

**The term *chiral* based upon the Greek word *cheir* (which means hand) was first introduced by Cahn, Ingold and Prelog in 1964. Thus chirality means 'handedness' i.e., the relationship which exists between the left and right hands. In recent years, the terms chiral and chirality have almost completely replaced the old terms dissymmetric and dissymmetry respectively.

3. Origin of chirality in organic compounds. Most of the organic compounds which are chiral in nature owe their chirality to the presence of a carbon atom bonded to four different groups. Such a carbon is termed as **chiral carbon** or **chiral centre** or **stereogenic centre** or **stereocentre** (earlier known as **asymmetric carbon**). A stereogenic centre or chiral centre or chiral carbon is a carbon atom which is bonded to four different monovalent atoms or groups such as C_{abcd} . There can be two different tetrahedral models for C_{abcd} which differ in the spatial arrangements of various groups attached to carbon as shown in Fig. 7.9.



Each of the two models is related to the other like an object to its mirror image and one cannot be superimposed on the other no matter how we turn or twist them. Each of these models, therefore, represents a chiral structure.

Similarly we can have two non-superimposable mirror image structures for any compound which contains a stereogenic centre or chiral centre. For example, lactic acid [$\text{CH}_3\text{CH}(\text{OH})\text{COOH}$] and 2-methyl-1-butanol [$\text{C}_2\text{H}_5\text{CH}(\text{CH}_3)\text{CH}_2\text{OH}$] are chiral molecules since each of them contains a chiral centre (the one marked*) Fig. 7.10.

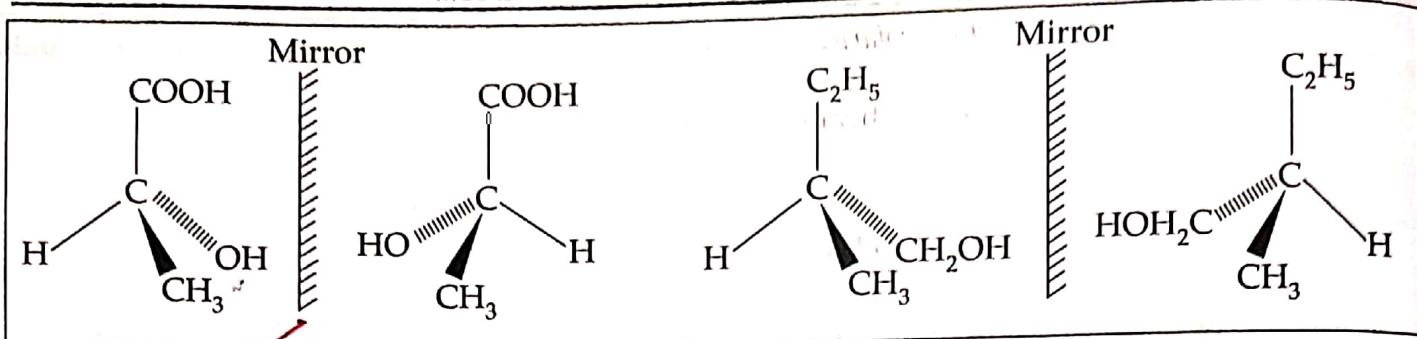
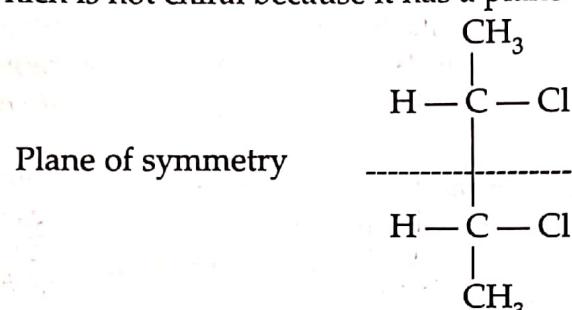
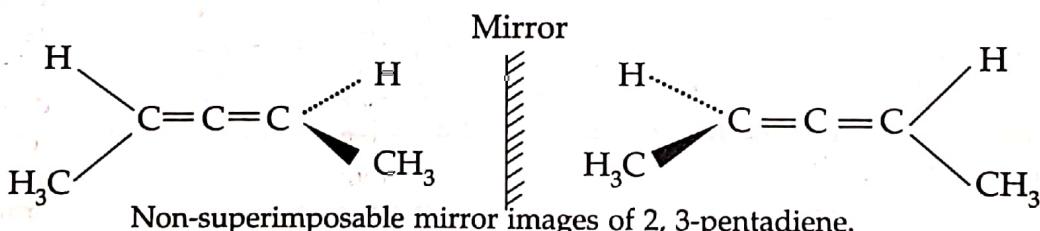


Fig. 7.10. Non-superimposable mirror image models of lactic acid and 2-methyl-1-butanol.

It must be emphasised, however, that *certain molecules may contain more than one stereogenic or chiral centre and still they may be achiral or non-disymmetric*. For instance, 2, 3-dichlorobutane, $\text{CH}_3-\overset{*}{\text{CHCl}}-\overset{*}{\text{CHCl}}-\text{CH}_3$, which has two chiral centres (those marked *) exists in many isomeric forms one of which is not chiral because it has a plane of symmetry as shown below :



Chiral molecules not containing any chiral carbon. There are certain molecules known to exist which are chiral even though they do not contain any chiral carbon. For example, allenes ($\text{RCH}=\text{C}=\text{CHR}$) represent a well known class of such compounds as illustrated below :

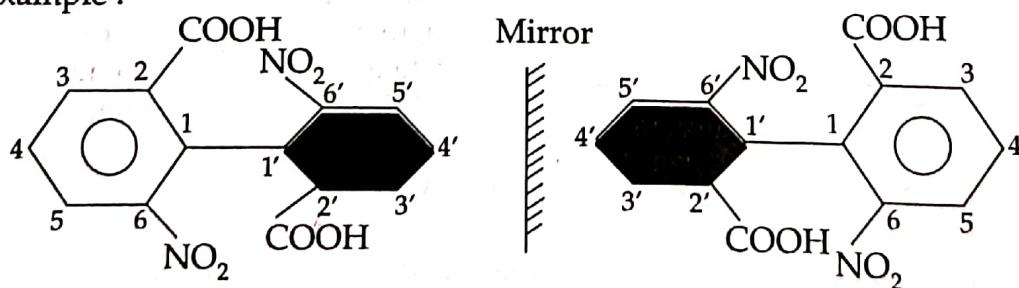


Non-superimposable mirror images of 2, 3-pentadiene.

It may be seen by molecular models that chirality in 2, 3-pentadiene arises due to the fact that the two groups singly bound to one of the end carbon atoms of allene system are in a different plane than the two groups singly bound to the other end carbon of the allene system.

Substituted biphenyls constitute another example of such compounds which are chiral without containing any chiral carbon atom. The chirality in such compounds arises due to the fact that the two benzene rings lie in different planes perpendicular to each other.

For example :



Non-superimposable mirror images of 6, 6'-dinitrophenic acid.

7.6. OPTICAL ISOMERISM : ENANTIOMERISM

It has been observed that optically active substances always exist in two or more isomeric forms, which differ with respect to their optical activity or their action on plane polarised light. As already stated, *the isomers which resemble one another in their chemical reactions and most of the physical*

properties but differ in their effect on polarised light are called optical isomers and the phenomenon is known as optical isomerism.

- There are two main types of optical isomerism. These are :
- Enantiomerism,
 - Diastereomerism.

We shall now discuss these two types starting with enantiomerism.

7.6.1. Enantiomerism

It is the simplest kind of optical isomerism which was discovered by Pasteur, in 1848, as a result of his work on the salts of tartaric acid. He observed that optically inactive sodium ammonium tartrate consisted of a mixture of two distinct types of crystals. These two types of crystals were not superimposable on each other although their shapes were like *mirror images* of each other. The relationship between the two types of crystals may be compared to that between a pair of right and left handed gloves. Pasteur separated the two types of crystals from the original sample with the help of a magnifying lens and a pair of tweezers. Unlike the original optically inactive sample, each type of crystals was found to be optically active in its aqueous solution. Moreover, the specific rotation of the solution of one type of crystals was found to be *equal but of opposite sign* to that of the solution of second type of crystals.

Considering the fact that difference in optical rotation was observed in solution where the solute exists in the form of simple molecules, Pasteur proposed that the molecules constituting the two types of crystals were also non-superimposable mirror images of each other. *(Such isomers whose molecular structures are non-superimposable mirror images of each other and which rotate the plane-polarised light equally but in opposite directions are now known as enantiomers or enantiomorphs.)* The phenomenon of mirror image isomerism is called enantiomerism. Since the mirror-image isomers differ only in the spatial arrangement of atoms, enantiomerism represents a type of stereoisomerism.

Explanation of enantiomerism. The existence of mirror-image isomers or enantiomers was justified by Van't Hoff on the basis of tetrahedral concept of carbon atom. Let us try to apply this concept to an imaginary compound of the type *Cabcd* in which a carbon atom is attached to four different groups. Such a compound can be represented by two different tetrahedral models which differ in the spatial arrangements of various groups attached to the carbon atom Fig 1.9 on page 4/9). The two models are related to each other like an object and its mirror image and one cannot be superimposed over the other, no matter how we turn or twist them. These models represent two enantiomers of the compound.

For example, let us draw tetrahedral formulae of substances such as lactic acid $[\text{CH}_3\text{CH}(\text{OH})\text{COOH}]$ and 2-methyl-1-butanol $[\text{C}_2\text{H}_5\text{CH}(\text{CH}_3)\text{CH}_2\text{OH}]$ which are known to exhibit enantiomerism. In each of these cases we find that it is possible to construct two formulae which are non-superimposable mirror images of each other and as such they represent the different enantiomers (Fig. 7.10 on page 7/10).

It may be pointed out, however, that if the compound, containing a tetrahedral carbon atom does not have four different groups attached to this carbon, then the molecules are superimposable on their mirror images. This is illustrated below with the help of bromochloromethane CH_2ClBr . Such compounds do not exhibit enantiomerism because all their molecules are of the same type.

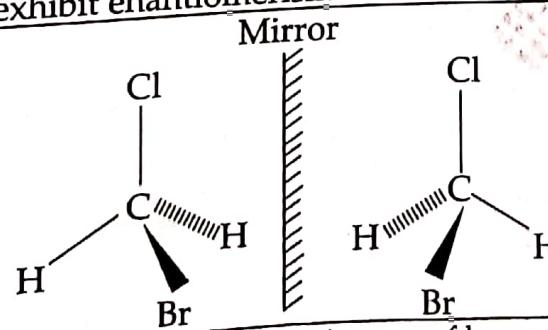


Fig. 7.11. No enantiomerism possible as mirror images of bromochloromethane are superimposable.

7.6.2. Fundamental condition for enantiomerism

It has been shown above that enantiomeric molecules are always non-superimposable mirror

images of each other. The non-superimposability of mirror images invariably arises due to chiral nature of the molecules. As already stated, a molecule is termed as chiral if it has no plane or centre of symmetry and is, therefore, non-superimposable on its mirror image.

Chirality in most of the enantiomeric molecules is itself due to the presence of at least one chiral carbon in the molecule. For example, lactic acid [$\text{CH}_3^*\text{CH}(\text{OH})\text{COOH}$] and 2-methyl-1-butanol [$\text{C}_2\text{H}_5^*\text{CH}(\text{CH}_3)\text{CH}_2\text{OH}$] contain one chiral carbon each (the one marked*) and therefore exist as enantiomeric forms as shown in Fig. 7.10 on page 7/10.

At the same time there can be molecules such as 2, 3-pentadiene and substituted biphenyls such as 6, 6'-dinitrophenic acid which do not contain any chiral carbon but they still possess the property of chirality and thus exhibit enantiomerism.

It may be concluded, therefore, that chirality (i.e. the property of existing as non-superimposable mirror images) is the fundamental and only condition of enantiomerism.

7.6.3. Characteristics of enantiomers

The important characteristics of the enantiomers of a given substance are described below :

(i) They have identical physical properties such as melting points, boiling points, densities, solubilities, refractive indices. The only difference lies in the direction of rotation of plane polarised light, although even here the magnitude of specific rotation is the same. For example, the specific rotations of the two enantiomeric 2-methyl-1-butans are $+5.76^\circ$ and -5.76° respectively.

(ii) They have identical chemical properties except in reactions with other optically active compounds. For example, the ordinary chemical reactions of (+) lactic acid are exactly like those of (-) lactic acid. Moreover, there is no difference in the speed of such reactions. There may be a difference, however, in the rates of reactions at which two enantiomers react with some other optically active compound. For instance, the rate of esterification of (+) lactic acid with (+) sec. butyl alcohol [$\text{CH}_3\text{CH}_2\text{CH}(\text{OH})\text{CH}_3$], which is optically active, would be different from the rate of esterification of (-) lactic acid with the same alcohol.

(iii) They have different biological properties. In contrast to physical and usual chemical properties, enantiomers are quite different in their biological properties. For example, (+) sugar plays an important role in animal metabolism whereas (-) sugar is not metabolised at all. Similarly, (+) tartaric acid is readily consumed by the mould *penicillium glaucum* while (-) tartaric acid is not.

(iv) When equal quantities of enantiomers are mixed together it results in the formation of an optically inactive form called racemic modification or racemic mixture or racemate. The racemic modification is distinguished by using the prefix (\pm) before the name of the compound. For example, if equal quantities of (+) lactic acid and (-) lactic acid are mixed with each other, we get racemic or (\pm) lactic acid which is optically inactive.

7.6.4. Enantiomerism and optical activity

We have just learnt that the fundamental condition for the phenomenon of enantiomerism is the chiral nature of the molecules and the fundamental difference between enantiomers of a given substance is the direction of optical rotation. Let us now examine as to what structural features give rise to optical activity and how is it related to the phenomenon of enantiomerism.

A single individual molecule of nearly every substance can cause some rotation of the plane polarised light when a beam of such light passes through the molecule. The direction and extent of rotation caused by a particular molecule depends upon its orientation in the beam of light. But in actual practice it is not possible to have with us only a single molecule of any substance; even a very small sample of a substance being made up of very large number of molecules distributed at random. Therefore, what happens in most of the cases is that for every molecule that rotates the plane of polarised light, there is another identical molecule oriented as the mirror image of the first which exactly cancels its effect. As such no optical rotation can be observed. This means optical inactivity of a substance is basically due to the random distribution of identical molecules which can serve as mirror images of each other.

But in case of chiral molecules the mirror image of any one molecule is not another identical molecule rather it is a different isomeric molecule. Now, if we take a pure sample consisting of a single enantiomer, no molecule can serve as the mirror image of another. As a result there cannot be exact cancellation of rotations and as such optical activity is observed. Thus a given sample of a

substance can exhibit optical activity only if the constituent molecules are non-superimposable mirror images of one another. In other words, chirality (i.e., non-superimposability of mirror images), is also the fundamental and sufficient condition for optical activity.

Problem 7.2. Classify the following objects as chiral or achiral :

- (i) Shoe
- (ii) Spoon
- (iii) Cup
- (iv) Ear
- (v) P

[Ans. Chiral - (i), (iv) and (v); Achiral - (ii) and (iii)]

Problem 7.3. Which of the following molecules are chiral in nature ?

- (i) $\begin{array}{c} \text{CH}_3 \\ | \\ \text{CH}_3 - \text{CH} - \text{CHCl} - \text{CH}_3 \end{array}$
- (ii) $\text{CH}_2\text{OHCHOHCHO}$
- (iii) $\text{CH}_3\text{CHOHCH}_3$
- (iv) $\text{CH}_3 - \text{CH}_2 - \underset{\text{CH}_3}{\text{CH}} - \text{CH}_3$
- (v) $\text{C}_6\text{H}_5\text{CHCl} - \text{CH}_3$
- (vi) $\text{CH}_2\text{NH}_2\text{COOH}$

Problem 7.4. Given below are the structural formulae of all alkanes having the molecular formula C_6H_{14} . Which of these exhibit enantiomerism ?

- (i) $\text{CH}_3(\text{CH}_2)_4\text{CH}_3$
- (ii) $\text{CH}_3(\text{CH}_2)_2\underset{\text{CH}_3}{\text{CH}}\text{CH}_3$
- (iii) $\begin{array}{cccc} \text{CH}_3 & - & \text{CH} & - \\ & | & | & \\ & \text{CH}_3 & \text{CH}_3 & \end{array} \text{CH}_3 - \text{CH}_2 - \text{CH}_3$
- (iv) $(\text{CH}_3)_3\text{C} - \text{CH}_2\text{CH}_3$
- (v) $\begin{array}{ccccc} \text{CH}_3 & \text{CH}_2 & \text{CH} & \text{CH}_2 & \text{CH}_3 \\ & | & & | & \\ & \text{CH} & & & \end{array}$

[Ans. None of these can exhibit enantiomerism.]

Problem 7.5. Point out the optically active compounds out of the following :

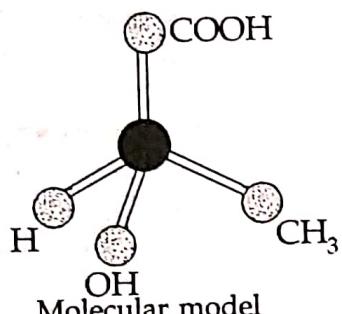
- (i) $\text{CH}_3\text{CHOHCH}_2\text{OH}$
- (ii) $\text{CH}_3 - \text{CH}_2 - \text{CH} = \text{C} = \text{CH} - \text{CH}_2\text{CH}_3$
- (iii) $\begin{array}{c} \text{COOH} \\ | \\ \text{H} - \text{C} - \text{OH} \\ | \\ \text{HO} - \text{C} - \text{H} \\ | \\ \text{COOH} \end{array}$
- (iv) $\text{CH}_2\text{OH} - \text{CHOH} - \text{CHO}$

[Ans. All are optically active.]

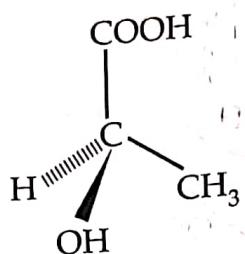
7.7. REPRESENTATION OF STEREOISOMERS

7.7.1. Flying Wedge Formulae

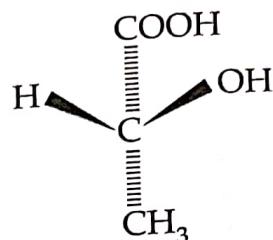
We have so far used the molecular models and three dimensional tetrahedral formulae to represent the stereoisomers. The tetrahedral formulae can also be drawn in a somewhat different, but more convenient, way known as **flying wedge formulae**. For drawing these formulae, the molecule is oriented in space in such a way that two bonds to the stereocentre point towards the observer while the other two bonds are directed away from the observer. The bonds pointing towards observer while the other two bonds are represented by wedges drawn horizontally (which may or may not be drawn along a straight line) The bonds pointing away from the observer are represented by hatched (or dotted) lines drawn vertically. For example, the molecular model, tetrahedral formula and flying wedge formula of one of the enantiomers of lactic acid $\text{CH}_3\text{CH}(\text{OH})\text{COOH}$ may be shown as follows :



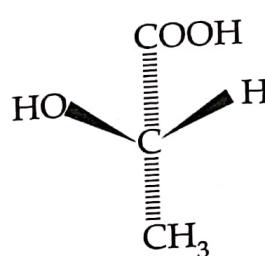
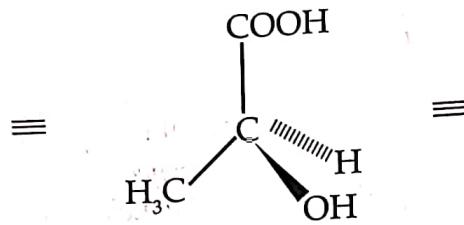
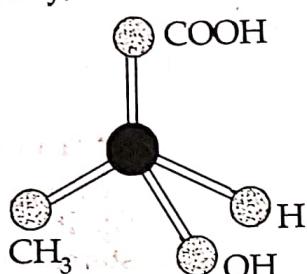
Molecular model



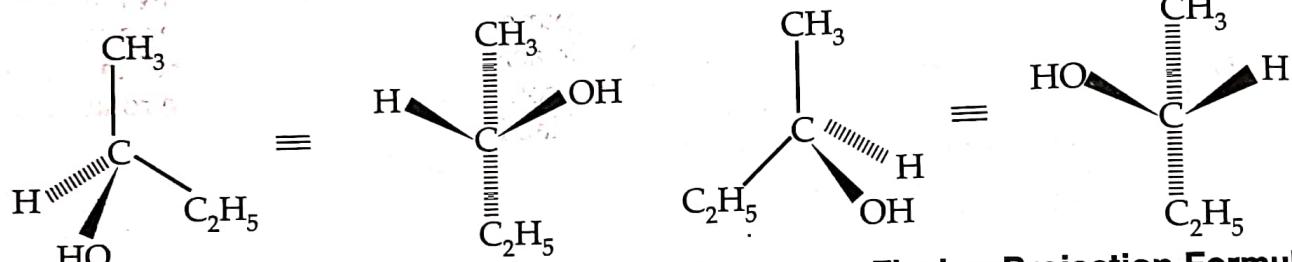
Tetrahedral formula

Flying wedge formula
Similarly, the three kinds of representations of the other enantiomer of lactic acid can be shown

as :



The tetrahedral and flying wedge formulae of the enantiomers of 2-butanol are given below:



7.7.2. Planar Representation of three Dimensional Formulae : Fischer Projection Formulae

The use of molecular models is, no doubt, the most suitable method of showing the spatial orientations of atoms constituting the molecules. But it is not very convenient to represent the formulae of compounds on paper. Therefore, a simple, although not foolproof method, was introduced by Emil Fischer (1891) for projecting three dimensional formulae of chiral molecules on planar surface. The planar representations are called **Fischer projection formulae**.

Procedure for writing Fisher projections. For writing the projection formulae, the following procedure is adopted :

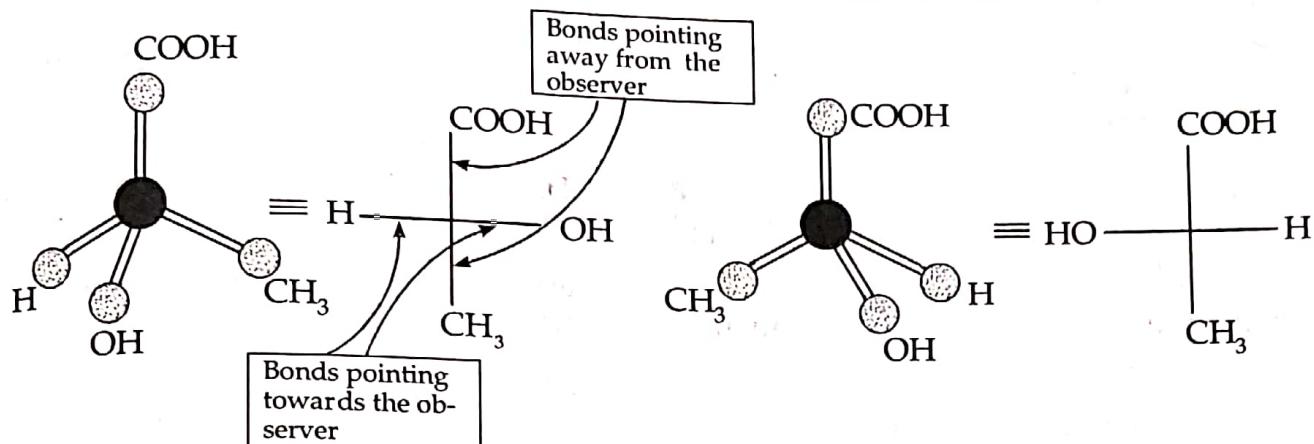
(i) *The chiral molecule is viewed in such a way that two groups bound to chiral carbon point towards the observer while the other two groups point away from the observer.*

(ii) *The various groups attached to the chiral carbon are then projected to the plane of the paper in the form of a cross so that horizontal lines represent bonds pointing towards the observer while vertical lines represent bonds pointing away from the observer. (If the chiral molecule contains two or more chiral carbons, each carbon is considered separately as described above).*

(iii) *The vertical part of the projection formula should represent, so far as possible, the longest chain of carbon atoms in the molecule with the carbon atom to be numbered as 1 according to IUPAC system being written at the top.*

(iv) *The chiral carbon atom is not written at all while writing the projection formulae. It is taken for granted that the chiral carbon is located where the horizontal and vertical lines cross each other.*

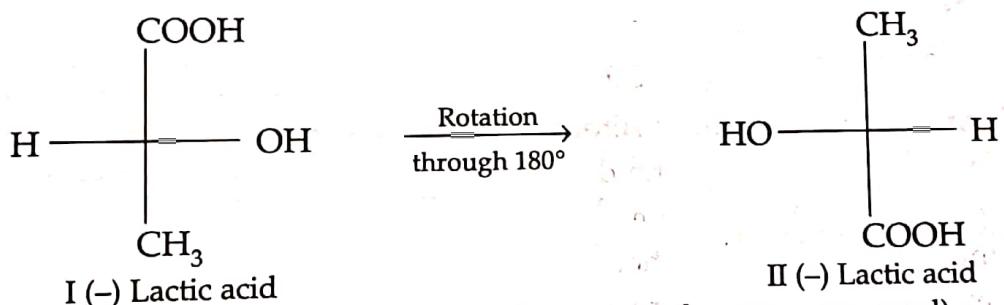
For instance the projection formulae of the two enantiomers of lactic acid may be represented as shown ahead.



Molecular models and Fischer projection formulae of the two enantiomers of lactic acid.

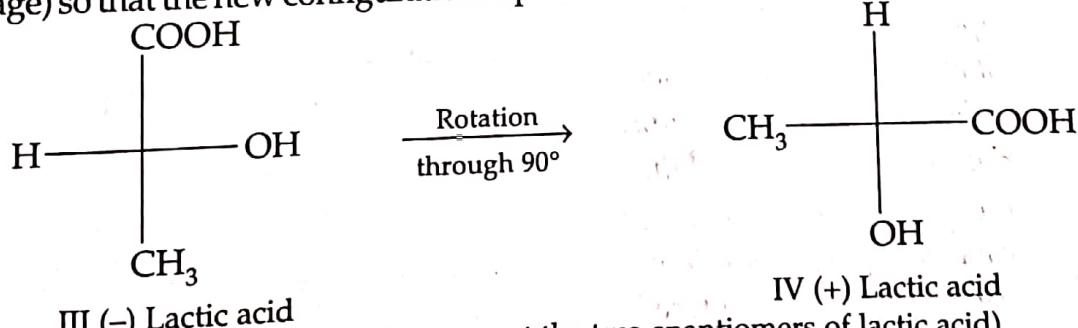
It should be noted that more than one Fischer projections can be written for the same compound depending upon which bonds are shown horizontally and which bonds are drawn vertically. It is, therefore, necessary to test whether the given Fischer projections represent the same stereoisomer of a compound or not. This can be done by using the following rules.

(i) A Fischer projection may be imagined to be rotated from end to end without lifting it from the plane of the paper. Rotation by 180° in the plane of the paper does not bring about any change in configuration. For example, if the projection I of lactic acid is rotated through 180° in the plane of the paper, it gives projection II. Since no change in configuration takes place in rotation by 180°, projections I and II represent the same stereoisomer of lactic acid.



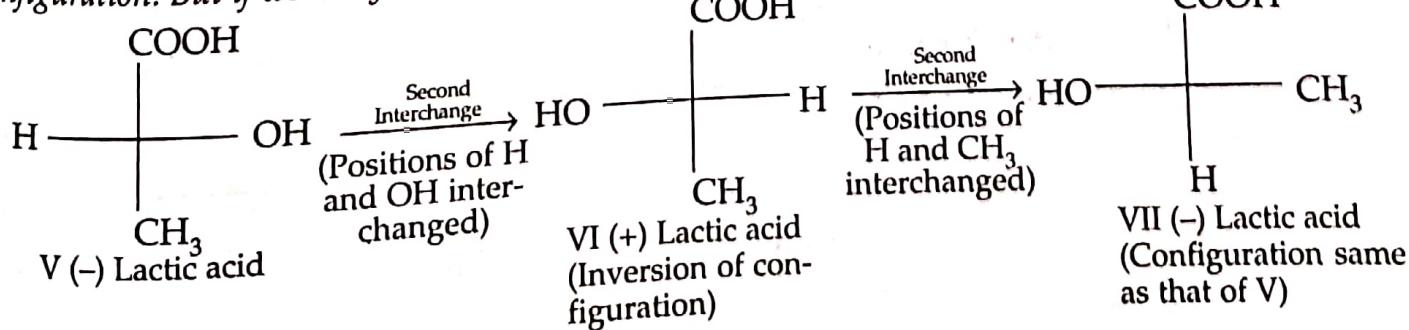
(No change in configuration; I and II represent the same compound)

But rotation by 90° or 270° leads to inversion of configuration (i.e., changes one configuration into its mirror image) so that the new configuration represents the enantiomer of the original compound.



(Inversion of configuration; III and IV represent the two enantiomers of lactic acid)

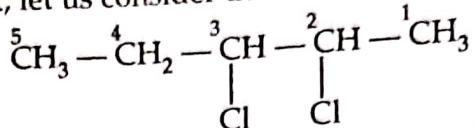
(ii) If positions of two groups or atoms about the chiral carbon are interchanged, it also leads to inversion of configuration. But if we carry out two such interchanges, the configuration remains unaltered.



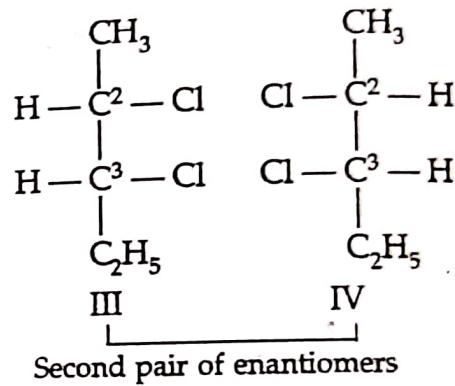
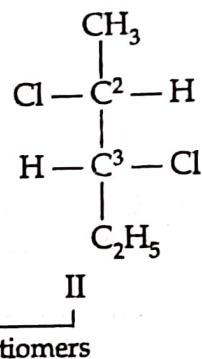
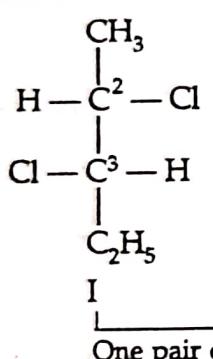
It is quite evident from above that one interchange is equivalent to rotation by 90° or 270° while two interchanges are equivalent to rotation by 180° .

~~7.8. CHIRAL AND ACHIRAL MOLECULES WITH TWO STEREOGENIC CENTRES : DIASTEREOMERISM~~

We have learnt that a compound containing one stereogenic centre exists in two stereoisomeric forms which are known as enantiomers of each other. What about compounds containing two stereogenic centres? Quite unexpectedly such compounds can exist in more than two stereoisomeric forms. To illustrate this statement, let us consider the case of 2, 3-dichloropentane:



which contains two stereogenic centres. Since the four different groups attached to one stereogenic centre are not the same as those attached to the other, the two chiral carbon atoms are dissimilar from the another. There are as many as four stereoisomers (I, II, III and IV) possible for this compound.

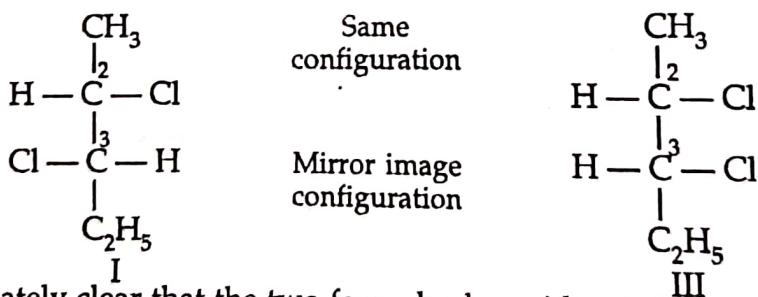


One pair of enantiomers

Second pair of enantiomers

Examination of formulae I and II reveals that they are non-superimposable mirror images of each other and hence represent a pair of enantiomers. Similarly, III and IV are also non-superimposable mirror images of each other and as such represent another pair of enantiomers.

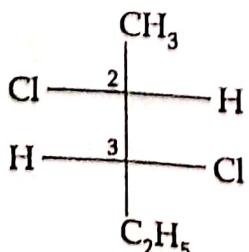
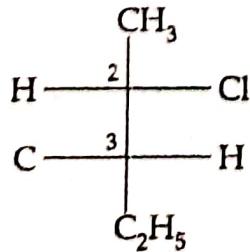
Let us now compare the formula I with formula III.



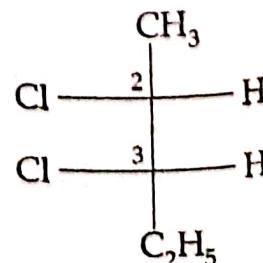
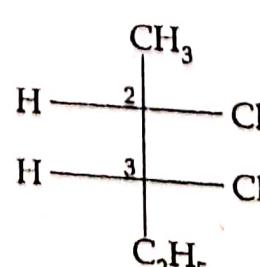
It becomes immediately clear that the two formulae have identical configurations about one chiral carbon (C^2) but mirror image configurations about the other chiral carbon (C^3). The net result is that the two forms are neither identical nor mirror images of each other. Such stereoisomers of a substance which are not mirror images of each other are known as diastereomers.

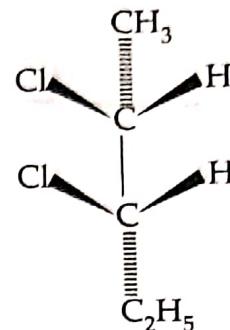
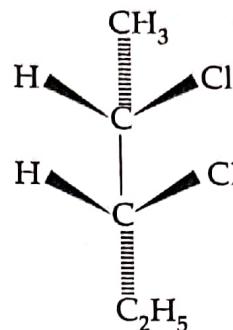
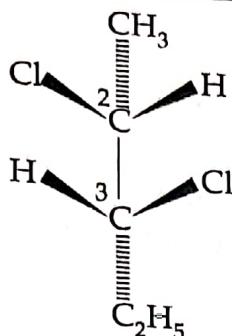
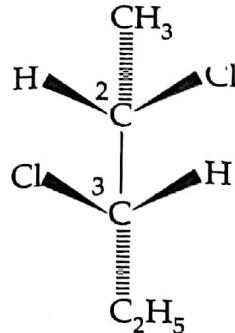
In addition to formulae I and III, formulae I and IV, II and III, II and IV also represent pairs of diastereomers.

Fischer projection formulae and flying wedge representations of the four stereoisomers of 2, 3-dichloropentane are given below.



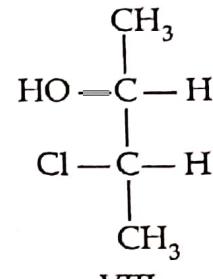
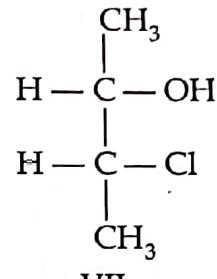
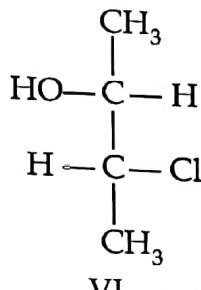
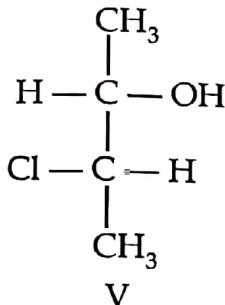
Fischer projection formulae.





Flying wedge representations.

3-Chloro-2-butanol affords another example of a compound having 2 dissimilar chiral carbon atoms which can exist in four stereoisomeric forms as given below :



It may be seen that structures V and VII; V and VIII; VI and VII; VI and VIII represent pairs of diastereomers.

Characteristics of diastereomers. The important characteristics of diastereomers are as follows :

(i) *They show similar, but not identical, chemical properties.* In the reactions of two diastereomers with a given reagent, the rates of reactions are generally different from each other. This is because diastereomers have different energies of activation for a particular reaction and, therefore, they react at different rates.

(ii) *They have different physical properties* such as melting points, boiling points, densities, solubilities and refractive indices.

(iii) *Their specific rotations are also different from each other.* In fact some of the diastereomers may be even optically inactive.

It should be noted that geometrical isomers are also diastereomers of each other but they are optically inactive.

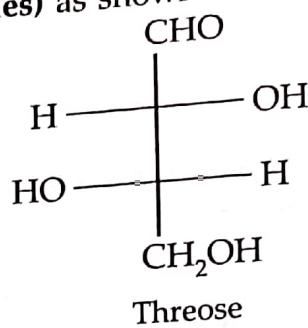
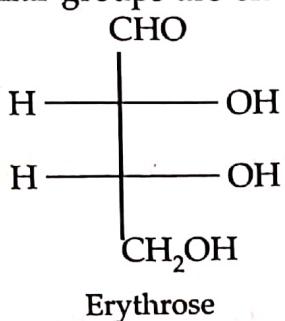
(iv) *On account of different physical properties, diastereomers can be rather easily separated from each other by physical methods such as fractional crystallisation, fractional distillation, chromatography, etc.*

Comparison of Diastereomers and Enantiomers

Diastereomers	Enantiomers
<ol style="list-style-type: none"> These are stereoisomers which do not have a mirror image relationship. These have different physical properties such as melting point, boiling point, solubility in a given solvent and density. These can be <u>separated by fractional distillation, fractional crystallisation and adsorption chromatography</u>. These may have optical rotation in the same or opposite directions but to a different extent. These have identical chemical properties but differ in the <u>rate of reactions with optically active compounds</u>. 	<p>These are stereoisomers which have a mirror image relationship.</p> <p>These have identical physical properties, such as melting point, boiling point, solubility in a given solvent and density.</p> <p>These cannot be separated by such methods.</p> <p>These have optical rotation in opposite directions but to the same extent.</p> <p>These have identical chemical properties except with other <u>optically active compounds</u>.</p>

7.8.1. Erythro and Threo isomers

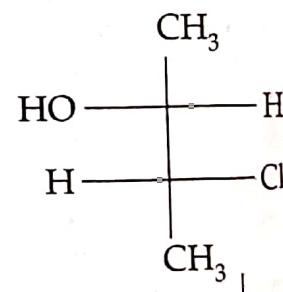
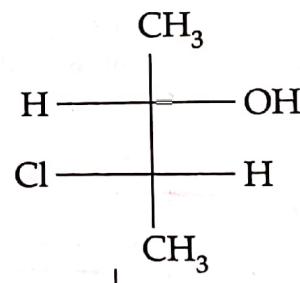
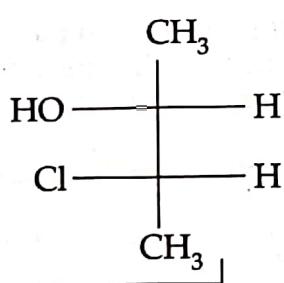
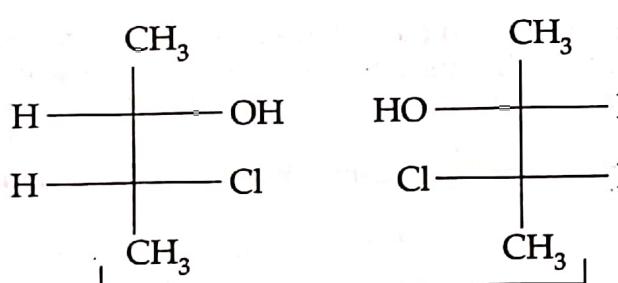
A special system of nomenclature is sometimes used for distinguishing between diastereomers in which two of the atoms or groups attached to one stereogenic centre are the same as the two atoms or groups attached to the other stereogenic centre. This method is derived from the names of two diastereomeric carbohydrates, *erythrose* (in which similar groups are on the same side) and *threose* (in which similar groups are on the opposite sides) as shown below :



If the two similar groups are on the same side in the Fischer projection formula of a molecule, the diastereomer is known as **erythro isomer**.

If the two similar groups are on the opposite sides in the projection formula, of a molecule the diastereomer is known as **threo isomer**.

For example, of the four isomers of 3-chloro-2-butanol, one pair of enantiomers is known as erythro while the other pair of enantiomers (which are diastereomers of the first pair) is known as threo as illustrated below :



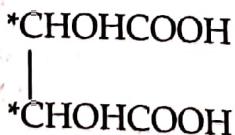
Erythro 3-chloro-2-butanol
(one pair of enantiomers)

Threo 3-chloro-2-butanol
(other pair of enantiomers)

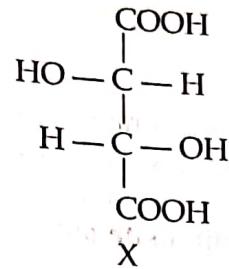
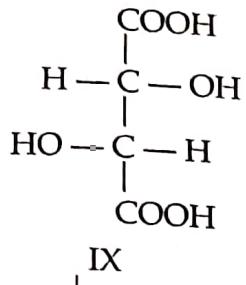
It may be seen that *any one* compound of *one pair* is diastereomer of *any one* compound of the *other pair*.

7.8. MESO COMPOUNDS

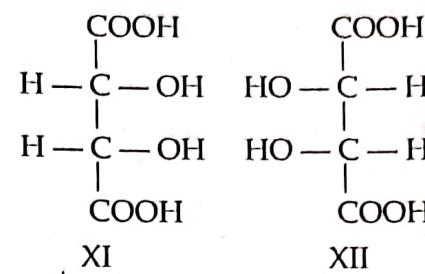
Let us now consider a compound containing two similar chiral centres i.e., having the same set of four different groups attached to each of the chiral carbon atom. A typical example of such a compound is provided by tartaric acid :



In view of the fact that it has two chiral centres, one may expect the existence of four stereoisomers of this acid having the configurations IX, X, XI and XII.

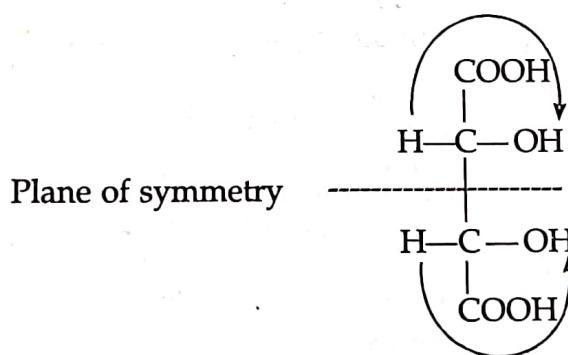


Pair of enantiomers

Superimposable mirror images;
represent only one compound

Formulae IX and X are non-superimposable mirror images of each other and, therefore, represent a pair of optically active enantiomers.

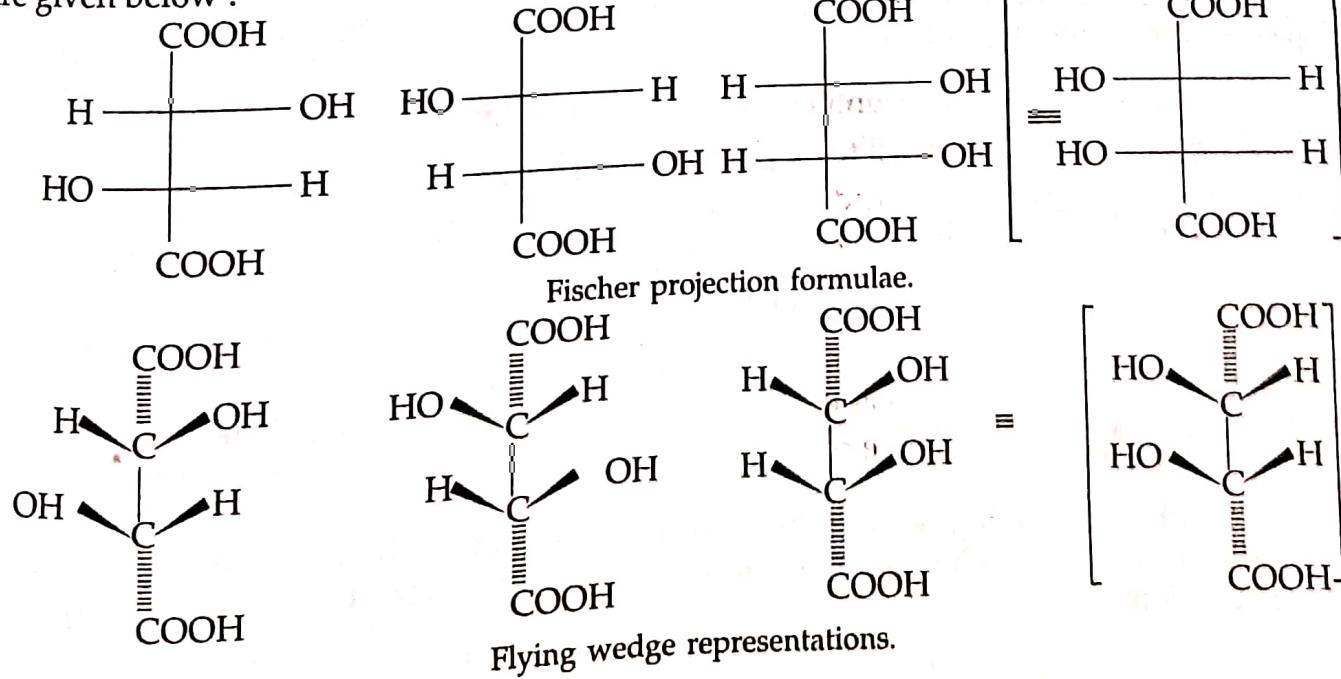
Formulae XI and XII again have a mirror image relationship. Close examination of these formulae, however, shows that one of these structures may be superimposed on the other just by rotating it through 180° *within* the plane of the paper. These two formulae, therefore, represent two superimposable mirror image molecules of the **same** compound. *Further examination of formula XI (or XII) reveals that in spite of two chiral centres in it, the molecule is achiral.* This is because it has a plane of symmetry; one half of its molecule being mirror image of the other half. As such the compound represented by formula XI (or XII) is optically inactive. Such an optically inactive compound whose molecules are not chiral even though they contain two (or more) chiral centres is known as a **meso compound**. As explained above the molecules of such compounds are superimposable on their mirror images.



Thus tartaric acid exists in **three forms** : (-) tartaric acid, (+) tartaric acid (formulae IX and X) and meso-tartaric acid (formula XI or XII).

Although optically inactive, the meso-tartaric acid represents a diastereomer of (-) or (+) tartaric acid.

Fischer projection formulae and flying wedge formulae of three stereoisomers of tartaric acid are given below :



It should be noted that meso compounds are permanently inactive and are said to be internally compensated. This is because one half of the molecule cancels the rotation due to the other half.

2, 3 -Dichlorobutane affords another example of a compound which contains 2 chiral carbons and exists in three forms : two optically active forms and one meso form.

~~7.10. NUMBER OF POSSIBLE STEREOISOMERS IN COMPOUNDS CONTAINING DIFFERENT NUMBER OF CHIRAL CENTRES~~

It may be stated that the maximum possible number of stereoisomers of a molecule is 2^n when n is the number of chiral centres in the molecule. Thus the molecules having 1, 2 and 3 chiral carbon atoms can exist in 2, 4 and 8 stereoisomeric forms respectively. But the actual number may be less than the maximum if some of the isomers exist in meso form. It is possible to predict the actual number of stereoisomers by simple calculations as explained below :

1. When the molecule contains n stereogenic centres (n may be odd or even number) and the molecule has no plane of symmetry.

$$\text{Number of optically active isomers (d- and l-forms)} = 2^n$$

$$\text{Number of meso forms} = 0$$

$$\text{Total number of isomers} = 2^n + 0 = 2^n$$

For example, 2, 3-dichloropentane ($\text{CH}_3-\text{CHCl}-\text{CHCl}-\text{CH}_2-\text{CH}_3$; two stereogenic centres) exists in the form of $2^2 = 4$ optically active isomers (as already shown on page 4/16).

2. When the molecule contains n stereogenic centres (where n = an even number) and the molecule has a plane of symmetry.

$$\text{Number of optically active forms} = 2^{n-1}$$

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

$$\text{Total number of isomers} = 2^{n-1} + 2^{n/2-1}$$

For example, tartaric acid ($\text{HOOC}-\text{CHOH}-\text{CHOH}-\text{COOH}$; two stereogenic centres with a plane of symmetry) exists as

$$2^{2-1} = 2 \text{ optically active isomers and}$$

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

$$\text{Total number of isomers} = 2 + 1 = 3 \text{ (already shown on page 4/19)}$$

3. When the molecule contains n stereogenic centres (where n = an odd number) and the molecule may have a plane of symmetry.

$$\text{Number of optically active forms} = 2^{n-1} - 2^{(n-1)/2}$$

$$\text{Number of meso forms} = 2^{(n-1)/2}$$

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

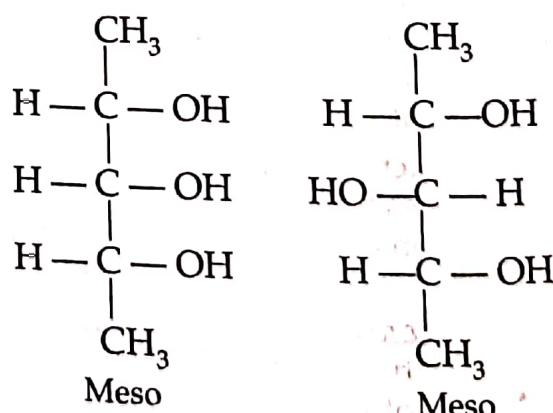
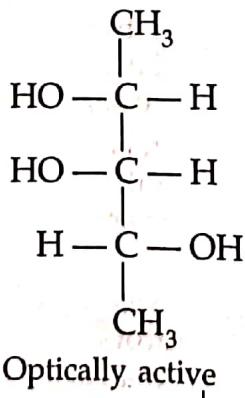
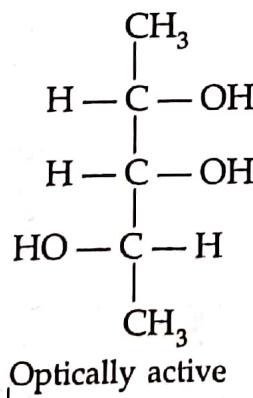
For example, pentane -2, 3, 4-triol ($\text{CH}_3-\text{CHOH}-\text{CHOH}-\text{CHOH}-\text{CH}_3$; 3 stereogenic centres with a possible plane of symmetry) exists as :

$$2^{3-1} - 2^{(3-1)/2} = 2^2 - 2^1 = 2 \text{ optically active forms}$$

$$2^{(3-1)/2} = 2^1 = 2 \text{ meso forms}$$

$$\text{Total number of isomers} = 2 + 2 = 4$$

These isomers are shown below :



[It is possible to draw four more structures. But each one of these would be found to be superimposable on one or the other of the above structures (as can be seen by rotation through 180°)