Mani Mobiles 3

UNIT - ■

STEREOCHEMISTRY

Stereochemistry deals with the three dimensional structure of the molecule and its effects on chemical behaviour.

The compounds having the same molecular formula but different properties (either physical (or) chemical) are known as isomers and the phenomenon is known as isomerism. Isomerism is of two types.

(i) Structural isomerism

(ii) Stereoisomerism

(i) Structural isomerism :-

In this isomerism the different isomers differ in the arrangement of atoms within the molecule without any reference to space. It is further divided into three types

a) Position isomerism

b) Chain isomerism

c) Functional isomerism

ii) Stereoisomerism:-

Stereoisomerism is exhibited by compounds having same structure but different configurations. These different configurations are possible because carbon mainly forms covalent bonds which have direction in space. Stereoisomerism is classified into two classes.

a) Configurational isomerism:-

The stereoisomers which are non-superimposable and non-interconvertible by rotation around single bonds are known as configurational isomers. They can be interconverted by breaking and making bonds, these are of two types.

(i) Enantiomers :-

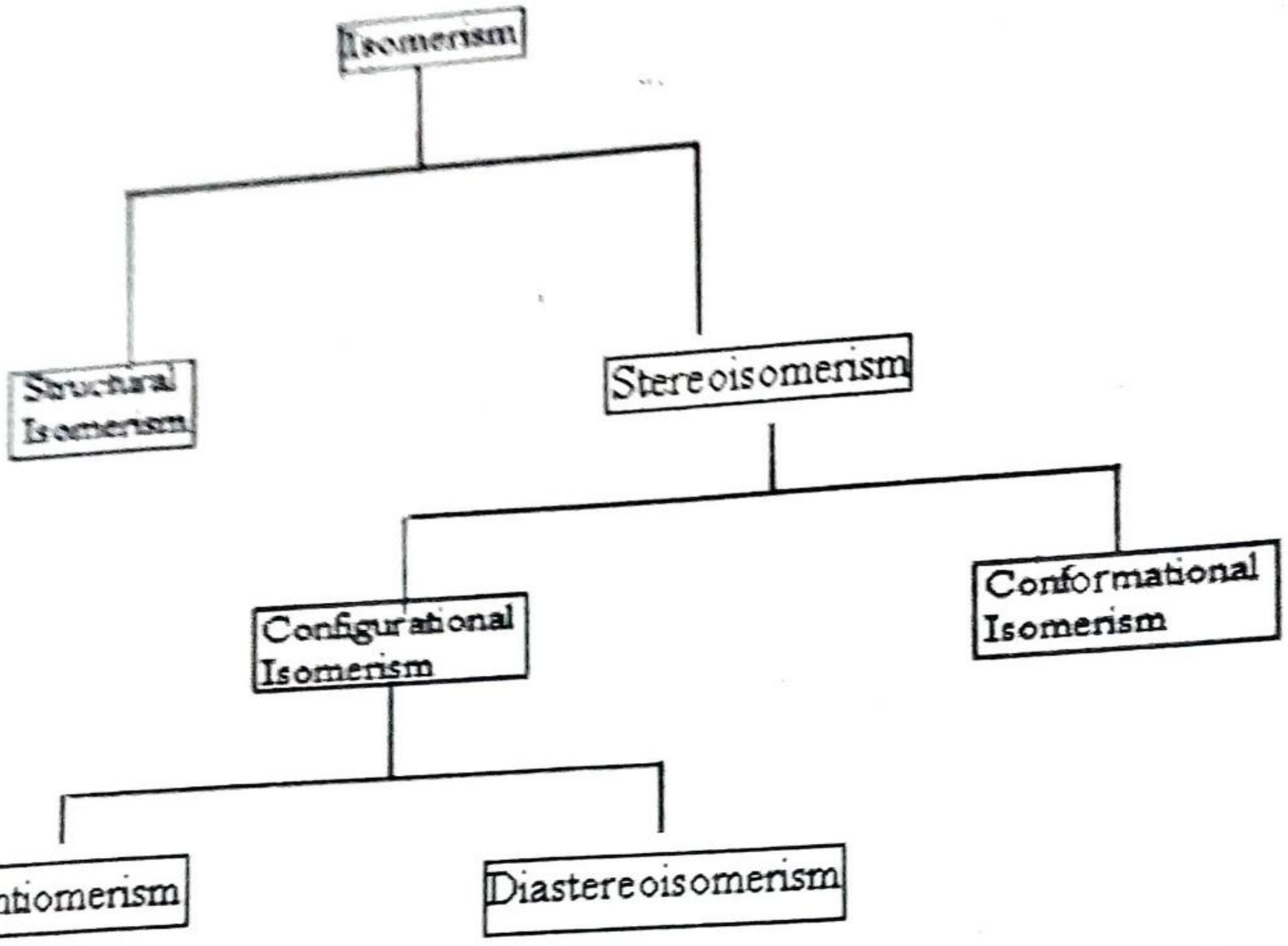
Enantiomers are compounds having same molecular formula but have different configurations which are minor images of each other.

(ii) Diastereomers

Diastereo isomers are compounds having same molecular formula but have different configurations which are not mirror images.

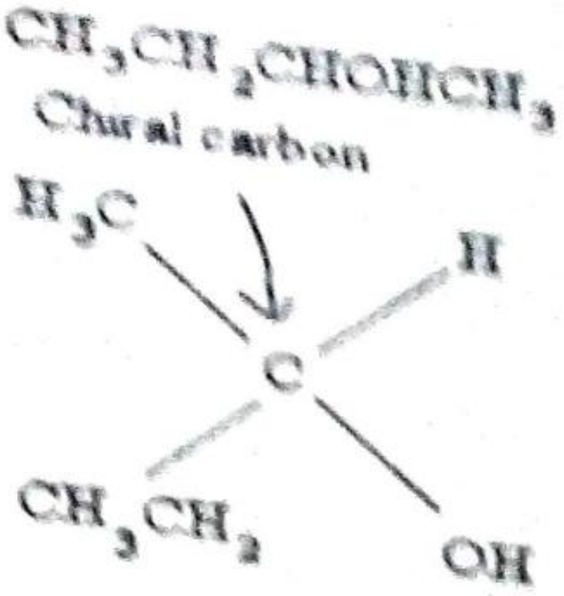
b) Conformational isomerism

The stereoisomers which are non-superimposable but easily interconvertible by rotation about single bonds are known as conformational isomers and the phenomenon is known as conformational isomerism.



Chirality

For any molecule to exhibit optical activity the main condition is that the geometric structure of the molecule must be such that it is non-superimposable on its mirror image. If the condition is not satisfied the molecule cannot exist in optically active forms. This property of asymmetry is exhibited by molecules and also environments. E.g., each of our hands is asymmetric. Enantiomorphs (mirror images) are related to each other in the same way that a right hand is related to the left hand that is, the structures of enantiomers differ only in handedness. Such molecules are said to possess chirality (from Greek Word, Kheir hand), e.g., the carbon atom of 2 – butanol carrying four different groups – H, -OH, $-CH_3$, $-C_2H_5$, is the 'Chiral atom' or the 'Chiral Centre' in the molecule. The molecule is asymmetric.



In organic chemistry asymmetric carbon atoms are the chiral centres which cause optical activity. These centres are sometimes also called stereocentres. When two ligands bonded to an atom are interchanged resulting in a new stereoisomer the atom is termed as stereocentre. In case the new Stereoisomer is an enantiomer, the stereocentre is a chiral centre. Not all stereocentres are chiral centres but all chiral centres are stereocentres.

Recognition of Symmetry Elements:-

Whether a molecule is symmetric or not is indicated by superimposing the original formula over its mirror image. If it is superimposable, the molecule is symmetric, if not it is asymmetric. A molecule having symmetrical form is optically inactive.

(a) Symmetry operations:-

The operations such as reflection, rotation, inversion etc. which leads to a configuration indistinguishable from original configuration are called symmetry operations.

(b) Elements of symmetry

The geometric elements of the molecule generating symmetry operations are called symmetry elements. These may be a point, an axis or a plane through which the operations are performed. The complete information of the symmetry of the molecule can be described in terms of symmetry. For a single molecule there are four symmetry elements corresponding to symmetry operations.

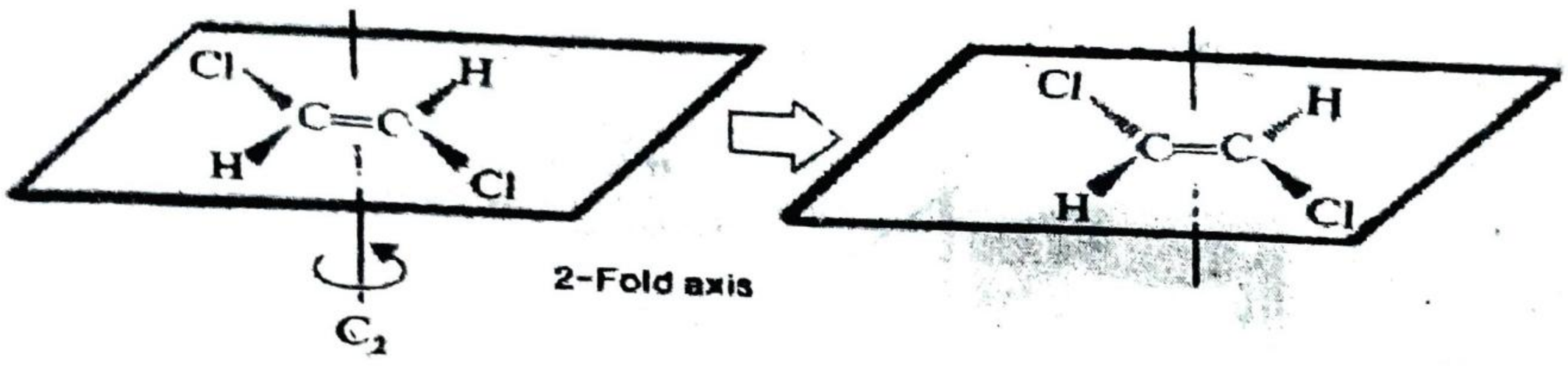
(i) Rotation axis or proper axis of symmetry (C_n).

If an imaginary axis can be constructed in a molecule around which the molecule can be rotated through an angle say Θ, to get an indistinguishable configuration, the molecule is said to possess a rotation axis. The symbol C, stands for axis of symmetry and subscript 'n' indicates, the order of axis.

The value of n (order of axis) can be calculated by the formula

$$n = \frac{360^\circ}{\Theta}$$

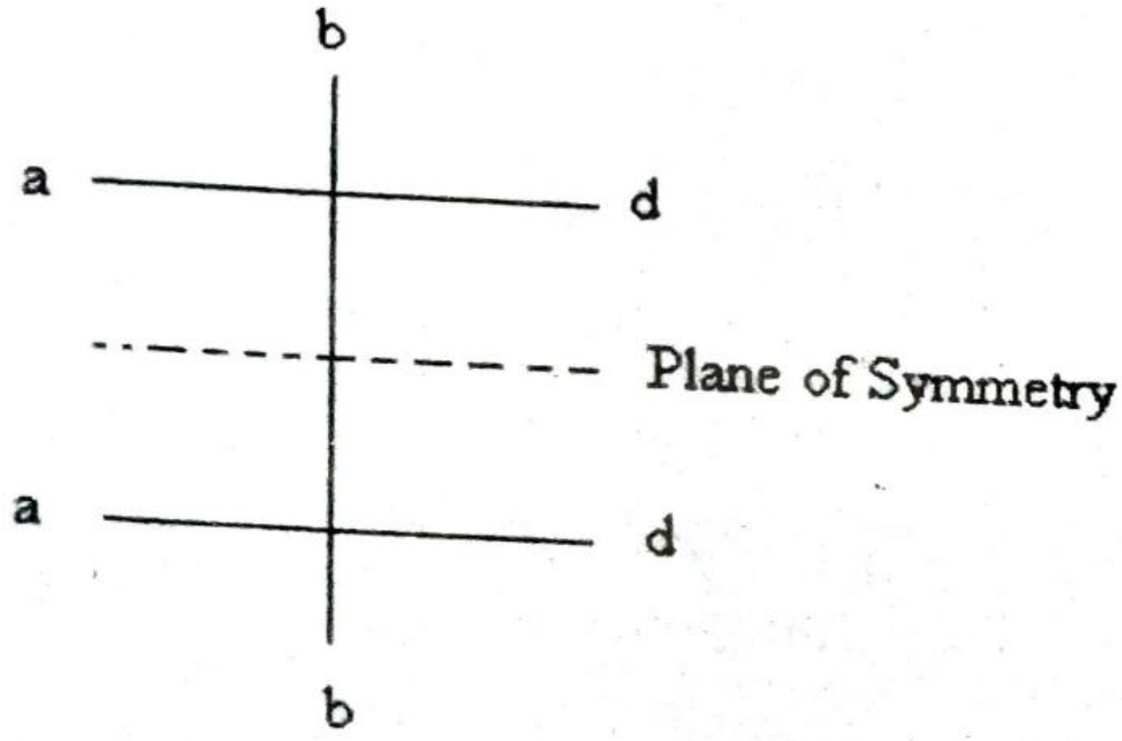
When n=1, it is a C_1 axis, also known as trivial axis. All molecules have a trivial axis. The symmetry operation C_1 is carried out by rotating the molecule through 360° which results to identical original molecule. When n=2; it is a C2 axis. For example (E)-1,2-dicholoroethene has a simple axis of rotation that passes through the midpoint of the molecule and is perpendicular to the plane described by the atoms of the molecule. Rotation through 180° about the axis leads to an arrangement identical to the original.

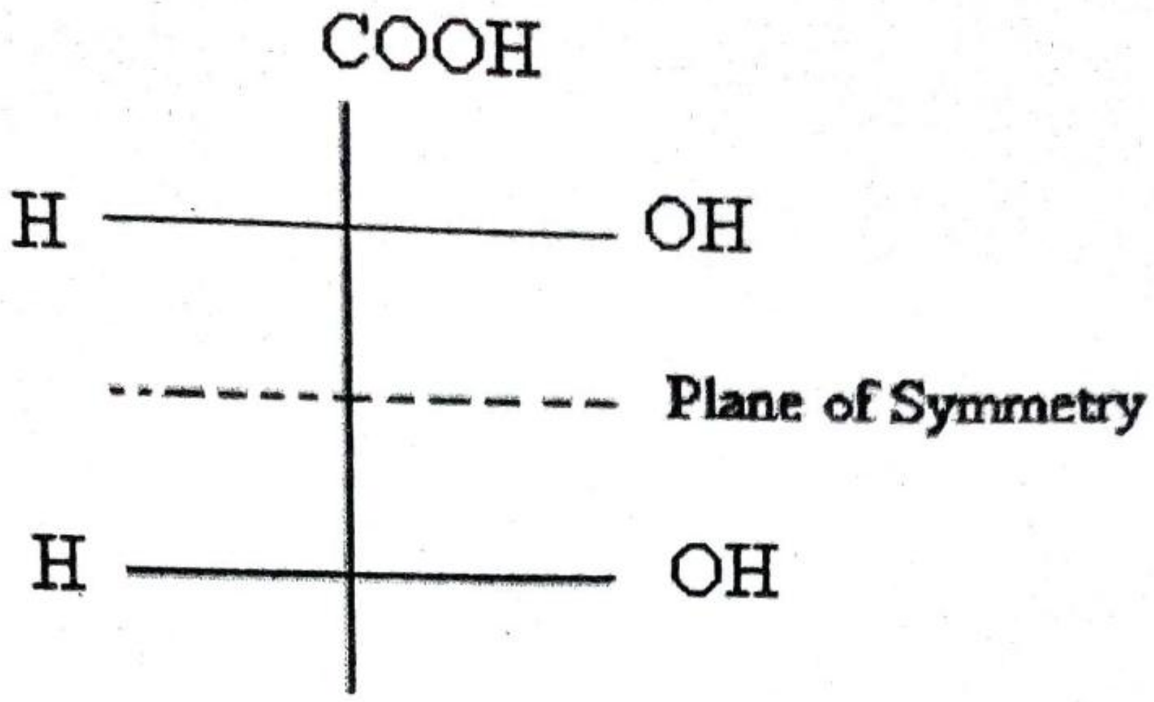


(ii) Plane of symmetry (σ)

The presence of at least two identical atoms or groups on the central atom gives a plane of symmetry. It divides a molecule in such a way that atoms or groups on one side of the plane form mirror images of those on the other.

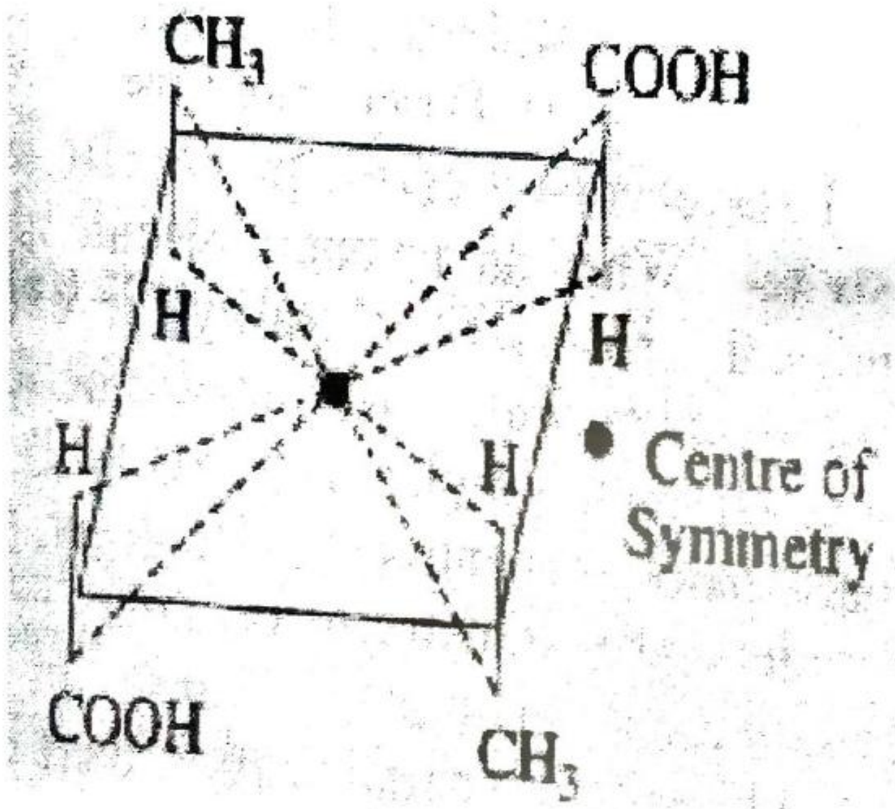
A compound with formula C_{abd} can have plane of symmetry like shown below –





(iii) **A centre of symmetry (i)** – It is a point within a molecule such that straight lines drawn through that point meet identical atoms or groups in both directions from that point. Generally even numbered rings have a centre of symmetry.

e.g. In 2,4 - dimethyl cyclobutane -1,3- dicarboxylic acid, the centre of symmetry is at the centre of the ring.



(iv) Alternating axis of symmetry (S_n) or Improper axis of symmetry

A molecule is said to possess an n-fold alternating axis of symmetry if, when it is rotated through an angle of $360°/n$ about this axis and then reflected across a plane perpendicular to the axis, an identical structure is obtained.

III year Organic chemistry - I

Unit - I

6 STEREOCHEMISTRY-I

6.0. GENERAL

Isomerism is a distinctive feature of organic chemistry. The concept of **structure** is inherent in the phenomenon of isomerism. The prime importance of structure in the study of organic chemistry cannot be over emphasized. A special type of isomerism called **stereoisomerism,** deals with **three-dimensional** aspect of organic molecules. **Stereochemistry**, the study of the structure and chemistry of stereoisomers, is becoming increasingly important in the study of organic chemistry. It has contributed significantly in establishing the **mechanisms** of organic reactions.

Important **biomolecules** (*steroids, carbohydrates, peptides/proteins, nucleic acids, enzymes, etc.,*) have a fascinating stereochemistry of their own. In addition, they function largely in a ***stereochemically important biological environment***. Stereochemical factors have also played an important role in determining the **efficacy** of many drugs.

This exposure to the subject of stereochemistry will help you in a better understanding of organic chemistry. Hopefully, you should also be in a better position to appreciate the important role that stereochemistry has played in the **chemical** and **biological** world.

6.1. CONCEPT AND TYPES OF ISOMERISM

Isomerism is the phenomenon that makes **two** or **more** organic compounds with the **same molecular formula** (MF) behave as *different* compounds. *Different compounds with the same MF are called* **isomers**. *When isomers have different orders of attachment of their atoms/groups within their molecules,* they are known as **structural isomers** (aka* **constitutional isomers**). In other words, **structural isomers** *are compounds with the same MF but with different orders of attachment of their atoms/groups within their molecules.* However, ***when isomers with the same MF have identical orders of attachment of atoms/groups within their molecules, but differ only in the relative positions of those atoms or groups in space, they are known as*** **stereo isomers** (the latter phenomenon is known as **stereoisomerism**). Thus, we have two broad classes of isomerism, namely **structural isomerism** and **stereoisomerism**. In due course, we shall see that structural isomerism and stereoisomerism can have subclasses too. It should be understood that the concept of structure implies not only the order of attachment of atoms/groups within a molecule, but also their orientation in space, where necessary.

* 'aka' is the shortened form of "

These may be further classified into the following sub-classes

(a) **Keto-enol tautomers** : Acetoacetic ester for example, exist in two **tautomeric** forms.

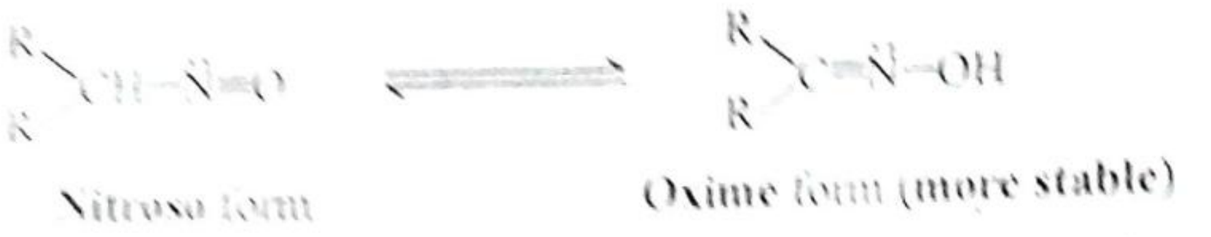
(*Keto*-form) 93% (*Enol*-form) 7%

Since the two tautomers are the **keto** and **enol** forms they are known as **keto** and **enol tautomers** phenomenon is known as **keto-enol** tautomerism.

(b) **Nitro-aci tautomers** : This type of tautomerism is shown by nitroalkanes.

Nitro form Aci form

(c) **Oxime–nitroso tautomers** : This type of **tautomerism** is shown by oximes.



Nitroso form **Oxime form (more stable)**

(d) **Imine–enamine tautomers**. This type of **tautomerism** is shown by imines.

Enamine **Imine (more stable)**

6.1.2. TYPES OF STEREOISOMERS

Stereoisomers have been divided into **three** types, namely **enantiomers** or optical **isomers**, geome or *cis-trans* **isomers** and conformational isomers. These stereoisomers have also been classified **enantiomers** and **diastereomers** or as **configurational isomers** and **conformational/rotational isome** The study of the **structure** and **chemistry of stereoisomers** is known as **stereochemistry**. The follow sections will be devoted to these terms and aspects of stereochemistry :

6.2. GENERAL STEREOCHEMISTRY

Before we take up a study of different kinds of stereoisomerism (***enantiomerism, geometri conformational isomerism***), it would be useful to understand some of the concepts and **terms used** i study of stereochemistry

6.2.1. CONCEPT OF CHIRALITY

Look at your left hand and right hand. They look similar, yet a left-handed glove does not fit the r hand. If you look at your hands in a mirror, you will notice that your two hands are really ***non-ident*** and ***non-superimposable*** mirror images of each other. An object that is **not superimposable** on its mirr **image** and has no plane of symmetry is called **chiral** (Greek : *cheir*, hand*). The property of an object th makes it nonsuperimposable on its mirror image is known as **chirality**. An object that **lacks chir**

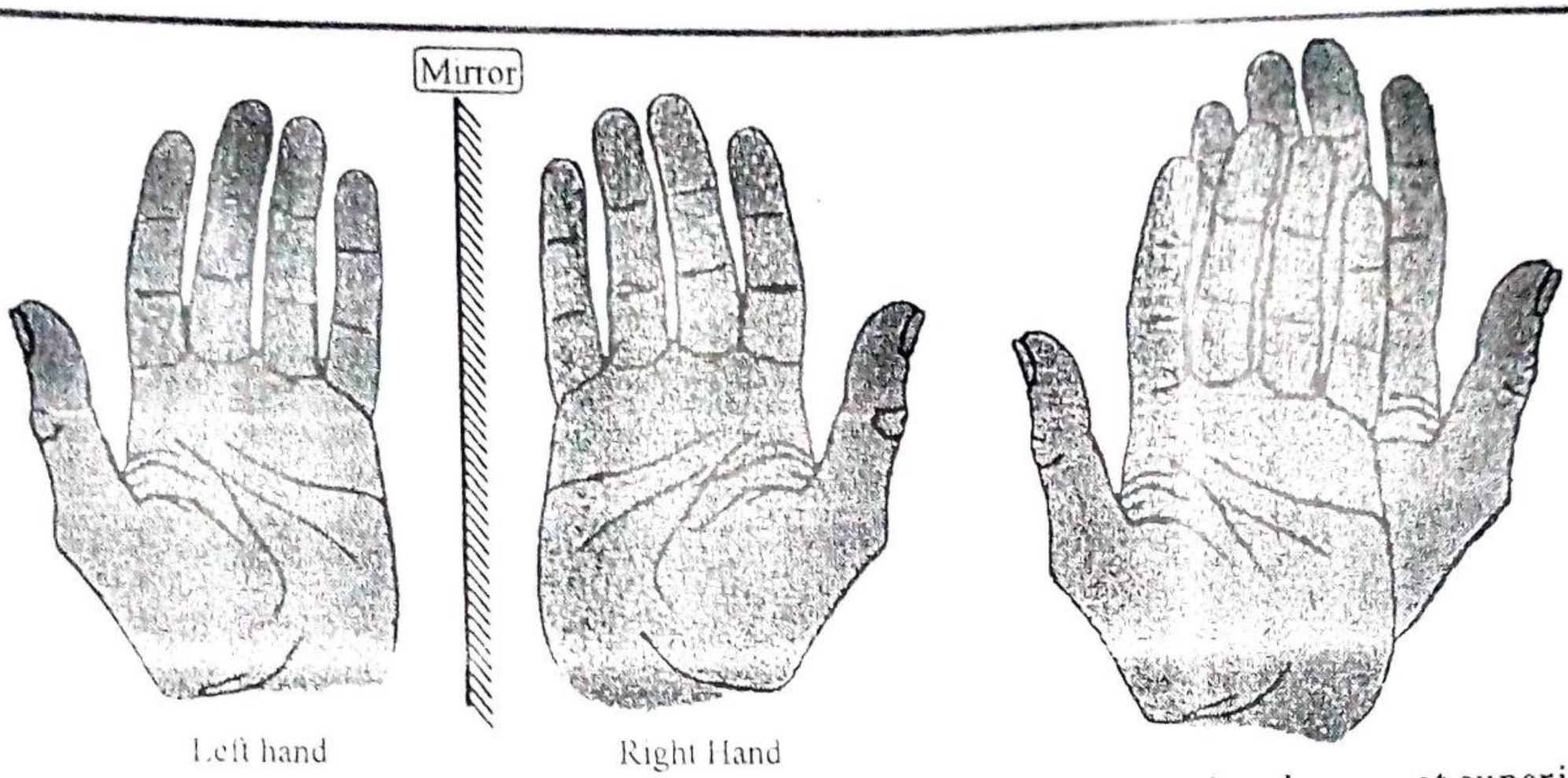


Fig. 6.1. The mirror image of a left hand is a right hand. Left and right hands are not superimposable.

6.2.2. TETRAHEDRAL CARBON

The concept of tetrahedral carbon (three-dimensional carbon in which its four valencies are directed to the four corners of a regular tetrahedron, carbon is located at the centre of the tetrahedron and the angle between different bonds is **109.5°** commonly known as the ***tetrahedral angle***) was put forward by **Van't Hoff** in **1874** on empirical grounds. It is now well-established on the basis of studies involving electron diffraction and X-ray diffraction of organic compounds. Since, all organic compounds must contain carbon, they have **three-dimensional**, rather than uniplanar, structures mostly.

The usual representation of the structure of an organic molecule within the plane of paper is convenient but not adequate, especially when we wish to depict the spatial relationships of atoms/groups attached to carbon(s). It is, therefore, necessary sometimes to construct a suitable **three-dimensional model** of the organic molecule. A number of kits have been designed to depict the three-dimensional structures of organic molecules, important being **Ball and Stick Models, Stuart Models and Barton Models**. Ball and Stick models, though crude, are simple and adequate for our immediate purpose. Fig. **6.2** shows the **Ball and Stick model** and the **Stuart model** of methane.

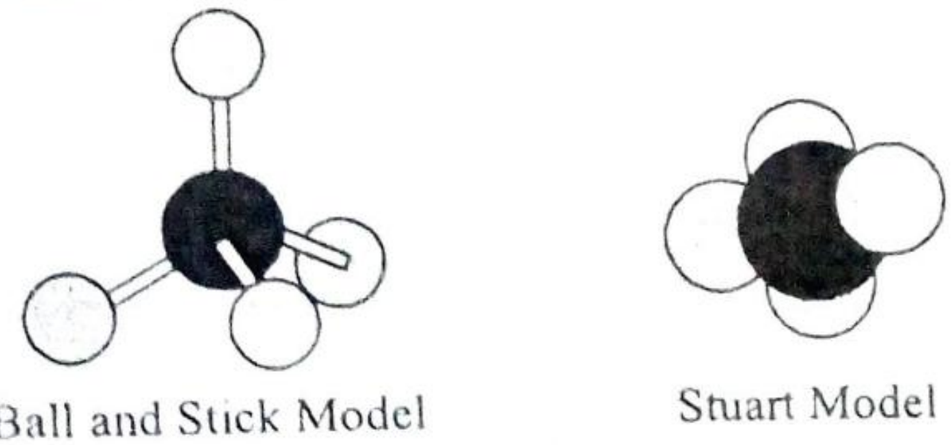


Fig. 6.2. Three-dimensional models of Methane.

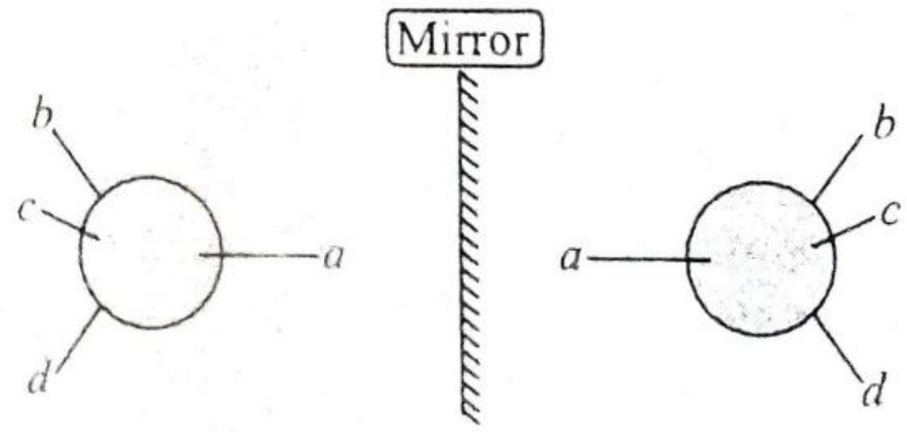


Fig. 6.3. Non-superimposable molecules (*show enantiomerism*).

6.2.3. CHIRALITY AND ENANTIOMERISM

Consider an organic compound, *Cabcd* (where *a*, *b*, *c* and *d* are different atoms/groups bonded to carbon). To determine, if such a molecule is chiral, construct its model and hold it before a mirror. Construct also the model of its mirror image (Fig. **6.3**). The two models are different and **non-superimposable**, *i.e.*, they do not coincide in all their parts, howsoever we turn or twist them without breaking any bond. By definition such an organic molecule would be **chiral**, and the two models (compound as well as of the

mirror image) would correspond to two **stereoisomers** of the molecule. Since, these two stereoisomers bear the relationship of an object and its mirror image, they are also known as **enantiomers**. Apparently these enantiomers have identical structures as far as the nature of the atoms/groups attached to the carbon are concerned, but they differ from each other in the distribution of atoms/groups in space. These **enantiomers** are a kind of **stereo isomers** and the phenomenon is called **enantiomerism**

Construct now the model of the organic compound, Ca_2bd, in which two of atoms/groups attached to the carbon atom are identical. As before, construct also the model of its mirror image (Fig. 6.4) and try to superimpose the two models. It will be seen that these two models are identical and superimposable after some twisting without breaking the bonds. The molecules correspond to these models are also identical and not different. It is thus seen that molecules, such as Ca_2bd have mirror images, but they are **superimposable** and lack chirality. In other words, such molecules are **achiral** and they do not show enantiomerism. It can be shown similarly that molecules, such as Ca_3d and Ca_4 are also **achiral** and do not show enantiomerism.

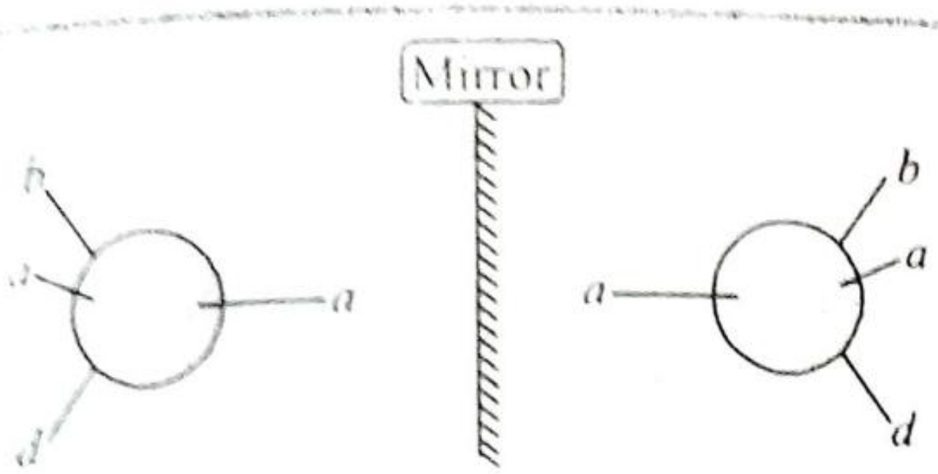


Fig. 6.4. Superimposable molecules
(*do not show enantiomerism*)

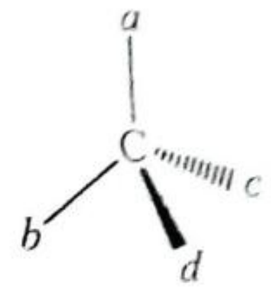


Fig. 6.5. Wedge and Dashed Bond Drawing
(Perspective drawing)

6.2.4. WEDGE AND DASHED BOND DRAWING OF ORGANIC MOLECULES (PERSPECTIVE DRAWINGS)

We can draw on paper tetrahedral molecules using **wedge** and **dashed bonds**. Fig. **6.5**. shows the wedge and dashed bond drawing (perspective drawing) of a tetrahedral carbon with four different atoms/ groups, *Cabcd*. In Fig. **6.5**, the central C and groups '*a*' and '*b*' are in the plane of the paper, group '*c*' (shown by a dashed bond, ┅┅) is pointing *into* the plane of the paper, and group '*d*' (shown by a wedge bond, ►) is pointing *out* of the plane of the paper. Such drawings of organic molecules are also known as **perspective drawings**. A quick way to draw the **enantiomer** of a chiral molecule is, to **interchange** any **two** groups.

6.2.5. ASYMMETRIC CARBON ATOM AND RELATED TERMS (STEREOGENIC ATOM)

Presence of a carbon atom bonded to four different atoms/groups in a molecule is the most important (though not the only one) feature that makes a molecule chiral. Such a carbon atom is called an **asymmetric carbon atom** or a **chiral carbon**, often designated by an asterisk (*) mark. **An asymmetric carbon is also known as a stereogenic centre or a chiral centre in recent literature.** Fig. **6.6** depicts the stereorepresentation of **lactic acid** (2-hydroxypropanoic acid) and its mirror image. C* is the asymmetric or chiral or **stereogenic carbon** because it is bonded to four different atoms/groups, namely **H, COOH, OH** and CH_3, and is responsible for the **chirality** of lactic acid.

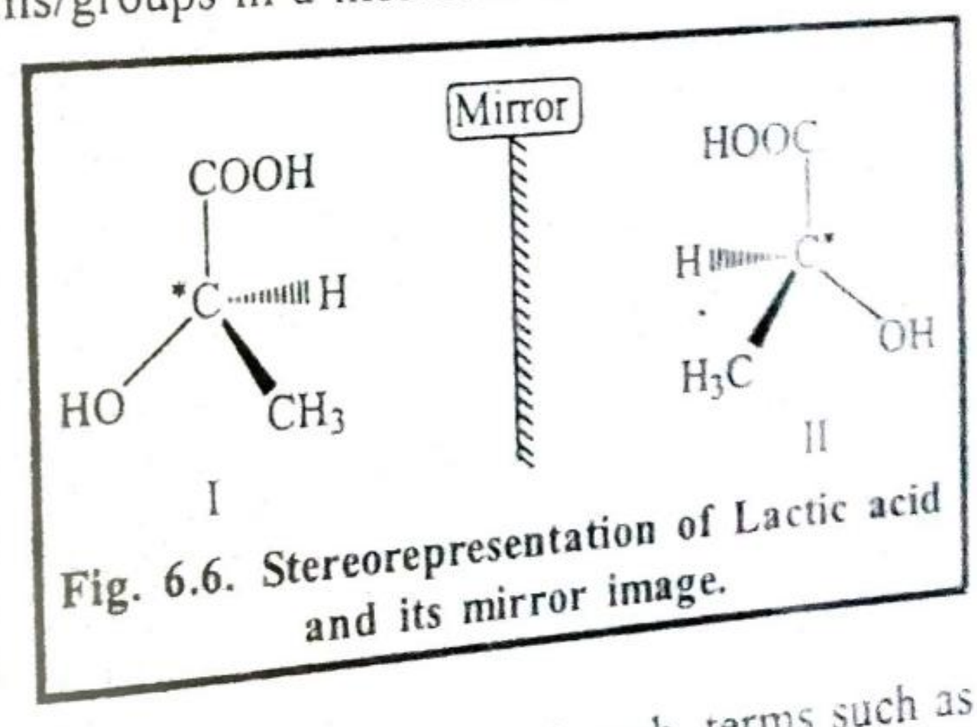


Fig. 6.6. Stereorepresentation of Lactic acid and its mirror image.

An asymmetric carbon atom is the common example of a **chirality centre**. Although, terms such as **stereocentre or stereogenic atom** have been used synonymously for an *asymmetric carbon or a chiral carbon*, they have a broader connotation too. A stereocentre or a **stereogenic atom** is ***any*** **atom** that leads

to ***chirality*** (and hence enantiomerism). So, a stereocentre or a stereogenic atom does not have to be a carbon atom always. It may be even **N** as in quaternary ammonium salt with **four different groups** bonded to N. Even enantiomers of tetrahedral **Si**, **P**, **Ge** compounds have been isolated. In due course, we shall come across even the **doubly bonded carbon** atoms in ***cis-trans*** or geometric isomers, show enantiomerism.

Fig. **6.7**, shows two chiral molecules (I and II), each having a C* and N* as the stereogenic atoms. C* in **I** is known as **asymmetric carbon**, but N* in **II** is better referred to as the **stereogenic atom**, though they can be collectively known as **stereogenic** atoms. Since both C* and N* are responsible for the chirality of these molecules, they are known as **chirality centres** of these molecules.

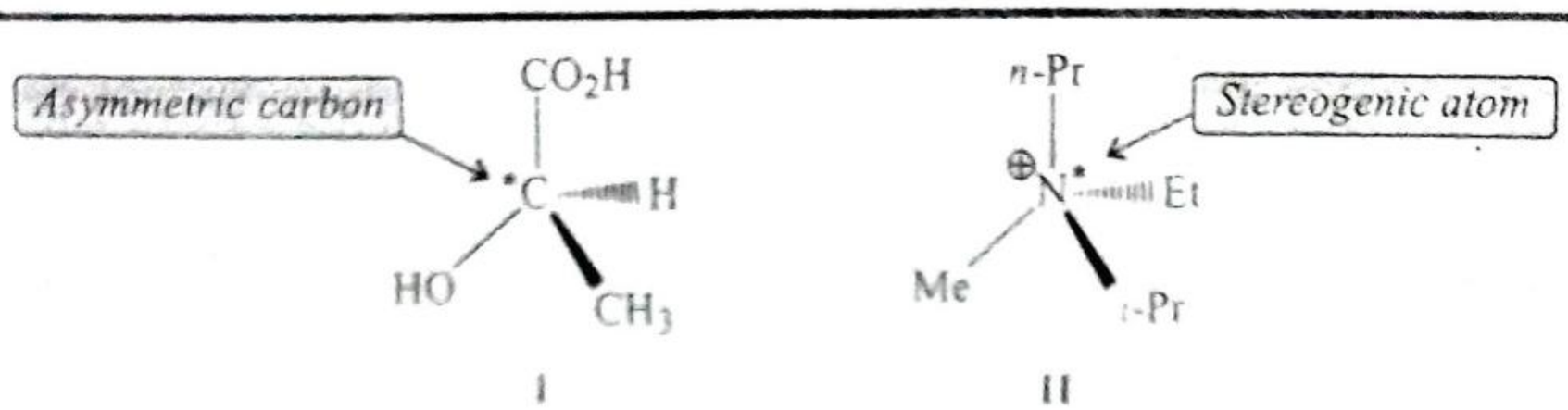


Fig. 6.7. Chirality centres in organic molecules.

6.2.6. ELEMENTS OF SYMMETRY

(*a*) Symmetry operations The geometric operations such as **reflection**, **rotation**, **inversion**, etc., which lead to a configuration indistinguishable from original configuration are called symmetry operations.

(*b*) Elements of symmetry The geometric elements of the molecule generating symmetry operations are called symmetry elements. These may be a **point**, an **axis** or a **plane**, through which the operations are performed. The complete information of the symmetry of the molecule can be described in terms of symmetry elements. For a single molecule, there are five symmetry elements correspond to symmetry operations. These are : (*i*) Identity E (*ii*) **Rotation axis or proper axis of symmetry** (C_n) (*iii*) Plane of symmetry (*iv*) Centre of symmetry (*v*) Alternating axis of symmetry or Improper axis of symmetry.

(*i*) Identity (*E*). In identity operation no change is made in the original molecule. We can say, identity is the operation of not doing anything. When we do not do anything we leave the system unchanged and identical to the original system.

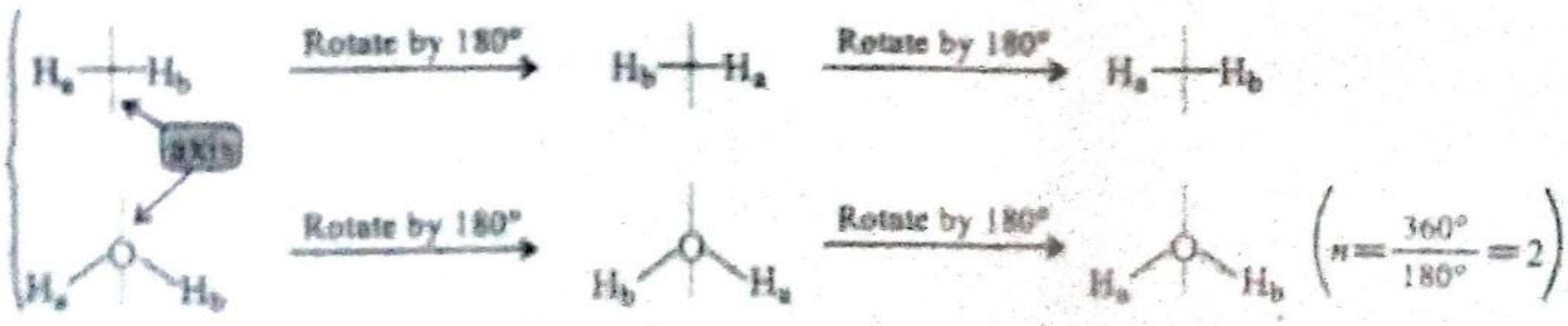
(*ii*) Rotation axis or proper axis of symmetry (C_n). If an imaginary axis can be constructed in a molecule around which the molecule can be rotated through an angle, say θ, to get an indistinguishable configuration, the molecule is said to possess a rotation axis. The symbol **C** stands for axis of symmetry and subscript ***n*** indicates the order of axis.

The value of *n* (order of axis) can be calculated by the formula –

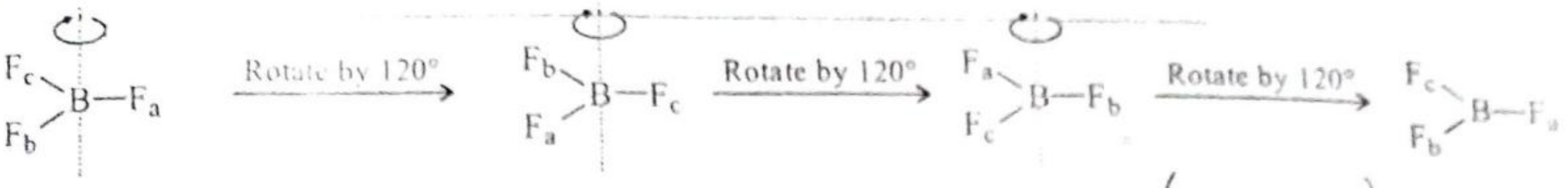
$$n = \frac{360^\circ}{\theta} \quad \text{or} \quad \theta = \frac{360^\circ}{n} \quad (n = \text{order of axis})$$

When $n = 1$, it is a C_1 axis, also known as **trivial axis**. All molecules have a trivial axis. The symmetry operation C_1 is carried out by rotating the molecule through 360° which results to identical original molecule.

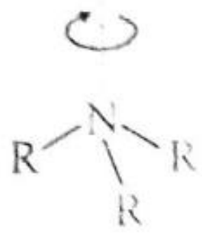
In H_2, O_2, Cl_2, N_2, etc., the proper axis of rotation is C_2 as the angle of rotation (θ) to get identical configuration is 180°.

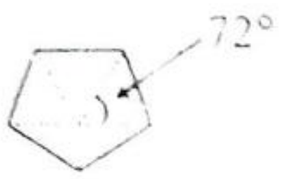


C_3 when $n = \frac{360^\circ}{120^\circ} = 3$ **(Three-fold axis)**



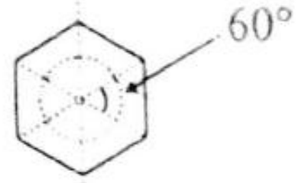
$\left(n = \frac{360^\circ}{120^\circ} = 3\right)$

Similarly,  has C_3 axis



$n = \frac{360^\circ}{72^\circ} = 5\ (C_5 \text{ axis})$

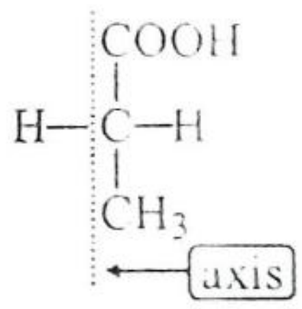
Cyclopentane



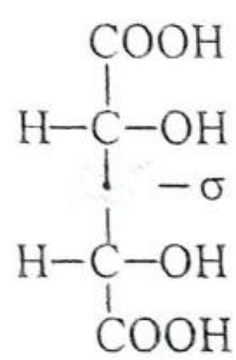
$n = \frac{360^\circ}{60^\circ} = 6\ (C_6 \text{ axis})$

Benzene

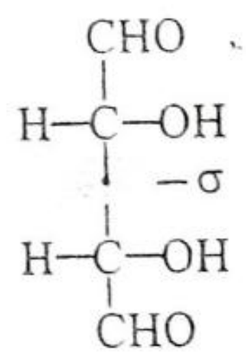
(*iii*) **Plane of symmetry** (σ). An imaginary plane that bisects molecule in such a way that the two parts are mirror images of each other. This element of symmetry is represented by symbol (σ). For example,



Propanoic acid



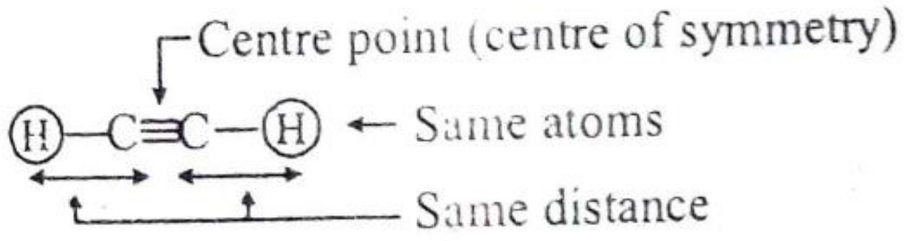
Tartaric acid

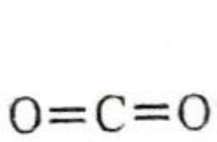


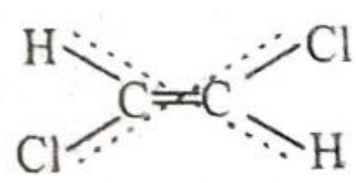
(plane of symmetry)

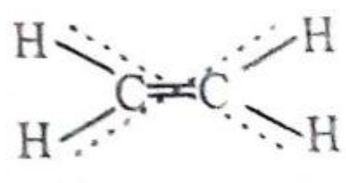
2, 3-Dihydroxy butane 1, 4-dial

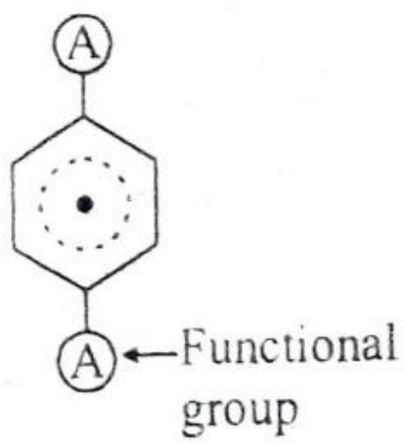
(*iv*) **Centre of symmetry** (*i*). This is such a point through which if a line drawn *meets identical atoms at equal distances* from the point in two opposite directions. The centre point is known as a centre of symmetry. The symbol used to indicate inversion centre is ***i***. For example,

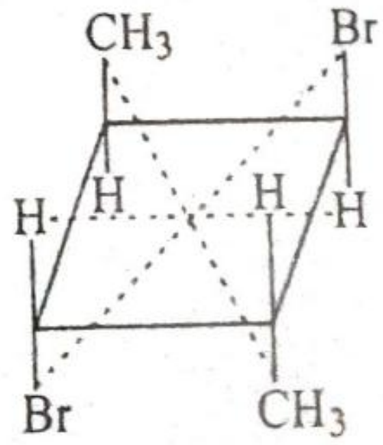


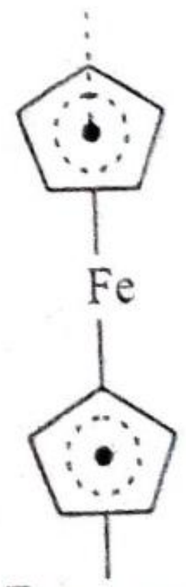








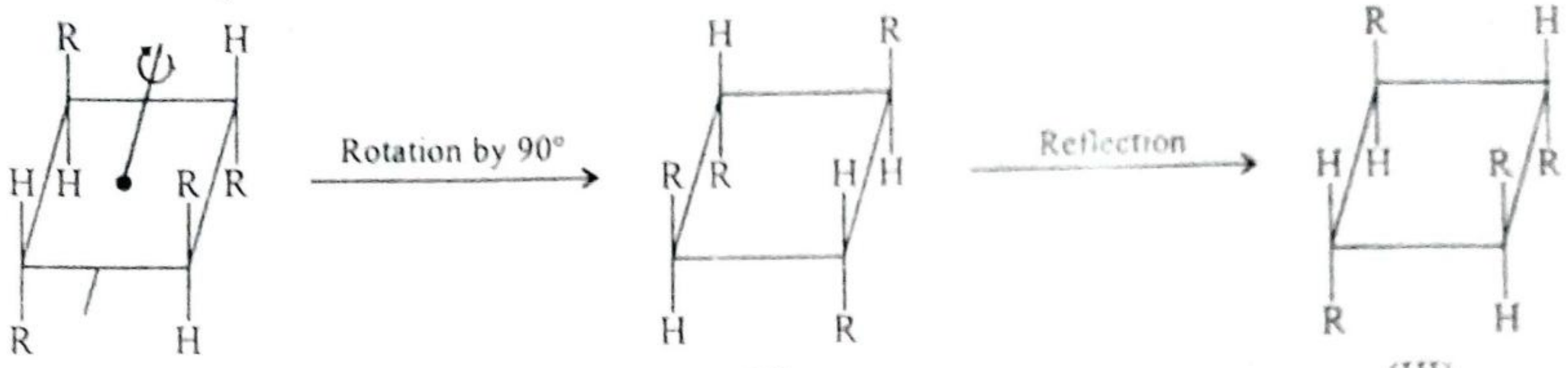




Ferrocene

(*v*) **Alternating axis of symmetry (Sn) or Improper axis of symmetry**. When a molecule has a *n*-fo alternating axis of symmetry is rotated through an angle $360^\circ/n$ about this axis and then followed by t reflection in a plane perpendicular to this axis, the molecule is indistinguishable from the original structu

For example,



(I) (II) (III)

R=(Alkyl, halide)

Since (I) and (III) are superimposable/indistinguishable, the molecule has 4-fold alternating axis of symmetry.

Optical Activity—Relation to Chirality and Symmetry Elements

We have seen that *asymmetric molecules* lack all elements of symmetry except a trivial axis *i.e.*, there is no simple axis of symmetry, plane of symmetry, alternating axis of symmetry and centre of symmetry.

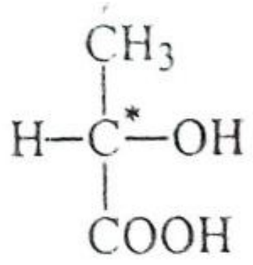
A dissymmetric molecule has simple or proper axis of symmetry, but lacking alternative axis of symmetry. The relationship to chirality and symmetry elements to optical activity is shown below in **Table 6.1**.

TABLE 6.1

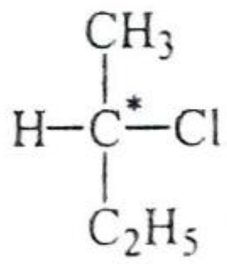
Term	Alternating axis of symmetry	Simple axis of symmetry	Optical activity
Asymmetric	Absent	Absent	Optically **active**
Dissymmetric	Absent	Present	Optically **active**
Symmetric	Present	May or may not be present	Optically **inactive**

6.2.7. THE ASYMMETRIC CARBON AND MOLECULAR CHIRALITY

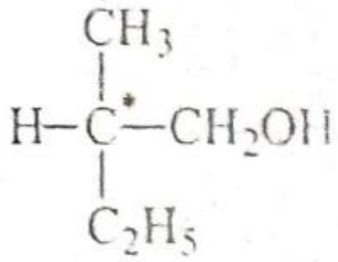
All the examples of dissymmetric or chiral molecules showing enantiomerism, can be presented by the general formula, *Cabcd*. Each such molecule contains a carbon (C*) with four ***different*** atoms/groups attached to it, as shown below.



Lactic acid



sec-Butyl chloride



2-Methyl-1-butanol

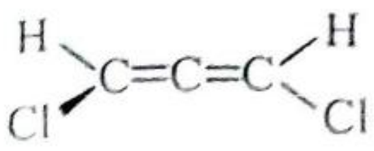
[Carbon atom with asterisk(*) has four different groups/atoms attached to it. Hence, **assymmetric or chiral**]

A carbon which has four different atoms or groups attached to it is called an **asymmetric carbon**. More recently, an asymmetric carbon is also known as a **chiral carbon**. It may appear that the presence of an **asymmetric** or **chiral** carbon in a compound is probably necessary for dissymmetry or **chirality** and hence enantiomerism. However, we find in actual practice that there are a few molecules which contain **asymmetric** or **chiral carbon** atoms and yet, do not show molecular dissymmetry or chirality. We shall see in due course that the *meso* form of **tartaric acid** contains **two** asymmetric carbon atoms, but it **does not** show **enantiomerism** and optical activity. **Again, there are a few molecules which do not contain asymmetric or chiral carbon atoms, but show dissymmetry or chirality and show enantiomerism.**

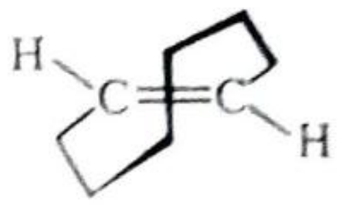
6.2.8. CHIRALITY WITHOUT CHIRAL CARBON AND AXIS OF CHIRALITY

Compounds like **allenes**, *trans*-**cyclooctene**, **spiranes** and *ortho*-**substituted biphenyls*** contain no

asymmetric carbon, yet, they show **molecular dissymmetry** and hence, enantiomerism.

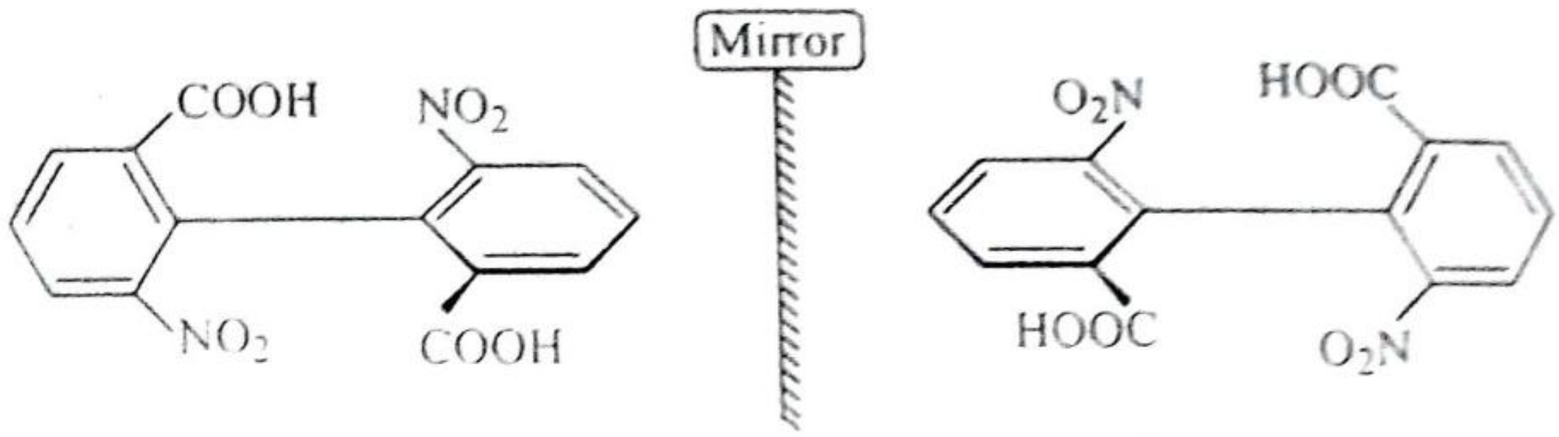


1, 3-Dichloropropadiene (an allene)



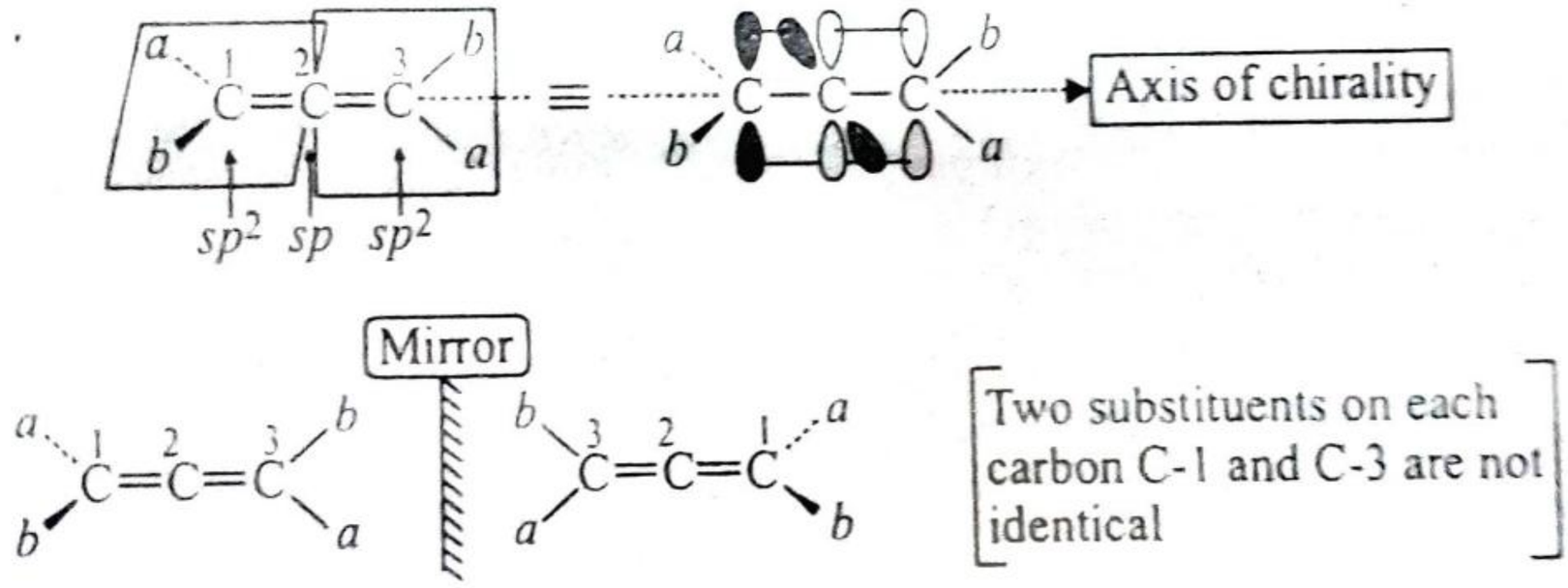
trans-Cyclooctene

a spirane



These cause **molecular dissymetry** due to the presence of **bulky atoms or groups** which make the molecule **coplanar** due to large space occupied by them and also **hindered rotation** on their axis.

In 1875, **J. Van't Hoff** pointed that an unsymmetrically substituted allene of the type $abC{=}C{=}C{<}^{a}_{b}$ or $^{a}_{b}$ should exist in two enantiomeric forms. The reason for the molecular dissymmetry is that the groups *a* and *b* at one end of the system lie in a plane at right angle to the other end (if the doubly bonded carbon atoms are viewed as tetrahedra joined edge to edge). At present, optically active allenes are regarded as compounds with an ***axis of chirality*** (in contrast to compounds with an assymetric carbon atom). The central carbon C-2 is *sp*-bonded and remaining two *p*-orbitals overlaps with *p*-orbital of each adjacent sp^2 carbon atom (C-1 and C-3). This forces the two remaining bonds of each carbon to lie in a perpendicular planes. (see Fig given below).



Enantiomers of unsymmetrically substituted allenes.

Two rings of spirane (linked by a common carbon) are similar to the *pi* bonds of the allene and the groups attached to two ends of the rings force to lie at perpendicular plane to each other. Hence such rings show optical activity **without a chiral carbon.** Similarly, unsymmetrically substituted biphenyls linked through **pivote bonds** lie in two different planes also show optical isomerism without a chiral carbon and can be resolved in two optically active forms. This type of isomerism is known as **atropisomerism**.

This shows that **the presence or absence of an asymmetric or a chiral carbon in a molecule has no criterion of dissymmetry or chirality** (*and hence enantiomerism*) in that molecule.

6.3. OPTICAL ACTIVITY

Ordinary light consists of rays of different wavelengths, vibrating in all directions, perpendicular to the path of propagation. Even a monochromatic light *i.e.*, light of a single wavelength (say, light from sodium lamp, $\lambda = 589$ nm) consists of waves, vibrating in many planes at right angles to the path of propagation. By suitable means say, by passing it through a ***Nicol prism*** (constructed by cementing together the two crystals of *Iceland spar** with Canada balsam), these vibrations can be so adjusted that

* **Nicol prism** constructed from it is name

they vibrate in a single plane only. The light whose vibrations occur in only one plane is called **plane polarised light**. The *device used to convert unpolarised light to polarised light* is called **polariser**.

The substances which **rotate** the **plane of polarised** light are said to be **optically active** and the property is known as **optical activity**. This phenomenon of optical activity was first observed in 1815 by the French physicist Biot. The instrument used to measure the angle of rotation of plane polarised light caused by an optically active substance is called **polarimeter**. A polarimeter consists of : a **source** of monochromatic light 'S' (usually sodium lamp of single wavelength, $\lambda = 589$ nm), (2) a **polariser (P)**, (3) a **sample tube (T)**, to be filling a solution of optically active substance, (4) an **analyzer (A)** and (5) a **scale** for measuring number of degrees that a plane of polarized light has been rotated.

When the sample tube (T) is empty (Fig. 6.8) or filled with optically **inactive** substance, the axes of the polariser (P) and analyzer (A), are exactly parallel and observer will detect the maximum amount of polarized light and instrument reads 0°.

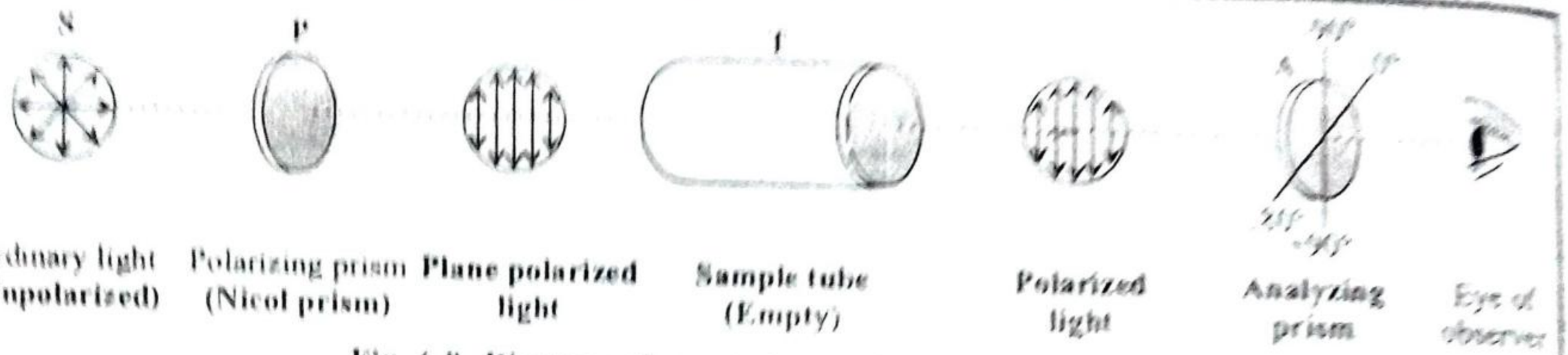


Fig. 6.8. Diagram of a polarimeter (sample tube empty)

When the sample tube (T) is filled with the solution of an **optically active** substance (**enantiomer**), the plane of the polarization of light has been rotated and observer will not detect any light. In order to detect maximum brightness of light, the observer will have to rotate the axis of analyzer (A) in either clockwise or anti-clockwise direction **Fig. 6.9**. If the scale mounted on analyzer (A) is rotated in a **clockwise** direction, the rotation (α) measured in degrees is said to be (+) and if **anticlockwise**, the rotation is said to be (–). An optically active substance that rotates the plane of polarized light in clockwise direction, is said to be dextrorotatory (Latin : **dexter**, right) and if rotates in **anticlockwise** direction, is said to be **laevorotatory** (Latin : *laevus*, left).

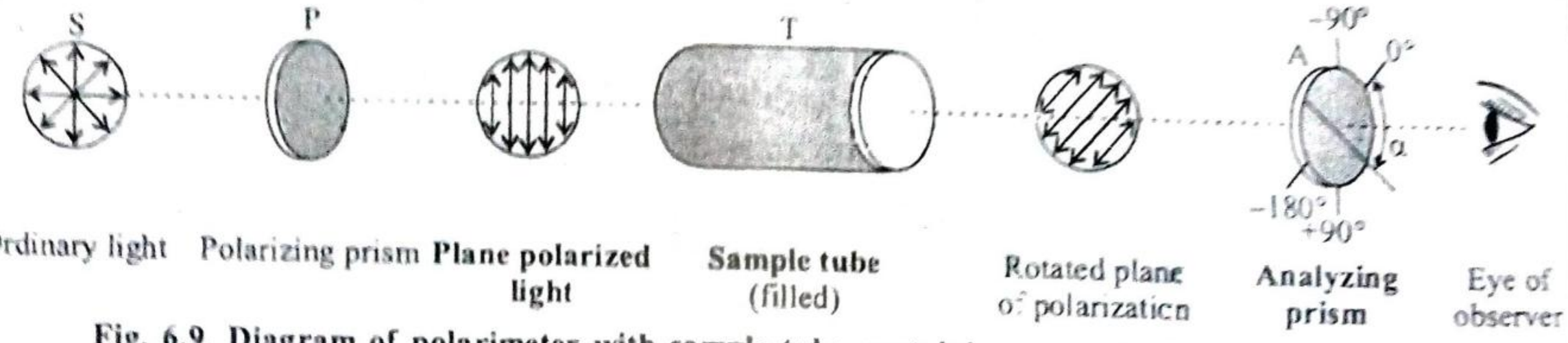


Fig. 6.9. Diagram of polarimeter with sample tube containing an optically active substance.

The actual **rotation** (α), observed by a polarimeter, or an optically active substance in a solution depends on (*i*) the **concentration**, *c*, of the solution, (*ii*) the **length**, *l*, of the light path through the solution *i.e.*, length of the sample tube T, in which the solution is filled for measuring its rotation, (*iii*) the **temperature** of measurement, (*iv*) the **wavelength** of the light used and (*v*) the **solvent** used for dissolving the substance. The **specific rotation**, $[\alpha]_D$, is given by following relationship :

$$[\alpha]_D = \frac{\text{Observed rotation } (\alpha)}{\text{Length}(l) \text{ of the polarimeter tube in } dm \times \text{Conc. (c) of the substance in } gms / ml}$$

$$[\alpha]_D^{20} = \frac{\alpha}{l \times c}$$

This relationship can also be used to calculate **observed rotation** (α), if **specific rotation**, l and c are given.

$$\alpha = [\alpha]_D^{20} \times l \times c$$

It is customary to indicate the **temperature** of the measurement and the nature or wavelength of the light used. For example, the specific rotation + 66·5° of **sucrose** solution in water at **20°C**, using sodium light, is shown as follows

$$\textbf{Specific rotation} = [\alpha]_D^{20} = +66{\cdot}5^\circ \text{ (in } H_2O)$$

The sign (+) denotes that sucrose is dextrorotatory, *i.e.*, it **rotates the plane of polarized light** to the **right** or in the **clockwise** direction. The sign (–) would be used when the substance is laevorotatory, *i.e.*, it rotates the plane of polarized light to the **left** or in the **anti-clockwise** direction. The notation D corresponds to the D-line of the sodium light ($\lambda = 589\ nm$). It is also desirable to indicate in braket the concentration in g *per ml* and also the solvent used for dissolving the substance. For example,

$$[\alpha]_D^{20} = +66{\cdot}5^\circ \text{ (c=0·02 g/ml. in water)}$$

Molecular rotation The product of multiplication **specific rotation** and **molecular mass** divided by hundred is known as **molecular rotation**.

$$\textbf{Molecular rotation (M)} = \frac{M \times [\alpha]_D^{20}}{100}$$ where, M=Molecular wt., $[\alpha]_D^{20}$ = Specific rotaion at 20°C

Problem 1. 3 gms. of an enantiomer is dissolved in ethanol to make 100 ml of solution. Find out the specific rotation at 20°C for sodium light (the D line), if the solution has an observed rotaion of **+2·10°** in 10cm (**1dm.**) polarimeter tube.

Solution. $\alpha = +2{\cdot}10^\circ$, $l = 10\text{cm} = 1\text{dm.}$, $c = 3\text{gms. in } 100\text{ ml} \equiv {\cdot}03\text{ gm per ml.}$

Substituting these values in the equaion :

$$[\alpha]_D^{20} = \frac{\alpha}{l \times c} = \frac{+2.10^\circ}{1 \times .03} = +.70^\circ \text{ (in ethanol)}$$

Problem 2. Calculate the observed rotation (α), if above solution (problem 1) that gives specific rotation +70° is filled in 5 cm. polarimeter tube.

Solution. Applying the formula, we get :

$$\alpha = [\alpha]_D^{20} \times l \times c$$

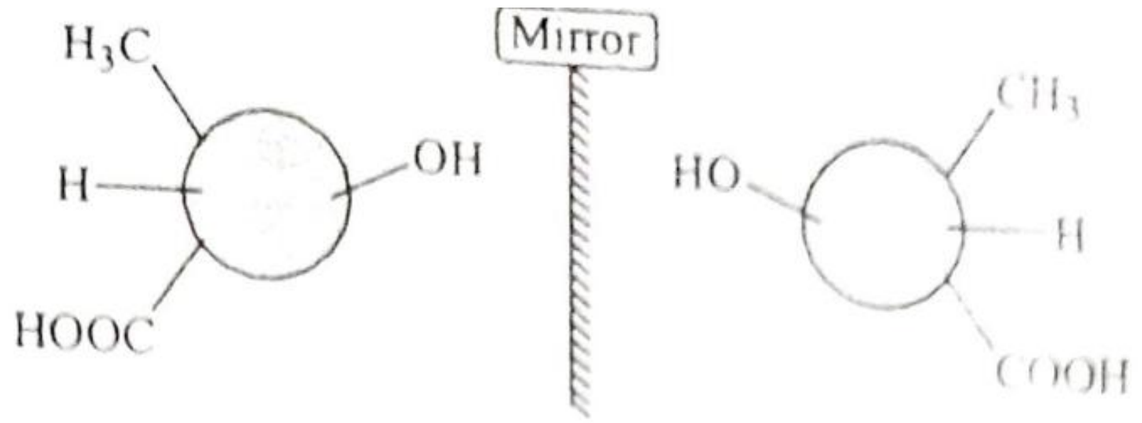
$$\alpha = 70^\circ \times 0.5 \times {\cdot}03 = +1.05^\circ$$

By reducing polarimeter tube to half allows only half as many molecules to act on the plane polarized light and therefore, observed rotation is half of the problem 1 vlaue.

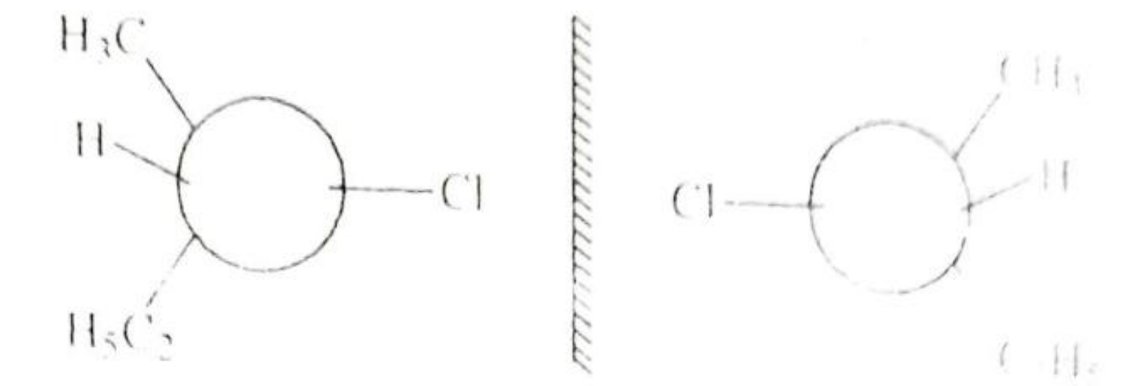
6.4. ACYCLIC MOLECULES WITH ONE ASYMMETRIC / CHIRAL CARBON Or STEREOGENIC CENTRE

Let us now consicer a few specific compounds, like **lactic acid** $CH_3CH(OH)COOH$, containing one asymmetric or chiral carbon (C*). Fig. **6.10**. lists a few such compounds together with their mirror images.

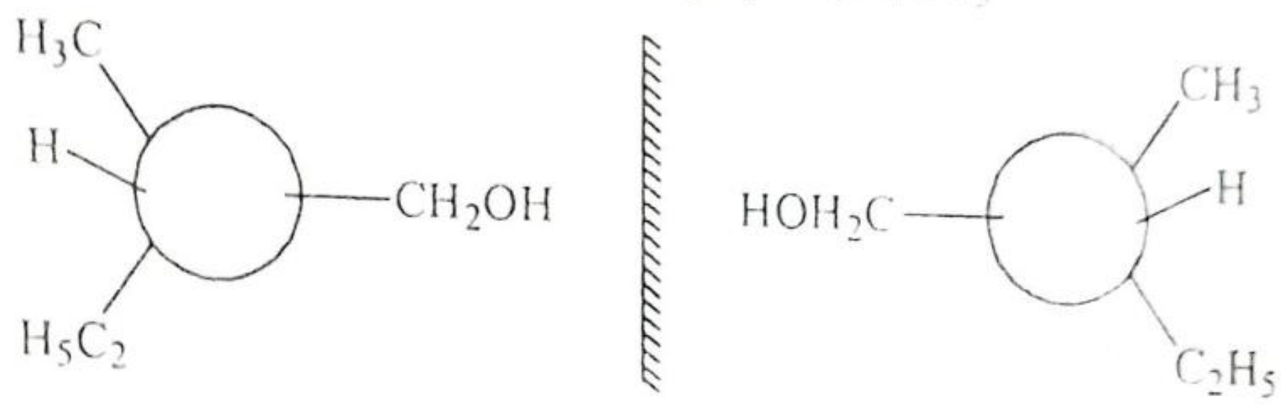
Each of these compounds, exists in **two** stereo ***isomeric*** (**enantiomeric**) forms.



Lactic acid $CH_3\overset{*}{C}H(OH)COOH$



***sec*-Butyl chloride** $C_2H_5\overset{*}{C}H(Cl)CH_3$



2-Methyl-1-butanol $CH_3\overset{*}{C}H(C_2H_5)CH_2OH$

Fig. 6.10. Possible enantiomers of Lactic acid, sec-Butyl chloride and 2-Methyl-1-butanol.
(In these structures, circle represents an asymmetric carbon atom)

The two stereoisomers of each pair depicted in Fig. **6.10** have identical structures as far as the atoms or groups attached to the central asymmetric carbon, C* are concerned. They have also identical physical properties except for the direction they rotate the plane of polarized light. Each enantiomer rotates the plane of polarized light by exactly the **same amount,** but in **opposite** direction. We cannot predict which direction a particular enantiomer will rotate the plane of polarized light. One enantiomer was arbitrarily said to be ***dextrorotatory,*** while the other was ***laevorotatory***. Thus, compounds shown in Fig. **6.10** are optically active.

It may be noted that before we knew the relationship between chirality and optical activity, these stereoisomers were called **optical isomers** because they were identical except for their opposite optical activity. However, the term 'optical isomer' was applied loosely to more than one type of isomerism among optically active compounds. This ambiguous term has now been replaced by the more well-defined term '**enantiomers**'. For similar reasons, the term optical isomerism is not favoured over the term **enantiomerism**.

It may be recalled that '**enantiomerism**' disappears, as soon as **two** or more atoms or groups, attached to carbon become identical. Therefore, compounds, like propionic acid CH_3CH_2COOH, *n*-propyl chloride ($C_2H_5CH_2Cl$) and *n*-butyl alcohol, ($C_2H_5CH_2CH_2OH$) **do not** show ***enantiomerism***.

6.5. ENANTIOMERS AND RELATED ASPECTS

We have already learnt that

(1) isomers, which are the **non-superimposable mirror images** of each other are **enantiomers.**

(2) ***Enantiomeric pairs have identical gross structure,*** *i.e.*, the sequences of atoms and groups in each are identical, but they differ from each other in having different spatial disposition of atoms and groups.

6.5.1. PROPERTIES OF ENANTIOMERS

We have already mentioned briefly in the earlier section while referring to the characteristics of a few specific compounds containing **one** asymmetric carbon atom (C*). Let us now consolidate the important **general properties** of enantiomers.

(1) Enantiomers have **identical physical properties** like m.p., b.p., density, refractive index, *etc.*, but they differ in their action on plane-polarized light. One of the enantiomers rotates the plane polarized light to the right (***dextrorotatory***) and the other rotates the plane of polarized light to the left (***laevorotatory***). These prefixes are generally shortned to the letters '*d*' and '*l*' (written in lower case to distinguish them from the upper case letters 'D' and 'L' used to define configurations of chiral molecules). It must be understood that directions of rotation in enantiomers are denoted usually by prefixing (+) for dextrorotatory and (–) for laevorotatory, before the names of compounds. The earlier practice of prefixing the letters '*d*' (for dextrorotatory) and '*l*' (for laevorotatory) is now discouraged. It must be noted that while the directions of rotation in such enantiomeric pairs are **different**, **the amounts of rotation are the same**.

(2) **Enantiomers have identical chemical properties except their action towards optically active reagents**. The two enantiomeric *sec-butyl* alcohols ($CH_3CH_2CH(OH)CH_3$), for example, give same 2-butene on treatment with H_2SO_4. They form the same *sec-butyl* bromide ($CH_3CH_2CH(Br)CH_3$) on treatment with hydrobromic acid, and they give the same *sec-butyl* acetate ($CH_3CH_2CH(OCOCH_3)CH_3$) on esterification with acetic acid. Even the rates of these reactions are identical in the case of each enantiomer. All this, is reasonable also because the two enantiomers of ***sec-butyl*** alcohol have exactly the **same *structural* environment** for reaction with reagents like H_2SO_4 or HBr or CH_3COOH.

Stereospecificity. When the **reagent itself is optically active, reaction rates would be different**. The reagent [say (–)-lactic acid in esterification] would not be subject to identical influences due to the different spatial disposition of –OH group in two enantiomers of *sec-butyl* alcohol. The rate of esterification of (+)-*sec-butyl* alcohol with (–)-lactic acid would be **different** from that of (–)-*sec-butyl* alcohol with (–)-lactic acid. These influences may sometimes be so different that reaction of an optically active reagent may **succeed with one enantiomer of the reactant, but not at all with other enantiomer**. These **reactions** are known as **stereospecific** reactions.

Such situations are quite common in biological systems, where ***enzymes*** (biocatalysts) and the compounds they act on (*substrates*) are both *chiral*. It is possible that reaction between an enzyme and a substrate would, be highly **stereospecific**, *i.e.*, only one stereoisomer or enantiomer of a substrate may respond to the action of the optically active enzyme. (+)-Glucose, for example, is easily metabolised in the animal system and is fermented by yeast, but (–)-glucose is **neither metabolised** by animals **nor** undergo fermentation. Therefore, **enantiomers have different biological properties also**.

Explanation for stereospecificity : To understand the above differences in terms of the ***transition state theory***, consider the reaction of two enantiomers, (+)-**A** and (–)-**A** with an optically inactive reagent B. The reactants in both the reactions have exactly the same energy. The two transitional states for the two reactions would obviously be mirror images (or enantiomers) and hence, of **equal** energy. Energeis of activation (E_{act}) of the two reactions and their reaction rates, would be identical. When (+)-A and (–)-A react with an optically active reagent [say (–)-B], their respective transitional states would ***not*** be **enantiomeric** and hence of **different** energies. Consequently, the energies of activation (E_{act}) of these reactions would be different and hence, their **reaction rates** would be **different**.

6.5.2. THE RACEMIC MODIFICATION

A *mixture of equal parts of enantiomers is called a* **racemic modification** or a **racemic mixture**. Such racemic modifications are *optically inactive*, because the **rotation caused by molecules of one isomer** is **cancelled out by an equal and opposite rotation** caused by an equal number of molecules of its enantiomer.

Racemic modifications are usually denoted by prefixing (±) before the name of that compound. The

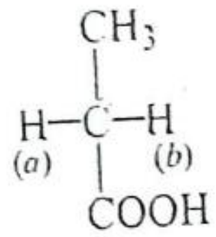
prefix *dl-* has also been used, especially in earlier literature, but the **prefix** (±) is now **preferred**. Thus we have (±) lactic acid, (±)-*sec-butyl* chloride, and (±)-2-methyl-1-butanol.

When a ***chiral*** compound is synthesized from ***achiral*** reactants, the product is always of the **racemic** variety. The reason for this will be readily understood from the following example :

When propionic acid (**achiral**) is brominated, α-bromopropionic acid (a **chiral** molecule) results. The reaction is brought about by the replacement of one of the two hydrogen atoms of CH_2 group in the molecule by Br. Both the hydrogen atoms at points (***a***) and (***b***) in the formula (see below) are equivalent and replacement of one or the other is equally possible. It is to be expected, that (+)-and (−)- bromo acid would be formed in equal amounts, that is, the product will be the **racemic** mixture. The conversion of **achiral** compounds into **chiral** compound is often referred as chiral synthesis

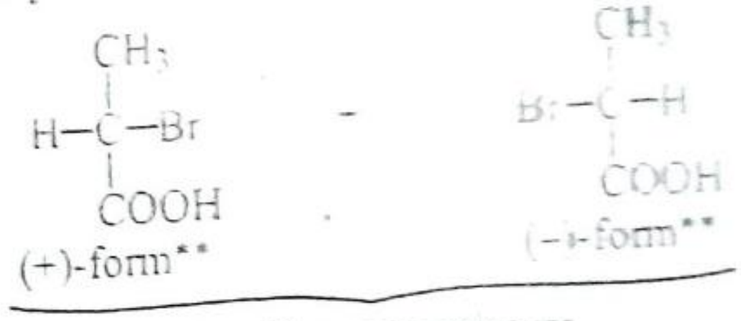
$$CH_3CH_2COOH + Br_2 \longrightarrow CH_3\overset{*}{C}HBrCOOH + HBr$$

(*Asymmetric carbon)



Propanoic acid
(Achiral)

Bromination →



(±)-or Racemic mixture

It may be recalled that the physical properties of enantiomers are identical. Thus, enantiomers have identical **melting** or **boiling** points and **solubilities** in a given solvent and they are held equally strongly on a given adsorbent. It is, therefore, not possible to separate a racemic modification into their enantiomeric components by conventional techniques like **fractional distillation, fractional crystallization**, etc. The **separation** of a **racemic** modification into its **enantiomeric** components, is known as **resolution**. This requires special methods and we shall consider in due course.

It may be pointed out that a **racemic modification** as well as an **achiral compound** are optically **inactive** for similar reasons. It has been stated earlier that due to the random distribution of a large number of molecules, for every achiral molecule that the light encounters, there is a second molecule a mirror image of the first, aligned just to cancel the effect of the first one. In fact, an achiral compound shows an overall optical inactivity. In a racemic modification, this second molecule happens to be an enantiomer of the first and there is an exact **cancellation of rotation** caused by the enantiomers. Hence, the **optical inactivity** of a **racemic** modification.

6.6. RACEMIC FORMS AND ENANTIOMERIC EXCESS (EE)

If a sample of an optically active substance contains a **single enantiomer**, it is said to be **enantiomerically pure** or an **enantiomeric excess** of 100%. For example, an enantiomerically pure sample of (−)-Tartaric acid shows a specific rotation of +12.7° *i.e.*, $[a]_D^{20} = +12.7°$ (H_2O). On the other hand, if a sample of (+)-Tartaric acid shows a **specific rotation** less than **+12.7°,** but greater than zero degree. Such a sample is said to have an **enantiomeric excess** less than 100%. Hence, **enantiomeric exess** (**ee**) may be defined by the following expression :

$$\% \text{ Enantiomeric excess} = \frac{\text{Observed specific rotation}}{\text{Specific rotation of pure enantiomer}} \times 100$$

(Remember that this calculation should be applied to a **single enantiomer** or to a **mixture of enantiomers** of **same** compound. It should **not be** applied to **mixtures** in which some other compounds are present.)

The signs of rotation for the enantiomeric pairs have been given here arbitrarily but it makes no difference in explaining "the optical inactivity of the product consisting of an **equimolecular mixture of the two isomers".

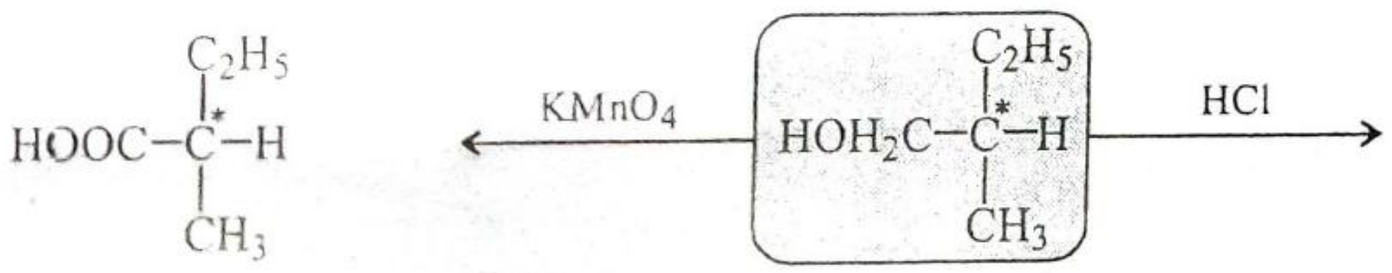
Suppose, a mixture of tartaric acid enantiomers shows a specific rotation of + 6.35°. We would then say that enantiomeric excess of (+) tartaric acid is 50% by applying above given relationship.

$$\text{Enantiomeric excess (ee)} = \frac{(+)6.35}{(+)12.70} \times 100 = 50\%$$

From this derivation we can say that enantiomeric excess of this mixture is 50%. This means that 50% of the mixture consists (+)-enantiomer and remaining 50% consists racemic form of 25% (+) and 25% (–) form which **cancel rotations** caused by each other in opposite direction. This mixture, **actually contain** 50 – 25 = 75% (+) enantiomer and 25% (–) enantiomer. This method is used to determine **optical purity** of enantiomer.

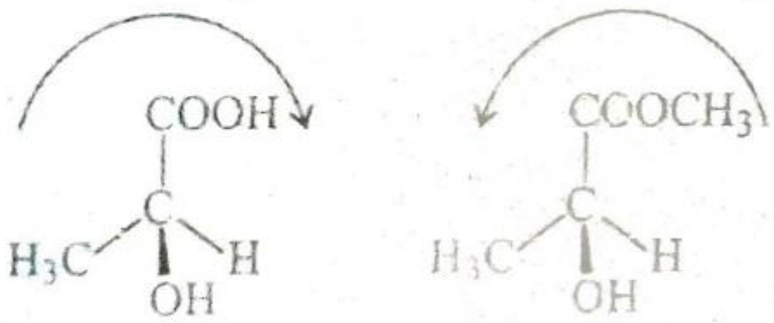
6.7. CONFIGURATION

In Fig. 6.6. we have represented the two enantiomers of **lactic acid** (I and II). *Arrangements of atoms or groups in space for each enantiomer define their* **configurations**. One of these configurations will represent (–)-lactic acid and the other will represent (+)-lactic acid. It is natural to enquire as to which of these two configurations represents the (–)-lactic acid or (+)-lactic acid. The ***actual*** arrangement in space of the atoms of a stereoisomer (*i.e.*, **absolute configuration**) can now be determined by using **Bijvoet's X-ray** analysis, but it is not essential to determine the absolute configuration of every optically active compound. It is usually sufficient to know the *configuration* of a compound and relate it to that of an other compound. *If a reaction does not involve the breaking of a bond at a chiral carbon, the configuration about that chiral carbon is retained.* The configurations of (+)-1-chloro-2-methylbutane (IV), obtained by the replacement of –OH in (–)-2-methyl-1-butanol (III) by Cl, would be similar to that of (III). Similarly, the configuration of (+)-2-methylbutanoic acid (V), obtained by the oxidation of (III) would also be similar to (III). This is called ***relative configuration*** that is required in most of the compounds.



(+)-2-Methylbutanoic acid (V) | (–)-2-Methyl-1-butanol (III) | (+)-1-Chloro-2-methylbutane (IV)

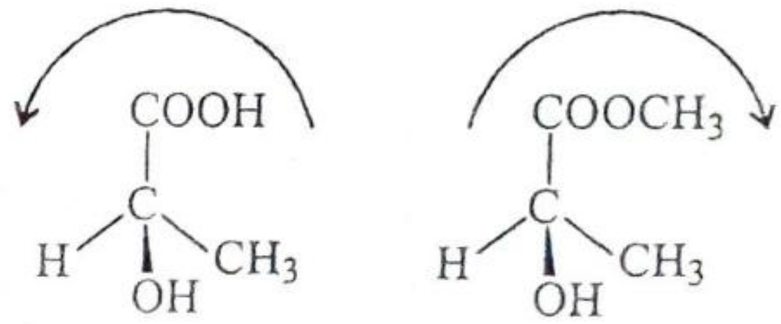
It may be noted that III, IV and V have **similar** configurations but **different** directions of rotation. It should, therefore, be clearly understood that **the direction** (*and even the magnitude*) **of rotation in a given stereochemical series** (*i.e.*, compounds possessing similar configurations) **varies greatly according to the nature of the groups attached to the chiral centre**. Thus, all dextrorotatory compounds do not necessarily have similar configurations. In fact, there are many compounds which have **similar configurations** but **different signs** of rotation. For example, two forms of lactic acid and their corresponding methyl lactate have similar configuration but **opposite sign** of rotation as shown below.



(+)-Lactic acid
$[\alpha] = (+)\ 3.82°$

(–)-Methyl lactate
$[\alpha] = (-)\ 8.25°$

Similar configuration but opposite sign of rotation



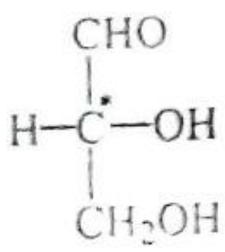
(–)-Lactic acid
$[\alpha] = (-)\ 3.82°$

(+)-Methyl lactate
$[\alpha] = (+)\ 8.25°$

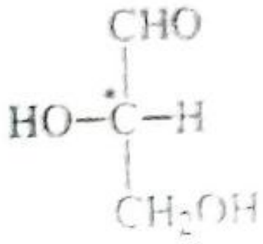
Similar configuration but opposite sign of rotation

6.7.1. RELATIVE SPECIFICATION OF CONFIGURATION 'D' AND 'L'* NOTATION

We have seen above that (+) lactic acid when esterified with methanol gave (–) methyl lactate without any change in **configuration at asymmetric carbon**. Therefore, it is very difficult to assign configuration to enantiomers on the basis of rotation alone. To solve this problem **Emil Fischer (1908)** used two forms of **glyceraldehyde** (I and II) as standard.



(I)
D(+)-Glyceraldehyde

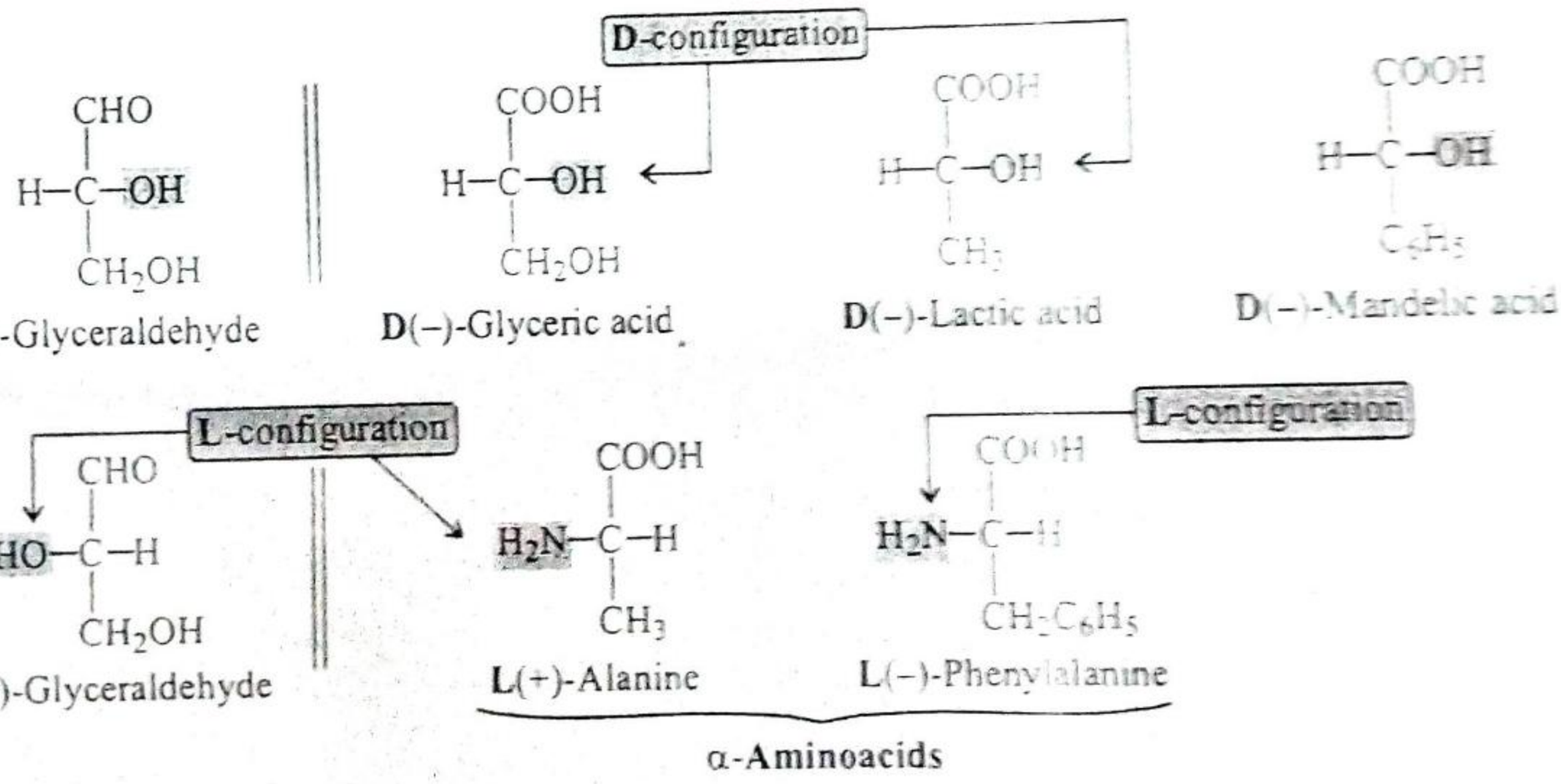


(II)
L(–)-Glyceraldehyde

(* Asymmetric carbon)

The structure (I) with **–OH** on the **right** hand side of the observer is known as **D**-glyceraldehyde whereas its mirror image (II) with **–OH** on the **left** and H on the **right** is known as **L**-glyceraldehyde. These configurations are denoted by capital letters **D** and **L**. In these designations (+) or (–) sign is also given in brackets as **convention** but **not** always **necessary**.

The configuration of other enantiomers at chiral carbon atom is then related to **D** and **L** forms of glyceraldehyde and **D** and **L** notations are given accordingly. For example,



Therefore, the sign of rotation of plane polarized light as (+) or (–) **does not specify configuration** (as D-configurational isomer may have (–) and L- may have (+) rotation).

Procedure for assigning D and L configuration. It involves following steps :

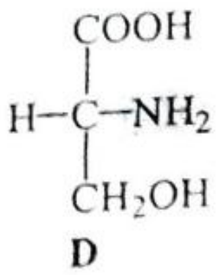
(1) Orient the main carbon chain in a **vertical line** with **priority group** (according to **IUPAC** nomenclature) **at the top**.

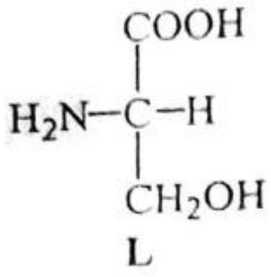
(2) Arrange the substituents at chiral carbon atom on **horizontal line** projecting towards the observer.

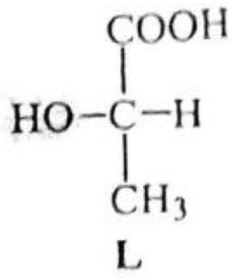
(3) Now, on examination if the main substituent (*e.g.*, OH, NH_2, etc) is on the **right** hand side of the observer (on horizontal line), the configuration is assigned **D** notation (without indicating any sign of optical rotation) and if on the **left** hand side **L** configuration. For example,

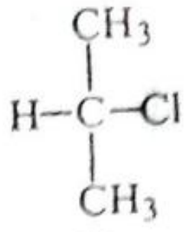
---

*D and L **do not specify the rotation of plane polarized light**, but specify the group on **right** and **left** hand side of the observer respectively on horizontal line. The sign (+) and (–) are given here only for the sake of **comparison**.

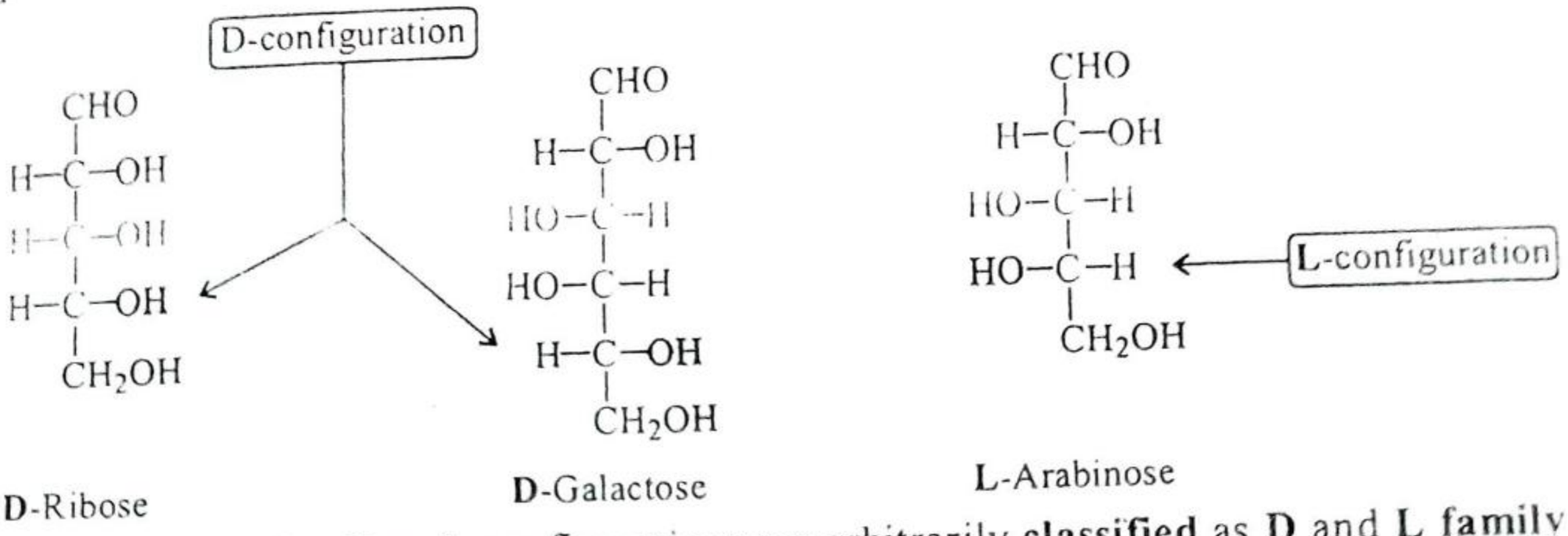

D


L


L


D

(4) The **D** and **L** notation can also be applied to multiple asymmetric (**chiral**) carbon containing compounds (*e.g.*, in carbohydrates). In such cases **bottom chiral carbon** containing **structure** is compared to corresponding **D** or **L** forms of glyceraldehyde. For *example,*



D-Ribose **D**-Galactose L-Arabinose

The compounds having **D** or **L** configurations are arbitrarily **classified** as **D** and **L family** of chiral compounds.

Limitation. D,L-nomenclature indicates configuration at only one **chiral** centre. It is therefore, **not satisfactory** for **assigning configuration** for compounds containing **more than one chiral** centre.

6.7.2. ABSOLUTE CONFIGURATION 'R' AND 'S' NOTATION*

Cahn, Ingold and **Prelog** have proposed a procedure to specify a particular configuration in a simpler and more convenient way than by always drawing its picture. This procedure involves the following steps :

Step 1. The four atoms or groups of atoms attached to the **chiral** carbon atom are assigned *priorities* in accordance to the following **sequence rules** :

(*a*) ***Sequence rule* 1**. *When the four atoms attached to the chiral carbon atom are all different, priority depends on* ***atomic*** *number. The atom of* ***higher atomic number*** *gets the* ***higher priority***. Thus, the priority in the compound bromo-chloro-iodomethane (C H Cl Br I) is I, Br, Cl, H.

When isotopes of the same element are attached to a chiral carbon, the isotopes with ***higher mass*** *number gets priority.* α-Deuterio ethyl bromide [$CH_3CH(D)Br$] for example, has the **priority sequence** of Br, CH_3, D, H.

In general, when the substituents are attached to **chiral** carbon, the **decreasing order of priority** is :

$$I > Br > Cl > SH > F > OH > NH_3 > CH_3 > D > H$$

(*b*) ***Sequence rule* 2**. *If* ***rule-1 fails*** *to decide the relative priority of two groups of atoms attached to a chiral carbon atom (e.g.,* the two groups may be $-CH_3$ and $-CH_2CH_3$: carbon is attached directly, in either case, to the chiral carbon), *the priority may be determined by* ***comparing the next atom*** *in the* ***group****. If it* is ***still not possible to decide the priority of the two groups****, the* ***comparison*** *may be* ***continued to the next atom****, and so on.* Thus, the priority sequence in *sec*-butyl chloride $CH_3\overset{CH_2CH_3}{\underset{|}{C}}HCl$, is Cl, C_2H_5, CH_3, H(C_2H_5 has priority over CH_3 because the second atoms in C_2H_5 are C,H,H whereas in CH_3 are H,H,H).

Therefore, when two of the atoms directly attached to the chiral centre are identical, the priority is decided by considering the next closest atoms. For example,

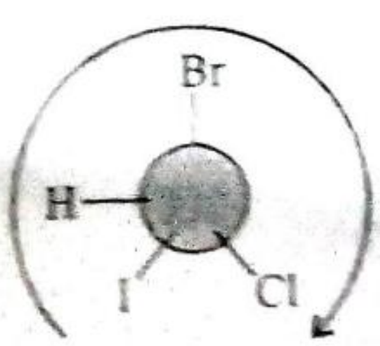
H_3C>CH– *has higher priority* than $CH_3CH_2CH_2$–, CH_3CH_2– *has higher priority* than CH_3–
H_3C

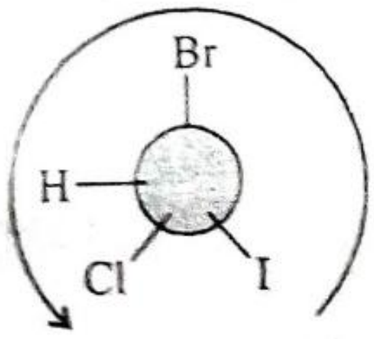
and CH_3CH_2O– ***has higher priority*** than HO–.

(c) ***Sequence rule 3***. *A doubly or triply bonded atom is equivalent to two or three such atoms.*

Thus, between the groups, –C(H)=O (O, O, H) and $-CH_2OH$ (O, H, H) the former (CH=O) will have priority in the compound glyceraldehyde, $OHCCH(OH)CH_2OH$.

Step 2. When the priorities of the four atoms or groups attached to an asymmetric or chiral carbon have been decided, the molecule is visualized so that the atom or group of the *lowest* priority is directed ***away*** from us. On looking at the arrangement of the remaining atoms or groups of atoms in decreasing order of priorities, if the eye travels in a **clockwise** direction the configuration is specified as **R**. If the eye travels in the **anti-clockwise** directoin, the configuration is specified as **S**. The following examples will illustrate the above procedure of specifying **R** and **S** notation to compounds containing an **asymmetric** or **chiral** carbon atom.

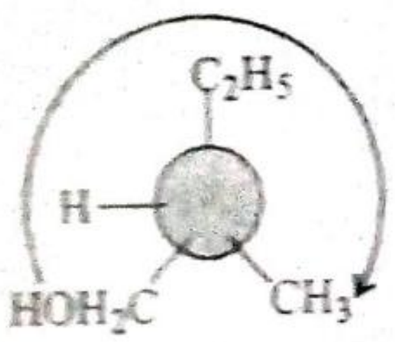




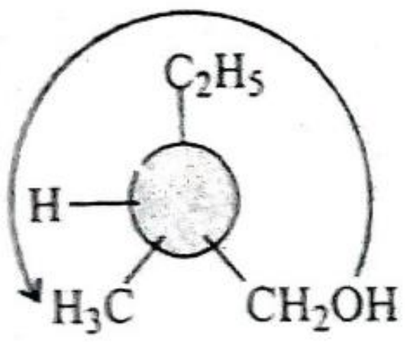
Priority sequence of groups :

I > Br > Cl > H

R

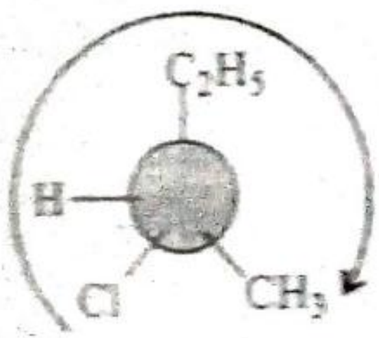


S

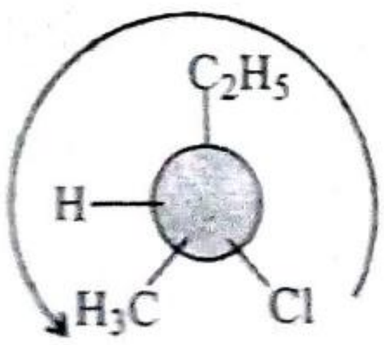


$CH_2OH > C_2H_5 > CH_3 > H$

R



S



$Cl > C_2H_5 > CH_3 > H$

R **S**

(These structures are also called steering wheel projections)

It may be pointed out that the *direction or rotation of an optically active compound is independent of the* **(R)**- *or* **(S)**-*configuration of the compound.*

---

*R and S are the symbols used for the Latin words **Rectus** (right) and **Sinister** (left). Occasionally, this convention has also been known as Rectus and Sinister system, but the shortened *forms* are more common. This method can also be used for compounds containing more than **one chiral carbon** atoms.

Thus, a complete description of an optically active compound must include **both the configurations** (**R** or **S**) and the direction of rotation (+ or –) prefixes. For example, R-(–)-*sec-butyl* chloride.

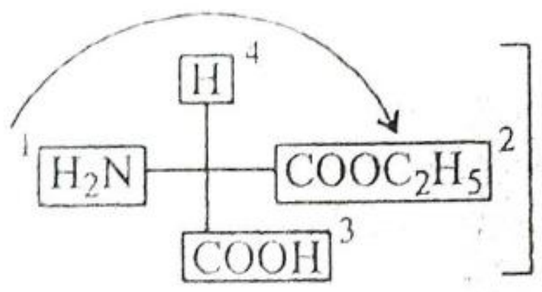
Such structures can be constructed on **Fischer projection** formulae (Planar structure) and equivalent structures can be constructed for **R-S** notation, if necessary.

The prefix (**RS**) is used to denote a **racemic** modification. For example, (RS)-*sec*-butyl chloride.

Problem 1. Designate R or S configuration to following compounds –

(*i*) $H_2N-\underset{COOH}{\overset{H}{C}}-COOC_2H_5$ (*ii*) $H_2C=CH-\underset{Cl}{\overset{H}{C}}-CH_2CH_3$ (*iii*) $ClCH_2-\underset{CH_3}{\overset{Br}{C}}-CH(CH_3)_2$

Answer. (*i*) The order of priorities is $NH_2 > COOC_2H_5 > COOH > H$



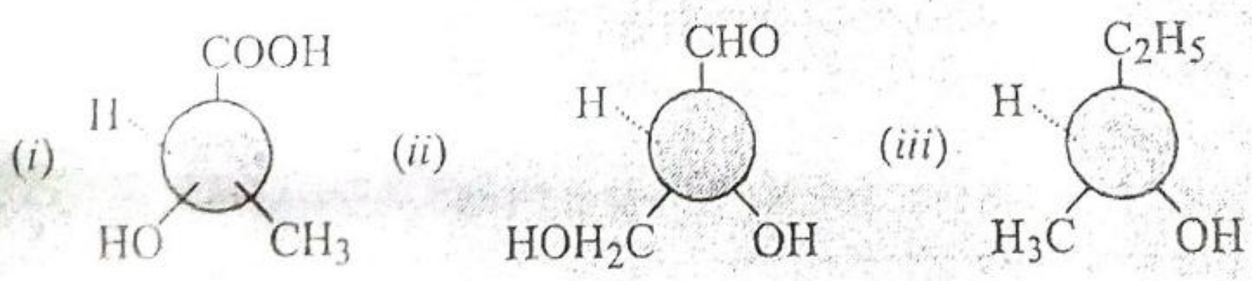
The sequence is clockwise or **R**.
Therefore, it has **R** configuration.

(*ii*) The sequential order of priorities is $Cl > H_2C=CH- > CH_3CH_2 > H$. The configuration of (*ii*) is, therefore, R.

(*iii*) The order of priority is $Br > CH_2Cl > CH(CH_3)_2 > CH_3$.

The sequence of decreasing priority order is counter clockwise. Therefore, configuration of (*iii*) is **S**.

Problem 2. Assign **R** and **S** configuration to following structures :



Answers : (*i*) Priority order HO > COOH > CH_3 > H, hence, it has **R** configuration.

(*ii*) Priority order HO > CHO > CH_2OH > H, hence, it has S configuration.

(*iii*) Priority order HO > C_2H_5 > CH_3 > H, hence, it has S configuration.

6.8. COMPOUNDS WITH TWO STEREOGENIC CENTRE / CHIRAL CARBONS

The two **chiral** carbons (C*) may be ***dissimilar*** (when the atoms or groups attached to one chiral carbon atom are different from those attached to the other) or ***similar*** (when the atoms or groups attached to the **two chiral carbon** atoms are identical). For example,

[**Both C* atoms contain different group/atom(OH,Cl)**] $H_3C-\overset{*}{C}H-\overset{*}{C}H-CH_3$ (OH, Cl)

3-Chloro-2-butanol
(***dissimilar chiral carbons***)

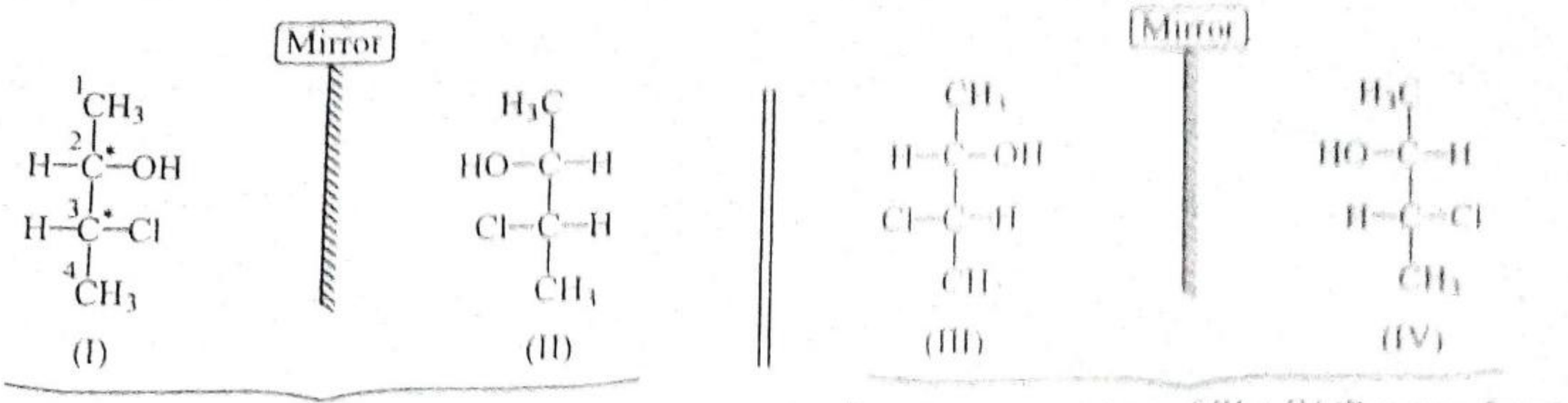
‖

[Both chiral C* atoms contain similar –OH group] $^{*}CH(OH)COOH$ | $^{*}CH(OH)COOH$

Tartaric acid
(***similar chiral carbons***)

The **stereochemistry** of these **two** representative compounds is described below :

1. **Stereochemistry of 3-chloro-2-butanol**. It contains **two dissimilar** chiral carbon atoms (C*), as shown below :



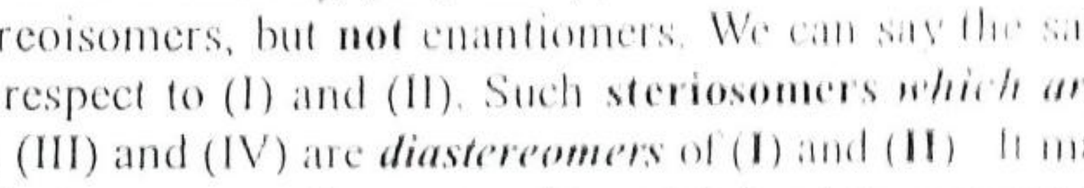
Diastereomers

If we write structure **I** and its mirror image II, we find that these structures are **not superimposable** (use models, if necessary). (I) and (II) therefore, constitute a pair of enantiomers. Structures (I) and (II) can be interconverted by rotation about carbon carbon bonds. Each stereoisomer can exist independently and can show **optical** activity.

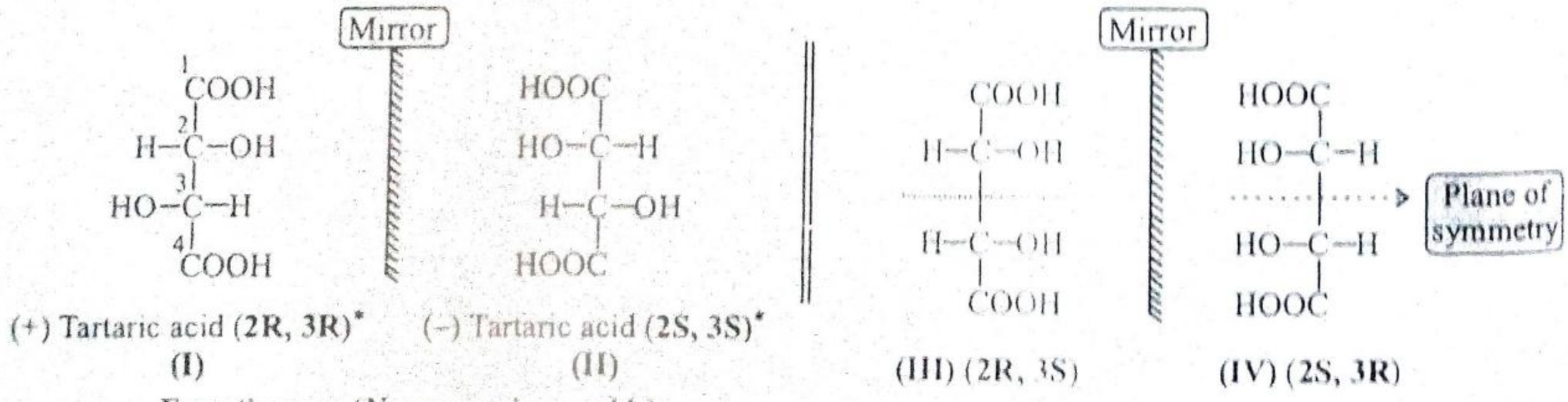
We can write yet another structure (III). It is **neither superimposable** on **(I) nor** on **(II)**. It is **not** a ***mirror image of*** **(I)** either. Obviously, **(III) and (I)** are stereoisomers but **not enantiomers**. Similarly, **(III)** and **(II)** are also stereoisomers, but **not** enantiomers. We can say the same thing about (IV), the mirror image of (III), with respect to (I) and (II). Such **steriosomers** ***which are not mirror images are called diastereomers.*** Thus, (III) and (IV) are ***diastereomers*** of **(I)** and **(II)**. It may be pointed out here that this is just an example of ***diastereomers***, of compounds containing two or more chiral centres. In due course, we shall see that compounds having **diasteriomers** do **not always** have to have **chiral**/asymmetric carbons. By definition, ***geometric isomers*** (or ***cis-trans***-isomers) are also ***diastereomers***.

For reasons similar to used above for (I) and (II), structures (III) and (IV) represent a **second pair** of **enantiomers**. Thus, **3-chloro-2-butanol** with **two** dissimilar stereoisomeric **chirality** centres can exist in ***four*** (I to IV) forms or **two pairs** of enantiomers. It can be shown similarly that other compounds containing two ***dissimilar*** asymmetric (chiral) carbon atoms are also capable of existing in ***four*** enantiomeric forms (two pairs of enantiomers). In general, it can be stated that a compound with ***n-different*** **chiral** carbon atoms, has 2^n **stereoisomers**, n is an integer ($n = 1, 2, 3 \cdots$).

(2) Stereochemistry of tartaric acid. Tartaric acid contains **two similar chiral carbon** atoms (C*), as shown below :



Using models as before, we arrive at structures (I), (II), (III) and (IV) for **tartaric acid** as shown below :



* It would be useful to recall here, the rules for assigning (R) and (S) notations around each asymmetric/chiral carbon [see sec. 6.7.2 and 6.10.2].

Structures **I** and **II** are mirror images of each other. They are neither superimposable nor interconvertible by rotation about carbon-carban bonds. Therefore, **I** and **II** are ***enantiomers*** capable of independent existence. When separated from each other, they show optical activity.

Structures III and IV also have a mirror image relationship, but become **superimposable** (identical) if one of the structures is just rotated through 180° within the plane of the paper. As the structures III and IV are identical, tartaric acid should be capable of existing in ***three***, rather than four, stereoisomeric forms. As the structure III (≡IV) is not the mirror image of I or II, it is really a **diastereomer** and **not** an **enantiomer**. Therefore, tartaric acid exists in **two** enantiomeric forms inspite of having two chiral carbons.

A closer examination of structure III (≡IV) shows that the structure is **not chiral** despite the presence of **two** chiral carbon atoms. It cannot exist in two optically active enantiomeric forms. Such an optically inactive compound is called a **meso** compound. An ***optically inactive compound whose molecules are superimposable on their mirror images despite the presence of chiral carbon atoms*** **is known as a meso compound**. The compound having structure III (or IV) is **meso-tartaric** acid.

It may be noted that a ***meso*** compound is optically **inactive** because the rotation caused by **one half** of the molecule is **cancelled** by the equal and opposite rotation of the **other half** of the molecule-the mirror image of the first half. In other words, **optical inactivity** in a ***meso*** compound is due to **compensation** ***within*** the molecule. This is known as **internal compensation**. In contrast, the ***racemic*** modification is optically **inactive due to cancellation of rotations caused by two different molecules** which are mirror images of each other (**external compensation**). In other words, optical inactivity in a **racemic modification** is caused by compensation between **two** molecules rather than between two halves of the same molecule. It will be seen shortly that an optically inactive ***racemic*** modification can be **separated** into optically **active** enantiomeric components, whereas an optically inactive ***meso*** compound **cannot** be **separated** into **optically active** components.

On examination of the model of ***meso*** structure III (or IV), we find that **it has a plane of symmetry**. The molecule can be imagined to be cut into two identical halves along the **plane of symmetry**. Such a molecule **cannot be chiral** inspite of having **two chiral** carbons.

Tartaric acid exists in **three** stereoisomeric forms, a pair of optically active enantiomers and an optically inactive ***meso*** form. It can be shown by similar reasoning that all compounds with two similar **chiral carbon** atoms (*e.g.*, 2,3dichlorobutane) can, exist in **three** stereoisomeric forms, a **pair** of optically active **enantiomers** and an optically inactive ***meso*** compound.

6.9. PROPERTIES OF DIASTEREOMERS

The important **properties of diastereomers** are :

(1) They have different physical properties such as melting points, boiling points, solubilities, refractive indices, densities, etc. This is in contrast to enantiomers. For example, *meso*-tartaric acid has m.pt. **149°C**, whereas its diastereomer (+ and –tartaric acid) has **m.pt. 170°C**.

(2) They may or may not be optically active. Geometric isomers (a kind of diastereomers), it will be seen in later chapter, may or may not be optically active. However, **diastereomers other than geometric isomers** can be **mostly optically active** as seen under 3-chloro-2-butanol.

(3) Unlike enantiomers, **diastereomers have similar, but not identical chemical properties**. The rates of reactions of diastereomers with reagents (chiral as well as achiral) are generally different, whereas enantiomers have identical chemical properties except the reactions with chiral reagents.

(4) Due to differences in their physical properties, **diastereomers can be separated from one another** through techniques such as ***fractional crystallization, fractional distillation, chromatography***, etc. It may be recalled that **enantiomers cannot be separated by these techniques**.

6.9.1. DISTINCTION BETWEEN DIASTEREOMERS AND ENANTIOMERS

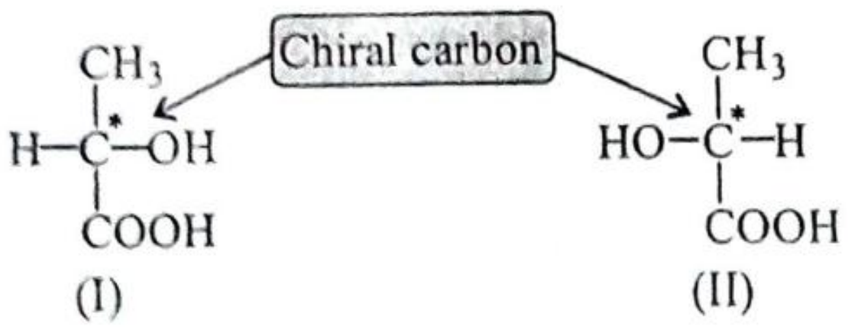
The distinction between diastereomers and enantiomers is given in **Table 6.2.**

Table 6.2. Distinction between Diastereomers and Enantiomers

S.No.	Diastereomers	Enantiomers
1.	These **do not** have **mirror image** relationship	These are **mirror images** of each other
2.	Diastereomers have **different physical properties**	Each enantiomeric pair has **similar physical properties**
3.	Due to **different physical properties**, these can be **separated** by **fractional distillation, fractional crystallization, chromatography** etc.	Due to **similar physical properties**, these **cannot** be **separated** by physical methods like **fractional distillation** and **fractional crystallization**.
4.	They **may have rotation** in the same direction, but to **different** extent.	Enantiomers have **rotation in opposite direction**, but to same extent.
5.	These **may** or **may not** be **optically active.**	These are **always optically active**.

6.10. FISCHER PROJECTIONS

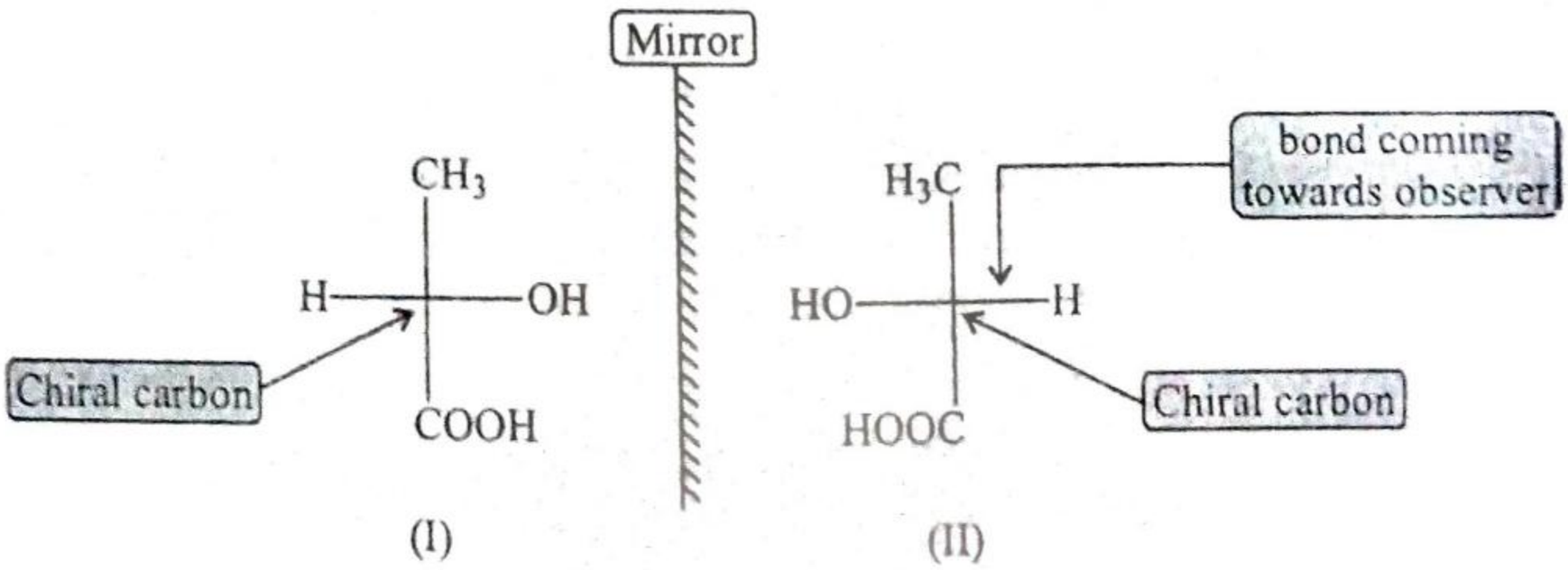
The steric aspects (*i.e.* space relationships of the different atoms/groups) of an organic compound can be understand by the examination of its **three**-dimensional model. It is sometimes necessary, and even convenient, to use the simpler **two dimensional** (planar) representations of three-dimensional compounds. These planar representations have obvious limitations, but with the help of certain conventions they also become quite clear. Let us illustrate this by taking the planar representation of the **two** enantiomeric forms of **lactic acid** (**I** and **II**).



C* = Asymmetric carbon

[**I** and **II** are **mirror images** (enantiomers)]

Two lines crossed at right angles to each other are drawn. The **chiral** or asymmetric **carbon** is not shown as such but it is believed to be situated **at the intersection** of these lines. The four atoms or groups are attached to four ends of **two** crossed lines, as shown below :



In such 'cross' representations (also known as **Fischer projections**), it is assumed that *the horizontal lines* (corresponding to the C–H and C–OH bonds in the above example) *represent bonds coming towards the observer out of the plane of the paper, whereas the vertical lines* (corresponding to C–CH_3 and C–COOH bonds in the above example) *represent bonds going away from the observer behind the plane of the paper.* While testing the superimposability of such flat, two-dimensional representations, the following rules have to be observed :

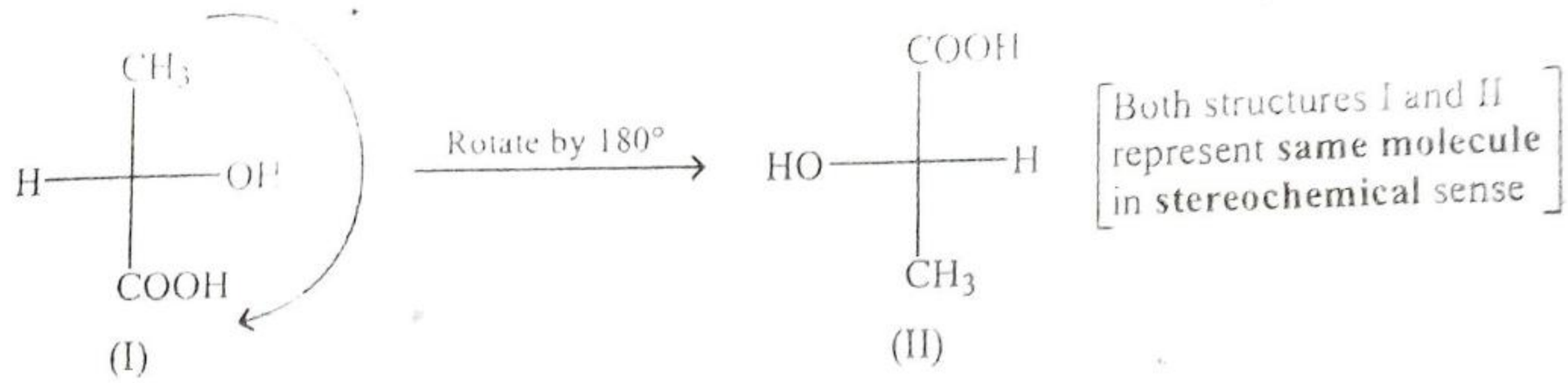
(1) These 'cross' representations are drawn only for molecules which contain atleast **one asymmetric or chiral** carbon.

(2) These formulae are not drawn at random. One of these formulae is drawn first and the other is drawn only as its mirror image.

(3) In our mind's eye we may rotate these formulae end for end, but we may not remove them from the plane of the paper

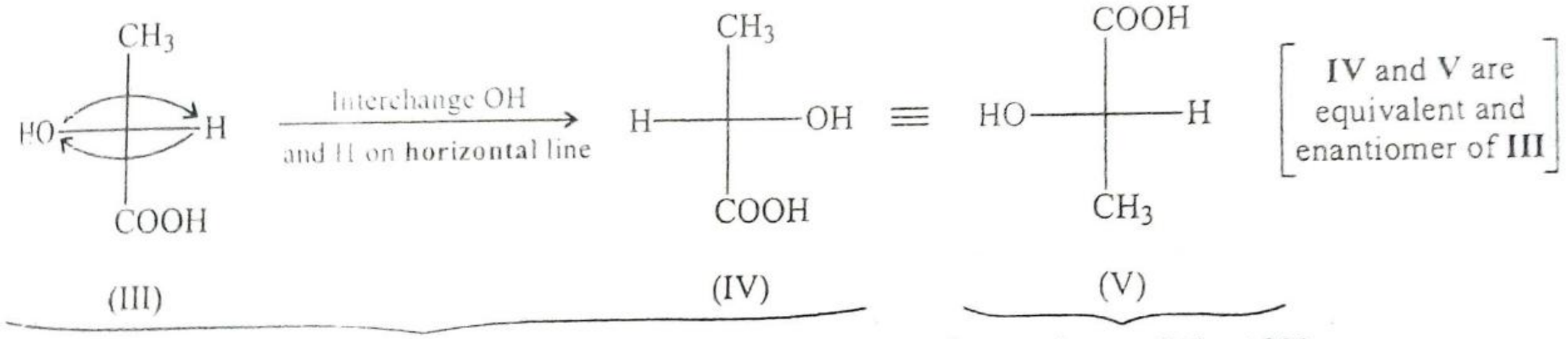
6.10.1. GUIDELINES FOR WRITING STEREOCHEMICALLY EQUIVALENT STRUCTURES ON FISCHER PROJECTIONS

(1) The stereochemical structure of the formula **does not change**, if rotated through 180° in the plane of the paper. For example, structure (I) and (II) for **lactic acid** are equivalent.



(I) (II)

(2) On interchanging the places of any **two** atoms or **groups** bonded to chiral carbon, the **enantiomer** of that isomer results. For example, III and IV are entiomers.

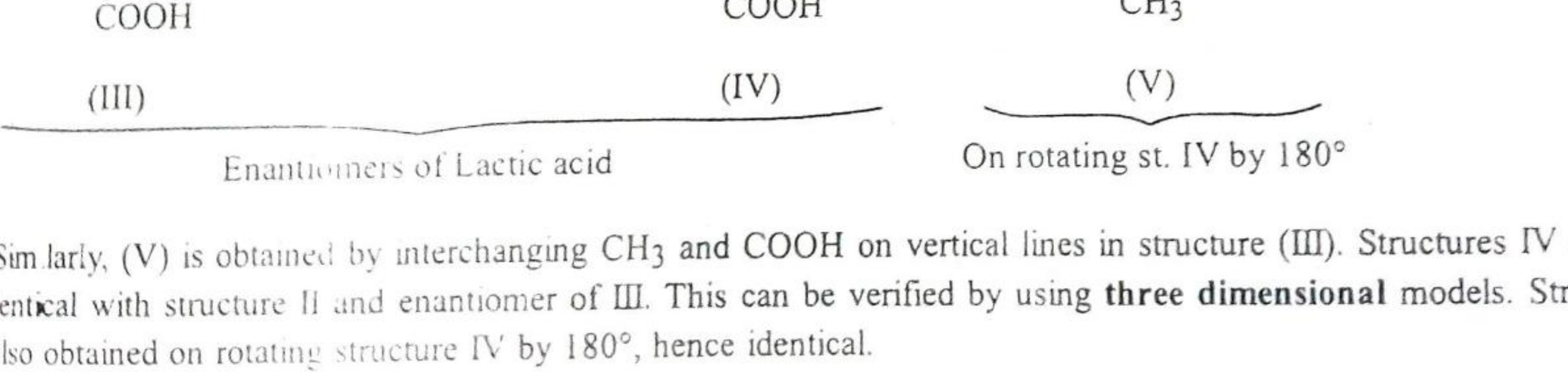


(III) (IV) (V)

Enantiomers of Lactic acid — On rotating st. IV by 180°

Similarly, (V) is obtained by interchanging CH_3 and COOH on vertical lines in structure (III). Structures IV and V are identical with structure II and enantiomer of III. This can be verified by using **three dimensional** models. Structure V is also obtained on rotating structure IV by 180°, hence identical.

(3) If the groups at the chiral carbon are interchangd **twice**, the resulting configuration is simlar to the original one i.e. there is **no net change** in configuration. For example, **VI** and **VIII** are identical.

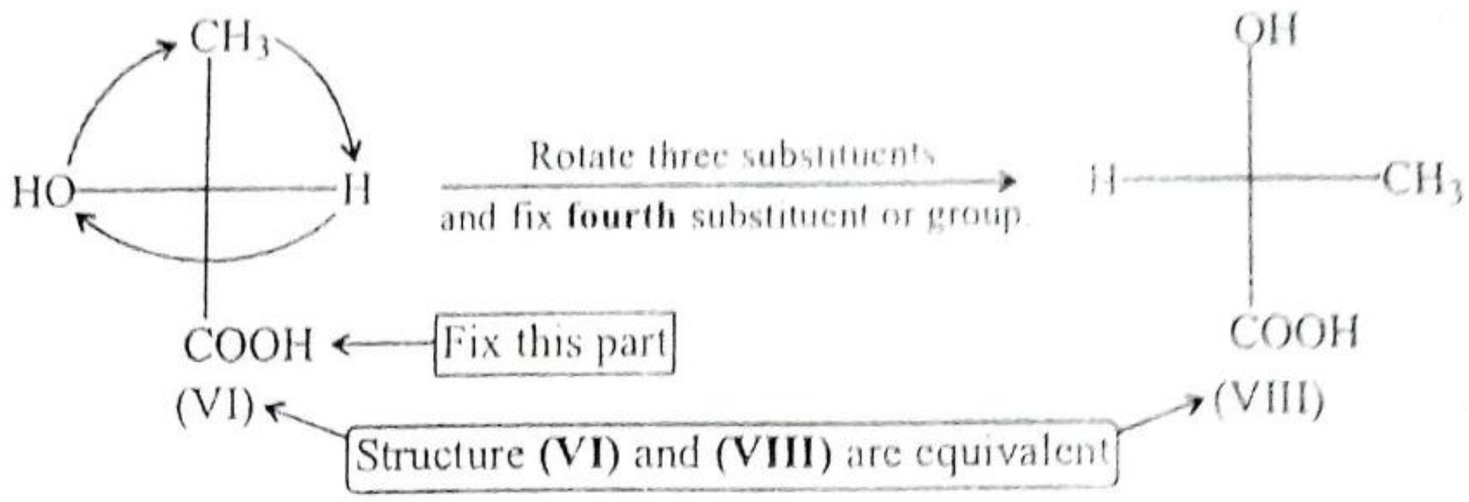


(VI) (VII) (VIII)

When checked by **three dimensional models**, the configuration (**VI**) and (**VIII**) were found to be identical.

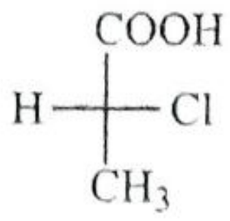
(4) Fischer Projections formulae can be transformed into equivalent structures by rotating a group of any **three** substituent in a **clockwise** or **anticlockwise** direction without changing the **position of fourth** substituent. Such a

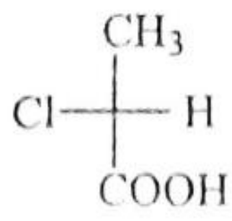
manipulation is **equivalent** to **two interchanges** given above under point (3). For example,

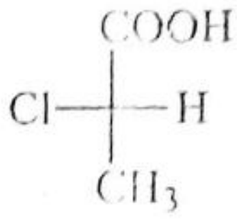


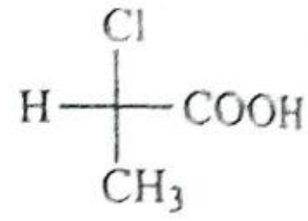
It can be concluded that the **rotation** of **three substituents** of a molecule **in clock-wise** or **anti-clockwise direction by fixing the fourth substituent**, **will give the structure of same molecule**. Whereas **rotation** of the whole formula through 90° or by interchanging any two substituents will give its enantiomer.

Problem 1. Which of the following Fisher projections of 2-chloropropanoic acid represent the same enantiomer ?

(*a*) 

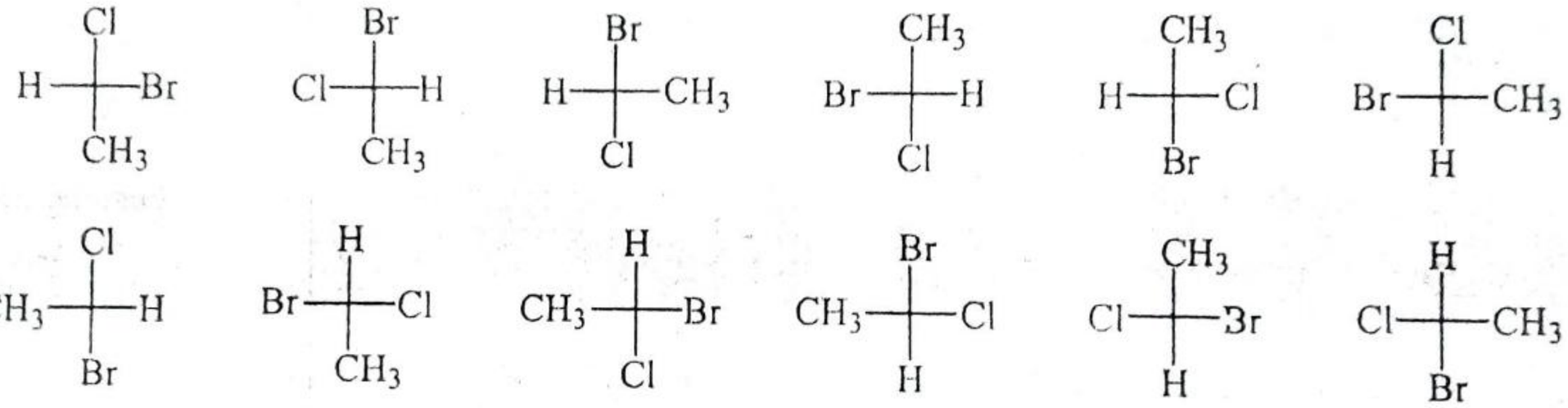
(*b*) 

(*c*) 

(*d*) 

Answer. (*a*) and (*b*) **identical** and **enantiomeric** with (*c*) and (*d*) which are **identical**.

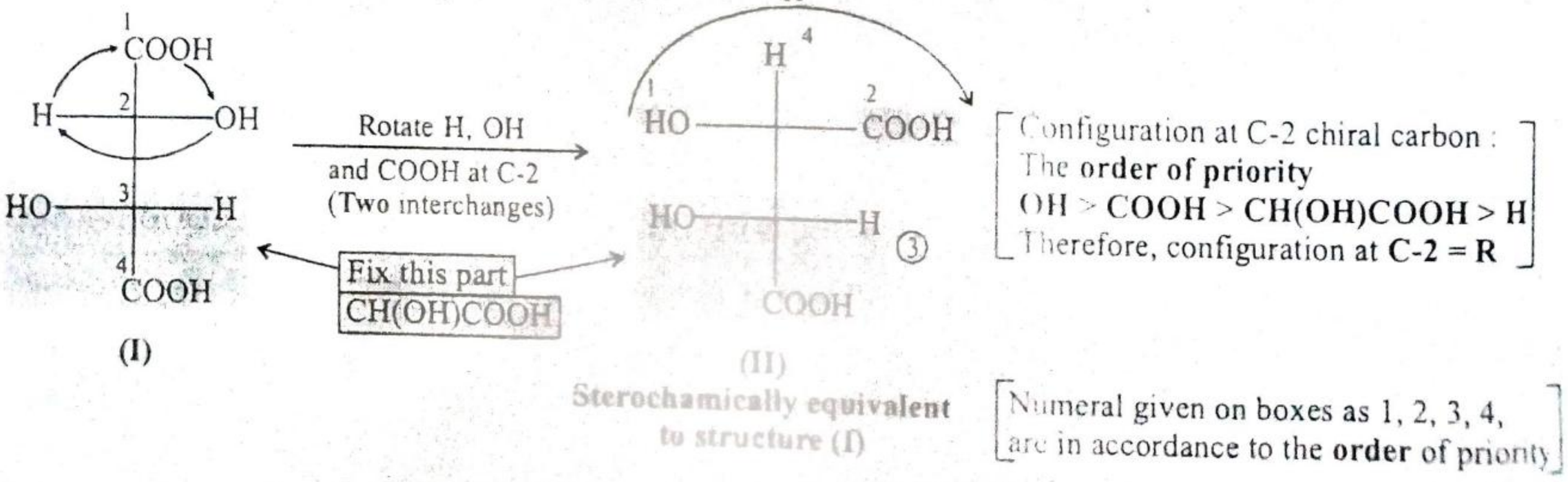
Problem 2. Are the following structures all equivalent ?



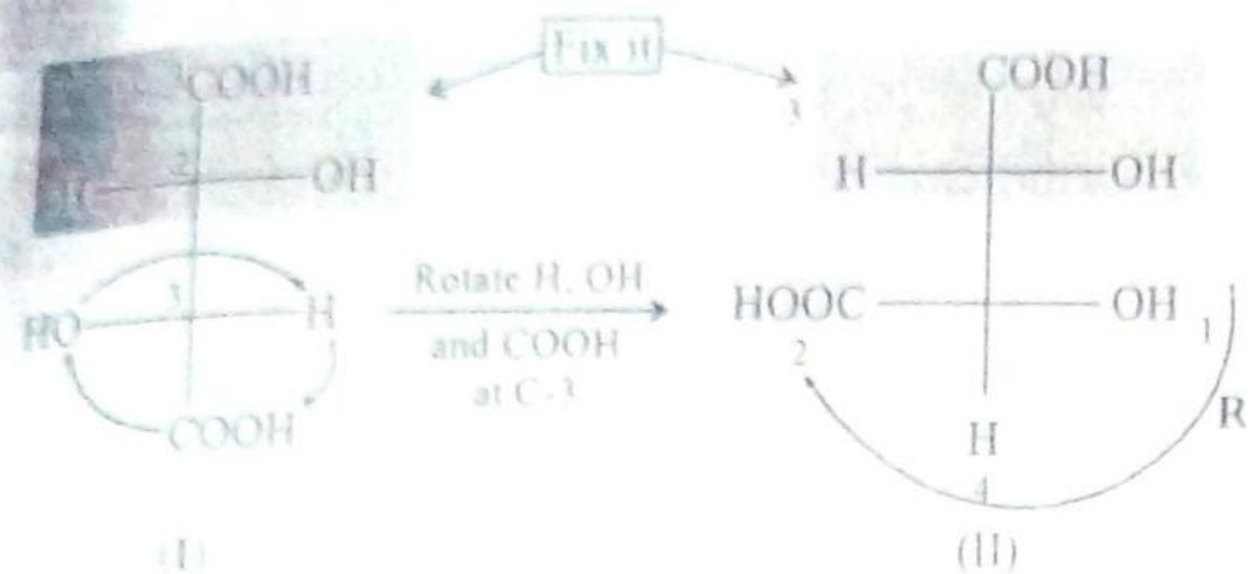
Answer. (R)-1-Bromo-1-chloroethane. These structures are all equivalent.

6.10.2. SPECIFYING R–S CONFIGURATIONS ON FISCHER PROJECTION

Consider the example of **tartaric acid** (**I**) to assign **R**–S notation at the **two chiral carbons** C-2 and C-3 on **Fischer projection**.



For configuration at C-3 in structure (I), **fix upper half part** and then rotate three substituents at chiral carbon **C-3** to get stereochemically equivalent structure



[Stereochemically equivalent to structure (I)]

Configuration at C-3, chiral carbon
The order of priority :
OH > COOH > CH(OH)COOH > H
Therefore, configuration at C-3 = *R*

Hence structure (I) has 2R3R notation at **chiral** carbon C-2 and C-3 respectively.

The **steps** involved in above operation or for any such compound are :

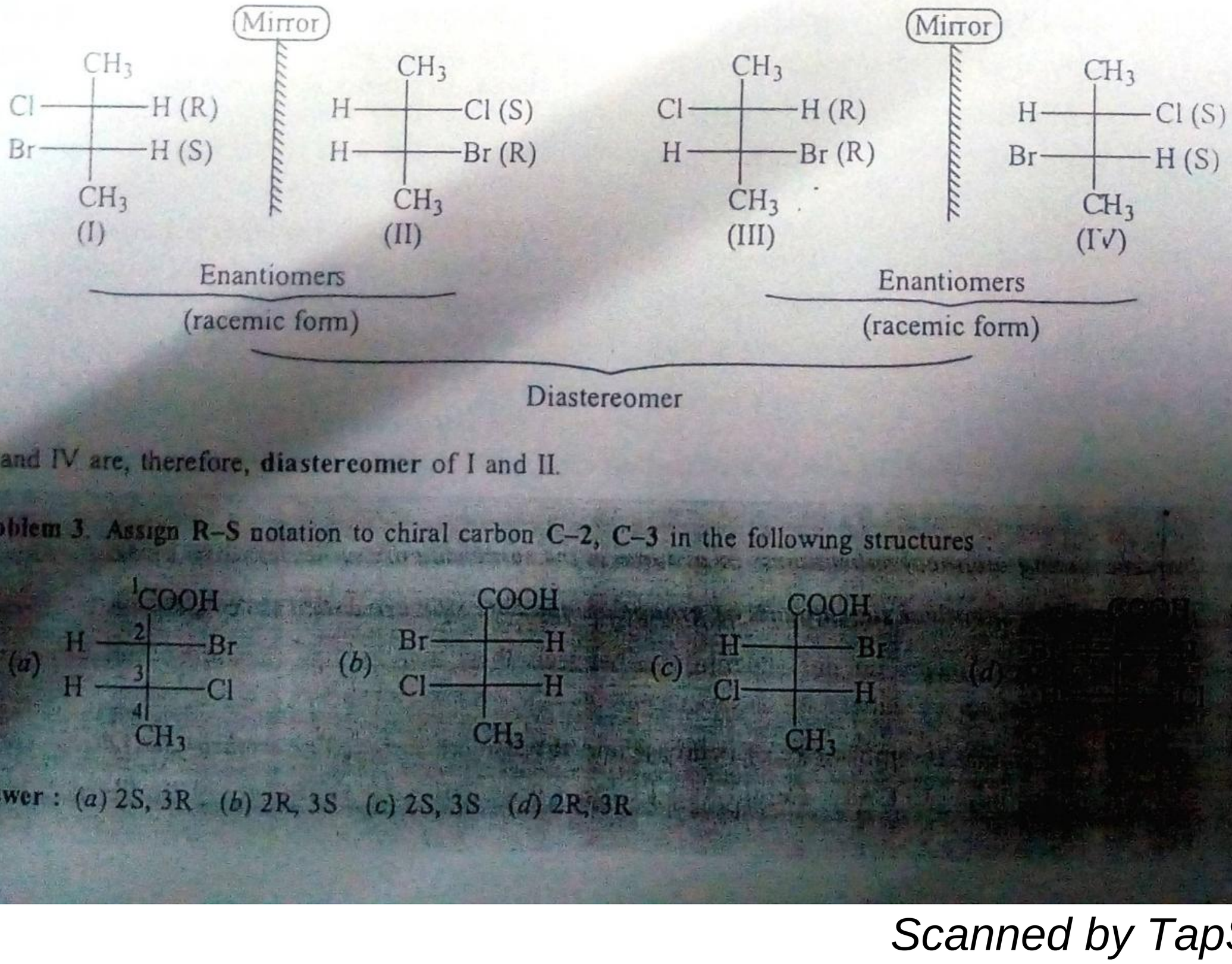
(1) Draw Fischer projection (as per guidelines given earlier) in such a way that substituent of lowest priority is at the **top** or **bottom** of the vertical line.

(2) Assign the order of priority to each substituent or group (as 1,2,3,4) on **chiral** carbon atom as per **Cahn, Ingold** and **Prelog** sequence rules, given under sec. 6.7.2.

(3) Observe the order of decreasing priority of other three substituents. If this is clockwise, the configuration is **R** (rectus), and if anticlockwise, it is **S** (sinister).

Following these steps, the **R-S** notation can be given to other compounds containing even **more** than two chiral or **stereogenic** centres/carbons.

Similarly, 2-bromo-3-chlorobutane ($n=2$), can have four enantiomers. The **R–S** configuration at concerned chiral carbon is shown below. You can try yourself to find the **notation** by following the **guidelines** given on previous page.

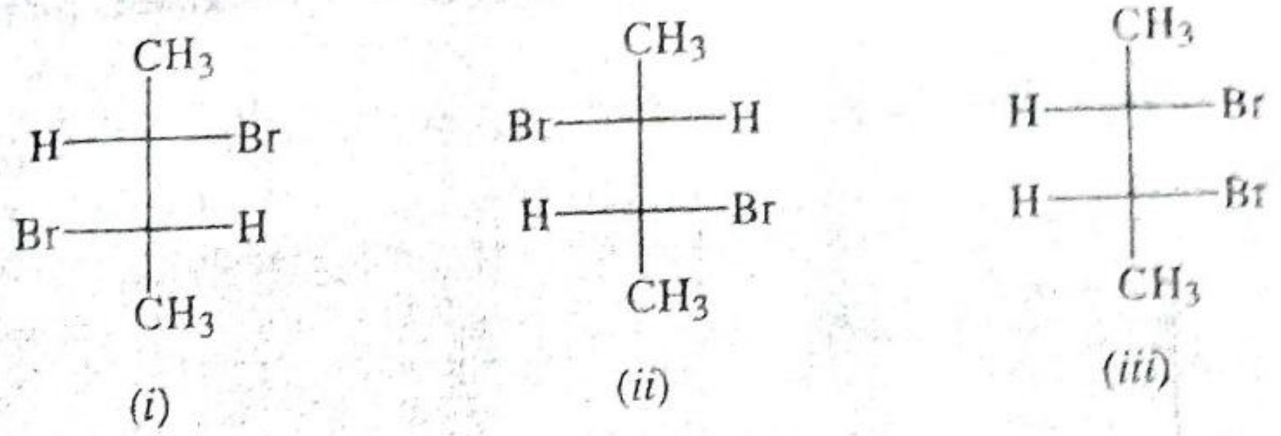


III and IV are, therefore, **diastereomer** of I and II.

Problem 3. Assign R–S notation to chiral carbon C–2, C–3 in the following structures :

Answer : (*a*) 2S, 3R (*b*) 2R, 3S (*c*) 2S, 3S (*d*) 2R, 3R

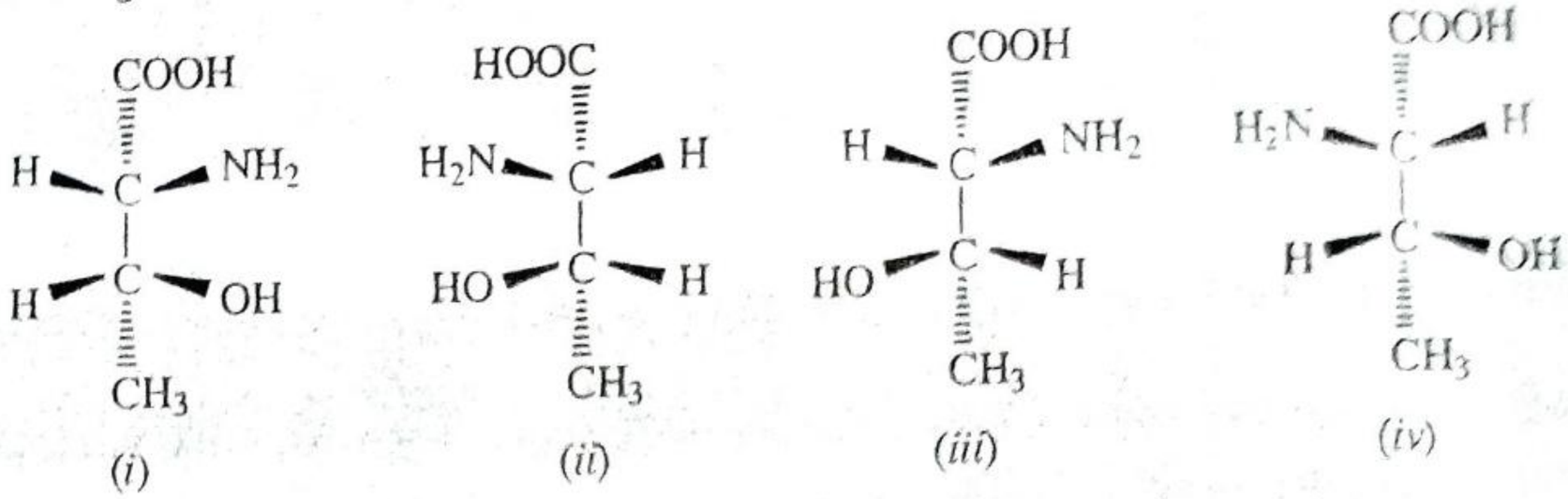
Problem 4. Assign the configuration to the following structures of 2,3-dibromobutane.



(*i*) (*ii*) (*iii*)

Answer : (*i*) 2S, 3S (*ii*) 2R, 3R (*iii*) 2S, 3R

Problem 5. Assign R, S notation to the following structures of threonines.



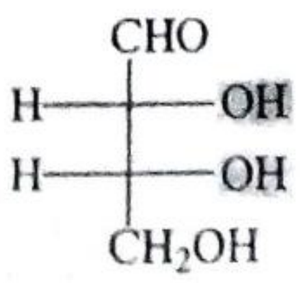
(*i*) (*ii*) (*iii*) (*iv*)

Answer : (*i*) 2R, 3R (*ii*) 2S, 3S (*iii*) 2R, 3S (*iv*) 2S, 3R

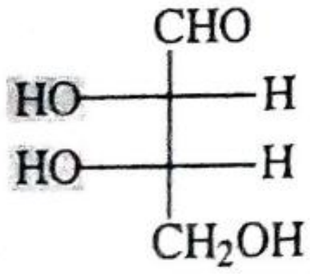
(*i*) and (*ii*) ; and (*iii*) and (*iv*) are **pairs of enantiomers.**

6.11. ERYTHRO AND THREO NOMENCLATURE (NOTATION) OF CONFIGURATIONS

Erythro- and *threo-* notations have been derived from the structural resemblance to two sugars **erythrose** and **threose**, having following structures :

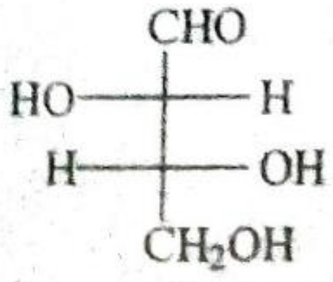


D (–) Erythrose

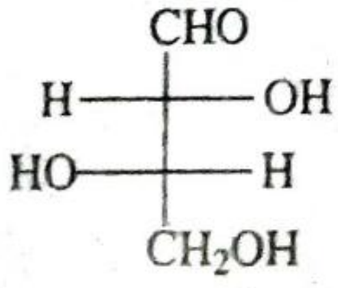


L (+) Erythrose

[Each form has OH groups on the same side, but their mirror images are not **superimposable** on **threose**. Hence, **Erythrose & threose** are **diastereomers** to each other]



D (–) Threose



L (+) Threose

[Each form has OH groups on the opposite side, but their mirror images are not superimposable on **erythrose**. Therefore, **Erythrose** and **threose** are **diastereomers**]

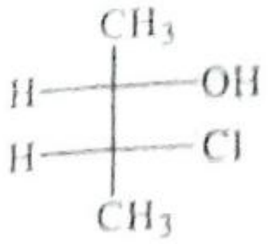
On reviewing above structures we **conclude** that :

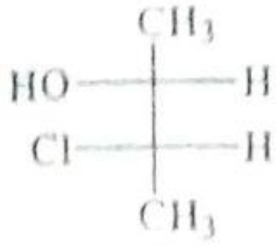
(1) *isomers having* ***identical substituents or groups*** *on the* ***same side*** *are called* **erythro forms.**

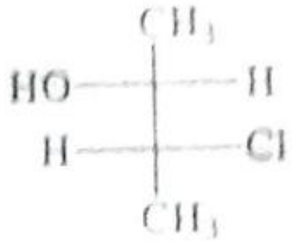
(2) *isomers having* ***identical substituents or groups*** *on* ***opposite side*** *are called* **threose forms.**

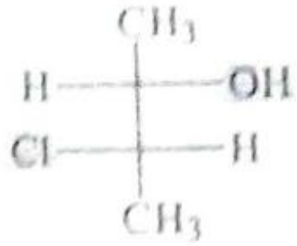
Further, their mirror images do not superimpose between these two groups (Erythrose and threose). Hence these are **diastereomers.**

Compounds with similar resemblance to **Erythrose** and **threose** are assigned as ***erythro-*** and ***threo-*** compounds. Two priority groups, according to **Cahn, Ingold and Prelog** sequence rule are considered to assign this configuration. For example,


Erythro-


Erythro-


Threo-


Threo-

6.12. RESOLUTION

The process used to separate a racemic modification into enantiomers is called **resolution**. Some important methods used to **resolve a racemic modification** into **enantiomeric forms** are :

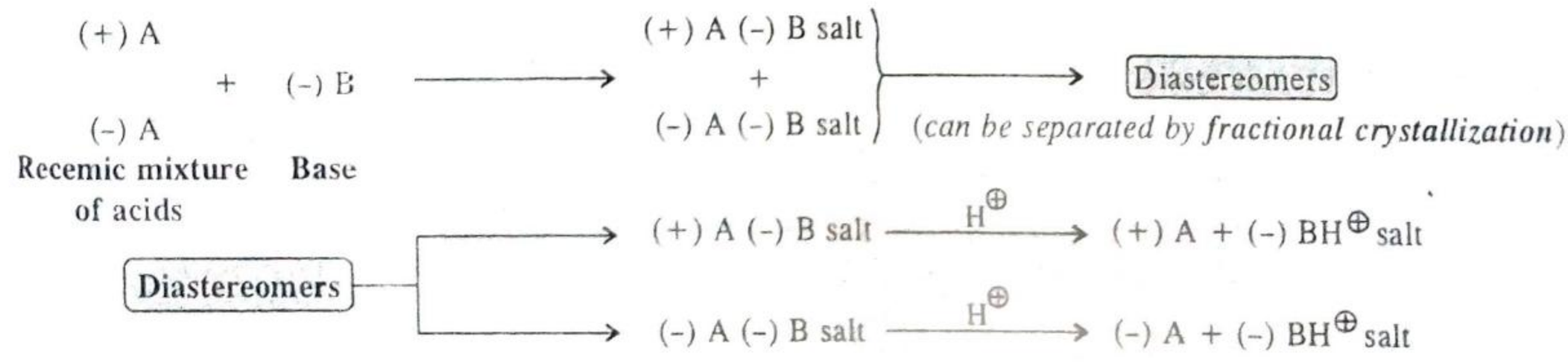
(a) **Biochemical method**. When certain micro-organisms are allowed to grow in racemic compound they prefer to take up one of the enantiomers. For example, when ***penicillium glaucum***, is added to racemic tartaric acid, it consumes only (+)-tartaric acid for its growth, leaving (–)-tartaric acid unused. Thus, (–) tartaric acid can be isolated in a *pure state*.

Limitations. *(i)* It leads to the **destruction** of **one** of the enantiomers. *(ii)* The recovery of the enantiomer is often very laborious. *(iii)* It is sometimes difficult to find a specific microorganism for racemic product.

(b) **Mechanical separation**. Sometimes, a racemic modification crystallizes out from a solution to produce a well-defined mixture of crystals of the (+)- and (–)-forms. These crystals, being enantiomeric can be separated by "**hand-picking**" or **forceps** with the help of a lens. Pasteur, discovered enantiomerism through such a resolution of racemic sodium ammonium tartrate.

Limitations. This method is also **laborious** and **limited** to only those cases in which the identification of two enantiomeric forms of crystals is possible by such means.

(c) **Chemical method (via diastereomers)**. The underlying principle of this method is that *the racemic modification is converted by an optically active reagent into a mixture of diastereomers which can then be separated*. Suppose the racemic substance under examination is an acid ***A***, consisting of an equimolecular mixture of (+)A and (–)A. It is made to react with an **optically active** base, say (–)B. Two salts namely (+)*A* (–)*B* and (–)*A* (–)*B* will be formed. These salts, being **diastereomers** will differ in physical properties such as solubility. These salts (+)*A* (–)*B* and (–)*A* (–)*B* can, be separated from one another by **fractional crystallization** and can be converted into (+)*A* and (–)*A* acids on treatment with strong mineral acids*. For example, (±)-**tartaric acid** on treatment with the optically active base, (–)-**cinchonidine**** forms (+)*acid* (–)*cinchonidine* and (–)*acid* (–)*cinchonidine* salts. The **two** salts can be separated from one another by **fractional crystallization**. The (–)acid (–)cinchonidine salts, being less soluble, separates out first. These salts can be reconverted into the corresponding (+)and (–)acids by treatment with dilute sulphuric acid. A **general scheme** of separation is outlined below:



*The optical purity of these enantiomeric acids will, of course, depend on the thoroughness, with which the mixture of diastereomeric salts are separated in the earlier step.

**It is an alkaloid (a nitrogenous heterocyclic base) of the cinchona bark. It is structurally related to *quinine*, the well-known antimalarial drug. These alkaloids are generally produced in plants in only one of the two possible enantiomeric forms.

Similarly, a (±)- **base** can be **resolved** by treacting it with an optically active acid, say (+)- tartaric acid

(+)-Base
+ (+)-Acid ⟶ (+)-Base (+)Acid, (−)-Base (+)Acid → **Diastereomers**
(−)-Base

(can be separated and recovered by treatment with **strong alkali***)*

These diastereomers are separated from one another by **fractional crystallization**. These salts can be reconverted into the corresponding (+) and (−) bases by treatment with strong base

(+)-Base (+)-Acid salt $\xrightarrow{\text{Base (B)}}$ (+) Base + Acid-B salt

(−)-Base (+)-Acid salt $\xrightarrow{\text{Base (B)}}$ (−) Base + Acid-B salt

Although this method has been **mainly used for the resolution of racemic acids** and **bases** that can form diastereoisomeric salts, it can be applied in principle to the resolution of racemic compounds belonging to other classes. Of course, the underlying chemistry in such cases will be different from that of salt formation just described above.

Resolution provides the most important method for the preparation of optically active compounds in the the laboratory. Of course, many optically active compounds, including some of the **reagents used** in the chemical method **for resolution** of racemic modifications, are obtained from **natural sources** [*e.g.*, (−)-malic acid *ex.* fruit juices, (−)-**quinine** *ex.* bark of the cinchona tree, (+)-lactic acid *ex* muscles, etc.].

***(d)* Selective adsorption in chromatographic column**. In this method, resolution of the racemate is achieved by passing its solution over a column of finely powdered starch as adsorbent. The surface of the adsorbent selectively absorbs one enantiomer and the solution comes out first if container is richer in one enatiomer. For example, (±) mandelic acid is separated by using **starch** as an optically active adsorbent in chromatographic column. Turner (1942), resolved the diastereomer of (−)menthyl(±)mendelate on alumina adsorbent.

***(e)* Kinetic method.** This is based on the different rate of reaction of enantiomers with an optically active compound. For example, (−) menthol reacts faster with (+) mandelic acid than (−) enantiomer. If the reaction is stopped before completion, on hydrolysis (−) menthyl (+) mandelate will dominate.

***(f)* Crystallization by inoculation (seeding).** In this technique, a supersaturated solution of the racemic mixture is inoculated with a crystal of one of the enantiomers or an isomorphous crystal of another chiral compound. For example, saturated solution of (±) sodium ammonium tartarate is **seeded** with the crystal of one enantiomer or a crystal of (−) asparagine, (−) sodium ammonium tartarate crystallizes out first and second isomer afterwards. The seed crystals is called **entrainer** and this method is also called entrainment. This method can be applied for the separation of D and L forms of amino acids

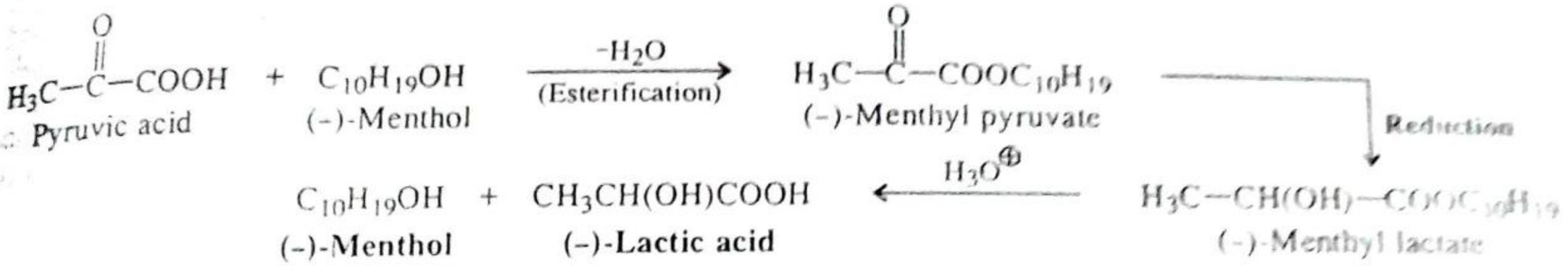
6.13. ASYMMETRIC (STEREOGENIC CENTRE) SYNTHESIS

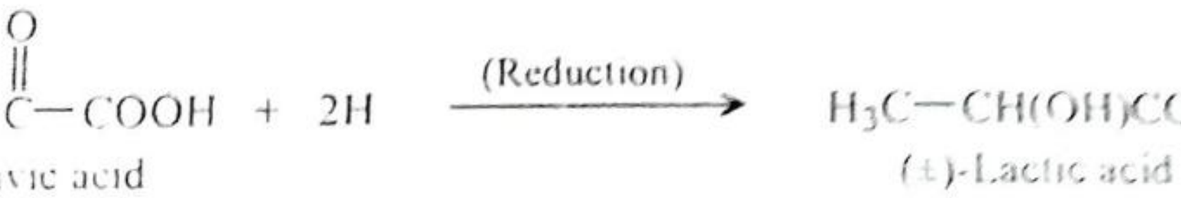
We have seen earlier that when propionic acid (**achiral** compound) is brominated, the racemic modification of a bromopropionic acid (a chiral compound) is obtained. In fact, this is a general phenomenon and ***synthesis of chiral compounds from achiral reagents*** *always gives the* ***racemic modifications***. Let us now consider the synthesis of **chiral** compounds from **achiral** compounds under the influence of some optically active substance.

For example, direct **reduction** of pyruvic acid gives the **racemic** modification of lactic acid, as expected. However, when pyruvic acid, **pre-esterified** with an optically active alcohol [say, **(−)-menthol***]. is reduced and the resulting alcohol hydrolysed, we get, **mainly (−)-lactic acid**. This asymmetric synthesis

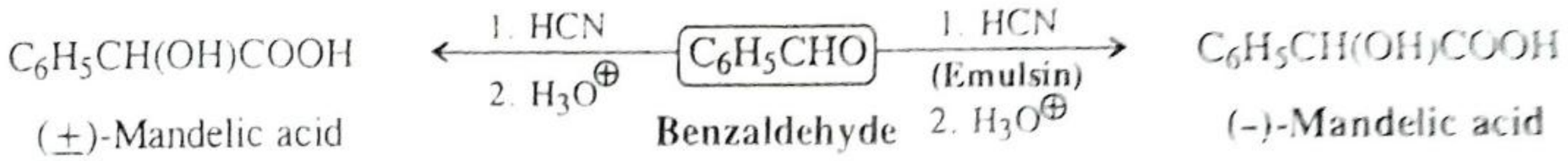
*(−)-Menthol is a high molecular weight monohydric alcohol ($C_{10}H_{19}OH$) occurring in peppermint oil.

is induced by (–) menthol (asymmetric) to get pure (–) lactic acid is also referred as **asymmetric induction**.





Similarly, when benzaldehyde is treated with hydrogen cyanide and the resulting cyanohydrin is hydrolysed, the product is the *racemic* modification of mandelic acid. However, if the same synthesis is carried out in the **presence of an optically active enzyme *emulsin***, the main product is (–)-mandelic acid.



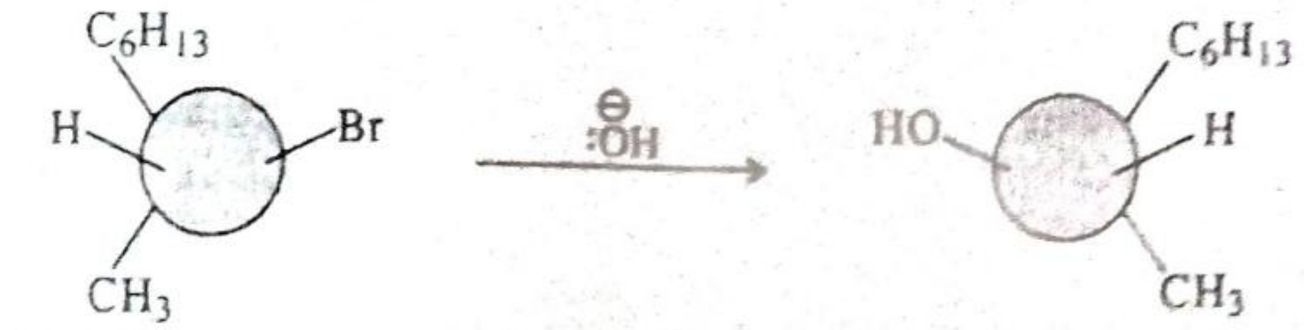
Thus, we find that we have achieved the laboratory synthesis of optically active dissymmetric (**chiral**) compounds from optically inactive non-dissymmetric (achiral) compounds under the influence of suitable optically active substances (these, of course, get removed subsequently). Possibly, the optically active substances like (–) **menthol** and **emulsin** used in the foregoing reaction sequences control the geometry of the main reactants in such a way that specific enantiomers are the main products in subsequent steps. It is necessary to stress here that the preferential formation of **laevorotatory** products in both the reaction sequences given above is only incidental. Under suitable conditions, **dextrorotatory** products could also form. The synthesis of the type described above is known as **asymmetric synthesis** as it leads to the formation of **asymmetric** or **dissymmetric** compound showing optical activity.

Thus, **asymmetric synthesis is the synthesis of an optically active chiral compound from non-dissymmetric (achiral) molecule, under the influence of some optically active substance**.

It is interesting to note here that most of the dissymmetric (**chiral**) compounds found in nature (*e.g.*, amino acids, carbohydrates, proteins, alkaloids, etc.) exist in optically active forms. This is possibly due to the fact that they are synthesized under the influence of other optically active species like enzymes. In other words, the **biological syntheses** are mostly **asymmetric** syntheses, induced by **biocatalysts**.

6.14. WALDEN INVERSION

If an atom or a group of atoms directly attached to an asymmetric carbon atom is replaced by another atom or a group of atoms, the configuration of the product is sometimes found to be different from that of the parent compound. This phenomenon, which involves the ***inversion*** of configuration during a reaction, is called **Walden inversion,** after the name of **Walden,** the discoverer of this phenomenon. Occasionally, Walden inversion is also known as **Optical inversion**. For example, S_N2 substitution of (–)-2-bromo-octane with alkali.



It may be stressed here that the inversion of configuration may or may not lead to a change in the direction of rotation. Change, if any, is incidental only.

6.15. RETENTION AND RACEMISATION

We have seen above how Walden inversion takes place, when an alkyl halide containing an asymmetric/chiral carbon reacts with a nucleophile (say, a base) by the back side attack. Consider now the reaction of a chiral alkyl halide [say, (*S*)-3-Bromo-2, 3-dimethylpentane] (I) with a mild base (say, solvent ethanol). We shall learn in due course that the reaction is a 2-step reaction involving the intermediate formation of a **carbocation (IA)**, as shown below in Fig. 6.11.

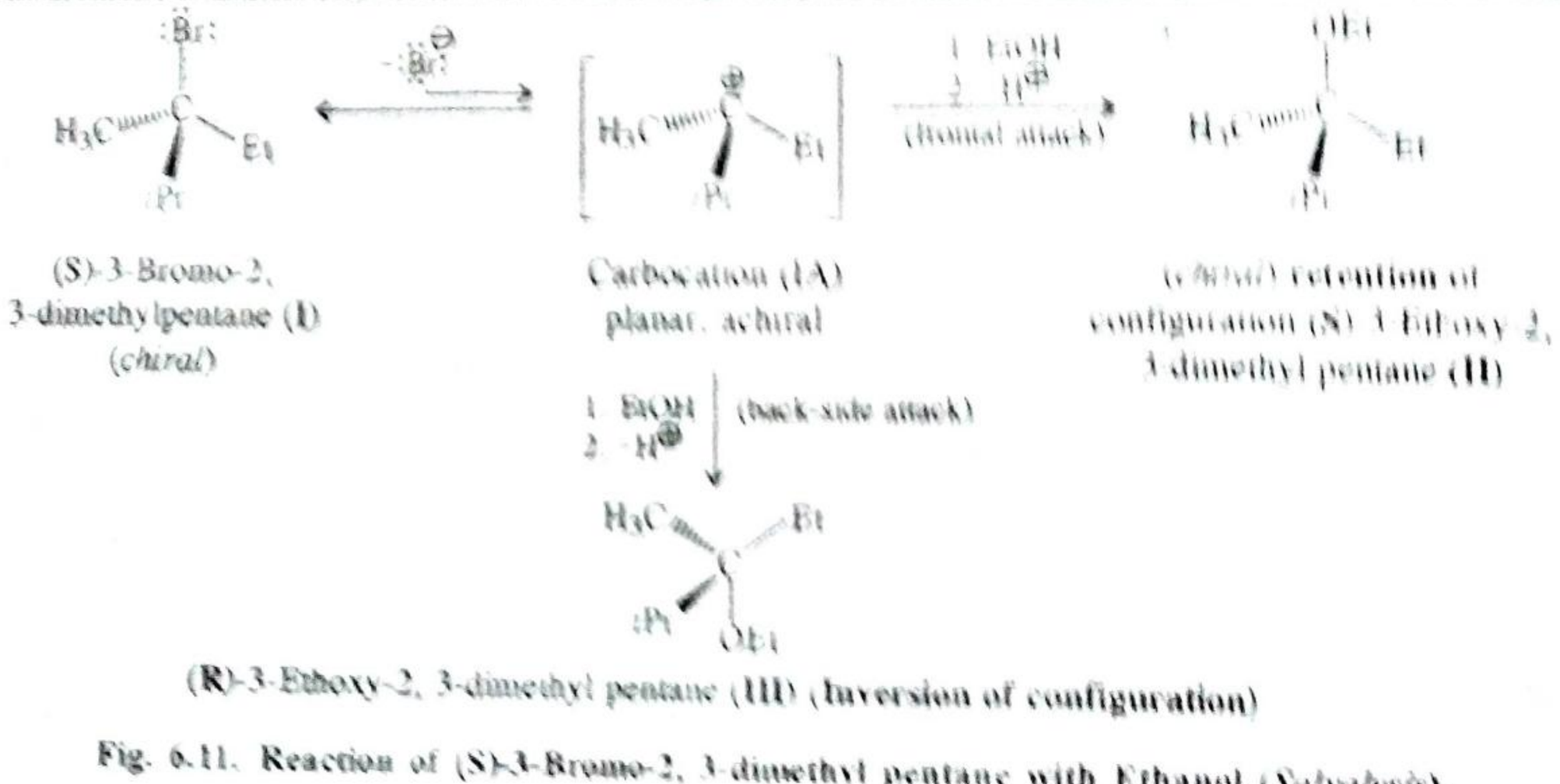


Fig. 6.11. Reaction of (S)-3-Bromo-2, 3-dimethyl pentane with Ethanol (*Solvolysis*).

The carbocation (IA), which is planar and achiral, is susceptible to attack from both faces. If the attack takes place from the **front side**, the chiral product has the same configuration (S) as I, *i.e.*, there is **retention of configuration** in going from I to II. However, when ethanol attacks IA from the **backside** or rear side, the product is III with configuration (R) opposite to that of I, *i.e.*, there is **inversion** of **configuration** in going from I to III. Apparently, II and III are *enantiomers*. If, both II and III are in equal amounts, the product would naturally racemic.

If II and III are in unequal amounts, **the product will be** *optically less pure than the starting material I*. A process that gives both enantiomers of the product in equal amounts during the reaction of the chiral starting material is called **racemisation**. When the enantiomers of the product are, however, in unequal amounts, the overall process is known **as partial racemisation**. The sign of rotation of the partially racemised product would, of course, depend on which route dominates back-side attack or the front-side attack. Thus, the **retention of configuration** *is the formation of the product (in a stereochemical reaction) with the* ***same configuration*** *as that of the reactant.* **Racemisation (complete or partial)**, on the other hand, *is the formation of the product (in a stereochemical reaction) that is a mixture of its two enantiomers in equal or unequal amounts.* Of course, **the complete racemisation occurs** only when the **enantiomers are formed in equal amounts.** Otherwise, it will be partial racemisation.