

Isomerism

In the study of organic chemistry we come across many cases when two or more compounds consist of equal number of like atoms. These compounds have the same molecular formula but differ from each other in physical or chemical properties, and are called **Isomers** and the phenomenon is called **Isomerism**. Since isomers have the same molecular formula, the difference in their properties must be due to different modes of combination or arrangement of atoms within the molecule. There are two main types of isomerism :

- (1) Constitutional Isomerism
- (2) Stereoisomerism

Constitutional Isomerism. When the isomerism is due to difference in the arrangement of atoms within the molecule, without any reference to space, the phenomenon is called *Constitutional Isomerism*. In other words, **Constitutional isomers are compounds that have the same molecular formula but different structural formulas.** Constitutional isomerism is of five types :

- (a) Chain Isomerism
- (b) Position Isomerism
- (c) Functional Isomerism
- (d) Metamerism
- (e) Tautomerism

Stereoisomerism. When isomerism is caused by the different arrangements of atoms or groups in space, the phenomenon is called *Stereoisomerism*. **The stereoisomers have the same structural formulas but differ in arrangement of atoms in space.** In other words, stereoisomerism is exhibited by such compounds which have the same structural formula but differ in *configuration*. (The term *configuration* refers to the three-dimensional arrangement of atoms that characterizes a particular compound). Stereoisomerism is of two types :

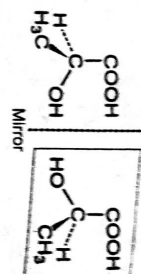
- (a) Geometrical or Cis-Trans Isomerism
- (b) Optical Isomerism

ISOMERS
(Same molecular formula)

Stereoisomers
(Same connectivity, different arrangement in space)

Diastereomers
(Nonsuperimposable, non-mirror images)

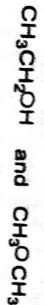
Enantiomers
(Nonsuperimposable, mirror images)



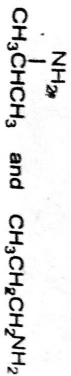
Different carbon skeletons :



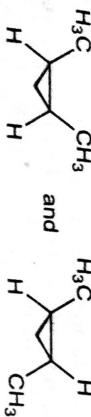
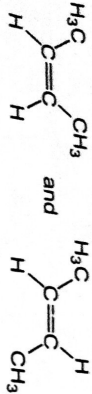
Different functional groups :



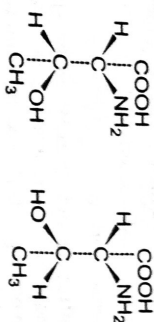
Different position of functional groups :



Cis-trans Diastereomers
(Double bond or Ring)



Chiral Diastereomers
(Multiple Chiral centers)



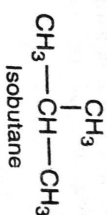
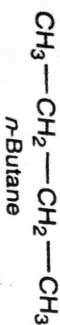
CONSTITUTIONAL ISOMERISM (STRUCTURAL ISOMERISM)

In constitutional isomerism the isomers have the same molecular formula but differ in constitutional formula, that is, in the order in which the different atoms are linked in the molecule. Constitutional isomerism is of five types :

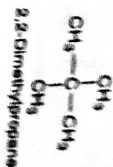
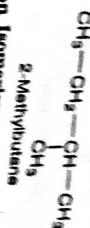
(1) Chain Isomerism

Chain isomers (also called skeletal isomers) have the same molecular formula but differ in the order in which the carbon atoms are bonded to each other.

Example 1. *n*-Butane and Isobutane



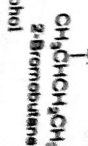
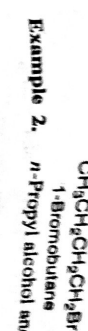
Example 2. 2-Methylbutane and 2,2-Dimethylpropane



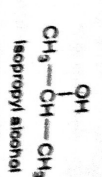
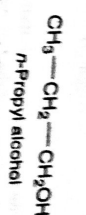
(2) Position Isomerism

Position isomers have the same molecular formula but differ in the position of a functional group on the carbon chain.

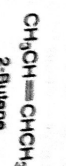
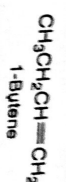
Example 1. 1-Bromobutane and 2-Bromobutane



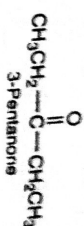
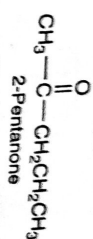
Example 2. *n*-Propyl alcohol and Isopropyl alcohol



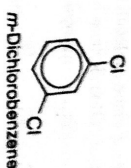
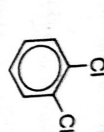
Example 3. 1-Butene and 2-Butene



Example 4. 2-Pentanone and 3-Pentanone



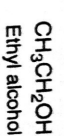
Example 5. *o*-Dichlorobenzene and *m*-Dichlorobenzene



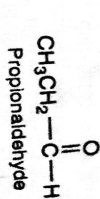
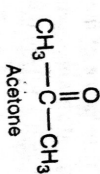
(3) Functional Isomerism

Functional isomers have the same molecular formula but different functional groups.

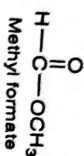
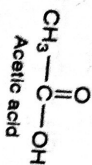
Example 1. Ethyl alcohol and Dimethyl ether



Example 2. Acetone and Propionaldehyde



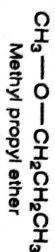
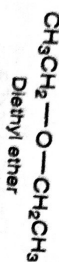
Example 3. Acetic acid and Methyl formate



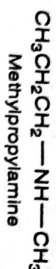
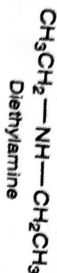
(4) **Metamerism**

This type of isomerism is due to the unequal distribution of carbon atoms on either side of the functional group. Members belong to the same homologous series.

Example 1. Diethyl ether and Methyl propyl ether



Example 2. Diethylamine and Methylpropylamine



(5) **Tautomerism**

It is a special type of functional isomerism in which the isomers are in dynamic equilibrium with each other. For example, ethyl acetate is an equilibrium mixture of the following two forms. At room temperature, the mixture contains 93% of keto-form plus 6% of the enol-form.



Points to Remember

1. Constitutional isomers are also called structural isomers.
2. Chain isomers have the same molecular formula but different arrangement of carbon atoms. Chain isomers are also called skeletal isomers.
3. Position isomers have the same molecular formula but differ in the position of a substituent or functional group.
4. Tautomers are interconvertible constitutional isomers that exist in equilibrium with each other.

GEOMETRICAL ISOMERISM

Geometrical isomerism (also called *cis-trans* isomerism) results from a restriction in rotation about double bonds, or about single bonds in cyclic compounds.

(1) **Geometrical Isomerism in Alkenes**

The carbon atoms of the carbon-carbon double bond are sp^2 hybridized. The carbon-carbon double bond consists of a σ bond and a π bond. The σ bond is formed by the overlap of sp^2 hybrid orbitals. The π bond is formed by the overlap of p orbitals. The presence of the π bond locks the molecule in one position. The two carbon atoms of the $\text{C}=\text{C}$ bond and the four atoms that are attached to them lie in one plane and their positions in space are fixed. Rotation around the $\text{C}=\text{C}$ bond is not possible because rotation would break the π bond (Fig. 7.1).

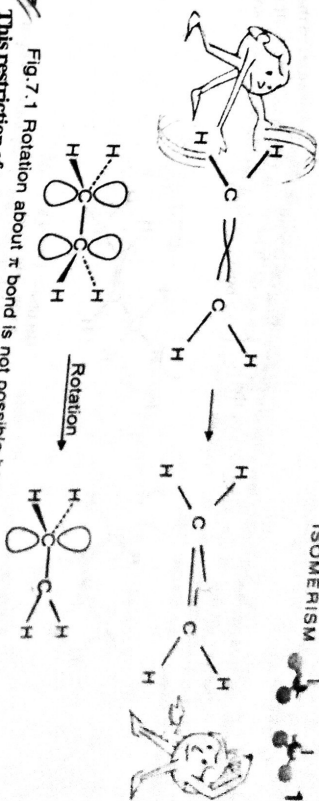
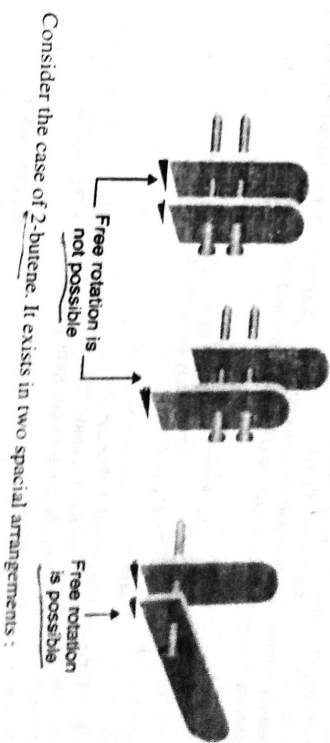
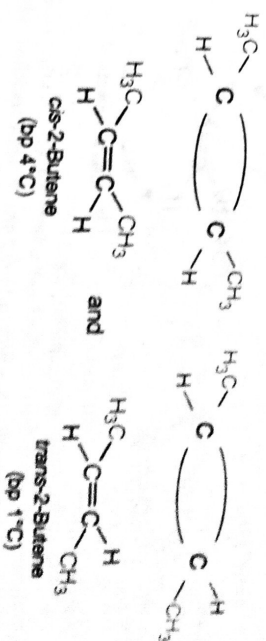


Fig. 7.1 Rotation about π bond is not possible because it would break the π bond. **Isomerism in alkenes.** A popular analogy for this situation is based upon two boards and two nails. Driving one nail through two boards will not prevent free rotation of the two boards. But once a second nail is used, the boards cannot be freely rotated.

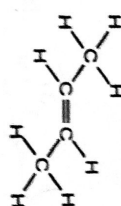
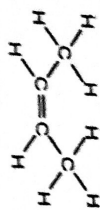


Consider the case of 2-butene. It exists in two spatial arrangements:



These two compounds are referred to as geometrical isomers and are distinguished from each other by the terms *cis* and *trans*. The *cis* isomer is one in which two similar groups are on the same side of the double bond. The *trans* isomer is that in which two similar groups are on the opposite sides of the double bond. Consequently, this type of isomerism is often called *cis-trans* isomerism. Geometrical isomers are stereoisomers, because they have the same structural formula but different spatial arrangement of atoms.

The *trans* isomers are more stable than the corresponding *cis* isomers. This is because, in the *cis* isomer, the bulky groups are on the same side of the double bond. The steric strain of the groups makes the *cis* isomer less stable than the *trans* isomer in which the bulky groups are far apart (they are on the opposite sides of the double bond).



Steric strain in *cis*-2-butene

No steric strain in *trans*-2-butene

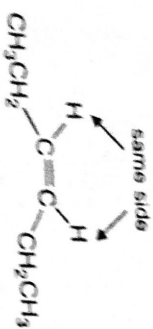
The geometrical isomers have different physical and chemical properties. They can be separated by conventional techniques like fractional distillation, gas chromatography etc.

All alkenes do not show geometrical isomerism. Geometrical isomerism is possible only when each double bonded carbon atom is attached to two different atoms or groups. The following examples illustrate this condition for the existence of geometrical isomers.

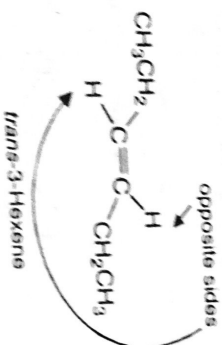
Example 1. Consider the case of Propene ($\text{CH}_3\text{CH}=\text{CH}_2$). This is because one of the double bonded carbons has two identical groups (H atoms) attached to it.



Example 2. Consider the case of 3-Hexene ($\text{CH}_3\text{CH}_2\text{CH}=\text{CHCH}_2\text{CH}_3$). This is because geometrical isomers are possible for 3-hexene ($\text{CH}_3\text{CH}_2\text{CH}=\text{CHCH}_2\text{CH}_3$ and H). The *cis* and *trans* isomers of 3-hexene are shown below:

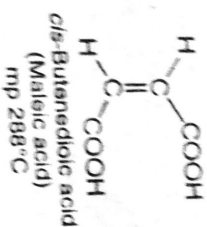
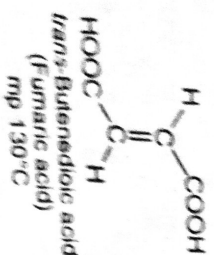


cis-3-Hexene



trans-3-Hexene

Example 3. Consider the case of Butenedioic acid ($\text{HOOC}-\text{CH}=\text{CH}-\text{COOH}$). This is because each double bonded carbon atom has two different groups attached to it (H and COOH).

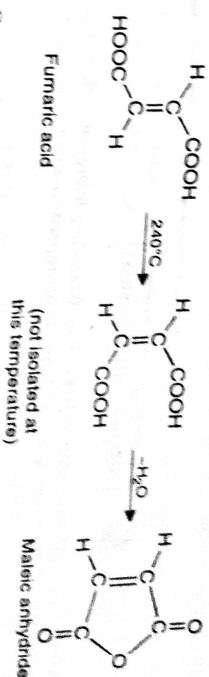
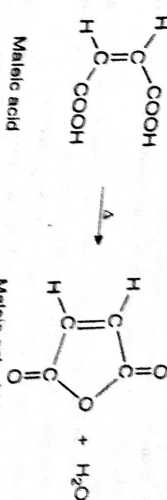


These isomers differ in physical properties such as melting point, dipole moment, and acidities. The *trans*-isomer has no dipole, since it is symmetrical, unlike the *cis*-isomer. The *cis*-isomer is stronger acid than the *trans*-isomer. Even chemical properties differ in the butenedioic acids. For example, the *cis*-acid undergoes dehydration at 100°C.

ISOMERISM

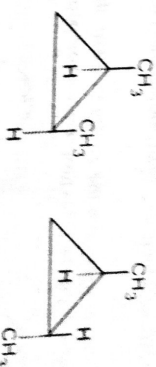
127

However, the *trans*-acid does not form an anhydride until heated to 240°C. At that temperature there is sufficient thermal energy to break the double bond, so that the *cis*-acid and the anhydride are formed in succession.

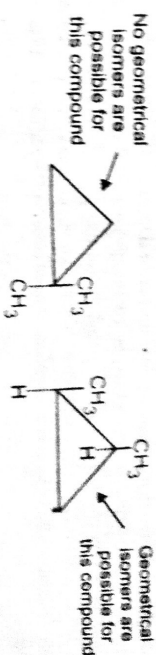


(2) Geometrical Isomerism in Cyclic Compounds

Geometrical isomerism is also possible in cyclic compounds. There can be no rotation about carbon-carbon single bonds forming a ring because rotation would break the bonds and break the ring. For example, 1,1-dimethylcyclopropane exists in two isomeric forms.



In *cis*-1,2-dimethylcyclopropane, the two methyl groups are on the same side of the ring. In *trans*-1,2-dimethylcyclopropane, they are on opposite sides. A requirement for geometrical isomerism in cyclic compounds is that there must be at least two other groups besides hydrogens on the ring and these must be on different ring carbon atoms. For example, no geometrical isomers are possible for 1,1-dimethylcyclopropane.



Geometrical isomers are possible for this compound

Points to Remember

1. Stereoisomers have the same structural formulas but differ in arrangement of atoms in space.
2. Geometrical isomerism is a type of stereoisomerism. It is also called *cis-trans* isomerism.
3. Restriction of rotation around carbon-carbon double bonds is responsible for the geometrical isomerism in alkenes.
4. *Cis* isomer is one in which two similar groups are on the same side of the double bond.
5. *Trans* isomer is one in which two similar groups are on the opposite sides of the double bond.
6. *Trans* isomers are more stable than the corresponding *cis* isomers.
7. All alkenes do not show geometrical isomerism. Geometrical isomerism is possible only when each double bonded carbon atom is attached to two different atoms or groups.
8. Geometrical isomerism is also possible in cyclic compounds.
9. A requirement for geometrical isomerism in cyclic compounds is that there must be at least two other groups besides hydrogens on the ring and these must be on different ring carbon atoms.

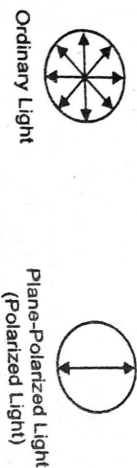


OPTICAL ISOMERISM

Optical isomerism is a type of *stereoisomerism*. The outstanding feature of optical isomers is that they have the ability to rotate plane-polarized light. This property is often referred to as optical activity and requires a brief discussion.

OPTICAL ACTIVITY: PLANE-POLARIZED LIGHT

Light from ordinary electric lamp is composed of waves vibrating in many different planes. When it is passed through Nicol prism (made of calcite, CaCO_3) or polaroid lens, light is found to vibrate in only one plane, and is said to be plane-polarized or simply polarized. The diagrams illustrate the vibrations of ordinary and polarized light from a beam propagated perpendicularly to the plane of paper.



Solutions of some organic compounds have the ability to rotate the plane of polarized light. These compounds are said to be optically active. This property of a compound is called optical activity.

Optical activity in a compound is detected and measured by means of a polarimeter. When a solution of a known concentration of an optically active material is placed in the polarimeter, the beam of polarized light is rotated through a certain number of degrees, either to the right (*clockwise*) or to the left (*anti-clockwise*). The compound which rotates the plane of polarized light to the right is said to be dextrorotatory. It is indicated by the sign (+). The compound which rotates (clockwise) is said to be levorotatory. It is indicated by the sign (-). The magnitude of the rotation, in degrees, is referred to as observed rotation, α . Fig. 7.2 shows the parts of a polarimeter.

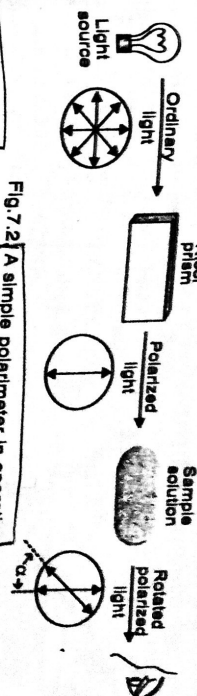


Fig. 7.2 A simple polarimeter in operation

SPECIFIC ROTATION

Optically active compounds rotate the plane of polarized light. The degree of rotation depends upon the number of molecules of the compound encountered by light along its path. It is, therefore, necessary to introduce some standard by which the rotating powers of different compounds may be compared.

Specific rotation is defined as the rotation produced by a solution of length 10 centimeters and unit concentration (1 g/ml) for the given wavelength of light at the given temperature. Consider a system in which the plane of polarized light is rotated through α degrees at a temperature

of $t^\circ\text{C}$ and using the sodium D-line as the source. The specific rotation $[\alpha]_D^t$ is given by $[\alpha]_D^t = \frac{100\alpha}{lc}$ where α is the observed rotation; l is the length of the tube in decimeters; and c is the number of grams per 100 ml of solution. The specific rotation varies with both the wavelength of light and the temperature.

Problem. A 1.20 g sample of cocaine, $[\alpha]_D = -16^\circ$, was dissolved in 7.50 ml of chloroform and placed in a sample tube having a path length of 5.0 cm. What was the observed rotation? Is cocaine dextrorotatory or levorotatory?

Solution. Use the following relationship:

$$[\alpha]_D^t = \frac{\alpha}{lc}$$

Where, α = observed rotation in degrees

l = length of tube (dm) = path length

c = concentration of sample (g/ml)

The given values are:

$$[\alpha]_D^t = -16^\circ$$

$$\alpha = ?$$

$$l = 5.0 \text{ cm} = 0.50 \text{ dm (1 dm = 10 cm)}$$

$$c = 1.20 \text{ g/7.50 ml} = 0.160 \text{ g/ml}$$

$$\text{Thus, } -16^\circ = \frac{\alpha}{0.50 \times 0.160}$$

$$\alpha = -16^\circ \times 0.50 \times 0.160$$

$$= -1.3^\circ$$

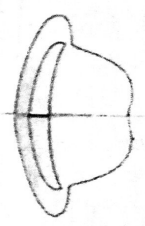
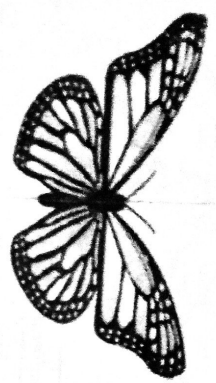
The observed rotation is -1.3° .

Cocaine is levorotatory.

PLANE OF SYMMETRY

A plane which divides an object into two symmetrical halves, is said to be plane of symmetry. For example, a person or a hat has a plane of symmetry (Fig. 7.3). A person's hand or gloves lack a plane of symmetry.

An object lacking a plane of symmetry is called **Chiral** (pronounced as *Ki-ral*) or **Dissymmetric**. A symmetric object is referred to as **Achiral**.



Plane of symmetry

Fig. 7.3. Planes of symmetry.

A chiral object cannot be superimposed on its mirror image. A left hand, for example, does not possess a plane of symmetry, and its mirror image is not another left hand but a right hand (Fig. 7.4). The two are not identical, because they cannot be superimposed. If we were to lay one hand on top of the other, the fingers and the thumbs would clash.

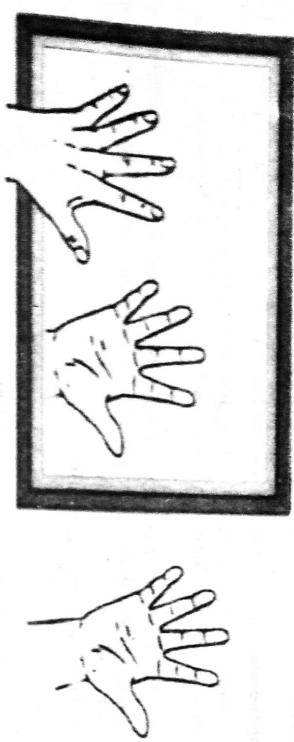
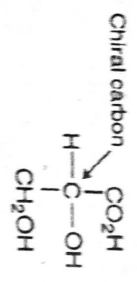
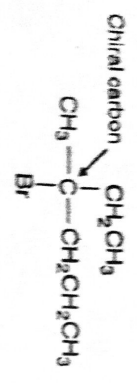


Fig. 7.4. The mirror image relationship of the left and right hands. Notice that right hand is the mirror image of the left hand.

CHIRAL (OR ASYMMETRIC) CARBON ATOM

A carbon atom which is bonded to four different groups is called a **Chiral** (or **Asymmetric**) **Carbon Atom**. For example,



The term **chiral** (Greek *handedness*; pronounced *Kairal*) carbon atom means that a carbon atom is bonded to four different groups and that a molecule of this type lacks a plane of symmetry. Such a molecule is also called **Asymmetric** or **Dissymmetric**.

OPTICAL ISOMERISM

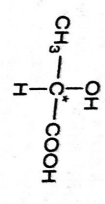
A substance which has the ability to rotate the plane of polarized light is said to be **optically active** and exhibits **optical isomerism**. Optical isomers are isomers that are identical in all properties except for their effect on plane of polarized light.

ISOMERISM

The isomer which rotates the plane of polarized light to the right (clockwise direction) is known as **Dextrorotatory Isomer** or **(+)-isomer**. The isomer which rotates the plane of polarized light to the left (anticlockwise direction) is known as the **Levorotatory Isomer** or **(-)-isomer**. The optical rotatory powers of two isomers are equal in magnitude but opposite in sign. An equimolar mixture of the two optical isomers will not rotate the plane of polarized light at all and is said to be **Racemic Mixture**. They have the same physical properties: melting point, boiling point, density, etc.

OPTICAL ISOMERISM OF LACTIC ACID

Lactic acid (2-Hydroxypropanoic acid) is an example of a compound which shows optical isomerism. It contains one chiral carbon atom.



Lactic acid. The chiral carbon is shown by an asterisk.

Two three dimensional structures are possible for Lactic acid (Fig. 7.5). These structures are not identical because they cannot be superimposed on each other. One is the mirror image of the other. Such nonsuperimposable mirror image forms are optical isomers and are called **enantiomers**. Thus, three forms of lactic acid are known. Two are optically active and the third is optically inactive.

1. **(+)-Lactic Acid** It rotates the plane of polarized light to the right (clockwise direction) and is called **dextrorotatory**.
2. **(-)-Lactic Acid** It rotates the plane of polarized light to the left (anticlockwise direction) and is called **levorotatory**. (-)-Lactic acid is the mirror image of (+)-lactic acid and vice versa.
3. **(±)-Lactic Acid** It does not rotate the plane of polarized light. That is, it is optically inactive. It is an equimolar mixture of (+)- and (-)-forms (racemic mixture).

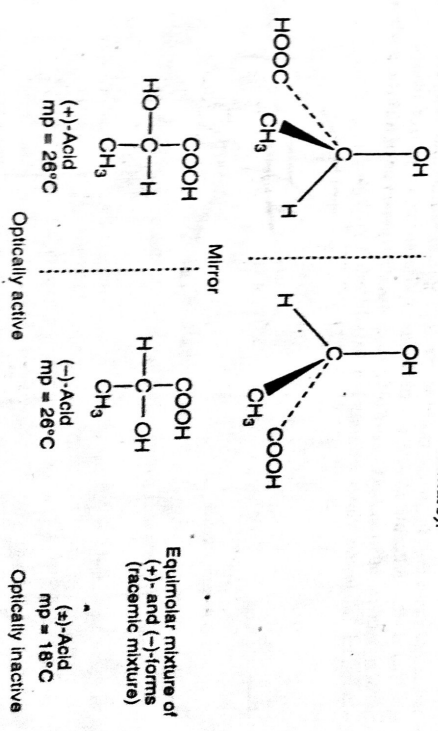


Fig. 7.5. Isomers of Lactic acid. In the upper line two three-dimensional structures are shown. In the lower line a commonly used Fischer projection is given. The vertical lines represent bonds going away from the observer/reader and horizontal lines represent bonds coming toward the observer.

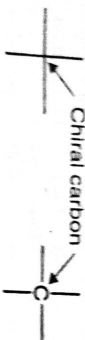
FISCHER PROJECTIONS

Fischer projections provide an easy way to draw three-dimensional molecules on paper. All atoms are projected onto one plane. The Fischer projection of one of the enantiomers of lactic acid is shown below:



Fischer projection of (+)-Lactic acid.

- The Fischer rules for showing the arrangement around a chiral carbon are as follows: the top. Or, put the carbon number 1 (as defined by nomenclature rules) at the top.
- Represent the chiral carbon(s) at the intersection of crossed lines. Some teachers like to show the chiral carbon also.



- Groups attached to the vertical lines are understood to be going back behind the plane of the paper. That is, the vertical lines represent bonds going away from the observer. The chiral carbon is in the paper plane.
- Groups attached to the horizontal lines are understood to be coming forward out of the paper plane. That is, the horizontal lines represent bonds coming toward the observer.

CONDITION FOR OPTICAL ISOMERISM

The necessary condition for a molecule to exhibit optical isomerism is that it should be *dissymmetric*. That is, the molecule should not be superimposable on its mirror image. In simple molecules, the dissymmetry (also called **Chirality**) results from the presence of a chiral carbon atom. Recall that a chiral carbon is one which is bonded to four different groups.

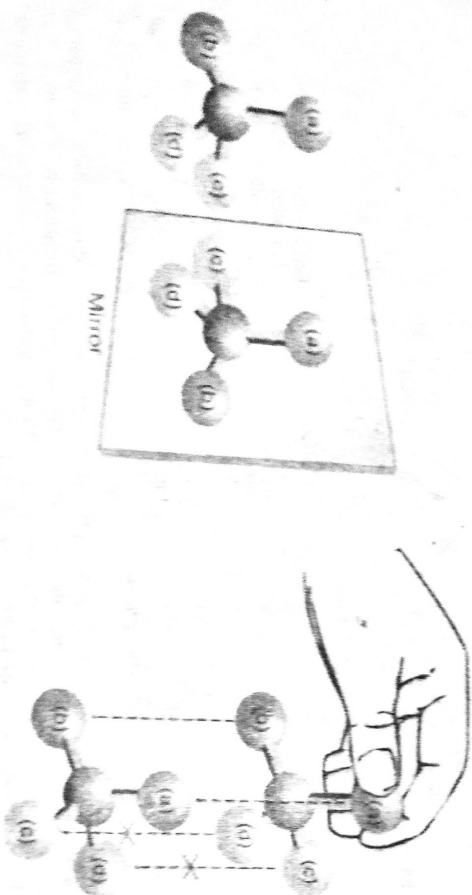


Fig. 7.6. The two forms (I and II) of C_{chiral} are nonsuperimposable.

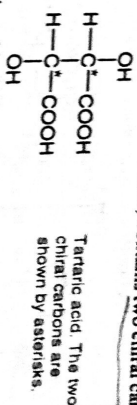
Consider a chiral molecule C_{chiral} . Fig. 7.6 shows two three dimensional models for this molecule. The form (II) is the mirror image of (I) and the two cannot be superimposed. If you try to superimpose the four groups attached to a chiral carbon atom in form (I) and form (II), only two of the four groups coincide, while the other two are in conflict. This shows that the two forms represent different compounds.

The nonsuperimposable mirror image forms of a chiral molecule are called **Enantiomers** (Greek, *enantio* = opposite). They represent two optical isomers: (+) and (-). Their opposite rotatory powers are due to the opposite arrangements of groups around the asymmetric carbon atom.

It is true that most of the compounds which contain chiral carbon atoms show optical isomerism. But it is not always so. There are some compounds (such as *meso*-tartaric acid) which have asymmetric carbons but being *achiral*, do not show optical isomerism. On the other hand, there are certain compounds (such as substituted alkenes and biphenyls) which have no chiral carbons but being *dissymmetric*, show optical isomerism.

OPTICAL ISOMERISM OF TARTARIC ACID

Tartaric acid (2,3-Dihydroxybutanedioic acid) contains two chiral carbon atoms.



Four forms of tartaric acid are known (Fig. 7.7). Two of them are optically active and two are optically inactive. The optically active forms are related to each other as an object to its mirror image. That is, they are *enantiomers*.

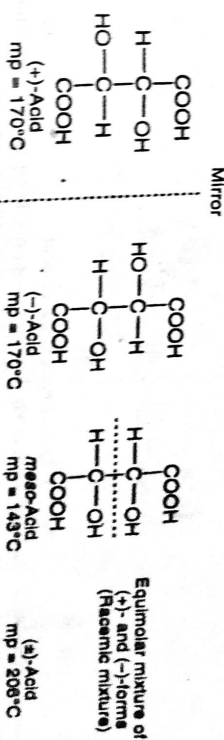


Fig. 7.7. Isomers of tartaric acid.

- (+)-Tartaric Acid: It rotates the plane of polarized light to the right (clockwise direction) and is called dextrorotatory.
- (-)-Tartaric Acid. It rotates the plane of polarized light to the left (anticlockwise direction) and is called levorotatory. (-)-Tartaric acid is the mirror image of (+)-tartaric acid and *vice versa*.
- meso*-Tartaric Acid. It possesses a plane of symmetry and is consequently optically inactive. This optically inactive form is said to be *internally compensated* (Optical rotation of one asymmetric carbon is cancelled by that of the other).
- (±)-Tartaric Acid. It does not rotate the plane of polarized light. That is, it is optically inactive. It is an equimolar mixture of (+)- and (-)-forms (racemic mixture).

A molecule containing n chiral centres can give rise to a maximum of 2^n optical isomers, unless the compound has a *meso* form, in which case it is $2^n - 1$. For example, four optical isomers are possible for 2-bromo-2-butanol. It has two chiral carbon atoms but no plane of symmetry (Fig. 7.8).

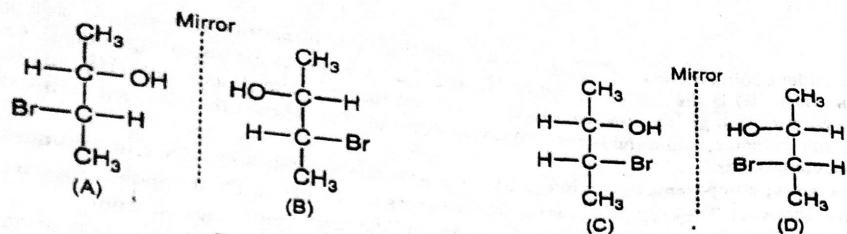


Fig. 7.8. Four isomers of 3-Bromo-2-butanol.

Optical isomers which are not enantiomers (mirror images) such as (A) and (C) or (B) and (D) of the above example, are known as **Diastereomers**.

PROPERTIES OF ENANTIOMERS

Optical isomers that are mirror images are called **Enantiomers**. These always exist as discrete pairs. For example, there are two optical isomers of lactic acid (Fig. 7.9). Notice that (A) is the mirror image of (B). They are a pair of enantiomers.

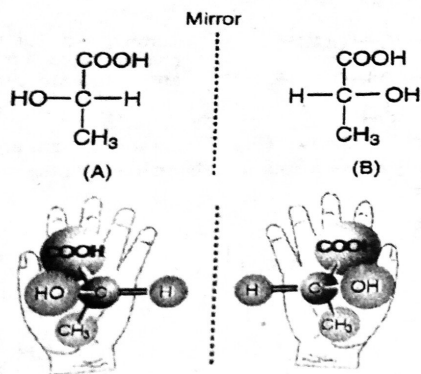


Fig. 7.9. Two isomers of Lactic acid.

Enantiomers are stable, isolable compounds that differ from one another in three-dimensional spatial arrangements. Enantiomers cannot be interconverted under ordinary conditions.

Enantiomers have identical properties in all respects except in their interaction with plane polarized light. Enantiomers have the same melting point, density, solubility, color, and reactivity toward acids and bases. They differ, however, in the direction in which they rotate the plane of polarized light. Both rotate the plane of polarized light to exactly the same extent (same angle) but one rotates the plane to the right (clockwise; called *dextrorotatory*), while the other rotates the plane to the left (anticlockwise; called *levorotatory*).

A mixture of equal amounts of two enantiomers is called a **Racemic Mixture**. Such a mixture is optically inactive (does not rotate the plane of polarized light) because the two components rotate the plane of polarized light equally in opposite directions and cancel one another.

PROPERTIES OF DIASTEREOMERS

In general, each chiral carbon atom in a molecule doubles the number of theoretically possible isomers. Hence, molecule with n chiral carbon atoms should have 2^n stereoisomers. Fig. 7.10 shows the four isomers of 3-bromo-2-butanol, which has two chiral carbon atoms.

Notice that (A) is the mirror image of (B); (C) is the mirror image of (D). Thus the four isomers are two pairs of *enantiomers*. Now compare (A) with (C). They are neither superimposable nor are they mirror images. They are called *diastereomers*. (A) and (D) are also diastereomers, as are (B) and (C), and (B) and (D). Stereoisomers that are not mirror images of each other are called **Diastereomers**.

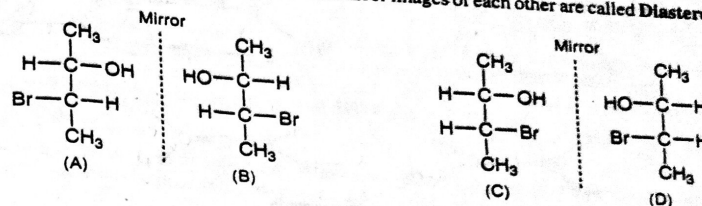


Fig. 7.10. Four isomers of 3-Bromo-2-butanol.

Diastereomers have different properties. Two diastereomers will have different melting points, boiling points, and solubilities. They will have different chemical reactivities toward most reagents.

PROPERTIES OF MESO COMPOUNDS

A compound with two or more chiral carbon atoms but also having a plane of symmetry (a mirror plane) is called the **Meso Compound**. Fig. 7.11 shows two meso compounds. These molecules have planes of symmetry dividing them midway between the two chiral carbons in each. Notice that one-half of the molecule is the mirror image of the other. Both molecules are optically inactive, even though each has two chiral centres. Neither will rotate the plane polarized light.

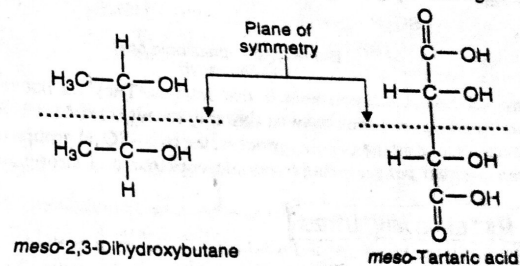


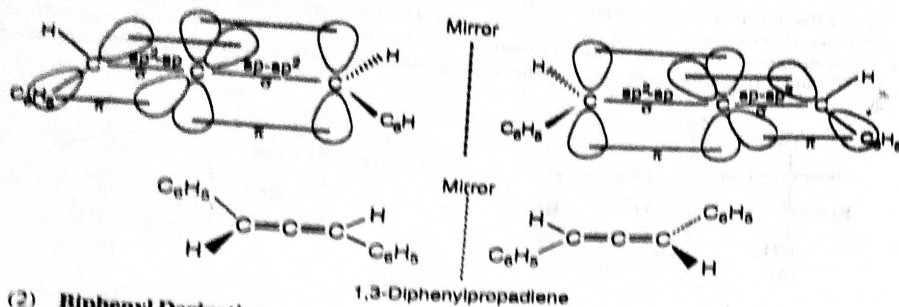
Fig. 7.11. Examples of meso compounds.

OPTICAL ACTIVITY WITHOUT CHIRAL CARBONS

Compounds containing a chiral carbon can exist in optically active forms. However, compounds which do not possess a chiral carbon atom can also exist in optically active forms provided that the molecule is dissymmetric. Example are:

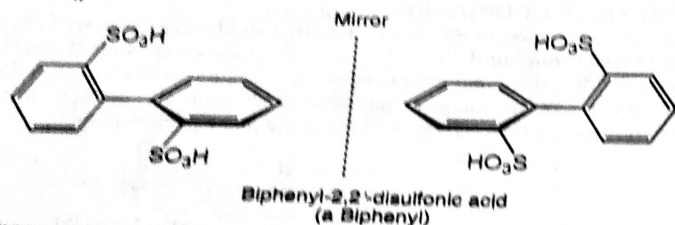
(1) Allene Derivatives

Some derivatives of allene ($\text{CH}_2=\text{C}=\text{CH}_2$) exhibit optical isomerism. Example is 1,3-diphenylpropadiene. In allenes, the central carbon is sp hybridized, and the terminal carbons are sp^2 hybridized. The central carbon forms two $sp-sp^2$ σ bonds. The central carbon also has two p orbitals which are mutually perpendicular. These form π bonds with the p orbitals on the other carbon atoms. As a result, the substituents at one end of the molecule are in a plane which is perpendicular to that of the substituents at the other end, so that the compound exists in two forms which are non-superimposable mirror images and are optically active.



(2) Biphenyl Derivatives

Substituted biphenyls show optical isomerism when substituents in the 2-positions are large enough to prevent rotation about the bond joining the two benzene rings. For example, biphenyl 2,2'-disulfonic acid exists in two forms.



These two forms are non-superimposable mirror images. They do not interconvert at room temperature because the energy required to twist one ring through 180° relative to the other is too high. This in turn is because, during the twisting process, the two $-SO_3H$ groups must come into very close proximity when the two benzene rings become coplanar and strong repulsive forces are introduced.

RESOLUTION OF RACEMIC MIXTURES

Synthesis of an optically active compound produces a mixture of both (+)- and (-)-isomers in equal amounts. Such a mixture is called a *racemic mixture* or a *racemate*. The separation of a *racemic mixture* into its two optically active components (+ and - isomers) is known as **Resolution**. Following methods are used:

(1) Chemical Resolution

Optically active isomers of the same compound resemble one another so closely in all properties except optical that it is not possible to separate them by ordinary laboratory methods. If, however, the racemic mixture is made to combine with another optically active compound, differences are set up which can be exploited for separation. Suppose for example, that racemic lactic acid is allowed to combine with the optically active base, (-)-strychnine. The salts formed will be:

(-)-strychnine (+)-lactate and

(-)-strychnine (-)-lactate

These salts are not true enantiomers. They differ considerably in properties and, in particular, in solubility in various solvents. By fractional crystallization from a suitable solvent, they can be separated. A treatment with dilute mineral acid removes the optically active base and leaves the two separate isomers of (+)-lactic acid and (-)-lactic acid.

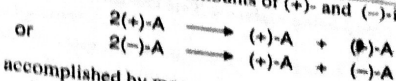
In a similar way, a racemic mixture of optically active forms of a base can be separated by the use of an optically active acid.

(2) Biochemical Resolution

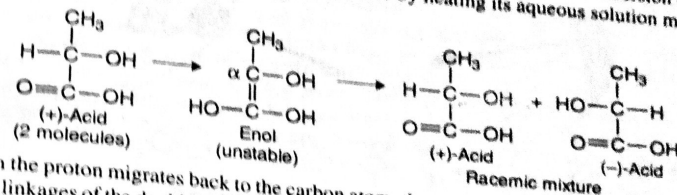
When certain bacteria or moulds are added to a solution of a racemic mixture they bring about the decomposition of one of the optically active forms more rapidly than the other. For example, *Penicillium glaucum* decomposes (+)-tartaric acid more readily than the (-)-isomer so that the latter can be obtained from the residue after treatment with the mould.

RACEMIZATION

Conversion of an optically active compound into a racemic mixture is called *racemization*. Recall: Racemic mixture is a mixture containing equal amounts of (+)- and (-)-isomers. Thus,



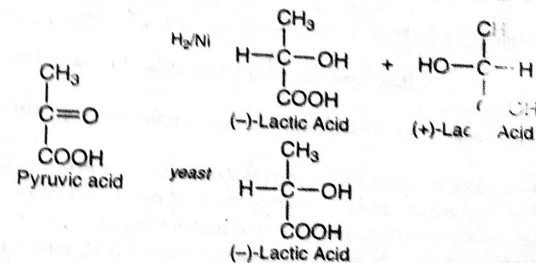
Racemization can be accomplished by means of heat, light, or by conversion of the isomer into an optically inactive intermediate which reverts to the racemic mixture. The conversion of either of the optically active lactic acids into a racemic mixture by heating its aqueous solution may proceed through an enol intermediate.



When the proton migrates back to the carbon atom, the process can involve the opening of either of the two linkages of the double bond and can produce either the original configuration or the opposite of it.

CHIRAL SYNTHESIS

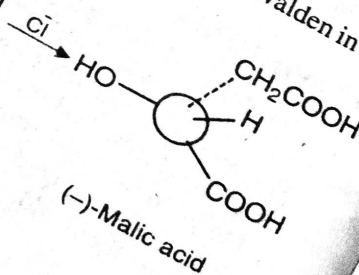
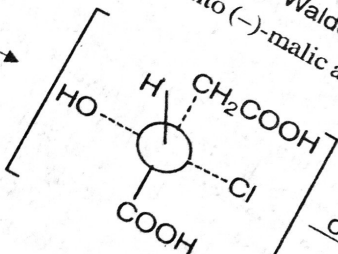
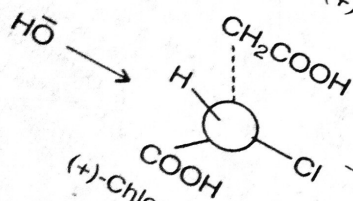
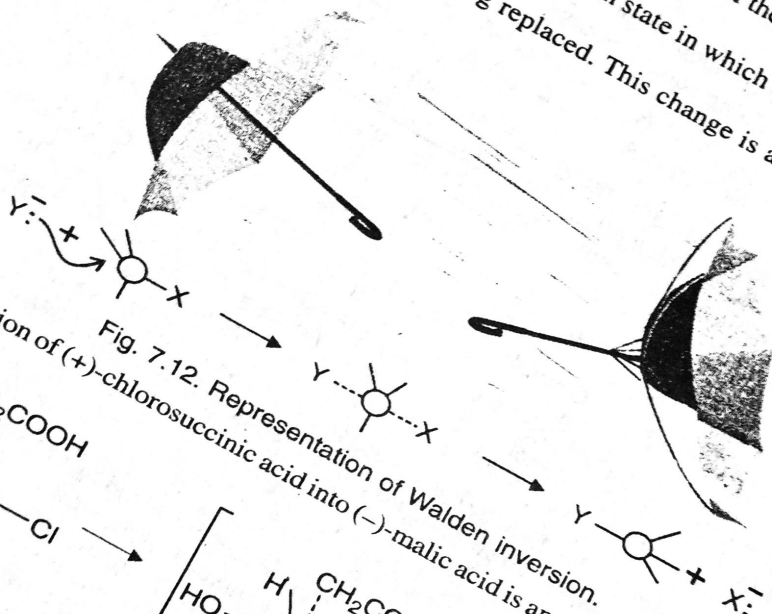
When a compound containing a chiral carbon atom is synthesized by ordinary laboratory methods from a symmetric compound, the product is a racemic mixture. If, however, such a synthesis is carried under the *asymmetric influence* of a suitable optically active reagent, only one of the optically active isomers (+ or -) is formed. This process in which a chiral compound is synthesized from a symmetric compound to yield the (+)-isomer or (-)-isomer directly is termed **Chiral Synthesis**. For example, the reduction of pyruvic acid, $\text{CH}_3\text{COCO}_2\text{H}$, in the laboratory leads to (\pm)-lactic acid (Racemic mixture). On the other hand, pyruvic acid is reduced by yeast to (-)-lactic acid only.



WALDEN INVERSION

When a group attached to a chiral carbon atom is replaced, the configuration of the new compound may be opposite to that of the original. This phenomenon is known as **Walden Inversion**. Factors which determine whether or not an inversion occurs are the nature of the reagent, the nature of the solvent, the temperature, and the nature of the substance being acted upon.

- The **mechanism** of Walden inversion involves three steps:
- (1) Approach of the attacking group from the side of the molecule opposite to the position of the group which is later replaced.
 - (2) Formation of an intermediate transition state in which three groups and the chiral carbon atom lie in one plane.
 - (3) Separation of the group being replaced. This change is analogous to an umbrella being blown inside out (Fig. 7.12).



Points to Remember

Enantiomers are isomers that have the same molecular formula, but different spatial arrangement of the groups.

Plane of symmetry is the plane that divides a structure into two symmetrical halves that are mirror images.

Asymmetric carbon (asymmetric carbon) is a carbon atom which is attached to four different groups.

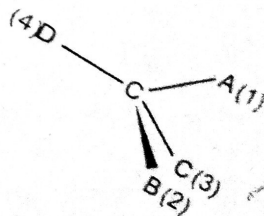
Chiral molecules (asymmetric molecules) do not have plane of symmetry.

Optically active molecules (asymmetric molecules) are nonsuperimposable on their mirror images.

Enantiomers are nonsuperimposable mirror images of a molecule with n chiral centers is 2^n , unless the compound has a plane of symmetry in which case it is 2^{n-1} .

R,S SYSTEM OF CONFIGURATION

The actual three-dimensional configuration of a chiral center is called the **Cahn-Ingold-Prelog** system, or the **R,S system**, which is based on the order of priority (1, 2, 3, 4) of the groups attached to the lowest priority group (4) in parentheses):



In the above example, A has the highest priority (1), B has the next highest priority (2), C has the next highest priority (3); and D has the lowest priority (4). We now go from A to B to C, and therefore we move in an **anticlockwise** direction. In the structure given below, we go from A to B to C, and therefore we move in a **clockwise** direction. We therefore assign to this structure an **S** configuration.

