CHAPTER 2

Stereochemistry

❖ Chirality

All the crystals or molecular geometries that cannot be superimposed on their mirror images have a special property to rotate the plane of polarized light when passed through them; such compounds are called as chiral compounds and the property is called as chirality or optical activity.

In 1811, a French physicist named François Jean Dominique Arago observed the rotation of the orientation of linearly polarized light when it is passed through quartz. A French physicist, Jean Baptiste Biot, also observed the rotation of the plane of polarized light in 1815 with some liquids and vapors of organic compounds like turpentine. After that, an English astronomer, Sir John F. W. Herschel, found in 1820 that all the different individual quartz crystals were actually the mirror images of each other, and rotated the plane of polarized light by equal magnitude but the directions of rotation were opposite. The crystal that rotates the plane of polarized light towards the right is called dextrorotatory, while the mirror image will rotate to left imparting a label of levorotatory. Now since all the crystals that were capable of rotating the plane of polarized light could not be superimposed on their mirror image crystals by any mean, the term 'chiral' (derived from Greek word, cheir = hand) become extremely popular to define such crystals as our hands also the non-superimposable mirror images of each other.

➢ *Experimental Measurement of Chirality or Optical Activity*

Optical activity or chirality is measured by an instrument called the 'polarimeter'. The basic experimental setup to measure the magnitude of optical activity is shown below.

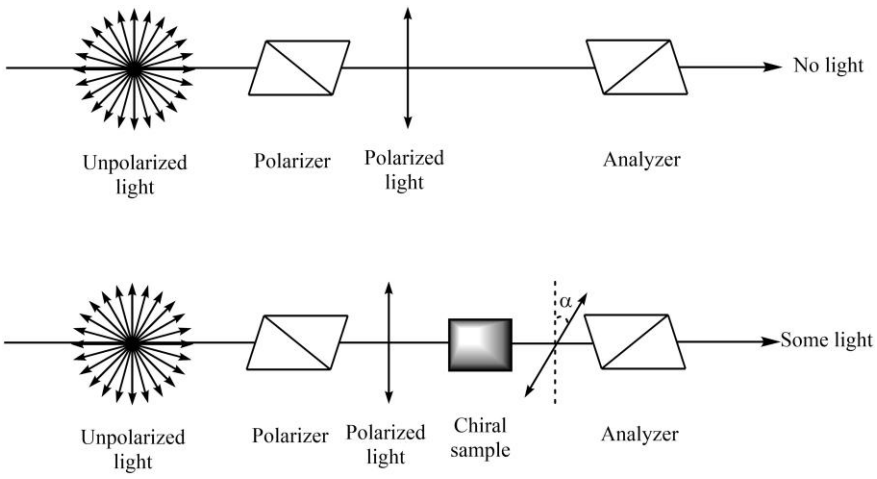


Figure 1. Schematic diagram of a polarimeter to measure chirality.

The angle through which the plane of polarized light gets rotated by the chiral molecules is symbolized by α and can be formulated as given below.

$$\alpha = [\alpha]^T_\lambda . l . c \quad (1)$$

Where l is the path length of the sample in cm whereas c represents the concentration of the sample in g/ml. The symbol represents the specific angle of rotation $[\alpha]^T_\lambda$ at temperature T and wavelength λ. It is also worthy to note that the observed angle of rotation also depends upon the nature of the solvent. Furthermore, the wavelength of the radiation used and the temperature of the system should be kept constant throughout the experiment. In order to determine the specific angle of rotation, use path length and concentration unity in the rearranged form of equation (1), i.e.,

$$[\alpha]^T_\lambda = \frac{\alpha}{l . c} \quad (2)$$

$$[\alpha]^T_\lambda = \frac{\alpha}{1\ cm \times 1\ g/ml} \quad (3)$$

or

$$[\alpha]^T_\lambda = \alpha \quad (4)$$

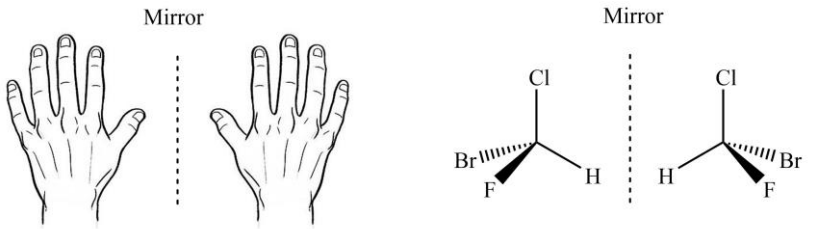
Therefore, the specific angle of rotation of any chiral molecule may simply be defined as the observed angle of rotation when the solution of the same compound with unit concentration and unit path length is placed in the path of polarized light.

- ***Conditions for Chirality***

In order to be optically active, any one of the following conditions can be used to define the chirality of a molecule to somewhat less or more strictly.

Condition 1: Since All the crystals or molecular geometries that are capable of rotating the plane of polarized light could not be superimposed on their mirror images, the primary condition for a molecule to be optically active or chiral can be summarized as follows.

If a molecular geometry wants to be optically active, it must not be superimposable on its mirror image.

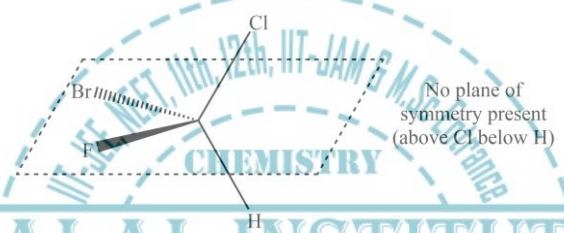


Non-superimoposable mirror images Non-superimoposable mirror images

This condition defines chirality in an absolute sense and will be chiral if it is satisfied.

Condition 2: Now although the first condition is successful in defining chirality, its application is quite difficult. This is because it is very difficult to imagine the mirror image of the molecular geometry in three dimensions (especially complex molecules), and then the confirmation of their superimposition is even more difficult to tackle for human imagination. Therefore, an alternate route is necessary to check the first condition. This problem can be solved by the fact that any molecular geometry lacking plane of symmetry cannot be superimposed on its mirror image; and therefore, the problem of 'visualizing the mirror image and its subsequent superimposition' is reduced to finding the plane of symmetry only. If a plane of symmetry is present, the molecule would be superimposable of its mirror image, and hence, will be achiral. Conversely, if a plane of symmetry is absent, the molecule would not be superimposable of its mirror image, and hence, will be chiral. Hence, this condition of chirality can be summarized as follows;

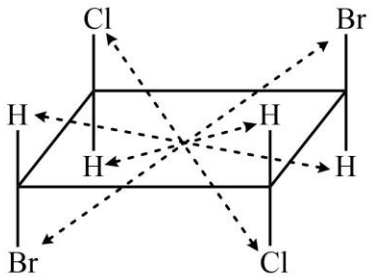
If a crystal molecular geometry wants to be optically active (or chiral), there should be no plane of symmetry.



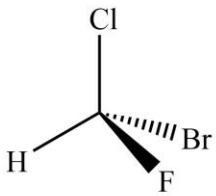
This condition defines chirality in part because there are molecules that don't have any plane of symmetry but still inactive.

Condition 3: Since there are molecules that don't have any plane of symmetry but still inactive, a more inclusive approach is needed to confirm the optical activity with ever treating mirror images. This problem can be solved by the fact that any molecular geometry lacking secondary symmetry elements (plane of symmetry, inversion center, and alternating axis of symmetry) can never be superimposed on its mirror image; and therefore, will be achiral. Hence, this condition of chirality can be summarized as follows;

If a crystal molecular geometry wants to be optically active (or chiral), there should secondary symmetry elements i.e., plane of symmetry (σ), center of symmetry (i), and alternating axis of symmetry (S_n).



No plane of symmetry present
yet achiral due to inversion (i.e. *i* or S_2)



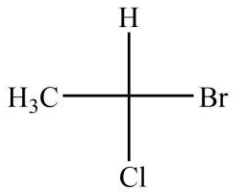
No secondary symmetry element (σ, *i*, S_n) present;
and therefore, chiral in nature.

This condition defines chirality in an absolute sense and will be chiral if it is satisfied.

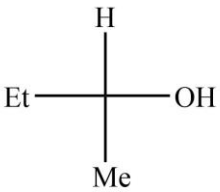
➢ ***Types of Chirality***

Depending upon the geometrical profile of molecular species, chiral compounds or chirality can primarily be divided into four categories as given below.

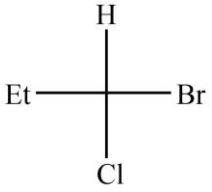
1. Chirality arising from a center (chiral center): This type of chirality arises when all the four groups around tetrahedrally coordinated carbon atom become different. In other words, an organic molecule can no longer be superimposed on its mirror image if it has a center with all different groups.



1-bromo-1-chloroethane



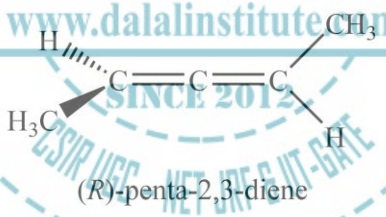
butan-2-ol



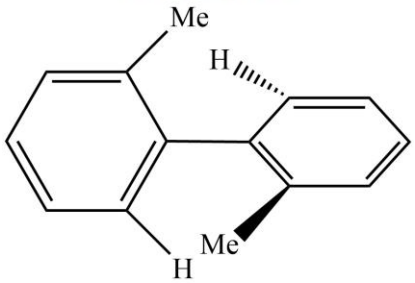
1-bromo-1-chloropropane

Some of the most simple examples of organic molecules with this type of chirality are CH_3-CHClBr, butan-2-ol, and 1-bromo-1-chloropropane.

2. Chirality arising from an axis (chiral axis): This type of chirality arises when a tetrahedrally coordinated prochiral molecule becomes chiral by extending the center along an axis. In other words, a prochiral molecule can no longer be superimposed on its mirror image if its center has been extended to a line with same groups at different ends.



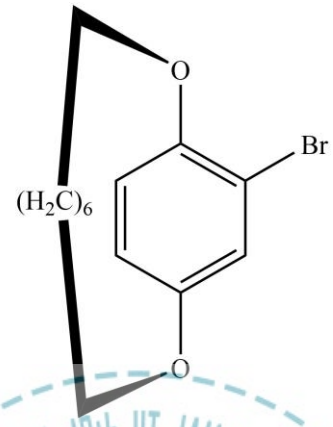
(*R*)-penta-2,3-diene



2,2'-dimethyl-1,1'-biphenyl

Some of the most simple examples of organic molecules with this type of chirality are penta-2,3-diene and 2,2'-dimethyl-1,1'-biphenyl (a biphenyl derivative).

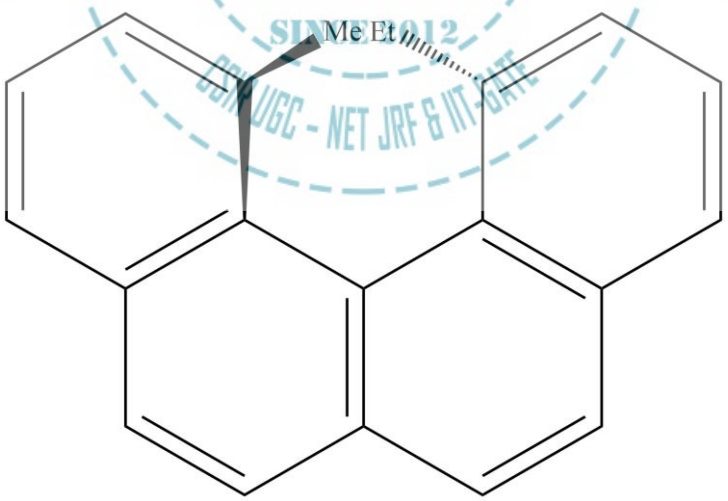
3. Chirality arising from a plane (chiral plane): This type of chirality arises when relacing a group in a plane makes the molecule chiral. In other words, an organic molecule can no longer be superimposed on its mirror image if the replacement of a particular group induces chirality.



13-bromo-1,10-dioxa[8]paracyclophane

Some of the most simple examples of organic molecules with this type of chirality are ansa compounds like 13-bromo-1,10-dioxa[8]paracyclophane.

4. Chirality arising from a spiral (helical chirality): This type of chirality arises when the molecule has a helical structure. In other words, an organic molecule can no longer be superimposed on its mirror image if its geometry resembles a helix.



1-ethyl-12-methylbenzo[*c*]phenanthrene

Some of the most simple examples of organic molecules with this type of chirality are helical compounds like 1-ethyl-12-methylbenzo[c]phenanthrene.

❖ Elements of Symmetry

Elements of symmetry may simply be defined as the point, line or plane inside or passing through the molecular geometry about which some operations like rotation, inversion, or reflection generate indistinguishable images. These operations are generally labeled as symmetry operations. A general discussion on different symmetry elements is given below.

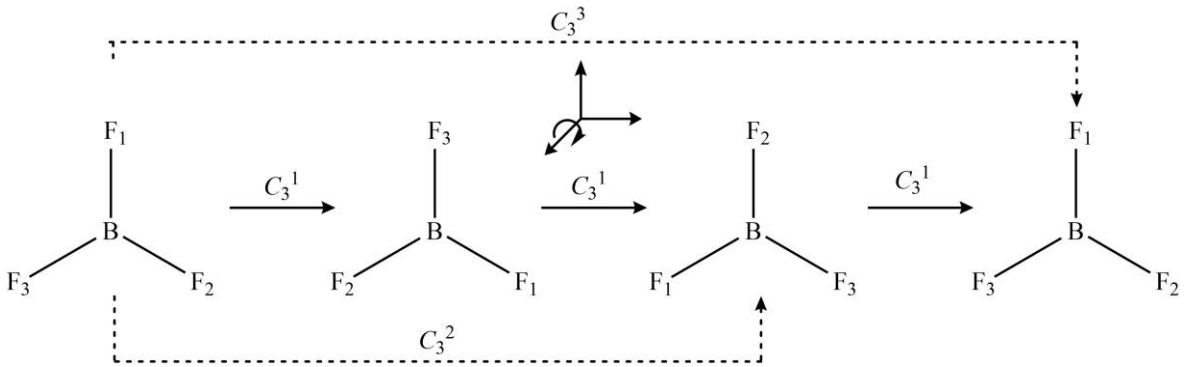
➢ *Axis of Rotation (C_n)*

The axis of rotation or simply the symmetry axis may simply be defined as the line passing through a molecular geometry about which the rotation through a certain angle generates indistinguishable images.

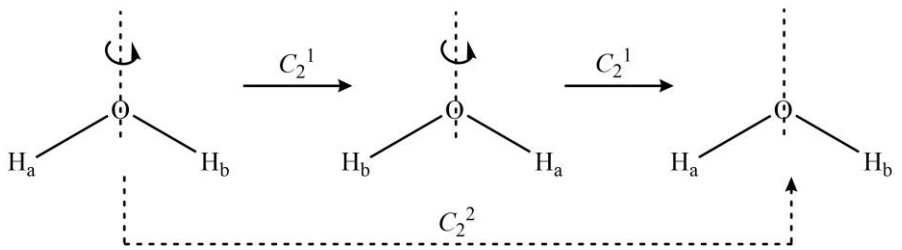
The axis of rotation is generally symbolized by C_n where n can have the value from 1, 2, 3, 4… and so on. The expression for n is

$$n = \frac{360°}{\theta} \tag{5}$$

Where θ is the minimum angle required to generate indistinguishable images. For instance, in the case of a regular trigone or BF_3 molecule, the geometry must be rotated through 120° minimum about the line perpendicular to the molecular plane to get indistinguishable images. Therefore, we can say that it is a C_3 (three-fold) axis of symmetry.



Where C_3^1, C_3^2 and C_3^3 are the symmetry operations via 120°, 240°, and 360°, respectively. Similarly, for the H_2O molecule, the minimum angle required to generate indistinguishable images is 180°, giving a C_2 axis of symmetry.

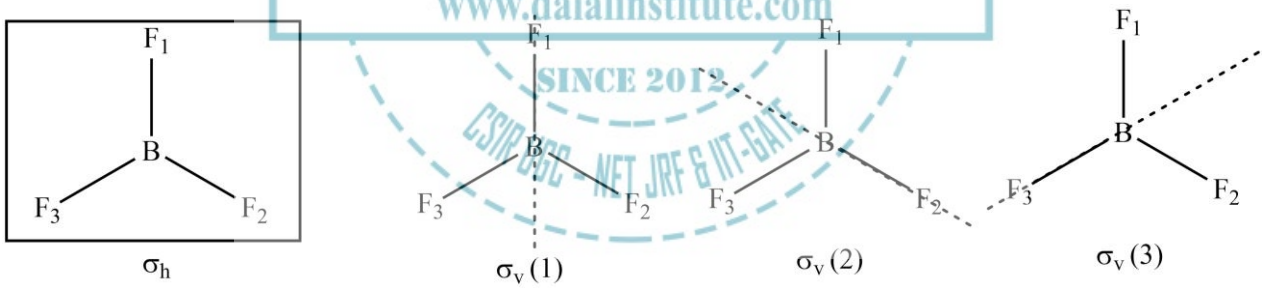


➢ ***Plane of Symmetry (σ)***

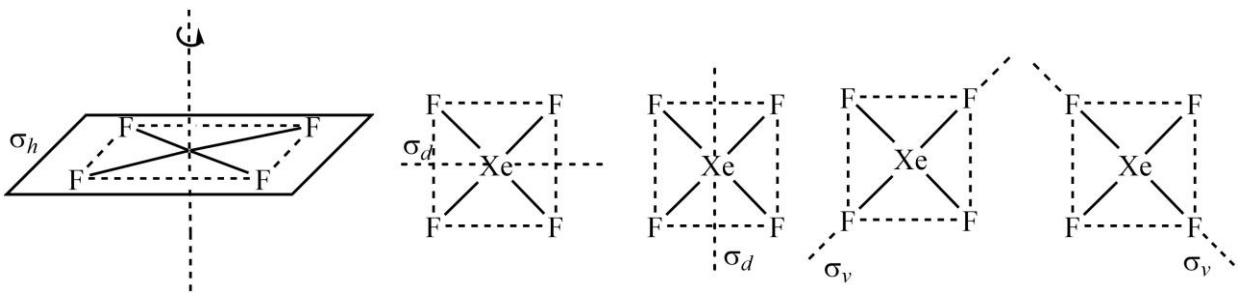
The plane of symmetry or simply the symmetry plane may be defined as the plane bisecting the molecular geometry in such a way that one half is the mirror image of the other.

The axis of rotation is generally symbolized by σ_h *or* σ_v where the subscript *h* or *v* is to denote wheater the plane is parallel or perpendicular to the principal axis (symmetry axis of the highest order). There is also a third kind of plane of symmetry called the dihedral plane (σ_d): In other words, we can say that a dihedral plane bisects two σ_v planes. On a final note, a plane of symmetry can also be designated by the Cartesian orientation encompassing it, e.g., (*yz*-plane) or (*xz*-plane). For instance, there are two σ_v planes in water molecules as shown below.

Similarly, there are a total of three vertical (σv) planes and one horizontal (σ_h) plane in the case of BF_3 molecules as shown below.



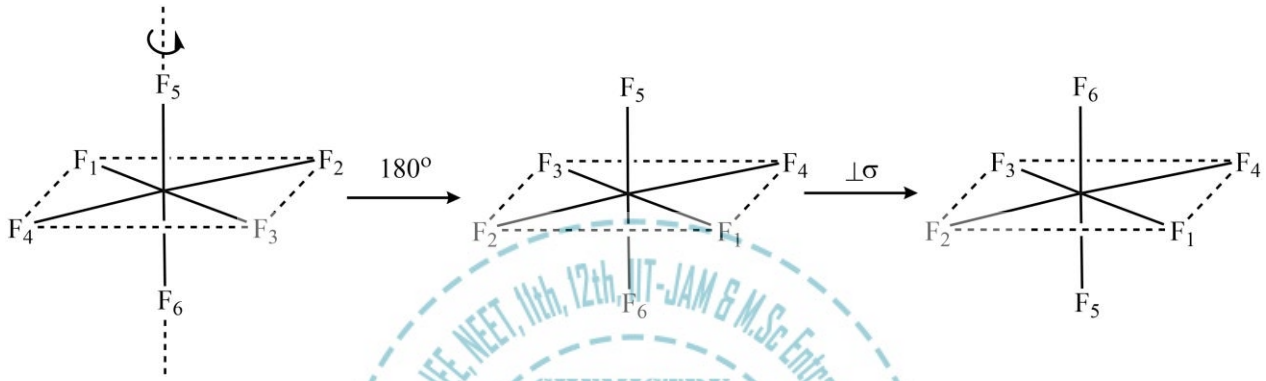
Similarly, there are a total of two vertical (σv) planes and one horizontal (σ_h) and two dihedral planes in the case of XeF_4 molecules as shown below.



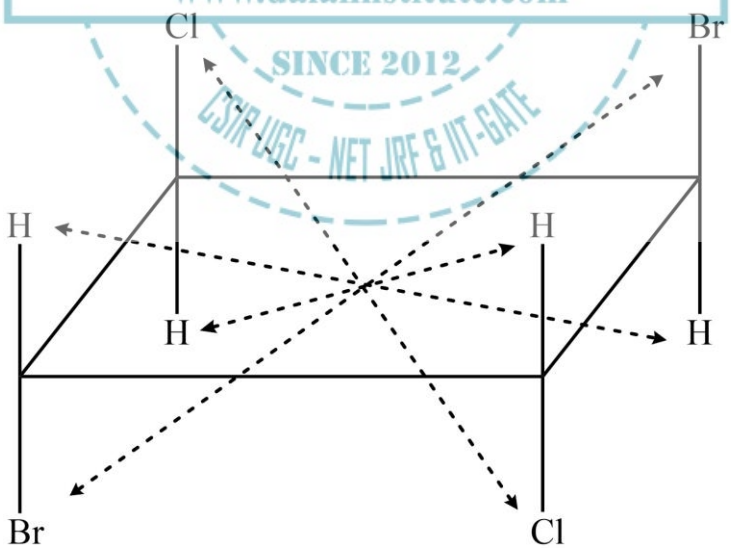
➢ ***Center of Symmetry (i)***

The molecular geometry is said to possess the center of symmetry if a rotation through 180° followed by the perpendicular reflection generates an indistinguishable image.

The center of symmetry or simply the 'inversion center is denoted by the symbol '*i*', which is a point inside the geometry at such a position that if an object is inverted about this point, the position vector of any point in an object ⟨say *x*, *y*, *z*⟩ is also inverted (–x, –y, –z⟩. For instance, consider the case of the SF_6 molecule.



Similarly, the complete staggered form of CHClBr–CHClBr also possesses the center of symmetry as it produces indistinguishable images after inverting through the center. Furthermore, the center of symmetry in any molecular geometry can also found by drawing lines of equal length in the opposite direction from the center, provide that similar points are observed.



Similarly, other examples of molecules with the center of symmetry are acetylene, a staggered form of ethane and ethylene.

➢ ***Alternating Axis of Symmetry (S_n)***

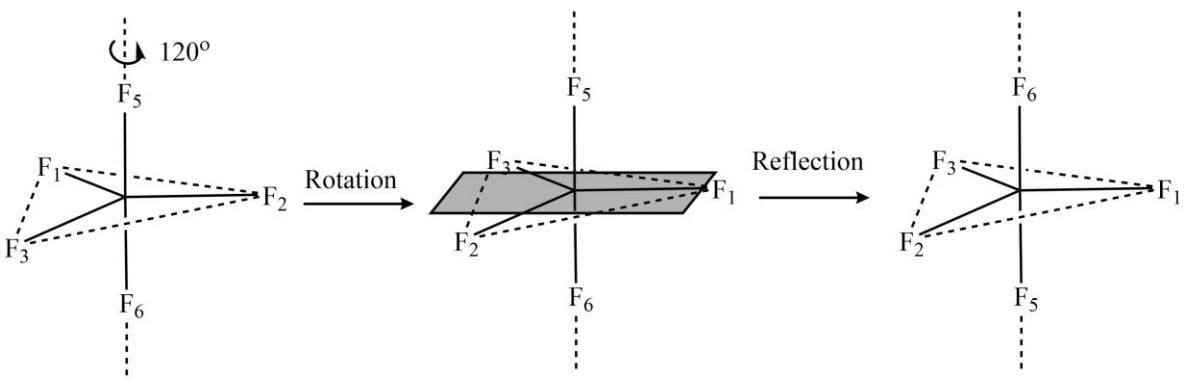
The alternating axis of symmetry or improper axis of rotation may simply be defined as the line passing through a molecular geometry about which a rotation followed by a perpendicular reflection generates indistinguishable images.

The improper axis of rotation is generally symbolized by S_n where n can have the value from 1, 2, 3, 4… and so on. The expression for n is

$$n = \frac{360°}{\theta} \tag{6}$$

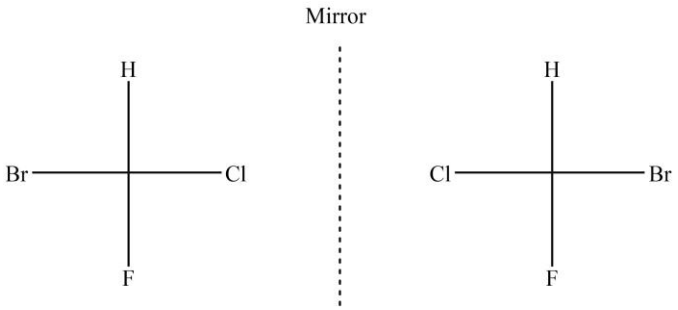
Where θ is the minimum angle required before perpendicular reflection to generate indistinguishable images. For instance, in the case of a regular trigone or CH_4 molecule, the geometry must be rotated through 90° before the reflection in a perpendicular plane is carried out to get indistinguishable images. Therefore, we can say that it is an S_4 (four-fold) alternating axis of symmetry.

Similarly, for the BF_3 molecule, indistinguishable images can also be obtained by rotating the molecule through 120° about a line perpendicular to the molecular plane followed by the reflection. Therefore, we can say that it is an S_3 (three-fold) alternating axis of symmetry.

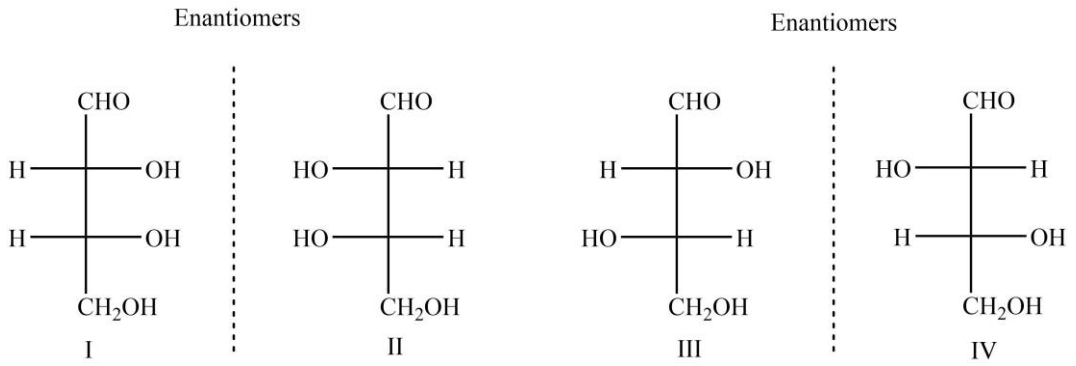


❖ Molecules with More Than One Chiral Centre: Diastereomerism

In most organic molecules, the optical activity or the chirality arises when all the four groups around an sp^3 hybridized carbon become different. Such carbon centers are typically called as chiral centers. Furthermore, it is also a quite well-known fact that the odd number of exchanges at a chiral center produce enantiomers. For instance, consider the case of CHClBrF.



However, if the organic molecule contains more than one chiral center, different possibilities of odd and even exchanges at these stereocenters may generate identical, enantiomers, or diastereomers. Unlike enantiomers, which are non-superimposable mirror images; diastereomers are simply the non-mirror-image stereomers. For instance, consider the case of an organic molecule with two chiral centers unsymmetrical ends.



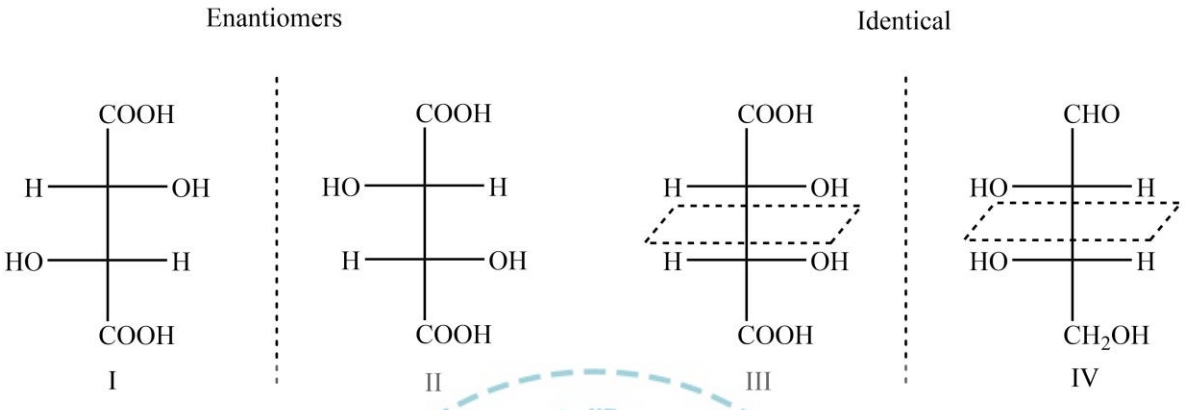
It is obvious that the odd number of exchanges at both chiral centers is creating non-superimposable mirror images (enantiomers); whereas the odd exchange at one chiral center and even exchange at other chiral centers is producing non-mirror-image isomers (diastereomers). It is also worthy to note that the even number of exchanges at both chiral centers will generate identical molecules just like in the case of molecules with a single chiral center. The calculation of the total number of optically active and meso forms for organic molecules with more than *n* chiral centers with unsymmetrical ends can be obtained by the following relations.

$$Number\ of\ optically\ active\ isomers = 2^n$$

$$Number\ of\ meso\ forms = 0$$

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

On the other hand, if we consider the case of an organic molecule with two chiral centers and symmetrical ends, the possibility of a meso compound also arises. The most popular example to prove the concept is tartaric acid.



It is obvious that the odd number of exchanges at both chiral centers in L-tartaric acid is creating a non-superimposable mirror image (R-tartaric); whereas the odd exchange at one chiral center and even exchange at other chiral center is producing non-mirror-image isomers (diastereomers). However, structures III and IV are identical although they are produced by odd-odd exchanges at both chiral centers. The obviously because of the presence of the symmetry plane perpendicular to the carbon-carbon bond. Such compounds are called as meso form. It is also worthy to note that the even number of exchanges at both chiral centers will generate identical molecules just like in the case of molecules with a single chiral center.

The calculation of the total number of optically active and meso forms for organic molecules with more than *n* chiral centers with symmetrical ends can be obtained by using the following relations.

i) When the number of chiral centers is even:

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

$$Number\ of\ meso\ forms = 2^{\left(\frac{n}{2}-1\right)}$$

$$Total\ number\ of\ isomers = 2^{(n-1)} + 2^{\left(\frac{n}{2}-1\right)}$$

ii) When the number of chiral centers is odd:

$$Number\ of\ optically\ active\ isomers = 2^{(n-1)} - 2^{\left(\frac{n}{2}-\frac{1}{2}\right)}$$

$$Number\ of\ meso\ forms = 2^{\left(\frac{n}{2}-\frac{1}{2}\right)}$$

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

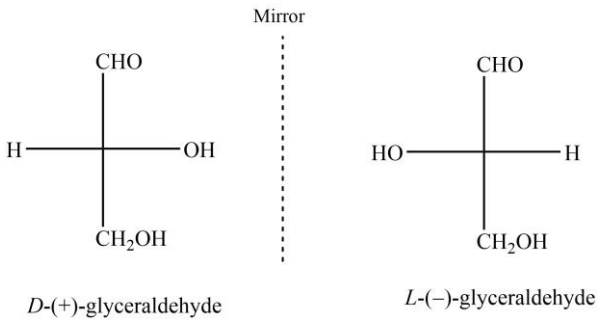
❖ Determination of Relative and Absolute Configuration (Octant Rule Excluded) with Special Reference to Lactic Acid, Alanine & Mandelic Acid

The three-dimensional character of organic molecules can be labeled absolutely or relative to some reference compound. In this section, we will study the relative and absolute configuration of various organic molecules with special reference to lactic acid, alanine & mandelic acid.

➢ *Relative Configuration*

The relative configuration of an organic stereoisomer may simply be defined as the correlation between two enantiomers even if the absolute configuration is unknown.

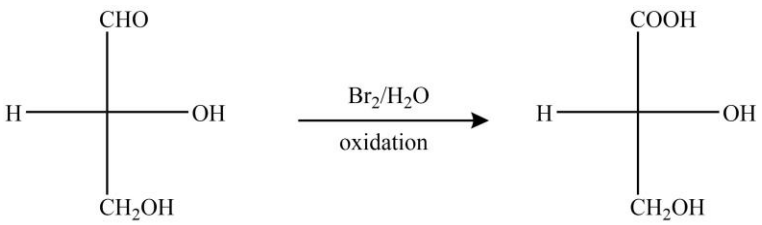
The elucidation of the absolute configuration of a chiral molecule was not possible before 1951 due to the absence of any such method. Therefore, the assignment of various groups in space was carried out relative to the groups of a standard reference compound.



D-(+)-glyceraldehyde *L*-(−)-glyceraldehyde

One of the most popular reference compounds for the determination of stereochemical notation of chiral organic molecules is glyceraldehyde.

General route to assign D-L nomenclature: All the compounds that can be obtained or transformed to *D*-(+)-glyceraldehyde are said to belong to D-series, whereas all the compounds that can be obtained or transformed to *L*-(−)-glyceraldehyde are said to belong to L-series. These predictions find their base in the fact that if no bond breaking-formation occurs at the chiral center, the configuration is retained. For instance, consider the case of (–)-glyceric acid.



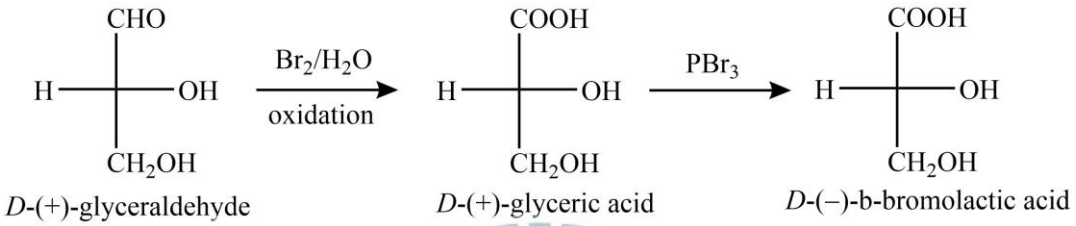
D-(+)-glyceraldehyde *D*-(−)-glyceric acid

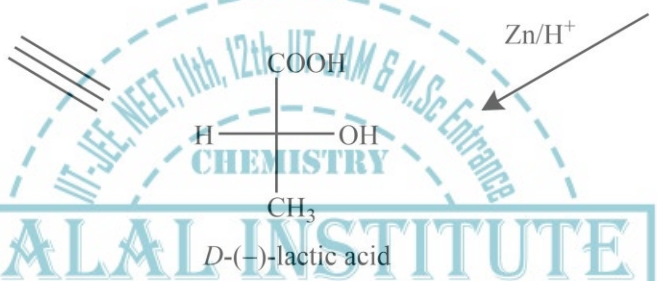
Since it can be obtained from D-(+)-glyceraldehyde, its name should be D-(–)-glyceric acid even though it is laevorotatory.

Determination of Relative Configuration Lactic Acid, Alanine & Mandelic Acid: The configuration of lactic acid, alanine & mandelic acid relative to glyceraldehyde (i.e., D-L configurations) can be obtained using the following chemical routes.

i) Determination of relative configuration of lactic acid:

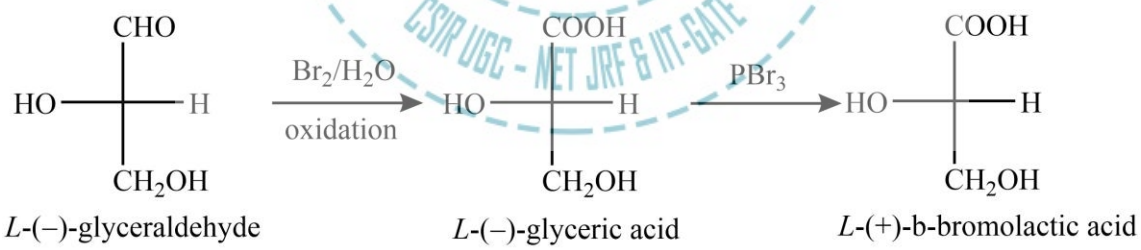
As we know that lactic acid is optically active, and therefore, is bound to exist as enantiomeric pair. The configuration of one enantiomer relative to the glyceraldehyde can be obtained as given below.

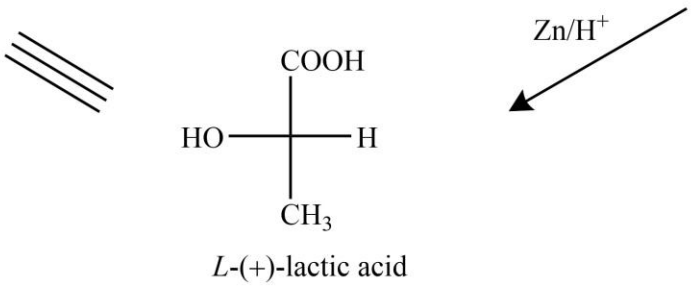




It is obvious that, unlike D-(+)-glyceraldehyde, the D configuration of lactic acid is found to be levorotatory.

Since lactic acid is optically active, the configuration of mirror image isomer relative to the glyceraldehyde can be obtained as given below.

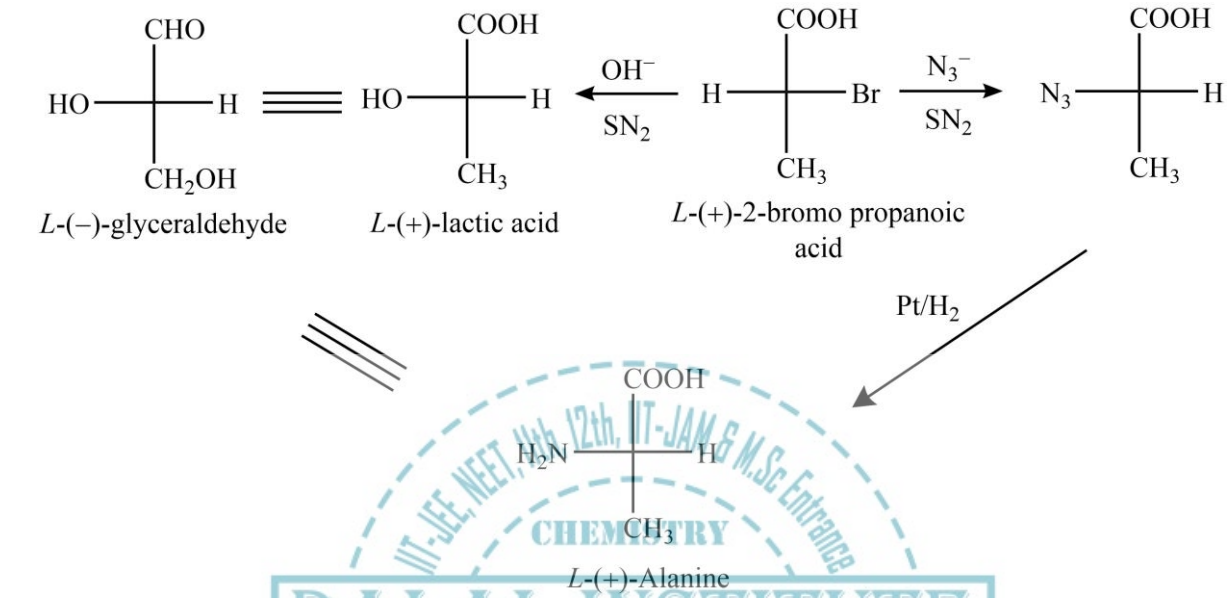




It is obvious that, unlike *L*-(–)-glyceraldehyde, the *L* configuration of lactic acid is found to be dextrorotatory.

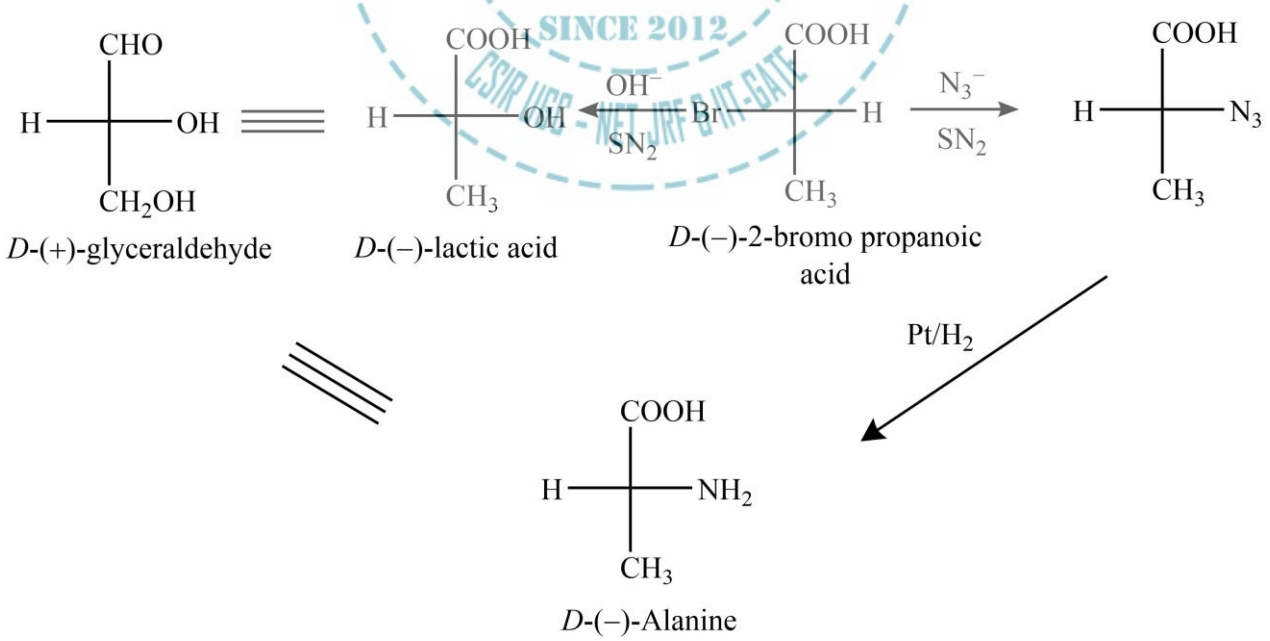
ii) Determination of relative configuration of alanine:

As we know that alanine is optically active, and therefore, is bound to exist as enantiomeric pair. The configuration of one enantiomer relative to the glyceraldehyde can be obtained as given below.



It is obvious that, unlike *L*-(−)-glyceraldehyde, the *L* configuration of alanine is found to be dextrorotatory.

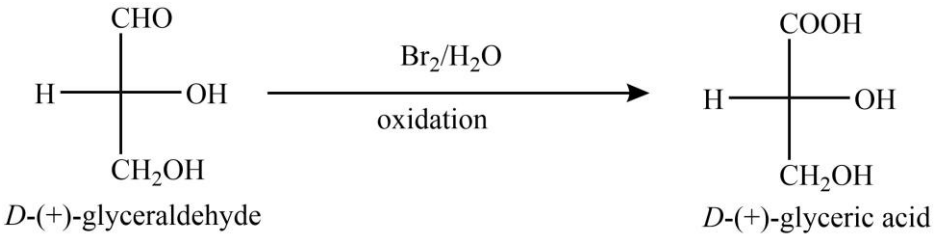
Since alanine is optically active, the configuration of mirror image isomer relative to the glyceraldehyde can be obtained as given below.



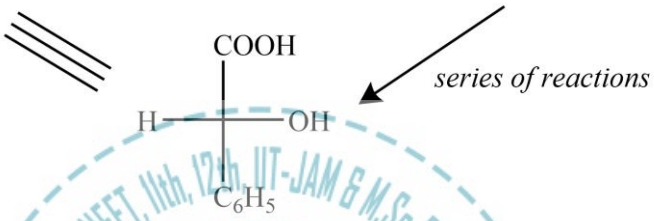
It is obvious that, unlike D-(+)-glyceraldehyde, the *D* configuration of alanine is found to be levorotatory.

iii) Determination of relative configuration of mandelic acid:

As we know that alanine is optically active, and therefore, is bound to exist as enantiomeric pair. The configuration of one enantiomer relative to the mandelic acid can be obtained as given below.



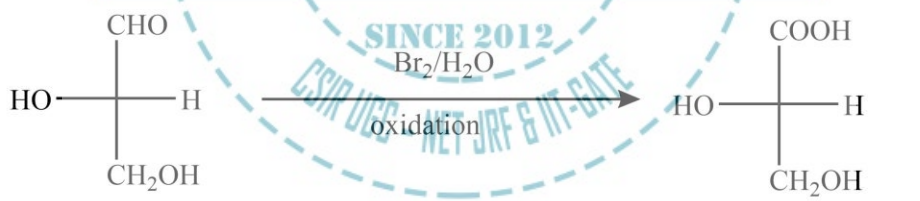
D-(+)-glyceraldehyde *D*-(+)-glyceric acid



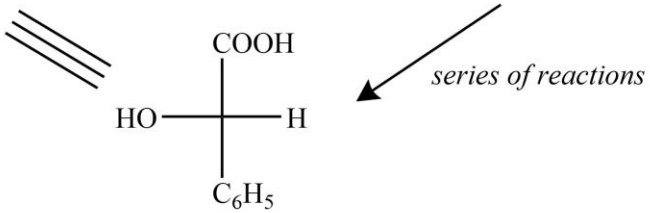
D-(−)-mandelic acid

It is obvious that, unlike D-(+)-glyceraldehyde, the *D* configuration of mandelic acid is found to be levorotatory.

Since mandelic acid is optically active, the configuration of mirror image isomer relative to the glyceraldehyde can be obtained as given below.



L-(−)-glyceraldehyde *L*-(−)-glyceric acid



L-(+)-mandelic acid

It is obvious that, unlike *L*-(−)-glyceraldehyde, the *L* configuration of mandelic acid is found to be dextrorotatory.

➢ ***Absolute Configuration***

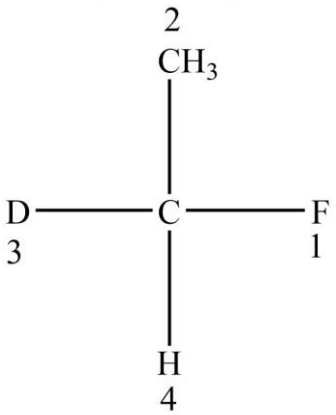
The absolute configuration of a particular stereoisomer of an organic molecule may simply be defined as the actual arrangement of atoms or groups in space.

Since the D-L system of stereoisomeric nomenclature was relative and difficult to apply, a more simplistic and robust approach was needed. The problem was solved by R. S. Chan, C. K. Ingold and V. Prelog by developing a nomenclature method that was free from limitations posed by the relative approach. This nomenclature technique is generally called as Chan-Ingold-Prelog or R-S system. The whole procedure includes two steps; the first is the priority assignment of different groups and the second step involves the assignment of absolute configuration.

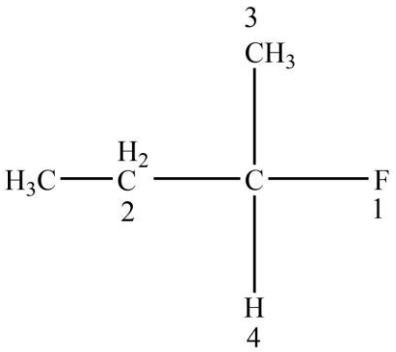
Rules for priority assignment of different groups: A priority sequence of (1), (2), (3), and (4) is assigned to all the four groups attached to the chiral center using the following set of rules.

i) If the substituents attached with the chiral center are simply atoms, substituents with a higher atomic number of bonded atoms are given higher priority and vice-versa.

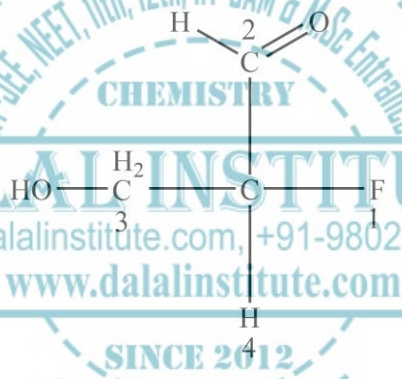
ii) If the bonded atoms of two groups are isotopes of the same element, a higher priority will be given to the group with a higher atomic mass.



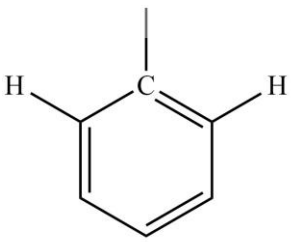
iii) Atoms next to the bonded atoms must be considered if the two above-mentioned rules are not able to distinguish the groups concerned.



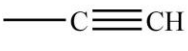
iv) For priority assignment, multiple bonds must be considered as multiple numbers of single bonds, i.e., double and triple bonds must be treated as two single and three single bonds, respectively.



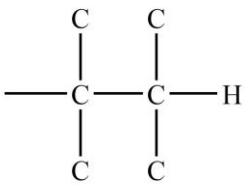
Now using all these rules, let us try to determine the priority sequence of phenyl and acetylenic groups.



Phenyl group



or



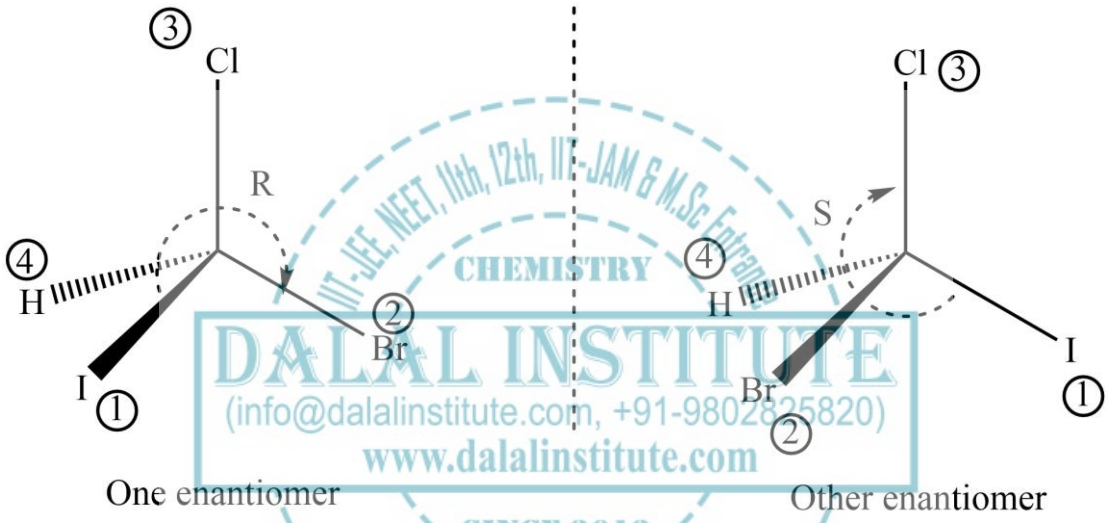
Vinyl group

According to the sequence rule, phenyl and should be prioritized over acetylenic; which can be attributed to the fact that the carbon in the former pair is attached with three other carbons whereas in the latter pair it binds with only two carbons. However, only one carbon has successive bonds in acetylenic (2C and 1H); whereas in the phenyl group, two carbons have successive bonds (2C and 1H) allotting it a higher priority.

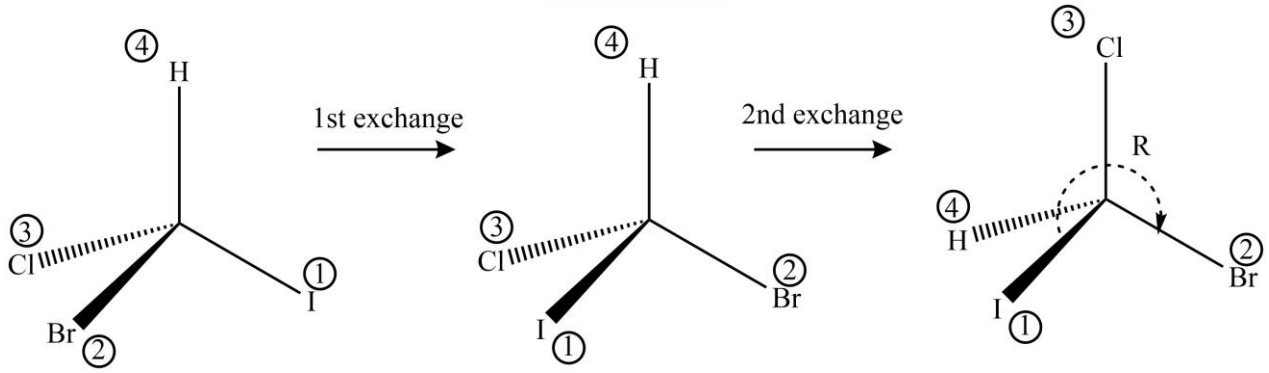
Assignment of absolute configuration: Since two of the most popular depiction of three-dimensional molecules on two-dimensional paper are Flying-Wedge and Fischer projection, we will study the determination of absolute configuration for both.

i) Assignment of absolute configuration in Flying-Wedge representation:

After assigning priorities to different groups the molecule is oriented in space such that the group of lowest priority goes away from the observer. Now if the tracking of decreasing priority of the remaining three groups comes gives rise to clockwise flight, the molecules should be labeled as R. However, if the tracking of decreasing priority of the remaining three groups comes gives rise to anticlockwise flight, the molecules should be labeled as S.



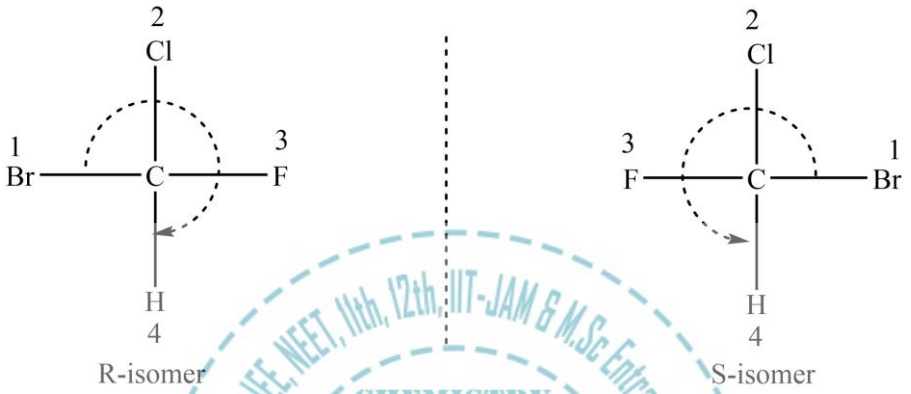
Furthermore, if the group with the lowest priority is toward the observer or in the plane of the paper, carry out an even number of exchanges to through the lowest-priority-group away from the observer before the R-S labeling.



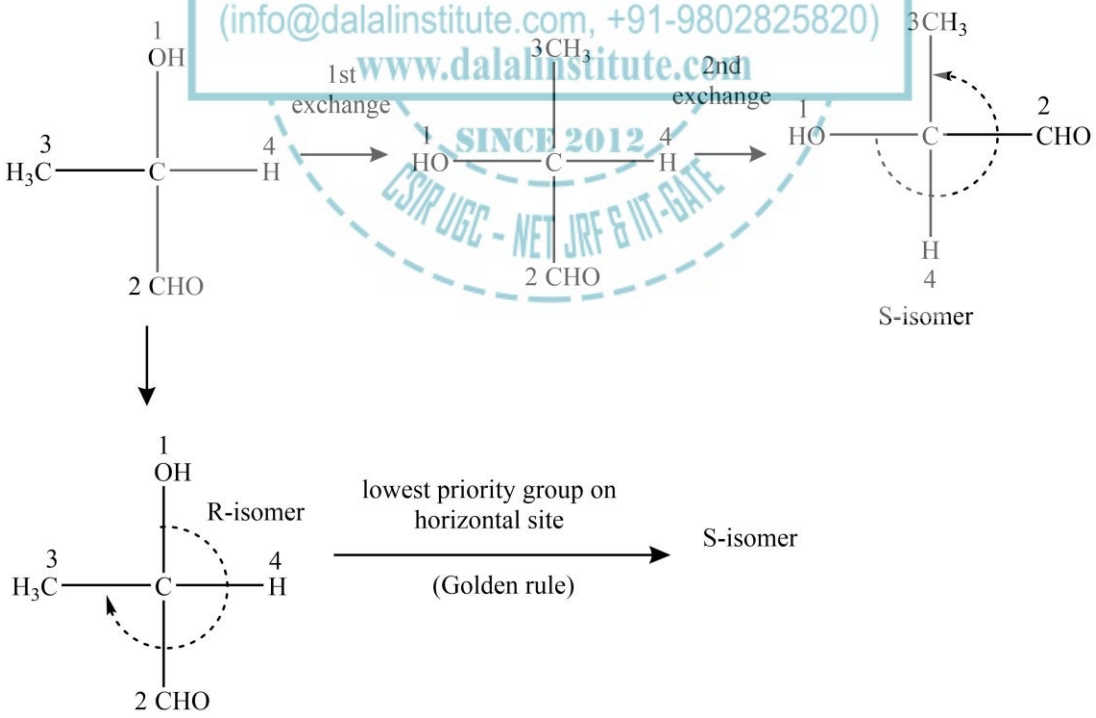
It is also worthy to note that the actual stereochemical notation can also be found by reverting the answer directly if the group with the lowest priority is toward the observer.

ii) Assignment of absolute configuration in Fischer representation:

After assigning priorities to different groups the Fischer projection of the molecule is transformed to an identical one by an even number of exchanges so that the group of lowest priority is at the vertical position. Now if the tracking of decreasing priority of the remaining three groups comes gives rise to clockwise flight, the molecules should be labeled as R. However, if the tracking of decreasing priority of the remaining three groups comes gives rise to anticlockwise flight, the molecules should be labeled as S.



Furthermore, if the group with the lowest priority is already located at the vertical position, nothing is needed but priority tracking only.

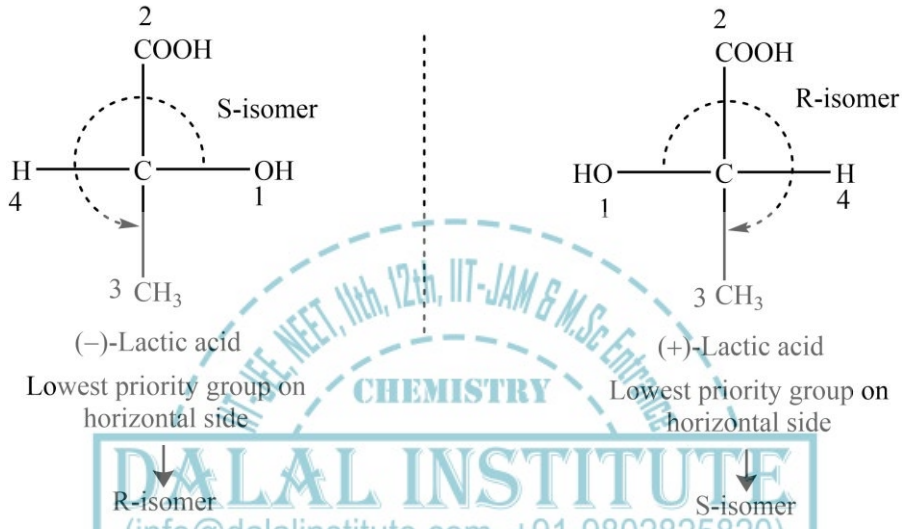


It is worthy to note that the actual stereochemical notation can also be found by reverting the answer directly if the group with the lowest priority is at the horizontal position, which is also called as the golden rule.

Determination of Absolute Configuration Lactic Acid, Alanine & Mandelic Acid: The absolute configuration of lactic acid, alanine & mandelic acid (i.e., R-S configurations) can be obtained using the following chemical routes.

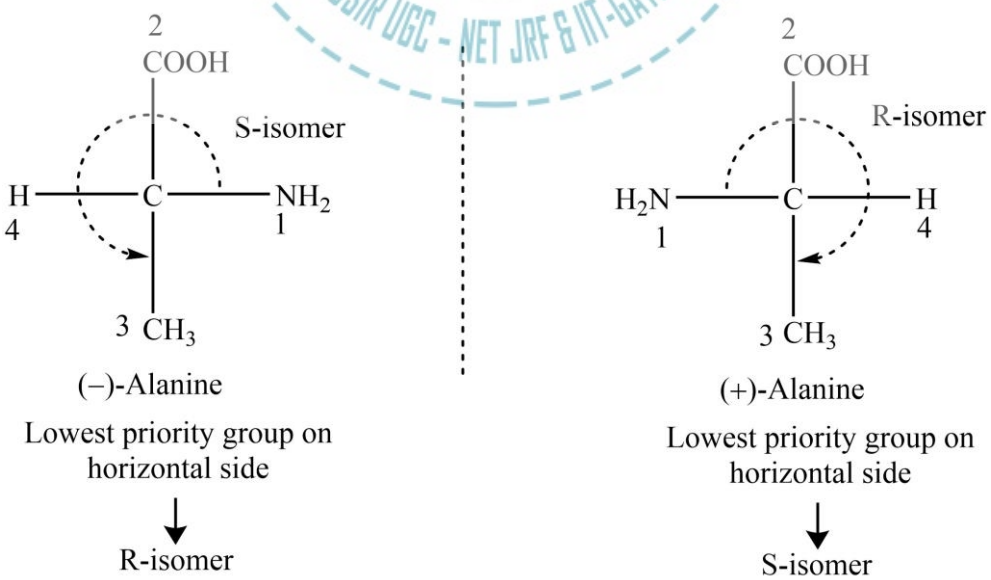
i) Determination of absolute configuration of Lactic Acid:

As we know that lactic acid is optically active, and therefore, is bound to exist as enantiomeric pair. The absolute configuration of both enantiomers can be obtained as given below.



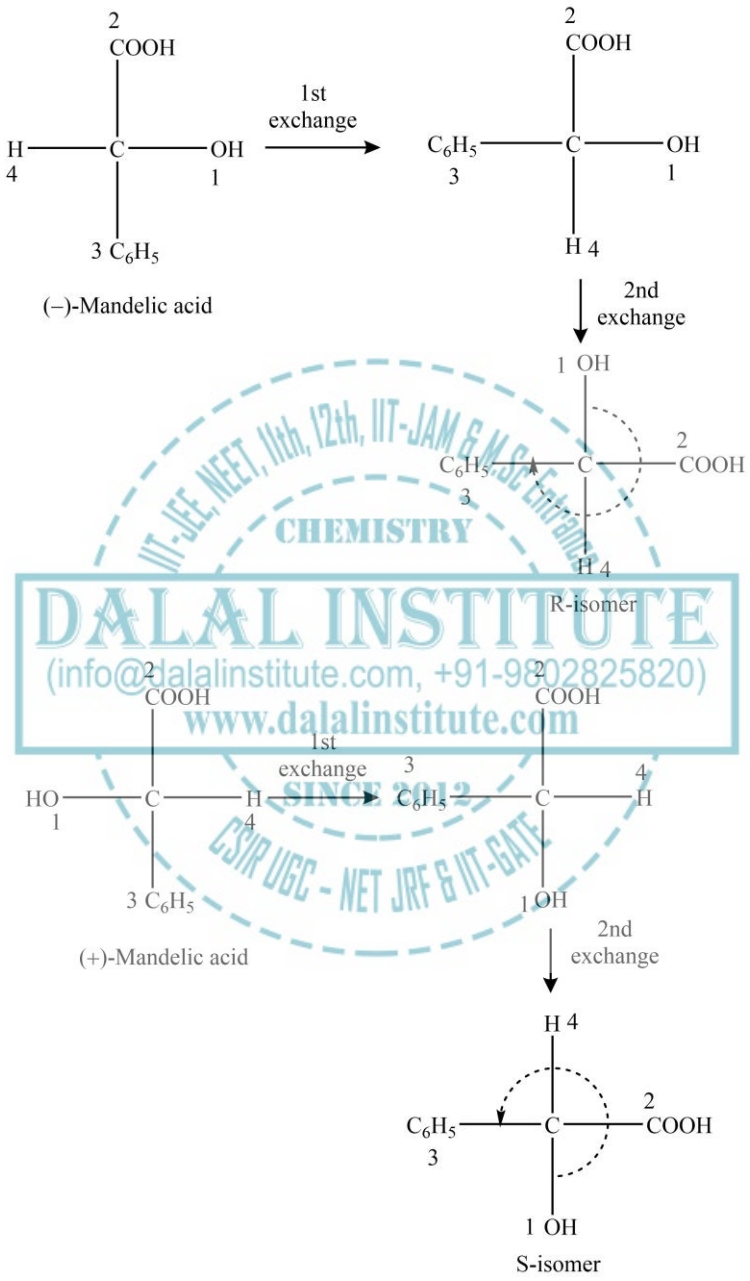
ii) Determination of absolute configuration of alanine:

As we know that alanine is optically active, and therefore, is bound to exist as enantiomeric pair. The absolute configuration of both enantiomers can be obtained as given below.



ii) Determination of absolute configuration of Mandelic acid:

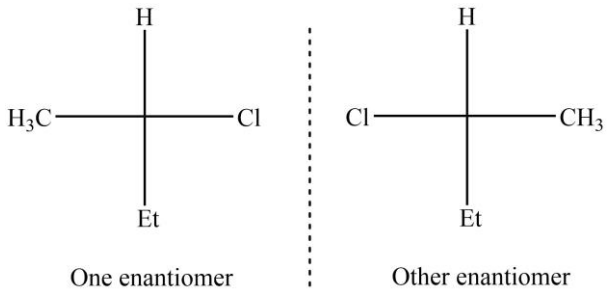
As we know that mandelic acid is optically active, and therefore, is bound to exist as enantiomeric pair. The absolute configuration of both enantiomers can be obtained as given below.



It is also worthy to note that *R*- and *S*-configuration are not bound to be dextro- or levorotatory in particular; in other words, *R*-configuration can be dextro-, as well as levorotatory. If R is dextro-, *S*-configuration will be levorotatory, and if *R* is levorotatory, *S*-configuration will be dextrorotatory.

❖ Methods of Resolution

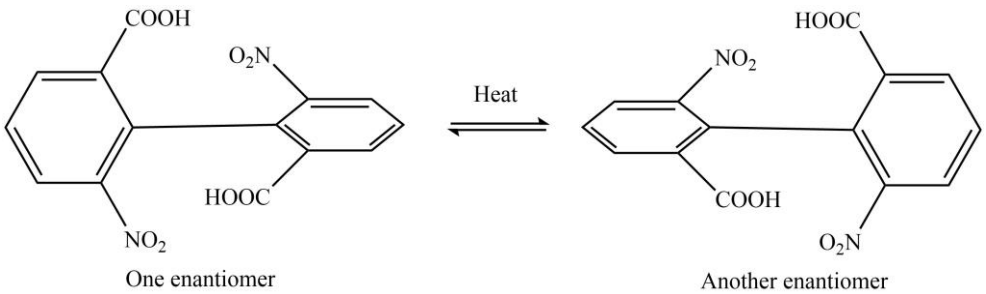
If the amount of laevorotatory and dextrorotatory enantiomers of a chiral molecule are equal in a solution, it will be called as a racemic mixture or racemate. One of the first racemic mixtures known was racemic acid, which is a mixture of the two enantiomeric forms of tartaric acid. A solution with only one enantiomer is called an enantiomerically pure or simply the enantiopure compound.



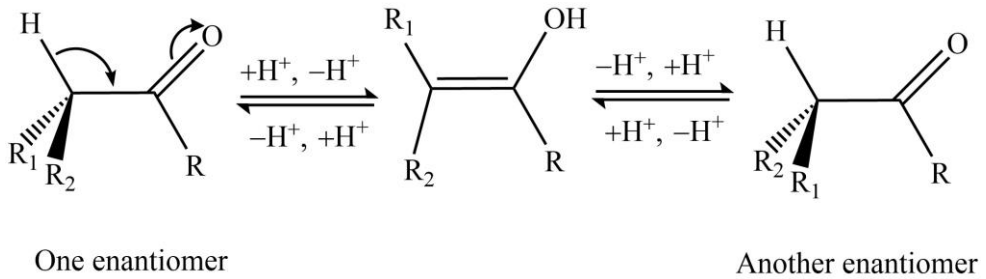
➢ *The Phenomenon of Racemization*

The phenomenon of racemization in most of the organic compounds can take place via the mechanisms given below.

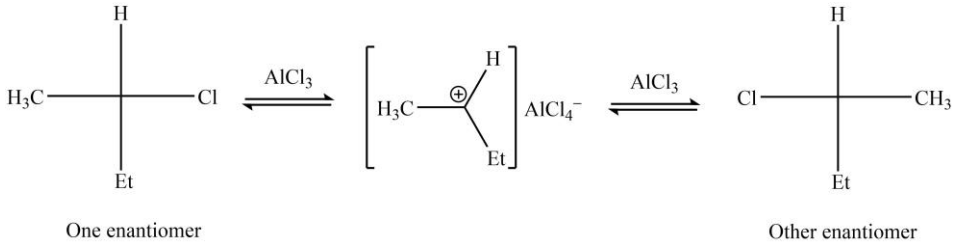
1. By the rotation about carbon-carbon single bond: When an enantiomer of optically active biphenyl derivative is heated, some of it can easily be converted into another enantiomer just by the rotation about carbon-carbon single bond.



2. By the phenomenon of enolization: When an enantiomer of optically active biphenyl derivative is heated, some of it can easily convert into another enantiomer just by the rotation about carbon-carbon single bond.

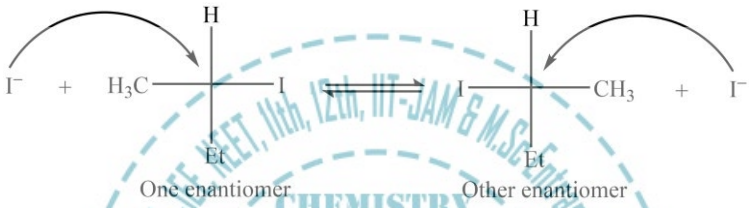


3. By SN_1 mechanism: The racemic mixture can also be obtained by subjecting an enantiomer in a typical SN_1 attack with the same nucleophile.



One enantiomer Other enantiomer

4. By SN_2 mechanism: The racemic mixture can also be obtained by subjecting an enantiomer in a typical SN_2 attack with the same nucleophile.



One enantiomer Other enantiomer

➢ ***The Resolution of Racemic Mixture***

The process of getting individual enantiomers from a typical racemic mixture by any physical or chemical route is called as the resolution of racemic mixtures. Some methods of resolution are given below.

1. Mechanical separation: This is the most popular and easy method to resolve an enantiomeric mixture into it components. This method involves the hand-picking of single crystals of R and S enantiomers using tweezers and a magnifying glass.

2. Chemical method: We know that enantiomers have the same physical properties but different chemical properties towards chiral reagents and differences in physical properties must be used for the act of separation. Therefore, is very much favorable to convert the enantiomers into corresponding diastereomers, which in turn, can be converted into corresponding enantiomers by using the difference between the physical properties.

3. Biochemical extraction: It is quite a well-known fact that many enantiomers are quite consumable by certain types of bacteria; and therefore, only one enantiomer of the racemic mixture will be left behind if the same is subjected to such conditions. For instance, penicillium glaucum eats (+)-tartaric acid leaving behind (+)-tartaric acid only. Now although the method is quite easy to follow, it suffers from the drawback of the destruction of almost half of the compound.

4. Chromatographic separation: The individual enantiomers of a racemic mixture can also be separated by employing the route of "column chromatography' when the adsorbent-taken is an optically active compound. Now since only one enantiomer will get attached strongly to the adsorbent, the elution of the column will result in the earlier extraction of weakly bound enantiomer.

❖ Optical Purity

Optical purity or the enantiomeric excess (ee) may simply be defined as the purity measurement used for chiral compounds and reflects the extent to which a sample contains one enantiomer in greater amounts than another enantiomer.

The enantiomeric excess of the racemic mixture 0%, whereas a single completely pure enantiomer has an enantiomeric excess of 100%. A sample having 60% of one enantiomer and 40% of the other has an ee of 20% (60% − 40%). The general expression for optical purity may be given by the following relation.

$$Optical\ purity = \%\ ee = \frac{\alpha_{obs}}{\alpha_{max}} = \frac{[R] - [S]}{[R] + [S]} \times 100 \tag{7}$$

Where α_{obs} and α_{max} are the observed angle of rotation of plane-polarized light by the racemic mixture under consideration and maximum angle of rotation that it could rotate when R is replaced by S enantiomer and vice-versa, respectively. The symbol $[R]$ and $[S]$ are simply the percentage of R and S enantiomer, respectively.

Furthermore, the percentage of major and minor enantiomers can be obtained if the enantiomeric excess is known as given below.

$$\%\ of\ major\ enantiomer = \frac{100 + \%\ ee}{2} \tag{8}$$

Similarly

$$\%\ of\ minor\ enantiomer = \frac{100 - \%\ ee}{2} \tag{9}$$

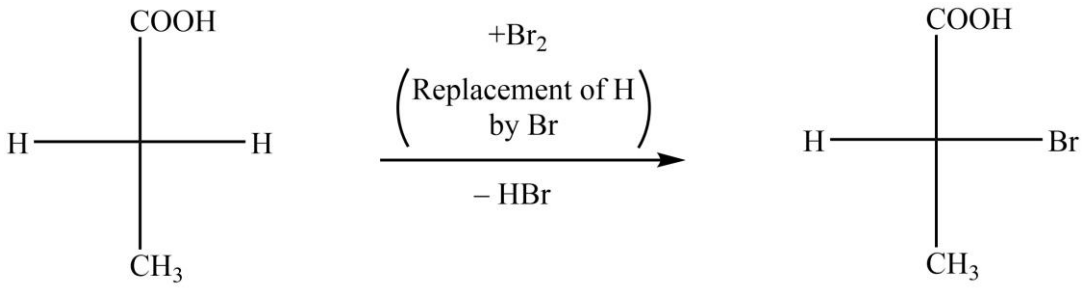
In an ideal situation, each component's contribution to the total magnitude of optical rotation is directly proportional to the corresponding mole fraction, and therefore, the optical purity should be identical to the enantiomeric excess. This gives rise to the informal usage of the two terms as interchangeable, especially due to the fact that optical purity was the conventional route of measuring enantiomeric excess. Nevertheless, other methods like NMR spectroscopy and chiral column chromatography are now quite popular for measuring the amount of each enantiomer separately.

The success of asymmetric synthesis is also quantified using enantiomeric excess. In the case of diastereomers mixtures, analogous definitions (diastereomeric excess) are employed for measurement. The term 'enantiomeric excess' was presented by Morrison and Mosher in 1971 in their paper entitled "Asymmetric Organic Reactions", indicating its historic ties with optical rotation. It has been proposed that the concept of 'enantiomeric excess' should be changed by that of 'enantiomeric ratio' which means S:R or S/R because the determination of optical purity has already been replaced by other experimental techniques which directly measure R and S for simplistic mathematical treatments. The same can be said for replacing the 'diastereomeric excess by 'diastereomeric ratio; though it seems very far from practice.

❖ Prochirality

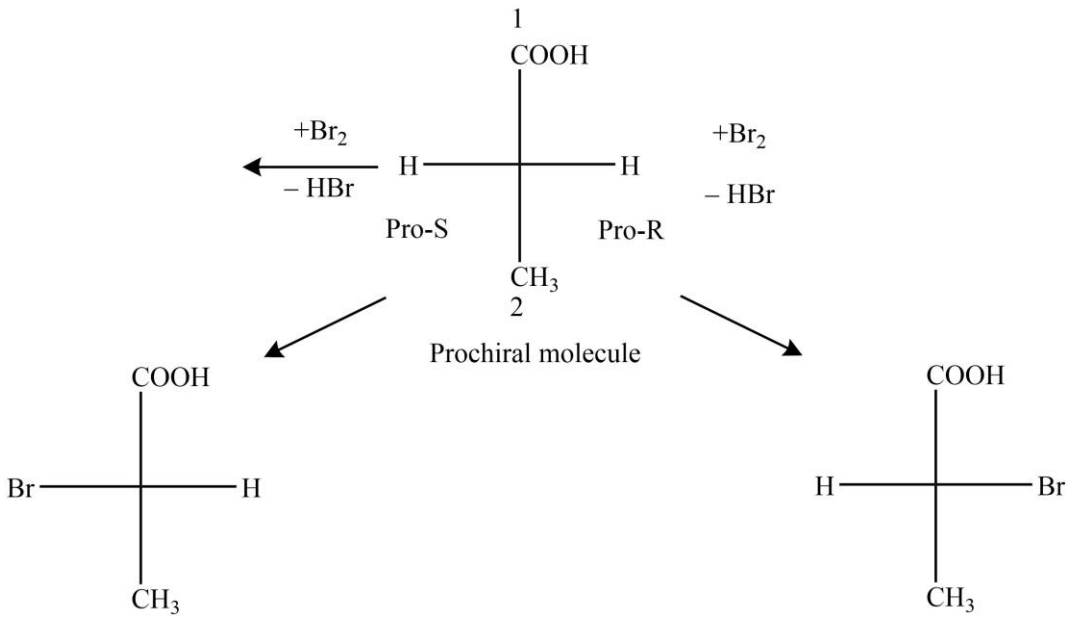
The prochirality in stereochemistry may simply be defined as the property of a molecule by which can be converted from achiral to a chiral entity in a single step, and such molecules are called as prochiral molecules.

This can be understood by taking the example of propanoic acid where two identical substituents are attached to an sp^3-hybridized carbon atom, and the pro-R and pro-S descriptors are used to differentiate between the two.



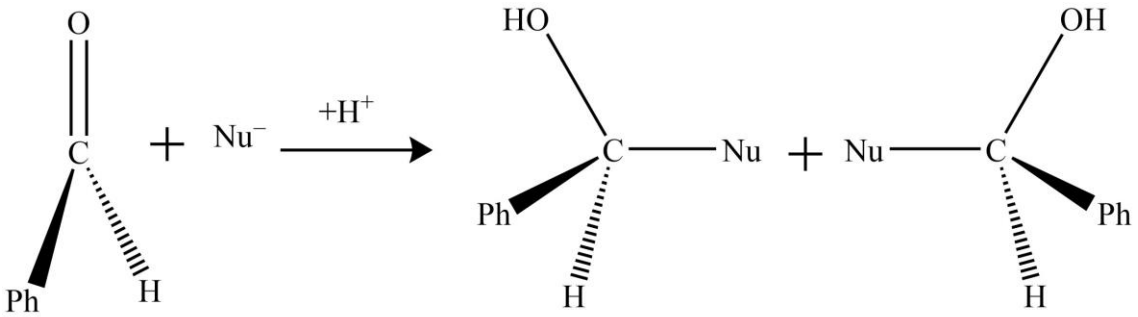
Prochiral molecule Chiral molecule

In other words, if we promote the pro-R substituent to a higher priority than the other identical substituent, we will get an R chirality center at the sp^3-hybridized carbon, and vice-versa is also true.



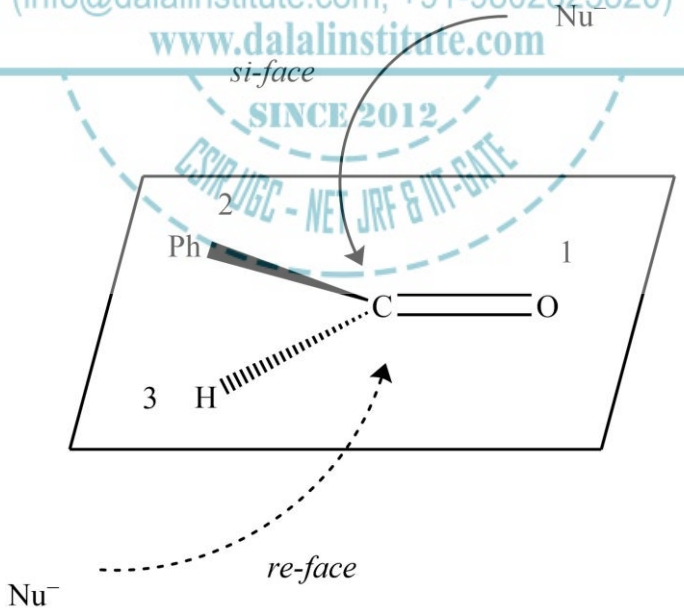
S-enantiomer R-enantiomer

An sp^2-hybridized carbon atom with trigonal planar coordination can also be converted to a chiral center if a group is attached to the '*re*' or '*si*' face of the organic molecule under consideration. For instance, imagine the case of benzaldehyde where the attack from the front and rear sides results in an enantiomeric pair.



Enantiomeric Pair

The face will be labeled '*re*' if the substituents priority decreases in clockwise order at the trigonal atom when looking at that face; the face will be labeled '*si*' if the substituents priority decreases in anticlockwise order at the trigonal atom when looking at that face. Also, the designation of the resulting optically active carbon as S or R is a function of the priority of the incoming substituent.



Furthermore, if an achiral species can be converted to a chiral one in two steps, it will be called a proprochiral. converted to a chiral one in two steps, it will be called a proprochiral.

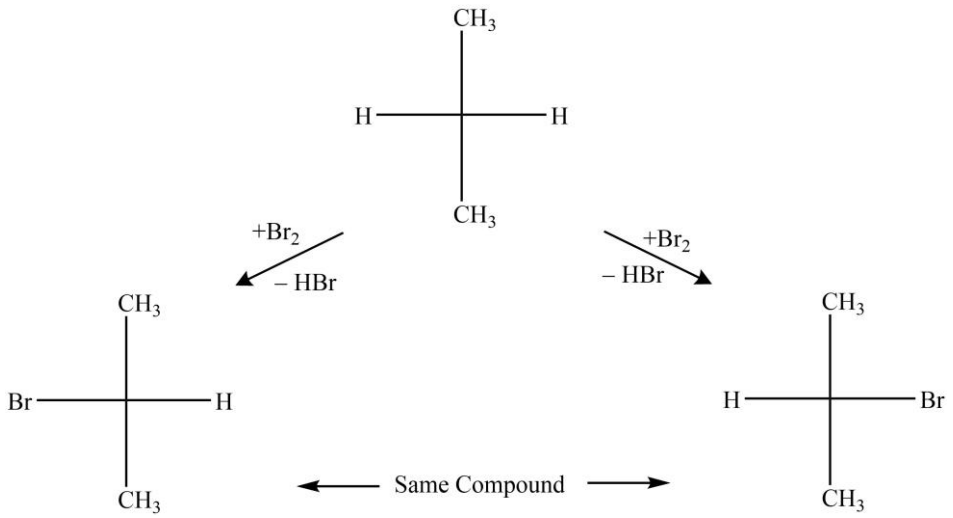
❖ Enantiotopic and Diastereotopic Atoms, Groups and Faces

The topicity in stereochemistry may simply be defined as the stereochemical relationship between substituents and the structure with which they are bonded. Based on such relationships, groups can be classified as homotopic, enantiotopic, or diastereotopic. A general discussion on these three types is given below.

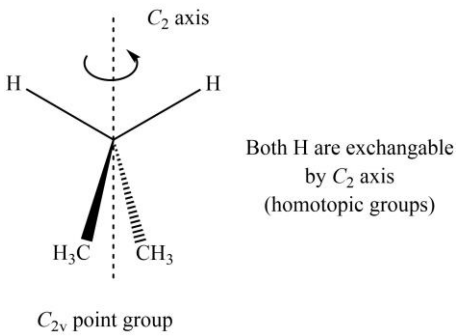
➢ *Homotopic Groups and Faces*

Homotopic groups and faces in an organic molecule can be found either based on chemical replacement or by using the symmetry criteria.

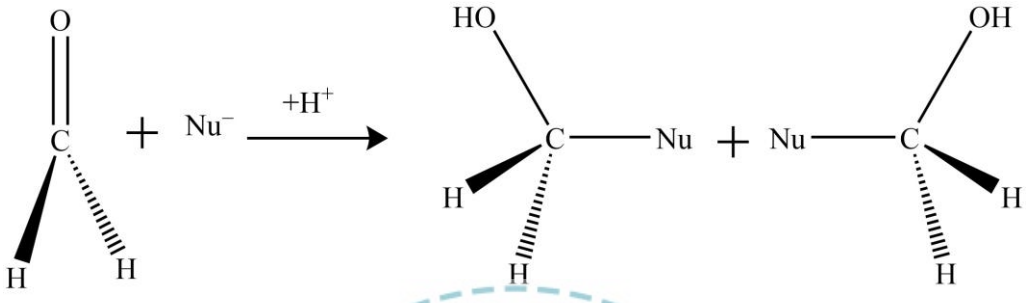
1. Homotopic groups: Homotopic groups in an organic molecule are equivalent groups. Two groups A and B are said to be homotopic if the resulting molecule remains the same (counting stereochemical notation also) when the groups are replaced with some other atom or group (such as bromine) whilst the remaining portion of the molecule is kept intact. Homotopic atoms or groups are always identical whether the environment is chiral or not. Also, NMR-active homotopic groups have the same chemical shift in NMR spectra. For instance, the four H of CH_4methane are homotopic, like two H or the two Cl groups in CH_2Cl_2).



On the basis of molecular symmetry, two groups are said to be homotopic in nature if they are exchangeable by a primary symmetry element i.e. proper axis of rotation (C_n).

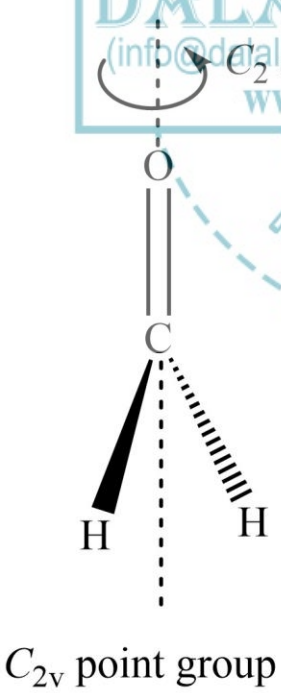


2. Homotopic faces: Homotopic faces in an organic molecule are equivalent faces, i.e., two faces A and B are homotopic if the molecule remains the same (including stereochemically) when the faces are attacked with some reagent (such as Cl^-) while the remaining parts of the molecule stay fixed. Homotopic faces are always identical, in any environment. For instance, two faces of methyl carbocation are homotopic, as the attack on two faces by an incoming nucleophile generates the same products.



Same compound

On the basis of molecular symmetry, two faces are said to be homotopic in nature if they are exchangeable by a two-fold axis symmetry (C_2).



C_{2v} point group

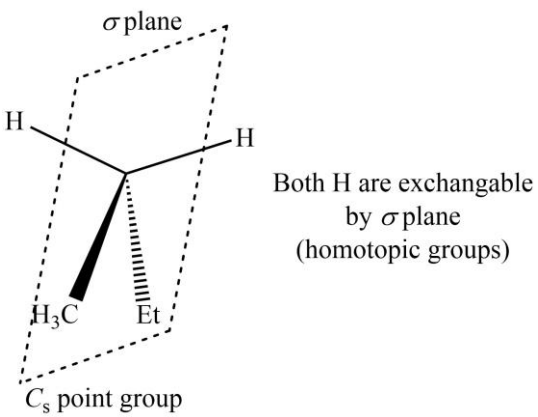
Both faces are exchangable by C_2 axis (homotopic groups)

➢ ***Enantiotopic Groups and Faces***

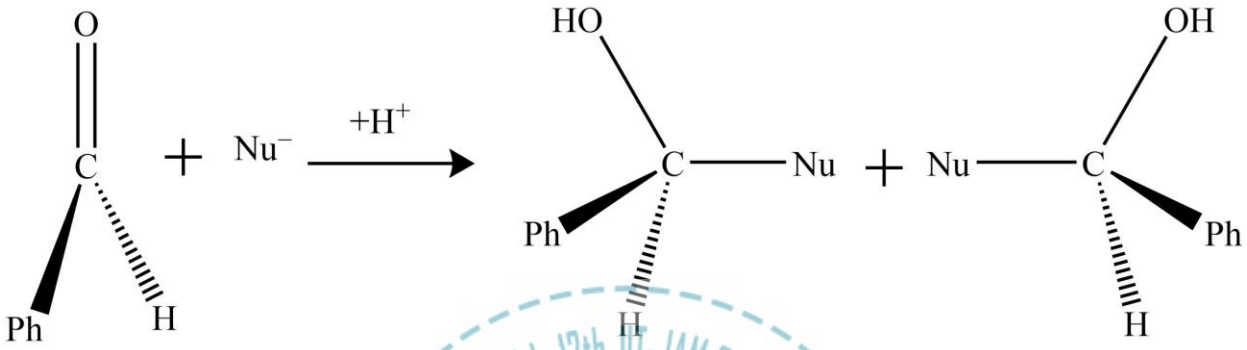
Homotopic groups and faces in an organic molecule can be found either on the basis of chemical replacement or by using the symmetry criteria.

1. Enantiotopic groups: Enantiotopic groups in a chemical compound are non-equivalent groups. Two groups A and B are enantiotopic if the enantiomers are obtained when the groups are interchanged with some other atom (such as bromine) while the remaining parts of the molecule stay fixed. Enantiotopic atoms are always identical in any achiral media while different in chiral media. Enantiotopic NMR-active nuclei have the same chemical shift in an NMR spectrum in achiral media and different chemical shifts in achiral media. For example, the two hydrogen atoms in CH_2ClBr are enantiotopic with one another, as the replacement by a third group gives rise to the enantiomeric pair.

On the basis of molecular symmetry, two groups are said to be enantiotopic in nature if they are exchangeable by a secondary symmetry element i.e. plane of symmetry (σ), the center of symmetry (*i*), or alternating axis of symmetry (S_n).

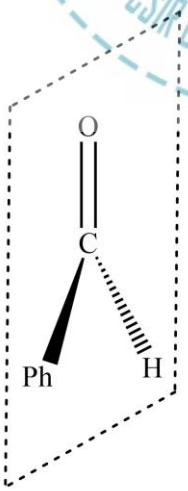


2. Enantiotopic faces: Enantiotopic faces in a chemical compound are non-equivalent faces, i.e., two faces A and B are enantiotopic if the molecule gives rise to enantiomeric pair when the faces are attacked with some reagent (such as Cl^-) while the remaining parts of the molecule stay fixed. Enantiotopic faces are always identical in the achiral environment and different in chiral media. For instance, two faces of primary carbocation are homotopic, as the attack on two faces by an incoming nucleophile generates enantiomeric pair.



Enantiomeric pair

On the basis of molecular symmetry, two faces are said to be enantiomeric in nature if they are exchangeable by a secondary symmetry element i.e. plane of symmetry (σ), the center of symmetry (i), or alternating axis of symmetry (S_n).



C_s point group

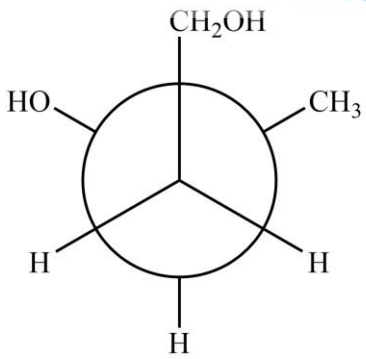
Both faces are exchangable by C_2 axis (homotopic groups)

➢ ***Diastereotopic Groups and Faces***

Diastereotopic groups and faces in an organic molecule can be found either on the basis of chemical replacement or by using the symmetry criteria.

1. Diastereotopic groups: Diastereotopic groups in a chemical compound are non-equivalent groups. Two groups A and B are diastereotopic if the diastereomers are obtained when the groups are interchanged with some other atom (such as bromine) while the remaining parts of the molecule stay fixed. Diastereotopic atoms are always different in any type of media whether it is chiral or achiral. Diastereotopic NMR-active nuclei have different chemical shifts in an NMR spectrum in any medium and different chemical shifts in achiral media. For example, the two hydrogen atoms in (Et)(OH)(Me)C–CH_2ClBr are CH2ClBr with one another, as the replacement by a third group gives rise to the diastereomeric pair.

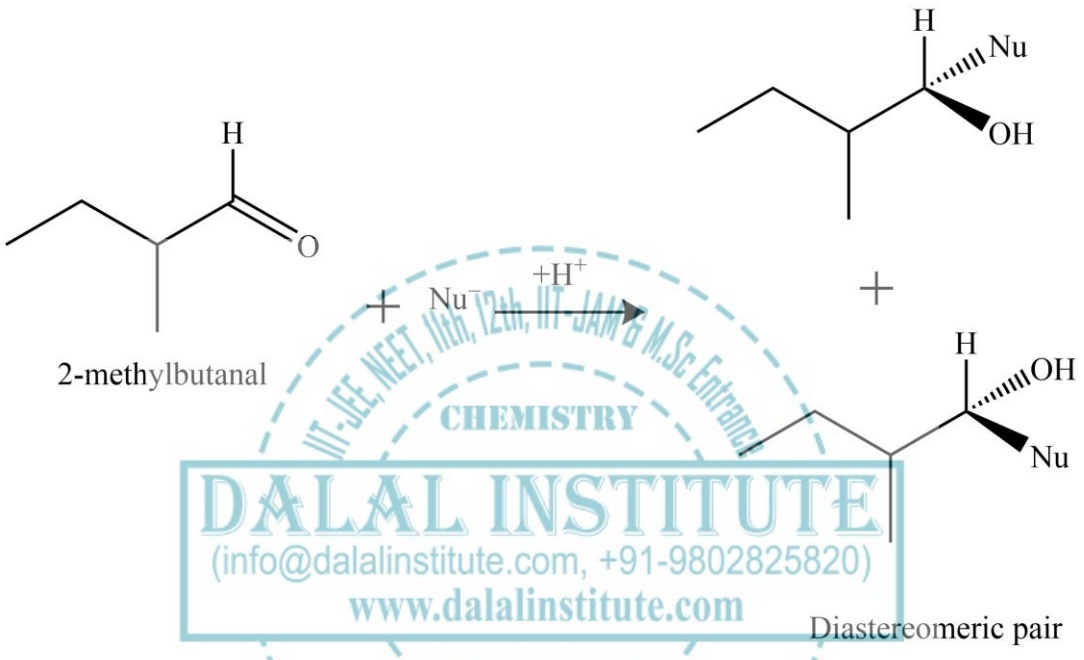
Based on molecular symmetry, two groups are said to be diastereotopic if they are not exchangeable by any symmetry element whether it is primary or secondary.



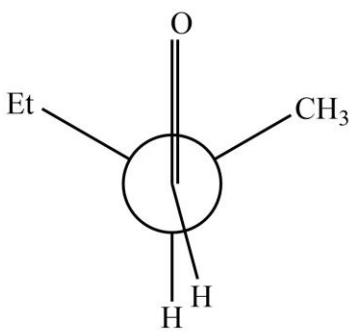
Both H are not exchangable by any symmetry element (diastereotopic groups)

C_1 point group

2. Diastereotopic faces: Diastereotopic faces in a chemical compound are non-equivalent faces, i.e., two faces A and B are diastereotopic if the molecule gives rise to diastereotopic pair when the faces are attacked with some reagent (such as Cl^-) while the remaining parts of the molecule stay fixed. Diastereotopic faces are always non-identical in any type of environment whether it is chiral or achiral. For instance, two faces of 2-methylbutanal are diastereotopic, as the attack on two faces by an incoming nucleophile generates diastereomeric pair.



On the basis of molecular symmetry, two faces are said to be diastereotopic in nature if they are not exchangeable by any symmetry element, i.e. neither by primary nor by secondary symmetry element.



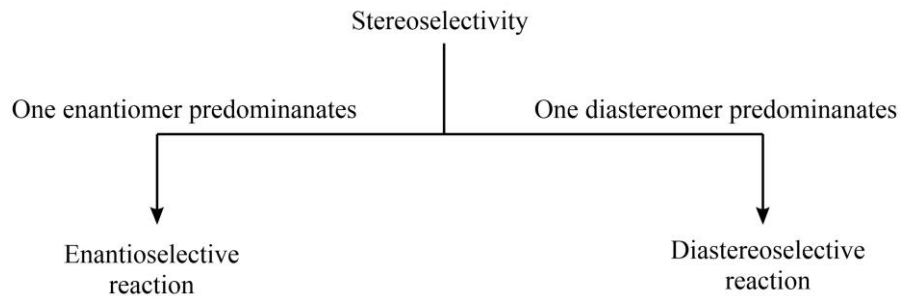
Both faces are not exchangable by any symmetry element (diastereotopic faces

C_1 point group

❖ Asymmetric Synthesis: Cram's Rule and Its Modifications, Prelog's Rule

Asymmetric synthesis or the stereoselective synthesis may simply be defined as the chemical synthesis in which one stereoisomer (enantiomer or diastereomer) is formed more predominantly than the other one, i.e. unequal amounts.

The phenomenon of stereoselectivity can primarily be classified into two categories; one as the enantioselective reactions and the other as the diastereoselective reactions. In enantioselective reactions, one enantiomer is formed in more amount than the other; whereas, in the case of diastereoselective reactions, the formation of one diastereomer dominates the other.



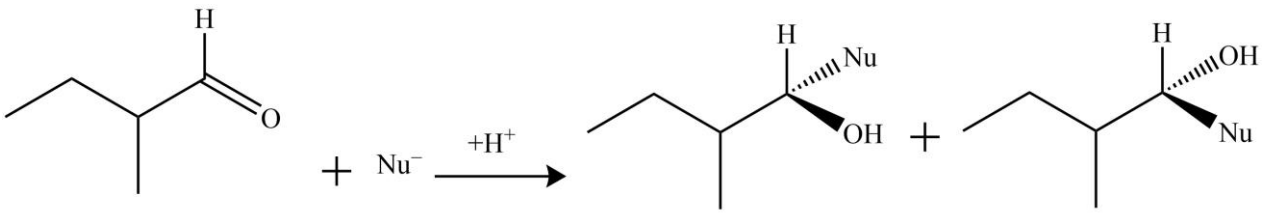
Now although the concept is quite wide and important, here we will only discuss the fundamental aspects of both types of stereoselective routes.

➢ *Diastereoselective Synthesis*

The diastereoselective synthesis may simply be defined as the chemical synthesis in which one diastereomer is formed more predominantly than the other one.

The diastereomer that will form in a higher amount can be predicted by Cram's rule in chiral ketones and by Prelog's rule in the case of chiral β-keto-esters.

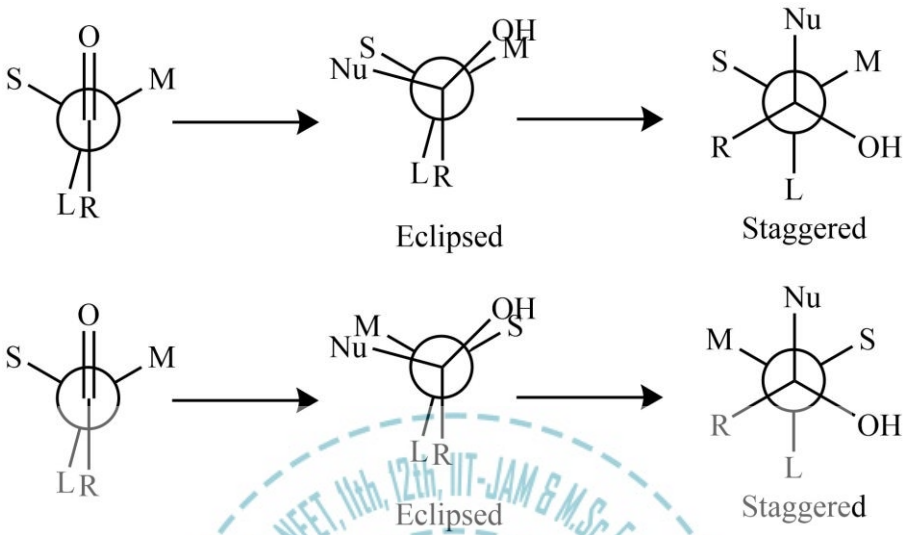
1. Cram's Rule: The Crams rule states that when the attacking group approaches the trigonal face of the double bond in a chiral ketone, it will prefer the side of the plane with a smaller group on the asymmetric carbon.



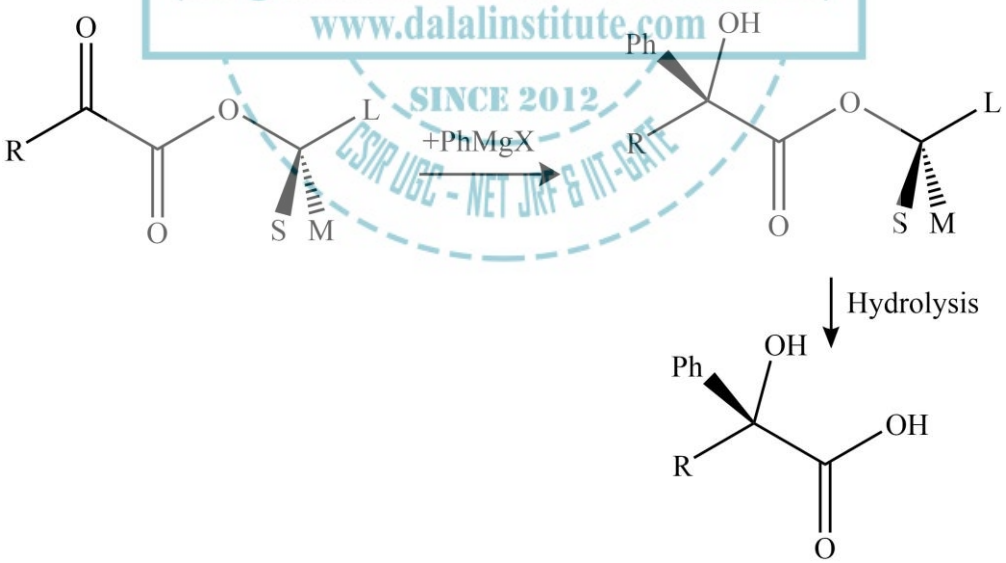
2-methylbutanal

Furthermore, it is also worthy to note that the reactive conformation will have the carbonyl group oriented between the medium and large group.

The modeling of the transition state of diastereoselective synthesis was also proposed by H. Felkin and N. Prudent and was different than the transition state given by the Cram as shown below.



2. Prelog's Rule: The extension of Cram's rule to rationalize the formation of unequal amounts of two diastereomers in the case of chiral α-keto-esters is called as Prelog's rule. This rule states that when the attacking group approaches the trigonal face of the double bond in a chiral α-keto-ester, it will prefer the side of the plane with a smaller group on the asymmetric carbon.

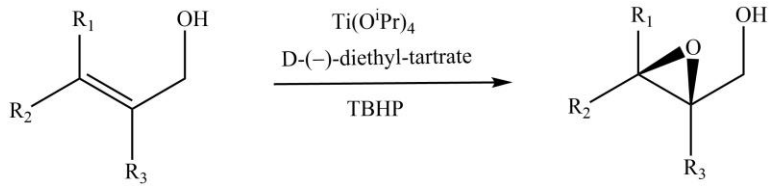


Furthermore, it is also worthy to note that the reactive conformation will have the carbonyl group oriented between the medium and large group.

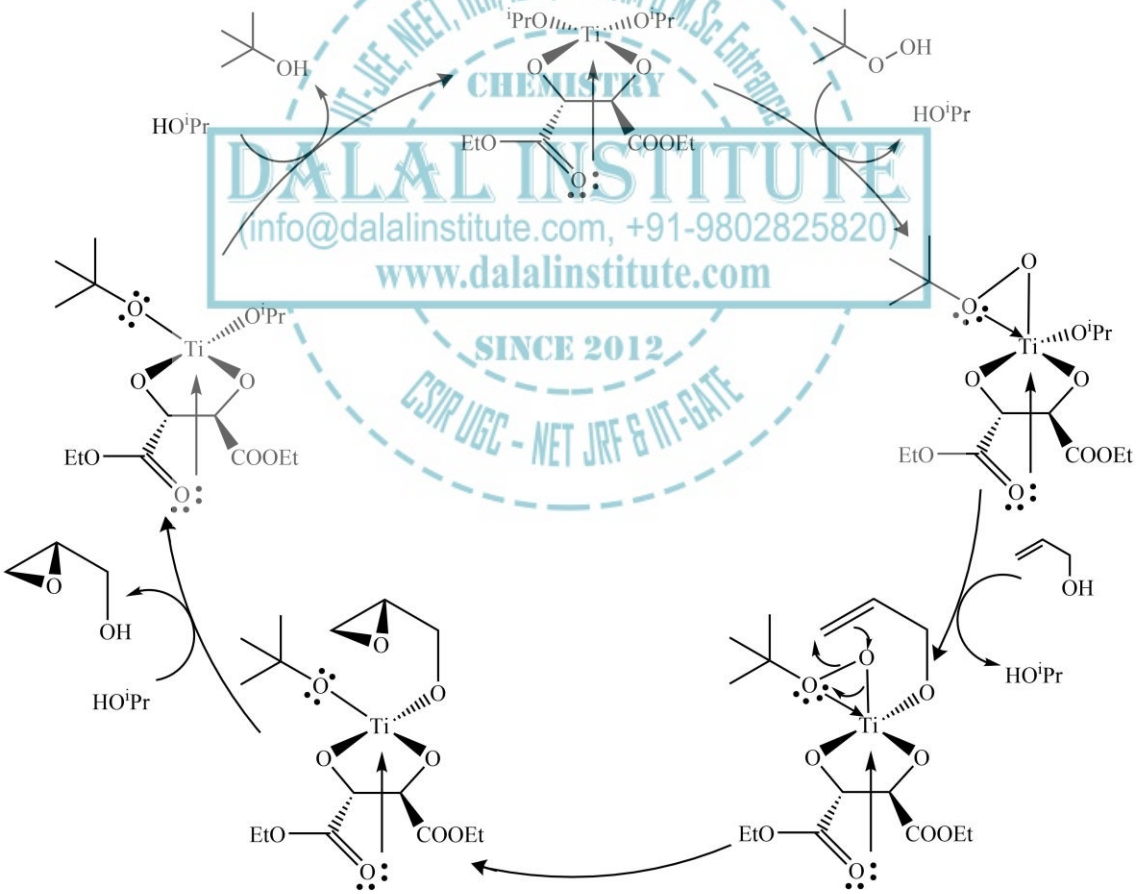
➢ ***Enantioselective Synthesis***

The enantioselective synthesis may simply be defined as the chemical synthesis in which one enantiomer is formed more predominantly than the other one.

The enantiomer that will form in a higher amount can be predicted by the attacking group itself. One of the most common examples to demonstrate the concept of enantioselective reactions is Sharpless asymmetric epoxidation in which allyl alcohols are converted into epoxy alcohols via a complex cycle.

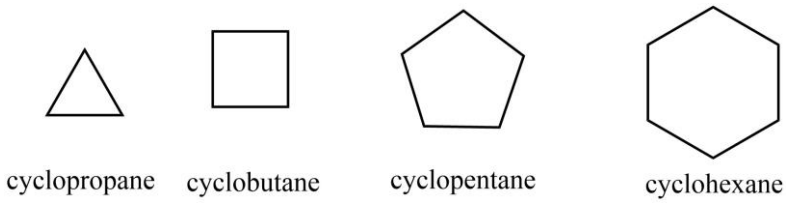


The typical catalytic cycle of the Sharpless asymmetric epoxidation is shown below.



❖ Conformational Analysis of Cycloalkanes (Upto Six Membered Rings)

Most of the cyclic compounds can be categorized on the basis of the number of atoms participating in the cyclic skeleton and their special properties. Rings with 3 or 4 atoms are quite rigid and extremely strained because of their large deviation from the normal tetrahedral angle (109°28') which gives rise to a very high angle strain and the presence of a very large magnitude of torsional strain as well.

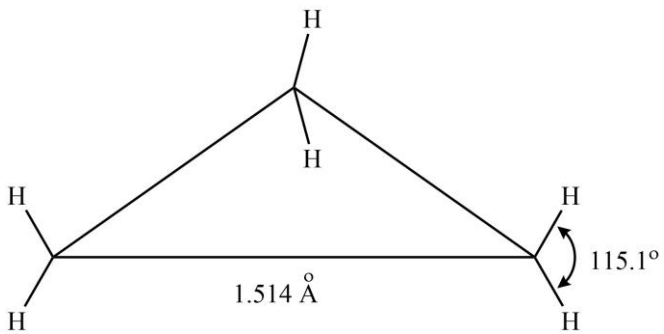


cyclopropane cyclobutane cyclopentane cyclohexane

Most common rings have 5–7 members and can be characterized by the normal tetrahedral angles and groups oriented outward from the cycle. Rings with 8–11 members are labeled as medium rings and can be characterized by transannular interactions which is a strain produced by groups pointing inward from the cycle. Furthermore, if the number of atoms is equals to or greater than 12 (large rings), very low strain exists and such rings are pretty much comparable with the corresponding acyclic hydrocarbons. In this section, we will discuss the conformational analysis of cycloalkanes up to six-membered rings.

➢ *Conformations of Cyclopropane*

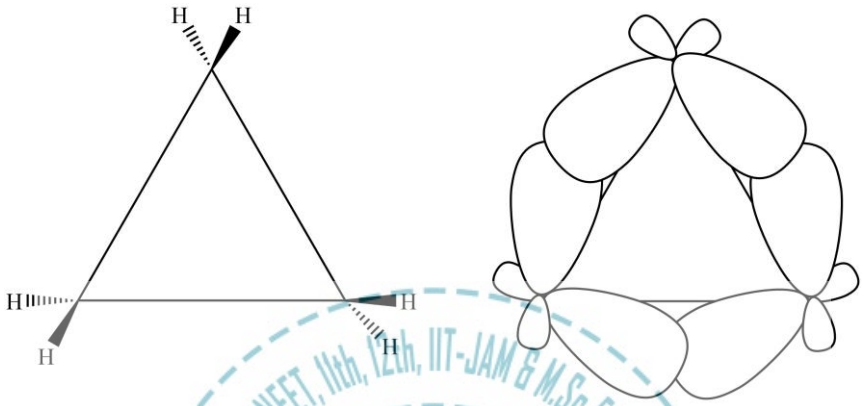
Cyclopropane is a kind of cycloalkanes with C_3H_6 as the molecular formula and is consisted of three carbon atoms that are connected with each other to give a cyclic structure. Each carbon atom is also bound with two hydrogens symmetrically so that the point group becomes D_{3h}. There is a huge ring strain in the cyclopropane due to its smaller size.



cyclopropane

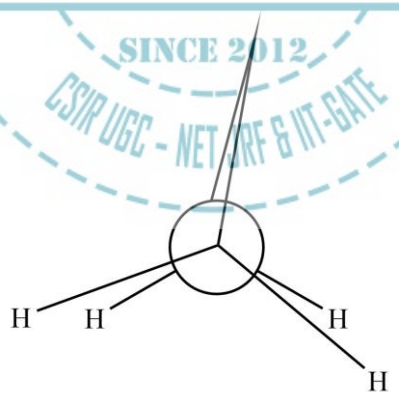
The trigonal structure of cyclopropane needs the carbon-carbon bond angles to be at 60°; however, it is much smaller than the ideal bond angle of 109.5° (most stable thermodynamically and is generated for bonds with sp^3 hybridized orbitals) and gives rise to the large magnitude of ring strain.

The cyclopropane molecule also possesses a very high torsional strain arising from the eclipsed conformation of its H atoms. Per se, the bonds between the C atoms are significantly weaker than in an archetypal alkane, giving rise to much higher reactivity in this case. Also, the nature of bonding between the carbon atoms is usually described in terms of bent or banana bonds, where the carbon-carbon bonds are bent outwards so that the inter-orbital angle becomes equal to 104°.



Banana bonds in cyclopropane

All this decreases the magnitude of bond strain and is obtained by distorting the sp^3 hybridized orbitals of carbon atoms to theoretically an sp^5 hybridized orbitals (i.e. 1⁄6 contribution of s orbital and 5⁄6 contribution of *p* orbital) so as to make C-C bonds have more π-character than usual (and giving s-character same time the carbon-to-hydrogen at the more bonds gain).

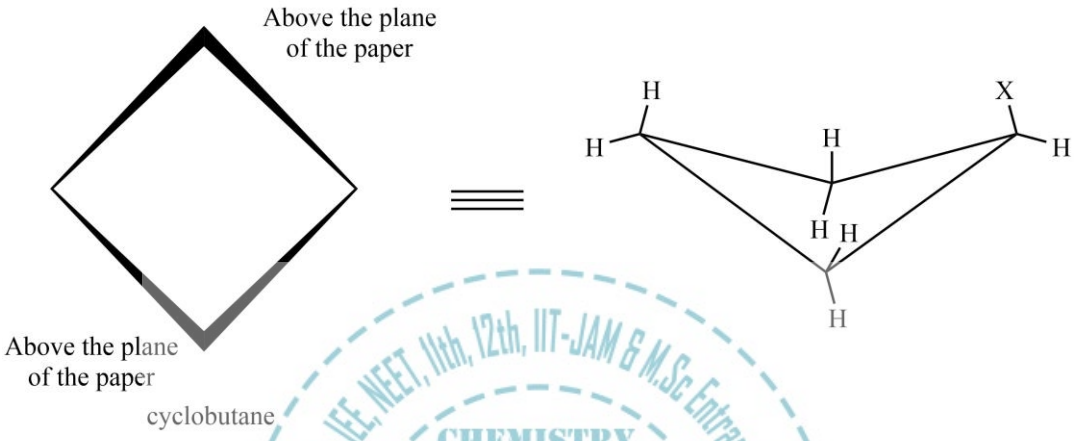


Newman projections of cyclopropane

One uncommon consequence of bending of bonds is that while the C–C bonds in cyclopropane are weaker than usual, the C atoms are also closer together than in a normal alkane bond: 151 pm versus 153 pm, when the average alkene bond length is about 146 pm.

➢ ***Conformations of Cyclobutane***

The angles between carbon-carbon bonds in cyclobutane are quite strained, and therefore, have lower bond dissociation energies than corresponding unstrained or linear hydrocarbons like cyclohexane or butane. Furthermore, the cyclobutane molecule is very unstable above 500 °C. As far as the structure is concerned, four carbons in cyclobutane are not in a single plane but adopts a puckered or somewhat "folded" conformation.



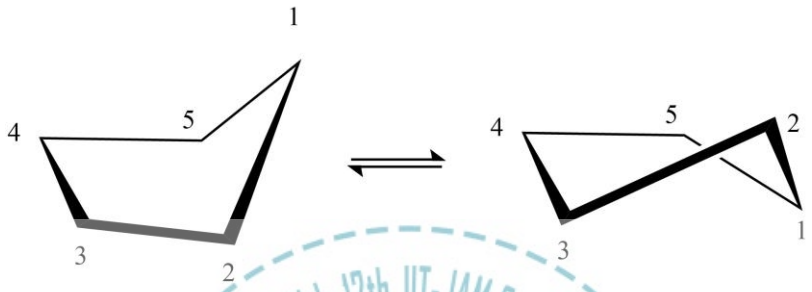
Any single carbon also has an angle of 25° with the plane of the remaining three carbon atoms. Like this, some of the interactions due to eclipsing are also diminished.

Newman projections of cyclobutane

The conformation of cyclobutene is also known as the "butterfly" structure. Furthermore, it is also worthy to note that equivalent puckered conformations of cyclobutene interconvert within each other at room temperature due to an appropriate supply of thermal energy.

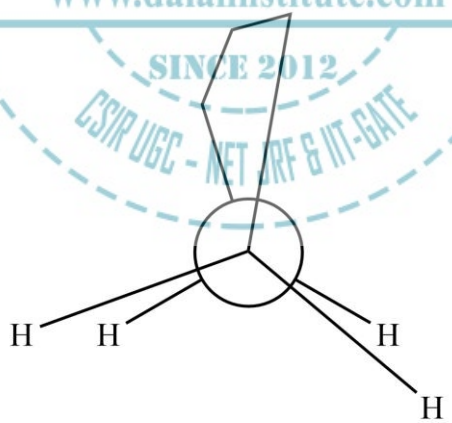
➢ ***Conformations of Cyclopentane***

The cyclopentane is the second-most common cycloalkane (after cyclohexanes) and stabler than cyclobutanes. Its planar conformation has almost zero angle strain but a huge magnitude of torsional strain resulting in a non-planar conformation, which in turn, actually increases angle strain slightly but still favorable due to stability from reduced torsional strain. The cyclopentane undergoes a rapid bond rotation process At room temperature where every carbon has its turns of being at the endo site eventually.



Conformational equilibrium of cyclopentane

The 'envelope' conformation (left) of cyclopentane is of the lowest energy where the out-of-plane carbon (i.e., 1 in the left side structure) is said to be in the 'endo or inside' site. The enveloping eliminates the torsional strain along the sides and the envelope's flapping happens. Nevertheless, the neighboring C atoms are eclipsed at the envelope's plane and are situated away from the fold.

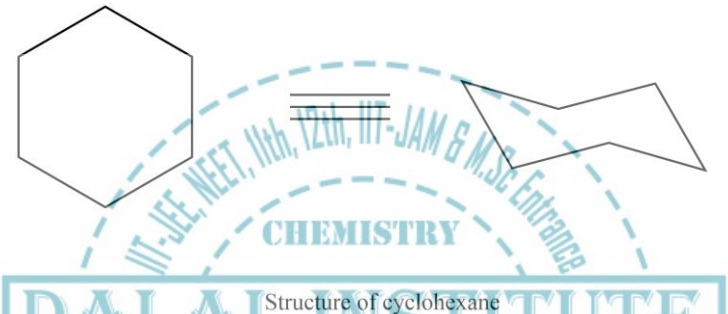


Newman projections of cyclopentane

Furthermore, if we view Newman's projection of cyclopentane molecule signed down one of the carbon-carbon bonds reveals the staggering nature of carbon-hydrogen bonds.

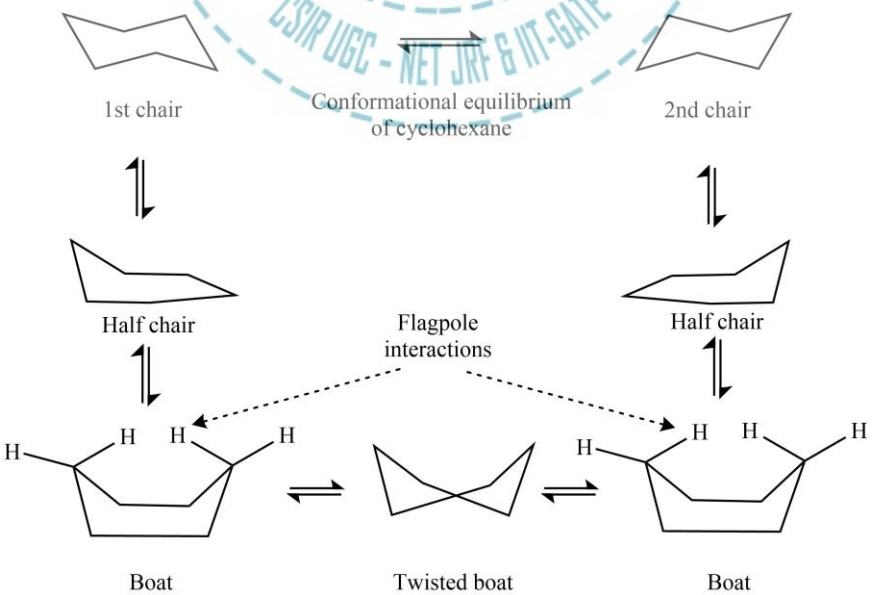
➢ ***Conformations of Cyclohexane***

Many students confuse the polygon formula of cyclohexane molecule with its actual structure and assume that it must be planar. Nevertheless, its structure is far from a perfect hexagon because the conformation of a flat 2-dimensional planar hexagon would have a huge magnitude of angle strain. After all, its carbon-carbon bonds would not be at the ideal tetrahedral angle (i.e., 109.5°). Furthermore, the torsional strain would also be of significant magnitude in hexagonal structure because all of the bonds would be of eclipsed type. So, to decrease torsional strain, the cyclohexane adopts a 3-dimensional geometry (chair form), which interconvert at room temperature very rapidly via the chair flipping mechanism during which 3 other intermediate conformations are met: the first one is the half-chair (most unstable), a more stable boat conformation, and the third one is the twist-boat (more stable than the boat but less stable than the chair form).



Structure of cyclohexane

In the potential energy diagram, the half-chair and the boat are at transition states and signify energy maxima whereas the chair form and twist-boat form are at energy minima inferring their conformer nature. The chair conformation was first suggested by Hermann Sachse in 1890 which gained acceptance at a widespread level in the later period.



In the chair form, the carbon-carbon bond angles become 109.5°, and therefore, the angle strain was completely eliminated. Also, six out of twelve hydrogens were parallel to the principal axis (C_3-axis), and are called axial hydrogens; whereas the remaining hydrogens are at higher angles from the principal axis imparting the label of equatorial hydrogens.

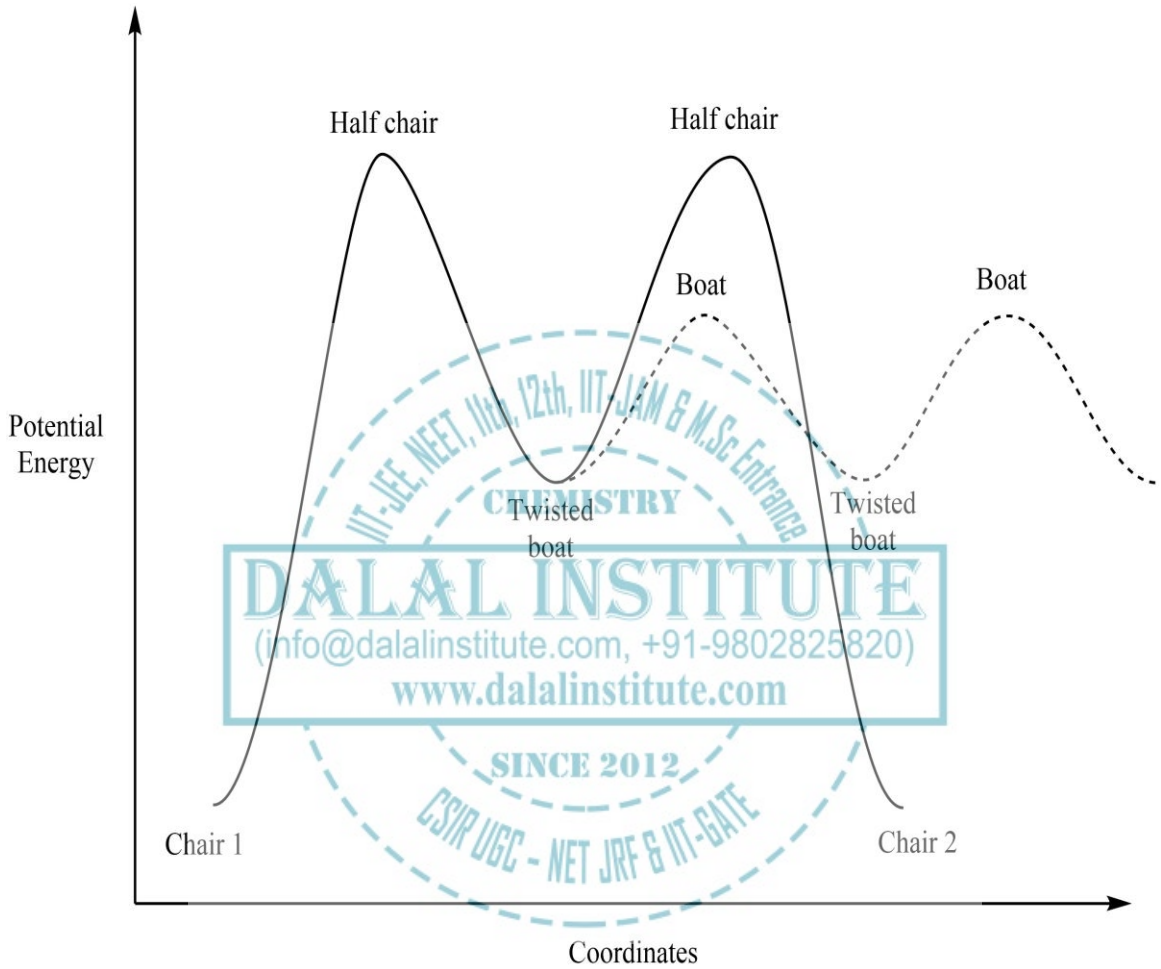


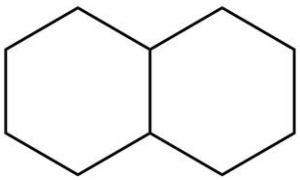
Figure 1. Potential energy diagram for different conformations of cyclohexane molecule.

Another important confirmation of cyclohexane molecule is known as the boat form which also gets interconverted to the more stable chair form. Furthermore, if the mono-substitution occurs at cyclohexane, it will most likely happen at the equatorial site because of the less torsional strain. Finally, the cyclohexane molecule has the lowest magnitude of torsional and angle strain of all cycloalkanes available making the cyclohexane a strain-free system.

❖ Decalins

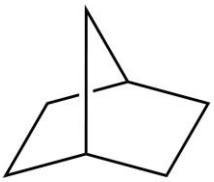
If two cyclic compounds are fused together, we will get a bicyclic system. These bicyclic compounds can be either bridged or fused systems. Two cycles share two adjacent C atoms in a fused system, whereas one or more carbon atoms act as a bridge between two non-adjacent carbon atoms in bridged systems. Here we will study one special kind of fused ring system called decalin or bicyclo-[4,4,0]-decane.

Fused bicyclo compound



Bicyclo-[4,4,0]-decane
(Decalin)

Bridged bicyclo compound

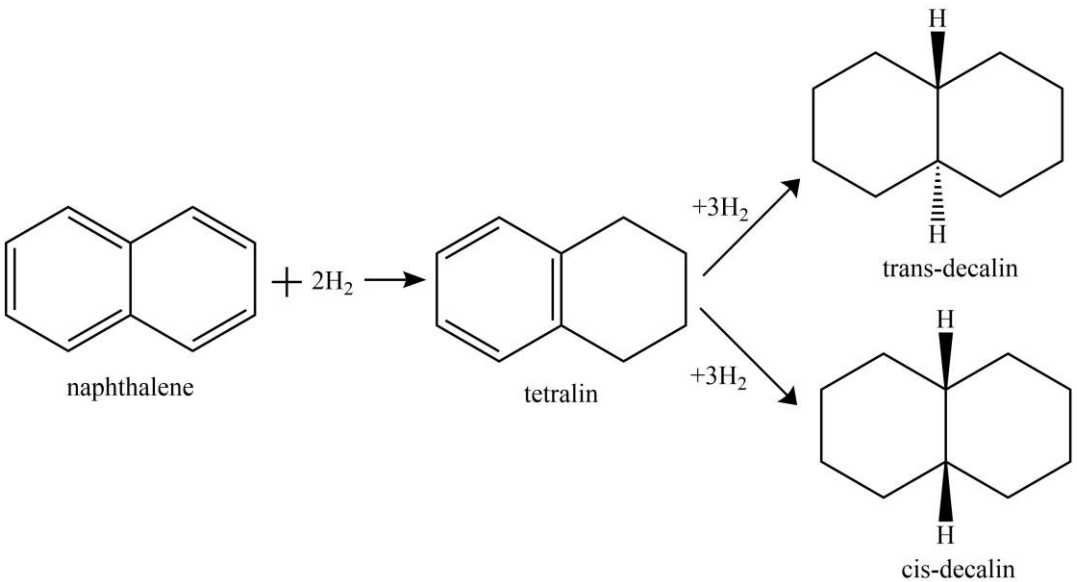


Bicyclo-[2,2,1]-heptane
(Norbornane)

Also, as far as the IUPAC name of decalin is concerned i.e. bicyclo-[4,4,0]-decane, the numbers 4, 4, 0 show the number of C atoms in each cycle (excluding the bridgehead carbon atoms).

➢ *Synthesis of Decalin*

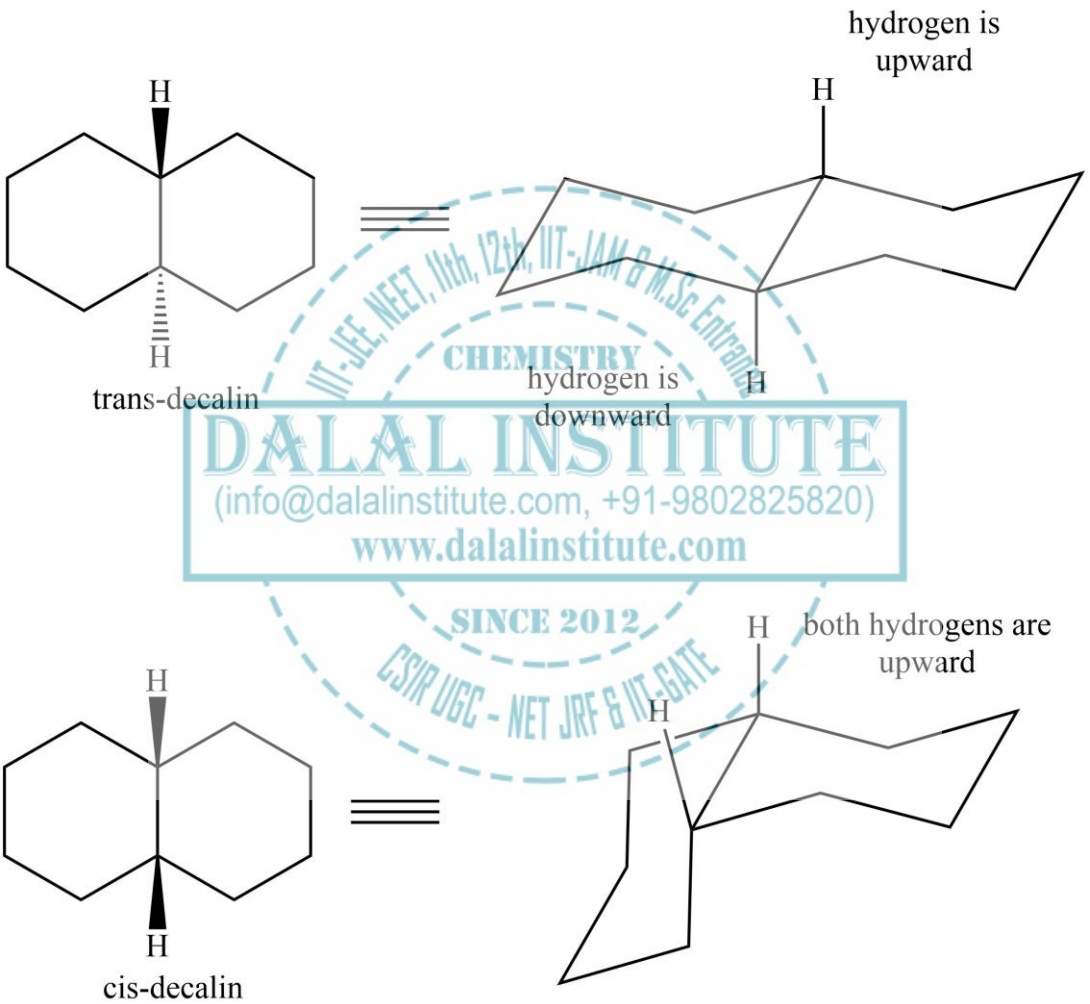
One of the most popular names of Decalin is decahydronaphthalene because it is a saturated counterpart of naphthalene molecule, and can also be obtained from the same by simple hydrogenation in a fused state.



The preparation gives two stereoisomers of decalin; where the first have both the hydrogens at the bridgehead carbons at 'cis' arrangement and trans hydrogens in the second one.

➢ ***Geometrical Isomerism in Decalin***

Since there are two cyclohexane rings fused in decalin, and those cyclohexenes are most stable in their chair form; it is reasonable to think that most stable should also have them in chair form. Using the same rationale, Sachse and Mohr proposed the decalin should be a puckered structure with no strain which exists as two isomers that cannot be interconverted without any bond-breaking. And therefore, they must be treated as diastereomers or configurational isomers. Both the puckered structures of decalin (cis and trans isomers) are shown below.



Now because both the stereoisomers have cyclohexane chairs, there should be no torsional or angle strain in either decalin molecule. It is also obvious that the two bridgehead hydrogens in trans decalin are directed in opposite directions, and therefore, both are axial hydrogens. Conversely, the two bridgehead hydrogens in cis decalin are pointing in the same direction with one axial and other of equatorial nature.

➢ ***Conformational Analysis of Decalin***

After studying the geometrical isomerism in decalin, we need to discuss the conformational behavior of the same in a more comprehensive and sophisticated way. To do so, we will first discuss the ring flipping in trans and cis-decalin one by one.

1. Ring flipping in trans-decalin: The two cyclohexane rings in trans decalin are connected via equatorial positions. Since we know that the flipping of the ring in cyclohexane converts all the axial bonds to equatorial bonds and the vice-versa is also true, the flipping of the ring in trans-decalin would give a conformation where the two cyclohexane units would be connected via axial bonds. Nevertheless, this ring flipping is strongly forbidden because it is not conceivable to build a 6-membered ring with two diagonally opposite bonds. We are bound to fail if we attempt to build a molecular model in which the cyclohexane units are connected via axial bonds.

Hence, we may conclude that the trans-decalin is actually 'conformationally locked' making ring flipping impossible. So, it keeps its equatorial confirmation for both the rings. Also, e,e-trans-decalin has an inversion center, and therefore, it is an optically inactive or achiral compound. In other words, trans-decalin is superimposable on its mirror image. There are also two C_2 symmetry axes, the first one through the equator and the other one passes through the axis.

2. Ring flipping in cis-decalin: Unlike trans-decalin, which is relatively flat, the cis-decalin resembles a tent-like geometry with less hindered (convex)and more hindered (concave) sides. Though in both cases the cyclohexanes are stable chair-like conformations, the cis decalin has them with equatorial and axial bond joining. The flipping of the ring is allowed in this situation which changes one cis form into another one and translates the equatorial bonds to axial ones.

The conformational study of cis-decalin also proved that it is an optically active or chiral molecule even if it has no chiral center. In other words, the cis-decalin cannot be superimposed on its mirror image. Nevertheless, a rapid flipping of the ring system cancels its optical activity and changes it into its mirror image. Consequently, we can not resolve the two chiral forms due to this rapid ring inversion, and it exists as a racemic mixture. The flipping of the ring in cis-decalin has also been supported by the NMR studies proving that only one peak H-NMR spectra; whereas, two proton peaks are observed in trans decalin. Two H-NMR peaks in the spectra of trans-decalin can be credited to its inflexibility. The equatorial and axial hydrogens are present in different chemical, as well as magnetic environments, and therefore, show the different magnitude of chemical shifts. On the other hand, the cis-decalin is able of very fast interconversion resulting in a single chemical shift for all the hydrogens.

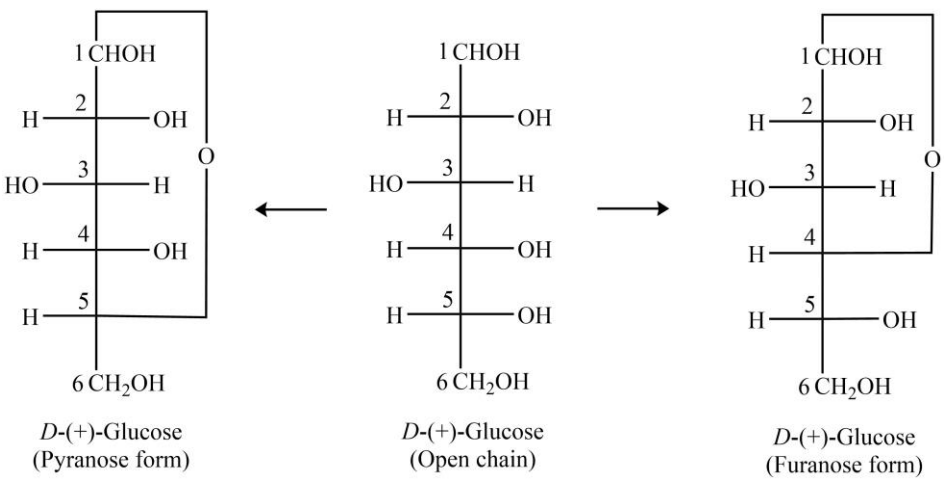
❖ Conformations of Sugars

It is quite a well-known fact that carbohydrates can primarily be classified into three categories; monosaccharides, oligosaccharides, and polysaccharides. The monosaccharides are the simplest carbohydrates that cannot be further hydrolyzed to simpler molecules. The general formula of monosaccharides is $(CH_2O)_n$ where n = 3–8. The oligosaccharides are the carbohydrate molecules that can produce 2–10 molecules of monosaccharides. Polysaccharides are carbohydrate molecules that can produce a very large number of monosaccharides' molecules upon hydrolysis.

Furthermore, in addition to the number of hydrolysis produce, the carbohydrates can also be classified on the basis of their taste. It has been found that all the monosaccharides and oligosaccharides (dia-, tri-, tetra-saccharides etc.) are crystalline compounds, soluble in water and sweet in taste; and typically labeled as sugars. On the other hand, polysaccharides are amorphous compounds, insoluble in water, and don't have any taste; and therefore, these carbohydrates are typically called as non-sugars. In this section, we will discuss the conformation of different types of sugars i.e. monosaccharides and oligosaccharides. The term "conformation" here refers to the overall three-dimensional structure adopted by a sugar (saccharide) molecule as a result of the through-bond and through-space physical forces it experiences arising from its molecular structure. The physical forces that dictate the three-dimensional shapes of all sugar molecules are sometimes summarily captured by such terms as "steric interactions" and "stereoelectronic effects".

➢ *Conformation of Monosaccharides*

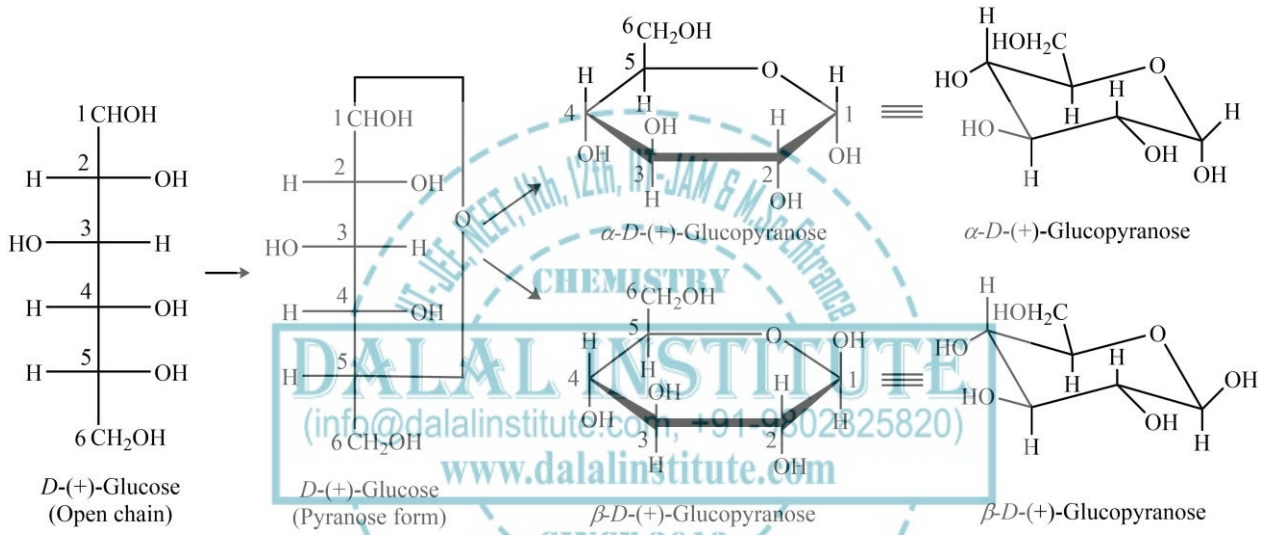
In 1883, Tollan proposed that the glucose molecule does not have a free aldehydic group but a cyclic structure via a hemiacetal carbon. The thought that the terminal aldehydic carbon may participate in hemiacetal formation by using the hydroxyl group of 4th carbon in open-chain glucose molecule, giving rise to a five-membered furan-like ring structure. Later on, in 1926, Haworth proposed that the formation of hemiacetal carbon takes place via 5th carbon, giving rise to a six-membered pyran-like ring structure.



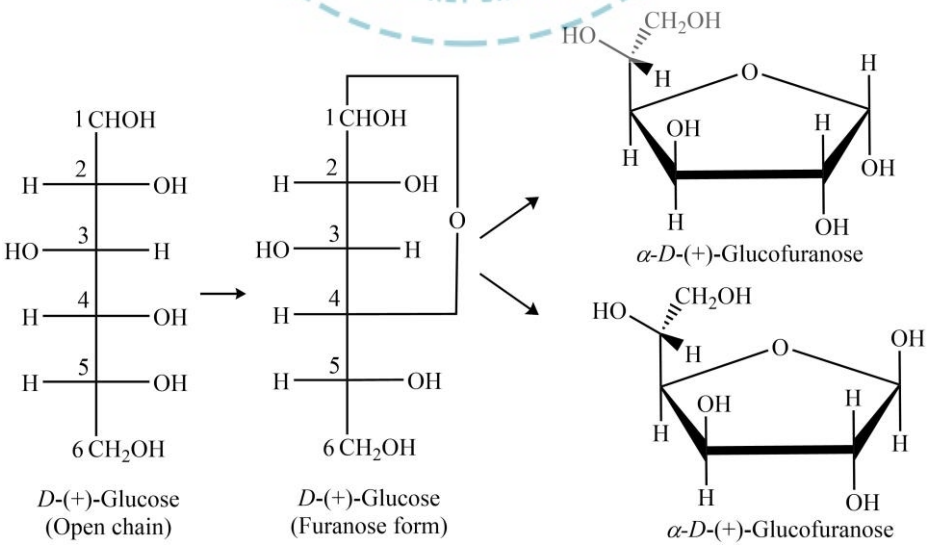
The general discussion on the conformational analysis of some typical monosaccharide sugar molecules is given below.

1. Glucose: The terminal aldehydic carbon in open-chain glucose molecule may participate in hemiacetal formation by using the hydroxyl group of 4th and 5th carbon in open-chain glucose molecule, giving rise to a five-membered furan-like and six-membered pyran-like ring structure, respectively. In solutions, the open-chain form of glucose (either "D-" or "L-") exists in equilibrium with several cyclic isomers, each containing a ring of carbons closed by one oxygen atom. In an aqueous solution, however, more than 99% of glucose molecules, at any given time, exist as pyranose forms. The open-chain form is limited to about 0.25% and furanose forms exist in negligible amounts.

i) Pyranose form: The terminal aldehydic carbon participate in hemiacetal formation by using the hydroxyl group of 5th carbon in open-chain glucose molecule to give pyranose form.

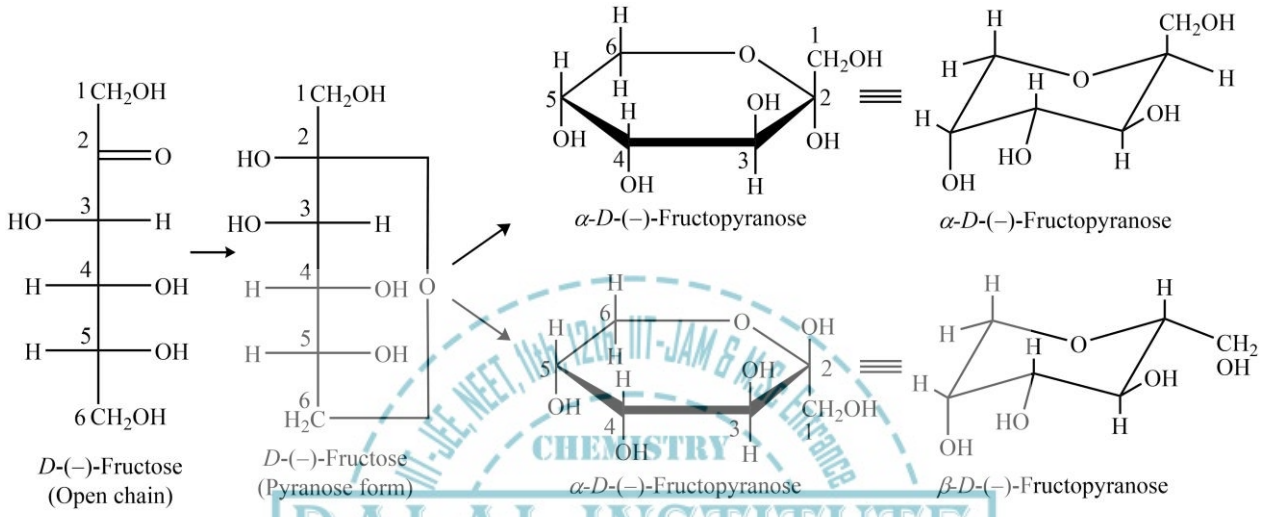


ii) Furanose form: The terminal aldehydic carbon participate in hemiacetal formation by using the hydroxyl group of 4th carbon in the open chain glucose molecule to give furanose form.

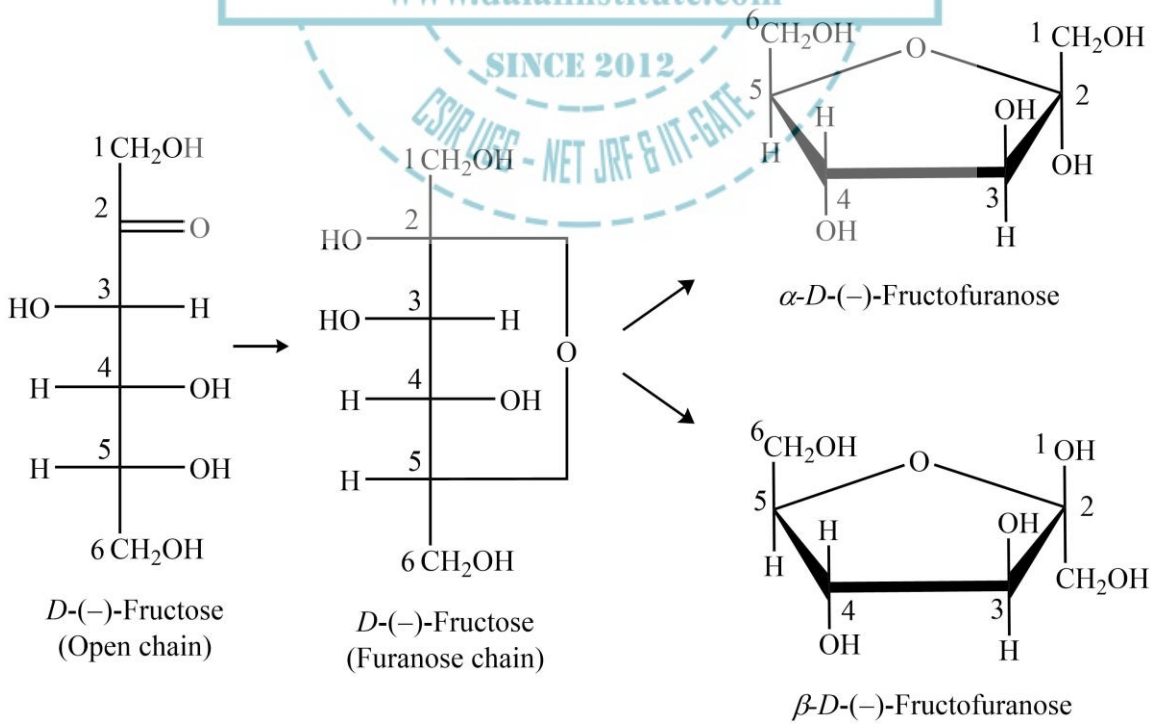


2. Fructose: The ketonic carbon in open-chain fructose molecule may participate in hemiketal formation by using the hydroxyl group of 5th and 6th carbon in open-chain glucose molecule, giving rise to a five-membered furan-like and six-membered pyran-like ring structure, respectively.

i) Pyranose form: The ketonic carbon participate in hemiketal formation by using the hydroxyl group of 6th carbon in open-chain glucose molecule to give pyranose form.

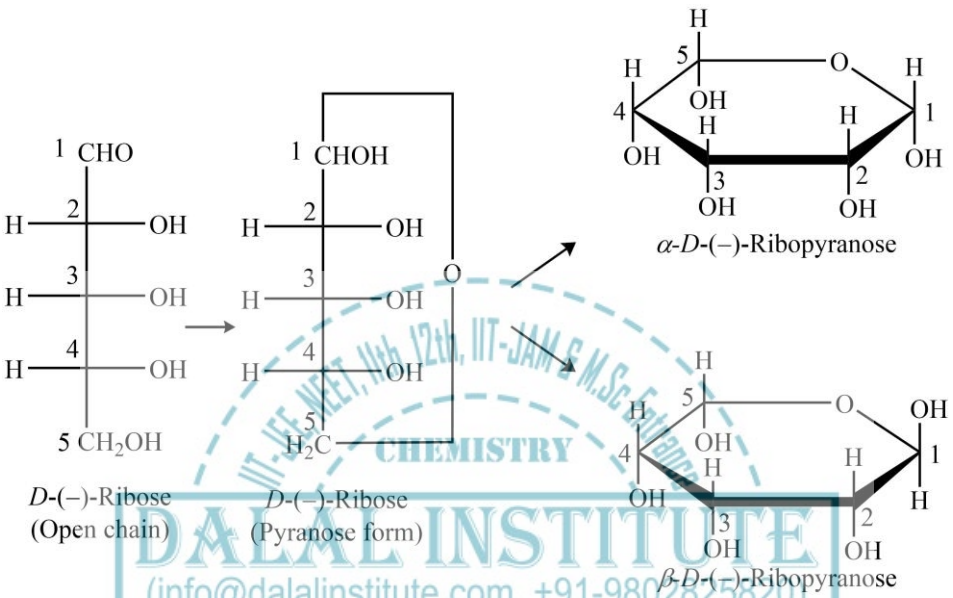


ii) Furanose form: The ketonic carbon participate in hemiketal formation by using the hydroxyl group of 6th carbon in open-chain glucose molecule to give furanose form.

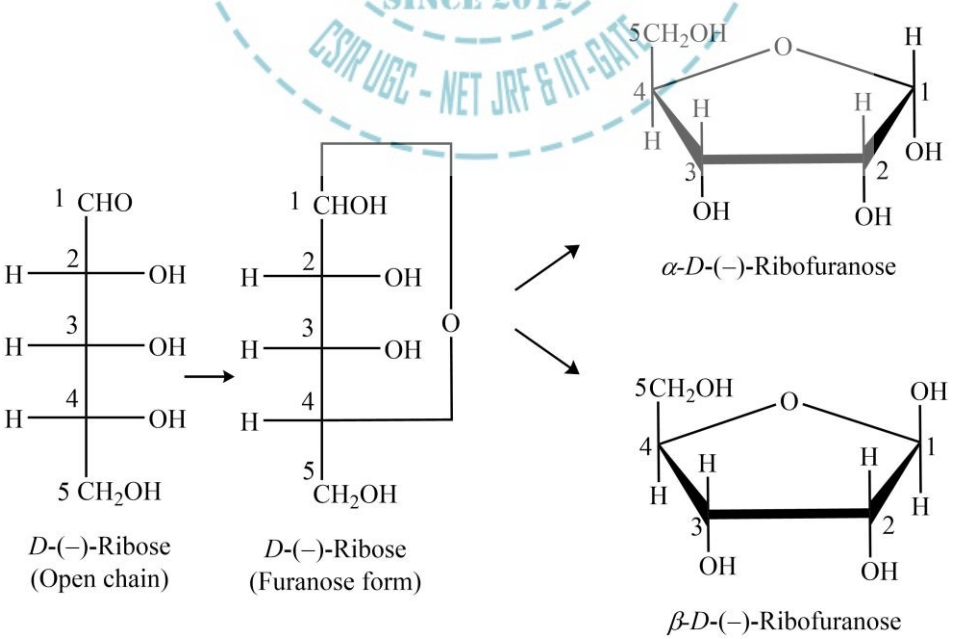


3. Ribose: The aldehydic carbon in open-chain ribose molecule may participate in hemiacetal formation by using the hydroxyl group of 4th and 5th carbon, giving rise to a five-membered furan-like and six-membered pyran-like ring structure, respectively.

i) Pyranose form: The aldehydic carbon participate in hemiacetal formation by using the hydroxyl group of 5th carbon in open-chain ribose molecule to give pyranose form.

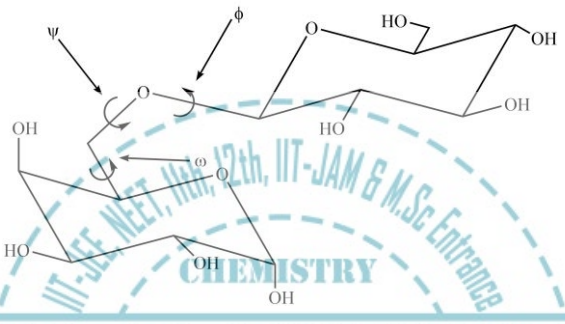


i) Furanose form: The aldehydic carbon participate in hemiacetal formation by using the hydroxyl group of 4th carbon in open chain ribose molecule to give furanose form.



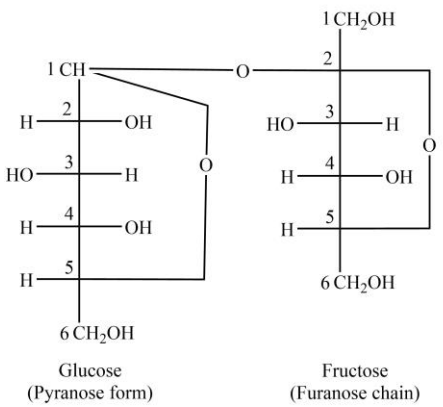
➢ ***Conformation of Oligosaccharides***

In addition to the factors affecting monosaccharide residues, conformational analysis of oligosaccharides requires the consideration of some additional factors. One such major factor is the exo-anomeric effect, which is similar to the endo-anomeric effect. The difference is that the lone pair being donated is coming from the substituent at C-1. However, since the substituent can be either axial or equatorial there are two types of exo-anomeric effects, one from axial glycosides and one from equatorial glycosides as long as the donating orbital is anti-periplanar to the accepting orbital. The other one is Glycosidic torsion angles which angles are described by φ, ψ, and ω (in the case of glycosidic linkages via O-6). Steric considerations and anomeric effects need to be taken into consideration when looking at preferred angles.

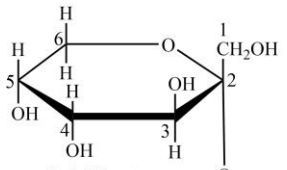


The general discussion on the conformational analysis of some typical monosaccharide sugar molecules is given below.

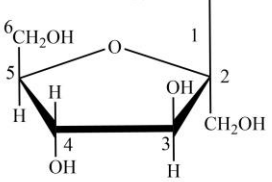
1. Sucrose: In sucrose, the components glucose and fructose are linked via an ether bond between C1 on the glucosyl subunit and C2 on the fructosyl unit. The bond is called a glycosidic linkage. Glucose exists predominantly as two isomeric "pyranoses" (α and β), but only one of these forms links to the fructose. Fructose itself exists as a mixture of "furanoses", each of which having α and β isomers, but only one particular isomer link to the glucosyl unit. What is notable about sucrose is that, unlike most disaccharides, the glycosidic bond is formed between the reducing ends of both glucose and fructose, and not between the reducing end of one and the nonreducing end of the other. This linkage inhibits further bonding to other saccharide units. Since it contains no anomeric hydroxyl groups, it is classified as a non-reducing sugar.



Glucose (Pyranose form) Fructose (Furanose chain)

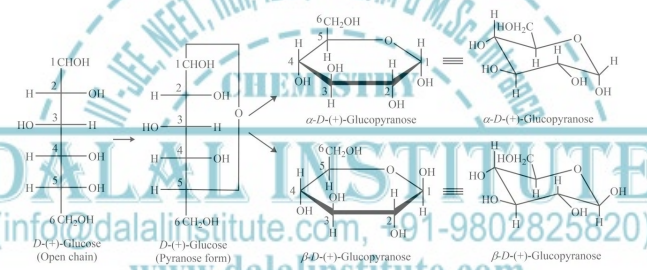


α-D-(−)-Fructopyranose

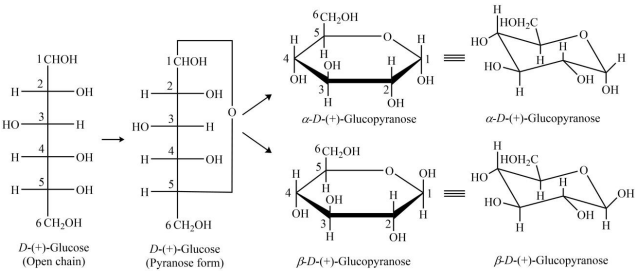


β-D-(−)-Fructofuranose

2. Maltose: Maltose is a disaccharide: the carbohydrates are generally divided into monosaccharides, oligosaccharides, and polysaccharides depending on the number of sugar subunits. Maltose, with two sugar units, is an oligosaccharide, specifically a disaccharide, because it consists of two glucose molecules. Glucose is a hexose: a monosaccharide containing six carbon atoms. The two glucose units are in the pyranose form and are joined by an O-glycosidic bond, with the first carbon (C1) of the first glucose linked to the fourth carbon (C4) of the second glucose, indicated as (1→4). The link is characterized as α because the glycosidic bond to the anomeric carbon (C1) is in the opposite plane from the CH2OH substituent in the same ring (C_6 of the first glucose). If the glycosidic bond to the anomeric carbon (C1) were in the same plane as the CH_2OH substituent, it would be classified as a β(1→4) bond, and the resulting molecule would be cellobiose. The anomeric carbon (C1) of the second glucose molecule, which is not involved in a glycosidic bond, could be either an α- or β-anomer depending on the bond direction of the attached hydroxyl group relative to the CH_2OH substituent of the same ring, resulting in either α-maltose or β-maltose. An isomer of maltose is isomaltose. This is similar to maltose but instead of a bond in the α(1→4) position, it is in the α(1→6) position, the same bond that is found at the branch points of glycogen and amylopectin.

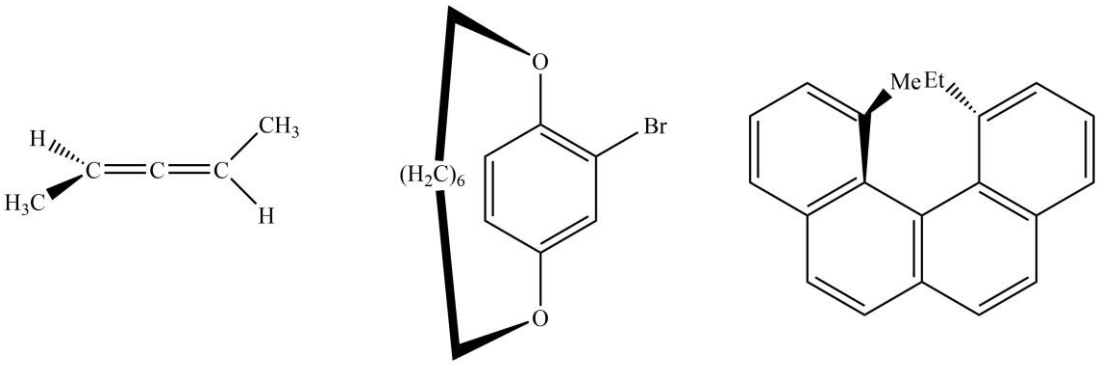


3. Lactose: Lactose is a disaccharide derived from the condensation of galactose and glucose, which form a β-1→4 glycosidic linkage. Its systematic name is β-D-galactopyranosyl-(1→4)-D-glucose. The glucose can be in either the α-pyranose form or the β-pyranose form, whereas the galactose can only have the β-pyranose form: hence α-lactose and β-lactose refer to the anomeric form of the glucopyranose ring alone. Detection reactions for lactose are the Woehlk-[6] and Fearon's test.[7] Both can be easily used in school experiments to visualize the different lactose content of different dairy products such as whole milk, lactose-free milk, yogurt, buttermilk, coffee creamer, sour creme, kefir etc. Lactose is hydrolyzed to glucose and galactose, isomerized in alkaline solution to lactulose, and catalytically hydrogenated to the corresponding polyhydric alcohol, lactitol.[9] Lactulose is a commercial product, used for the treatment of constipation.



❖ Optical Activity in Absence of Chiral Carbon (Biphenyls, Allenes and Spiranes)

As we discussed earlier in this chapter, optically active compounds can primarily be divided into four categories on the basis of their geometrical profile; molecules with the chiral center, chiral axis, chiral plane, and helical chirality.

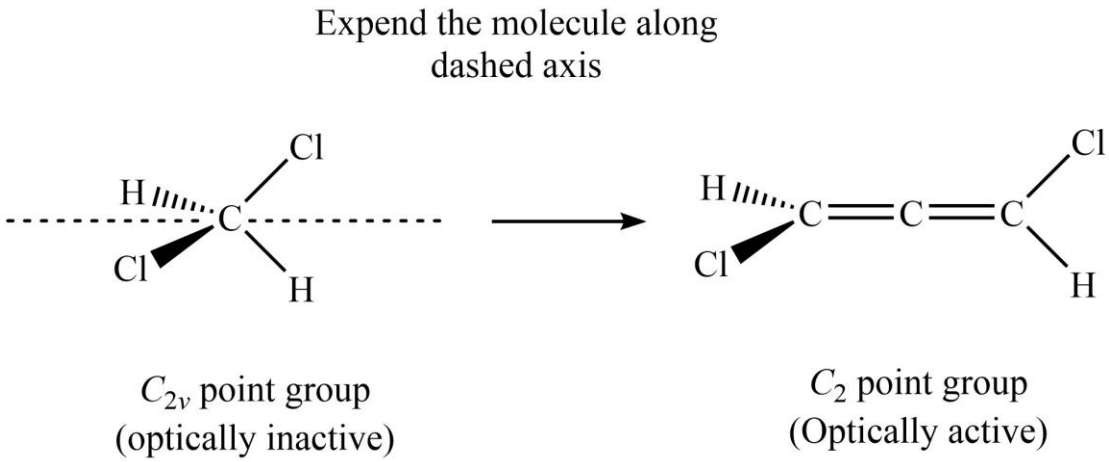


Chiral axis | Chiral plane | Helical chirality

In this section, we will study two kinds of optically active molecules without chiral carbon, compounds with chiral axis, and chiral plane.

➢ ***Optically Active Compounds with Chiral Axis***

This type of chirality arises when a tetrahedrally coordinated prochiral molecule becomes chiral by extending the center along an axis. In other words, a prochiral molecule can no longer be superimposed on its mirror image if its center has been extended to a line with the same groups at different ends.



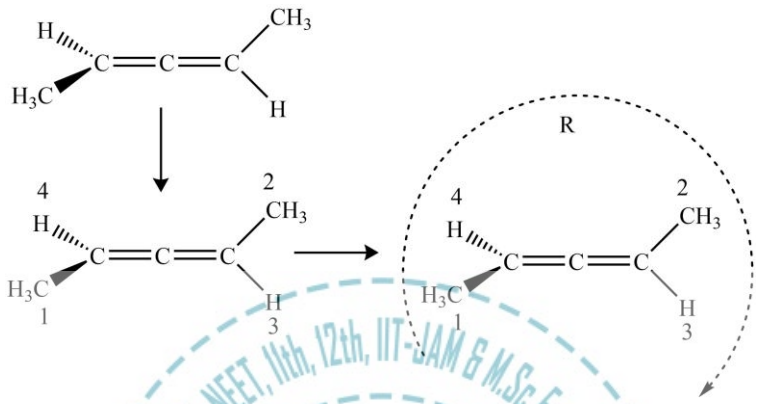
C_{2v} point group
(optically inactive)

C_2 point group
(Optically active)

Figure 3. Conversion of an optically inactive molecule to optically active via chiral axis.

1. R-S nomenclature of Optically active compounds with chiral axis:

The whole procedure includes two steps; the first is the priority assignment of different groups at both ends using Chan-Ingold-Prelog and the second step involves the assignment of absolute configuration. It is worthy to note that the highest and lowest priorities (1, 4) should be assigned to the "out-of-plane" unit and intermediatory priorities (2, 3) must be assigned to the "in-plane" unit.

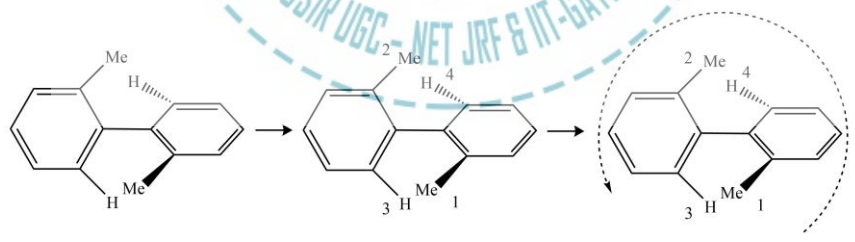


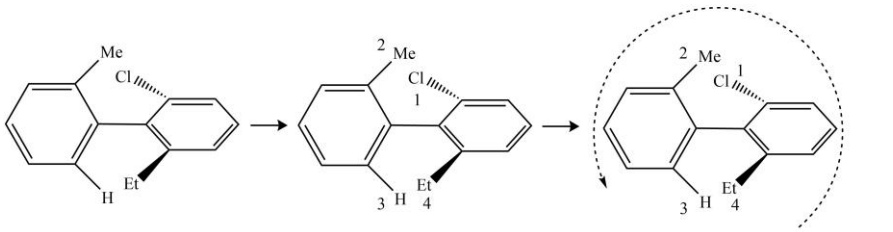
After assigning priorities to different groups, if the tracking of decreasing priority of the remaining three groups comes gives rise to clockwise flight, the molecules should be labeled as R and vice-versa. However, if the group of lowest priority is towards observer, revert the result from R to S and vice-versa.

2. Examples of Optically active compounds with chiral axis:

Some of the most common examples of organic molecules with this type of chirality are biphenyls, allenes, and spiranes derivatives.

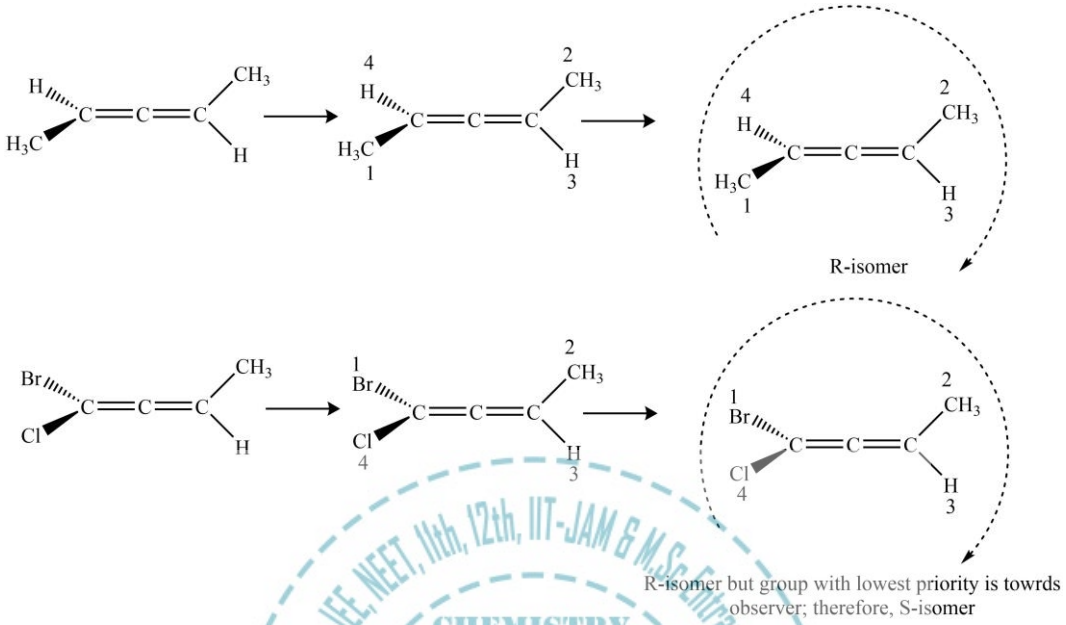
i) Optically active biphenyls:





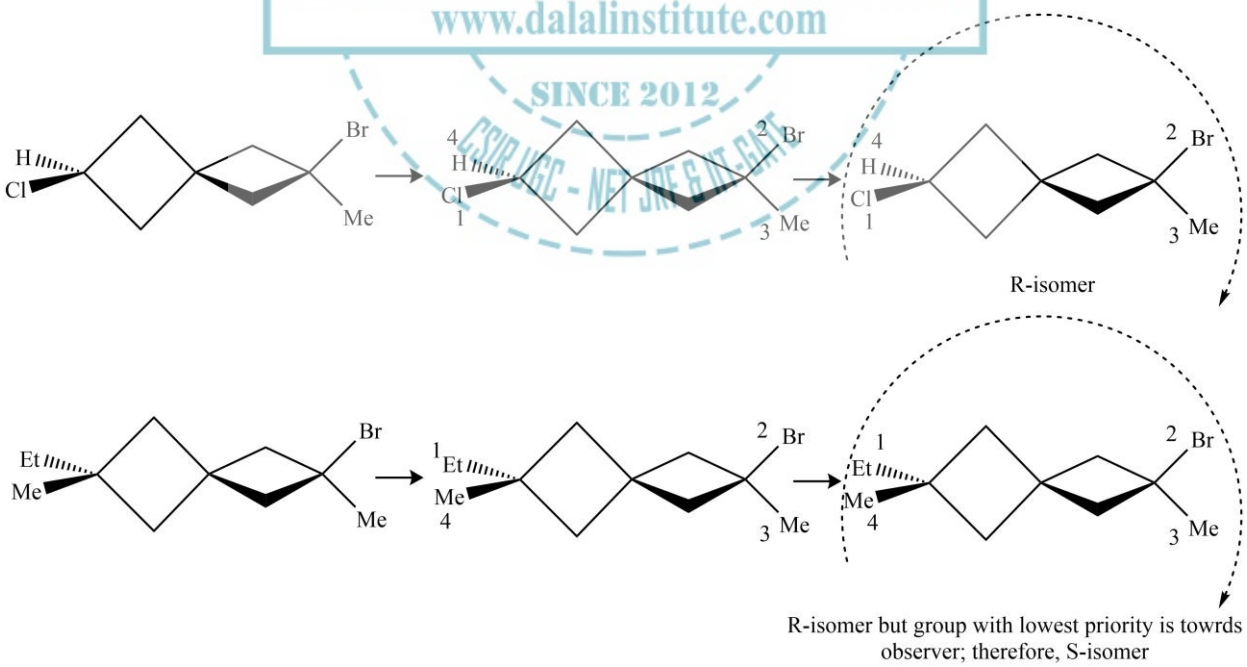
It is clear that biphenyl derivative will only be optically active groups on both ends are not the same.

ii) Optically active allenes:



It is also obvious that the allene derivative compounds will only be optically active groups on both ends are not the same.

iii) Optically active Spiranes:



It is also obvious that the spirane derivative compounds will only be optically active groups on both ends are not the same.

➢ ***Optically Active Compounds with Chiral Plane***

This type of chirality arises when relacing a group in a plane makes the molecule chiral. In other words, an organic molecule can no longer be superimposed on its mirror image if the replacement of a particular group induces chirality.

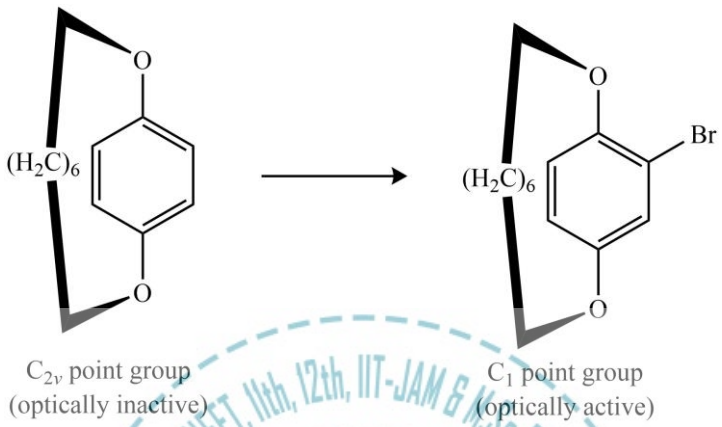
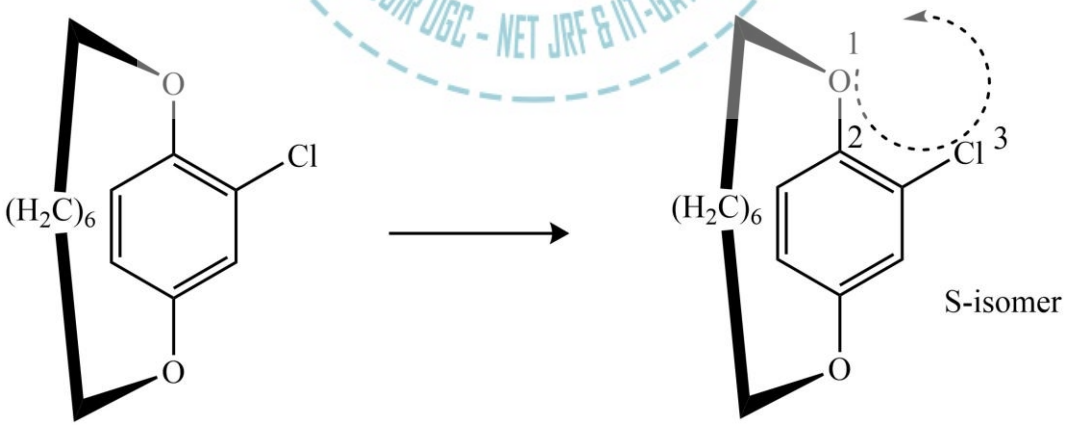


Figure 4. Conversion of an optically inactive molecule to optically active via chiral plane.

1. R-S nomenclature of Optically active compounds with chiral plane:

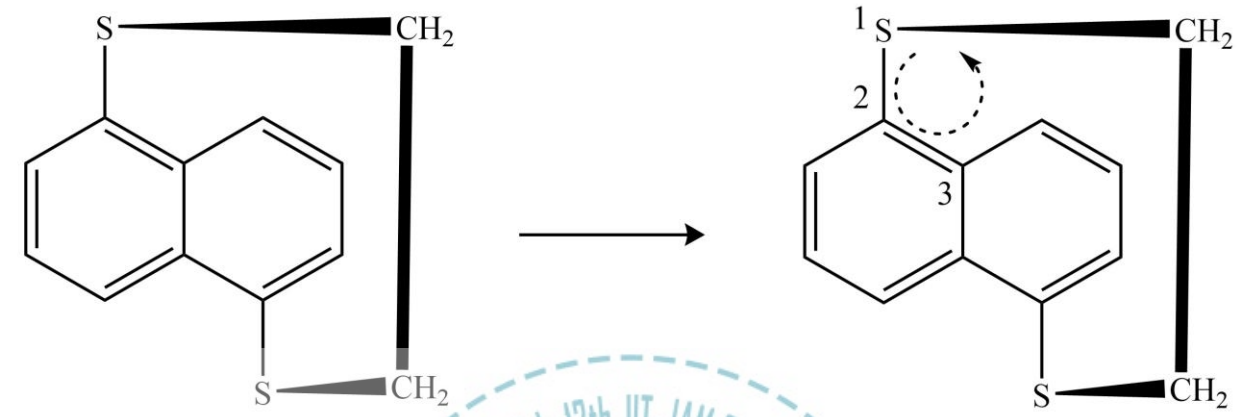
The whole procedure includes two steps; the first is the priority assignment of different groups next to the "pilot atom" (the directly bonded atom above the chiral plane). The atom next to the pilot atom is always assigned 1st priority, followed by the 2nd priority to next atom, and then deciding the priority of the next group using Chan-Ingold-Prelog rules.



After assigning priorities to different groups, if the tracking of decreasing priority of the remaining three groups comes gives rise to clockwise flight, the molecules should be labeled as R. However, if the tracking of decreasing priority of the remaining three groups comes gives rise to anticlockwise flight, the molecules should be labeled as S.

2. Examples of Optically active compounds with chiral plane:

Some of the most common examples of organic molecules with this type of chirality are ansa compounds' derivatives.



S-isomer

R-isomer

The enantiomer of any optically active ansa compound can simply be obtained by flipping the chain below the chiral plane.

❖ Chirality Due to Helical Shape

This type of chirality arises when the molecule has a helical structure. In other words, an organic molecule can no longer be superimposed on its mirror image if its geometry resembles a helix.

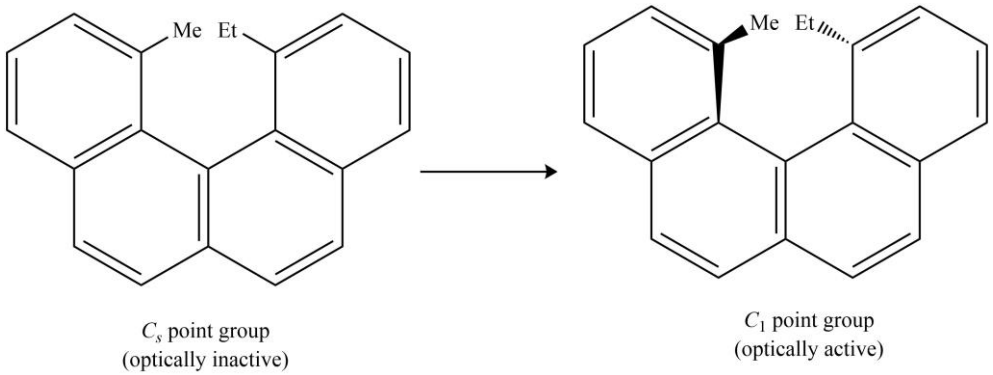
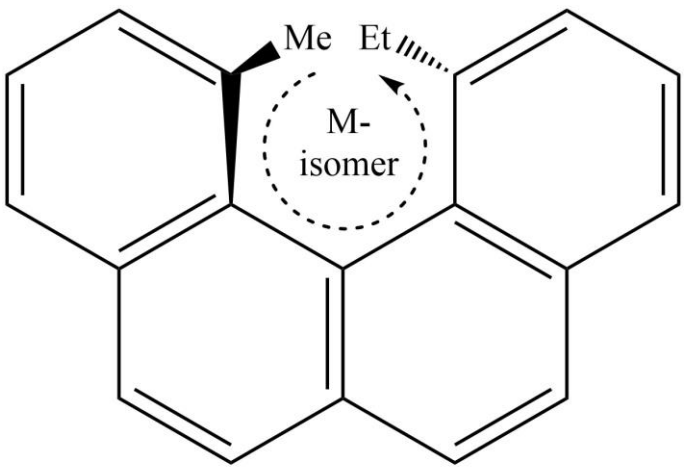


Figure 5. Conversion of an achiral molecule to optically active via the induction of helical shape.

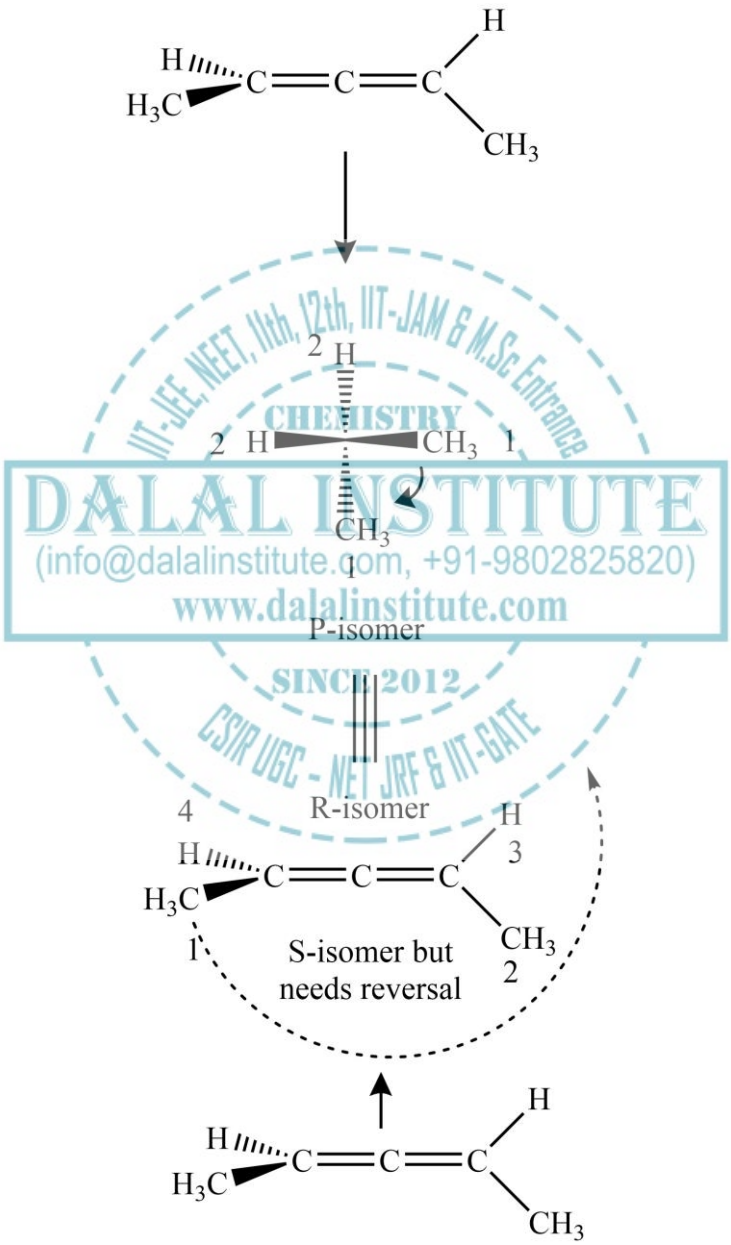
➢ *R-S Nomenclature of Optically Active Compounds with Helical Chirality*

Many molecules (such as a helix) lack a chiral center, chiral axis, or chiral plane but still are optically active. Since we can view a helix along the axis, we need to check the behavior of the near and far end of the same. If the deboarding from the near end of the helix to the far end gives rise to clockwise flight, the molecules should be labeled as P. Conversely, if the deboarding from the near end to the far end gives rise to anticlockwise flight, the molecules should be labeled as M.



Anticlockwise deboarding

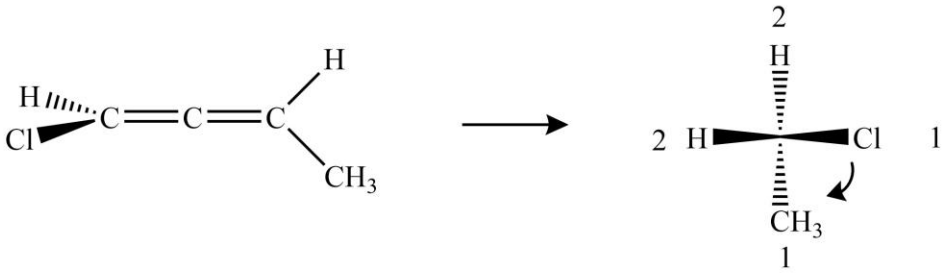
Furthermore, some optically active molecules; like allenes, biphenyls, and spiranes; can have axial as well as helical chirality. The route to do so is the same except for the fact that such molecules must be viewed along the chiral axis first, and priorities are assigned separately at both ends. Now if the deboarding from near highest priority group to the far highest priority group gives rise to clockwise flight, the molecules should be labeled as P. Conversely, if the deboarding from near highest priority group to the far highest priority group gives rise to anticlockwise flight, the molecules should be labeled as M.



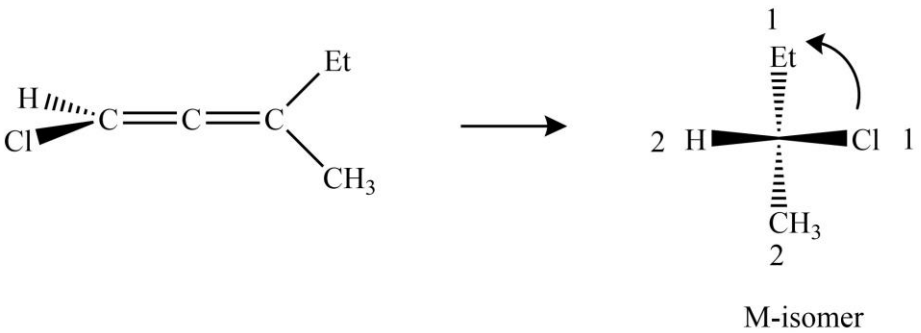
It is also very important to note the fact that the R and S labels for molecules with chiral axis translate P and M; respectively.

➢ ***Examples of Optically Active Compounds with Helical Chirality***

Some of the most common examples of organic molecules with this type of chirality (due to helical shape) are given below.



P-isomer

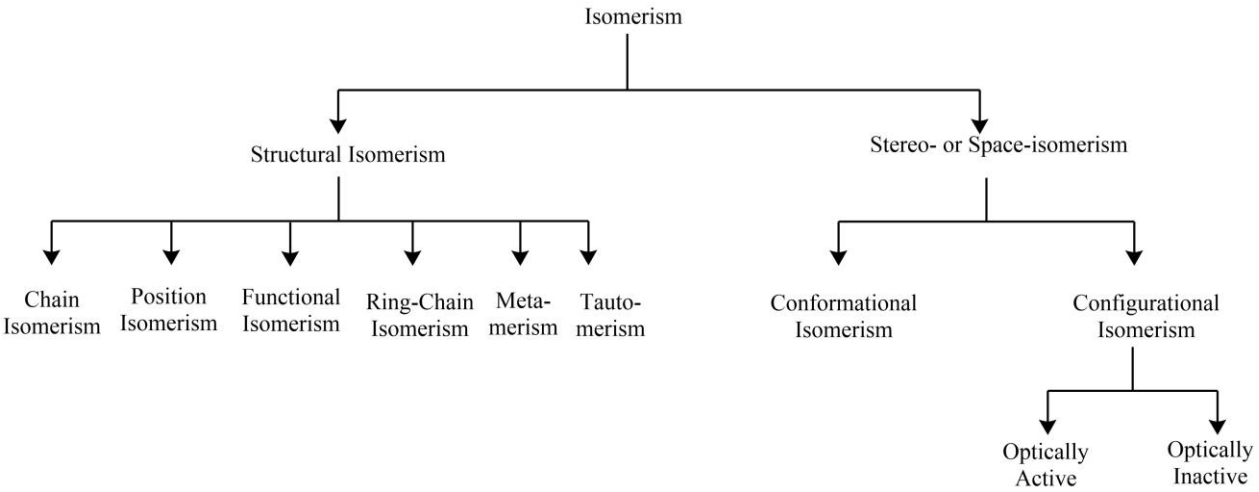


M-isomer

The enantiomer of any compound with helical chirality can simply be obtained by twisting the helix in the opposite direction.

❖ Geometrical Isomerism in Alkenes and Oximes

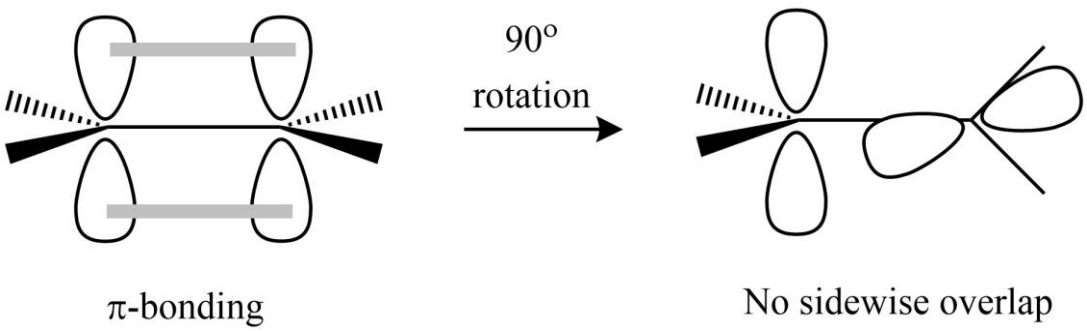
Before we study the geometrical isomerism in alkenes and oximes, we need to recall the general flow chart for different kinds of isomerisms first.



Since stereoisomerism can either be conformational or configurational, the latter possibility is of more importance in the case of oximes and alkenes as the rotation about the double bond is restricted. In this section, we will discuss the geometrical or configurational isomers of alkenes and oximes one by one.

➢ *Geometrical Isomerism due to Double Bond*

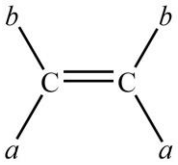
The carbon atom in alkenes is an sp^2-hybridized one, and therefore, it has a half-filled atomic orbital perpendicular to the molecular plane. After using all its three hybrid orbitals for σ-bonding, the half-filled p_z orbital can be used for side-wise overlap to form a π-bond. Nevertheless, if we rotate one of the half-filled p_z by an angle of 90°, it will not be able to do so anymore.



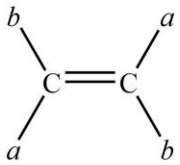
Hence, we can conclude that groups attached to sp^2-hybridized carbon cannot be exchanged simply by rotating about the double bond as it is restricted by the orbital picture. This eliminates the possibility of conformational isomerism, and therefore, we are only left with the case of the configurational one.

➢ ***Condition for Geometrical Isomerism arising from Double Bond***

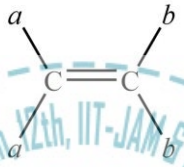
The presence of a double bond does not ensure the existence of geometrical isomers but some other conditions must also be satisfied. The primary condition is that two carbons of the double bond must have different kinds of substituents not only to carbons but to each other also.



cis-isomer



trans-isomer



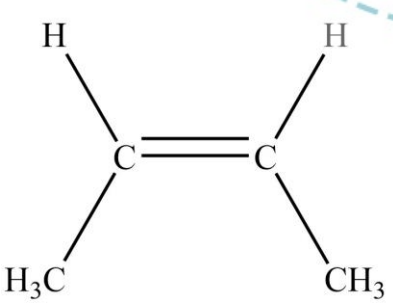
No geomtrical isomerism possible

In other words, we can also say that no geometrical isomerism will be observed if one or both carbons carry the same kind of substituents.

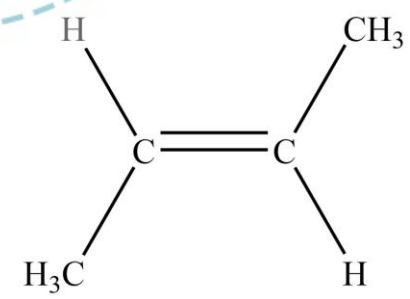
➢ ***Geometrical Isomerism in Alkenes***

The geometrical isomers of alkenes are primarily labeled as cis-trans or Z-E types, depending upon the nature of the groups on each side of the double bond.

1. Geometrical isomerism in disubstituted alkenes (cis-trans nomenclature): If the alkene under consideration is a disubstituted one, we can label it as cis or trans isomer, depending upon their mutual orientation.



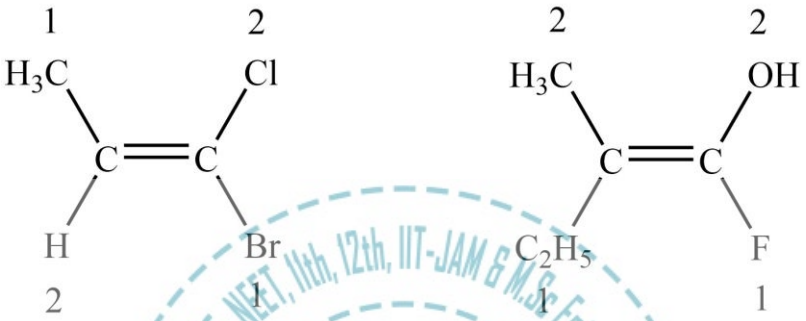
cis-isomer



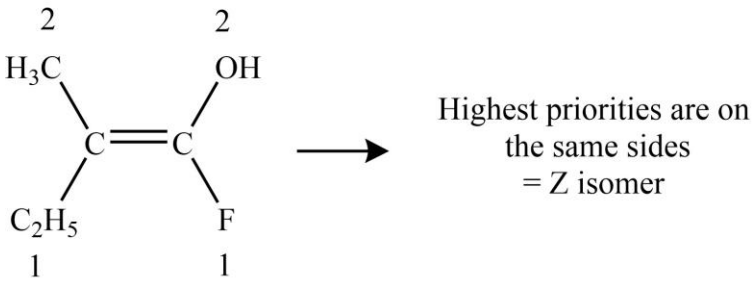
trans-isomer

2. Geometrical isomerism tri- or tetra-substituted alkenes (Z-E nomenclature): If the alkene under consideration is a tri- or tetra-substituted one, we cannot label it as cis or trans isomer, and therefore, we need to follow a special system for such compounds, called Z-E nomenclature. This system of nomenclature is also based upon the Chan-Ingold-Prelog system of priority assignment. The main postulates of the Z-E system of nomenclature are given below.

i) Priorities are assigned to different groups individually at both ends as per the sequence rule from the Chan-Ingold-Prelog system.



ii) Once the priorities are assigned, check if groups with higher priorities are on the same or opposite side of the double bond. If they are on the same side, the system is 'Z'; and if they are on the opposite side, the compound should be labeled as 'E' isomer.



3. Geometrical isomerism in compounds with two or more double bonds: If the alkene under consideration has two or more double bonds, the number of geometrical isomers depends not only upon the number of double bonds only but also upon whether the ends are symmetrical or not. This can be classified into two categories as discussed below.

i) When ends are unsymmetrical: If the ends of the alkenes are unsymmetrical, the total number of geometrical isomers (whether the number is odd or even) is given by the following equation.

$$N_{isomer} = 2^n \tag{7}$$

Where *n* represents the number of double bonds.

ii) When ends are symmetrical: If the ends of the alkenes are symmetrical, the total number of geometrical isomers (whether the number is odd or even) is given by the following equation.

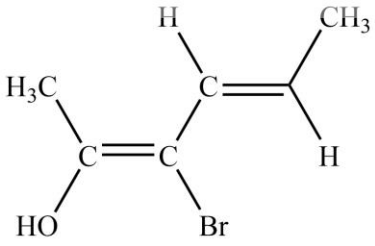
$$N_{isomer} = 2^{n-1} + 2^{(n/2-1)} \quad if\ n = even \tag{8}$$

$$N_{isomer} = 2^{n-1} + 2^{(n/2-1/2)} \quad if\ n = odd \tag{9}$$

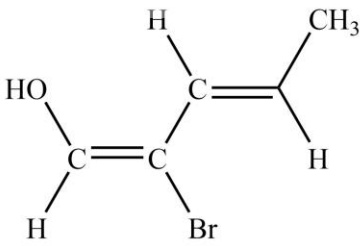
Where *n* represents the number of double bonds.

(2*E*,4*E*)-3-bromohexa-2,4-diene

(2*Z*,4*E*)-4-bromohexa-2,4-dien-2-ol



(2*Z*,4*E*)-3-bromohexa-2,4-dien-2-ol

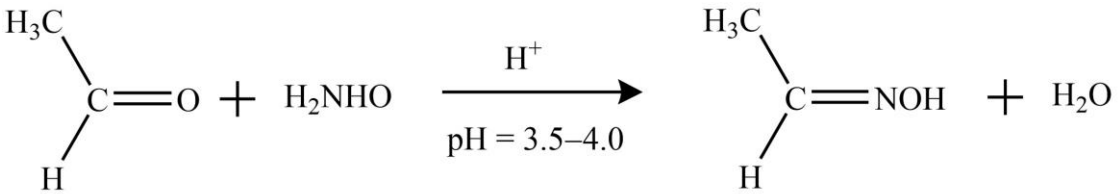


(1*E*,3*E*)-2-bromopenta-1,3-dien-1-ol

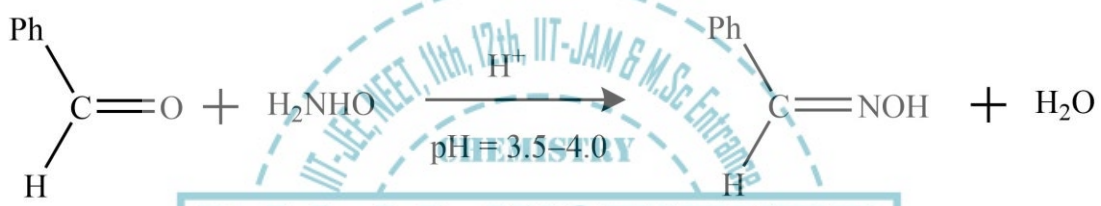
It is also obvious from the structures given above that besides tri- and tetra-substituted alkenes, the E-Z system of nomenclature also finds its application in compounds with many double bonds.

➢ ***Geometrical Isomerism in Oximes***

Oximes are compounds that have a carbon-nitrogen double bond, and can easily be prepared by treating hydroxylamine with ketones or aldehydes in somewhat acidic solutions.

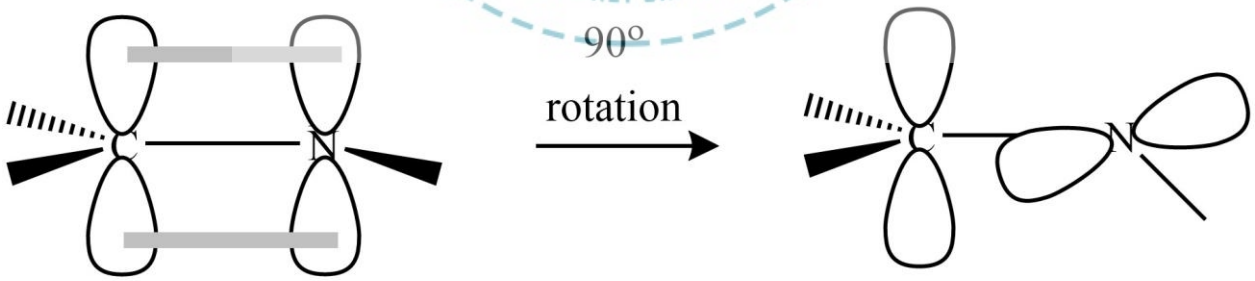


acetaldehyde acetaldehyde oxime



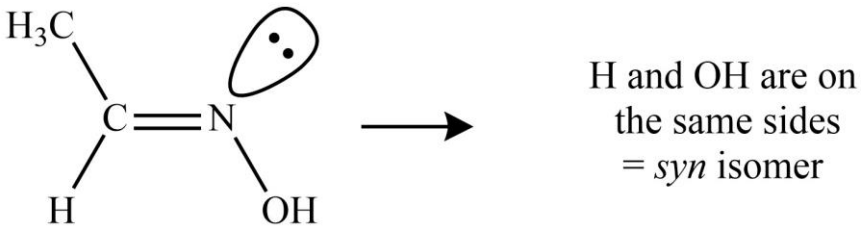
benzaldehyde benzaldehyde oxime

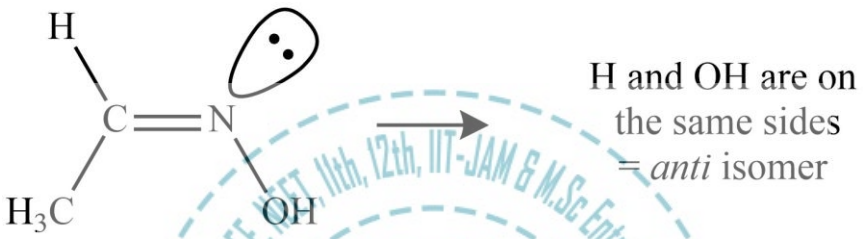
The carbon atom in oxime is an sp^2-hybridized one, and therefore, it has a half-filled atomic orbital perpendicular to the molecular plane. After using all its three hybrid orbitals for σ-bonding, the half-filled p_z orbital can be used for side-wise overlap to form a π-bond. Nevertheless, if we rotate one of the half-filled p_z by an angle of 90°, it will not be able to do so anymore because the nitrogen atom is also sp^2-hybridized with lone pair residing in one of the hybrid orbitals.



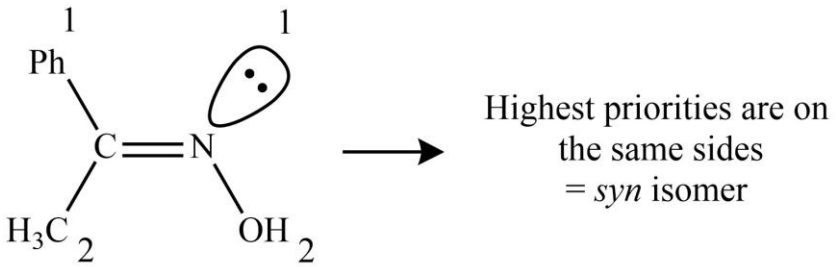
π-bonding No sidewise overlap

Now, if the H and OH are on the same side of the double bond, the compound will be called as *syn*; whereas if H and OH are on the opposite side of the double bond, the compound should be labeled as *anti*.





The nomenclature rule using H and OH is only applicable to aldoximes and cannot be applied to ketoximes because there is no H present. In such cases, we need to use priorities assignment using the Chan-Ingold-Prelog system with lone pair having the highest priority.



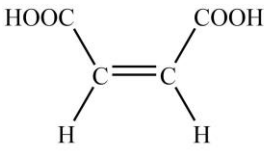
❖ Methods of Determining the Configuration

After studying the geometrical isomerism in alkenes, it's time to discuss the route by which know their configurations. The methods of determining the configuration of geometrical isomers are based upon either physical or chemical properties.

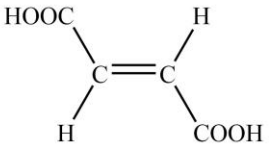
➢ *Determination of Configuration Using Physical Properties*

The geometrical isomers of alkenes can be identified with various kinds of physical properties like melting point, solubility, dipole moment, or boiling point, etc. Some of the important physical methods for determining the configuration of geometrical isomers are given below.

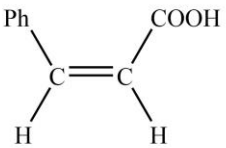
1. Melting point: The melting points of trans-isomers are generally higher than that of cis-isomers, which makes it a suitable tool for configuration prediction. The reason for such behavior is the fact that trans-isomers are symmetrical, and consequently, are well packed to give stronger intermolecular forces than cis-isomers.



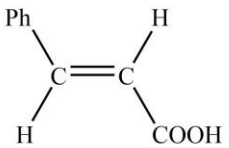
Maleic acid
melting point = 403 K



Fumaric acid
melting point = 575 K

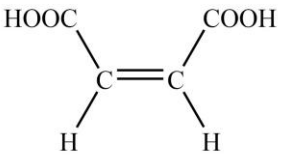


Allocinnamic acid
melting point = 341 K

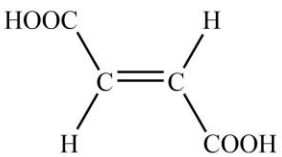


Cinnamic acid
melting point = 406 K

2. Solubility: The solubility of cis-isomers are generally higher than that of trans-isomers, which makes it a suitable tool for configuration prediction. The reason for such behavior is the fact that cis-isomers are unsymmetrical, and consequently, are not well packed, giving weaker intermolecular forces than trans-isomers.

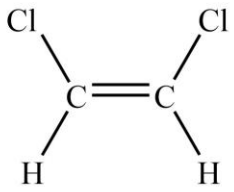


Maleic acid
Solubility = 790g per liter water

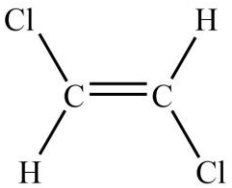


Fumaric acid
Solubility = 7g per liter water

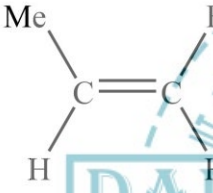
3. Dipole moment: The dipole moments of cis-isomers are generally higher than that of trans-isomers, which makes it a suitable tool for configuration prediction. The reason for such behavior is the fact that trans-isomers have individual dipoles in the exact opposite direction which may or may not get canceled completely.



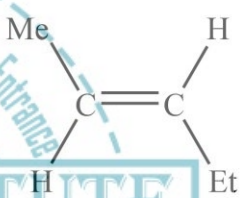
cis-dichloroethene
Dipole moment = 1.85D



trans-dichloroethene
Dipole moment = 0D

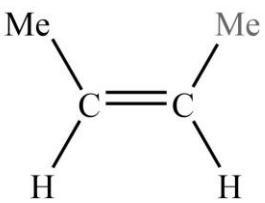


(*Z*)-pent-2-ene
More polar
Higher dipole moment



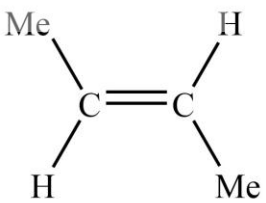
(*E*)-pent-2-ene
Less polar
Lower dipole moment

4. Boiling Point: The boiling points of cis-isomers are generally higher than that of trans-isomers, which makes it a suitable tool for configuration prediction. The reason for such behavior is the fact that the boiling points are typically the function of dipole moments, which are higher for cis-isomers.



(*Z*)-but-2-ene

Boiling point = 277K
Dipole moment = 0.4 D



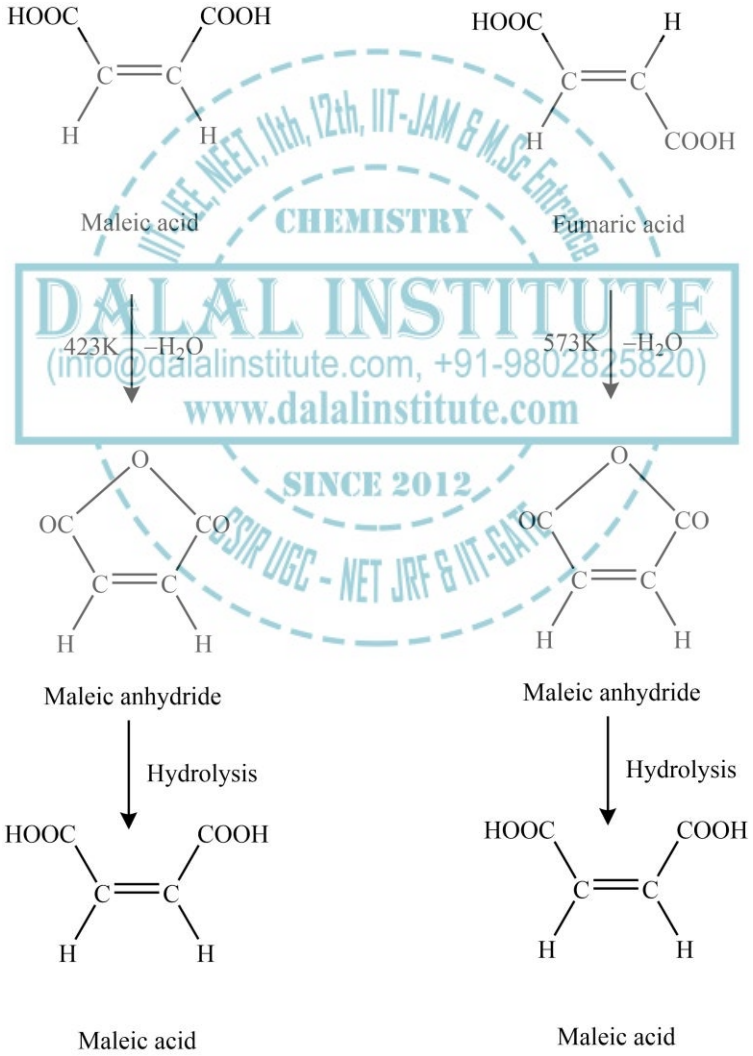
(*E*)-but-2-ene

Boiling point = 274K
Dipole moment = 0.0 D

➢ ***Determination of Configuration Using Chemical Properties***

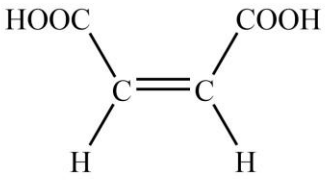
The geometrical isomers of alkenes can be identified with various kinds of chemical properties like the formation of cyclic compounds, or the optical properties of the stereoisomers formed during bromination and hydroxylation reactions, etc. Some of the important chemical methods for determining the configuration of geometrical isomers are given below.

1. Generation of cyclic systems: Since the reactive groups of the substrate are on the same side in cis-isomer, the formation of cyclic systems will be an easy task. Conversely, if the reactive groups of the substrate are on the opposite side (in trans-isomer), the formation of cyclic systems will be much more difficult to carry out. This can be illustrated by the case of maleic acid and fumaric acid where the generation of maleic anhydride requires much more temperature for the later substrate.

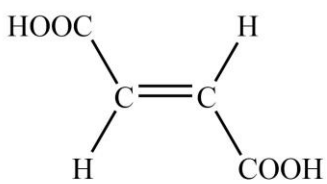


Furthermore, it is also worthy to note that the hydrolysis of maleic anhydride gives back only maleic acid and no fumaric acid.

2. Optical properties of stereoisomers formed: The geometrical isomers of alkenes can be identified with the optical properties of the stereoisomers formed during bromination and hydroxylation reactions. Since the alkene's hydroxylation with dilute $KMnO_4$ or OsO_4 is cis-addition, we should get a meso-product with cis-isomer and racemic mixture for trans-substrate.



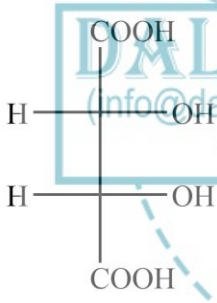
Maleic acid
(*cis*-isomer)



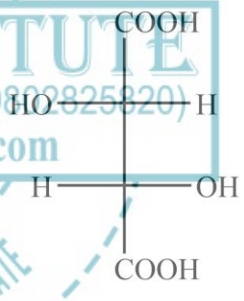
Fumaric acid

Aq. $KMnO_4$
or OsO_4

Aq. $KMnO_4$
or OsO_4

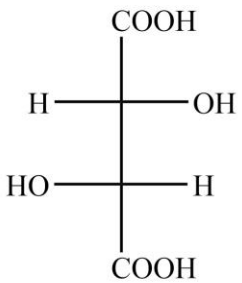


meso-Tartaric acid



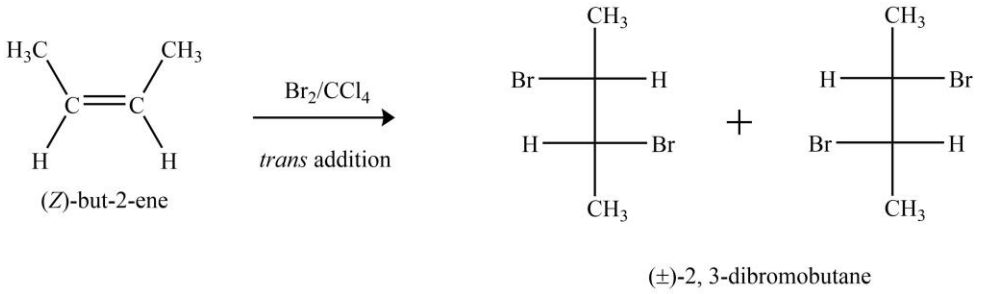
(+)-Tartaric acid

&



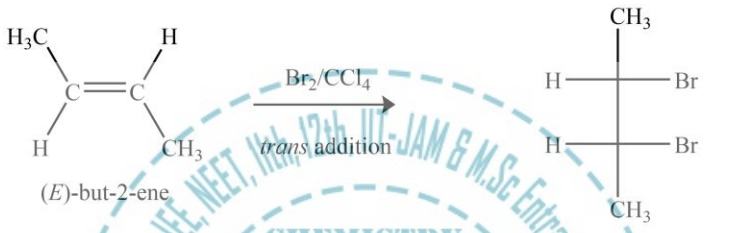
(–)-Tartaric acid

On the other hand, the alkene's bromination with CCl_4 is trans-addition, we should get a meso-product with trans-isomer and racemic mixture for cis-substrate.



(*Z*)-but-2-ene

(±)-2, 3-dibromobutane



(*E*)-but-2-ene

meso-dibromobutane

❖ Problems

Q 1. What is the meaning of chirality in chemistry? Explain with necessary historical background.

Q 2. Define and discuss various symmetry elements.

Q 3. What is a secondary symmetry element? How is it related to the concept of optical activity?

Q 4. Discuss and differentiate the phenomenon of diastereomerism from enantiomerism.

Q 5. Discuss the absolute nomenclature of optically active compounds with suitable examples.

Q 6. Give various methods of resolution of racemic mixtures.

Q 7. Define optical purity. How is it calculated?

Q 8. What do you mean by the term 'prochirality'?

Q 9. What are enantiotopic groups and faces? How are they different from diastereotopic faces and groups?

Q 10. State and explain asymmetric synthesis.

Q 11. Draw and discuss various conformations of cyclohexane.

Q 12. What is the significance of the twisted boat form of cyclohexane?

Q 13. Define and discuss decalins.

Q 14. Discuss the conformational analysis of sugars.

Q 15. What is the chiral axis? How is it different from the chiral plane?

Q 16. Discuss the chirality arising from helical structures in detail.

Q 17. Discuss the geometrical isomerism in alkenes and oximes.

❖ Bibliography

1. K. Mislow, *The Relative Configuration of (levo)-Mandelic Acid*, J. Am. Chem. Soc., 73 (1951) 3954−3956.

2. M. B. Smith, *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, John Wiley & Sons, Inc., New Jersey, USA, 2013.

3. D. Klein, *Organic Chemistry*, John Wiley & Sons, Inc., New Jersey, USA, 2015.

4. C. A. Coulson, B. O'Leary, R. B. Mallion, *Hückel Theory for Organic Chemists*, Academic Press, Massachusetts, USA, 1978.

5. R. L. Madan, O*rganic Chemistry*, Tata McGraw Hill, New Delhi India, 2013.

6. H. Zimmerman, *Quantum Mechanics for Organic Chemists*, Academic Press, New York, USA, 1975.

7. J. Clayden, N. Greeves, S. Warren, *Organic Chemistry*, Oxford University Press, Oxford, UK, 2012.

CLASSES

CSIR UGC – NET JRF, IIT-GATE, M.Sc Entrance, IIT-JAM, IIT-JEE, NEET, 11th and 12th

Want to study chemistry for CSIR UGC – NET JRF + IIT-GATE; IIT-JAM + M.Sc Entrance; IIT-JEE + NEET + 11th +12th; and all other postgraduate, undergraduate & senior-secondary level examinations where chemistry is a paper?

READ MORE

BOOKS

Publications

Are you interested in books (Print and Ebook) published by Dalal Institute ?

READ MORE

VIDEOS

Video Lectures

Want video lectures in chemistry for CSIR UGC – NET JRF + IIT-GATE; IIT-JAM + M.Sc Entrance; IIT-JEE + NEET + 11th +12th; and all other postgraduate, undergraduate & senior-secondary level examinations where chemistry is a paper?

READ MORE

Postgraduate Level

CSIR UGC – NET JRF & IIT-GATE

First Chemistry Batch
(1st January – 31st May)

Second Chemistry Batch
(1st July – 30th November)

Regular Program

Online Course

Result

Senior-Secondary Level

11TH, 12TH, NEET & IIT-JEE

First Chemistry Batch
(1st April – 31st August)

Second Chemistry Batch
(1st October – 28th February)

Regular Program

Online Course

Result

Undergraduate Level

M.SC ENTRANCE & IIT-JAM

First Chemistry Batch
(1st February – 30th June)

Second Chemistry Batch
(1st August – 31st December)

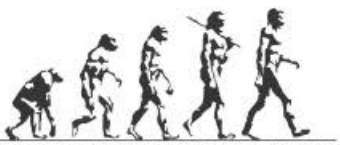
Regular Program

Online Course

Result

Join the revolution by becoming a part of our community and get all of the member benefits like downloading any PDF document for your personal preview.

Sign Up



JOIN THE REVOLUTION FROM BEAST TO BUDDHA

..... India's Best Coaching Center for Academic and Competitive Chemistry Exams .....

(CSIR UGC – NET JRF + IIT-GATE; IIT-JAM + M.Sc Entrance; IIT-JEE + NEET + 11th +12th; and all other postgraduate, undergraduate & senior-secondary level examinations where chemistry is a paper)

DALAL INSTITUTE

.....Chemical Science Demystified.....

Main Market, Sector 14, Rohtak, Haryana 124001, India
(+91-9802825820, info@dalalinstitute.com)
www.dalalinstitute.com

International Edition

A TEXTBOOK OF ORGANIC CHEMISTRY

Volume I

MANDEEP DALAL

First Edition

DALAL INSTITUTE

Table of Contents

Mandeep Dalal
(M.Sc, Ph.D, CSIR UGC – NET JRF, IIT-GATE)
Founder & Educator, Dalal Institute
E-Mail: dr.mandeep.dalal@gmail.com
www.mandeepdalal.com

Mandeep Dalal is an Indian research scholar who is primarily working in the field of Science and Philosophy. He received his Ph.D in Chemistry from Maharshi Dayanand University, Rohtak, in 2018. He is also the Founder of "Dalal Institute" (India's best coaching centre for academic and competitive chemistry exams), the organization that is committed to revolutionize the field of school-level and higher education in Chemistry across the globe. He has published more than 40 research papers in various international scientific journals, including mostly from Elsevier (USA), IOP (UK), and Springer (Netherlands).

Other Books by the Author

A TEXTBOOK OF INORGANIC CHEMISTRY – VOLUME I, II, III, IV

A TEXTBOOK OF PHYSICAL CHEMISTRY – VOLUME I, II, III, IV

A TEXTBOOK OF ORGANIC CHEMISTRY – VOLUME I, II, III, IV

ISBN: 978-81-952427-3-3

MRP: Rs 800.00

DALAL INSTITUTE
..... Chemical Science Demystified .....
Main Market, Sector 14, Rohtak, Haryana 124001, India
(info@dalalinstitute.com, +91-9802825820)
www.dalalinstitute.com