

## Unit -2

### Part –I Spectroscopic Techniques and Applications

**Spectroscopy** is the analysis of the electromagnetic radiations scattered or absorbed or emitted by molecules. It is study of interaction between electromagnetic radiation with the matter and is a most powerful technique to study the atomic and molecular structure of the compound.

#### UV-VISIBLE SPECTROSCOPY

UV-Visible spectroscopy is an analytical technique that records the wavelengths of UV or visible light that are absorbed by or transmitted through a sample in comparison to a reference or blank sample.

#### Theory of UV- visible spectroscopy

- Ultraviolet- visible spectroscopy involves the absorption of ultraviolet/visible light by a molecule causing the transition of an electron from a ground electronic state to an excited electronic state.
- The region of UV-visible spectroscopy: 200 nm to 800 nm.
- The common solvent used for preparing sample to be analyzed is either ethyl alcohol or cyclohexane.
- Ultraviolet- visible spectroscopy is used to measure the number of conjugated double bonds and also aromatic conjugation within various molecules.

#### Absorbance Law or Beer's-Lambert's Law

Ans. The Beer-Lambert's Law: It states that for a parallel beam of monochromatic radiation passing through a homogenous solution the absorbance is proportional to the product of the concentration and path length.

$$A \propto c \cdot l$$

$$A = \epsilon \cdot c \cdot l$$

where:

A = absorbance

$\epsilon$  = absorptivity

l = path length

c = concentration

$\epsilon$  is absorptivity constant. Its value depends on the substance, solvent, wavelength and the units used for the concentration and path-length.

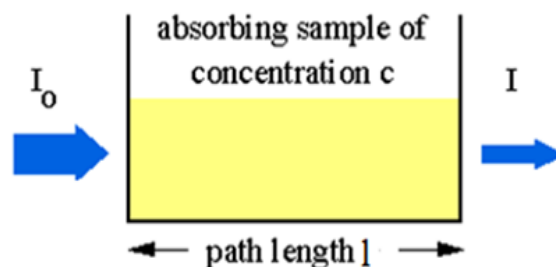
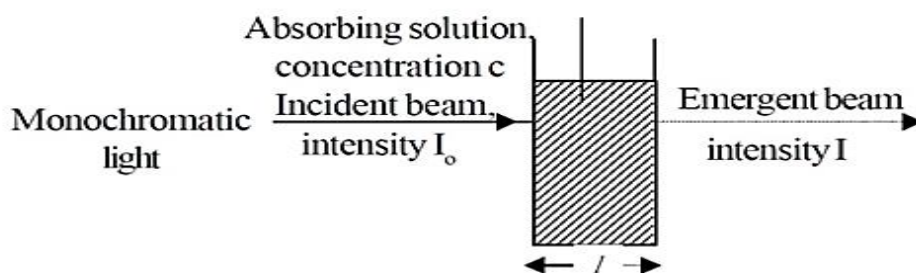


Figure 1: Light absorbed by sample in a cuvette

#### Derivation:

When a beam of monochromatic light is passed through a solution of an absorbing substance, the rate of decrease of intensity of radiation ( $dI$ ) with thickness of absorbing solution ( $dl$ ) is directly proportional to the intensity of incident radiation ( $I$ ), as well as concentration of the solution ( $c$ ).



Mathematically, according to Beer-Lambert's law;

$$-\frac{dI}{dl} \propto C \cdot I$$

$$-\frac{dI}{dl} = k \cdot C \cdot I$$

$$-\frac{dI}{I} = k \cdot C \cdot dl \quad \text{--- (1)}$$

On integrating Eq. (1);

When intensity is  $I_0$  (incident), the path length is zero and when intensity becomes  $I_t$  (transmitted), the path length becomes  $l$ ;

$$I = I_0 \text{ at } l = 0$$

$$I = I_t \text{ at } l = l$$

We get,

$$-\int_{I_0}^{I_t} \frac{dI}{I} = k \cdot C \cdot \int_0^l dl$$

$$-\ln \frac{I_t}{I_0} = k \cdot C \cdot l$$

$$\ln \frac{I_0}{I_t} = k \cdot C \cdot l \quad \text{--- (2)}$$

By taking log base 10

$$2.303 \log \frac{I_0}{I_t} = k \cdot C \cdot l$$

$$\log \frac{I_0}{I_t} = \frac{k}{2.303} \cdot C \cdot l$$

$$\log \frac{I_0}{I_t} = \epsilon \cdot C \cdot l \quad \text{--- (3)}$$

where,

$\epsilon = k/2.303$ , is called the absorption coefficient or absorptivity

$\log I_0 / I_t = A$ , is called the absorbance

But  $A = \log \frac{I_0}{I_t}$ ;

$$A = \epsilon \cdot C \cdot l$$

**Transmittance (T):** It is the ratio of the intensity of transmitted light ( $I_t$ ) by the sample to the intensity of incident light on the sample ( $I_0$ ).

$$T = I_t / I_0$$

$$\%T = T \times 100$$

**Absorbance (A):** It is the reciprocal of the logarithm of the transmittance.

$$A = -\log T = -\log (I_t / I_0) = \log (I_0 / I_t)$$

This relationship may be expressed as:

$$A = \log \frac{I_0}{I_t} = \epsilon cl = -\log T$$

Let  $I_0$  is the intensity of incident and  $I_t$  is the intensity of transmitted light.

Limitation of Beer-Lambert's law:

- (i) The electromagnetic radiation should be monochromatic.
- (ii) The light beam should not be scattered.
- (iii) The solution should be diluted.
- (iv) Deviation may occur, if the solution contains impurities.

**Example** A compound having concentration  $10^{-3}$  g/L resulted absorbance value 0.20 at  $\lambda_{\max}$  510 nm using 1.0 cm cell. Calculate its absorptivity and molar absorptivity values. Molecular weight of compound is 400. [UPTU, Sem., 1st, 2008-09]

**Solution.** Given : Concentration of compound =  $C = 10^{-3}$  g/L,  
Length of the cell =  $l = 1.0$  cm,  
Absorbance =  $A = 0.20$

Let, absorptivity =  $\epsilon$

According to Beer-Lambert's law,

$$A = \epsilon Cl$$

$$\epsilon = \frac{A}{Cl}$$

$$\Rightarrow \epsilon = \frac{0.20}{(10^{-3}) \times (1.0)} = 200 \text{ L g}^{-1} \text{ cm}^{-1} \quad \dots(1)$$

Given : Molecular weight of compound = 400

$$\therefore \text{Molar concentration} = C_M = \frac{10^{-3}}{400} = 0.25 \times 10^{-5} \text{ mole/L.}$$

Let, molar absorptivity =  $\epsilon_M$

As per Beer-Lambert's law,

$$A = \epsilon_M C_M l$$

$$\epsilon_M = \frac{A}{C_M l}$$

$$\Rightarrow \epsilon_M = \frac{0.20}{(0.25 \times 10^{-5}) \times 1} = 8 \times 10^4 \text{ L mol}^{-1} \text{ cm}^{-1} \quad \dots(2)$$

## Electronic transitions

Absorption of UV-Visible radiation by an organic molecule leads to electronic transitions between various energy levels. These transitions consist of an excitation of an electron from an occupied molecular orbital to unoccupied molecular orbital.

The possible electronic transitions:

### I. $\sigma \rightarrow \sigma^*$ transition:

- These transitions occur by the saturated hydrocarbons.
- Transition occur by  $\sigma$  electron from bonding orbital is excited to corresponding  $\sigma^*$  anti-bonding orbital.
- These transitions require higher energy and thus absorb radiation at lower wavelength.
- e.g. Methane, ethane, propane etc.

### II. $n \rightarrow \sigma^*$ transition:

- These transition occur by the saturated compounds containing atoms with lone pair of electrons like O, N, S and halogens.
- They are capable of  $n \rightarrow \sigma^*$  transition.
- These transitions usually require less energy than  $\sigma \rightarrow \sigma^*$  transitions.
- e.g. Amine, aldehydes, alcohol, alkyl halide, ethers, etc.

### III. $\pi \rightarrow \pi^*$ transition :

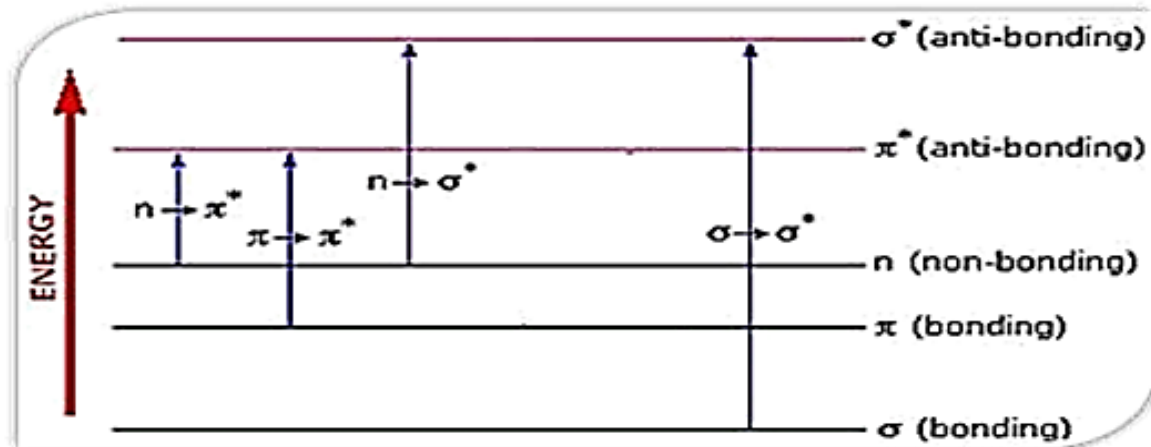
- These transitions occur by the  $\pi$  electron in a bonding orbital to corresponding anti-bonding orbital  $\pi^*$ .
- These transitions are associated with compounds containing double or triple bond and aromatic compound.
- These transitions require less energy and occur at higher wavelength.
- Compounds like alkenes, alkynes, carbonyl, nitriles, aromatic compounds, etc. undergo  $\pi \rightarrow \pi^*$  transitions.

### IV. $n \rightarrow \pi^*$ transition:

- Unsaturated compounds containing heteroatoms such as O, N, S show this type of transition.
- An electron from non-bonding orbital is promoted to anti-bonding  $\pi^*$  orbital.
- Compounds containing double bond involving hetero atoms ( $C=O$ ,  $C\equiv N$ ,  $N=O$ ) undergo such transitions.
- $n \rightarrow \pi^*$  transitions require minimum energy and show absorption at longer wavelength around 300 nm.
- Aldehydes, ketones, cyanides, carboxylic acid etc.

**Electronic transitions in the order of increasing energy:**





### Important terms in UV-visible Spectroscopy

#### Chromophores :

- The part of a molecule responsible for imparting colour, are called as chromophores.
- It is covalently bonded unsaturated group responsible for electronic absorption.
- Chromophores show absorptions due to  $n \rightarrow \pi^*$  &  $\pi \rightarrow \pi^*$  transitions.
- There are two types of chromophores:

(a) Chromophores containing  $\pi$  electrons; they undergo  $\pi \rightarrow \pi^*$  transitions,  
For e.g. ethene ( $-\text{C}=\text{C}-$ ), ethylene ( $-\text{C}\equiv\text{C}-$ ) etc.

(b) Chromophores containing both  $\pi$  and  $n$  electrons; they exhibit two types of transitions:  $\pi \rightarrow \pi^*$  and  $n \rightarrow \pi^*$

For e.g.  $>\text{C}=\text{O}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{N}=\text{O}$

- When double bonds are conjugated in a compound  $\lambda_{\text{max}}$  is shifted to longer wavelength.  
e.g. 1,5 - hexadiene has  $\lambda_{\text{max}} = 178 \text{ nm}$   
2,4 - hexadiene has  $\lambda_{\text{max}} = 227 \text{ nm}$

**Q.** Which one of the following have higher  $\lambda_{\text{max}}$  in U.V. spectroscopy.

- 1,3 pentadiene and 1,4 pentadiene
- Anthracene and Benzene
- $\text{CH}_3\text{COCH}_3$  and  $\text{CH}_2=\text{CH}-\text{CO}-\text{CH}_3$

#### Auxochrome

- An auxochrome is colour enhancing group.
- When it is attached to chromophore, it changes intensity as well as the wavelength of the absorption maximum.
- They are saturated groups having lone pairs of electrons.

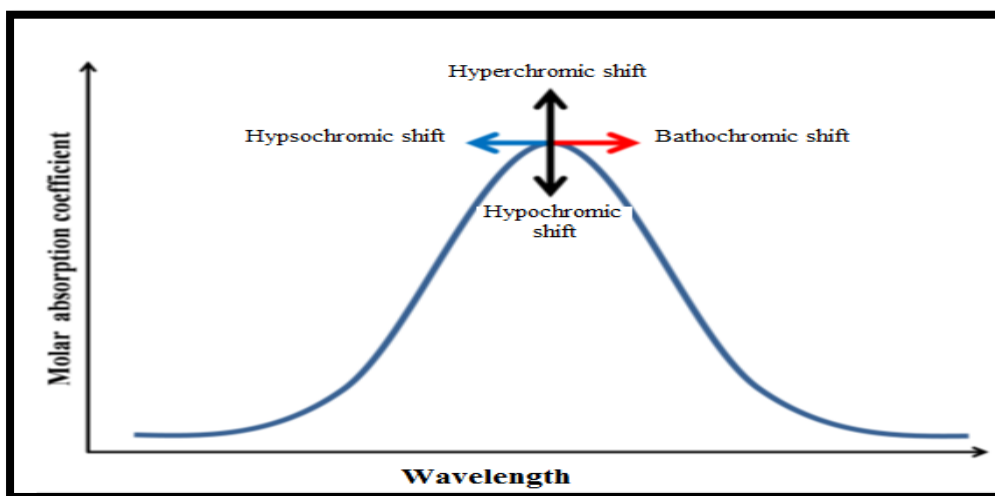
- Auxochrome generally increases the value of absorption maxima by extending the conjugation through resonance.
- e.g  $\text{NH}_2$ ,  $\text{OH}$ ,  $\text{OR}$ ,  $\text{NHR}$ ,  $-\text{SH}$  etc.

### Intensity and Absorption shift

When an absorption in a molecule is affected either by any structural environment or by solvent, it gets shifted. The absorption may shift by intensity or by wavelength. The various shifts are:

#### (i) Bathochromic shift (Red shift) :-

- The effect which cause shifting of absorption maximum towards longer wavelength is called Bathochromic shift.
- Red shift may be affected by:
  - a. The change of medium.
  - b. The presence of an auxochrome.
  - c. The presence of conjugation.



**Fig: Absorption and Intensity Shift**

#### (ii) Hypsochromic shift (Blue shift) :-

- The effect which cause the shifting of absorption maximum towards shorter wave-length is called Hypsochromic shift.
- Blue shift may be produced by-
  - a. The removal of conjugation
  - b. The removal of an auxochrome
  - c. The change in solvent polarity.

#### (ii) Hyperchromic shift :-

- The effect which cause an increase in the intensity of absorption maximum ( $\epsilon_{\text{max}}$ ) is called hyperchromic shift.
- It is usually affected by the introduction of an auxochrome.

(iii) **Hypochromic shift:-**

- The effect which cause the decrease in the intensity of absorption maximum ( $\epsilon_{\max}$ ) is called hypochromic shift.
- It is caused by the groups which distorts the geometry of the molecule.

**Solvent effect:**

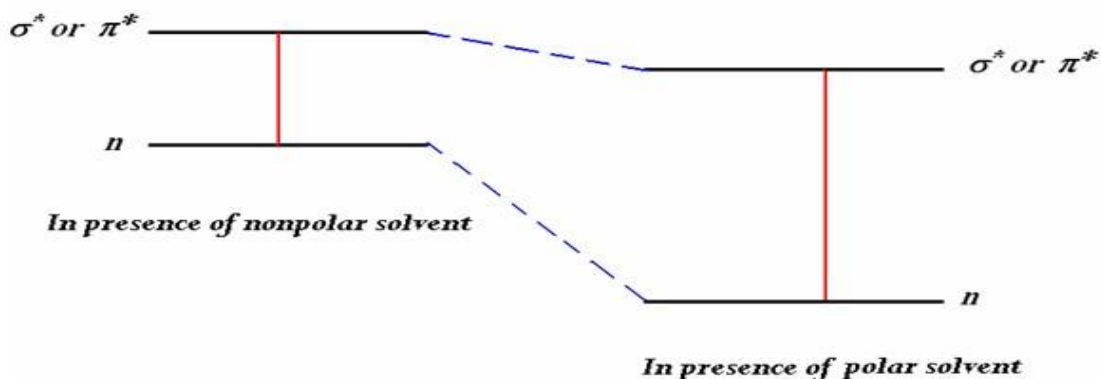
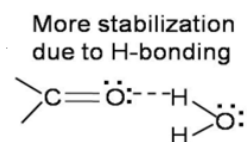
- The most suitable solvent for UV spectroscopy is the one which does not absorb in the region under investigation. Ex: Ethanol, Hexane, Methanol, Cyclohexane etc.

**Unsaturated carbonyl compounds** (ex: methyl vinyl ketone (butenone) or  $\text{CH}_2=\text{CHCOCH}_3$ ) show two different shifts on increasing the polarity of the solvent.

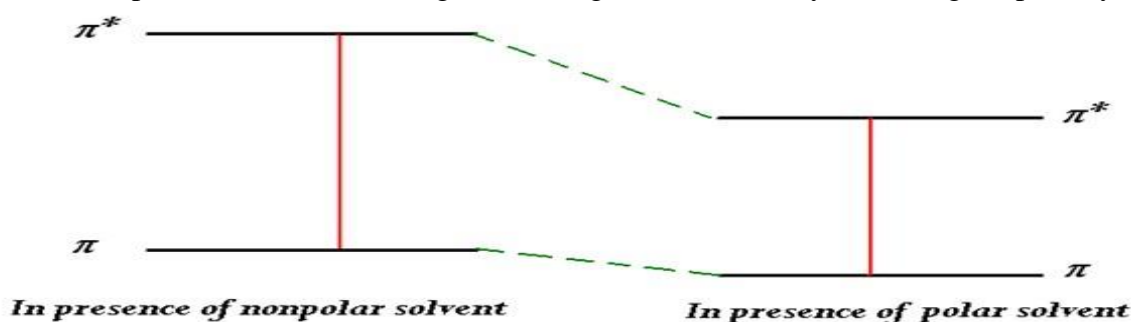
 **$n \rightarrow \pi^*$  transition**

- A net increase in energy required for a  $n \rightarrow \pi^*$  transition is thus observed in protic solvents like water or alcohols.

- Hydrogen bonding stabilizes  $n$  more than  $\pi^*$  in polar solvents.
- Thus absorption band moves to shorter wavelength i.e. blue shift by increasing the polarity of the solvent.

 **$\pi \rightarrow \pi^*$  transition**

- In the presence of a polar solvent, the more polar  $\pi^*$  orbital will be more stabilized than  $\pi$  orbital leading to a net decrease in the transition energy.
- The dipole-dipole interaction with the solvent molecules lower the energy of excited state more than that of the ground state.
- Absorption band moves to longer wavelength i.e. red shift by increasing the polarity of the solvent.



**Application of UV- visible spectroscopy:**

- i. **Detection of Conjugation:** UV-visible spectroscopy is an important tool to determine the extent of conjugation in polyenes (compounds having more than one double bond). With increase in conjugation the  $\lambda_{\text{max}}$  shifts towards the longer wavelength.
- ii. **Detection of impurities:** UV- visible absorption spectroscopy is one of the best methods for determination of impurities in organic molecules. Additional peaks can be observed due to impurities in the sample and it can be compared with that of standard raw material.
- iii. **Quantitative analysis:** Determination of molecular weight using Lambert's Beer's law.  $A = \epsilon \cdot c \cdot l$   
where: A = absorbance,  $\epsilon$  = absorptivity, l = path length, c = concentration.
- iv. **Detection of geometrical isomers:** Geometrical isomers can be distinguished by UV-visible spectroscopy. The trans isomer exhibit  $\lambda_{\text{max}}$  at slightly longer wave length than the cis-isomers.
- v. **Qualitative analysis:** UV- visible absorption spectroscopy can characterize the compounds which absorb UV-visible radiation. Identification is done by comparing the absorption spectrum with the spectra of known compounds.
- vi. **Study of kinetics of chemical reaction.** The UV-visible radiation is passed through the reaction cell and the absorbance changes can be observed. As we know that absorbance is directly proportional to concentration.
- vii. **Quantitative analysis:** Used in quantitative analysis of pharmaceutical substances and drugs.

**Infrared Spectroscopy****Theory of IR spectroscopy**

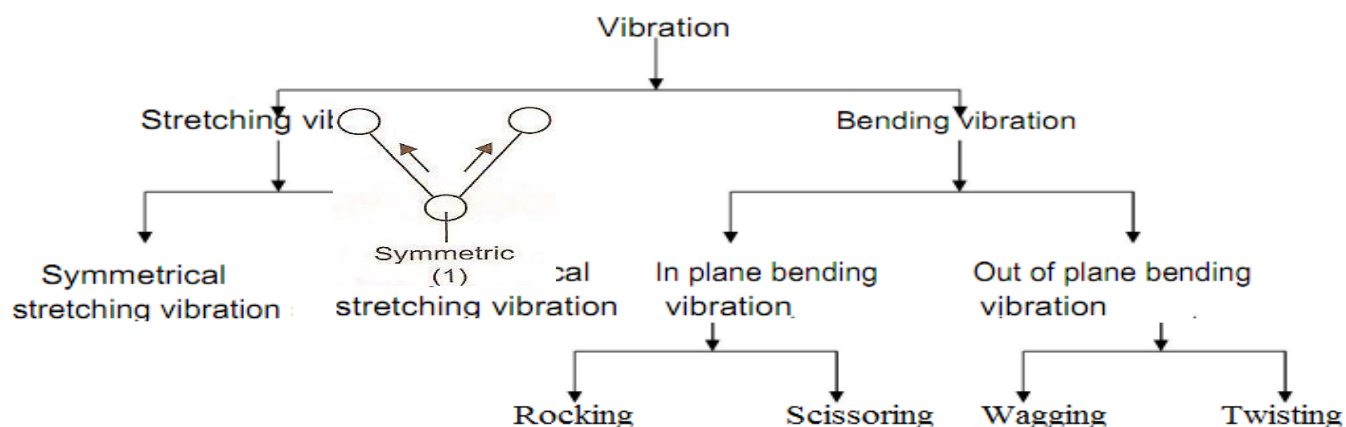
- IR spectroscopy deals with **the infrared region** of the electromagnetic radiation.
- It involves the transitions between **vibrational energy levels**.
- Infrared spectroscopy region lies between **4000-625  $\text{cm}^{-1}$  (2.5-16  $\mu\text{m}$ )**.



- IR spectra can be used to provide information on the **functional group** as well as the **structure of a molecule**.

### Fundamental mode of vibration for $XY_2$ molecule.

Types of vibrations in IR spectroscopy:

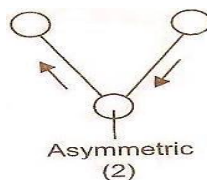


(i) **Stretching Vibration**:- In this type of vibrations, the distance between two atoms increases or decreases but the center atom remain in the same bond axis. During the stretching vibration, there is change **in bond length but no change in bond angle**.

### Types of Stretching Vibration :

(a) **Symmetric Stretching**: When the stretching and compressing occurs in a symmetric way, it is called symmetric stretching.

(b) **Asymmetric Stretching**: When one bond is compressed and the other is stretched, it is known as asymmetric stretching.

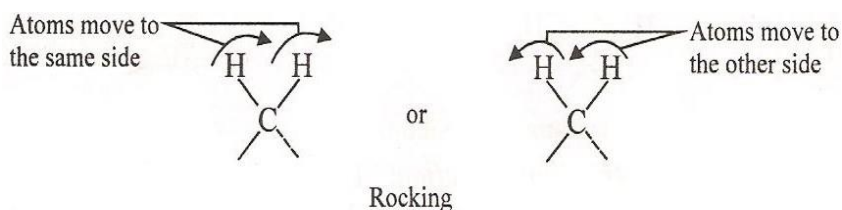


(ii) **Bending Vibration**:- In this type of vibrations, the position of the atoms changes with respect to the original bond axis but the distance between the atoms remain same. In other words, bond angle changes but the bond length remains same.

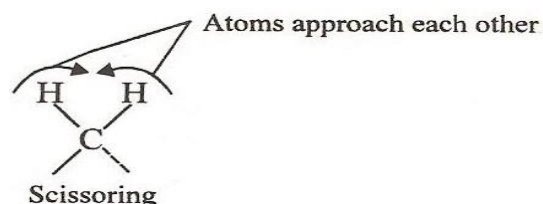
Types of Bending Vibration:

**In plane Bending vibrations :** In this type atoms remain in the same plane.

a) **Rocking**:-The mode of bending vibration in which both the atoms move to the same side and then both move to the other side.

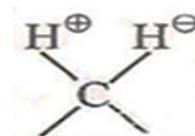


b) **Scissoring** :- The mode of bending vibration in which both the atoms approach each other.

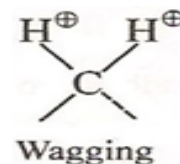


**Out plane Bending vibrations:** In this type atoms remain in the different plane.

c) **Twisting** :- The mode of bending vibration in which one of the atoms moves up the plane while the other moves down the plane with respect to the central atom.



d) **Wagging**:-The mode of bending vibration in which two atoms moves up the plane and below the plane with respect to the central atom.



### Calculation of Fundamental mode of vibration

The number of fundamental vibrations depend upon the structure of the molecule.

For linear molecules:

$$\text{Vibrational degrees of freedom} = 3N - 5$$

For Non-linear molecules:

$$\text{Vibrational degrees of freedom} = 3N - 6$$

where, N is the number of atoms in the molecule.

Example:

H<sub>2</sub>O is non-linear molecule.  $3N - 6 = 3 \times 3 - 6 = 3$  fundamental vibrations.

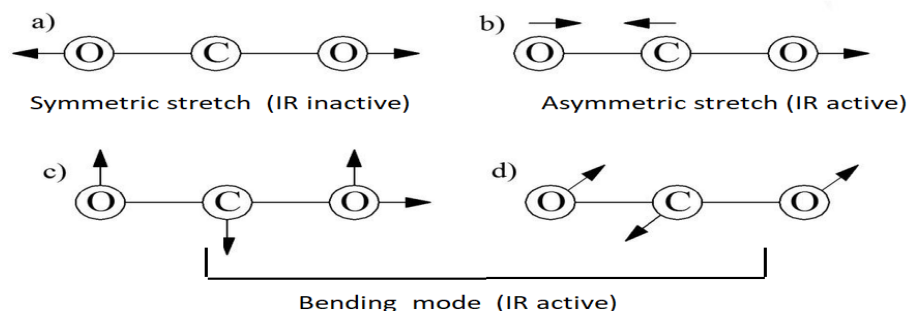
HCN is linear molecule.  $3N - 5 = 3 \times 3 - 5 = 4$  fundamental vibrations.

Fundamental vibrations of CO<sub>2</sub> molecule

CO<sub>2</sub> is linear molecule.  $3N - 5 = 3 \times 3 - 5 = 4$  vibrations

It has expected four vibrational mode but actually three are considered.

Because in bending vibration, there are two modes, but they have same frequency, so they are said to be degenerate state. So out of 4 only 3 are consider as vibrational mode.



### Regions of IR Spectroscopy:

#### (i) Functional-group region:

- Peaks in this region are characteristic of specific functional group.
- This region lies in between  $4000\text{ cm}^{-1}$  to  $1300\text{ cm}^{-1}$ .
- Different functional group absorb at characteristic frequencies in this region of the spectrum.
- Eg. OH-  $3610\text{--}3650\text{ cm}^{-1}$ , carbonyl CO-  $1750\text{ cm}^{-1}$ , aromatic ring C-H - $3000\text{--}3100\text{ cm}^{-1}$

#### (ii) Fingerprint region:

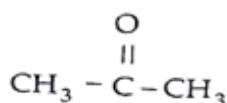
- The area from  $1300\text{ cm}^{-1}$  to  $687\text{ cm}^{-1}$  is called the fingerprint region.
- The IR spectrum of an unknown substance compared with spectra of possible substance.
- The pattern of bands in this region are dependent on the structure of the molecule as a whole.
- Fingerprint region is associated with complex vibrational and rotational energy changes and is characteristic of the molecule as a whole.

### Applications of IR spectroscopy:

- (1) Identification of functional groups.
- (2) Determination of impurities in a sample.
- (3) Determination of shape or symmetry of a molecule.
- (4) Determination of force constant.
- (5) Provides a valuable information of dipole-moment, bond-lengths etc.
- (6) Useful to distinguish between inter and intra molecular hydrogen bonding in a molecule.

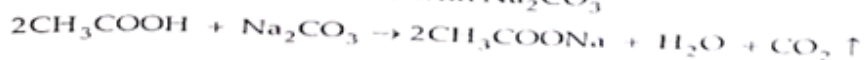
**Example** Determine the structure of the compound,  $C_3H_6O$  showing the following absorption bands in IR spectrum ; (i)  $2950\text{ cm}^{-1}$  and (ii)  $1720\text{ cm}^{-1}$ . The compound gives negative test with Tollen's reagent. [IPTU, IInd Sem., 2009-10] 12]

**Solution.** As the compound ( $C_3H_6O$ ) show absorption bands in IR spectrum at  $2950\text{ cm}^{-1}$  and  $1720\text{ cm}^{-1}$ . It means, this compound has carbonyl functional group. Further, the compound gives negative test with Tollen's reagent so it must not be an aldehyde. Thus, the compound is a ketone. It must be acetone.



$\therefore$  Possible compound :  $\begin{array}{c} \text{O} \\ || \\ \text{CH}_3 - \text{C} - \text{OH} \end{array}$  (Ethanonic acid or Acetic acid)

**Confirmation :** It gave effervesces with  $\text{Na}_2\text{CO}_3$



**Example** A compound having molecular formula  $C_2H_4O_2$  while studied for its IR analysis resulted the following peaks in its spectrum :  $2900 - 2950\text{ cm}^{-1}$ ,  $1710\text{ cm}^{-1}$  and  $3500 - 3650\text{ cm}^{-1}$ . The compound also gave effervesces with  $\text{Na}_2\text{CO}_3$ . Suggest structure of the compound.

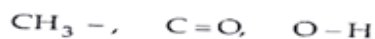
**Solution.**

[IPTU, Ist Sem., 2011-12]

Position of peak in IR spectrum	Interpretation
(i) $2900 - 2950\text{ cm}^{-1}$ -	C-H stretching of alkyl group say $-\text{CH}_3$ group
(ii) $1710\text{ cm}^{-1}$	C=O stretching in carboxylic acid
(iii) $3500 - 3650\text{ cm}^{-1}$	O-H stretching of carboxylic acids

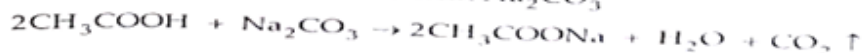
Given molecular formula :  $C_2H_4O_2$

Possible functionalities as per IR spectra :



$\therefore$  Possible compound :  $\begin{array}{c} \text{O} \\ || \\ \text{CH}_3 - \text{C} - \text{OH} \end{array}$  (Ethanonic acid or Acetic acid)

**Confirmation :** It gave effervesces with  $\text{Na}_2\text{CO}_3$



## NMR Spectroscopy

### Theory NMR Spectroscopy

- Nuclear Magnetic resonance is the branch of Spectroscopy in which **radio frequency** waves induce transitions between magnetic energy levels of spin active nuclei of a molecule when they are placed in magnetic field.
- Radio frequency range is 4 to 900 MHz used in NMR Spectroscopy.
- Spin active nuclei shows the NMR Spectroscopy. (Nuclei in which the sum of protons and neutrons is odd (ie., mass number is odd and atomic number odd or even).  
For Example:  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{15}\text{N}$ ,  $^{31}\text{P}$
- NMR techniques gives the following information:
  - The number of signals
  - The position of signals.
  - The intensities of the signals
  - The splitting if signal into several peaks

### Number of signals and Splitting of Proton Signals

The **number of NMR signals** represents the **number of different types of protons** in a molecule.

- **Equivalent Protons:** In a molecule, protons in the same magnetic environment absorb at the same applied magnetic field strength,  $B_0$  are known as equivalent protons.
- **Non-Equivalent Protons:** In a molecule, protons in the different magnetic environment absorb at the different applied magnetic field strength,  $B_0$  are known as non-equivalent protons.
- **Spin- Spin Coupling:** The magnetic interaction between the spins of neighboring, non –equivalent NMR- active nuclei may cause splitting of NMR spectrum which is known as spin – spin coupling. The splitting pattern of a given nucleus (or set of equivalent nuclei) can be predicted by the **n+1 rule**, where n is the number of protons present on the adjacent carbon(s).

S.No.	Compounds	Number of signals	Splitting pattern
1.	$\text{CH}_4$ A	1	a = 1 (singlet), No Splitting
2.	$\text{CH}_3 \text{ CH}_2 \text{ CH}_3$ a    b    a	2	a = 3 triplet b = 7 septet
3.	$\text{CH}_3\text{CH}_2\text{OH}$ a    b    c	3	a = 3 triplet b = 4 quartet c = 1 (singlet), No Splitting
4.	$(\text{CH}_3)_3 \text{ CO CH}_3$ a                    b	2	a = 1 (singlet), No Splitting b = 1 (singlet), No Splitting
5.	$\text{CH}_3 . \text{CH}(\text{Cl}). \text{CH}_2\text{Cl}$ a    b    c	3	a = 2 doublet b = 6 sextet c = 2 doublet

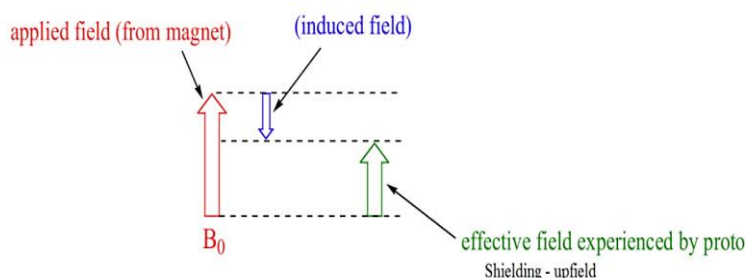
6.	$\begin{array}{cccc} \text{CH}_3 & \text{CH}_2 & \text{CH}_2 & \text{OH} \\ \text{a} & \text{b} & \text{c} & \text{d} \end{array}$	4	a = 3 triplet b = 6 sextet c = 3 triplet d = 1 (singlet), No Splitting
7.	$\begin{array}{c} \text{O} \\ \parallel \\ \text{H}_3\text{C} - \text{C} - \text{CH}_2 - \text{CH}_3 \\ \text{a} \qquad \qquad \text{b} \quad \text{c} \end{array}$	3	a = 1 (singlet), No Splitting b = 4 quartet c = 3 triplet

### Position of signals, Chemical Shift

When a molecule is placed in a magnetic field its electrons are made to circulate and thus generate a secondary magnetic field called induced magnetic field which may either reinforce or oppose the applied magnetic field.

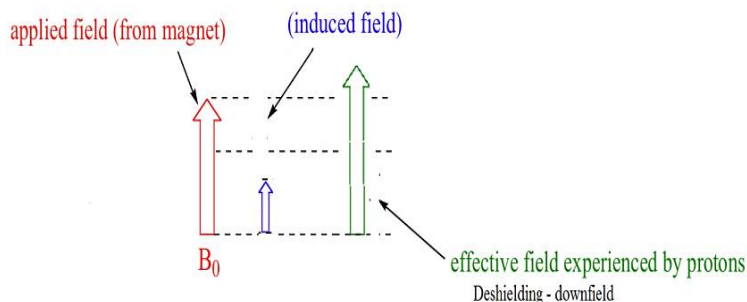
#### Shielding of Protons

- In case the induced field opposes the applied field, the field felt by the proton is diminished, such a proton is said to be shielded.
- This shielded proton requires a stronger magnetic field to produce an absorption signal (as compared to a native proton) and thus is said to absorb upfield.



#### Deshielding of Protons

- If the induced field reinforces the applied field, the field felt by the proton is increased, such a proton is said to be deshielded.
- A deshielded proton requires a lower applied field to produce an absorption signal and thus is said to absorb downfield.



The shifts in the position of NMR signals arising from shielding or deshielding by electrons are referred to as **Chemical Shift**.

The **chemical shift** in absolute terms is defined by the frequency of the resonance expressed with reference to a standard compound which is *defined* to be at 0 ppm. The scale is made more manageable by expressing it in parts per million (**ppm**) and is independent of the spectrometer frequency.

$$\text{Chemical shift, } \delta = \frac{\text{frequency of signal} - \text{frequency of reference}}{\text{spectrometer frequency}} \times 10^6$$

Chemical shifts are measured with the reference to fixed standard i.e., Tetramethylsilane (TMS),  $(\text{CH}_3)_4\text{Si}$  is the standard in the proton magnetic resonance spectroscopy.

**The choice of TMS as the standard has following advantages:**

- i) TMS is chemically inert.
- ii) It is miscible with almost all organic substance
- iii) It is highly volatile and is readily removed from the system.
- iv) TMS gives single intense peak in its NMR spectrum.
- v) It has low boiling point.

### Applications of NMR spectroscopy

- i. Structure elucidation
- ii. Mixture analysis
- iii. Sample purity determination
- iv. Quality assurance and control
- v. Quantitative analysis
- vi. Raw materials fingerprinting
- vii. Compound identification and confirmation
- viii. Analysis of inter- and intramolecular exchange processes
- ix. Molecular characterization
- x. Reaction kinetics examination

## Part –II Stereochemistry

[Optical isomerism in compounds without chiral carbon, Geometrical isomerism, Chiral Drugs]

### Stereoisomerism:

The phenomenon exhibited by two or more compounds with the same molecular and structural formula, but different spatial arrangements of atoms or groups, is known as stereoisomerism. Stereoisomerism can be categorized into two categories:

- I. Geometrical isomerism
- II. Optical isomerism

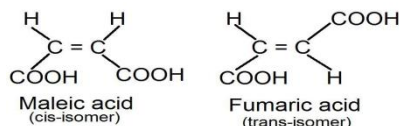
**Geometrical isomerism:** *The geometrical isomerism arises when atoms or groups are arranged differently in space due to restricted rotation of bonds in a molecule.*

### cis or trans isomers

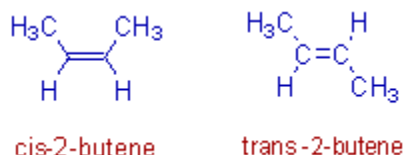
When a similar group is placed at an adjacent position the compound is named with the prefix *cis*

When a similar group is placed at the opposite position the compound is named with the prefix *trans*

1) butenedioic acid:



2) cis-2-butene and trans-2-butene



### E-Z notation

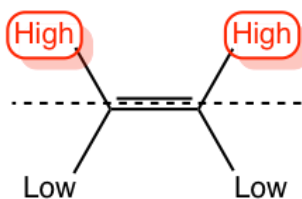
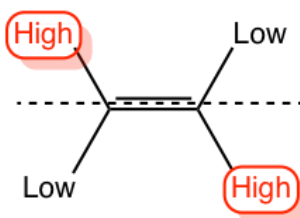
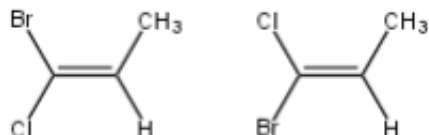
According to this method, if the groups with higher priorities are present on the opposite sides of the double bond, that isomer is denoted by E. Where E = Entgegen (the German word for 'opposite')

However, if the groups with higher priorities are on the same side of the double bond, that isomer is denoted by Z. Where Z = Zusammen (the German word for 'together')

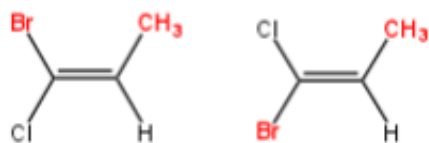
The following procedure is to be adopted to denote the geometrical isomers by E & Z descriptors.

- First determine the higher priority group on each end of the double bond.
- If the higher priority groups are on the opposite sides of double bond, the isomer is denoted by the descriptor, E.
- Otherwise if they are on the same side of double bond, the Z descriptor must be used.
- The priorities are assigned by following **Cahn-Ingold-Prelog sequence rules (CAN rules)** described below.
  - (i) Rank the atoms directly attached to the olefinic carbon according to their atomic number. High priority is given to the atom with higher atomic number.
  - (ii) If isotopes of same element are present, the higher priority is given to the isotope with higher atomic mass. E.g.
  - (iii) The Deuterium isotope ( $\text{H}^2$  or D) has more priority than protium ( $\text{H}^1$  or H).
  - (iv) The  $\text{C}^{13}$  isotope has more priority than  $\text{C}^{12}$ .
  - (v) If the atoms are still identical, examine the next atoms along the chain until a “first point of difference” is found. This is done by making a list of atoms linked directly to the first atom. Each list is arranged in order of decreasing atomic number. Then the higher priority is given to the list which contain atom with higher atomic number at first point of difference.

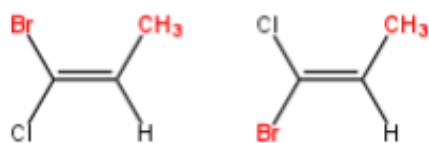


**Z - isomer****E - isomer****Example 1**

Step 1: Identify the higher priority groups.



Step 2: Assign E/Z based on orientation.

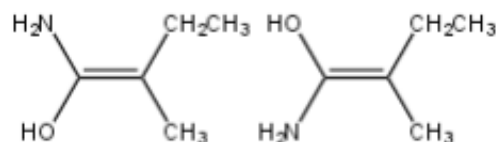


same side -&gt; Z

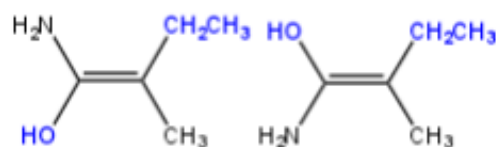
(Z) Isomer

opposite sides -&gt; E

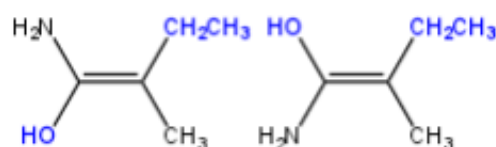
(E) Isomer

**Example 2**

Step 1: Identify the higher priority groups.



Step 2: Assign E/Z based on orientation.



opposite sides -&gt; E

(E) Isomer

same side -&gt; Z

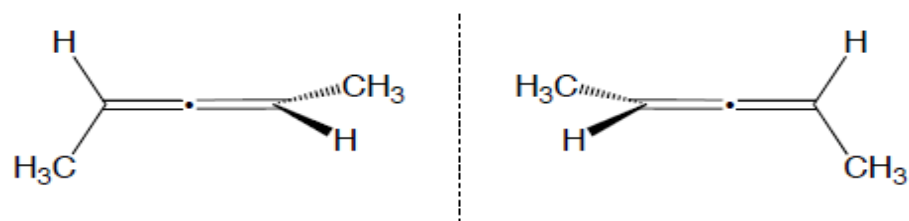
(Z) Isomer

### Optical isomerism of Organic compounds without chiral carbon

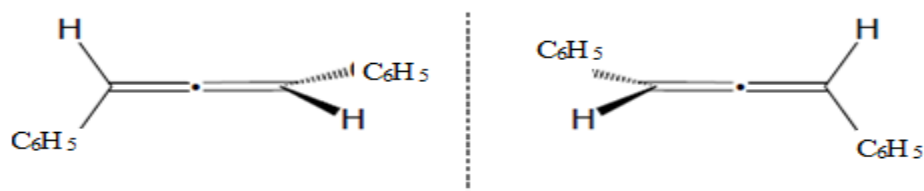
Some compounds which do not have asymmetrically substituted carbon atoms (or any other atom type) may still be chiral if they feature two perpendicular planes which are not symmetry planes. If these *disymmetric* (chiral) planes cannot freely rotate against each other, the corresponding compounds are chiral.

There are some molecules that do not contain chiral carbons but are chiral. E.g.

- (i) **Allenes:** Compounds containing a  $C=C=C$  unit are called allenes. In allene, the central C atom is  $sp$  hybridized, but the two outer carbons are  $sp^2$  and the planes containing the substituents on either end of the double bonds are aligned perpendicular to each other. The whole molecule does not lie in the same plane. An allene is chiral if each end has two distinct substituents.

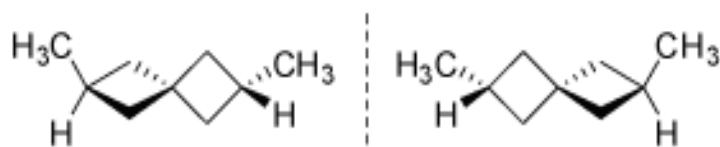


2,3-propadiene



1,3 Diphenyl propadiene

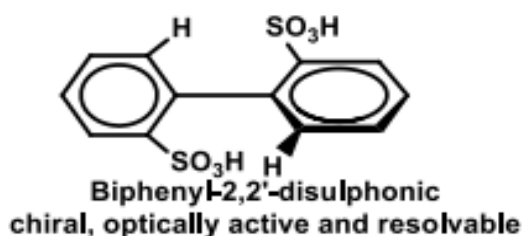
**(ii) Spiro compounds** :A spiro compounds are bi- or polycyclic organic compounds with rings connected through just one atom. The rings can be different in nature or identical. These two rings are perpendicular to each other .Because of restricted rotation spiranes exhibit optical isomerism. The connecting atom is also called the spiro atom .



enantiomers

2,6-dimethyl-spiro[3.3]heptane

**(iii) Biphenyls:** Biphenyls also exhibit optical isomerism due to restricted rotation around the single bond between the two benzene nuclei. In the biphenyls, the *ortho*-substituents must be large enough to prevent rotation around the central single bond; if hydrogen atoms are present in these positions the barrier of rotation may be too small to prevent interconversion of the enantiomeric .



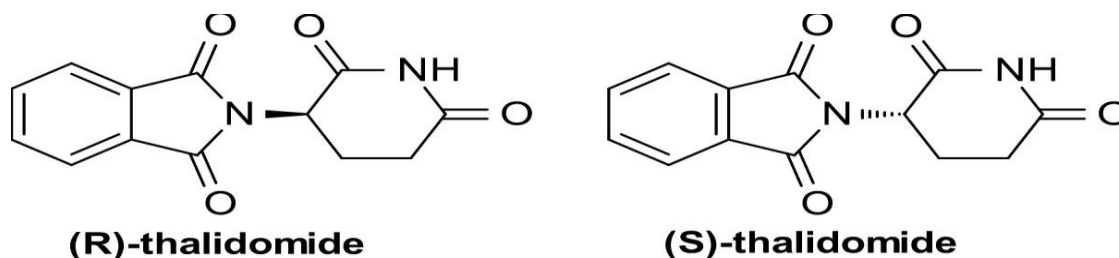
## Chiral Drugs

- Chirality is a property of an object which is non-superimposable with its mirror image.
- Drugs that exhibit chirality are referred to as chiral drugs.
- A chiral molecule is a molecule having at least one asymmetric carbon. Carbon is not the only atom that can act as an asymmetric center. Sulfur, phosphorus and nitrogen can sometimes form chiral molecules.
- In pharmaceutical industries, 56% of the drugs currently in use are chiral molecules and 88% of the last ones are marketed as racemates (or racemic mixtures), consisting of an equimolar mixture of two enantiomers.
- Although the enantiomers of chiral drugs have the same chemical connectivity of atoms; they exhibit marked differences in their pharmacology, toxicology, metabolism etc. Therefore, when chiral drugs are synthesized, as much effort goes towards the rigorous separation of the two enantiomers.

Few examples of chiral drugs, whose enantiomers vary drastically in their properties

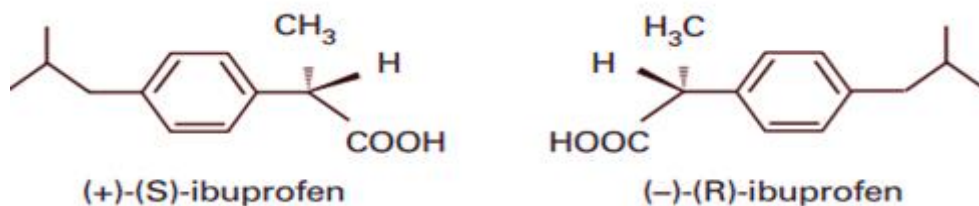
### 1. *thalidomide*.

The R-enantiomer is an effective sedative, which has a soothing effect that relieves anxiety and makes the patient drowsy; while, the S-enantiomer is known to cause teratogenic birth defects.



### 2. *Ibuprofen*:

A well-known painkiller, ibuprofen, the (S)-enantiomer has the desired pharmacological activity while the (R)-enantiomer is totally inactive.



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