



SCHOOL OF SCIENCE AND HUMANITIES
DEPARTMENT OF CHEMISTRY

UNIT-1 – Stereochemistry-I – SCYA5203

1. Symmetry and Symmetry Elements

Symmetry Operation: A symmetry operation is an action that leaves an object looking the same after it has been carried out. A classification of molecules is done with reference to five symmetry operations. Each symmetry operation is performed relative to a point, line, or plane - called a symmetry element. There are four symmetry elements that a molecule may possess.

Proper axis of Symmetry or n-fold axis of rotation (C_n): It denotes a rotation through an angle of $360^\circ/n$, thereby yielding an image indistinguishable from the original. The n-fold axis C_n is the respective symmetry element. Some molecules have more than one C_n axis, in which case, the highest value of n is called the principal axis. Rotations are counter clockwise about the axis.

Plane of symmetry (σ): Reflection in the plane leaves the molecule looking the same. In a molecule that also has an axis of symmetry, a mirror plane that includes the axis is called a vertical mirror plane and is labeled σ_v , while one perpendicular to the axis is called a horizontal mirror plane and is labeled σ_h . A vertical mirror plane that bisects the angle between two C_2 axes is called a dihedral mirror plane, σ_d .

Centre of symmetry (i): Inversion through the center of symmetry leaves the molecule unchanged. Inversion consists of passing each point through the center of inversion and out to the same distance on the other side of the molecule.

Improper axis of Symmetry or n-fold improper rotation axis (S_n): This operation consists of rotation through an angle $360^\circ/n$ about the axis, followed by reflection in a plane perpendicular to the axis.

2. Chirality and Optical Activity

Optical activity is the ability of a chiral substance to rotate the plane of plane-polarized light and is measured using an instrument called a polarimeter.

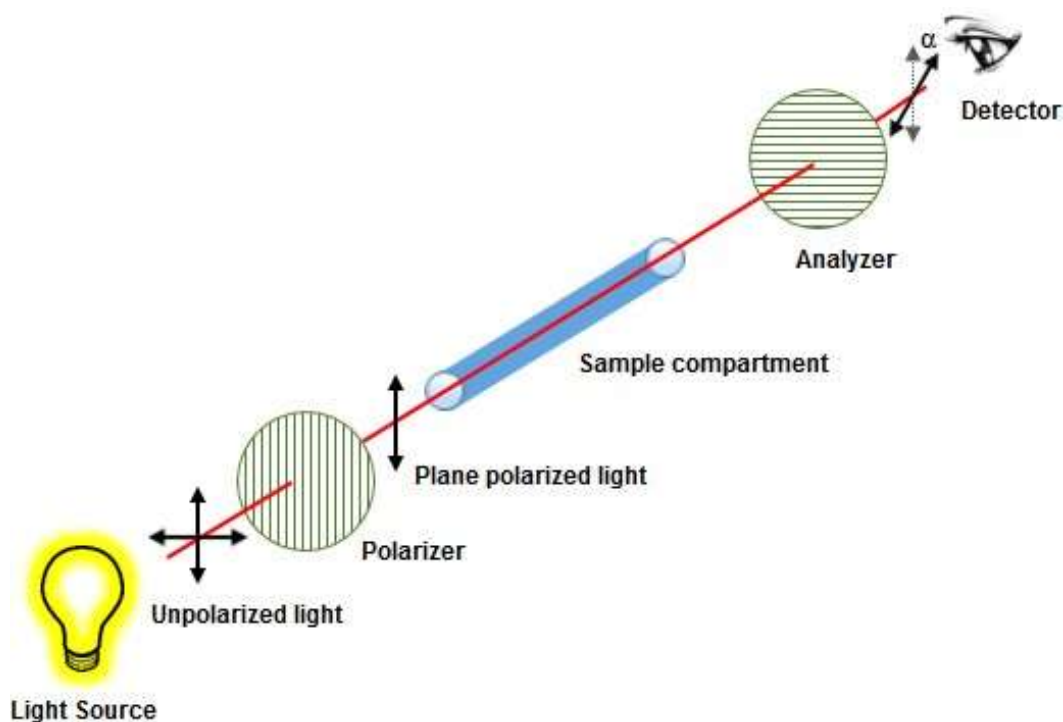


Figure 1: Block Diagram of Polarimeter

A beam of unpolarized light is transformed to plane-polarized light by passing it through a polarizing filter. This filter is usually a Nicol prism made up of calcite. This plane polarized light now passes through the sample tube containing the substance to be examined. The sample is optically active if it rotates the plane of polarized light. The direction and magnitude of rotation are measured using a second polarizing filter (the analyzer) and is given as α , the observed rotation. A substance that does not rotate the plane of polarized light is said to be optically inactive. All achiral substances are optically inactive. Rotation of plane polarized light in the clockwise direction is called dextrorotatory (+), and rotation in the anticlockwise sense is called laevorotatory (-) rotation. Optical activity is given in terms of specific rotation $[\alpha]$. Specific rotation is calculated from the observed rotation according to the expression

$$[\alpha] = \alpha / c \cdot l$$

where c – concentration in g/mL and l – length of the polarimeter tube in dm.

For a compound to be optically active, it should not possess plane of symmetry, centre of symmetry and improper axis of rotation. Presence of proper axis of symmetry is not a required condition for optical activity. Optically active compounds may or may not contain C_n . Chirality is not a necessary condition for optical activity since there are molecules that do not possess a chiral centre and yet display optical activity. Absence of symmetry or the three symmetry elements mentioned above is a necessary condition for optical activity.

Important Terminology

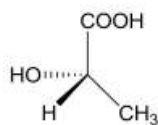
- a. **Dissymmetric molecules** - Molecules that do not possess a plane of symmetry, centre of symmetry and improper axis of rotation are called Dissymmetric molecules.
- b. **Asymmetric molecules** - Molecules that do not contain any element of symmetry are called Asymmetric molecules.
- c. **Enantiomers** – Enantiomers are stereoisomers that form non-superimposable mirror images of each other.
- d. **Diastereomers** – Diastereomers are stereoisomers that do not form mirror images of each other.
- e. **Epimer** – These are diastereomers that differ in the configuration of a single chiral centre.
- f. **Anomer** - Anomers are diastereoisomers of cyclic forms of sugars or similar molecules differing in the configuration at the newly formed chiral centre.
- g. **Chiral centre** – A tetrahedral carbon containing four different groups is said to be a chiral centre. It is also called a stereogenic centre.
- h. **Achirality** – If a molecule is superimposable on its mirror image, it is said to be achiral.
- i. **Chirality** – If a molecule is not superimposable on its mirror image, it is said to be possess chirality.

3. Representation of organic molecules

Since stereochemistry refers to molecules in three dimensions, appropriate modes of representations of three dimensional molecules on two-dimensional paper is essential. The wedge formula is most commonly used. Of the projection formula, Fischer, Newmann and Sawhorse projections are the most important.

i. Wedge formula

In the wedge formula, there are two line bonds, one solid wedge bond and one broken wedge bond for a tetrahedral stereogenic centre. The two line bonds are on the plane of the paper, the solid wedge is pointing towards the observer out of the plane and the broken wedge is pointing away from the observer out of the plane.



ii. Fischer Projection formula

In the Fischer projection formula, the horizontal bonds are coming out of the plane of the paper

and the vertical bonds are going away from the plane of the paper.



Rules for Fischer projection

- a. 90° in plane or out of plane rotation is not allowed.
- b. 180° in plane rotation is allowed.
- c. 180° out of rotation is not allowed.
- d. Exchange in groups of 2 is not allowed.
- e. Exchange in groups of 3 is allowed.

iii. Newmann projection formula

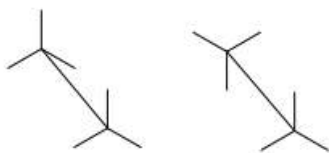
This is applicable for two carbon systems. The front carbon is written as a dot. The second carbon is represented as a circle behind the dot. The substituents on the dot are usually written



in the form of a Y or inverted Y. The back carbon substituents are written in a similar fashion.

iv. Sawhorse Projection formula

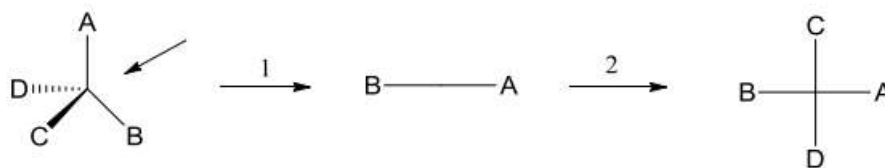
This is also applicable to two carbon systems. The C-C bond is elongated to represent a sawhorse in an angular fashion. The substituents on each carbon can be represented in the form of a Y or inverted Y.



Interconversion between Fischer and Wedge Formulae

A. Compounds with one stereocenter

i. Conversion of wedge structure into Fischer projection

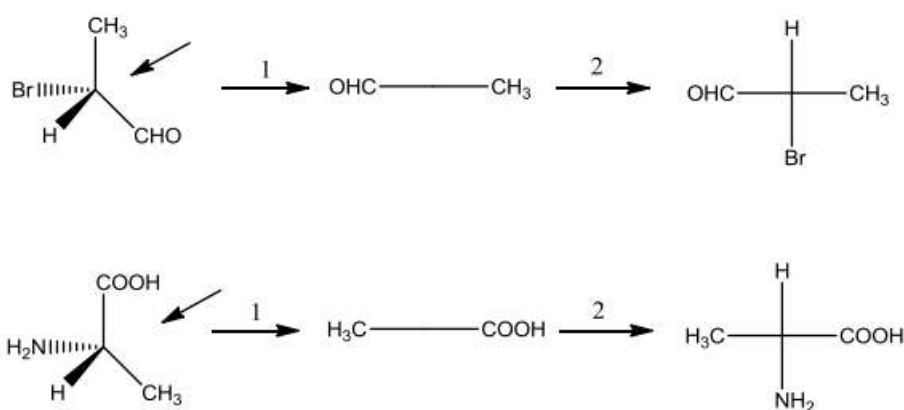


Step 1: View the molecule from in between the two bonds on the plane of the paper. The observer is standing perpendicular to the plane of the paper.

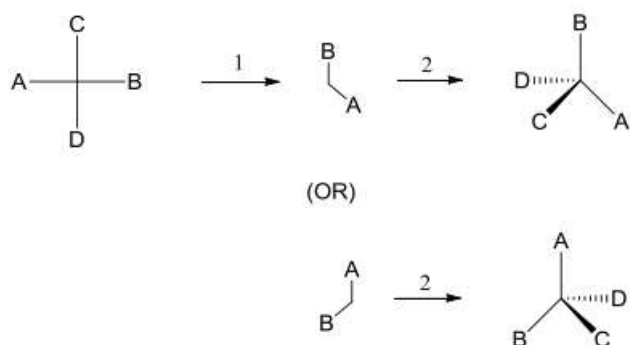
Step 2: The group A is to the right of the observer. The group B is to the left of the observer. Hence these two groups should be drawn on the horizontal plane of the Fischer projection with A to the right and B to the left.

Step 3: The group C in the solid wedge is above the observer and group D in the broken wedge is below the observer. Hence these two groups should be drawn on the vertical plane of the Fischer projection with C to the top and D to the bottom.

The same rules will apply no matter how the wedge formula is drawn. The observer should always be placed in between the bonds on the plane of the paper and stand perpendicular to the plane.

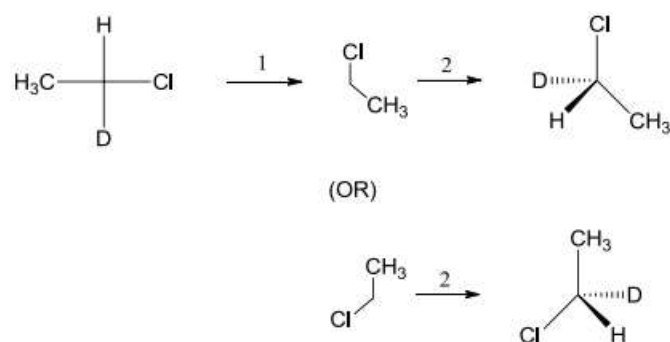


ii. Conversion of Fischer projection into wedge structure



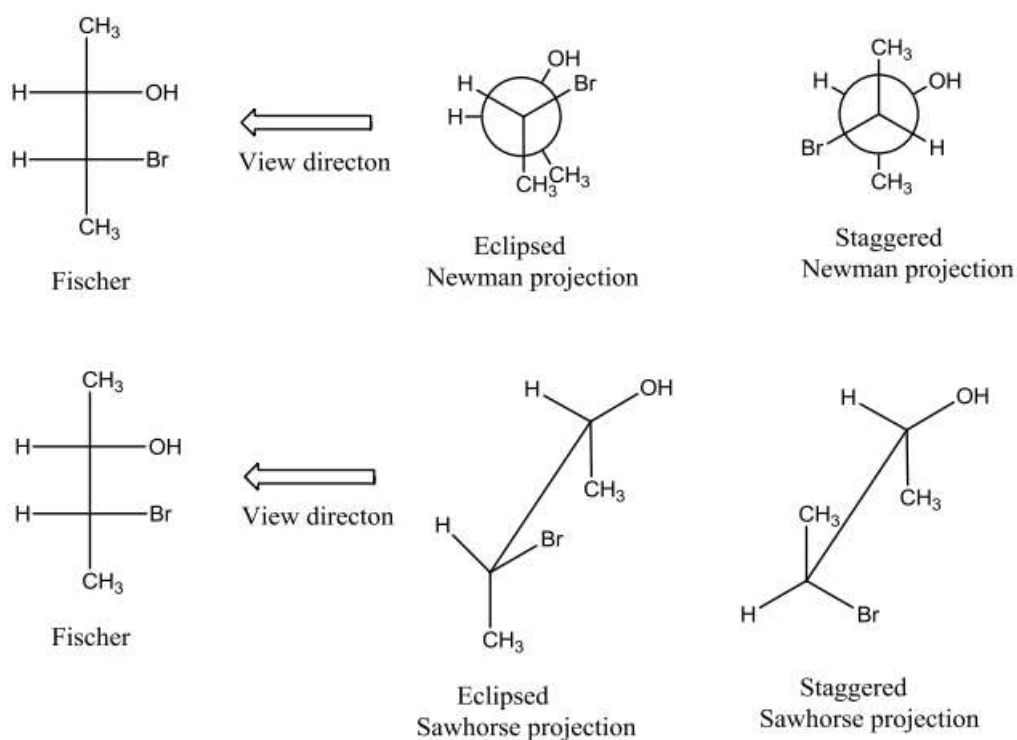
Step 1: The horizontal groups should be placed on the two bonds on the plane of the paper in either of the two ways shown above.

Step 2: The top group C should be written on the solid wedge and the bottom group D should be written on the broken wedge. Both forms will give the same representation.

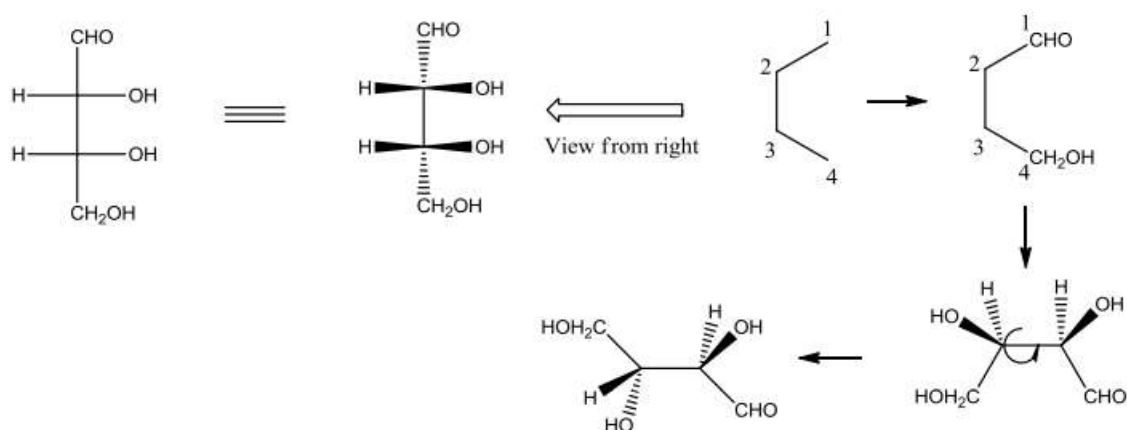


B. Compounds with two stereocenters

i. Interconversion of Fischer into Sawhorse and Newman projections

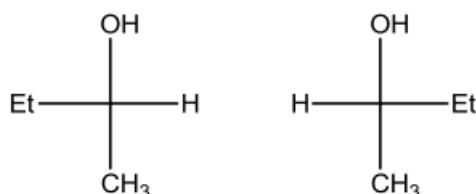


ii. Conversion of Fischer projection into Dashed-wedge line or Zig-zag projection

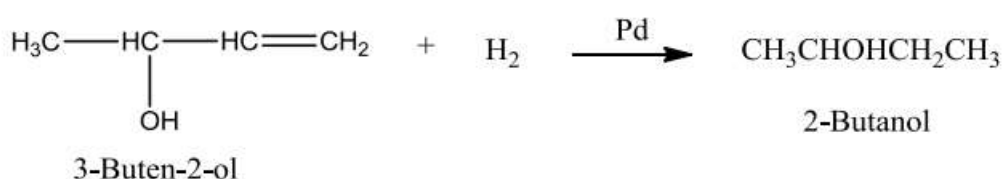


4. Absolute Configuration

The spatial arrangement of substituents at a stereogenic center is its absolute configuration. Neither the sign nor the magnitude of rotation by itself can tell us the absolute configuration of a substance. Thus, one of the following structures is (+)-2-butanol and the other is (-)-2-butanol, but without additional information we can't tell which is which.



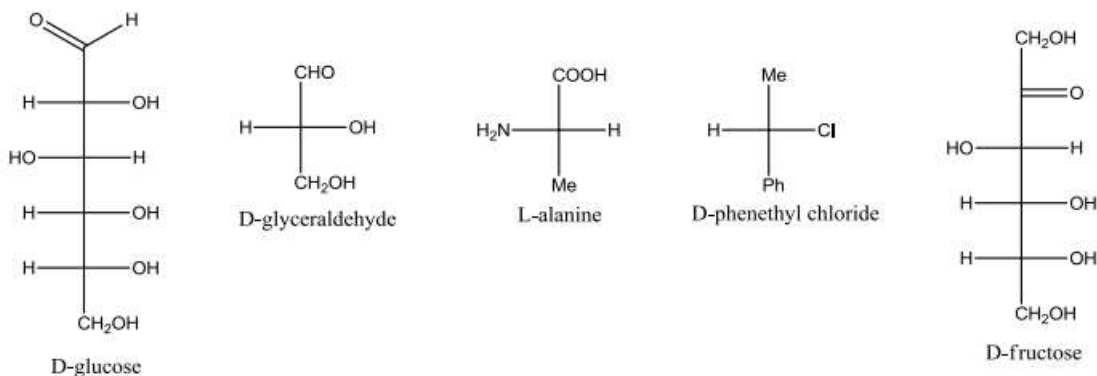
Although no absolute configuration was known for any substance before 1951, organic chemists had experimentally determined the configurations of thousands of compounds relative to one another (their relative configurations) through chemical interconversion. To illustrate, consider (+)-3-buten-2-ol. Hydrogenation of this compound yields (+)-2-butanol.



Since hydrogenation of the double bond does not involve any of the bonds to the stereogenic center, the spatial arrangement of substituents in (+)-3-buten-2-ol must be the same as that of the substituents in (+)-2-butanol. The fact that these two compounds have the same sign of rotation when they have the same relative configuration is established by the hydrogenation experiment; it could not have been predicted in advance of the experiment.

i. D and L Notation

There are several systems of configurational nomenclature. The oldest one is the D and L system and is applicable to molecules of the type R-CHXR' where R-C-R' is the main chain e.g. carbohydrates and amino acids. The number one carbon of the main chain is at the top in a Fischer projection. Then, if X is to the right of the stereocentre, the molecule is called D, if to the left, it is called L.



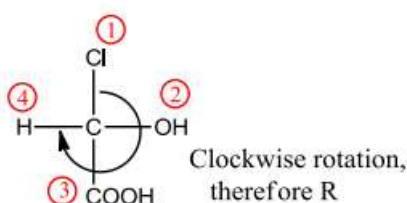
ii. R and S Notation (Cahn-Ingold-Prelog's rules)

This system is based on the actual three dimensional formula of the compound to be named. In order to name a compound Xabcd (X-asymmetric atom), the groups a, b, c and d are first arranged in a priority sequence according to the sequence rules. If in this sequence, the order of priority is $a > b > c > d$, then the molecule is viewed with d on the vertical line.

If $a \rightarrow b \rightarrow c$ traces a clockwise or right handed turn, the configuration is R (rectus). If it traces an anti-clockwise turn, the configuration is S (sinister).

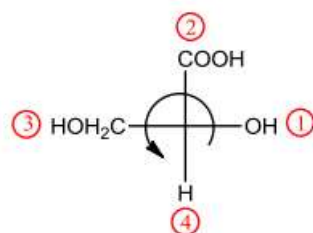
Sequence Rules

1. The groups are arranged in order of decreasing atomic number of the atoms directly attached to the asymmetric atom. The group with lowest priority should be in the vertical plane (back). If not, the order of priority is determined and the resulting configuration is inverted.



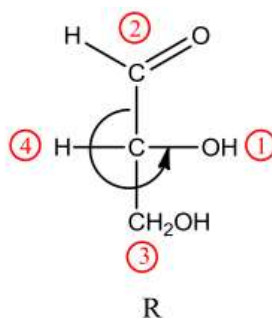
Since H is in the horizontal plane (front), the configuration is S

2. If two atoms attached to the asymmetric atom are the same, their respective states of substitution are considered. The atoms substituted with other atoms of higher atomic number takes priority or if two atoms are equivalent in that respect, then with more substituents of high atomic number comes first. If the second atoms afford no choice, then the third is selected.



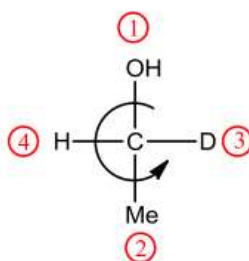
Anticlockwise rotation, therefore S

- For multiple bonds like double bonded N, O, etc, substitute N or O twice, for triple bonded N, substitute N thrice, etc. Phenyl group corresponds to C bonded to three other carbon atoms. Two N or O atoms attached to C takes priority over =N or =O.



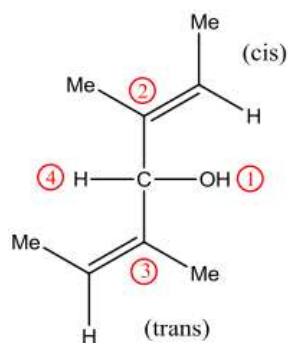
R

- In a case such as XabHD, the isotope of higher mass number precedes that of lower mass number



R

- In a case such as Xaa'bc, where a and a' are stereoisomeric, the cis takes precedence over the trans group and R takes precedence over S group.

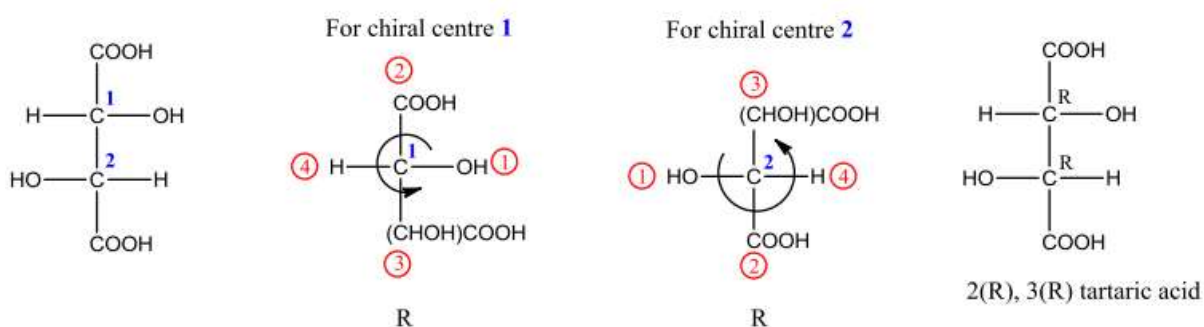


R

6. By applying these rules to some common substituents, one obtains the following sequence (group of highest priority first)

-I	-OH	-CH ₂ OH	-CH ₂ -CH=CH ₂
-Br	-NO ₂	-C ₆ H ₅	-CH ₂ (CH ₂)NCH ₃
-Cl	-NO	—C≡CH	-CH ₂ CH ₃
-SO ₂ R	-NHCH ₃	-C(CH ₃)	-CH ₃
-SOR	-NH ₂	-CH=CH ₂	-D
-SH	-COOH	-CH(CH ₃) ₂	-H
-F	-CONH ₂	-CH ₂ C ₆ H ₅	
-OC ₆ H ₅	-COR	—H ₂ C—C≡CH	
-OCH ₃	-CHO		

7. This system can be used for compounds with more than one asymmetric atom also.



5. Relative Configuration

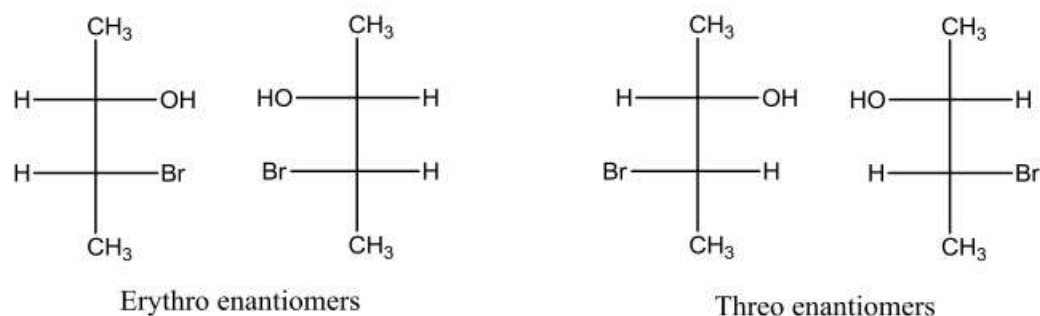
Relative configuration is the position of atoms or groups in space relative to something else in the molecule.

Prior to 1951 only relative configuration of compounds were known. For example, if (+) glyceraldehyde is converted to glyceric acid using a reaction that is known to put the COOH group where the CHO was, then the two compounds have the same relative configuration at their stereocenters even though one may not know their absolute configuration.

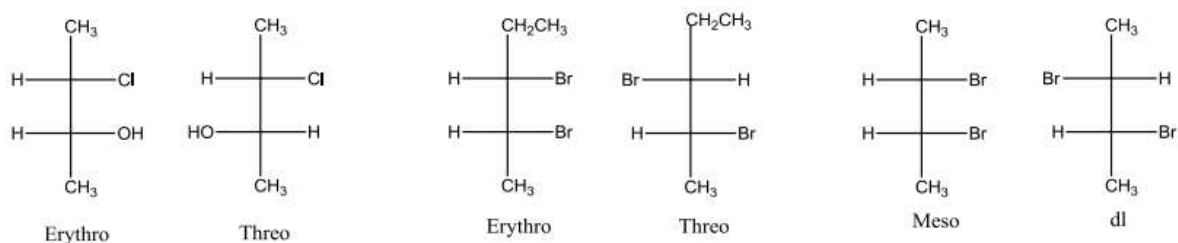
Relative configuration at a stereocenter is also the relation with that of any other stereocenter in the same molecule.

A. Erythro and Threo Nomenclature

A molecule with two adjacent stereocenters, when there are two groups which are common to each carbon while the third is different i.e., Cabx-Caby gives rise to erythro and threo diastereomers. Since erythrose and threose are diastereomers, other diastereomeric pairs of molecules which have two adjacent stereocenters are designated as erythro or threo depending on whether similar groups are on the same side (erthyro) or on opposite sides (threo) of the Fischer projection respectively. Thus 3-bromo-2-butanol with two stereocenters has (2²) four stereoisomers.



Erythro and threo is the short hand method employed by organic chemists to name appropriate compounds. R and S is used to refer to a particular enantiomer of the erythro and threo pair. The terms erythro and threo are applied only to those molecules which do not have symmetric ends. When, however, the ends are symmetric as in 2, 3-dibromobutane and tartaric acid, the terms meso and dl are preferred since the use of these terms show if the diastereomer has an enantiomer or not.

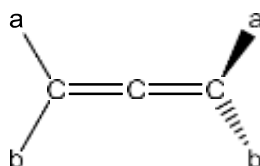


6. Optical activity in the absence of chiral carbon

Stereoisomerism in organic compounds is usually based on chiral centres acting as stereogenic units. Two other elements of chirality (axes and planes) also behave as stereogenic units. Hence, compounds such as allenes, hemispiranes, spiranes and biphenyls exhibit optical activity even in the absence of a chiral carbon. These two elements of chirality are called stereoaxis and stereoplanes.

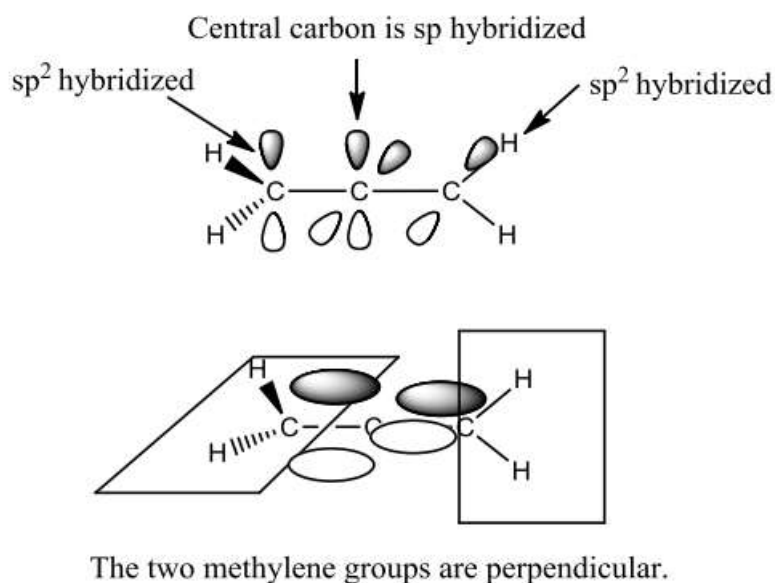
i. Allenes and Spiranes

An allene is said to be chiral if the two substituents at each end are different from each other ($a \neq b$).

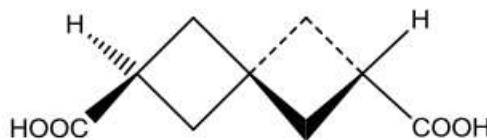
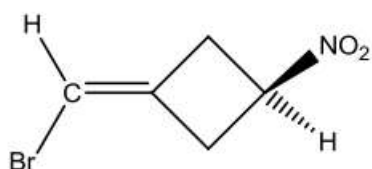


In an allene, the central carbon is sp hybridized and linear and the two other carbon atoms are

sp^2 hybridized and trigonal. In allene, the $C=C=C$ is a potential chiral axis. The two double bonds lie in perpendicular planes. Hence unsymmetrical substituents give chirality to the molecule.



The replacement of one double bond in allene with a ring gives a hemispirane. These type of molecules are also chiral provided the groups at each end are not identical. The replacement of both double bonds by ring systems gives a spirane. Similar rules of optical activity apply here.

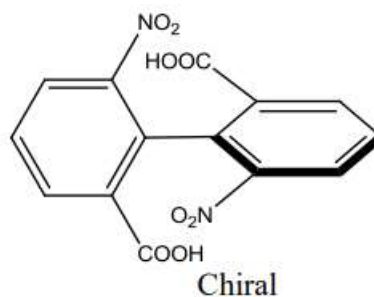
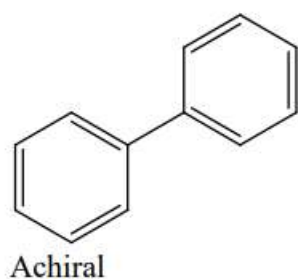


ii. Optical activity in Biphenyls

Atropisomers are stereoisomers resulting from hindered rotation about single bonds. Biphenyls is a class of compounds that exhibit atropisomerism. In the crystal state, both benzene rings of biphenyl lie in the same plane. In solution, the two rings are twisted with respect to each other by an angle of 45° due to steric interactions between the 2, 2' and 6, 6' pairs of hydrogens. These interaction effects are further enhanced by ortho substituents larger than hydrogen.

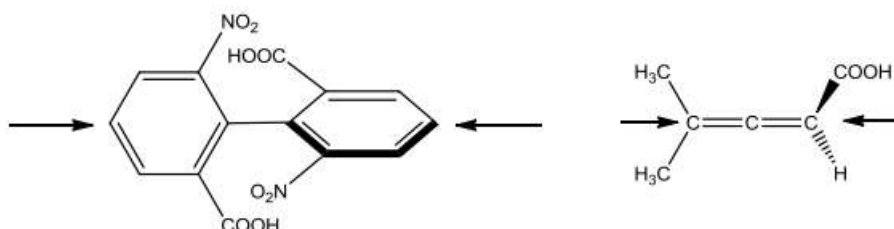
- The rotation about the bond linking the two phenyl rings does not occur due to steric hindrance between the bulky ortho groups.
- The two rings lie in different planes which are perpendicular to each other.
- Chiral biphenyls must contain two different ortho substituents on each ring.

- In order to display optical activity, the substituents in the ortho position must be large enough to prevent the two rings from becoming coplanar.

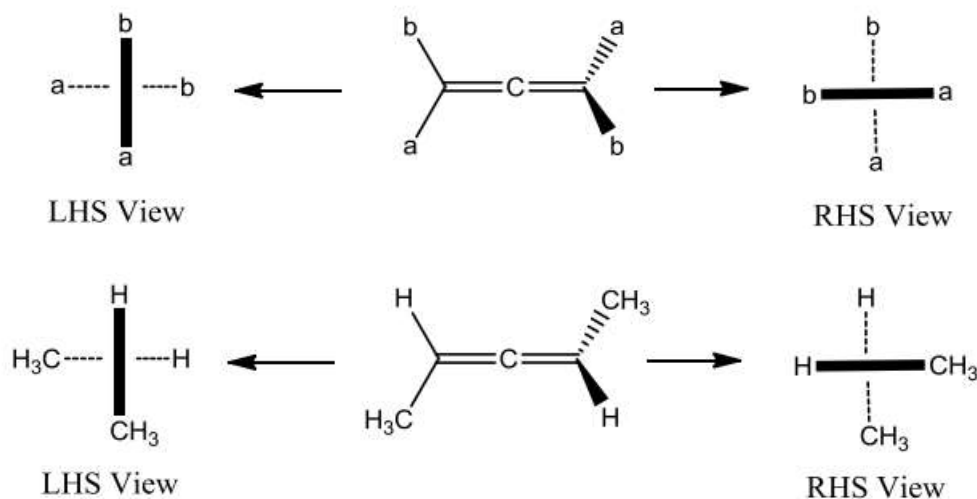


iii. Absolute Configuration for allenes, spiranes and biphenyls

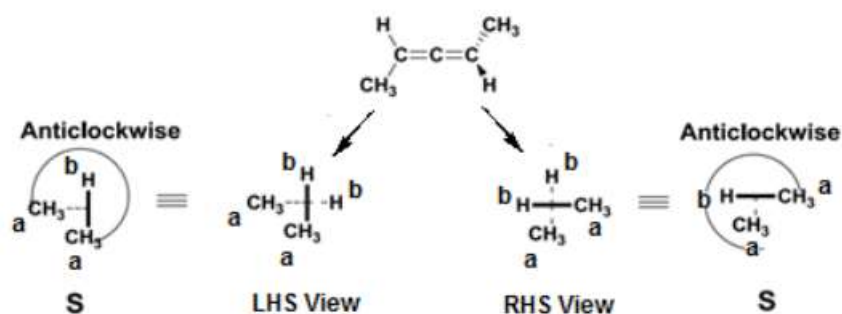
- The CIP rules are used to assign priority to the end groups but with one addition: That the front groups take precedence over the rear groups. Thus the two front and two groups are ranked according to the priority rules.
- The chiral axis is viewed end on and the observer is standing parallel to the plane of the paper.



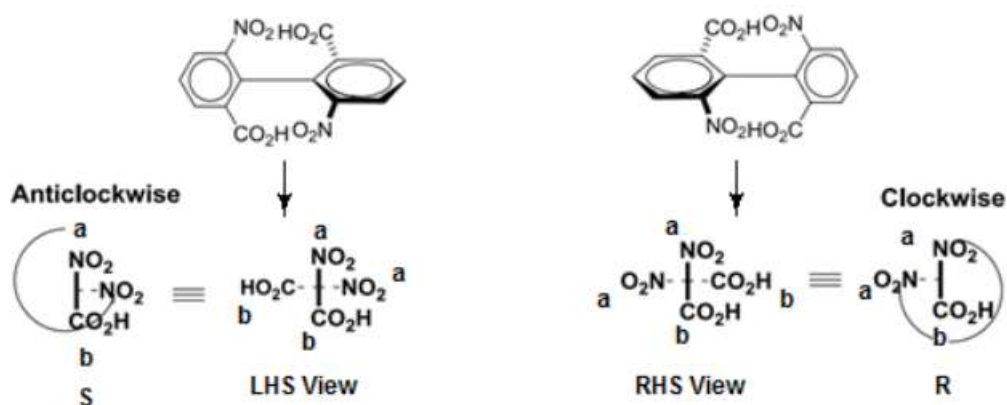
- The model below shows the side views and representation of the allene along the chiral axis.



4. Assigning priority to substituents - assign priority to the substituents on each of the terminal carbons of the allene system (you may use a (higher priority) and b (lower priority)).



5. The same rule applies for biphenyls also.



6. Racemic modifications or racemic mixture or racemates

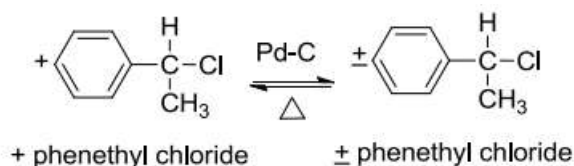
A racemic mixture consists of equal amounts of dextrorotatory and laevorotatory molecules such that the average optical rotation is zero.

A. Racemization

Racemization is the process of producing a racemic modification starting with one of the pure enantiomers. Since the two enantiomers have the same free energy, the equilibrium mixture will correspond to a 50-50 composition.

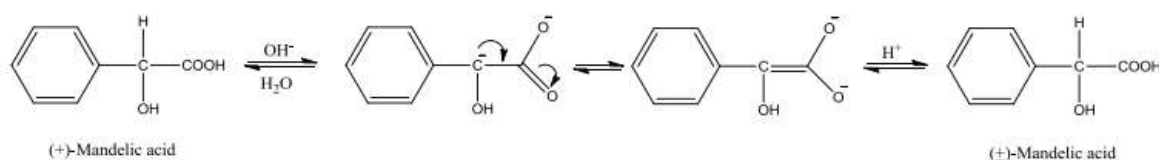
There are several chemical methods for reaching the racemization equilibrium.

i. Thermal racemization – One method of racemization of an optically active material is by breaking, temporarily one of the four bonds in an asymmetric carbon. If in the subsequent reformation of the bond, the group separated exchanges places with one of the remaining groups, the dissymmetric molecule is converted to its enantiomer. Homolytic cleavage takes place.

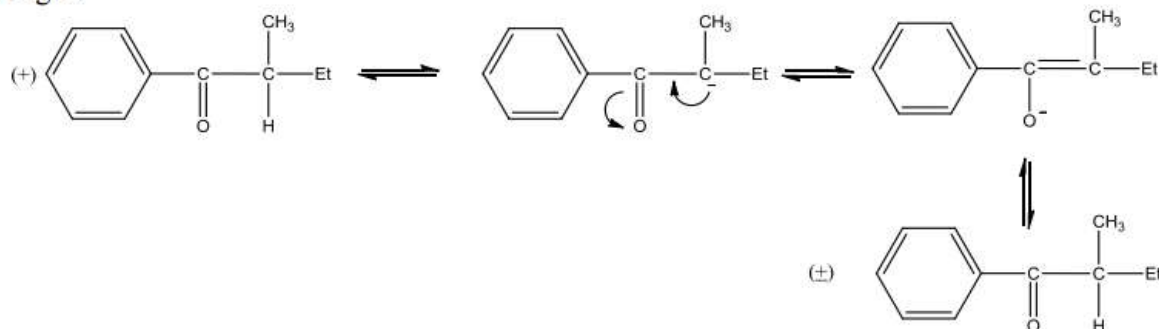


ii. By Anion formation – This is an example of heterolytic cleavage. Racemization occurs through anion formation. If a group is removed from a tetrahedral and chiral carbon leaving behind a carbanion, it undergoes rapid inversion so that when the group recombines, it can do so either from the right or the left. Hence the product is racemic. The group that leaves without its electrons is usually a proton.

E.g. 1



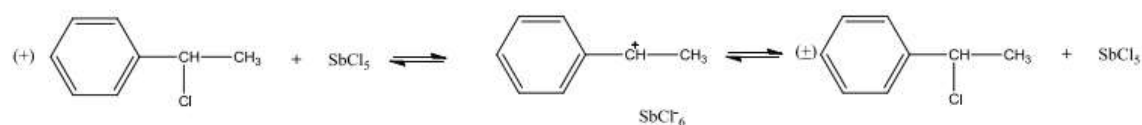
E.g. 2



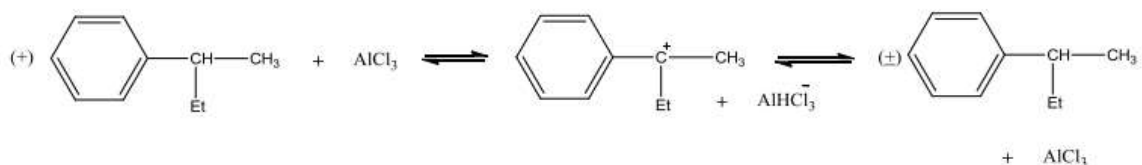
The anion in each case is stabilized by resonance. The base used to abstract the acidic proton is usually NaOH or NaOEt. If enolisable hydrogen is not present, racemization does not take place.

iii. By cation formation – This is also an example of heterolytic cleavage. Racemization is done by removing the group R with its pair of electrons and leaving a carbonium ion or carbocation. It is brought about by a Lewis acid. The carbocation formed must be stable. The reagents used are Lewis acids like SbCl₅, AlCl₃, ZnCl₂, etc.

E.g. 1

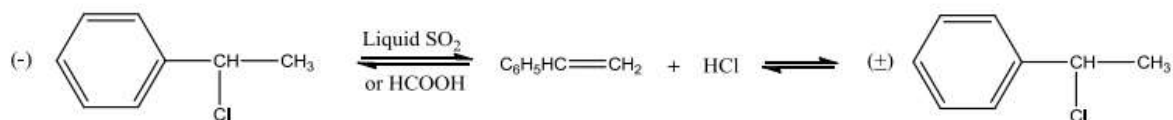


E.g. 2



iv. By reversible formation of stable inactive intermediate – The carbocations and carbanions involved in the racemization have very short half-life. In this method, symmetric intermediates which are stable entities are formed.

E.g. 1



E.g. 2



B. Resolution of Racemic Modifications

Resolution is the separation of a racemic mixture into its enantiomeric constituents. An optically active compound can be obtained from a racemic mixture by using two methods.

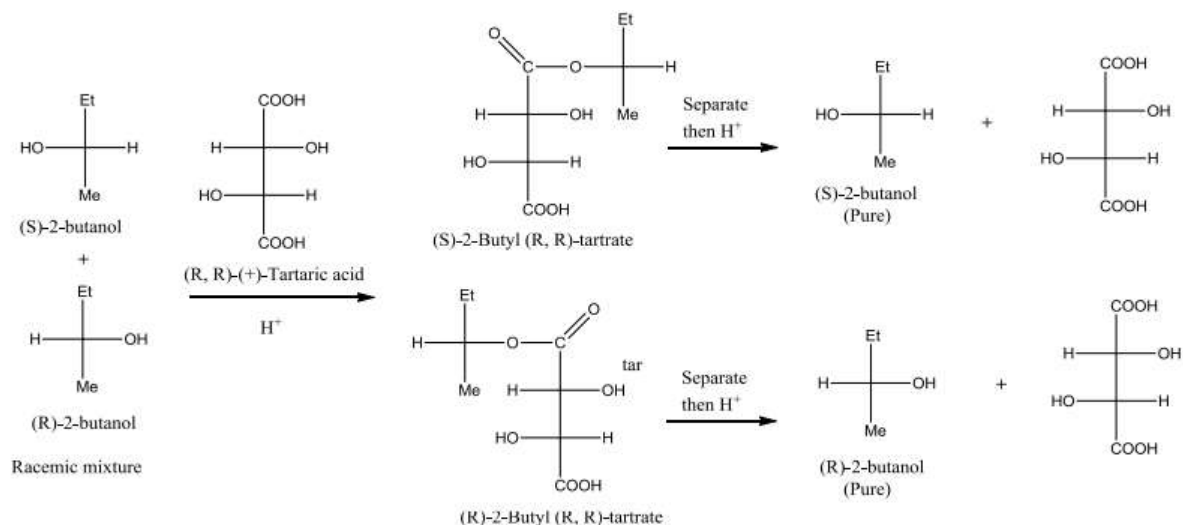
1. Via resolution of individual enantiomers from a racemic mixture and
2. By carrying out an asymmetric synthesis using a chiral reagent or a catalyst

i. Resolution through the formation of diastereomers

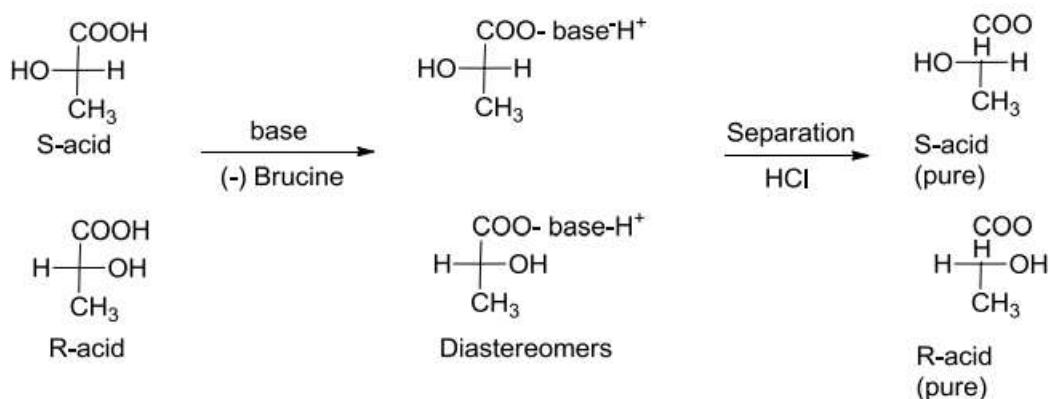
A racemic mixture of an alcohol e.g. 2-butanol reacts with pure (+)-tartaric acid to give diastereomeric esters. These esters are separated by chromatography easily since they are now

diastereomeric. The resolving agent is then cleaved from the separated enantiomers of 2-butanol by hydrolysis to give (R)-2-butanol and (S)-2-butanol in their pure form.

E.g. 1



E.g. 2

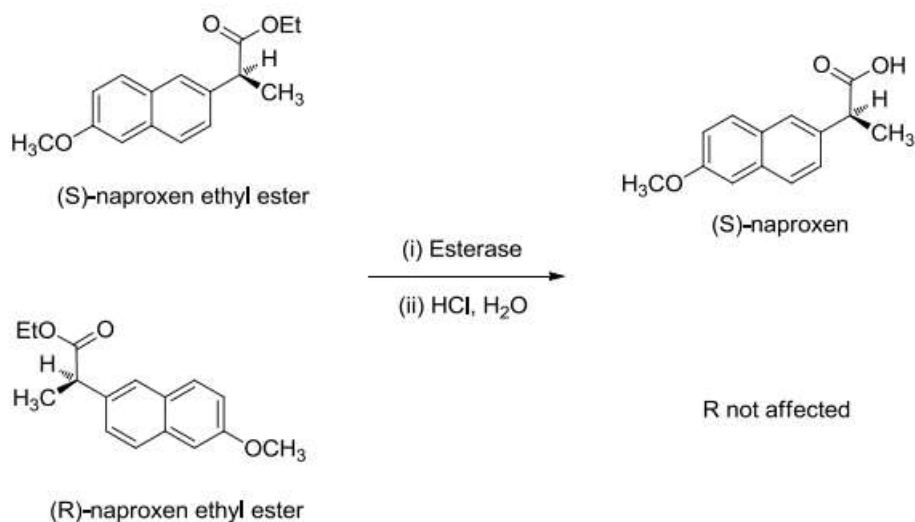


The most important criterion is the proper choice of the resolving agent. Thus a racemic mixture of organic acids can often be separated into its pure enantiomers by using the naturally occurring alkaloid brucine (a base).

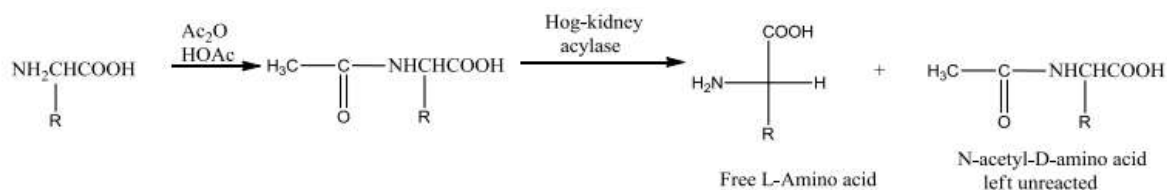
ii. Resolution with the use of enzymes

Amino acids can be resolved with the help of enzymes.

E.g. 1 - The enzyme esterase hydrolyzes only the S enantiomer of naproxen ethyl ester leaving the R enantiomer unaffected. Thus the racemic mixture can be separated.

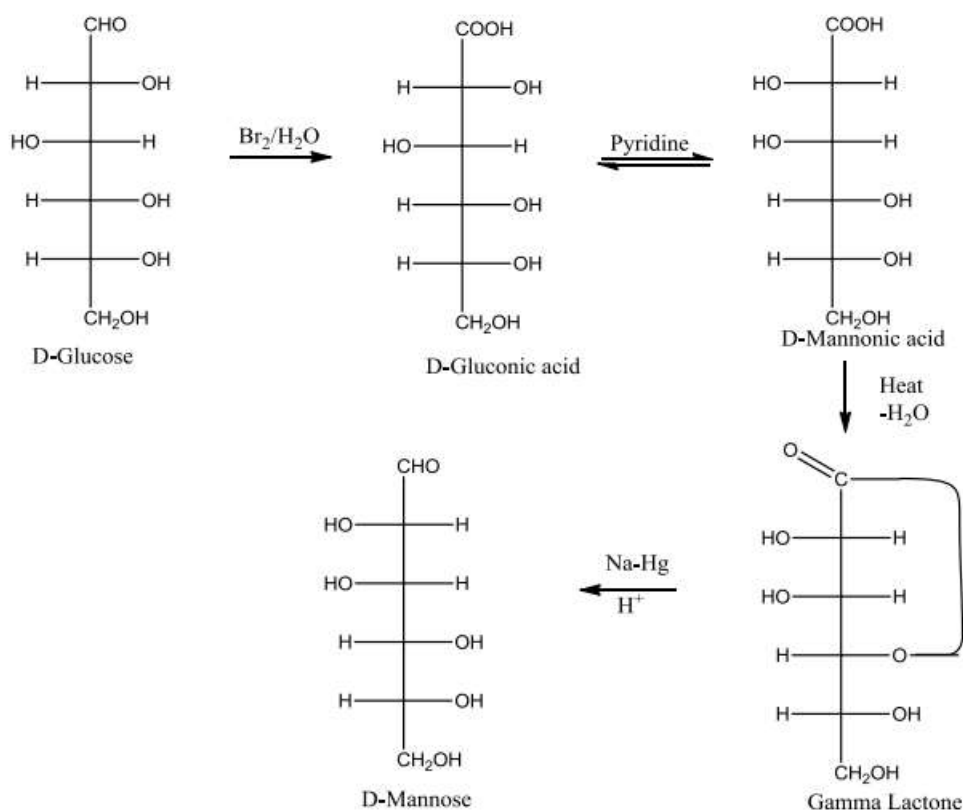


E.g. 2 - A (±) amino acid is acylated and the acylated racemic mixture is treated with an enzyme acylase 1 (hog kidney acylase). This enzyme is capable of hydrolyzing amide links of L-amino acids only (stereospecificity). Thus at the end, a free L-enantiomer with the acylated D-enantiomer is obtained. The mixture can now be easily separated by various methods.



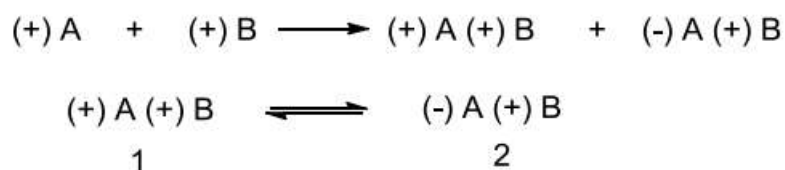
7. Epimerization

Epimers are diastereomers that differ in the configuration of a single chiral centre. They are related by the inversion of configuration at a single chiral center. Epimerization is the process of conversion of one form of epimer into another. E.g. conversion of D-glucose to D-mannose. Glucose is an epimer of both mannose and galactose because they differ by the configuration of a single chiral center. Mannose and galactose have different configurations at both C2 and C4 and are not epimers.



8. Asymmetric Transformations

When a racemic mixture is converted into a pure enantiomer or a mixture in which one enantiomer predominates, it is called asymmetric transformation. It holds true for diastereomers as well. This is sometimes called deracemisation. There are two types of asymmetric transformation – first order and second order.



When a racemic mixture A is reacted with an optically active reagent B, it forms two isomers. If for eg. 2 is more than 1, then the equilibrium will shift towards the right and more and more of 1 will be transformed to 2. This is asymmetric transformation. The change in optical rotation will take place naturally.

First and Second Order asymmetric transformations

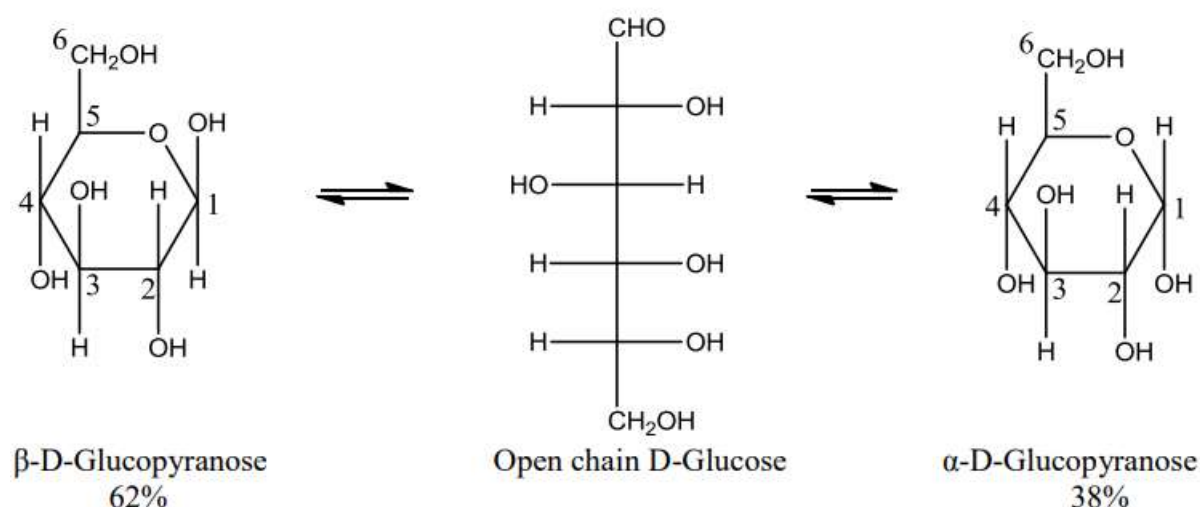
This occurs when a compound containing a chiral centre undergoes a spontaneous configurational change in solution. If there is a second chiral element present, then one of the enantiomers predominates in equilibrium. Mutarotation is an example of first order asymmetric transformation.

If in an asymmetric transformation, one of the species crosses the phase boundary and precipitates out of the solution, it is called **second order asymmetric transformation**. For example, a concentrated solution of glucose in ethanol precipitates out in the α form, while a concentrated solution of glucose in pyridine precipitates out the β form.

9. Mutarotation

Two crystalline forms of D-Glucose have been isolated. α -D-glucose crystallized from a concentrated aqueous solution at 30°C. It has a melting point of 146°C and a specific rotation of +112°. β -D-glucose crystallized from hot, glacial acetic acid solution. It melts at 148-150°C and has a specific rotation of +19.2°. When either of these forms of D-glucose is dissolved in water and allowed to stand, a gradual change in specific rotation occurs. The specific rotation of the alpha form falls and that of the beta form rises until a constant value of +52.7° is reached. **This change in optical rotation of a solution of a chiral substance until a constant value is reached is called mutarotation.**

Glucose forms a stable cyclic hemiacetal between the CHO group and the OH group on the fifth carbon. In this process, the first carbon becomes asymmetric, giving two isomers which differ only in the configuration of the new asymmetric carbon. They are called anomers and the new asymmetric carbon is called anomeric carbon. **Anomers are diastereoisomers of cyclic forms of sugars or similar molecules differing in the configuration at the anomeric carbon (C-1 atom of an aldose or the C-2 atom of a 2-ketose).**



10. Enantiomeric excess or Criteria for Optical Purity

Optical activity can be measured in a mixture of enantiomers if these are present in unequal amounts. For example, if a solution of (+) and (-) isomers consist of 75% (+) isomer and 25% (-) isomer, the racemic mixture present is 25%, and the (+) enantiomer exists in excess. This is called enantiomeric excess. The 25% (-) enantiomer cancels the rotation of a corresponding amount of the (+) enantiomer. This mixture is called 50% optically pure. Optical purity can be found from the following relationship.

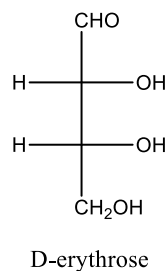
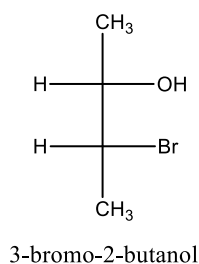
$$\% \text{ Optical Purity} = \left(\frac{[\alpha]_{\text{observed}}}{[\alpha]} \cdot 100 \right) = \text{Enantiomeric excess}$$

Where $[\alpha]_{\text{observed}}$ = specific rotation of mixture
 $[\alpha]$ = specific rotation of pure enantiomer

QUESTIONS

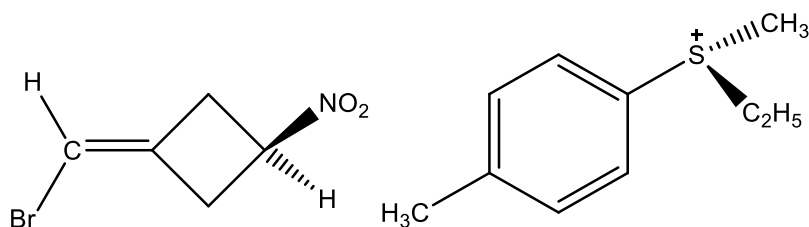
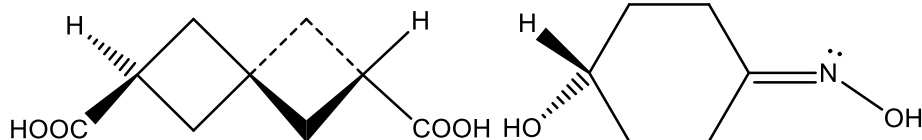
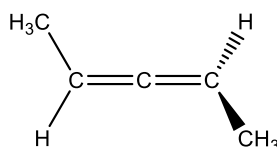
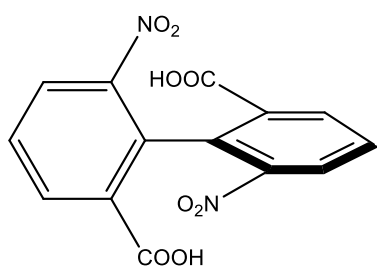
PART-A

1. What is a symmetry operation? Discuss the various elements of symmetry.
2. Define racemization. How is racemization done through anionic intermediate? Explain with an example.
3. Explain racemization through cationic intermediate formation.
4. Explain racemization through stable unreactive intermediate formation.
5. Explain how D-glucose is converted into D-mannose.
6. What is mutarotation? Explain the concept of mutarotation in D-glucose.
7. Define the following terms a) enantiomer b) diastereomer c) epimer d) anomer e) asymmetry.
8. Convert the following Fischer projections into Newman and Sawhorse projections.

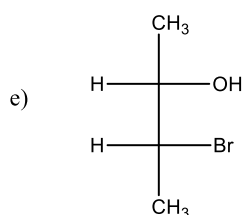
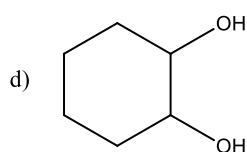
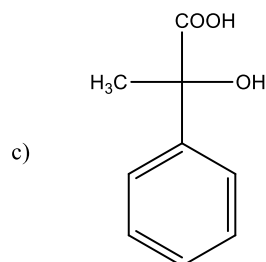
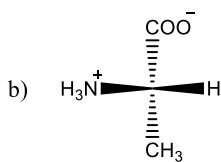
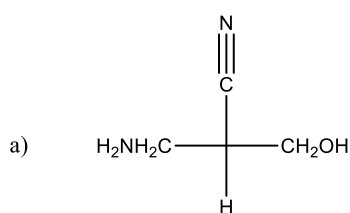


PART B

1. Explain resolution of racemic modifications through the formation of diastereomers.
2. Explain resolution of racemic modifications through the use of enzymes.
3. What is stereospecificity? Discuss stereospecificity in the bromination and epoxidation reactions of cis and trans-2-butene.
4. Explain optical activity in the allenes with suitable examples.
5. Explain atropisomerism in biphenyls.
6. Assign R/S configuration



7. Assign R/S configuration in the following compounds.



References

1. P. S. Kalsi, Stereochemistry Conformation and Mechanism, 8th Edition, New Age International Publishers.
2. Ernest L. Eliel, Stereochemistry of Carbon Compounds, Tata McGraw-Hill Publishing Company Limited.
3. D. Nasipuri, Stereochemistry of Carbon Compounds – Principles and Applications, 3rd Edition, New Age International Publishers.



SCHOOL OF SCIENCE AND HUMANITIES
DEPARTMENT OF CHEMISTRY

UNIT-2 – Stereochemistry-II – SCYA5203

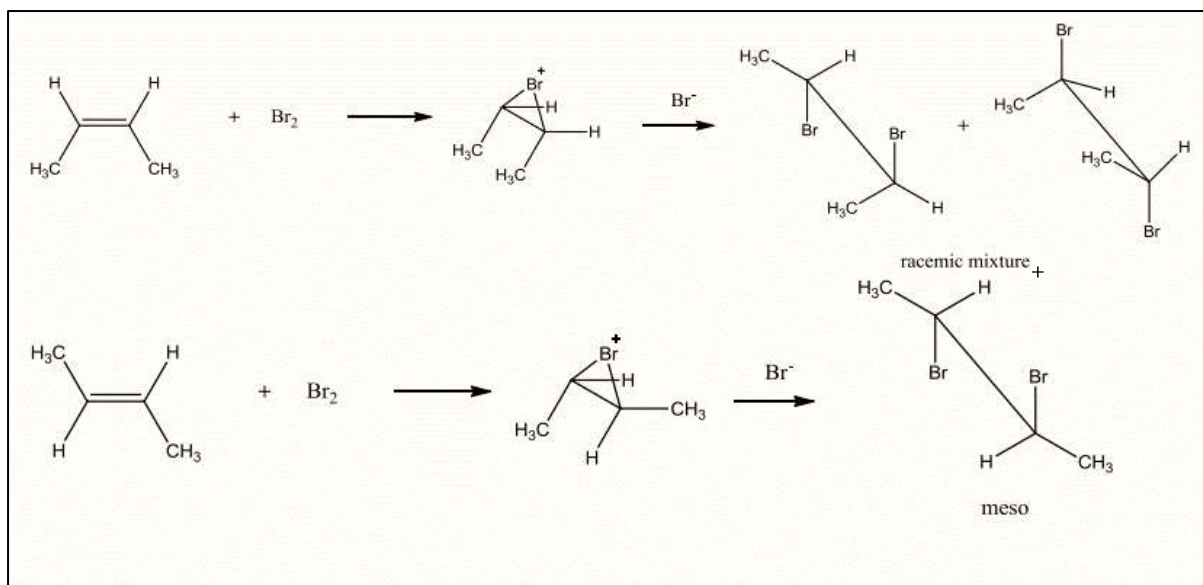
1. Stereospecific Synthesis

A reaction is stereospecific provided the reactant can exist as stereoisomers and each stereoisomeric reactant gives a different stereoisomeric product which may be a $\pm$ pair.

i. Bromination of cis and trans-2-butene

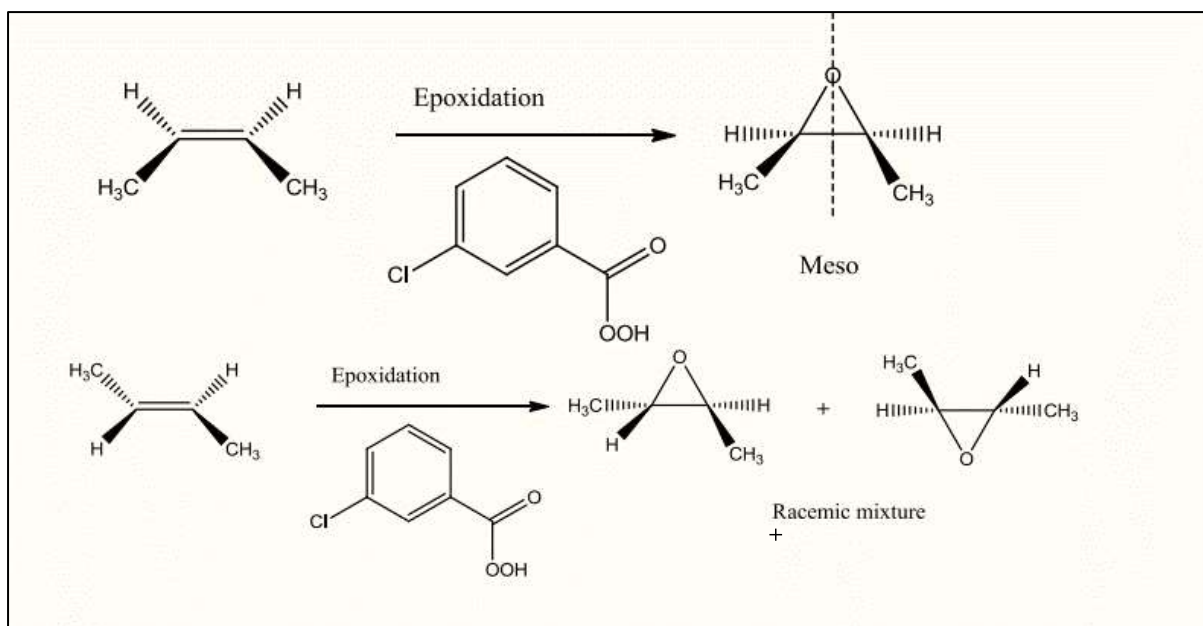
Addition of bromine to cis-2-butene gives a racemic mixture of 2, 3 – dibromobutane while addition to trans-2-butene gives the *meso* stereoisomer. Cis-2-butene add bromine from the top face to give the intermediate bromonium ion which is achiral. The bromide ion then attacks the bromonium ion at either carbon from bottom (S_N2) type of displacement at equal rates to yield the two enantiomers in equal amounts i.e. the racemic form.

Trans-2-butene reacts with bromine from the top face to give a chiral bromonium ion. When the bromonium ion is opened by S_N2 type displacement at either carbon, the same achiral *meso* compound is formed.



ii. Epoxidation of cis and trans-2-butene

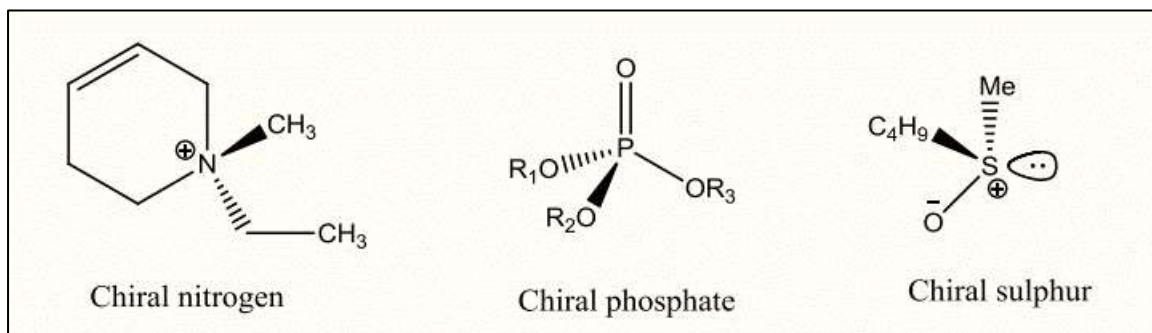
The reaction of alkenes with peroxy acid takes place in a stereospecific way, cis-2-butene for example yields only cis-2, 3-dimethoxyoxirane (*meso*) and trans-2-butene yields only the racemic trans-2, 3-dimethyloxirane.



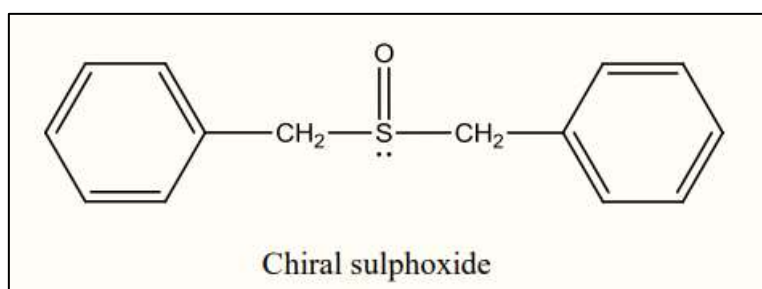
2. Stereochemistry of compounds containing nitrogen, phosphorous and sulphur

Single-bonded nitrogen is pyramidal in shape, with the non-bonding electron pair pointing to the unoccupied corner of a tetrahedral region. If the nitrogen in these compounds is bonded to three different groups, its configuration is considered to be chiral. Amines are approximately tetrahedral with the lone pair being assigned the lowest priority group. Pyramidal nitrogen is normally not configurationally stable. It rapidly inverts its configuration by passing through a planar, sp^2 hybridized transition state, leading to a mixture of interconverting R and S configurations.

Phosphines, phosphine oxides, sulfoxides and amine oxides display chirality provided the ligands are non-equivalent. The phosphorus centre of phosphate ion and organic phosphate esters is tetrahedral, and is a stereocenter. Consider a chiral phosphine in which the electron lone pair and the phenyl group are in the plane of the paper while pentafluorophenyl is projected in front of the plane and the methyl group is projected away. Absolute configuration can be assigned by viewing from below or from the side.



Sulphur exhibits pyramidal bonding in sulphoxides, sulphonium salts, etc many of which have been resolved.



Absolute Configuration (R and S designations) for compounds containing nitrogen, phosphorous and sulphur.

3. Conformation Analysis

S. No.	Conformation	Configuration
1.	It refers to different arrangement of atoms or groups relative to each other and raised due to free rotation round a sigma bond.	It refers to different arrangement of atoms or groups in space about a central atom.
2.	The energy difference between two conformers is lower.	The energy difference between two configuration forms is large.
3.	Conformers are not isomers and they cannot be separated from each other.	These are optical isomers and can be separated from each other.
4.	These are easily inter converted to one another.	These are not easily converted to one another.

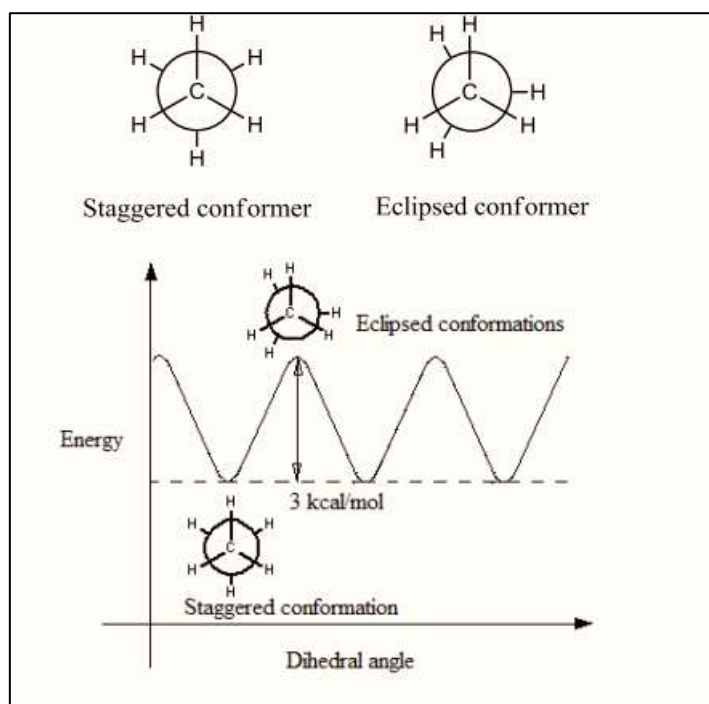
Conformational Analysis

The different spatial arrangements that a molecule can adopt due to rotation about σ bonds are called conformations and hence conformational isomers or conformers. The study of the energy changes that occur during these rotations is called conformational analysis. Conformers are stereoisomers that are separated by relatively low energy barriers (< 60 kJ/mol). A molecule can have an infinite number of conformations, but only one configuration.

1. Conformational Analysis in Acyclic systems

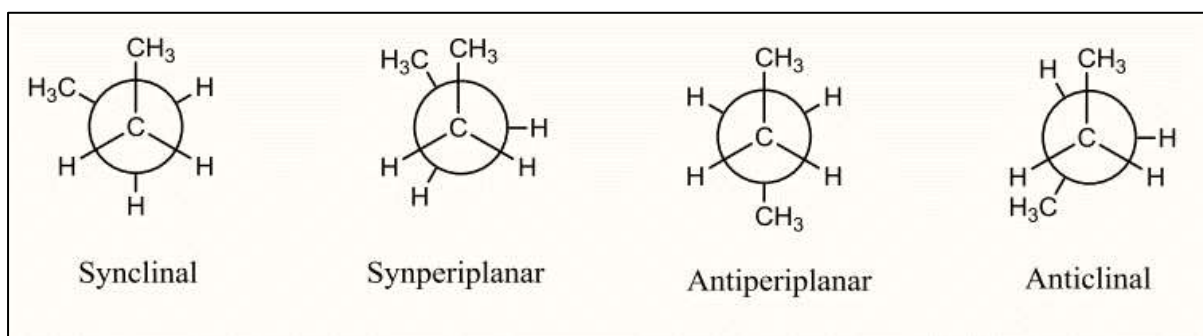
i. Conformational analysis of ethane

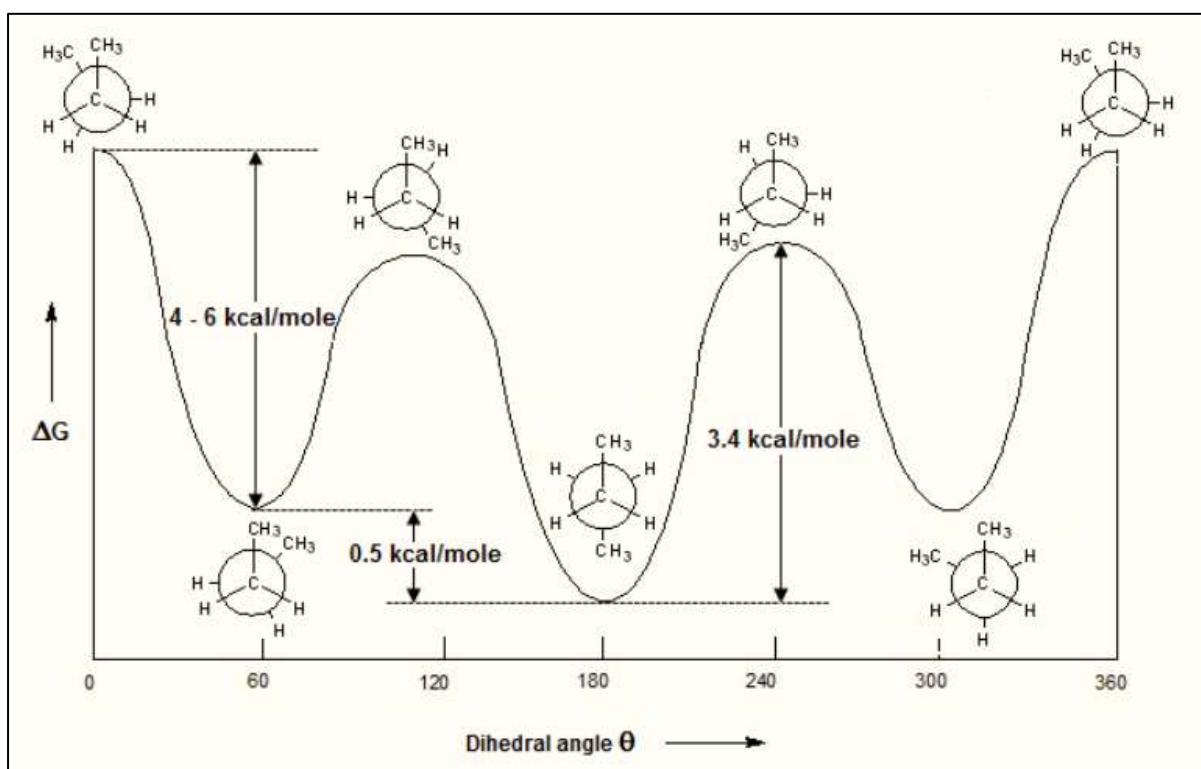
- There are two conformations of ethane – eclipsed and staggered conformations.
- The staggered conformations of ethane are the low energy forms while the eclipsed conformations represent transition states.
- The energy difference between the two conformers which represent the barrier of interconversion between two staggered conformers is about 3 kcal/mol.
- The activation energy for rotation about the C-C bond in ethane is small.



ii. Conformational analysis of 1, 2-disubstituted ethane derivatives Butane

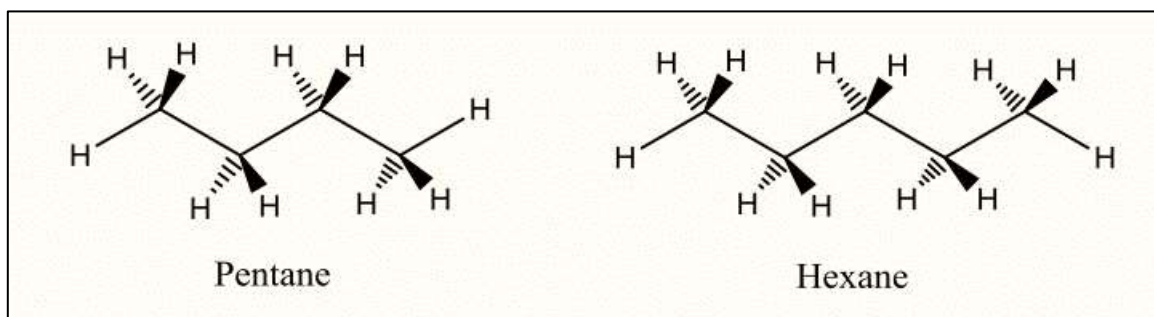
- For a compound of the type A-CH₂-CH₂-B, there are four extremes - A fully eclipsed conformation (**syn-periplanar**), partly eclipsed conformation (**anticlinal**), a fully staggered conformation (**anti-periplanar**) and another staggered conformation (**gauche or syn-clinal**).
- In ethane, all the staggered conformations are equivalent, but in butane, there are two different staggered conformations.
- The fully staggered form is the most stable because the methyl groups are far apart.
- Two groups are said to be gauche when the dihedral angle between them is 60°.
- In the anti-conformation, the groups are maximum distance apart and the dihedral angle between them is 180°.
- The methyl groups in the gauche conformation are close enough to each other so that the van der Waals forces between them are repulsive.
- The eclipsed conformation represents the energy maxima in the potential energy diagram.
- Eclipsed conformations not only have torsional strain, but also additional van der Waals repulsions from the eclipsing methyl groups and hydrogen atoms.



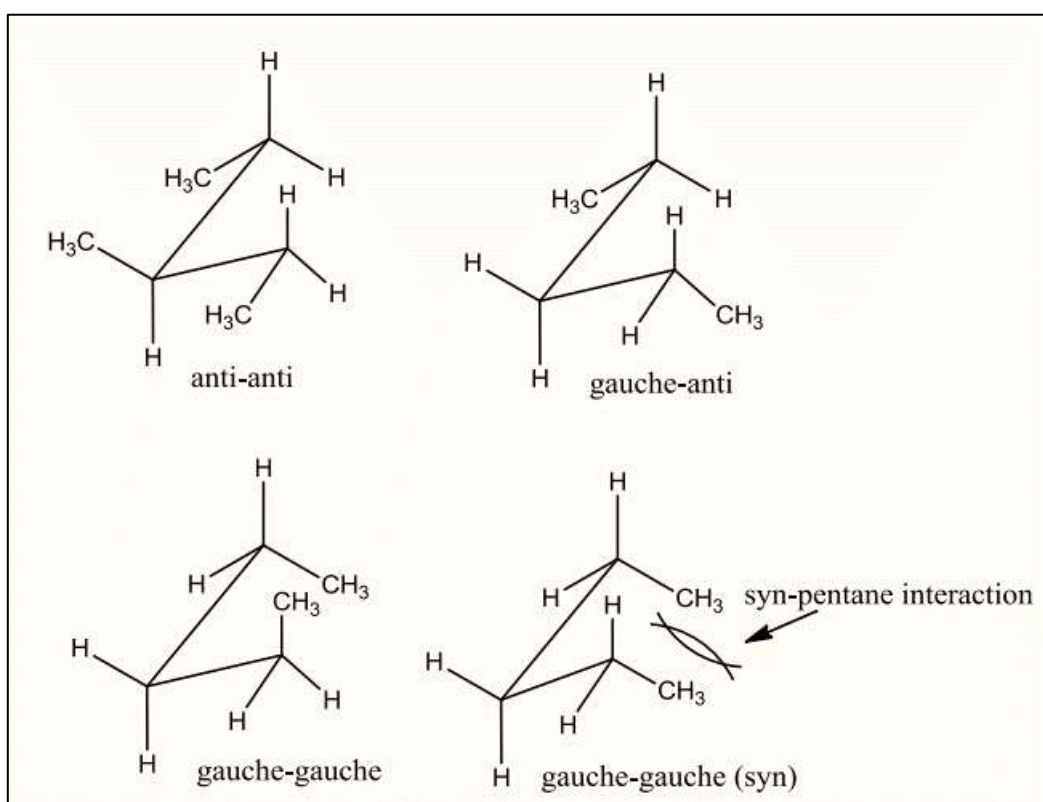


iii. Conformations of unsymmetrically substituted ethane n-pentane

- Pentane and higher alkanes have conformational preferences similar to ethane and butane.
- Each dihedral angle tries to adopt a staggered conformation and each internal C-C bond attempts to take on an anti-conformation to minimize the potential energy of the molecule.
- The most stable conformation of any unbranched alkane follows these rules to take on zigzag shapes:



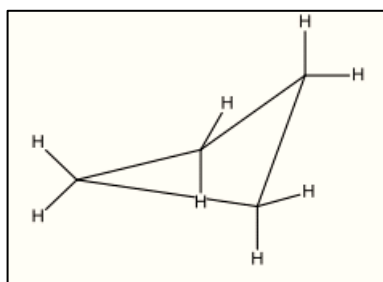
- In n-pentane, conformations about the C2-C3 and C3-C4 bonds.
- The most stable conformation is anti at both bonds, whereas less stable conformations contain gauche interactions.
- One gauche-gauche conformer is particularly unfavorable because methyl groups are aligned with parallel bonds in close proximity. This conformation is called syn.
- This type of steric hindrance across five atoms is called a syn-pentane interaction.
- Syn-pentane interactions have an energetic cost of about 3.6 kcal/mol relative to the anti-anti conformation and are therefore disfavored.



2. Conformational analysis of cyclic systems

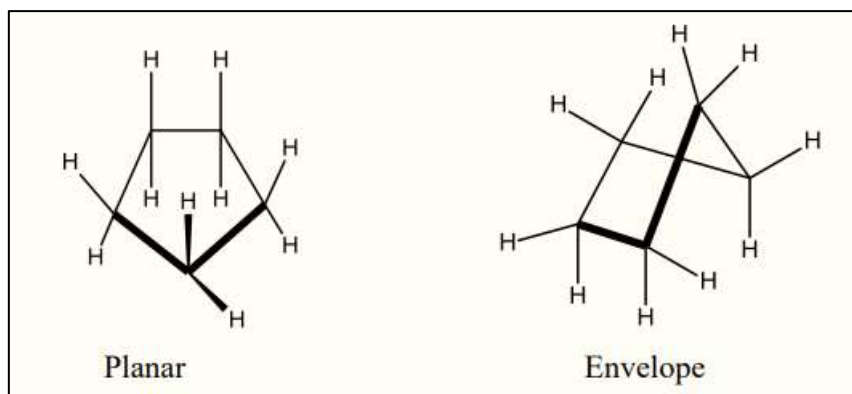
i. Conformational analysis of cyclobutane

- In cyclobutane, the internuclear angle is 90° and the C-C bonds are not. There are four strained bonds and there are eight eclipsed hydrogen atoms.
- Cyclobutane exists in a non-planar conformation.
- One methylene group is bent at an angle of 25° from the plane of the other three ring carbons. In this conformation, some increase in bond angle strain is compensated by the reduction in the eclipsed hydrogen interactions.



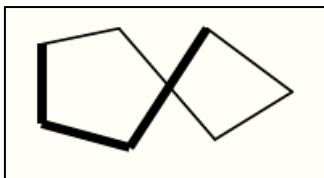
ii. Conformational analysis of cyclopentane

- In planar cyclopentane, all the hydrogens are completely eclipsed and there would be torsional strain.
- The molecule undergoes distortion to form a non-planar conformation.
- The structure has an envelope shape and the out of plane methylene group is approximately staggered with respect to its neighbours.



iii. Conformational analysis of cycloheptane

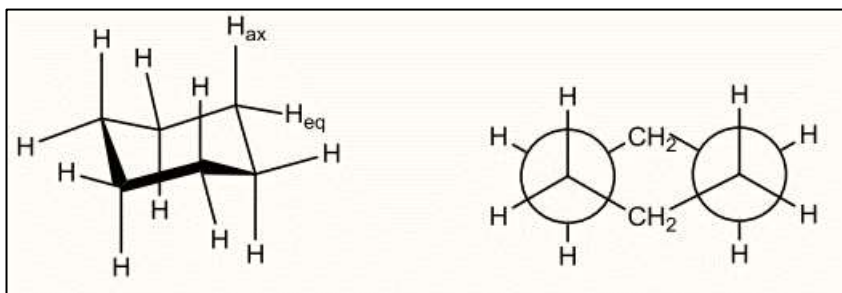
- It exists in non-planar conformation.
- The instability is due to torsional strain and van der Waal's repulsions between hydrogens across rings.
- The conformation is called the twist chair.



iv. Conformational analysis of cyclohexane

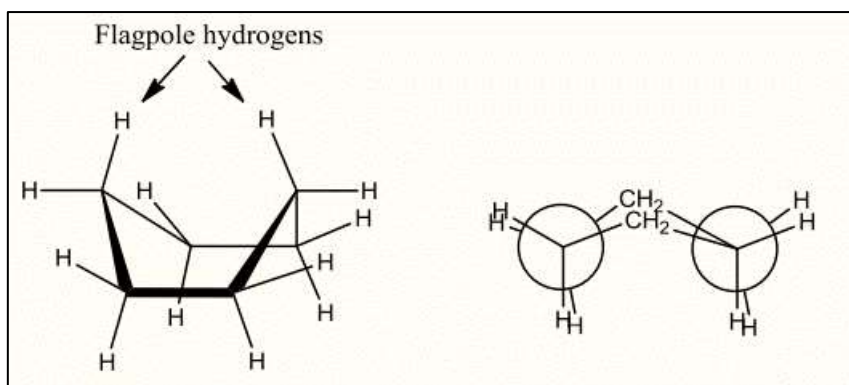
• Chair Conformation

Cyclohexane exists predominantly in a non-planar puckered conformation called the CHAIR conformation. All the bonds are staggered. However, there is gauche interactions between neighbouring methylene groups leading to steric strain. Bond angle is 111° . Dihedral angle is 56° .



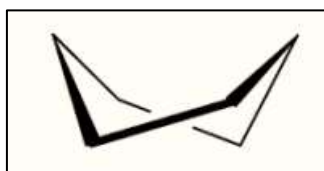
• Boat conformation

There is complete eclipsing of the hydrogens. The inside hydrogens on C1 and C4 interfere sterically in transannular interaction. The Newmann projection has two butane type units eclipsed. Dihedral angle is 54° . The two hydrogens are called flagpole hydrogens.

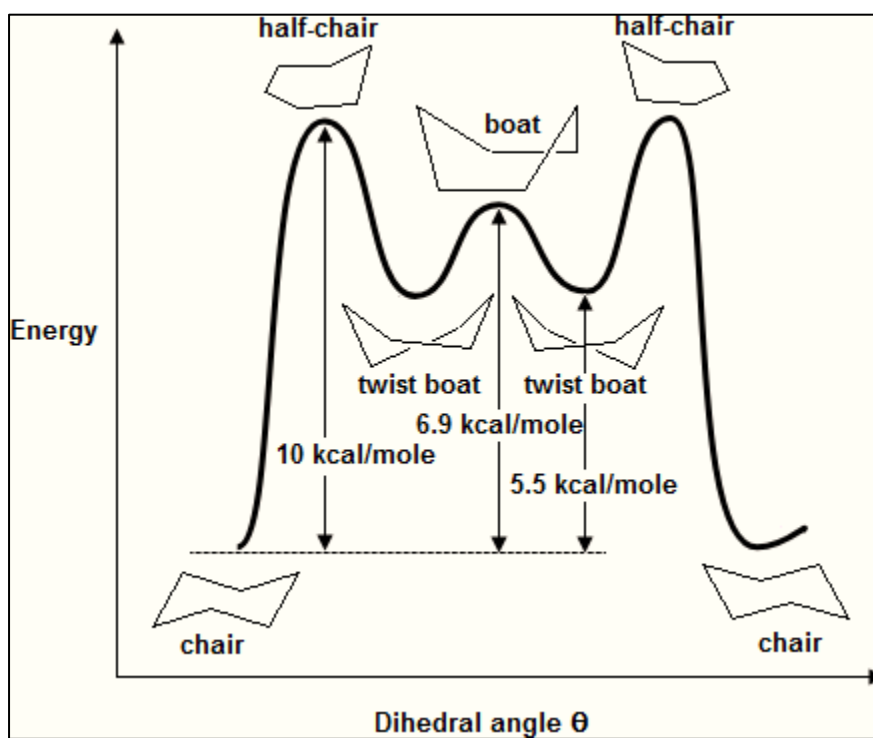


- **Twist Boat Conformation**

The boat conformation is slightly stabilized by moving apart the C1 and C4 hydrogens. This is called the TWIST BOAT. The molecule is chiral.

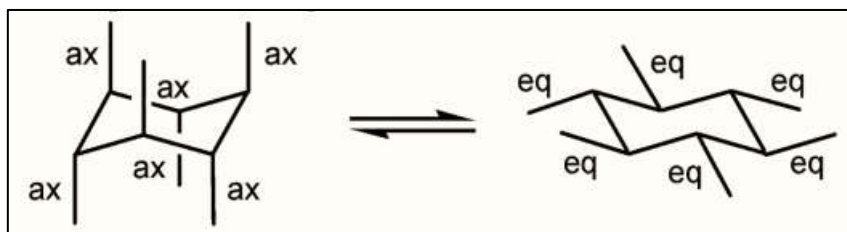


- **Energy diagram**



- The transition state conformation is called half chair.

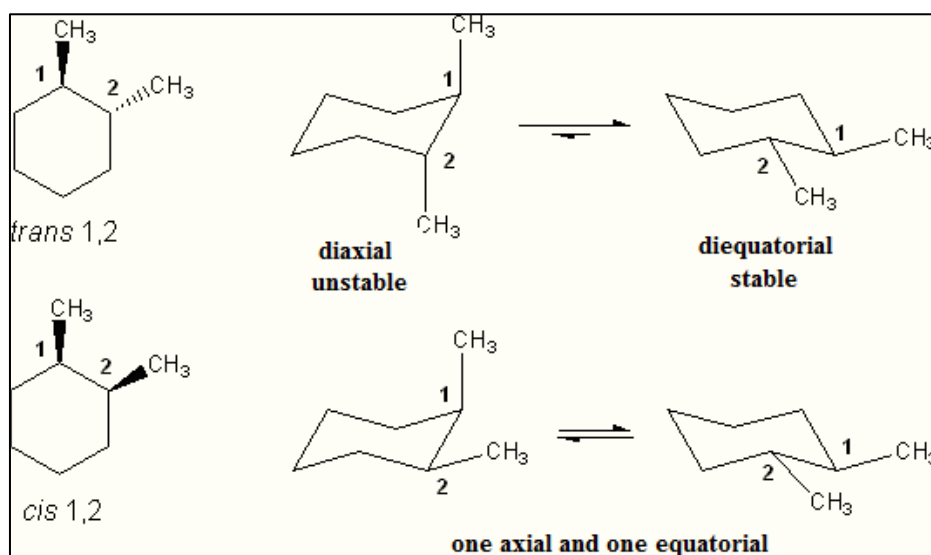
- Ring flipping is fast and occurs $\sim 100,000$ times per second
- During inversion, the chair is converted into twist boat first which lies 5.5kcal above the chair.
- The full boat lies above the barrier separating two twist forms and is also a transition state.
- The twist boat passes through a second half chair to give the other cyclohexane.
- **Equatorial and Axial bonds in the chair form of cyclohexane**
- The 12 C-H bonds in the chair form of cyclohexane are of two types.
- Six of these are parallel to the three fold axis of symmetry of the chair.
- These are represented by vertical lines in the plane of the paper and are designated as axial.
- The remaining six bonds are inclined at an angle of $109^\circ.28'$ to the three fold axis and are called equatorial.
- Of the six axial bonds, three are above and three below.
- Similarly, three equatorial bonds point above and three below.



3. Conformation and Reactivity in disubstituted cyclohexanes

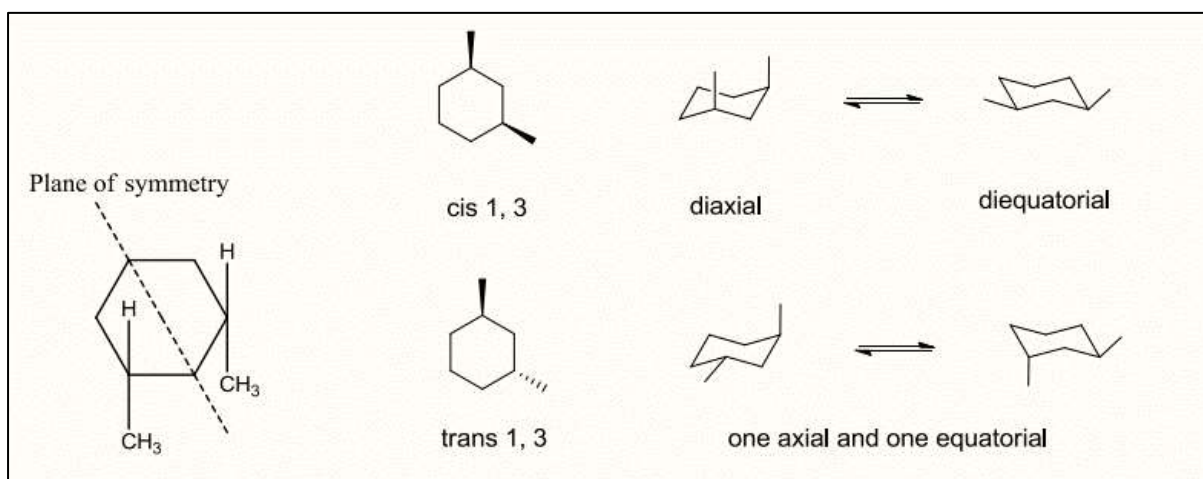
i. 1, 2-disubstituted cyclohexanes

- 1, 2-Dimethyl cyclohexane has 2 stereocentres, hence there are four isomers.
- The trans isomer exists as enantiomers where the equatorial conformer is the most stable.
- In 1, 2 substituents, the trans form has substituents in the two axial or equatorial position.
- The cis form has substituents in one axial and one equatorial position.



ii. 1, 3 – di-substituted cyclohexane

- 1, 3 – dimethyl cyclohexane has two stereocenters. Hence 4 isomers are expected ($2^n = 2^2 = 4$)
- However, only 3 isomers exist since the cis form has a plane of symmetry and exists as a meso compound.
- The trans isomer does not have a plane of symmetry and exists as a pair of enantiomers.
- In trans, one group is axial and the other equatorial. In cis, the two groups are either equatorial or axial.

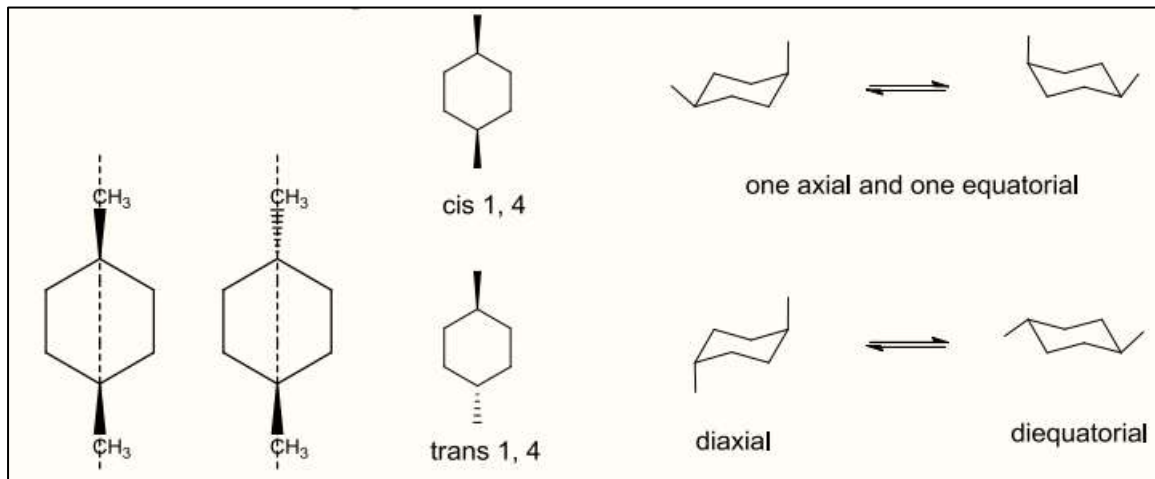


iii. 1, 4-disubstituted cyclohexane

- The cis isomer exists in two identical conformations (axial-equatorial and equatorial-axial) while the trans exists in two non-equivalent conformations (axial-axial and

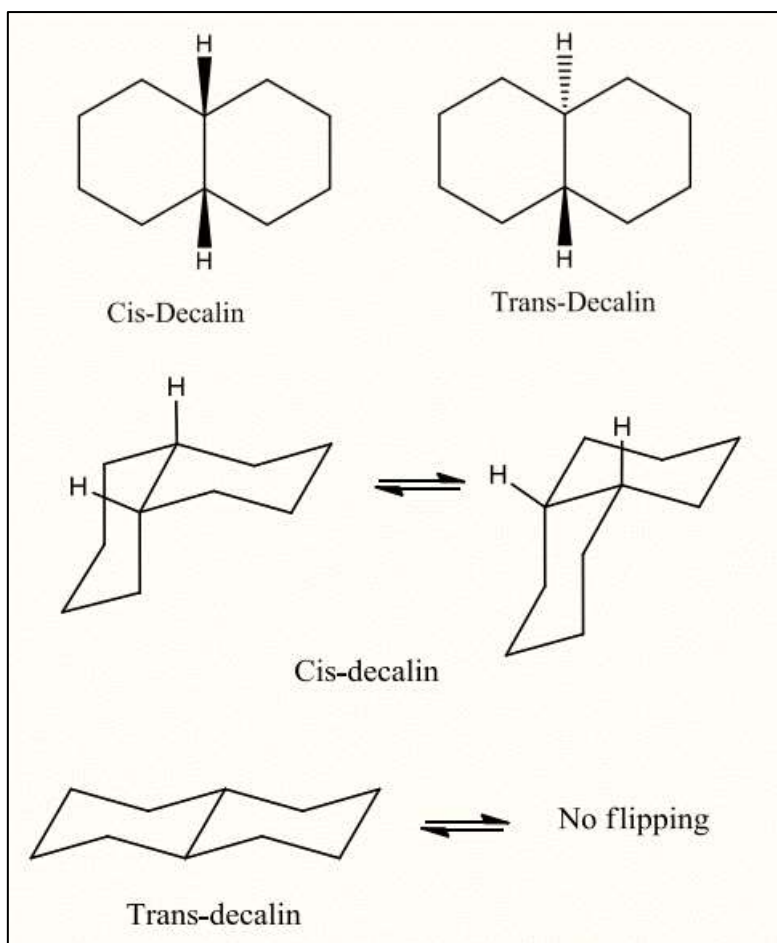
equatorial- equatorial).

- It has a plane of symmetry so both conformers are achiral.
- The cis and trans forms represent diastereomers.



4. Cis and Trans Decalins

The compound bicyclo [4.4.0] decane, known as decalin, exists in two diastereomeric forms. The cis and trans forms are diastereomers since they cannot be interconverted into each other by bond rotations. Decalin may be considered as a fusion of a four carbon chain connected to the chair form of cyclohexane. Trans decalin is fused with this 4-carbon chain in equatorial position while the cis decalin has equatorial-axial position.

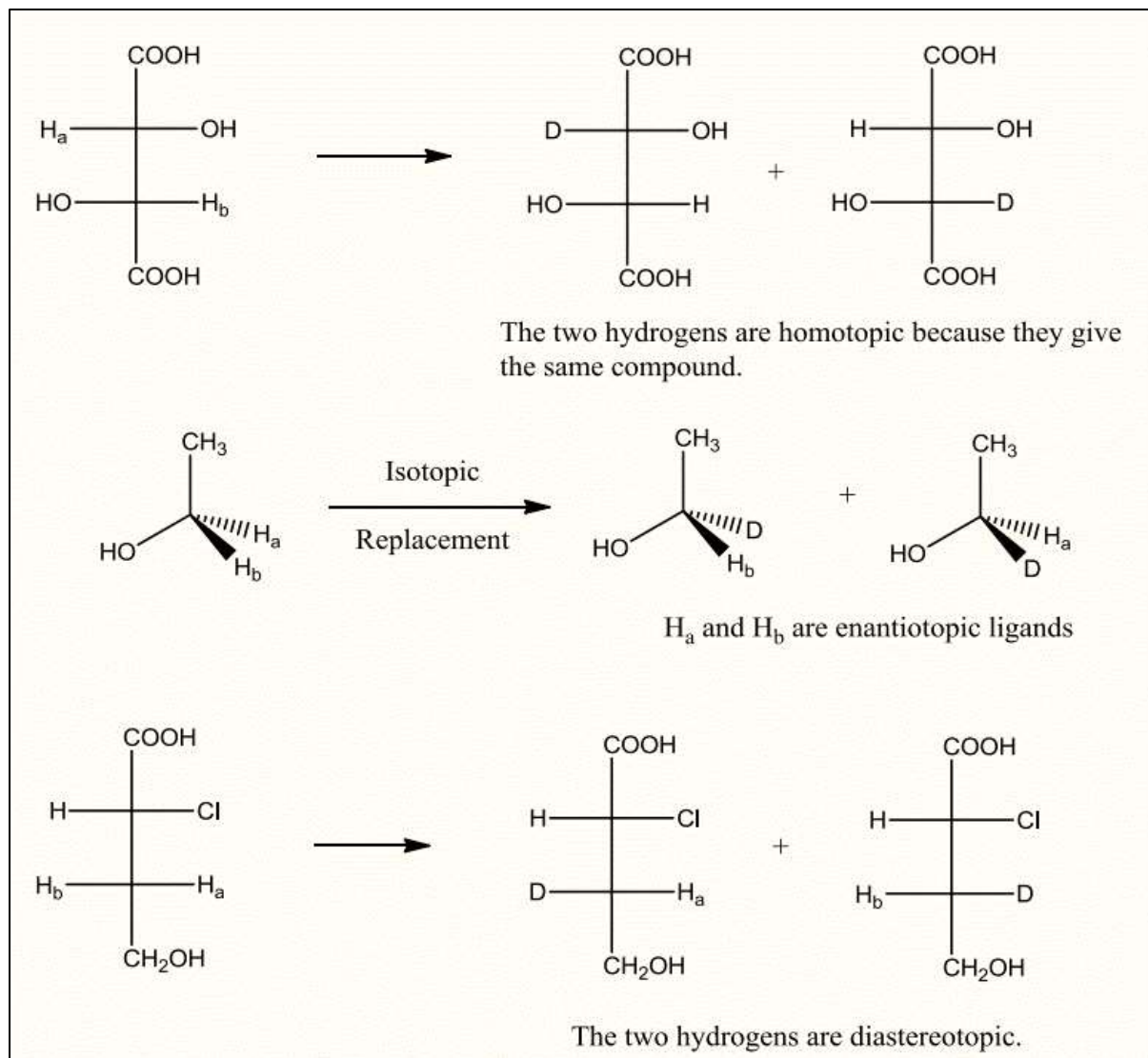


Cis decalin exists as an equilibrium between two enantiomeric all chair conformations which are interconvertible. Any substituent attached to the cis decalin system is free to adopt the equatorial conformation. Trans decalin has a unique and rigid conformation. Inversion is not possible. A substituent is forced to remain in a particular conformation which depends on its configuration.

5. Topicity of Ligands and Faces

Topicity is the spatial relationship between constitutionally and configurationally identical atoms or groups of atoms in a molecule. The groups are homotopic to mean that they occupy equivalent places in the molecule as in propane. The groups may also be heterotopic which are further subdivided into enantiotopic and diastereotopic groups. Such alteration or replacement

of one or other of the ligands leads to stereoisomeric compounds. The idea of topism is also applied to spaces on either face of a trigonal atom which may become occupied by an incoming atom or group and are again classified as homotopic, enantio or diastereotopic based on the environment generated by the ligands.



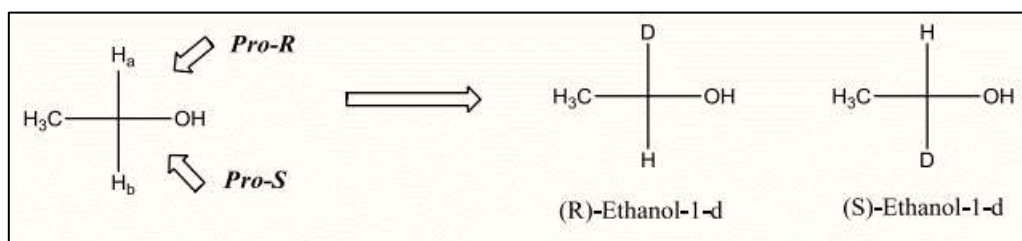
i. Nomenclature of Heterotopic ligands and faces

A. Pro-R and Pro-S nomenclature

To name the enantiotopic ligands at a prochiral centre, e.g. H_a and H_b in ethanol, the ligand to be labelled is arbitrarily assigned a higher priority over the other.

If H_a is preferred over H_b in the sequence rule, the sequence is $\text{OH} > \text{CH}_3 > H_a > H_b$, then the

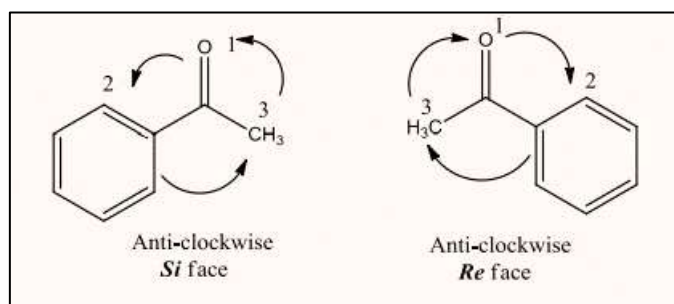
configurational symbol at the prochiral centre will be R, thus H_a is designated **pro-R**. Then by default, H_b becomes **pro-S**.

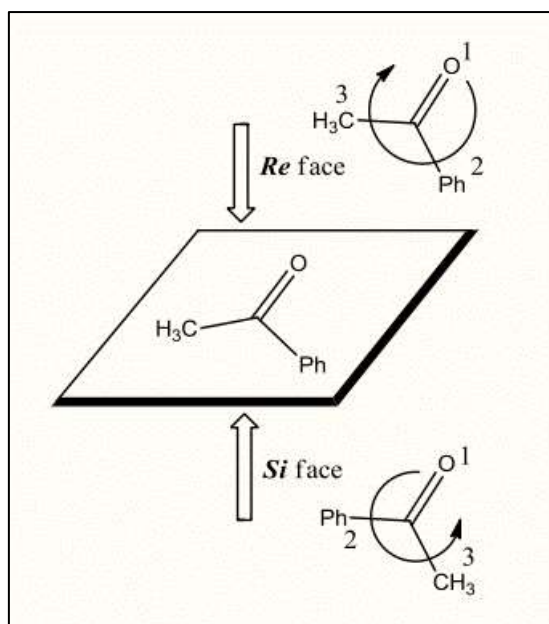


B. Heterotopic faces of carbonyl compounds (*Re*, *Si* nomenclature)

The groups and faces in a molecule which are enantiotopic or diastereotopic are collectively termed as heterotopic. In the case of carbonyl compounds when the groups R and R' are different, the two faces of the trigonal centre are different and the carbonyl carbon is called prostereogenic carbonyl carbon.

The faces of the carbonyl group are differentiated by the *Re*-*Si* nomenclature. The groups around the carbonyl group are given priorities as per Cahn-Ingold-Prelog's rules. If going from the group of highest priority to the group of lowest priority, the path is clockwise, the face is ***Re*** and if it is anti-clockwise, the face is ***Si***.





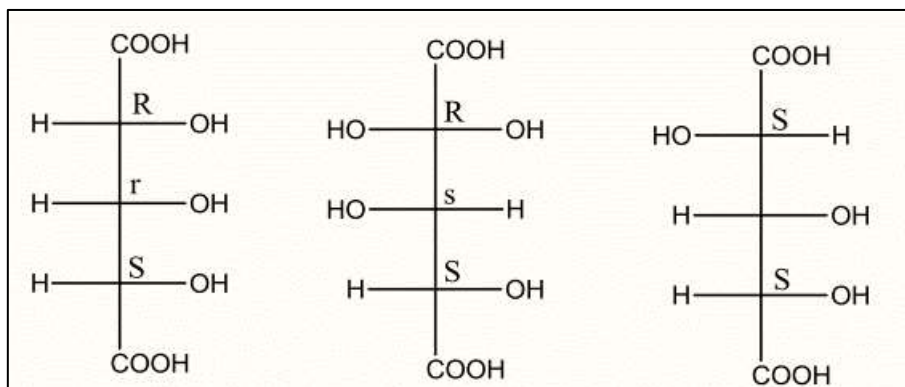
Summary of topic relationship

Topicity	Substitution-addition criterion	Symmetry criterion	Difference
Homotopic	Identical product	Ligands related through C_n and faces by C_2 axis	No difference by any method.
Enantiotopic	Enantiomeric products	Ligands and faces related through σ , i or S_n	Distinguishable in principle in chiral media (NMR) by chiral reagents, and enzymes.
Diastereotopic	Diastereomeric products	Ligands and faces not related by any symmetry elements	Distinguishable in principle by all methods

C. Pseudo asymmetry

In compounds in which two or more chiral ligands of the central atom are constitutionally identical but have the opposite configuration the central atom is formally chiral because it has

four different ligands. However, since such a compound also has a plane of symmetry it is, in fact, achiral as a whole. The central atom is termed a pseudo asymmetric center. The configuration of such atom is determined according to normal precedence rules assuming that R takes priority over S.

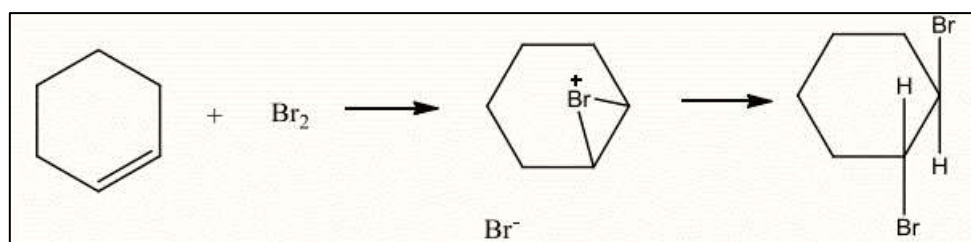


6. Stereoselective reaction

A reaction in which there is a choice of pathway, but the product stereoisomer is formed due to its reaction pathway being more favourable than the others available is called a stereoselective reaction. When this selectivity results in the formation of an excess of one enantiomer over the other from an achiral or racemic substrate, it is sometimes called asymmetric induction.

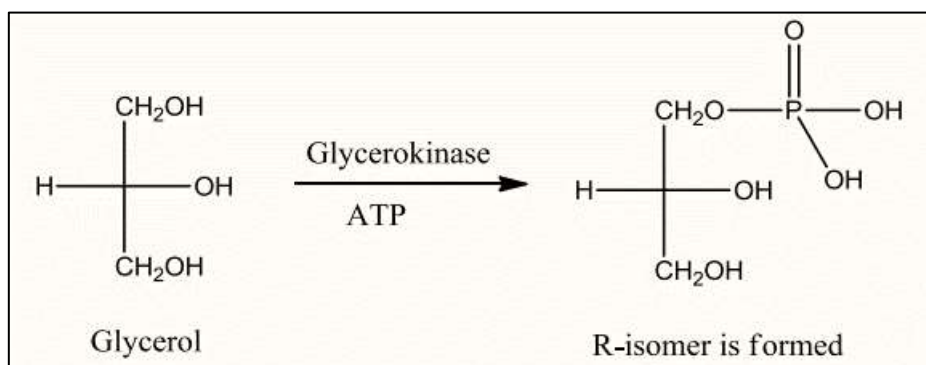
i. Bromination of cyclohexene

Cyclohexene can only exist in one stereoisomeric form with cis geometry of the double bond. When cyclohexene is brominated, the product is one stereoisomeric product trans 1,2-dibromocyclohexane is formed. No cis isomer is formed.



ii. Stereoselectivity of enzymes

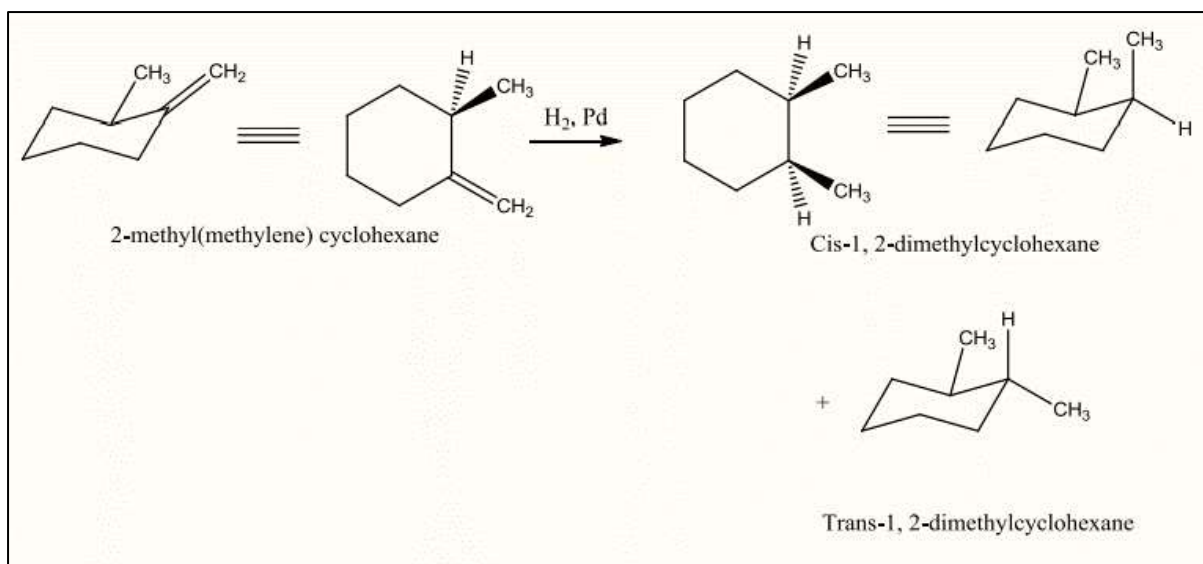
The enzymes when in contact with prochiral molecules react only with one of the enantiotopic ligands or faces, a property called stereoselectivity. E.g. glycerol undergoes phosphorylation exclusively at the pro-R hydroxymethylene group with ATP in the presence of enzyme-glycerol kinase.



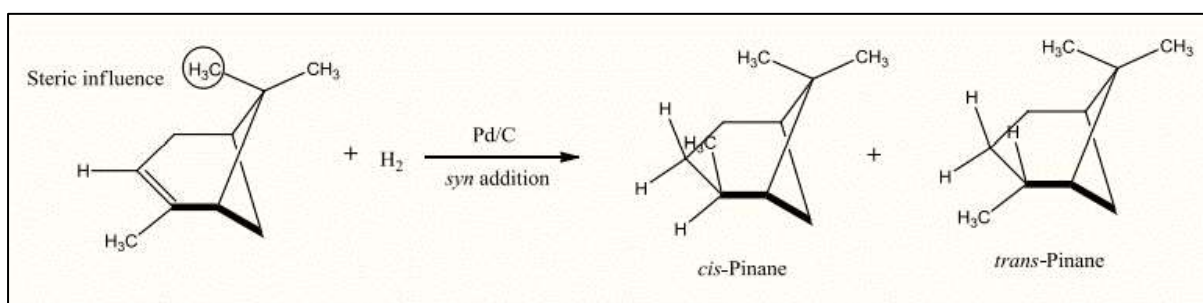
iii. Hydrogenation (syn addition) of a chiral alkene

A reaction which introduces a second stereocenter into a starting reactant which already has one may not give equal quantities of two possible diastereomers.

E.g. 1: The catalytic hydrogenation of 2-methyl (methylene) cyclohexane gives cis and trans-1, 2-dimethyl cyclohexane, but in unequal amounts. The major product is the cis and the minor product is the trans. The less hindered face of the double bond approaches the catalyst surface, and this is the face to which hydrogen is added – syn addition.



E.g. 2: The catalytic hydrogenation of α -pinene is also a stereoselective syn addition of hydrogen. It depends on the mode of alkene approach to the catalyst surface. The two hydrogens are added on the less hindered side of α -pinane. Cis-pinane is formed exclusively.



iv. Asymmetric synthesis

If an enantiomer or diastereomer is to be synthesized, then either the reactant or the reagent or the solvent must be the pure enantiomeric form. The chiral agent must play an active part in the reaction and has to be integral to the transition state so that two diastereoisomeric transition states are formed. Hence, one stereoisomer is produced more rapidly than the other. Thus, asymmetric synthesis involves competing reactions with diastereoisomeric transition states which takes place at different rates.

There are several categories of asymmetric synthesis

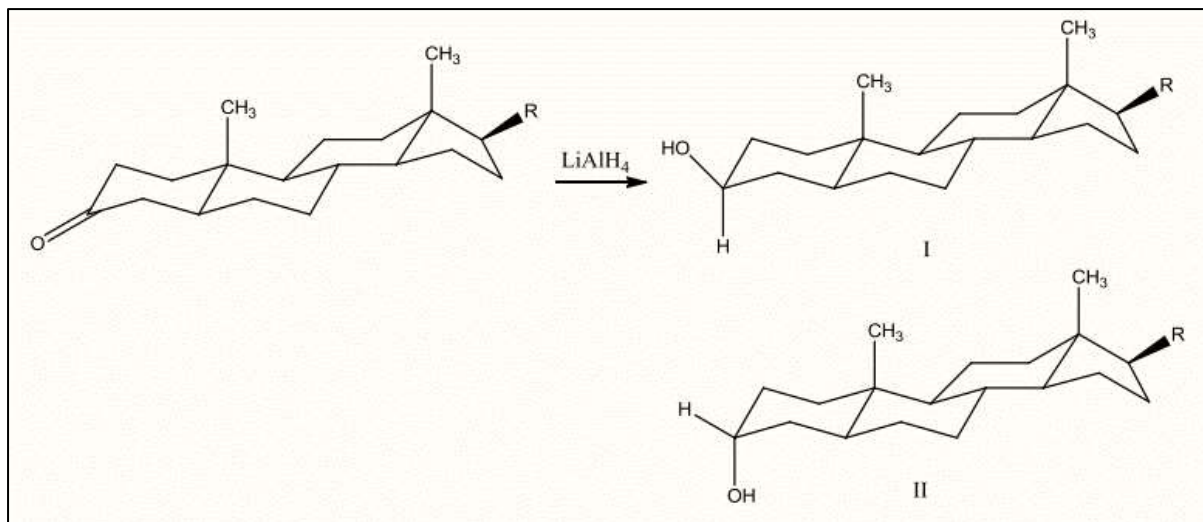
- The use of chiral substrates
- Diastereoselectivity in Aldol reactions
- The use of chiral auxiliaries

- Use of chiral reagents and chiral catalysts

a. The use of chiral substrates

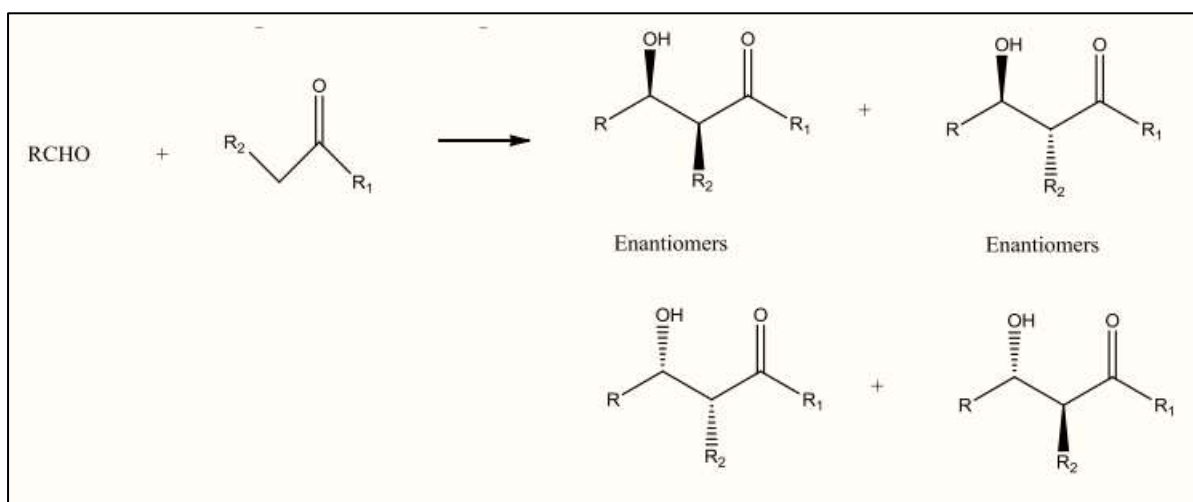
Stereoselective reduction of cholestan-3-one (Diastereoselectivity)

Cholestan-3-one on reduction with lithium aluminium hydride gives exclusively the equatorial alcohol by attack of the reagent from the less hindered face of the molecule. The alcohol I is the only product since it is more stable than II since II has sterically hindered beta face due to angular methyl groups.

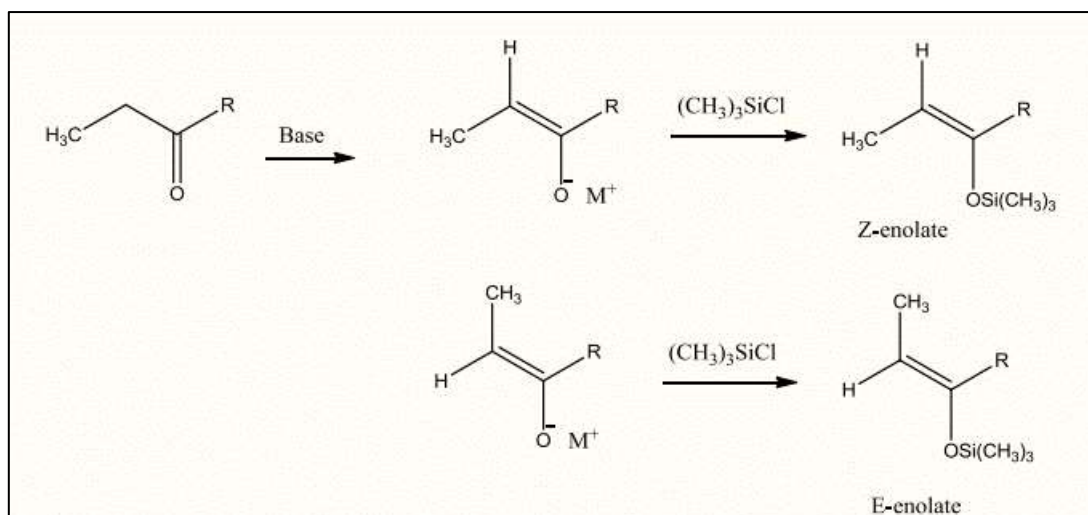


b. Diastereoselectivity in Aldol reactions (Directed Aldol reaction)

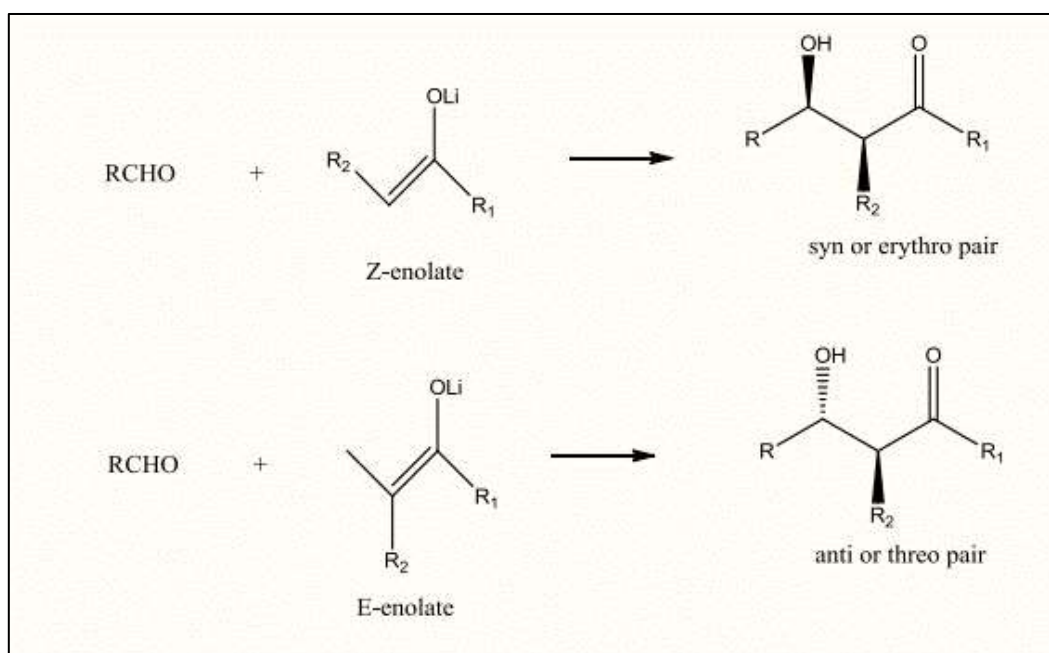
An aldol reaction creates two stereocenters from achiral starting materials. Thus syn and anti diastereomers are produced, each a pair of enantiomers.



Diastereoselectivity in aldol reaction is achieved by employing the enolate of desired stereochemistry.



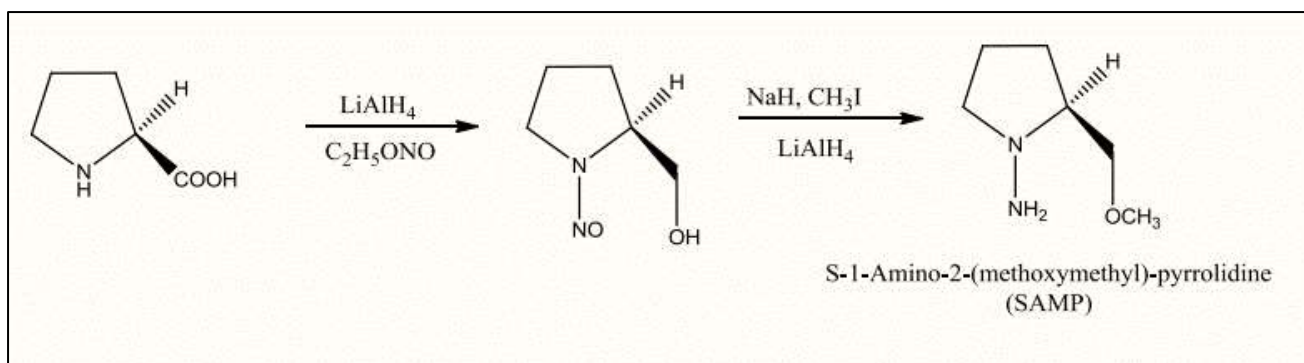
These are separated and purified and converted into pure Z or E enolate with fluoride ions. Z-enolates give mainly syn aldols while the E-enolates give anti aldols.



c. Use of chiral auxiliaries

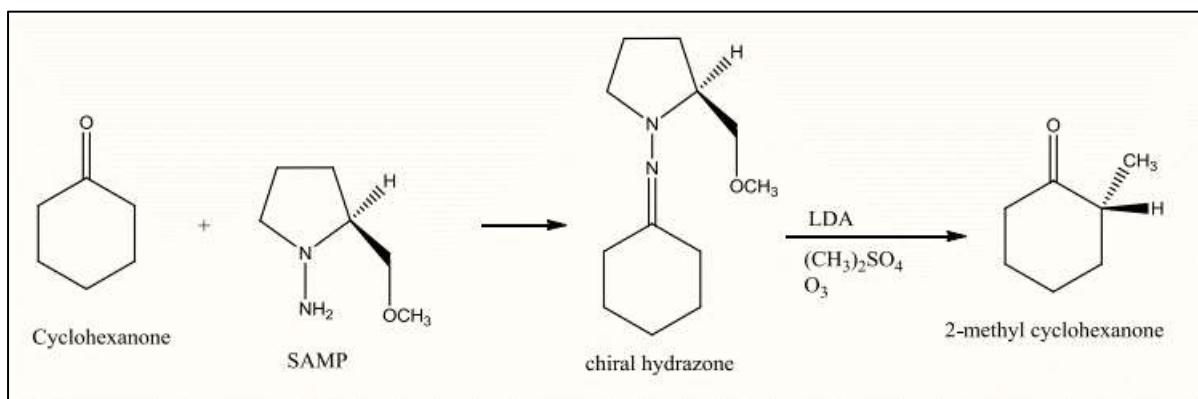
During asymmetric synthesis, a chiral auxiliary is attached chemically to the achiral substrate to give a chiral intermediate. This is followed by the reactions of asymmetric synthesis. At the end, the chiral auxiliary is removed.

Enantioselective alkylation of aldehydes and ketones via chiral hydrazones



SAMP and its enantiomer RAMP are prepared from S- and R- prolines respectively. They bear a chelating methoxy group and are used as chiral auxiliaries in enantioselective alkylation of aldehydes and ketones.

Conversion of cyclohexanone into 2-methyl cyclohexanone

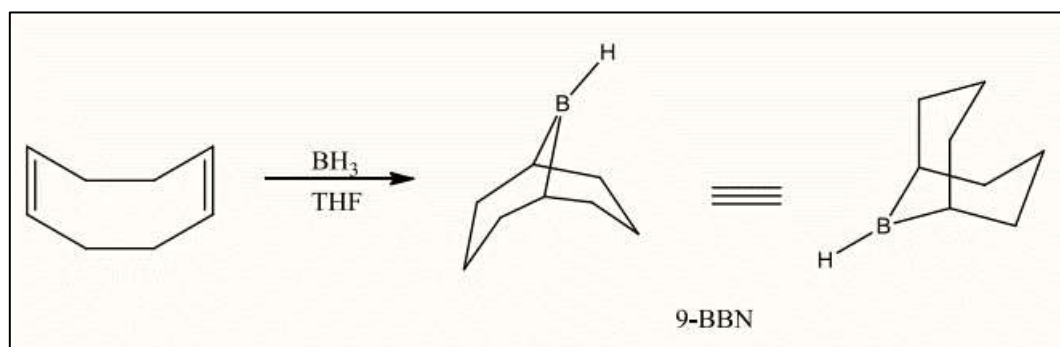


d. Use of chiral reagents and catalysts

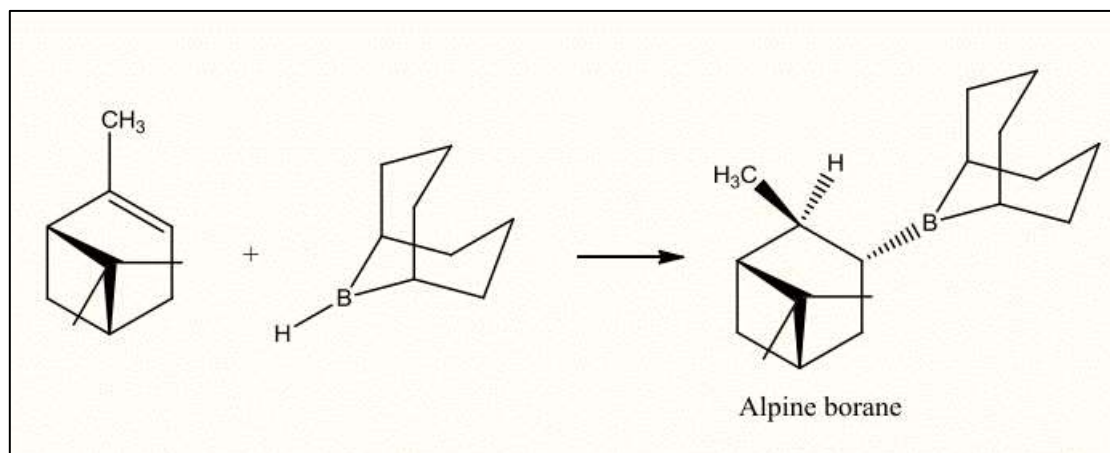
Asymmetric reduction using chiral trialkylboranes (enantioselective reduction of aldehydes and ketones)

Useful reagents:

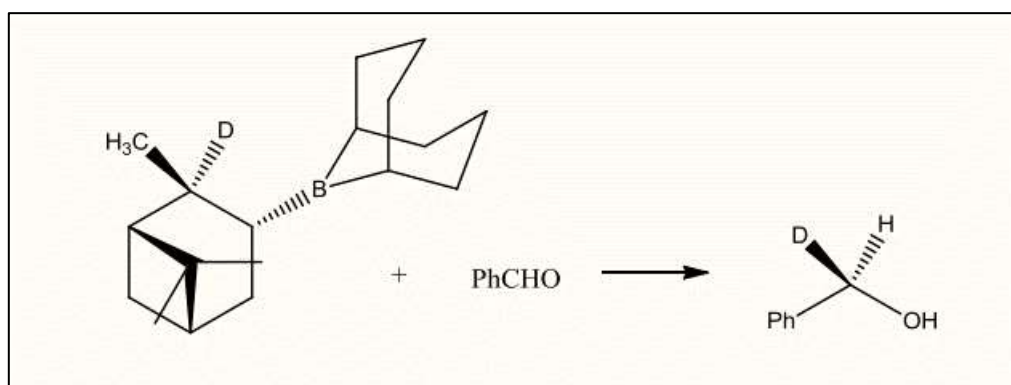
9-BBN (9-borabicyclo (3.3.1) nonane)



Alpine borane



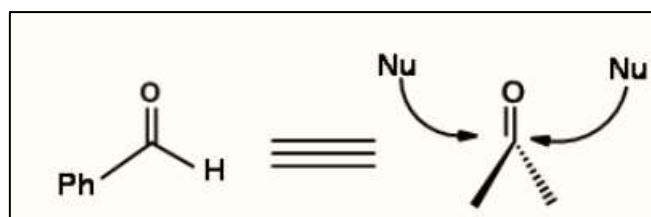
Hydroboration of α -pinene with 9-BBN gives alpine borane, which is used as a chiral reagent. It reduces a variety of carbonyl compounds. Monodeuteriated and chiral primary alcohols can be made by using this reagent.



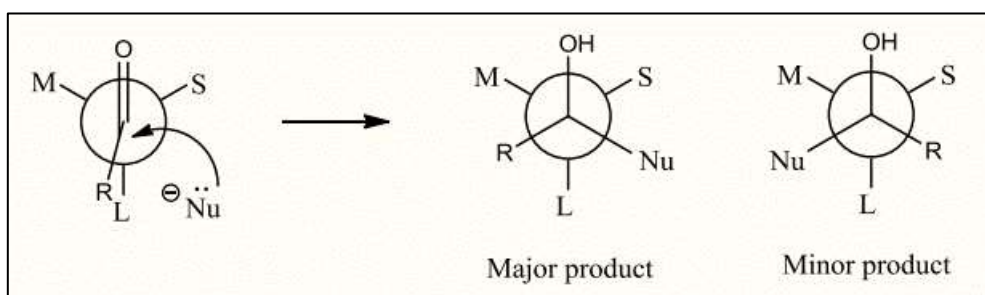
7.Cram's Rule, Felkin-Ahn Modification and Prelog's Rule

In carbonyl compounds, the carbonyl carbon and the three other atoms attached to it would be in one plane. A nucleophile attacking the carbonyl carbon could attack from either side of this plane with equal ease.

E.g. benzaldehyde. The phenyl group is also flat. Nucleophilic attack on benzaldehyde could take place from either side with equal ease. Since a new asymmetric center is now created by this reaction, both enantiomers could be formed with equal ease, resulting in a racemic mixture.

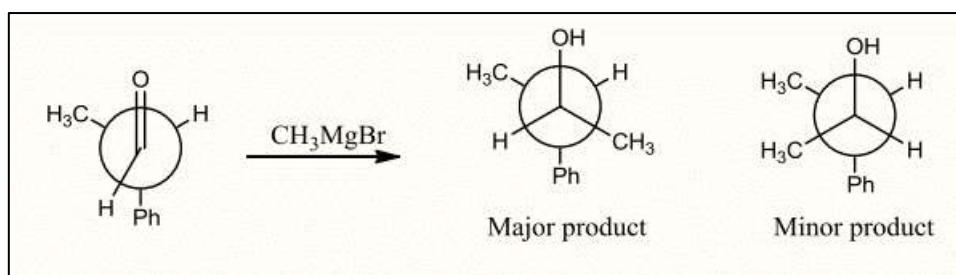


In complex organic molecules, the nucleophile would experience more steric hindrance from one side, leading to unequal synthesis of the two enantiomers. Hence, reaction would take place in the conformation having the least steric strain.



A. Cram's Rule

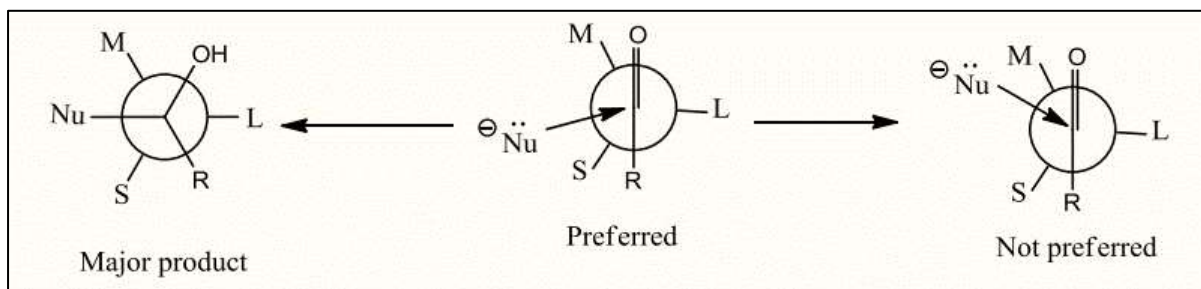
- The existing asymmetric center would have a Small, Medium and Large group, denoted S, M and L respectively.
- In the reactive conformation, the carbonyl group would orient itself in such a way that it will rest between the Small group and the Medium group.
- The attacking nucleophile would prefer to attack from the side of the small group, resulting in the predominant formation of one diastereomer in the product.



B. Felkin-Ahn modification

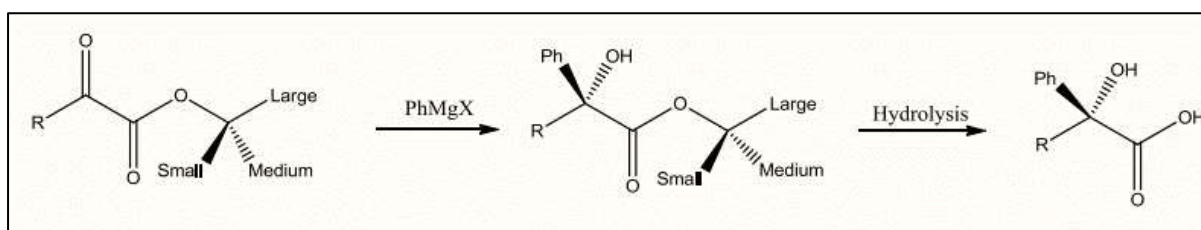
- The Felkin-Ahn model differs from Cram's rule in the conformation adopted by the carbonyl compound.
- The C-L bond is positioned perpendicular to the carbonyl group.
- This arrangement removed unfavourable eclipsing interactions between L and R.
- The nucleophile approaches the carbonyl carbon in a plane perpendicular to that of the

- -CO- fragment from the side opposite the C-L bond and at an obtuse angle with C=O .



C. Prelog's Rule

An extension of Cram's idea of reactive conformation is the Prelog's Rule. The rule has been applied for asymmetric synthesis of α -hydroxyl acids and for assigning the configuration of secondary and tertiary alcohols.



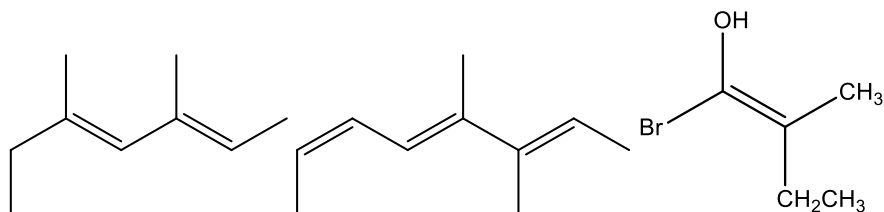
The Grignard reagent approaches the electrophilic carbon from the side of the small group (S) rather than from the side of the medium group (M). Thus, the major product is formed by attack from this side. This on hydrolysis gives the acid.

QUESTIONS

PART-A

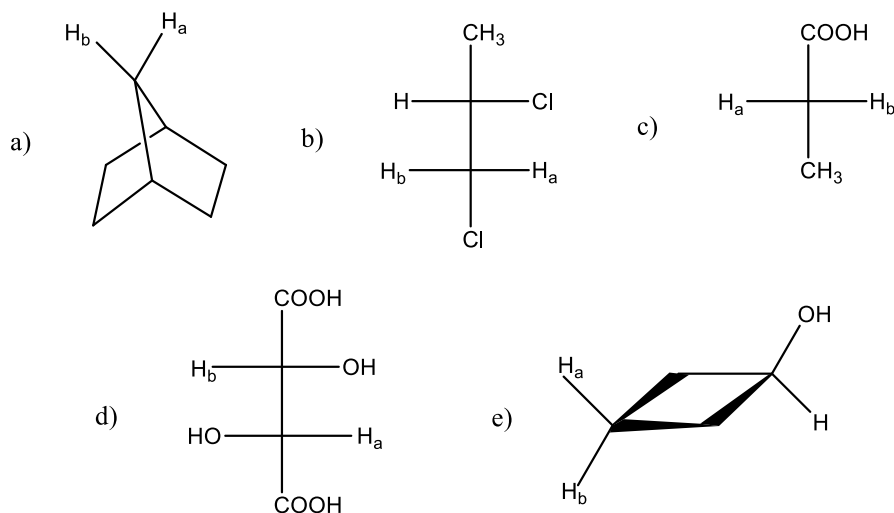
1. Discuss the conformational analysis of ethane.
2. Discuss the stereochemistry in cis and transdecalins.
3. Explain pseudoasymmetry with suitable examples.
4. Differentiate between configuration and conformation.
5. Write the structures of
 - a) cis-1,2-diethyl cyclohexane
 - b) trans-1-methyl-2-isopropyl cyclohexane
 - c) gauche and staggered forms of n-butane

- d) puckered conformation of cyclopentane
6. Explain Cram's rule with examples.
 7. Explain the Felkin-Ahn's modification of Cram's rule.
 8. Explain Prelog's rule with an example.
 9. Assign E/Z nomenclature to the following compounds.

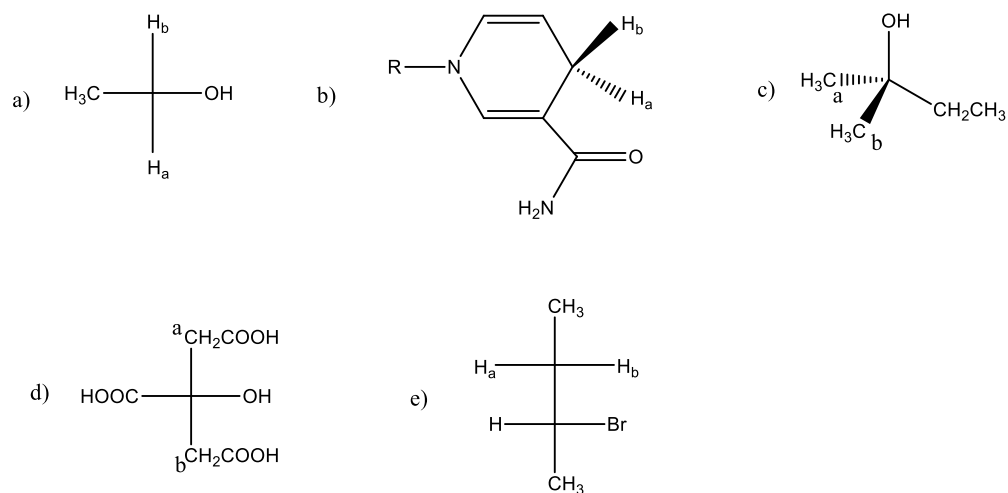


PART B

1. Explain the conformational analysis of n-butane.
2. Discuss the stereochemistry in 1, 2 and 1, 3 disubstituted cyclohexanes.
3. Explain the conformational analysis of cyclohexane.
4. Discuss the diastereoselectivity in aldol reaction as a means of asymmetric synthesis.
5. Explain asymmetric synthesis with the use of chiral reagents and catalysts.
6. Indicate if the hydrogens marked H_a and H_b in the following compounds are homotopic, enantiotopic or diastereotopic.



7. Assign *pro-R* or *pro-S* to the groups labelled 'a' and 'b' in the following compounds.



References

1. P. S. Kalsi, Stereochemistry Conformation and Mechanism, 8th Edition, New Age International Publishers.
2. Ernest L. Eliel, Stereochemistry of Carbon Compounds, Tata McGraw-Hill Publishing Company Limited.
3. Nasipuri, Stereochemistry of Carbon Compounds – Principles and Applications, 3rd Edition, New Age International Publishers.



SCHOOL OF SCIENCE AND HUMANITIES

DEPARTMENT OF CHEMISTRY

UNIT-3 – Pericyclic Reactions – SCYA5203

1. Pericyclic Reactions - Characteristics

Pericyclic Reactions:

A pericyclic reaction is one in which bonds are made or broken in a concerted cyclic transition state. A concerted reaction is one which involves no intermediate.

Characteristics of Pericyclic Reactions:

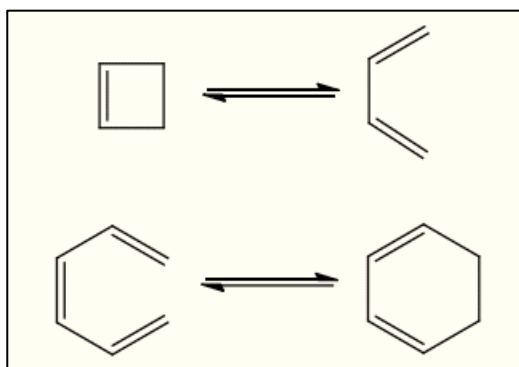
Pericyclic reactions have certain characteristic properties.

- There is no nucleophilic or electrophilic component.
- No catalyst is needed.
- They show very high stereospecificity.
- They can be promoted by heat or light.
- Can occur in gas phase with no solvent.
- They occur in a single step.
- Bond breaking and making occur simultaneously.
- The configuration of the product depends on the configuration of the reactants and reaction conditions.
- At least one reactant is unsaturated.
- It involves formation or break up of sigma and pi bonds.

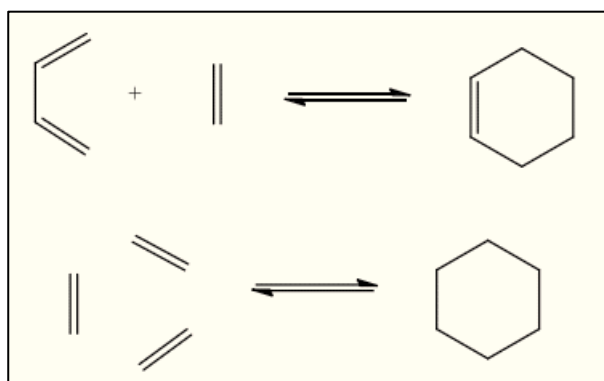
2. Types of Pericyclic Reactions

Based on the identification of certain common features, Woodward and Hoffmann classified pericyclic reactions into five basic types.

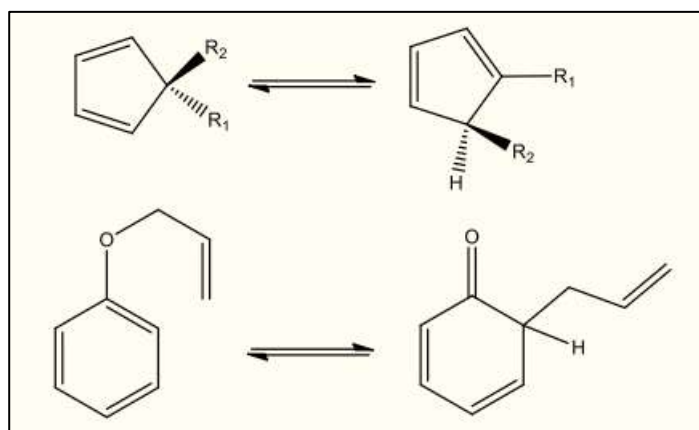
i. Electrocyclic reactions – An electrocyclic reaction is a reversible intramolecular reaction that involves ring opening or ring closure of sigma bonds to pi bonds or vice versa.



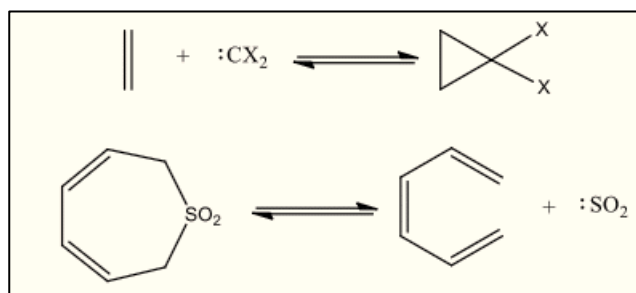
ii. Cycloaddition reactions – These are characterized by cyclization between 2 or more molecules to form a ring via transformation of pi bonds or vice versa.



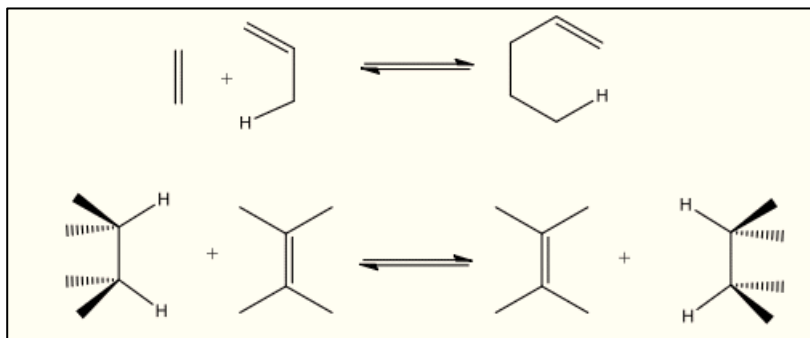
iii. Sigmatropic reactions – These are the reactions in which a bond migrates over a conjugated system.



iv. Cheletropic reactions – They are a special class of cycloaddition/cycloreversion reactions in which 2 bonds are formed or broken at a single atom.



v. Group transfer reactions – One or more groups are transferred from one component to the other.



3. Reaction profile for a concerted reaction

A concerted reaction is one in which the conversion of reactants R into the products P occurs directly by way of a single transition state TS. When the conversion of reactants into products proceeds by way of more than one transition state, such that one or more intermediates are formed, the processes are accordingly non-concerted.

The transition state of organic reactions may be placed into one of three broad categories

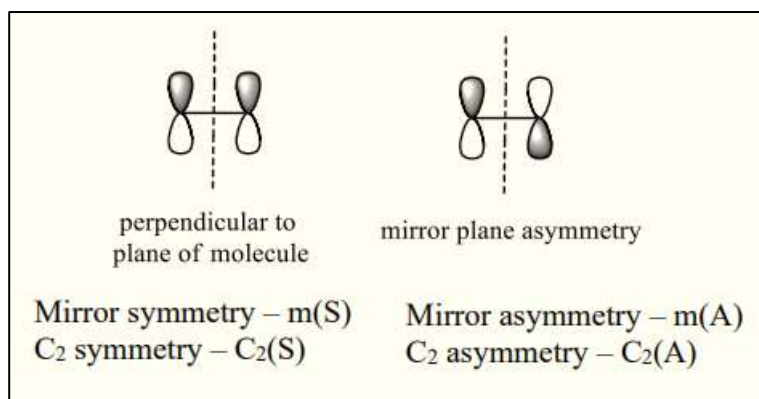
- Polar (involves separation or dispersal of charge)
- Free radical (involves creation or transfer of unpaired electrons)
- Isopolar (neither polar nor radical in nature) Pericyclic reactions proceed through isopolar transition states.

Background of Molecular Orbitals

Molecular orbital (MO) theory describes bonds as the mathematical combination of atomic orbitals that forms a new set of orbitals called molecular orbitals (MOs). The number of atomic orbitals used equals the number of molecular orbitals formed.

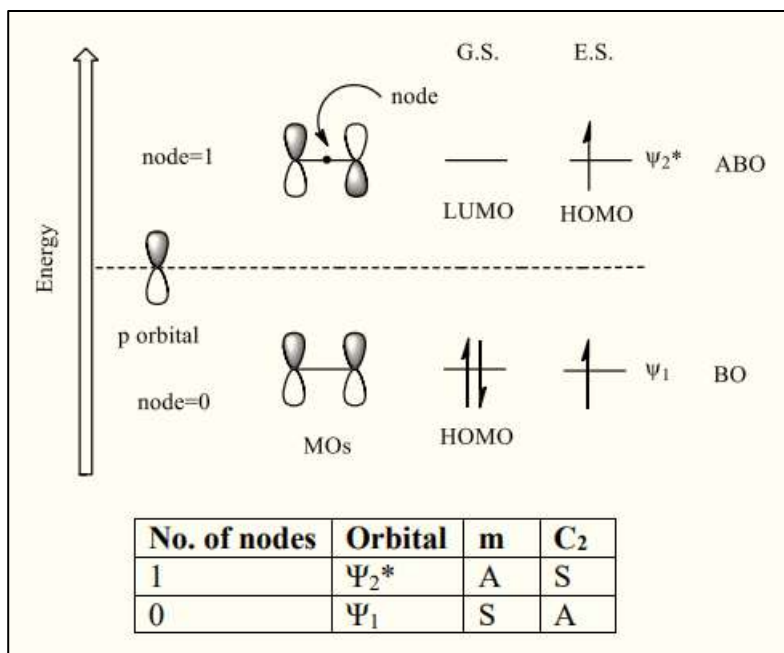
Symmetry in pi molecular orbitals

Pi molecular orbitals contain either the mirror plane or centre of symmetry. Both will not be present together.



i. Ethylene

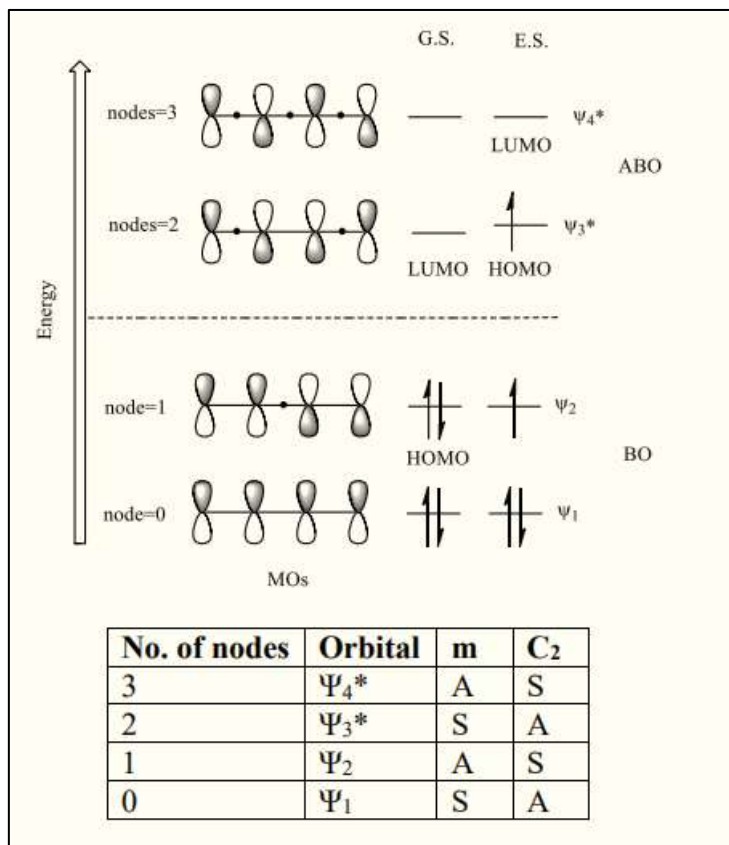
The π bond in ethylene ($\text{CH}_2\text{-CH}_2$) is formed by side-by-side overlap of two p orbitals on adjacent carbons. Two p orbitals can combine in two different ways. When two p orbitals of similar phase overlap, a π bonding molecular orbital (designated as Ψ_1) results. Two electrons occupy this lower-energy bonding molecular orbital. When two p orbitals of opposite phase combine, a π^* antibonding molecular orbital (designated as Ψ_2^*) results. A destabilizing node occurs when two orbitals of opposite phase combine.



ii. 1, 3-butadiene

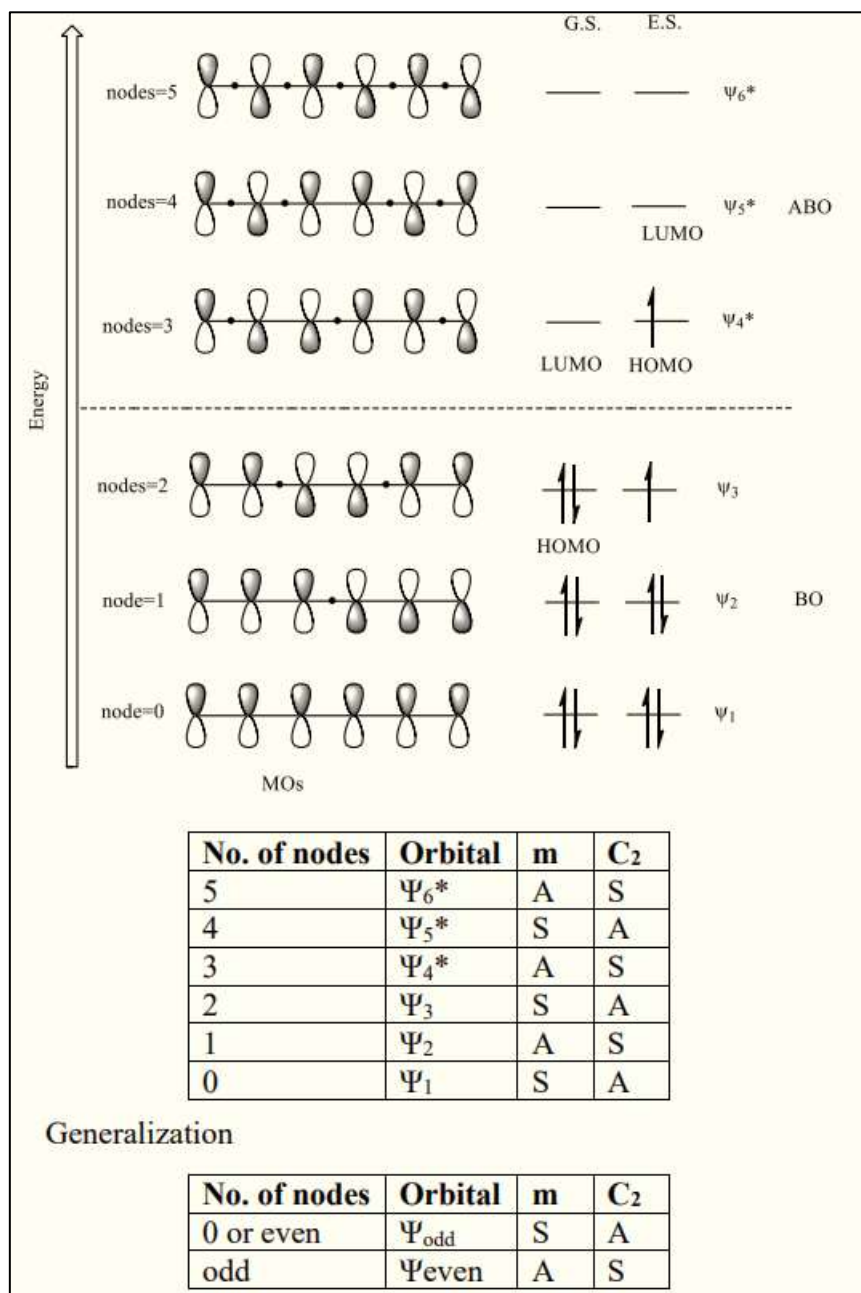
The two π bonds of 1, 3-butadiene ($\text{CH}_2=\text{CH}-\text{CH}=\text{CH}_2$) are formed by overlap of four p orbitals on four adjacent carbons. The four p orbitals can combine in four different ways to form four molecular orbitals designated as Ψ_1 – Ψ_4 . Two are bonding molecular orbitals (Ψ_1 and Ψ_2), and two are antibonding molecular orbitals (Ψ_3^* and Ψ_4^*). The two bonding MOs are

lower in energy than the p orbitals from which they are formed, whereas the two antibonding MOs are higher in energy than the p orbitals from which they are formed.



iii. 1, 3, 5-Hexatriene

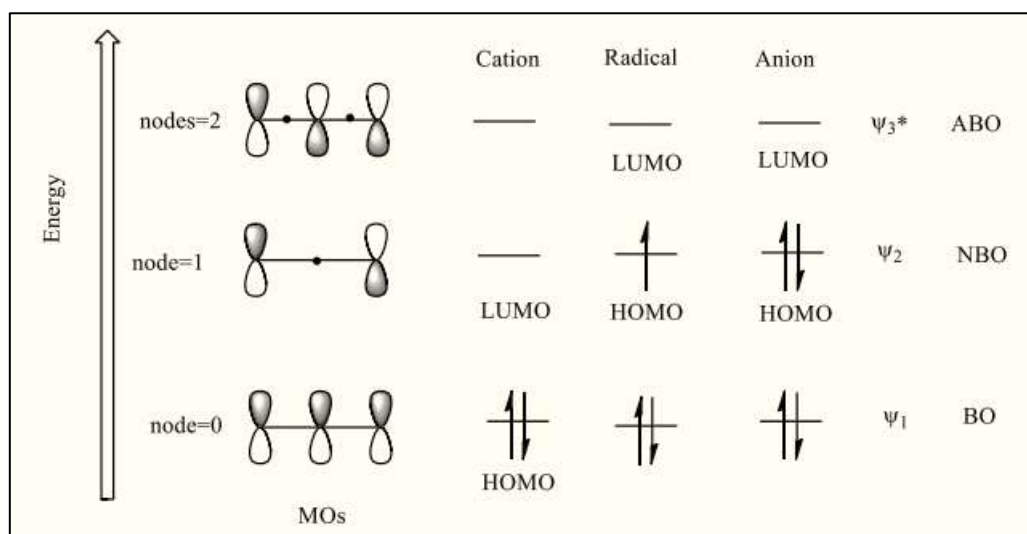
The three π bonds of 1, 3, 5-hexatriene ($\text{CH}_2=\text{CH}-\text{CH}=\text{CH}-\text{CH}=\text{CH}_2$) are formed by overlap of six p orbitals on six adjacent carbons. The six p orbitals can combine in six different ways to form six molecular orbitals designated as Ψ_1 – Ψ_6 . Three are bonding molecular orbitals (Ψ_1 – Ψ_3), and three are antibonding molecular orbitals (Ψ_4^* – Ψ_6^*). In the ground state electronic configuration, the six π electrons occupy the three bonding MOs, Ψ_3 is the HOMO, and Ψ_4^* is the LUMO. In the excited state, which results from electron promotion from Ψ_3 to Ψ_4^* , Ψ_4^* is the HOMO and Ψ_5^* is the LUMO.



Construction of molecular orbitals of conjugated ions and radicals

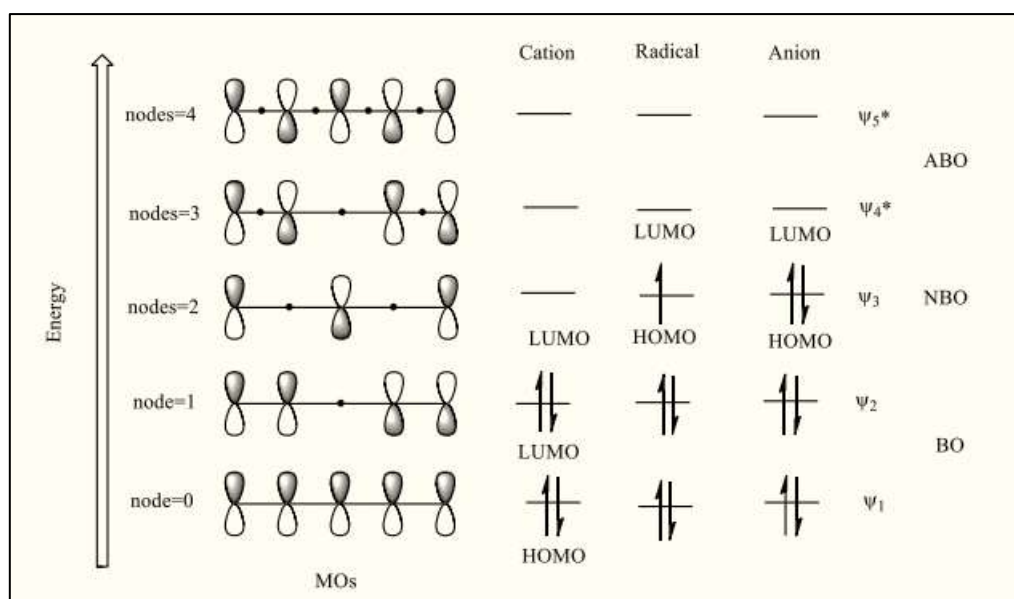
1. Allyl system

$\text{CH}_2=\text{CH}-\text{CH}_2^+$ (cation), $\text{CH}_2=\text{CH}-\text{CH}_2^-$ (anion), $\text{CH}_2=\text{CH}-\text{CH}_2^\bullet$ (radical)



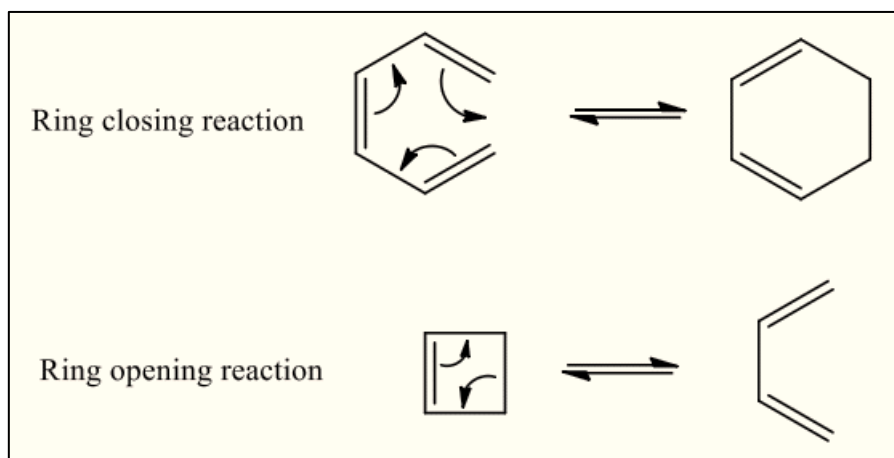
2. 2, 4-pentadienyl system

$\text{CH}_2=\text{CH}-\text{CH}=\text{CH}-\text{CH}_2^+$ (cation), $\text{CH}_2=\text{CH}-\text{CH}=\text{CH}-\text{CH}_2^-$ (anion), $\text{CH}_2=\text{CH}-\text{CH}=\text{CH}-\text{CH}_2^\cdot$ (radical)



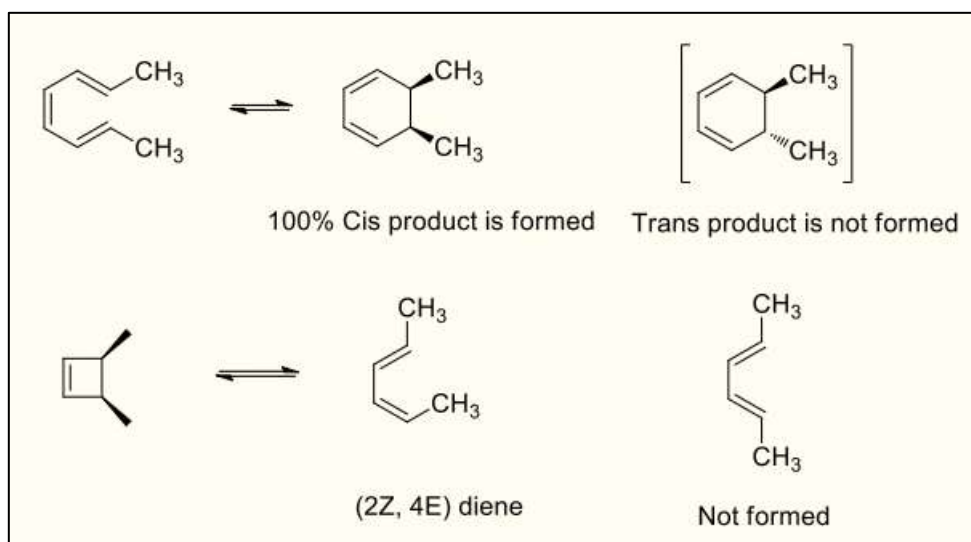
4. Electrocyclic Reactions

An electrocyclic process is defined as the formation of a single bond between the termini of a conjugated polyene and the reverse reaction.

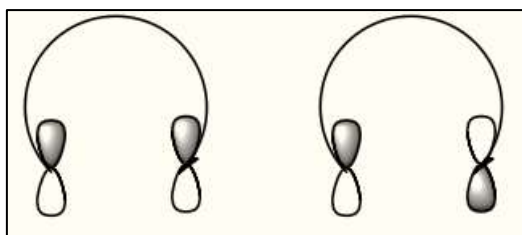


Stereochemistry and Orbital Symmetry

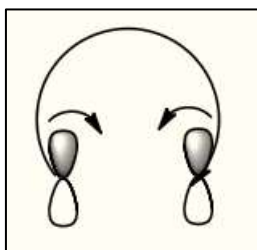
Electrocyclic reactions are completely stereospecific. For example, ring closure of (2E, 4Z, 6E)-2, 4, 6-octatriene yields a single product with cis methyl groups on the ring. Ring opening of cis-3, 4-dimethylcyclobutene forms a single conjugated diene with one Z alkene and one E alkene.



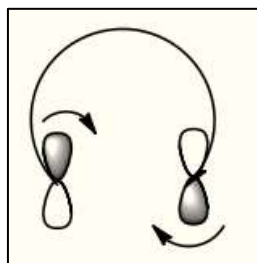
An electrocyclic reaction occurs only when like phases of orbitals can overlap to form a bond. Such a reaction is symmetry allowed. An electrocyclic reaction cannot occur between orbitals of opposite phase. Such a reaction is symmetry forbidden. For this, the p orbitals on the terminal carbons of the HOMO must be examined and determined whether like phases of the orbitals are on the same side or on opposite sides of the molecule.



When like phases of the p orbitals are on the same side of the molecule, the two orbitals must rotate in opposite directions—one clockwise and one counterclockwise. Rotation in opposite directions is said to be disrotatory.



When like phases of the p orbitals are on opposite sides of the molecule, the two orbitals must rotate in the same direction—both clockwise or both counterclockwise. Rotation in the same direction is said to be conrotatory.



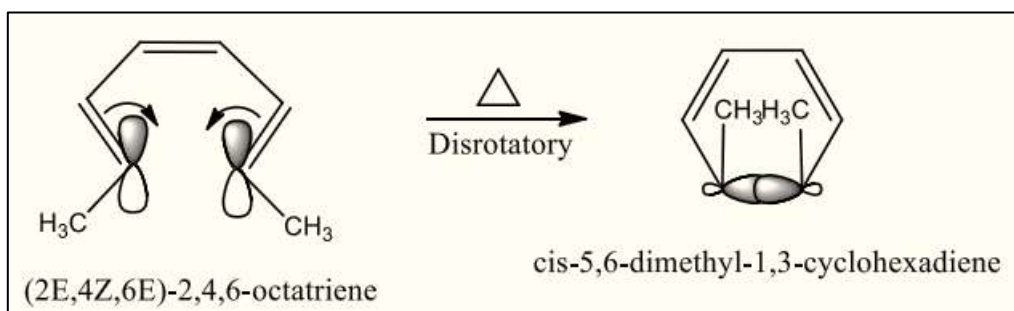
Thermal Electrocyclic reactions

In a thermal reaction, the HOMO of the ground state electronic configuration is considered. Rotation occurs in a disrotatory or conrotatory fashion so that like phases of the p orbitals on the terminal carbons of this molecular orbital combine.

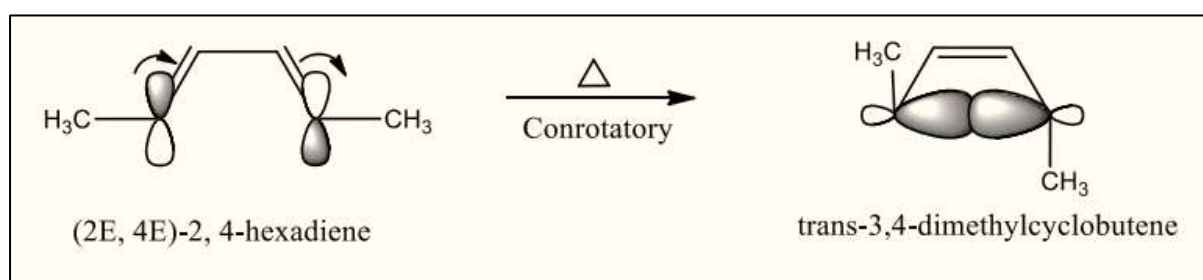
The number of double bonds in the conjugated polyene determines whether rotation is conrotatory or disrotatory.

Two examples illustrate different outcomes. Thermal electrocyclic ring closure of (2E,4Z,6E)-2,4,6-octatriene yields a single product with cis methyl groups on the ring. Cyclization occurs

in a disrotatory fashion since the HOMO of the triene has like phases on the same side of the molecule.



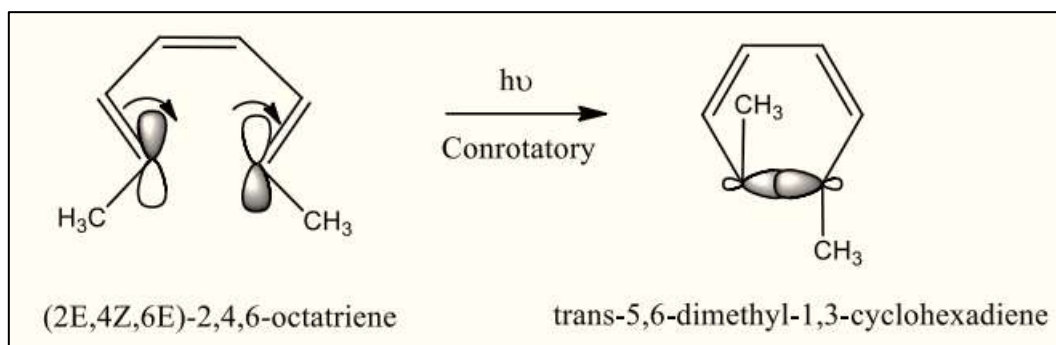
In contrast, thermal electrocyclic ring closure of (2E,4E)-2,4-hexadiene forms a cyclobutene with trans methyl groups.



Cyclization occurs in a conrotatory fashion since the HOMO of the diene has like phases on the opposite side of the molecule. A conrotatory ring closure is symmetry allowed since like phases combine to form the sigma bond.

Photochemical electrocyclic reactions

In photochemical reactions, the orbitals of the HOMO of the excited state are considered to determine the course of the reaction. The excited state HOMO has the opposite orientation of the outermost p orbitals compared to the HOMO of the ground state. Hence, the method of ring closure of a photochemical electrocyclic reaction is opposite to that of a thermal electrocyclic reaction for the same number of pi bond.



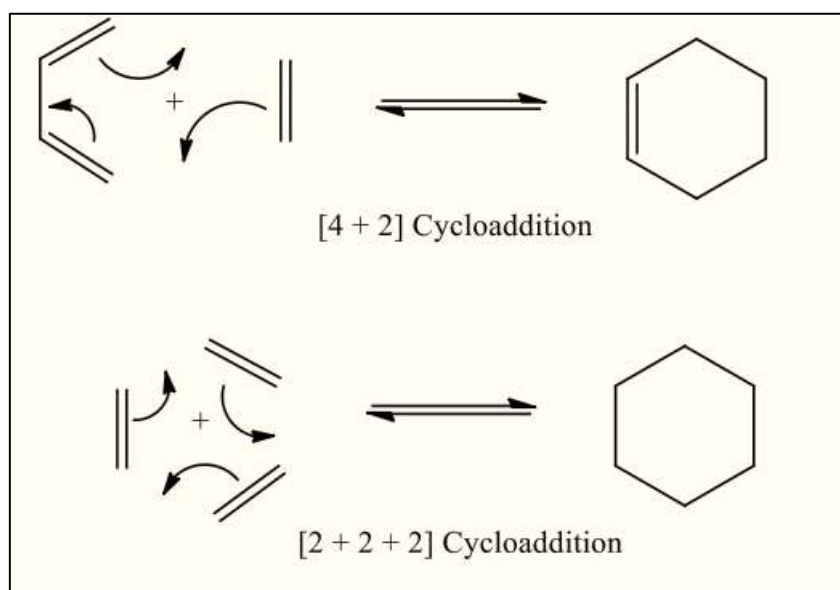
Cyclization occurs in a conrotatory fashion because the excited state HOMO of a conjugated triene has like phases of the outermost p orbitals on the opposite sides of the molecule.

From the above examples, the Woodward-Hoffmann rules for electrocyclic reactions under thermal or photochemical conditions can be summarized.

No. of π bonds	No. of π electrons	Thermal Reaction	Photochemical Reaction
$4n$	Even	Conrotatory	Disrotatory
$4n + 2$	Odd	Disrotatory	Conrotatory

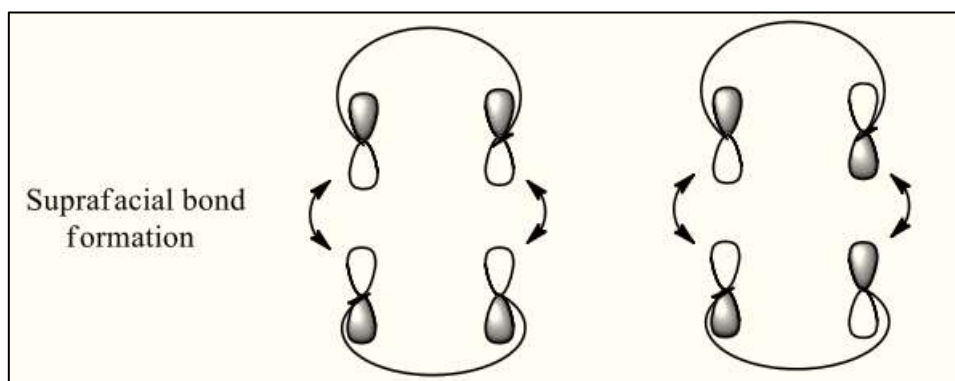
5. Cycloaddition Reactions

A cycloaddition is a reaction between two compounds with π bonds to form a cyclic product with two new σ bonds. Cycloaddition reactions are initiated by heat or light and are identified by the number of π electrons in each reactant.



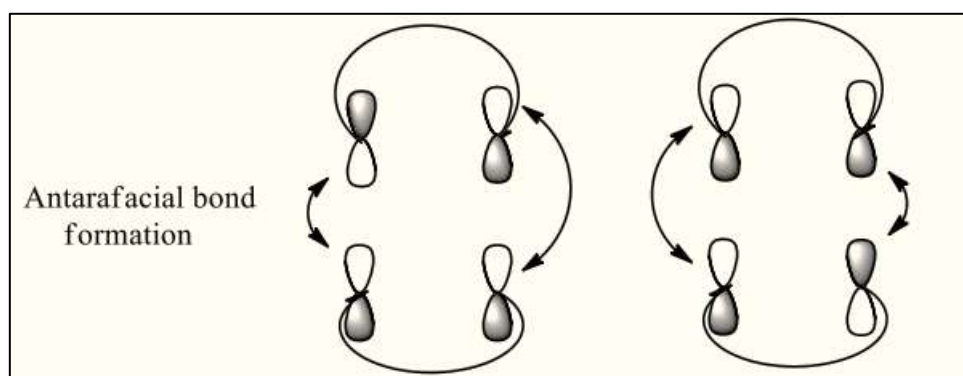
Orbital Symmetry in Cycloaddition

Bonding in cycloaddition can take place only if the p orbitals of the terminal carbons having like phases combine. Similar to electrocyclic reactions, two modes of reactions are possible.



A suprafacial cycloaddition occurs when like phases of the p orbitals of both reactants are on the same side of the π system, so that two bonding interactions result.

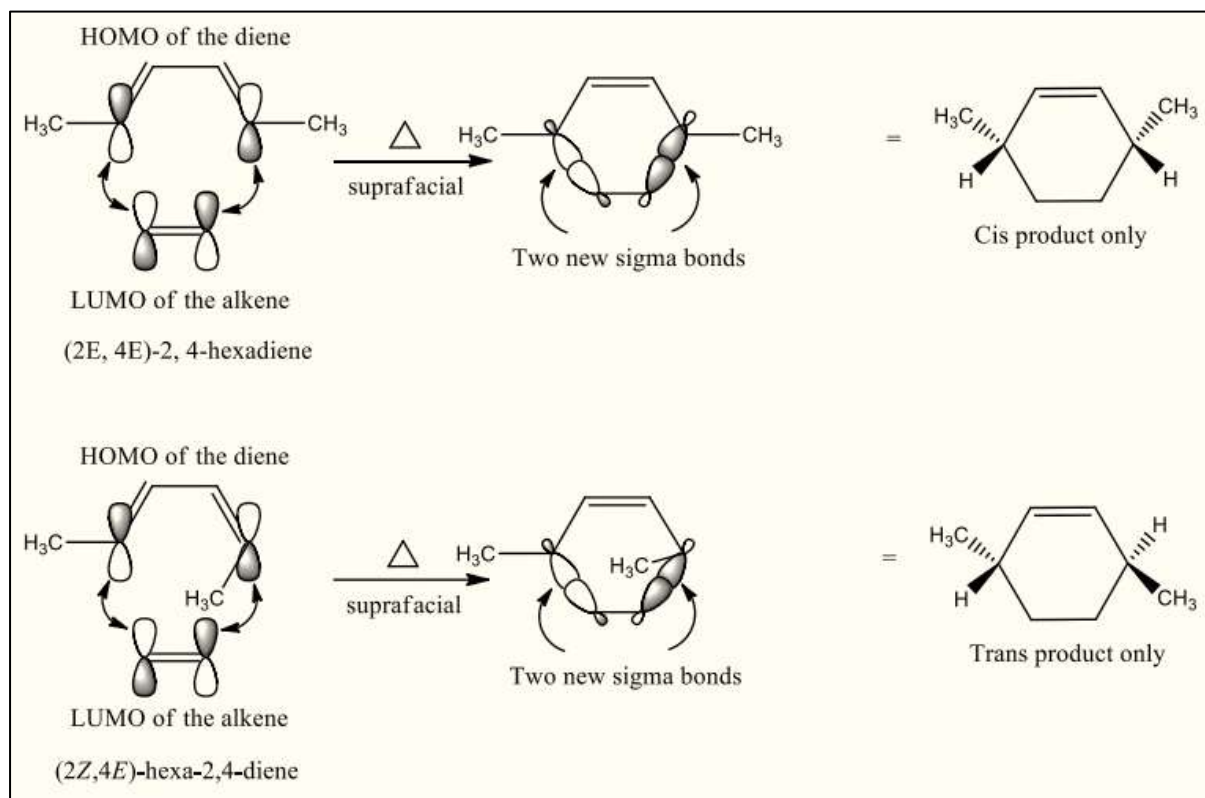
An antarafacial cycloaddition occurs when one π system must twist to align like phases of the p orbitals of the terminal carbons of the reactants.



Since cycloaddition involves the donation of electron density from one reactant to another. One reactant donates its most loosely held electrons (HOMO) to a vacant orbital that can accept electrons (LUMO) of the second reactant. The HOMO of either reactant can be used for analysis. Hence, the HOMO of one component is used to interact with the LUMO of the other component.

6. Diels – Alder Cycloaddition - [4 + 2] Cycloaddition

Consider the HOMO of the diene and the LUMO of the alkene. A [4 + 2] cycloaddition occurs readily by suprafacial reaction under thermal conditions.



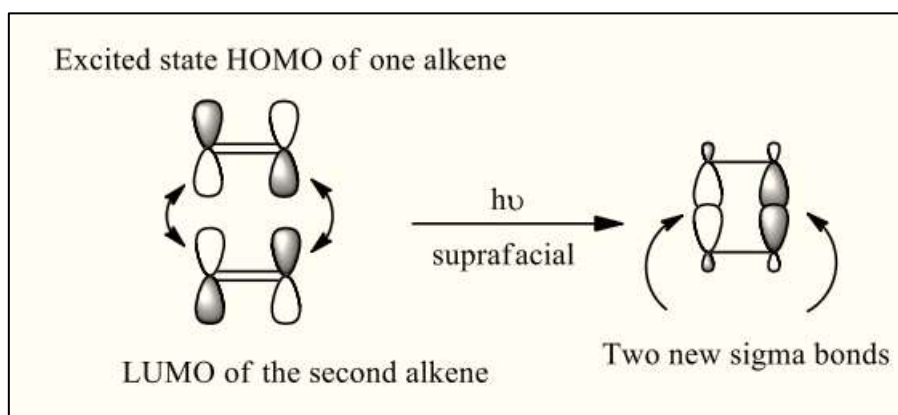
[4 + 2] cycloaddition follows a concerted, suprafacial pathway. The stereochemistry of the diene is retained in the product.

The Diels-Alder cycloaddition is classified as a [4+2] process because the diene has four pi-electrons that shift position in the reaction and the dienophile has two.

The Diels-Alder reaction is an important and widely used method for making six-membered rings, as shown on the right. The reactants used in such reactions are a conjugated diene, simply referred to as the diene, and a double or triple bond co-reactant called the dienophile, because it combines with (has an affinity for) the diene.

[2 + 2] Cycloaddition

[2 + 2] Cycloaddition does not occur under thermal conditions but takes place photochemically. Like phases of the p orbitals on only one set of terminal carbons can overlap. For like phases to overlap on the other terminal carbon, the molecule must twist to allow for an antarafacial pathway. This process cannot occur to form small rings.

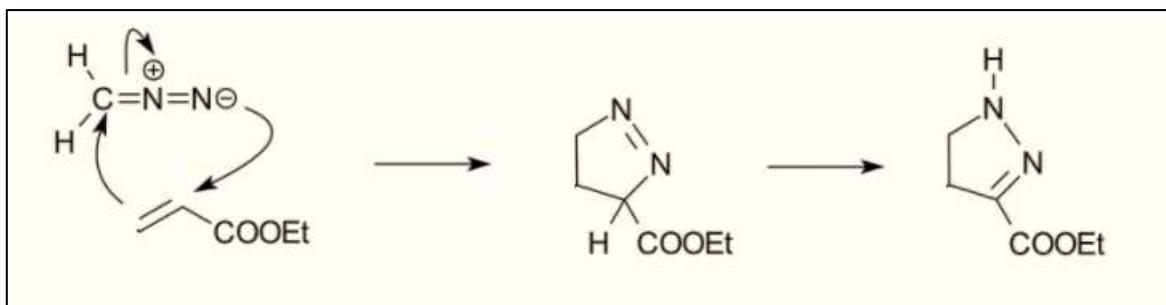


Woodward-Hoffmann rules for Electrocyclic and Cycloaddition reactions

Reaction conditions	Number of π bonds	Electrocyclic reactions	Cycloadditions
Thermal	Even	Conrotatory	Antarafacial
	Odd	Disrotatory	Suprafacial
Photochemical	Even	Disrotatory	Suprafacial
	Odd	Conrotatory	Antarafacial

7. 1,3-Dipolar cycloaddition

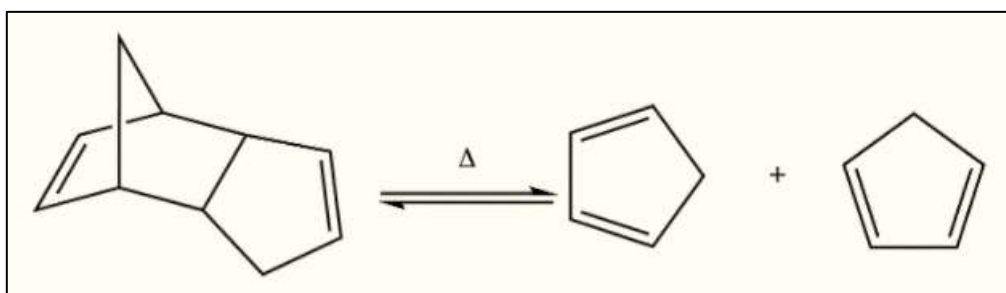
These cycloadditions are analogous to the Diels – Alder reaction in that they are Concerted [$\pi^{4s} + \pi^{2s}$] reactions. The 1,3-dipolar components are compounds whose representation requires ionic structures which include one with charges on atoms bearing 1, 3 – relationship as in diazomethane. These types of molecule are called 1, 3- dipoles are isoelectronic with allyl anion. These have 4 π electrons and each has atleast one charge separated resonance structure with opposite charges in a 1, 3- relationship. These reactions are useful for the synthesis of five membered heterocyclic rings.



8. Retro Diels – Alder reaction

The retro Diels – Alder reaction is the exact reverse of Diels-Alder reaction and passes through the same transition state. In the most common case, where the reverse Diels – Alder is exactly same as the forward Diels – Alder all that is an equilibrium is established between the diene/ dienophile and the Diels – Alder product. However, there are cases where the Diels – Alder product can undergo more than one possible retro Diels – Alder reaction and this can result in the formation of products that differ from the original diene and dienophile. In retro Diels – Alder reaction, a six membered ring is broken

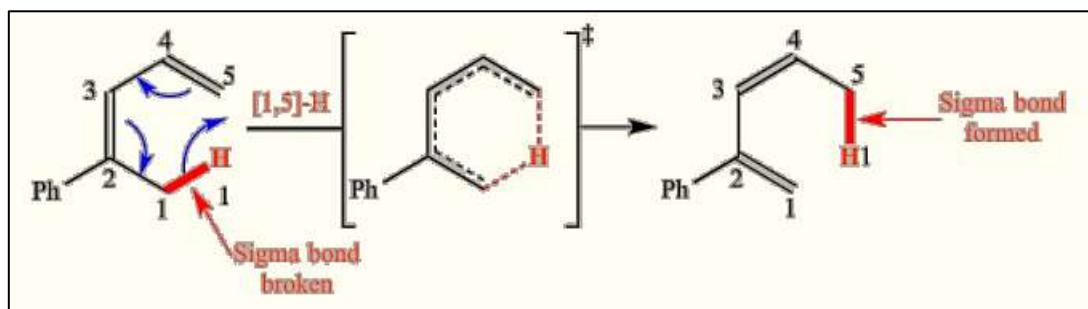
- Three π bonds are formed
- Two single bonds + one π bond are broken
- Bonds formed: C1 – C2 (π), C5 – C6 (π) and C3 – C4 (π)
- Bonds broken: C1 – C6, C4 – C5 and C2 – C3 (π)



9. Sigmatropic Rearrangement

A sigmatropic rearrangement is a Concerted intramolecular shift of an atom or a group of atoms. Molecular rearrangements in which a σ -bonded atom or group, flanked by one or more π -electron systems, shifts to a new location with a corresponding reorganization of the π -bonds are called sigmatropic reactions. The total number of σ -bonds and π -bonds remain unchanged.

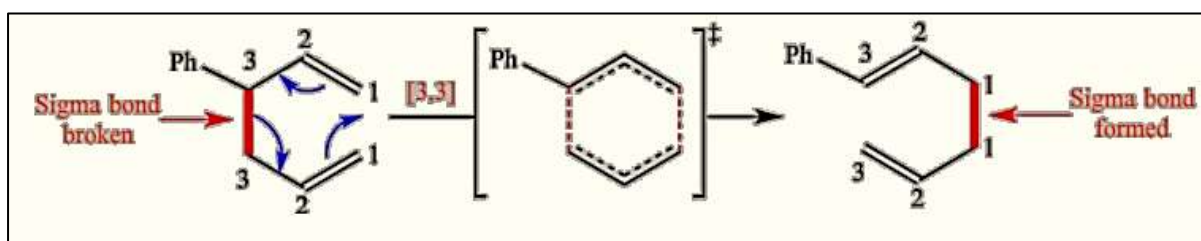
These rearrangements are described by two numbers set in brackets, which refer to the relative distance (in atoms) each end of the σ -bond has moved, as illustrated by the first equation in the diagram below. The most common atom to undergo sigmatropic shifts is hydrogen or one of its isotopes.



10. The Cope Rearrangement

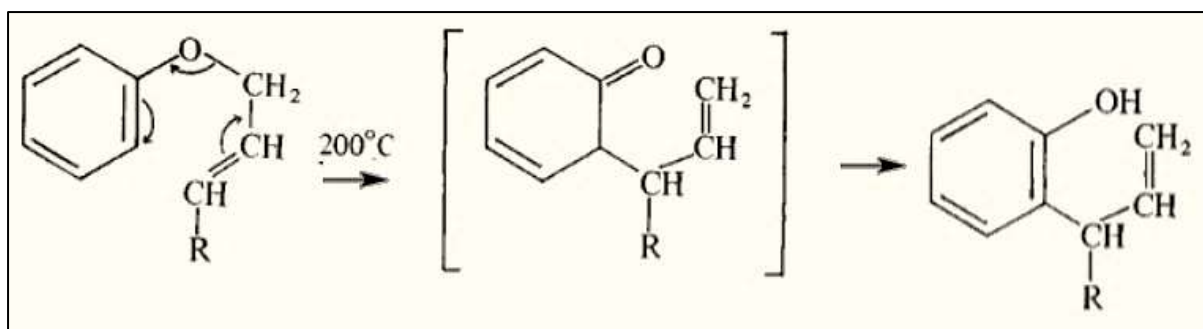
The equation shows a facile [1,5] hydrogen shift which converts a relatively unstable allene system into a conjugated triene. Note that this rearrangement, which involves the relocation of three pairs of bonding electrons, may be described by three curved arrows.

1, 5- diene on heating is rearranged to another 1,5-diene by concerted formation of a 1,6-bond, breaking of the 3 , 4 – bond and migration of both the double bonds in a [3, 3] sigmatropic rearrangement is known as Cope rearrangement.



11. The Claisen Rearrangement

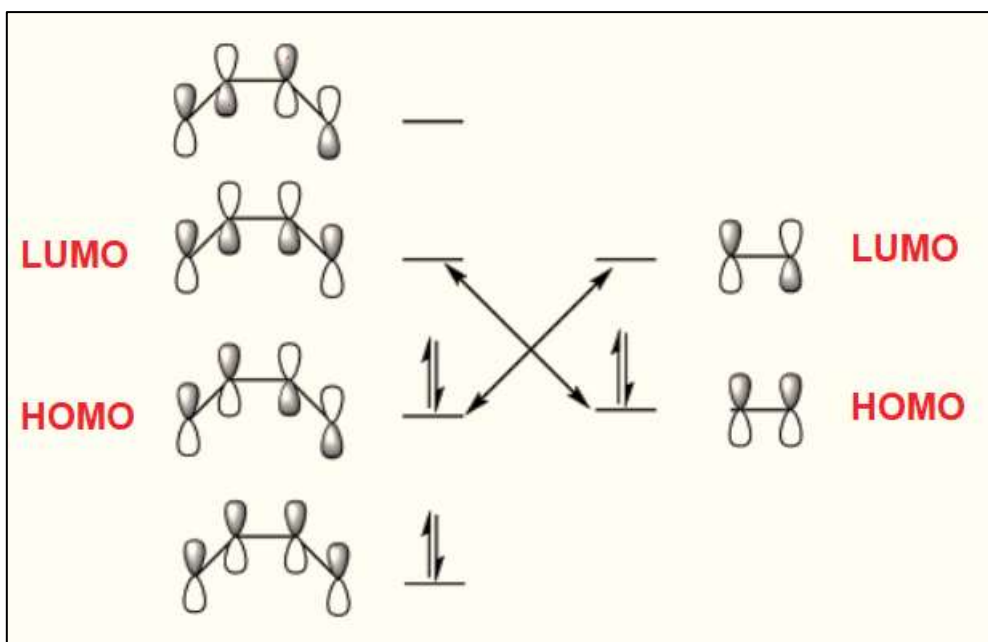
The Claisen rearrangement also involves a [3,3] sigma tropic rearrangement, however in Claisen rearrangement the substrates incorporate one or more hetero atoms in place of Carbon in the 1, 5 – hexadiene system



12. Fukui Frontier Orbital Theory concept (FMO)

Valence electrons occupy the highest filled electronic levels and when chemical reactions occur, these electrons are transferred into the molecular bonding and non-bonding levels. These may be referred to as the frontier electrons since they suffer the greatest perturbation on interaction with the empty acceptor orbitals of the attacking reagent. The frontier electrons of an unsaturated delocalized system such as butadiene reside in the highest occupied pi molecular orbital or HOMO. In the case of photochemically excited butadiene, the frontier orbital or HOMO is Ψ_3 , since this now contains the most energetic electron. In ground state butadiene, the Ψ_3 orbital is unoccupied and is the LUMO. The HOMO levels have electron donor properties, whilst the LUMO levels can accept electrons. The basis of the frontier orbital analysis of concerted pericyclic reactions is the assumption that these processes take place at the position and in the direction of maximum overlap between the HOMO and LUMO of the reacting species. If the reacting species possess a singly occupied molecular orbital SOMO, it is assumed to play the part of the HOMO or of the LUMO or of both, since it has some electron donor and some electron acceptor character. The theory developed by Fukui emphasizes the importance of the LUMO-HOMO interaction.

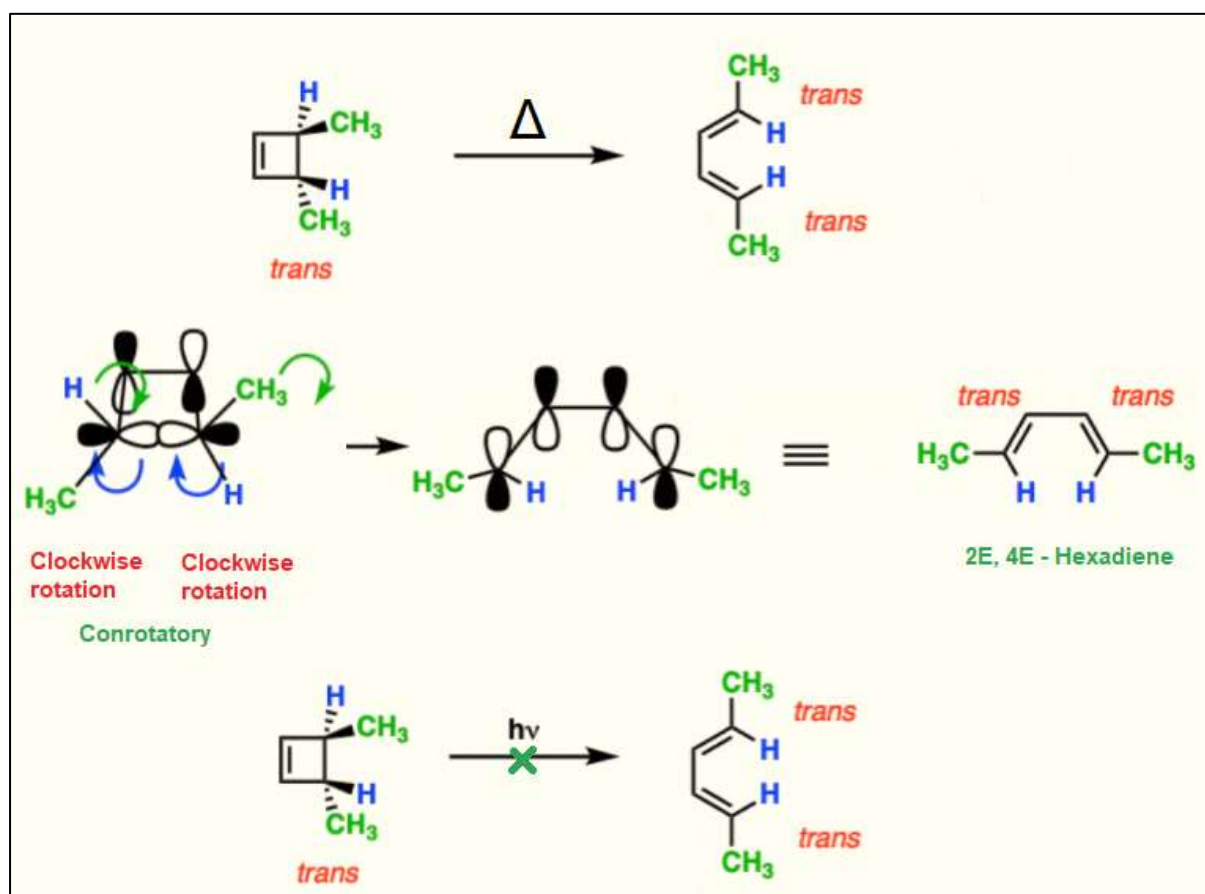
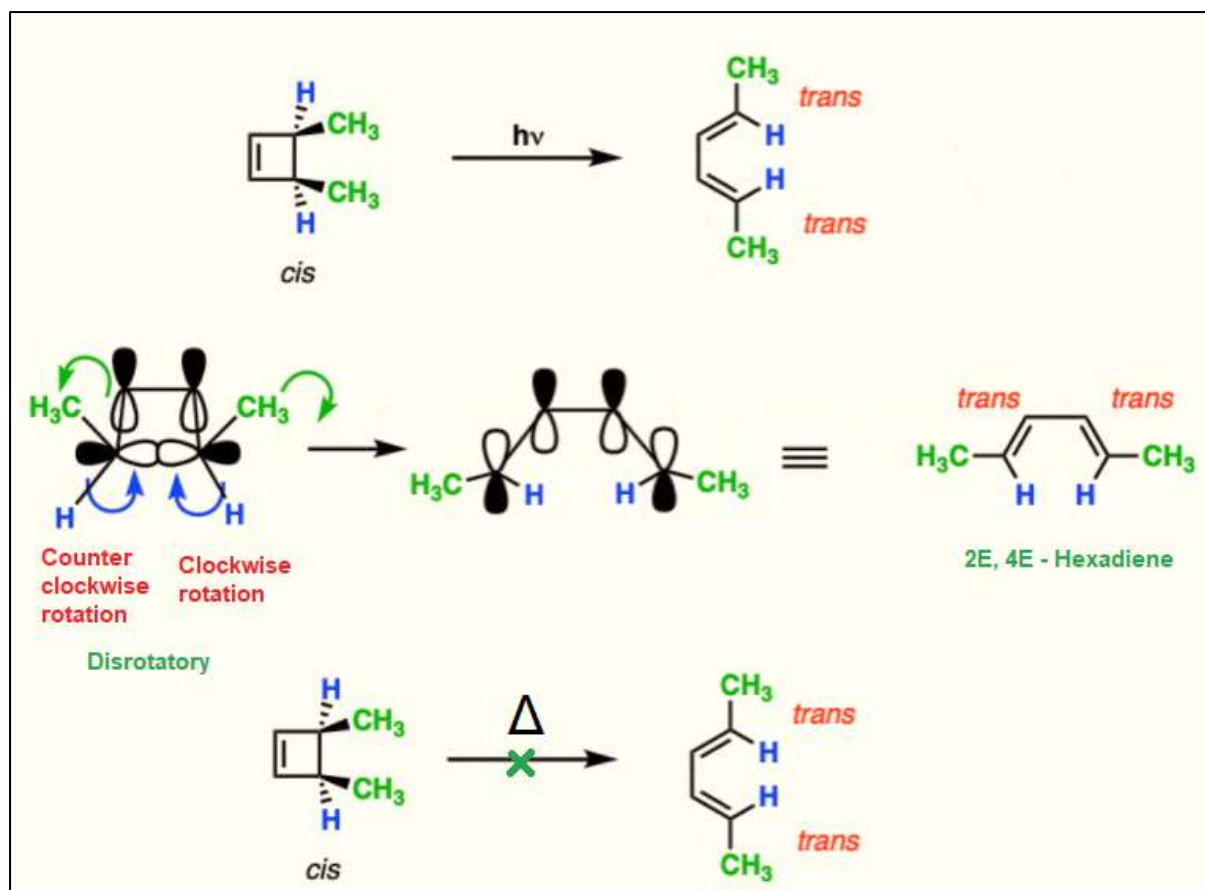
The two π bonds of 1, 3-butadiene are formed by overlap of four p orbitals on four adjacent carbons. The four p orbitals can combine in four different ways to form four molecular orbitals designated by ψ_1 - ψ_4 . Out of these four orbitals, two are bonding molecular orbitals (ψ_1 and ψ_2), and two are anti bonding molecular orbitals (ψ_3^* and ψ_4^*). The p-orbitals from which they are formed are at higher energy than the two bonding MOs, whereas the two anti-bonding MOs are higher in energy than the p orbitals from which they are formed.



13. Mobius- Huckel Analysis (PMO) Approach

The Concerted reactions are analyzed by the classification of transition states as aromatic or anti-aromatic. Huckel's rule of aromaticity states that a monocyclic planar conjugated system with $(4n + 2) \pi$ electrons is aromatic and stable in ground state. On the otherhand a system with $4n \pi$ electrons is unstable and is called anti aromatic.

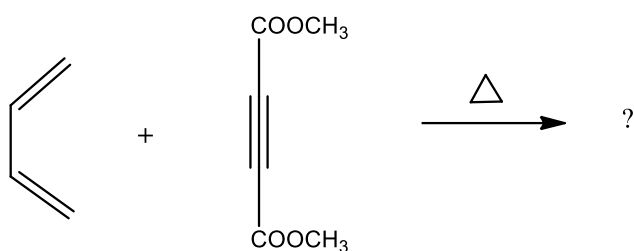
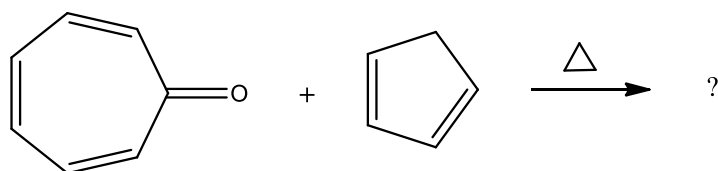
The Huckel – Mobius approach also predicts conrotatory motion under thermal conditions and predicts the formation of same diene. The transition state for conrotatory ring opening has one sign inversion (phase dislocation) and with four electrons it is aromatic . The conrotatory transition state for cyclobutene ring opening is therefore aromatic. The transition state for disrotatory cyclobutene ring opening however it is anti-aromatic (No phase dislocation with 4 electrons). Thus, the PMO approach like FMO method also predict That for butadiene - cyclobutene interconversion the conrotatory transition state is the favoured aromatic transition state and thus thermal conrotatory ring opening in cyclobutene is allowed and dis rotatory opening is forbidden.



QUESTIONS

PART-A

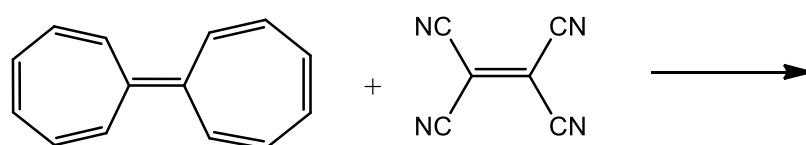
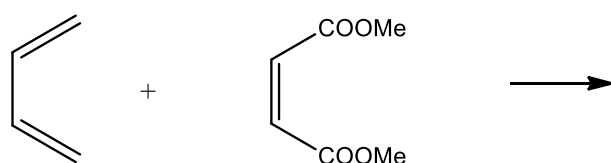
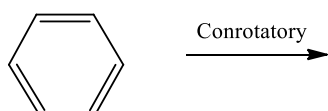
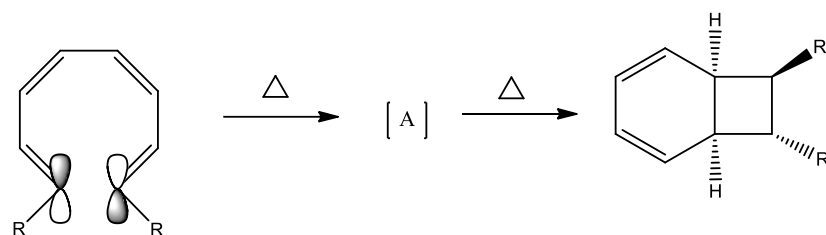
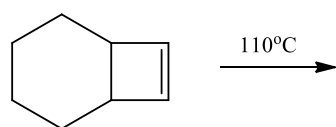
1. Discuss the different types of pericyclic reactions with suitable examples.
2. Draw the pi molecular orbitals for 1,3-butadiene in the ground and excited states.
3. Draw the pi molecular orbitals for 1, 3, 5-hexatriene indicating the HOMO and LUMO in the ground and excited states.
4. Explain the Woodward-Hoffmann rules for electrocyclic reactions.
5. Explain sigmatropic rearrangements involving hydrogen migration.
6. Predict the product and justify.



7. Explain thermal and photochemical [2+2] cycloaddition.
8. Explain endo and exo product formation in Diels-Alder reaction.
9. Explain the Cope rearrangement with mechanism.

PART B

1. Explain the Diels-Alder reaction with orbital interactions and explain whether it is thermally or photochemically allowed.
2. Explain the Claisen arrangement with mechanism.
3. Each transformation shown below is believed to involve a concerted reaction. Explain what is happening in each case.



4. Draw the correlation diagram for the Diels-Alder reaction of butadiene with ethylene. Deduce and explain whether the reaction is allowed thermally or photochemically.
5. Apply Fukui FMO method to explain disrotatory and conrotatory ring closure of 1,3,5-hexatriene.
6. Draw the correlation diagram of the supra-supra cycloaddition of two ethylene molecules to form cyclobutane and predict whether the reaction will proceed thermally or photochemically.
7. Explain the types of orbital interactions possible in cheletropic reactions. Apply Woodward-Hoffmann rule and point out which of the reactions will take place thermally and which photochemically.
8. Explain disrotatory and conrotatory ring opening and closure in electrocyclic reactions with suitable examples.

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3. Ian Fleming, Pericyclic Reactions, OUP Oxford Publishers, 1999.
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SCHOOL OF SCIENCE AND HUMANITIES

DEPARTMENT OF CHEMISTRY

UNIT-4 – Organic Photochemistry-I – SCYA5203

1. Organic Photochemistry – Introduction

Photochemistry is a branch of chemistry which reported its first reaction in the middle of 18th century. A photochemical reaction can be treated as a normal chemical reaction where, in some cases, the high energy content of the excited state of a reagent can be seen as the transition state. The interaction of the matter or of a molecule with the light, i.e. a photo-physical process, is always the starting point for any other processes, chemical reactions included. The knowledge of the principal photo-physical processes and of the primary photo-chemical processes is essential for a deep comprehension of organic photochemistry.

Chapmann defined photochemical process as the science which has been arising from the application of photochemical methods to organic chemistry and organic chemical methods to photochemistry. A very important naturally occurring photochemical process is the process of photosynthesis and the carbohydrates formed from which is the basis of life on earth.

Electromagnetic Spectrum

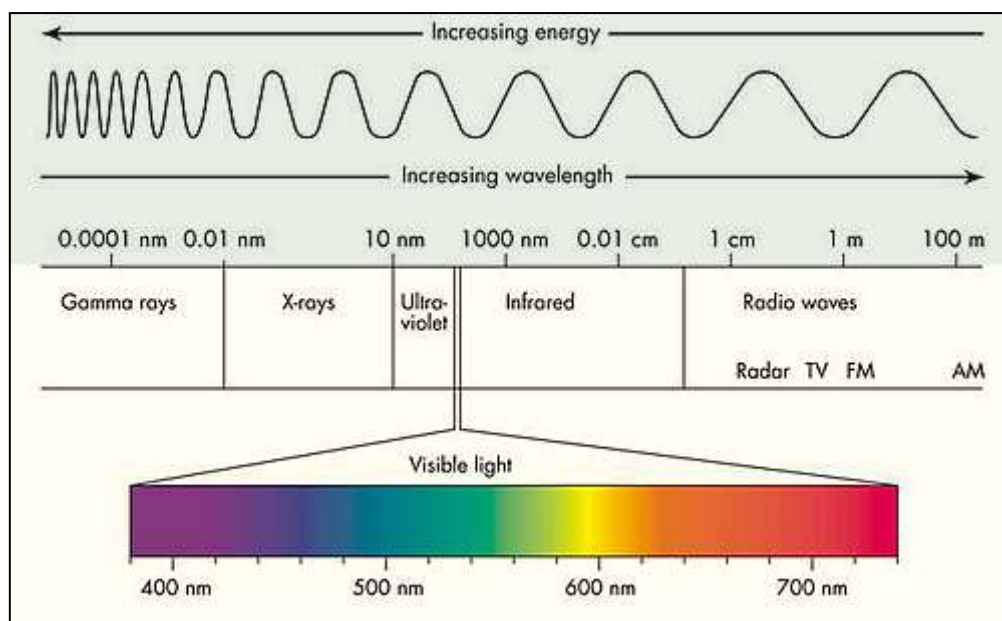


Fig. 1: Electromagnetic Spectrum

When the energy of the electromagnetic radiation in the ultraviolet (UV) or visible region (VIS) falls on molecule it is sufficient to promote electrons to excited states and photochemical processes can be observed. In photochemical reactions light is the reagent which interacts with the electrons (σ and π electrons and lone pairs) in the molecule. In a thermally stimulated reaction, the extra energy supplied to the reagents, is necessary for overcoming the transition state at higher energy and for its conversion into the final products. In photochemical reaction, when the light interacts with the electrons of a molecule or an atom, a high energy state is generally produced which is similar to the transition state called electronically excited state of

the molecule. Thermal and photochemical stimulated processes are strongly different: in thermal processes all atoms of the molecule in its ground states are stimulated with a continue variation of the energy along the reaction coordinate; photo-chemical process deals directly with the quantum or discrete nature of the light-matter interaction.

Criteria for all photochemical reactions

1. Molecule must absorb light
2. Radiation energy must match energy difference of ground and excited state

Typical absorption range of some important classes of organic compounds

- | | |
|--|--------------|
| 1. Simple alkene | 190 - 200 nm |
| 2. Acyclic diene | 220 - 250 nm |
| 3. Cyclic diene | 250 - 270 nm |
| 4. Styrene | 270 - 300 nm |
| 5. Saturated ketones | 270 - 280 nm |
| 6. α,β -Unsaturated ketones | 310 - 330 nm |
| 7. Aromatic ketones/aldehydes | 280 - 300 nm |
| 8. Aromatic compounds | 250 - 280 nm |

Advantages of Photochemical reactions

1. The excited states are rich in energy and therefore endothermic reactions in ground state may also easily occur.
2. In the excited state antibonding orbitals are occupied. This may allow reactions which are not possible for electronic reasons in the ground state.
3. Photochemical reaction can include singlet and triplet states. Thermal reactions usually only show singlet states.
4. In photochemical reaction intermediates may be formed which are not accessible at thermal conditions.

Key points in Photochemical reactions

1. Purity of starting materials

Photochemical reactions are very sensitive and presence of coloured or light absorbing impurities in starting material or formed during reaction interfere in the photochemical process.

2. UV spectra of Reactants

UV/Vis spectrum of the “photoactive” compound is recorded prior to a photochemical reaction. The “photoactive” compound should be electronically excited and undergo or

initiate a reaction from its excited singlet or triplet state. UV spectra from the reaction mixture may help to identify ground state interactions of compounds or CT complexes, and the best reaction conditions.

3. Criteria for Solvent

- Solvent must dissolve reactants
- Solvent should be transparent at the irradiation wavelength
- Solvent must be free of impurities
- If a reactive intermediate needs to be stabilized by the solvent, this has to be tried out until a solvent is found which matches all criteria.

4. Direct or sensitized photolysis

The absorption characteristics do not tell anything about the behavior of a molecule in the excited state. It may rapidly deactivate via fluorescence or radiationless, it may undergo intersystem crossing into the triplet manifold.

Sensitizers and quenchers can help to investigate a photochemical reaction:

- Pure singlet reactivity: No reaction in the presence of appropriate triplet sensitizers.
- Pure triplet reactivity: enhanced product formation in the presence of appropriate sensitizers; no reaction in the presence of triplet quenchers.
- Triplet as well as singlet reactivity: combination of methods a) and b) gives a product pattern corresponding to the specifically activated states.

5. Reaction control: Spectroscopy and chromatography

In the course of the reaction more and more product is formed which competes with the starting material for light. UV spectroscopy and Chromatographic methods, such as TLC, GC or HPLC should be used to gain information about the course of the reaction.

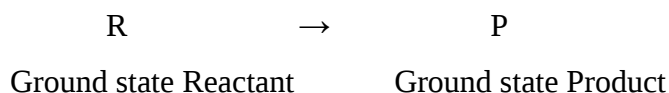
6. Side reactions

Side reactions of photochemical reactions can in some cases become the major reaction pathway. Free radicals produced during the reaction may cause side reactions. Radical scavengers, such as phenols, are added to trap them. Examples are photosensitizers, which are used in catalytic or stoichiometric amounts to mediate the wanted photochemical process, but they may also act as photoinitiator of a radical chain reaction.

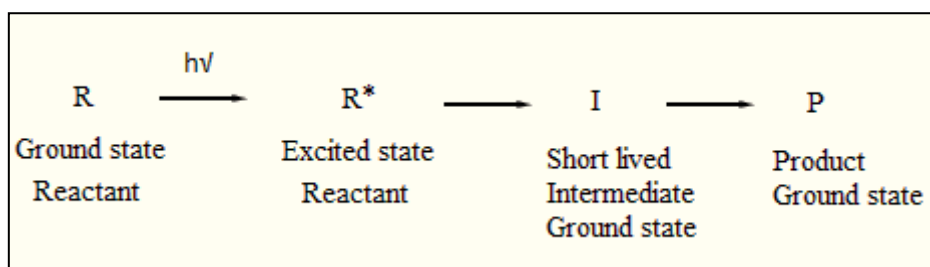
2. General Principles

Simple Photochemical reaction

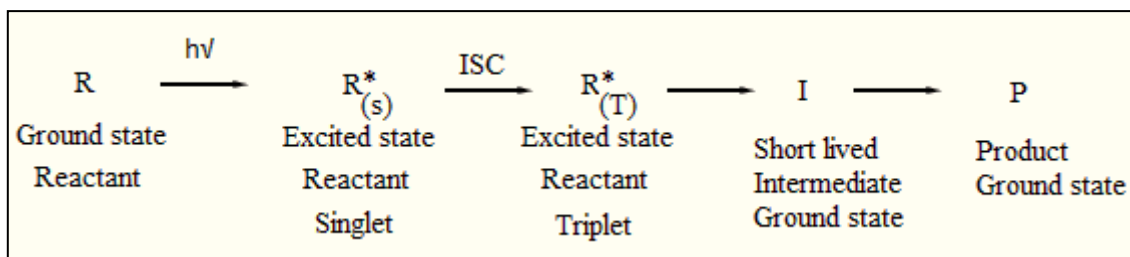
when a light interacts with your ground state reactant R, it undergoes different types of transformation and gives the product P. The simplest representation of organic photochemistry can be written as



When R, ground state reactant, is shined with light $h\nu$, it undergoes different transformation to give the ground state product P.



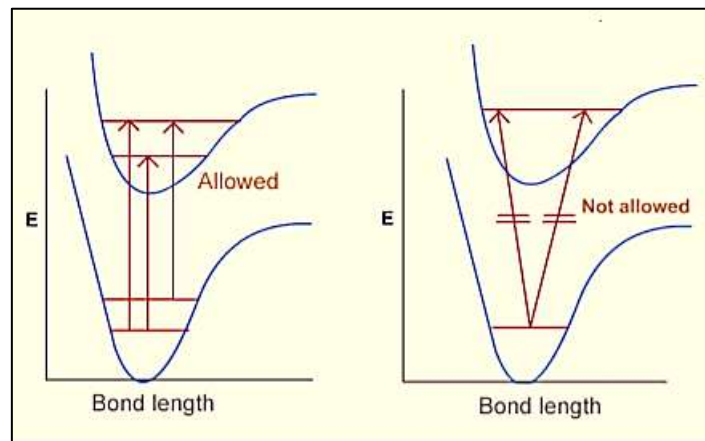
In organic photochemistry the reagent is $h\nu$. When light strikes the ground state reactant R, it transforms to an excited state energy R*. This R* does an electron transfer, or an atom transfer, or break the bond, or make a bond to give an intermediate (I). The intermediate (I) is a ground state species, but it is a very short lived species, so it is immediately transformed to give the product P. The short lived intermediate can be carbide, nitride, diradicals, etc. The ground state product can be isolated.



3. Franck – Condon Principle

- An electronic transition is so fast compared to the nuclear motion that during an electronic transition the vibrating molecule does not change its internuclear distance.
- All transitions are assumed to be drawn by vertical lines and not slanted lines as in the figure below.

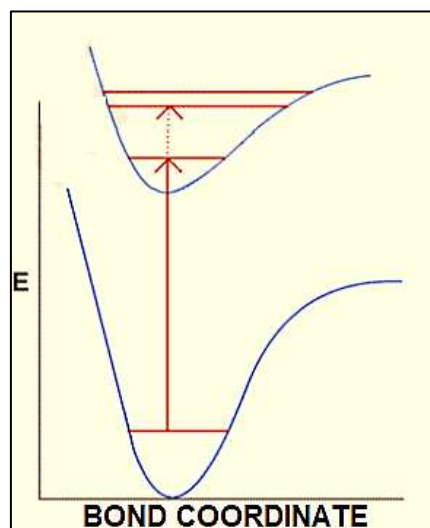
- The electronic potential energy of a diatomic molecule with bond length as the nuclear coordinate is depicted below. The molecule is assumed to be stable both in the ground and excited electronic state.
- The left hand figure illustrates Franck-Condon principle.
- The transitions are vertical from one state to another state
- The right hand figure shows that the bond length of the diatomic molecule in the excited state is not the same as that of the ground state.
- Such transitions are not possible (not allowed) The general reason for this is that the inter-nuclear distance changes due to vibration or rotation of the molecule (centrifugal distortion) which are very slow compared to the time taken for an electronic transition.



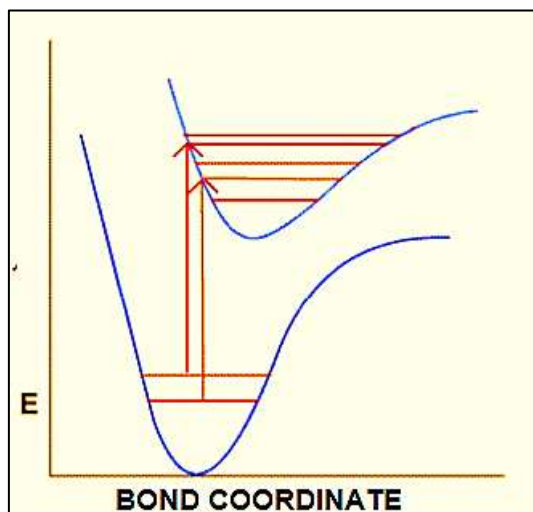
Types of electronic transitions for a diatomic molecule

Several possible cases arise for Franck-Condon transitions which do or do not lead to any dissociation of diatomic molecule.

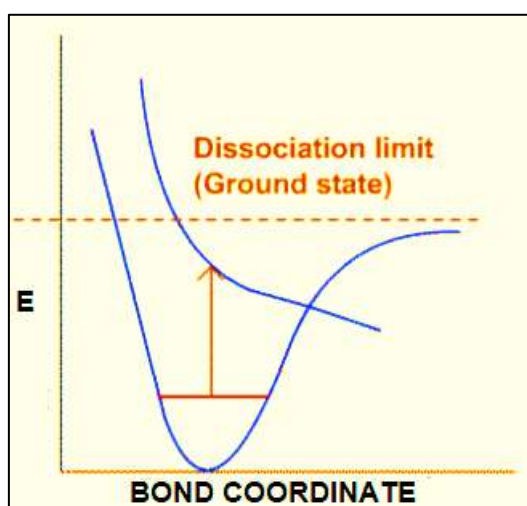
- The equilibrium bond distance is approximately the same in both the ground as well as the first excited electronic state. (The potential energy minima are the same for both curves)



ii. The minimum in the energy of the first excited state corresponds to a slightly more stretched bond, than that of the ground state.



iii. The potential energy curves for the ground and excited electronic state cross each other below the dissociation region of the ground state. (Such a phenomenon is called pre-dissociation)



4. Electronic Transitions

- Three types of electronic transitions are common:
 1. $d - d$ (bonding d orbital to bonding d orbital) transitions
 2. $\pi - \pi^*$ (bonding π orbital to antibonding π^* orbital) transitions
 3. $n - \pi^*$ (non-bonding orbital to antibonding π^* orbital) transitions
- $d - d$ transitions are important in coordination chemistry (transition metal complexes).

- The d-orbitals of transition metal complexes are not five-fold degenerate, but split into at least two different energy levels. They are often not completely filled, leading to the possibility of electrons in the lower d-orbital being excited by visible light to higher d-orbitals. This explains why many transition metal complexes are highly colored.
- $\pi - \pi^*$ and $n - \pi^*$ are usually transitions of an electron from a bonding (π) or a non-bonding (n) orbital to an antibonding orbital (π^*). eg. absorption in C=O bonds is a transition from non-bonding oxygen orbital to an antibonding orbital of C=O molecule.

5. Jablonski Diagram

The absorption of the UV/VIS radiation by the electrons in the molecule occupies high energy molecular orbitals. When a molecule absorb light the electrons gets excited to higher energy and the electrons can return back to the ground state in different ways such as releasing the excess energy through collisions or by emitting photon. Various electronic and molecular processes that occurs following excitation are usually represented on a Jablonski diagram. The S_0 , S_1 , S_2 represents singlet electronic states while T_1 represents the first triplet electronic state. The various processes are

i. Absorbance

S_0 state is the state of lowest energy and highly populated state. Absorption of a photon results in excitation to S_1 state. This process usually occurs in 10^{-15} sec. this transition is indicated by a straight arrow pointing up.

ii. Internal Conversion and Vibrational relaxation

Non-radiative electronic transition (heat is given off) from higher energy singlet states to S_0 or from T_1 to S_0 is termed as Internal conversion. Relaxation from a higher vibrational level of S_1 to lowest vibrational state is termed as Vibrational relaxation. This occurs so fast (10^{-14} sec).

iii. Fluorescence

Internal conversion is so rapid and completes before fluorescence is observed (10^{-5} to 10^{-6} sec). Fluorescence emission is returning back to S_0 from S_1 emitting a photon. It is indicated as straight arrow pointing down.

iv. Intersystem crossing

The process is indicated by a horizontal curved line from S_0 to T_1 with an emission of photon. In this process the electron spin changes from an excited singlet state (S_0) to excited triplet state (T_1). It occurs at 10^{-8} to 10^{-12} sec.

v. Phosphorescence

The molecule in the triplet state T_1 can return back to S_0 state emitting a photon. It takes place in 10^{-2} to 10^{-3} sec. In this transition the electron spin changes from T_1 to S_0 . It is indicated by a straight-line arrow pointing down.

Characteristics of Fluorescence

i. Stoke's shift

Fluorescence emission spectrum is always towards the longer wavelength with respect to the absorption spectrum. This shift is known as Stoke's shift.

ii. Kasha's rule

A fluorescence emission is completely independent of the excited state that is always takes place from singlet excited state (S_1).

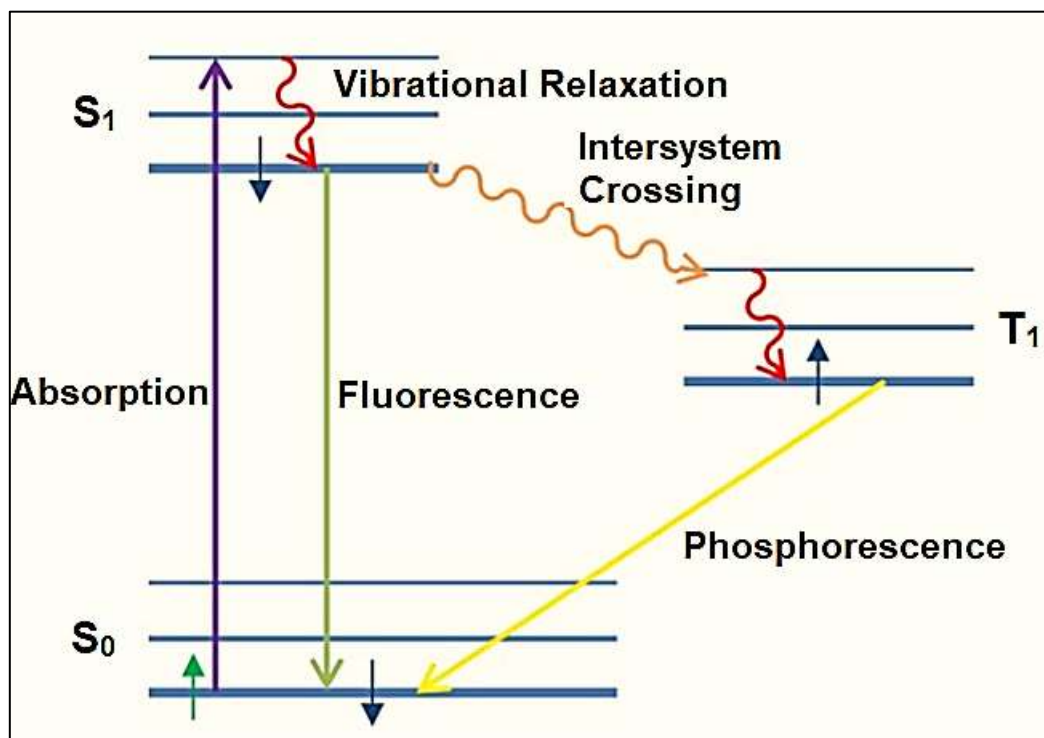


Fig. 2: Jablonski Diagram

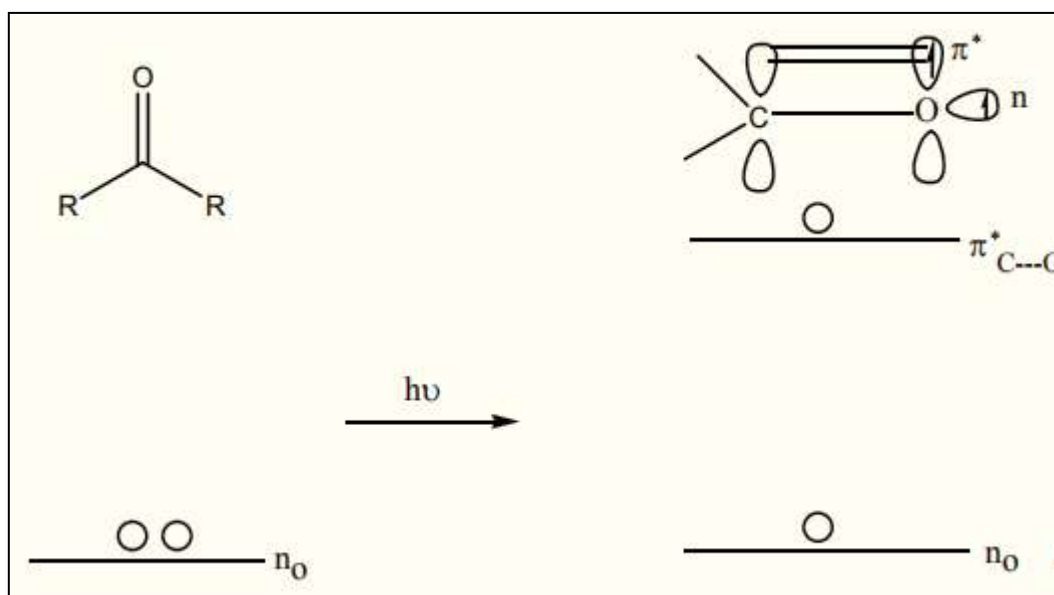
6. Photochemistry of Carbonyl Compounds

The absorption properties of ketones and aldehydes are convenient for irradiation around 300 nm ($n - \pi^* = 330 - 280$ nm). Triplet-singlet energy gap is small (20-70 kJ/mol); intersystem crossing rates are high. Lifetime of first excited singlet state is in the nanosecond region for aliphatic aldehydes and ketones; in the subnanosecond region for aromatic aldehydes and ketones. Singlet photochemistry can be detected with aliphatic aldehydes or ketones, while

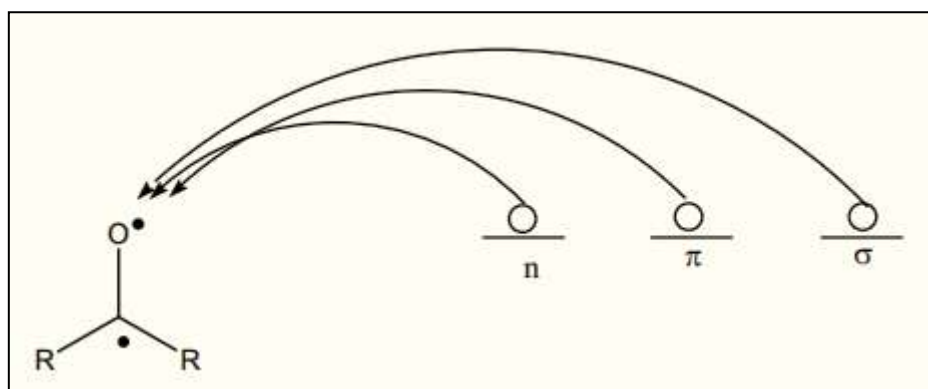
aromatic substrates, such as benzophenone or acetophenone, react exclusively from their corresponding triplet states and are excellent triplet sensitizers.

Reactivity of $n - \pi^*$ Transitions

When light of wavelength > 310 nm is irradiated on carbonyl group the electrons gets excited and the π^* electrons distribute between carbon and oxygen. Since the non-bonded electrons is more towards oxygen due its electronegative nature and oxygen doesn't prefer to be radical. Thus non-bonded electrons is more reactive than π^* electrons and $n - \pi^*$ chemistry is dominated by non-bonded electron on the oxygen atom.

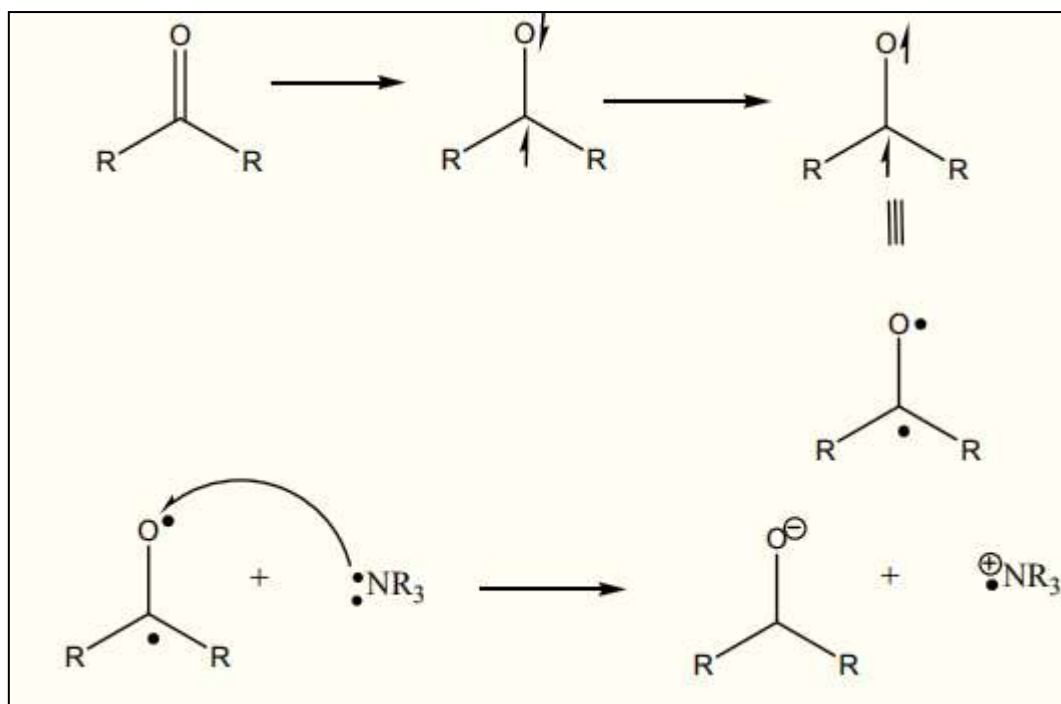


If the carbonyl group is irradiated with light it gets excited to excited singlet S_1 and does an intersystem crossing and forms excited triplet state T_1 . The radical oxygen is more reactive and tries to get electron from the environment (π , non-bonded or σ electrons).

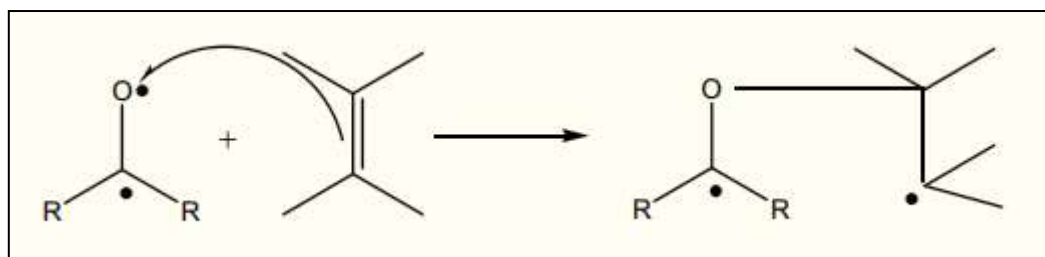


There are 5 reactions in $n - \pi^*$ chemistry they are

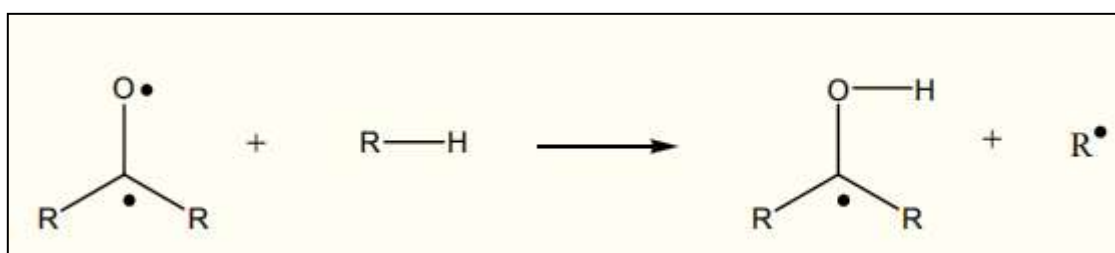
i. Electron abstraction reaction:



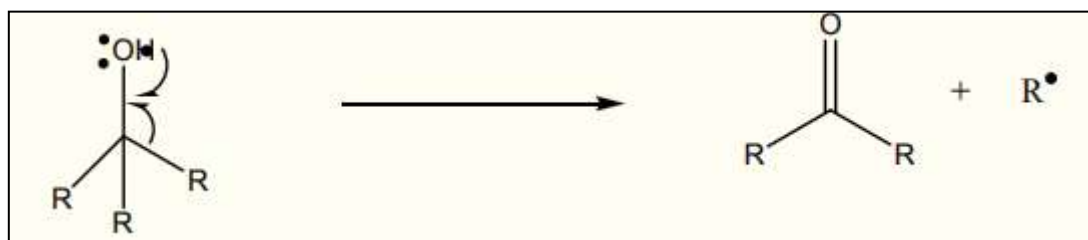
ii. Addition to π system or double bond:



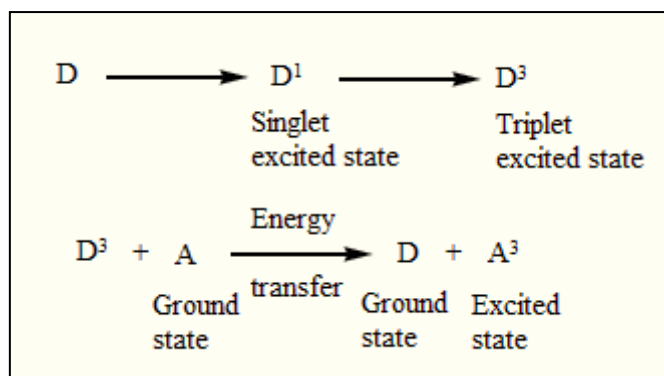
iii. Hydrogen abstraction reaction:



iv. Cleavage reaction:

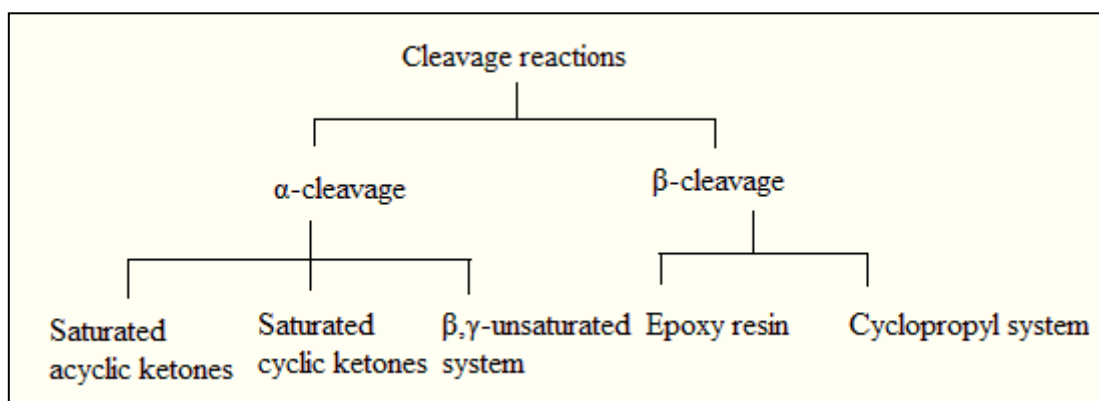


v. Energy transfer reaction:



7. α – Cleavage or Norrish Type I Reactions

Cleavage reactions are classified as follows



A. α -cleavage reactions:

When light is made to strike carbonyl group of ketones it undergoes α -cleavage followed by decarbonylation reactions which was first observed by Norrish and these α -cleavage reactions are called Norrish type I reactions. The different carbonyl compounds that undergo α – cleavage reactions are as follows

i. Saturated acyclic ketones:

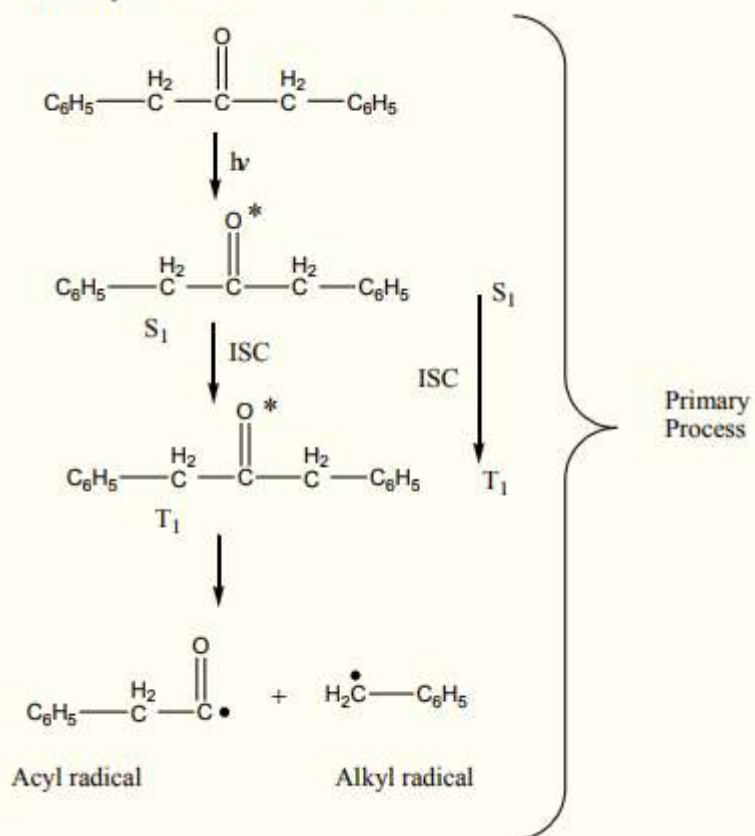
UV spectrum of these saturated acyclic ketones shows 4 bands at 155 nm, 170 nm, 195 nm, 280 nm. Among these 4 wavelengths 280 nm wavelength is used for $n - \pi^*$ transaction. Thus > 280 nm light is used.

When light is shined on saturated acyclic ketones, initially primary process occurs which is followed by secondary process through radical chemistry. The second step chevage is more probable based on stability of radical formed.

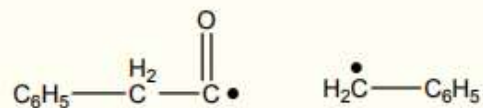
The stability of radical is as follows

Tertiary radical $>$ secondary radical $>$ primary radical

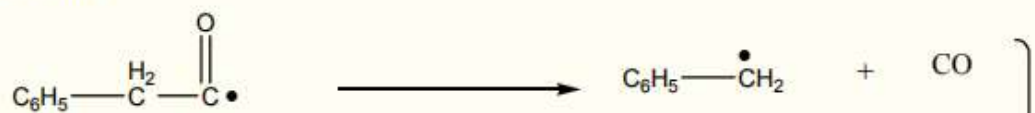
Primary Process of α - Cleavage



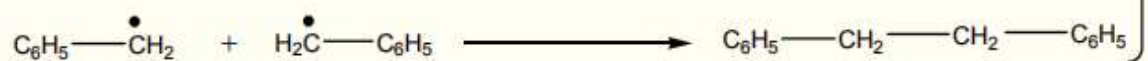
Secondary Process



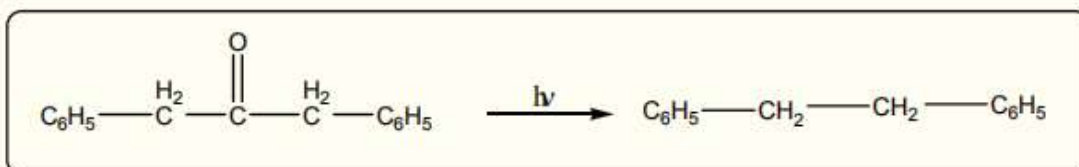
Decarbonylation



Radical Recombination



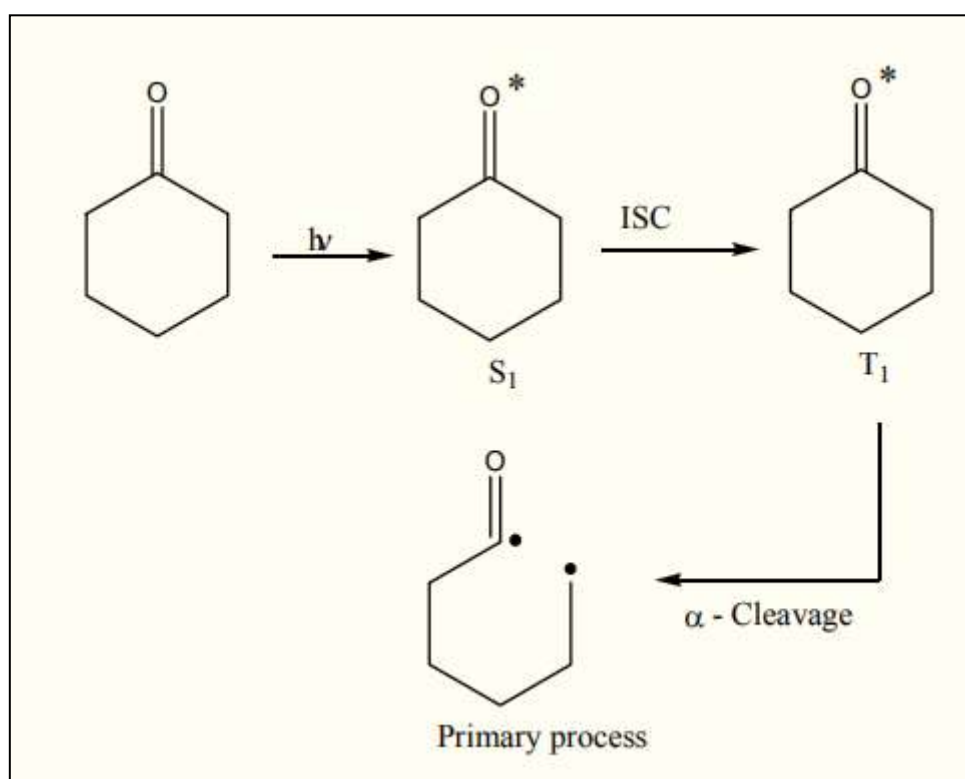
Secondary Process

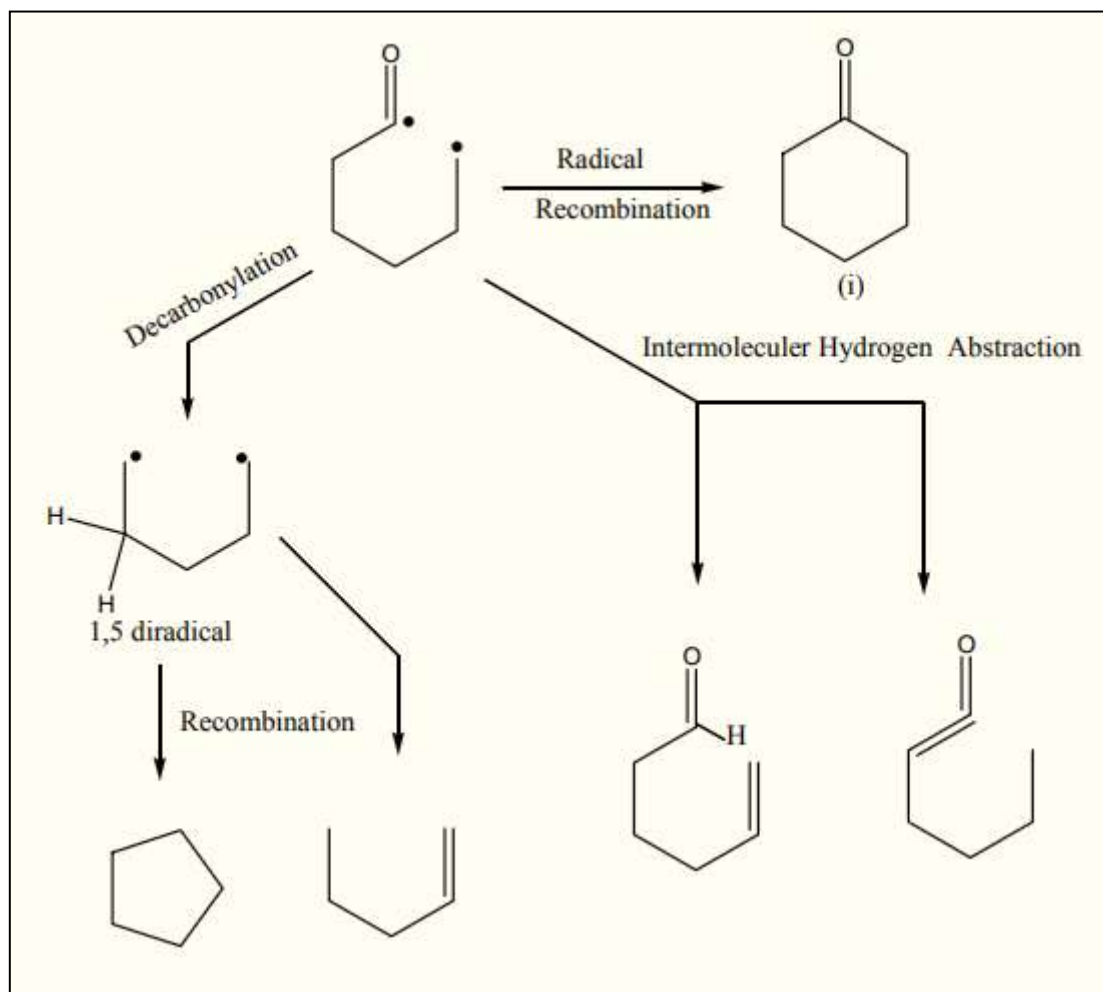


ii. Saturated cyclic ketones:

a. Six membered cyclic ketone

when light is shined on six membered saturated cyclic ketones, initially the primary process of α -cleavage occurs which is followed by secondary process. The secondary process depends on the presence or absence of solvent. In vapour phase reaction, the secondary process occurs by decarbonylation and proceed by Norrish type I reaction. In liquid phase or solvent secondary process occurs through intramolecular hydrogen abstraction reaction.



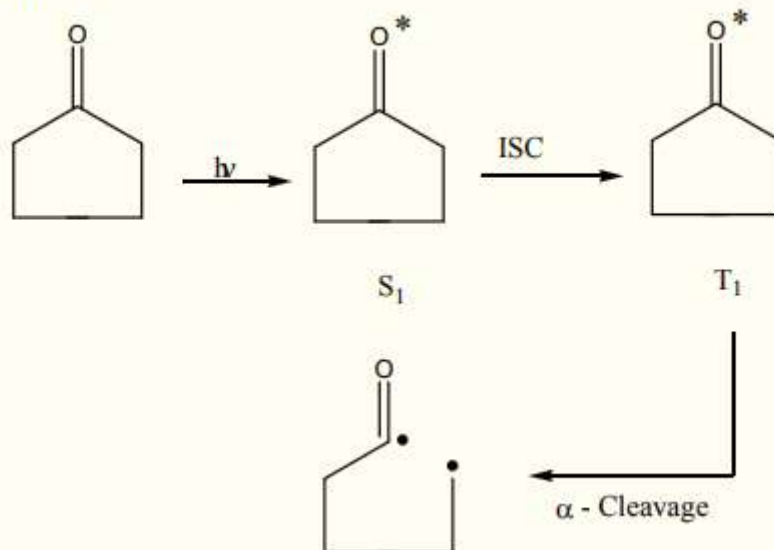


b. Five membered cyclic ketone:

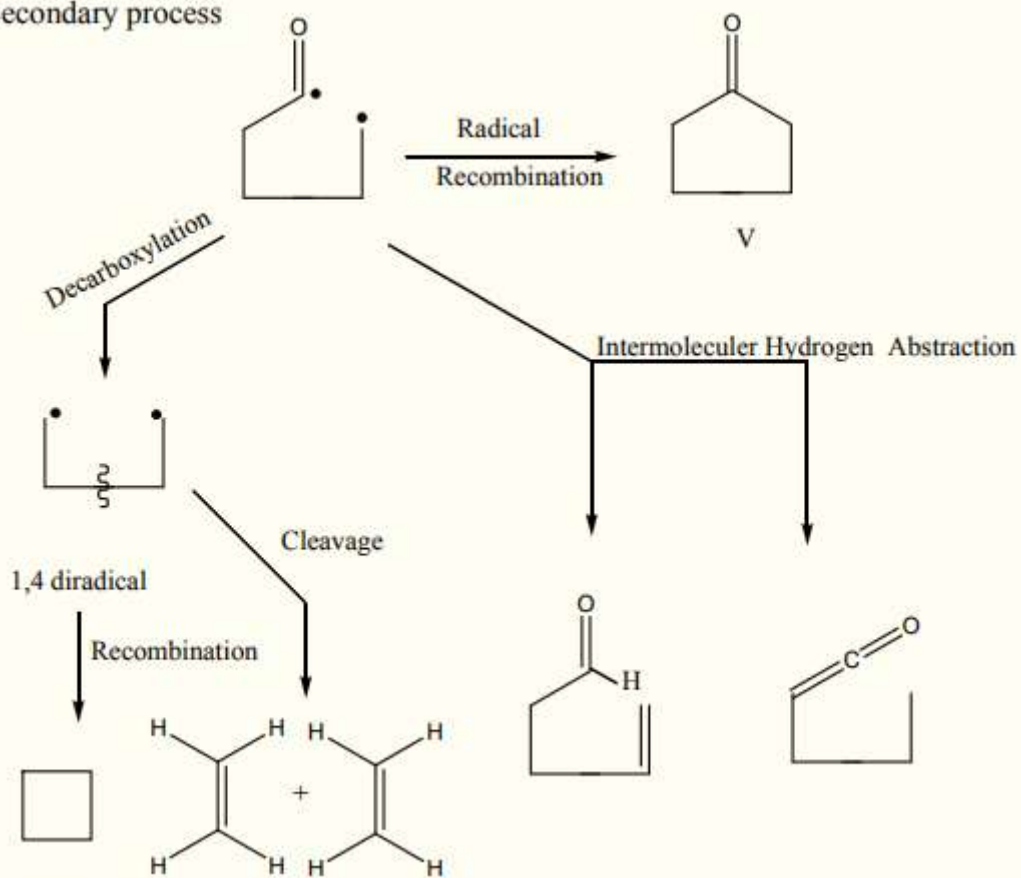
when light is shined on five membered saturated cyclic ketones, initially the primary process of α -cleavage occurs which is followed by secondary process. The secondary process depends on the presence or absence of solvent. In vapour phase reaction, the secondary process occurs by decarbonylation and proceed by Norrish type I reaction. In liquid phase or solvent secondary process occurs through intramolecular hydrogen abstraction reaction similar to six membered saturated cyclic ketones.

The 1, 4 – diradical formed may also undergo β -cleavage to form the products.

Primary process

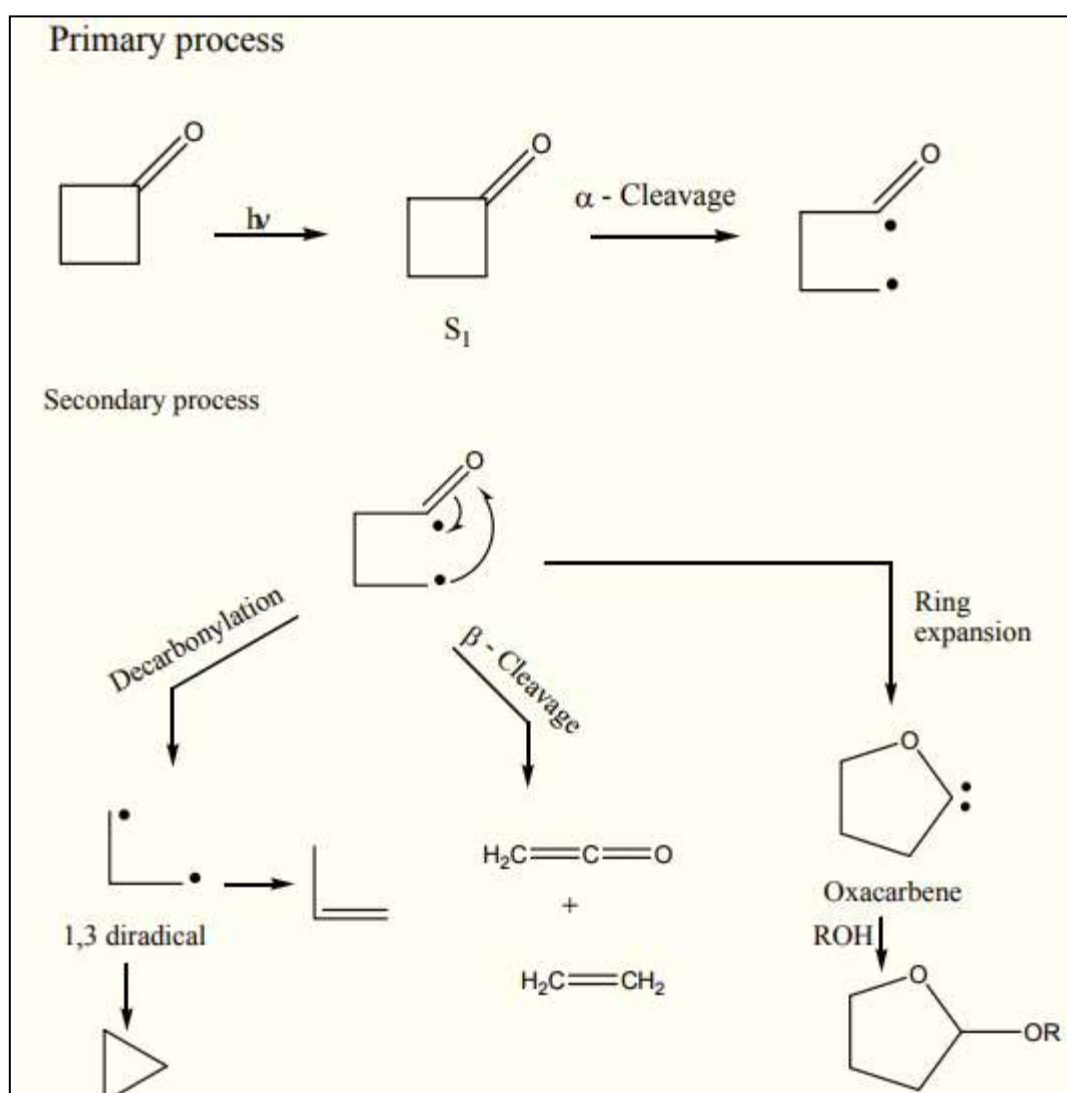


Secondary process



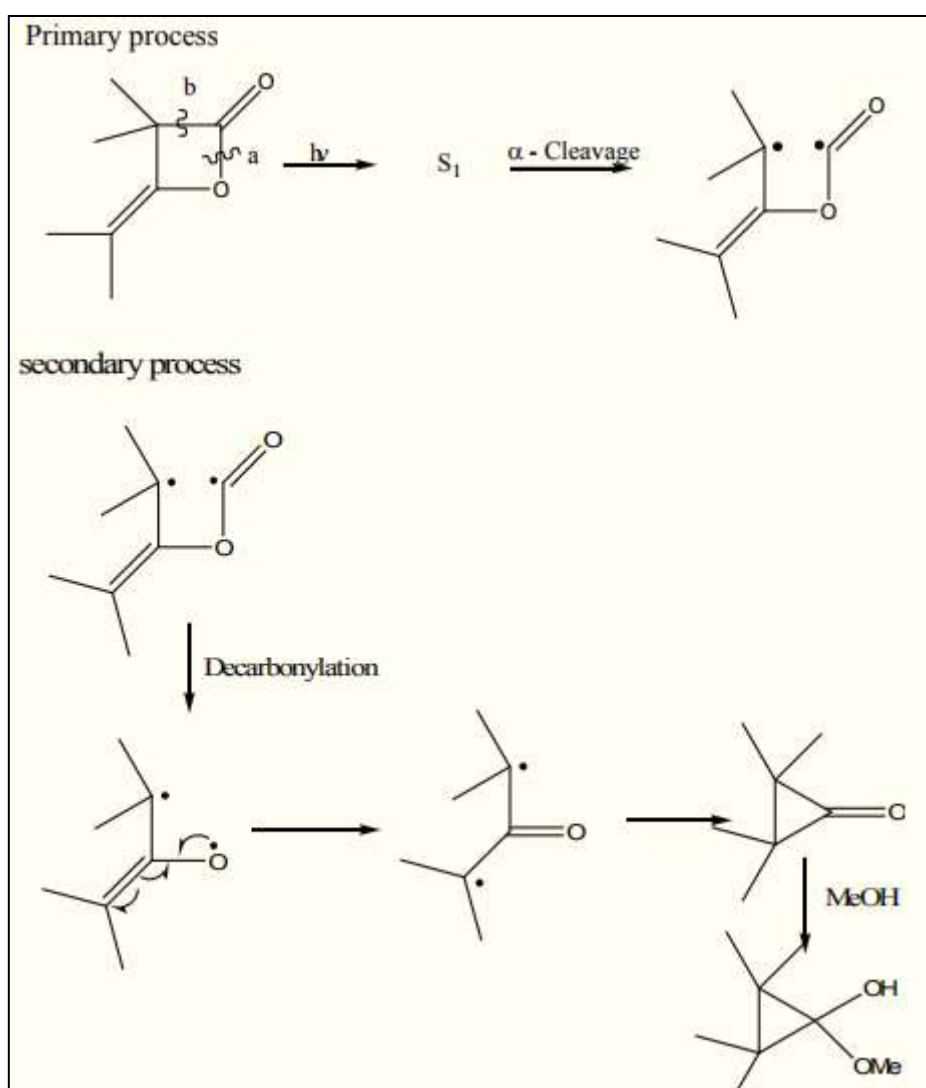
c. Four membered cyclic ketone:

when light is shined on four membered saturated cyclic ketones, initially the primary process from singlet state and doesnot do ISC to form triplet state followed by α - cleavage. The α -cleavage result in the formation of 1,4- diradical which is followed by secondary process. The secondary process occurs either by decarbonylation , ring expansion and β - cleavage and forms the product.



iii. β,γ -Unsaturated system:

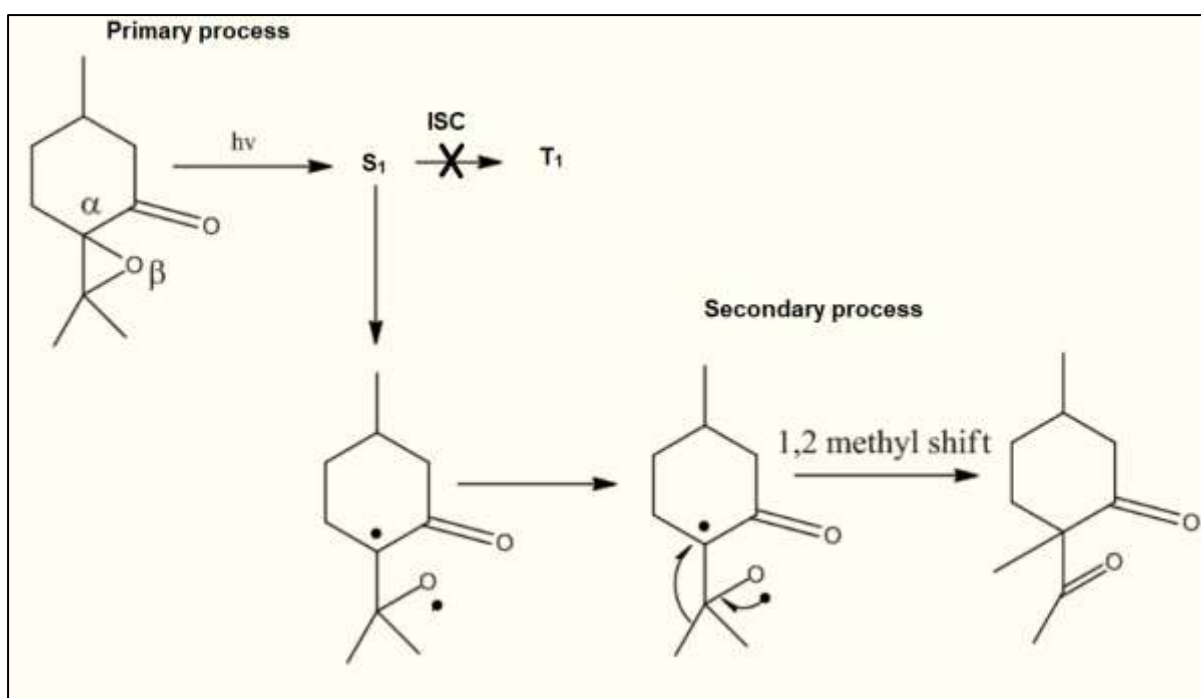
when light is shined on β,γ -unsaturated ketones, initially the primary process of α -cleavage occurs which is followed by secondary process. The secondary process occurs by decarbonylation and proceed by Norrish type I reaction. Radical recombination is not possible. Similarly ring expansion results in oxocarbene which is very rare reaction and doesnot takes place.



B. β – cleavage reactions

Carbonyl compound in which $C_\alpha - C_\beta$ bond is weak and undergo β -cleavage because of the strain in cyclic structure ($\alpha - \beta$ carbon bond is weak). The reaction can proceed from both S_1 or T_1 . when carbonyl is excited it has excited energy that is transferred to $C_\alpha - C_\beta$ Carbon – Carbon bond and it gets cleaved.

In epoxy ketones, ISC never happens and photochemistry occurs from S_1 whereas in cyclopropane ketones, photo chemistry occurs from T_1 . The 1, 3 – diradical cannot recombine to give cyclized product and a 1, 2 – methyl shift or 1, 2 – hydrogen shift occurs which results in products.

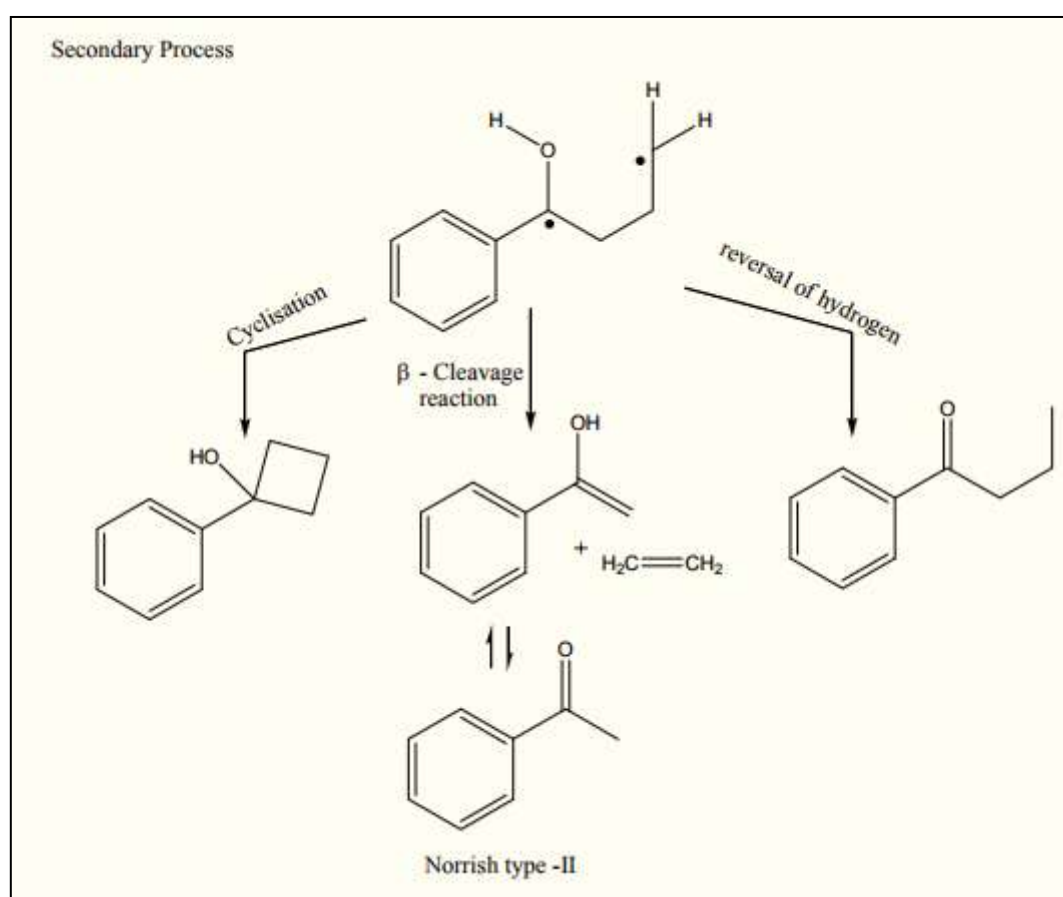
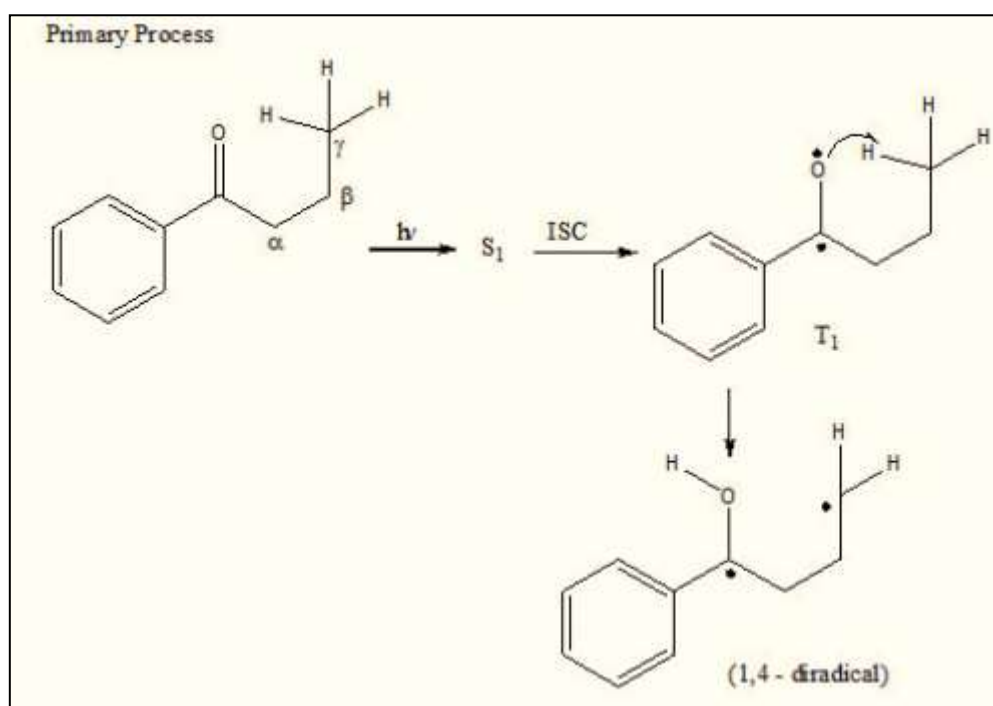


8. γ –Hydrogen Transfer or Norrish Type II Reactions

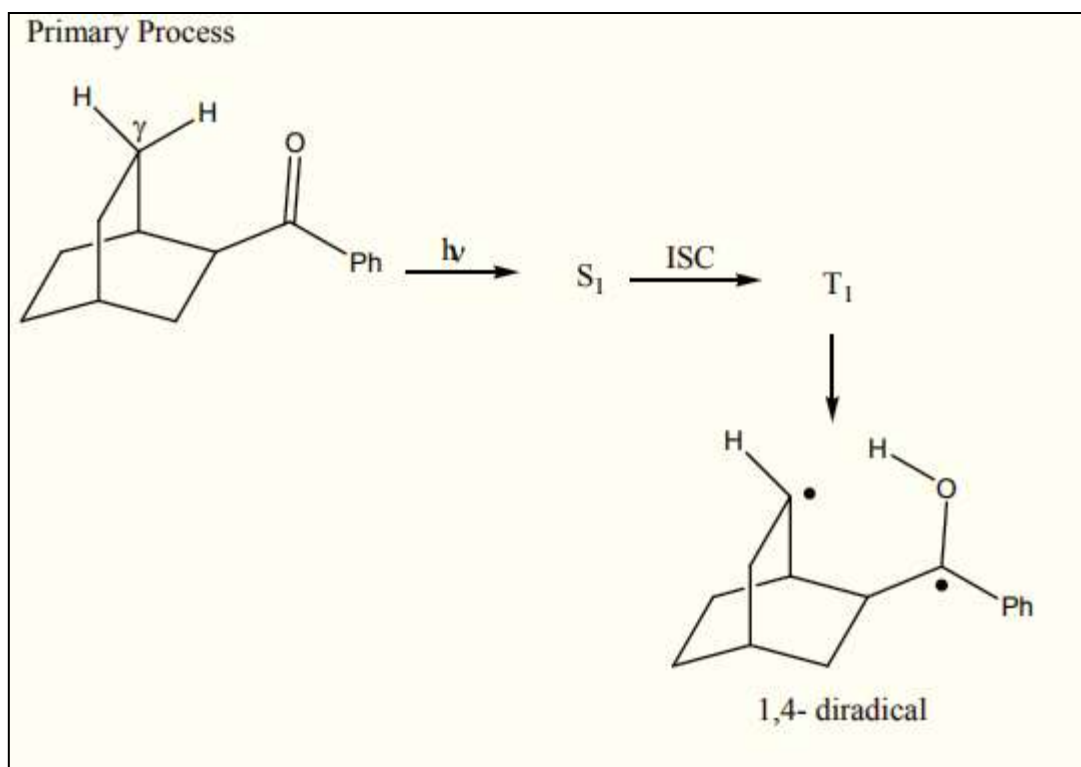
Intramolecular hydrogen abstraction takes place when γ -carbon has hydrogen. In Norrish type II reaction, a ketone undergoes excitation and forms 1,4-diradical by abstracting γ -hydrogen by forming a six membered transition state which is followed by β -cleavage.

In Case of 1,4 – diradical both cyclisation and Norrish type II reactions can predominate. This depends on the nature of the substituent that is attached and the nature of product that is formed (strained product).

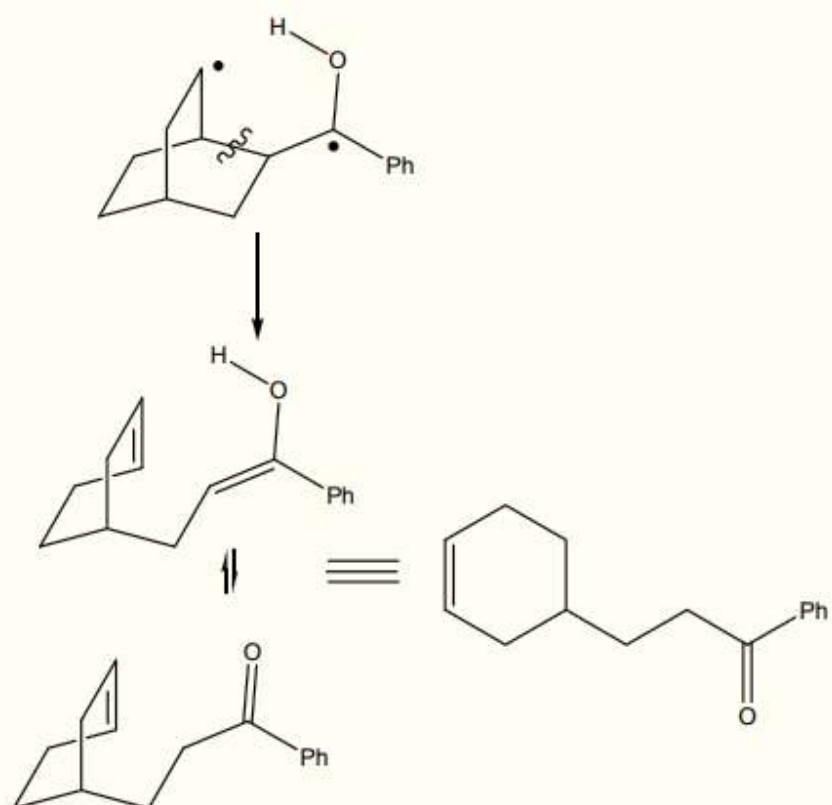
Fig. 1:



Eg. 2: Aromatic Ketone



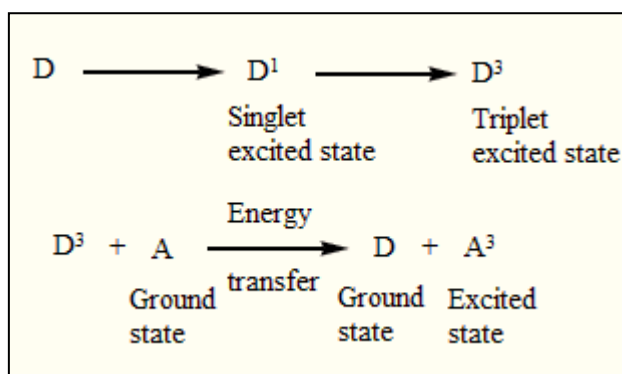
Secondary Process



9. Energy Transfer Reactions

Energy transfer reaction is a photo physical process and is not a photochemical. Let us consider a donor molecule and shined light it goes to its singlet and undergoes an intersystem crossing to triplet state. This excited triplet donor collides with ground state acceptor and energy is transferred to acceptor.

Basically spin exchange happens between donor and acceptor and donor becomes singlet and comes to ground state and acceptor becomes the excited triplet state. This process is a type of spin exchange process and it happens because of electronically excited state. Finally, the products are formed from the excited triplet acceptor.



Criteria for Donor and Acceptor

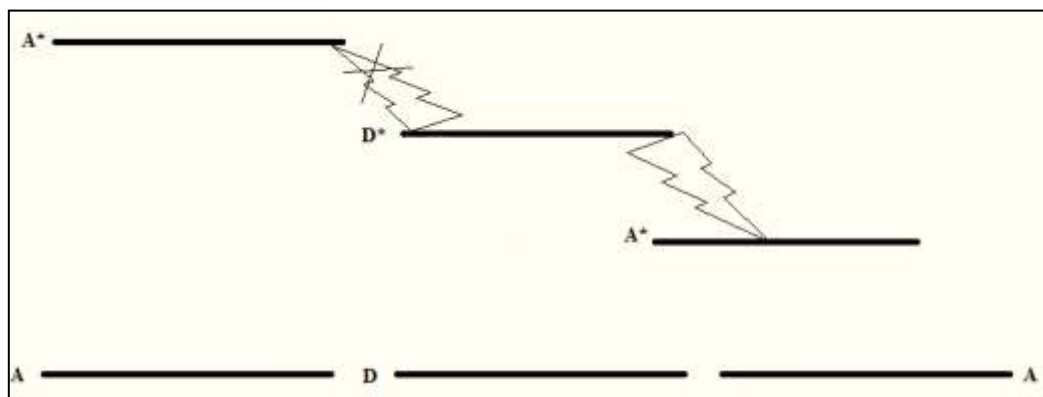
The criteria for a donor to transfer its energy to acceptor are

1. Rate of collision must be greater than rate of diffusion for energy transfer reactions to occur. Thus the rate constant of energy transfer (K_{ET}) is greater than rate constant of diffusion (K_D).

$$K_{\text{Electron Transfer}} > K_{\text{Diffusion}}$$

$$K_{ET} \sim 10^9 \text{ to } 10^{10} \text{ mol/sec}$$

2. The energy of donor should be greater than energy of acceptor.

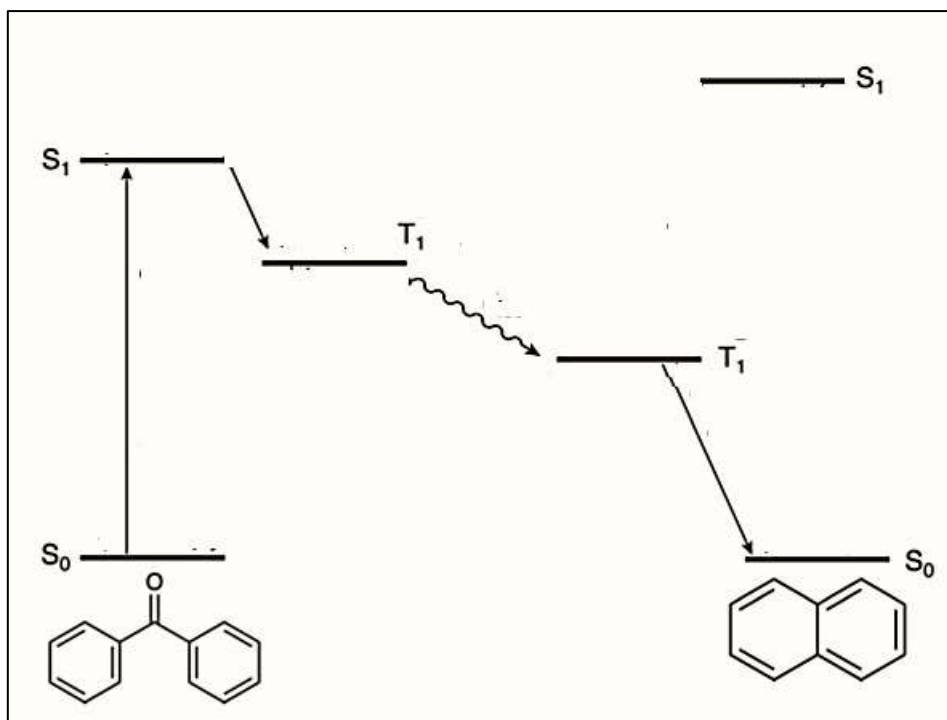


Energy of Donor > Energy of Acceptor

10. Sensitizer and Quencher

A. Quenching process

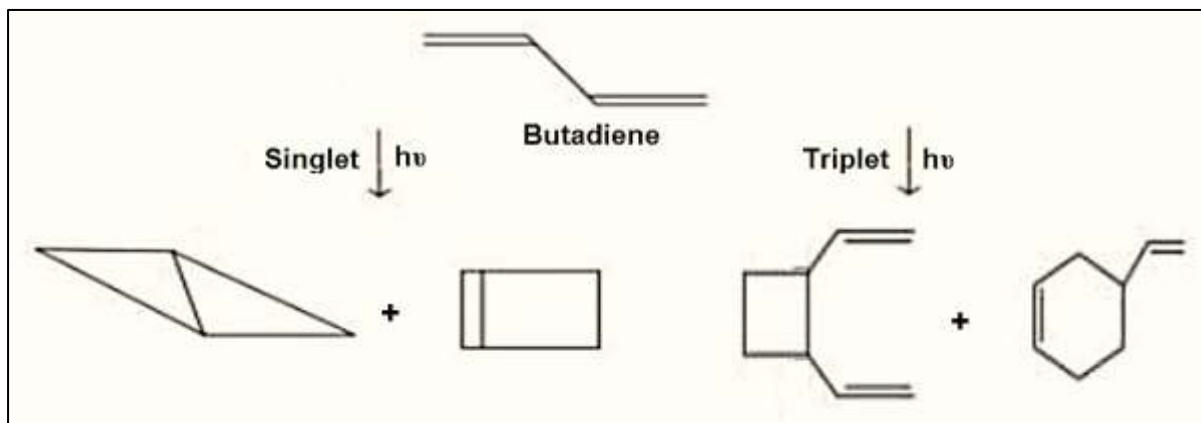
If the 2 conditions of donor and acceptor is satisfied the energy is transferred from donor molecule to acceptor molecule. For example, when benzophenone or any ketone is photolyzed it forms product from either from the singlet excited state or from the triplet excited state or from both singlet and triplet. The singlet excited energy of benzophenone is 74 Kcal/mol and triplet is 69 Kcal/mol. when naphthalene is added to benzophenone, the benzophenone converts its S_1 to T_1 by ISC. The energy of T_1 of naphthalene is still less thus the energy is transferred to T_1 of naphthalene then benzophenone doesn't form product. The excited singlet state of naphthalene is 90 Kcal/mol and 60 Kcal/mol for triplet excited state. Because the T_1 of naphthalene is the lowest excited state, most of the photochemistry happens from the lowest excited state. This is called as quenching process. Here naphthalene plays a quencher and benzophenone – naphthalene system is a donor – acceptor system.



B. Sensitization process

In certain systems where the energy difference between S_1 and T_1 is high and the reaction proceeds from S_1 . If we require the products from triplet which 1, 3 – butadiene does not normally produce (since it doesn't convert to T_1 triplet state). Thus, sensitizer is added to obtain product from T_1 state. Thus, the singlet products are bypassed and photochemistry takes place only from triplet of acceptor. When benzophenone is added as sensitizer, it absorbs light and converts from S_1 to T_1 and then transfers its energy from its T_1 to butadiene T_1 state and the

products are formed from the triplet state of butadiene. Here benzophenone is donor and acts as sensitizer and butadiene is acceptor. The sensitizer should not form the products, it should transfer its energy to the acceptor and the acceptor should form the products. This type of reactions are known as sensitization process.



QUESTIONS

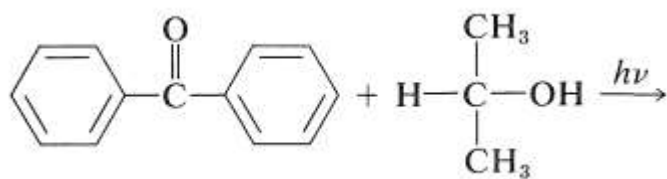
PART-A

1. Define Kasha's rule, Stoke's shift, photochemical inefficient steps, product inefficient steps, Quantum yield.
2. Write short notes on Quenching process.
3. Write short notes on Sensitization reaction.
4. What is singlet and triplet state? Explain with suitable example.
5. Explain internal conversion and Inter-system crossing.
6. Explain fluorescence and phosphorescence.
7. Explain the energy transfer reactions and discuss its applications with suitable examples.
8. Discuss the mechanism of electron transfer reactions with suitable examples.
9. With a suitable example explain the β -cleavage reactions.

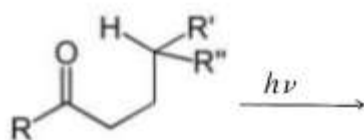
PART-B

1. Explain the Jablonski diagram and discuss various process involved.
2. Explain Franck-Condon principle and discuss several possible transitions.
3. Explain the Norrish type – II reactions and discuss the factors influencing it.
4. Explain Norrish type – I reactions with a suitable example.
5. Predict the products

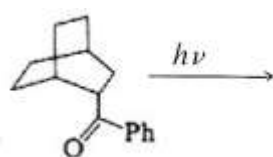
i.



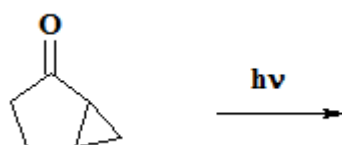
ii.



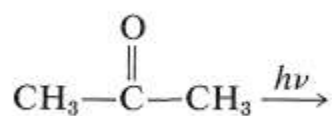
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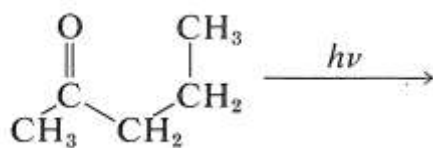
iv.



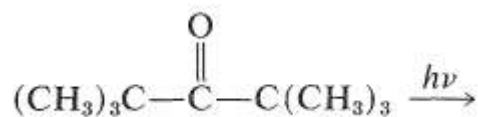
6. With the mechanistic approach predict whether the compound undergoes Norrish type I or Norrish type II



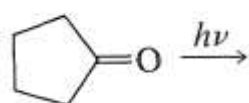
a.



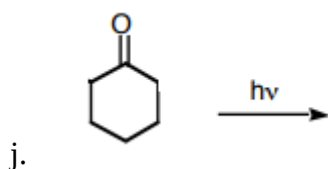
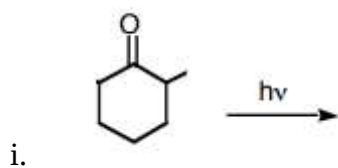
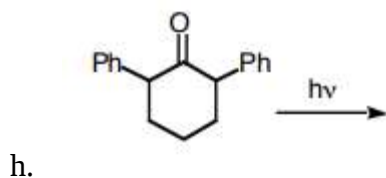
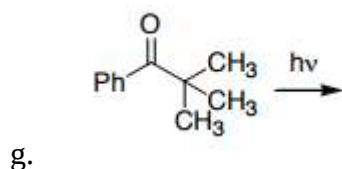
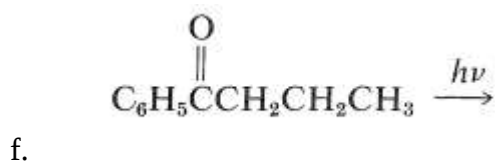
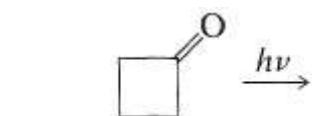
b.



c.



d.



References

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2. K. K. Rohatgi and K. K. Mukherjee; Fundamentals of Photochemistry, 3rd ed. New Age International (P) Ltd., 2014.
3. N. J. Turro, V. Ramamurthy and J. C. Scaiano, Modern Molecular Photochemistry of Organic Molecules, 1st ed. University Science, Books, CA, 2010.
4. Ninomiya, T. Naito, Photochemical Synthesis, 1st ed. Academic Press, New York, 1989.
5. <https://nptel.ac.in/content/storage2/courses/104106083/tutorial12forweek7/lec1.pdf>
6. <https://nptel.ac.in/courses/104/105/104105038/>



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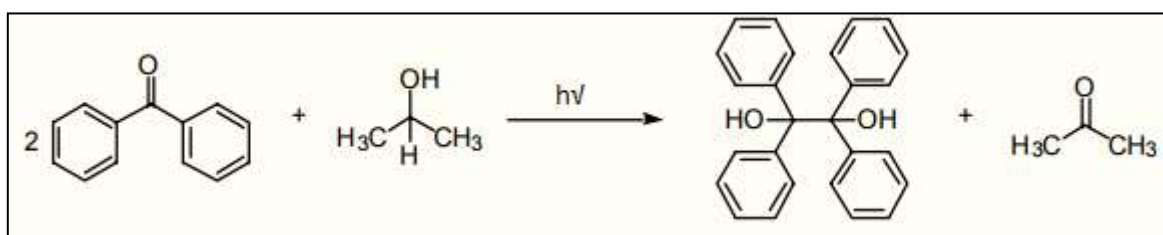
SCHOOL OF SCIENCE AND HUMANITIES

DEPARTMENT OF CHEMISTRY

UNIT-5 – Organic Photochemistry-II – SCYA5203

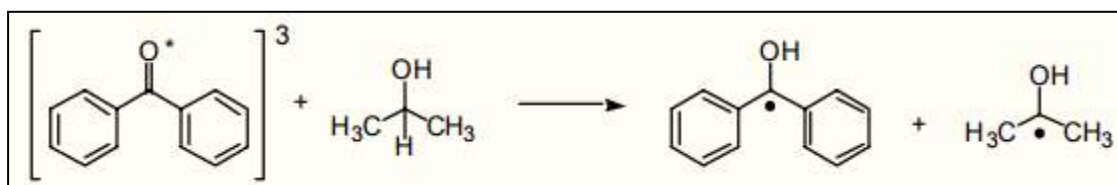
1. Photoreduction

The electron transfer of a certain functional groups can be induced by irradiation with light source. Reductions are possible when a proton source along with a sensitizer and a source of irradiation are employed. The reduction proceeds via photo-induced electron transfer (PET). Photoreduction takes place by hydrogen abstraction by photoexcited benzophenone from 2-propanol yields benzopinacol and acetone as products. When benzophenone is photoexcited it forms its $n \rightarrow \pi^*$ triplet state which does an intermolecular hydrogen abstraction reaction of photoexcited benzophenone from 2-propanol.

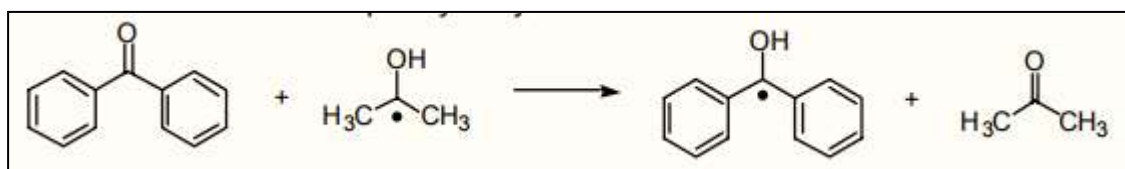


Mechanism

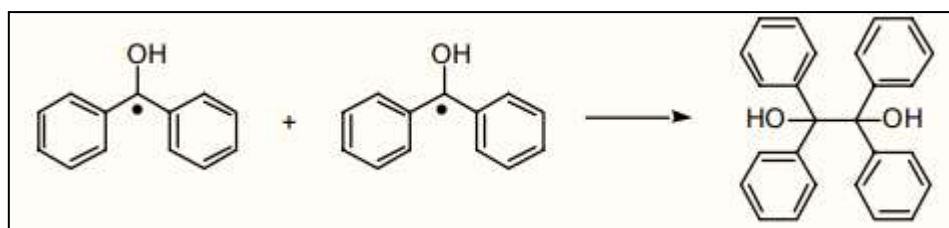
- i. The $n \rightarrow \pi^*$ triplet state of benzophenone abstracts hydrogen from isopropanol to yield the diphenyl ketyl and dimethyl ketyl radicals



- ii. The second molecule undergoes radical transfer from the dimethyl ketyl radical to benzophenone to yield acetone and another diphenyl ketyl radical

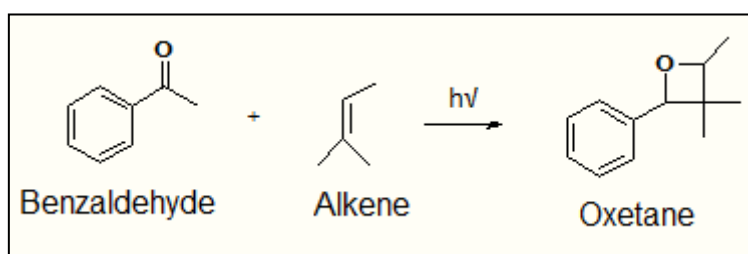


- iii. The two diphenyl ketyl radical dimerize to yield benzopinacol

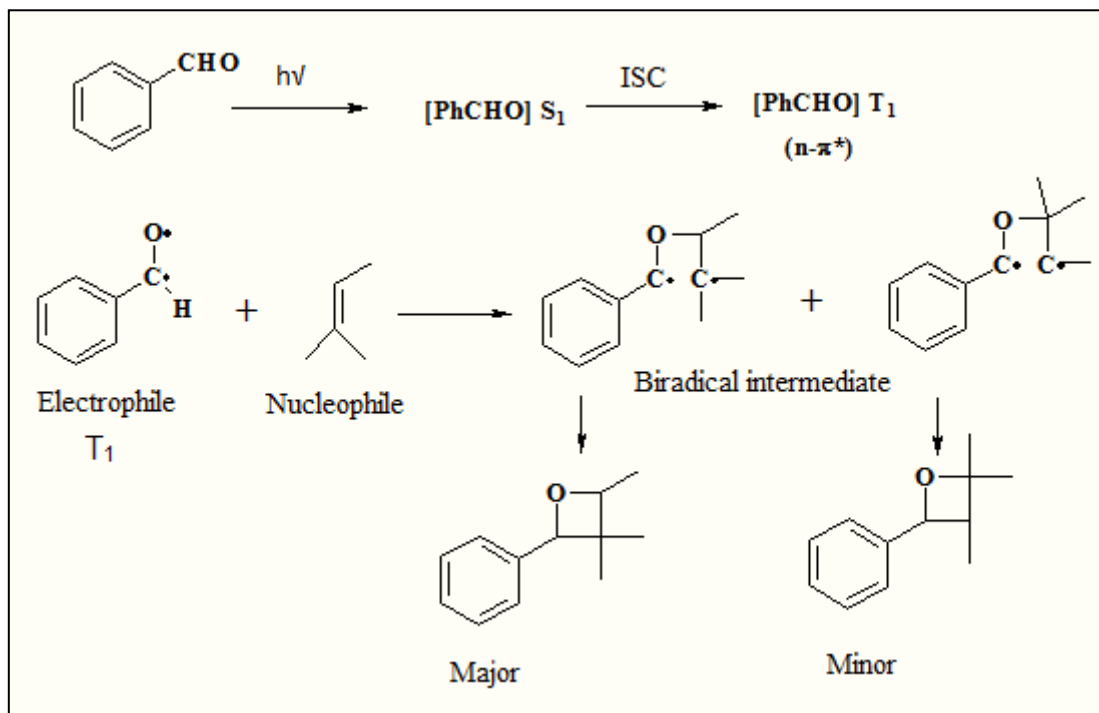


2. Paterno – Buchi Reaction

In 1909 Paterno and Chieffi first observed the photochemical [2+2] cycloaddition of an alkene and a carbonyl group (ketone or aldehyde). The mechanistic investigation was proposed by Buchi in 1954 and the reaction is famously called the Paternó Büchi reaction. Inter- and intramolecular examples are known. High diastereoselectivities can be observed in many examples.

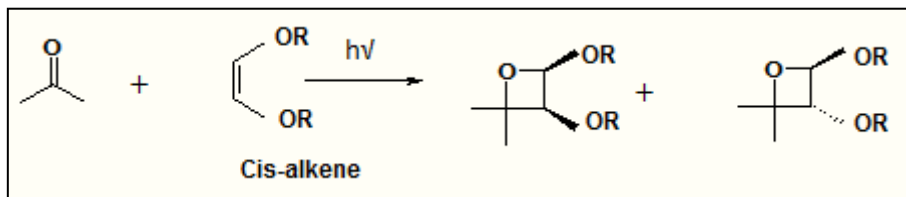


Mechanism

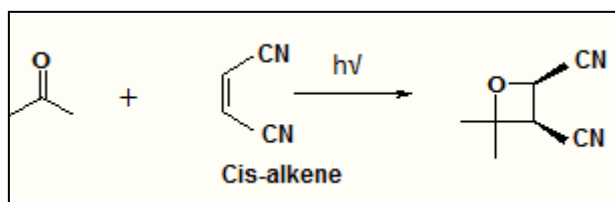


These reactions mostly depend on the alkene. There are two types of alkenes

i. Electron rich alkenes: These alkenes have electron donating substituent. These reactions are not stereospecific and not regiospecific.

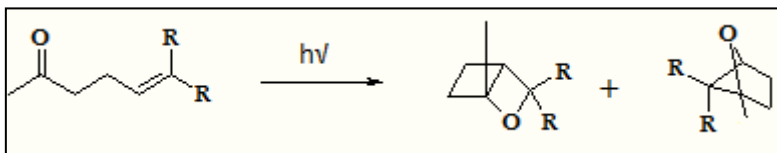


ii. Electron rich alkenes: These alkenes have electron withdrawing substituent. These reactions are stereospecific and regiospecific.



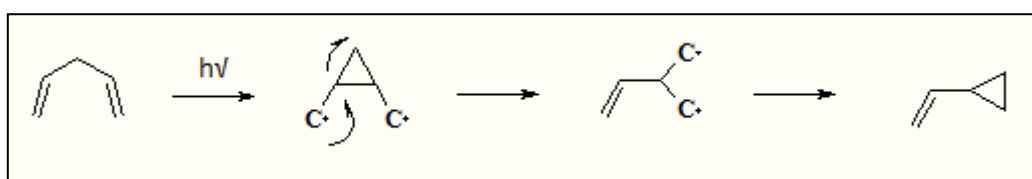
Intramolecular Paterno-Buchi reaction

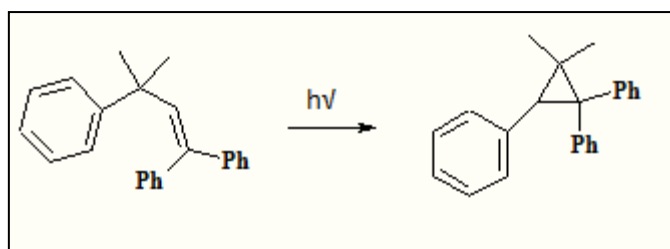
If the carbonyl group and alkene present in the same molecule it undergoes intramolecular Paterno-Buchi reaction.



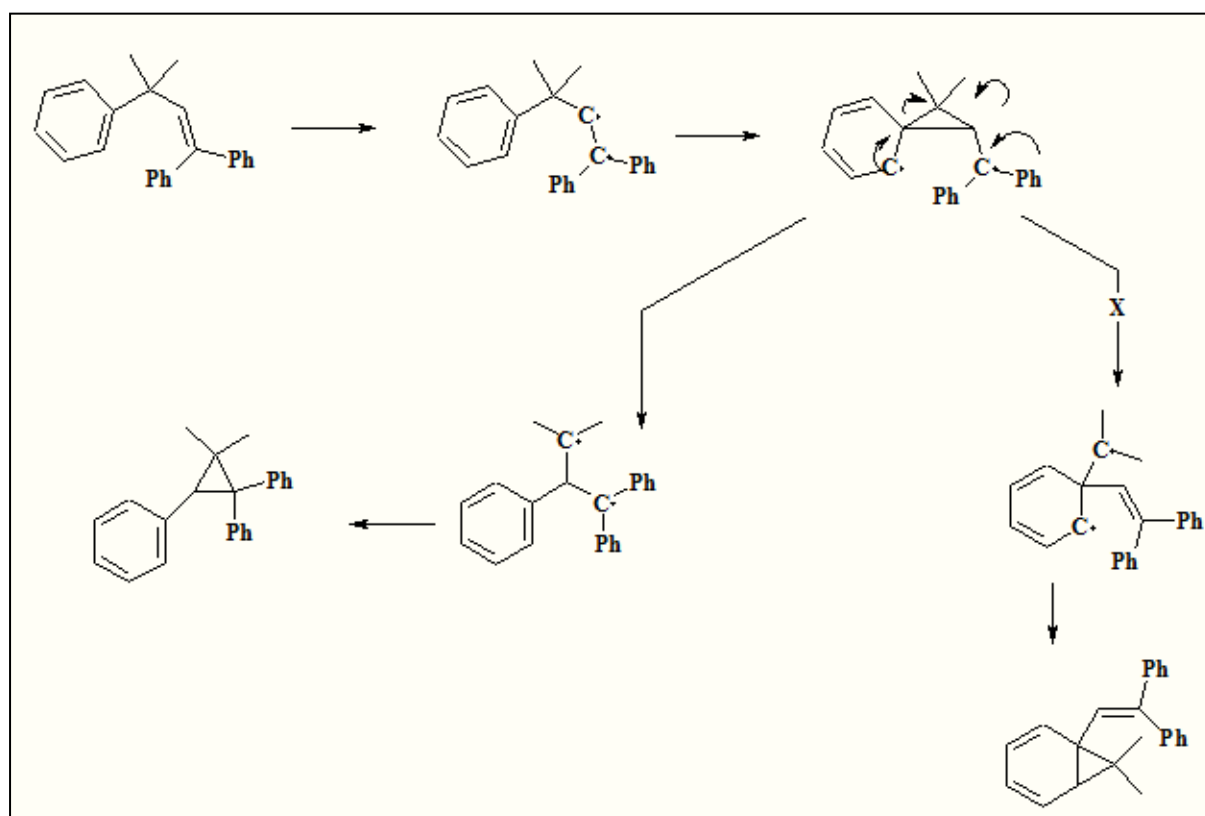
3. Di – π Methane Rearrangement

Non conjugated diene system separated by a sp^3 central carbon can undergoes di- π methane rearrangement. This rearrangement is commonly known as Zimmermann di- π methane rearrangement. The mechanism can take place via singlet or triplet. Majority of di – π methane rearrangement takes place via radical chemistry.

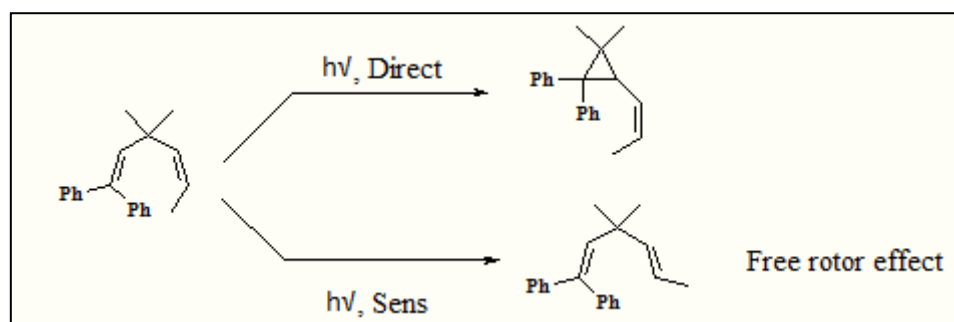




Mechanism

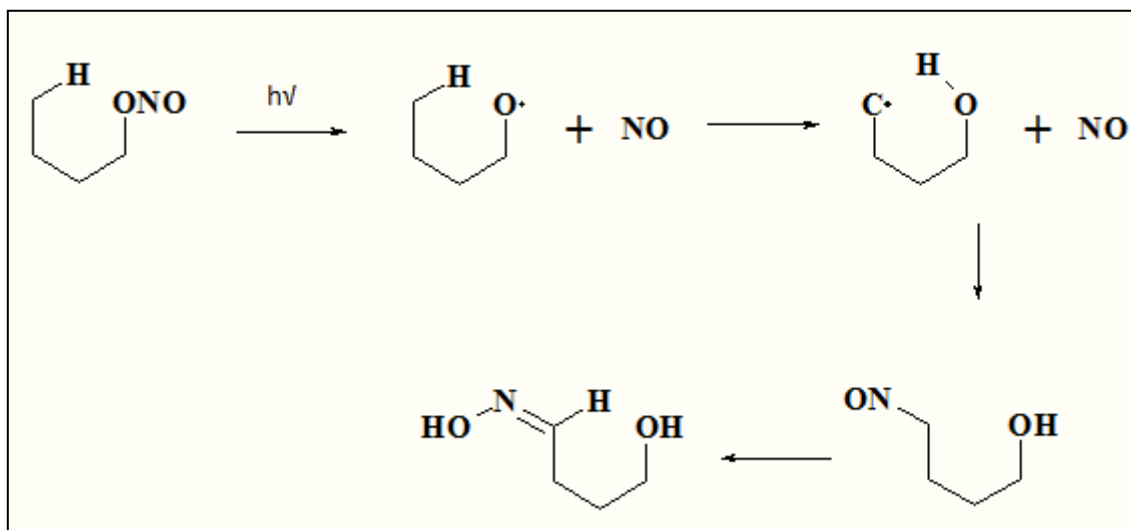


Systems in which double bonds are not in cyclic rings or not inhibited from free rotation undergo free rotor effect instead of di- π methane rearrangement in presence of a sensitizer.



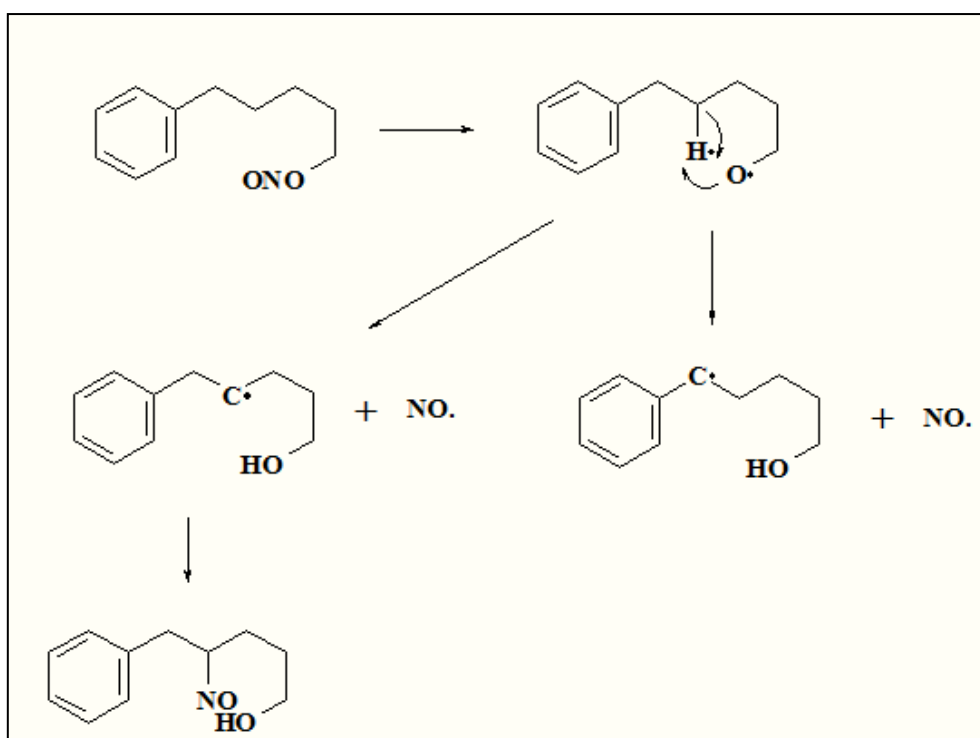
4. Barton Rearrangement

Remote functionalization of groups in compounds finds major applications in organic chemistry. One of the famous reaction in this category is Barton reaction. If the 5th carbon methyl should be functionalized it is called Remote functionalization.

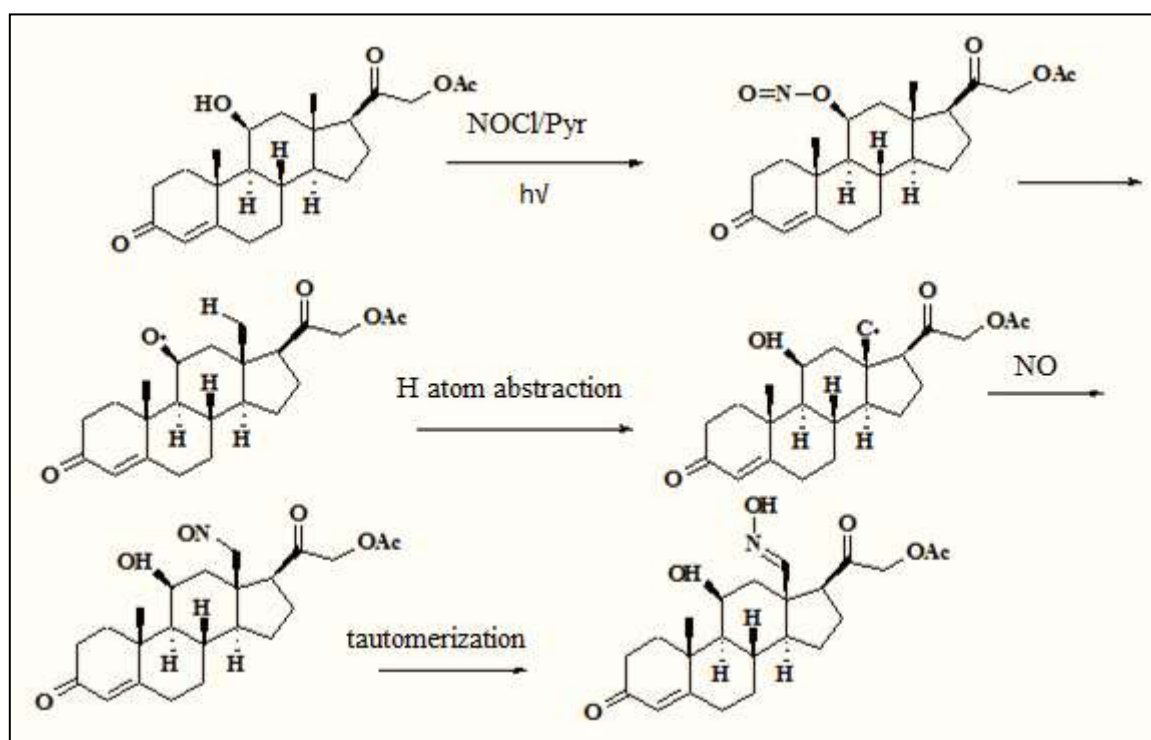


Compounds containing OH group can be functionalized by formation of six membered transition state for γ -hydrogen abstraction using NOCl/pyridine.

It can abstract H $\cdot$ from 5th 6th carbon . The 6th Carbon gives seven membered transition state but 5th carbon gives six membered more stable transition state (δ – hydrogen abs transaction takes place).

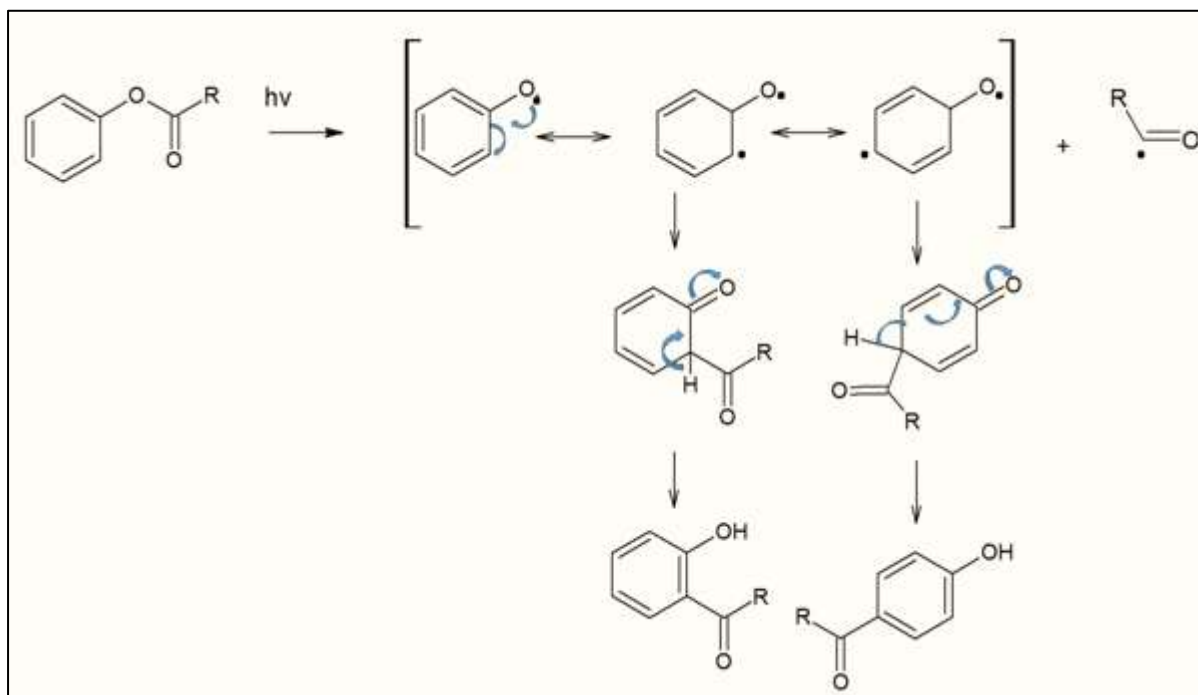


Natural products can be functionalized by Barton reaction.

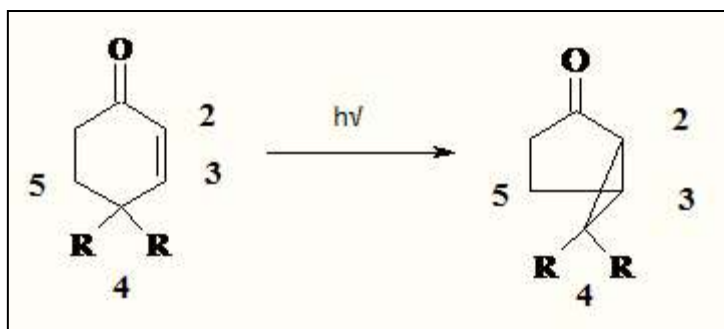


5. Photo – Fries Rearrangement

Photo-Fries rearrangement works as a radical reaction mechanism. In this reaction the rearrangement of COR group takes place to ortho and para position on the aromatic ring. The yield is low and thus it is not used in commercial production. This reaction takes place naturally by UV light at a wavelength of about 310 nm.

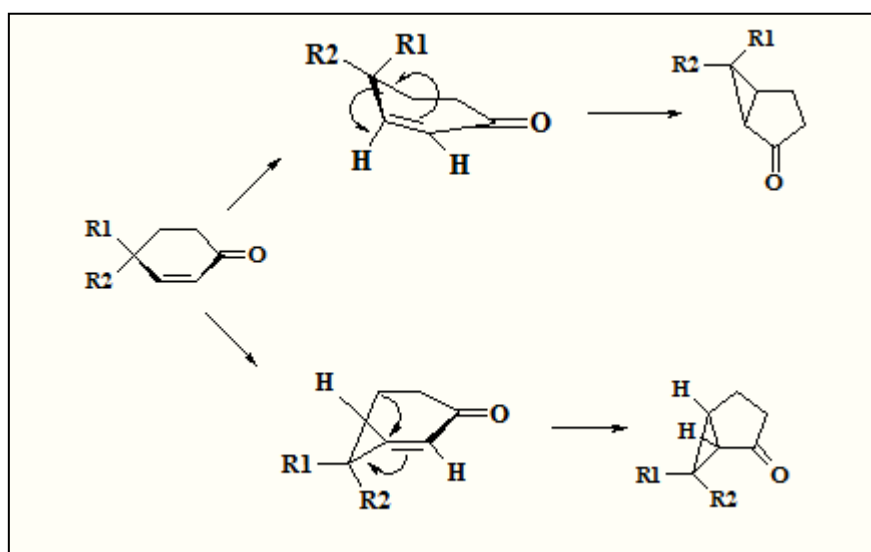


6. Photochemistry of α,β Unsaturated Ketones

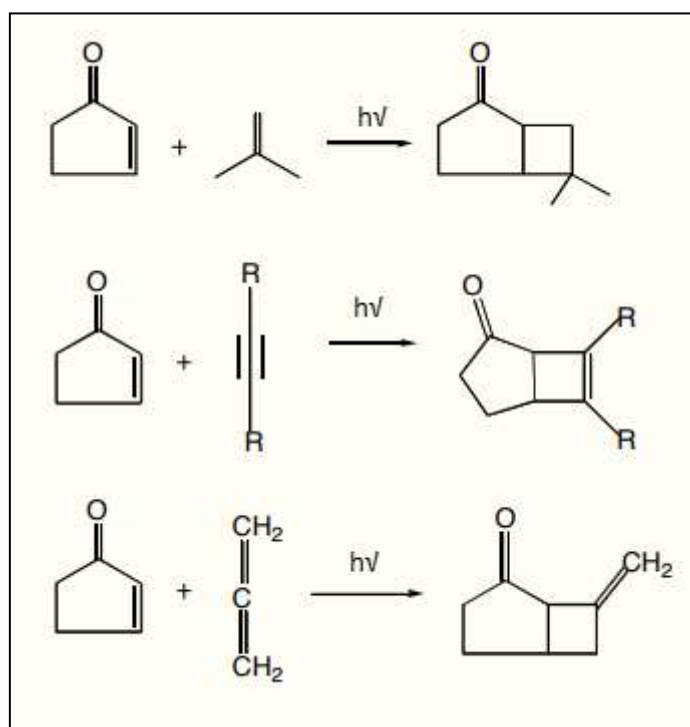


In molecules containing a carbonyl group with α,β -unsaturated double bond they rearrange in presence of light. Zimmerman and Chapman found that 4,4-dialkyl-2-cyclohexenones undergoes rearrangement in which the C3 and C4 carbon atoms actually exchange places producing a bicycle [3.1.0] hexan-2-one. This conversion was later postulated to involve a triplet excited state undergoing the initial rearrangement, followed by electron demotion to an

ionic species which then rearranges to products. The electron demotion leads to a zwitterion and product is formed.



The photochemical addition of α,β -unsaturated ketones to carbon-carbon double bonds (Olefins, alkynes, Alkenes) is most important cycloaddition. It has been synthetically very valuable and syntheses of numerous natural and unnatural products have utilized this reaction as a key step.

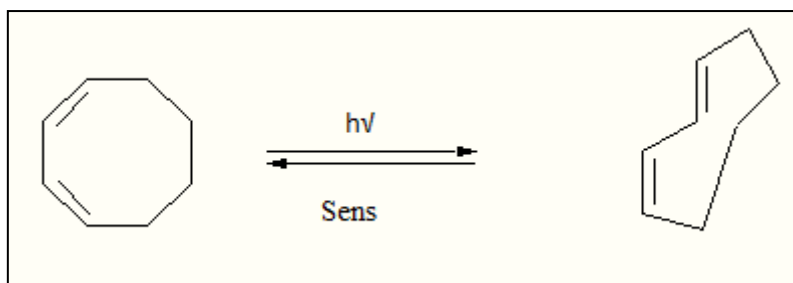
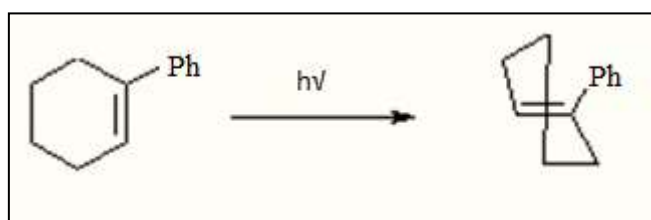
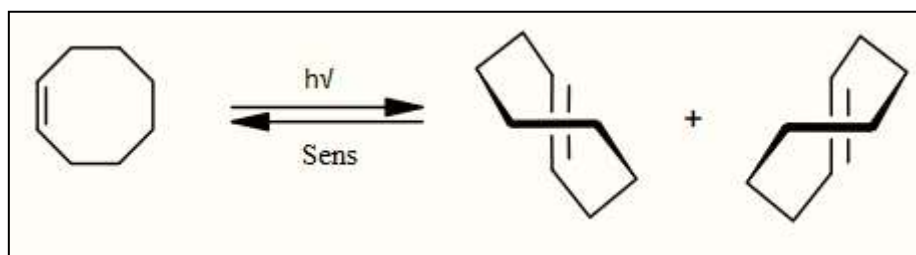


7. Olefin Photochemistry

The formation of the lowest excited singlet state of simple alkenes arises from the allowed π - π^* transition. This generally requires short wavelength irradiation extending to about 200 – 210 nm. Absorption of solvents and lack of suitable light sources make the use of simple alkenes in preparative photochemistry difficult. Substituted or conjugated derivatives are mainly used. Another possibility to circumvent the problem of absorption at short wavelengths is the use of sensitizers.

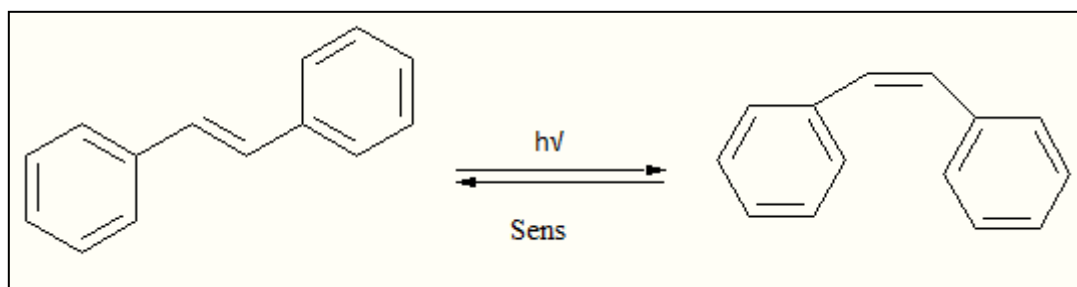
i. Cis-Trans Isomerization

When irradiated with uv-light olefins usually undergo cis -trans isomerization. The transformation can be carried out either by direct irradiation of the olefins or by sensitized irradiation. It may either occur through a singlet or a triplet excited species. It has been reported that isomerization in the triplet state has a lower barrier to rotation around the carbon-carbon bond.



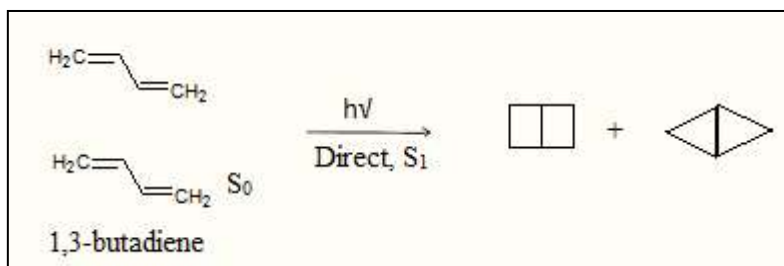
ii. Photoisomerization of Stilbenes

Direct irradiation of solutions of either cis or trans- stilbene gives rise to a constant mixture having 93% cis- stilbene and 7 % trans- stilbene. Initial absorption of light by either of these isomers has been found to be rapidly followed by intersystem crossing to the corresponding triplet states. Photoisomerization then takes place via inter conversion or probably via a common triplet intermediate.

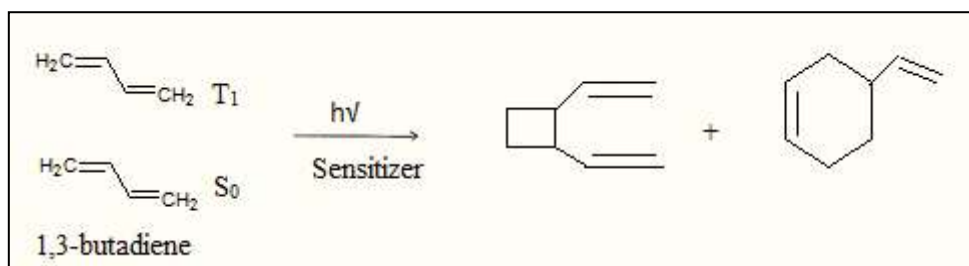


8. Photochemistry of Conjugated Dienes

The conjugated dienes exist in both cis and trans isomer and they react differently in direct light or presence of sensitizer. In direct light it forms the product from singlet state. The excited singlet state butadiene forms product via zwitter ion formation.

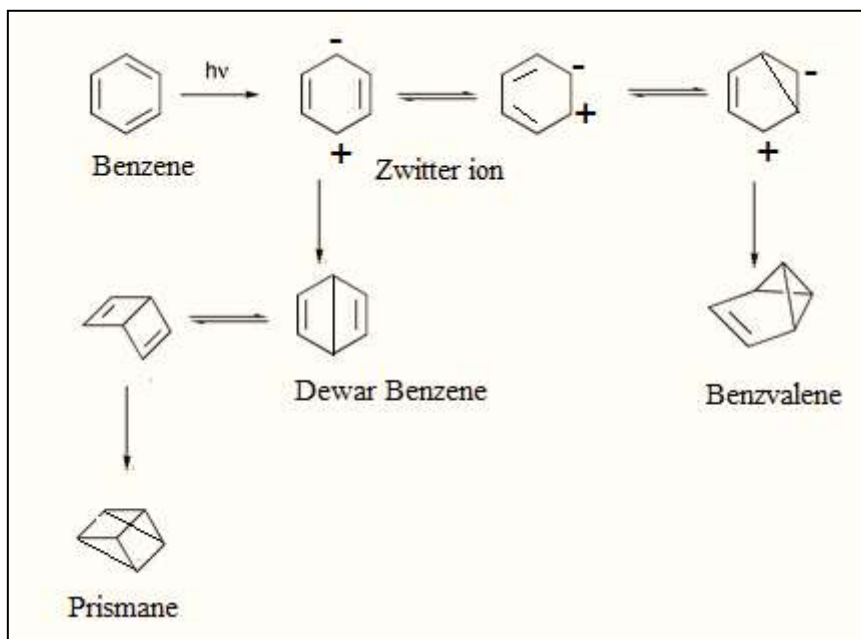


In presence of a sensitizer the excited singlet state butadiene undergoes ISC and form triplet state butadiene which reacts with ground state butadiene to form the products. In presence of sensitive, energy transfer taken place and does radical chemistry.

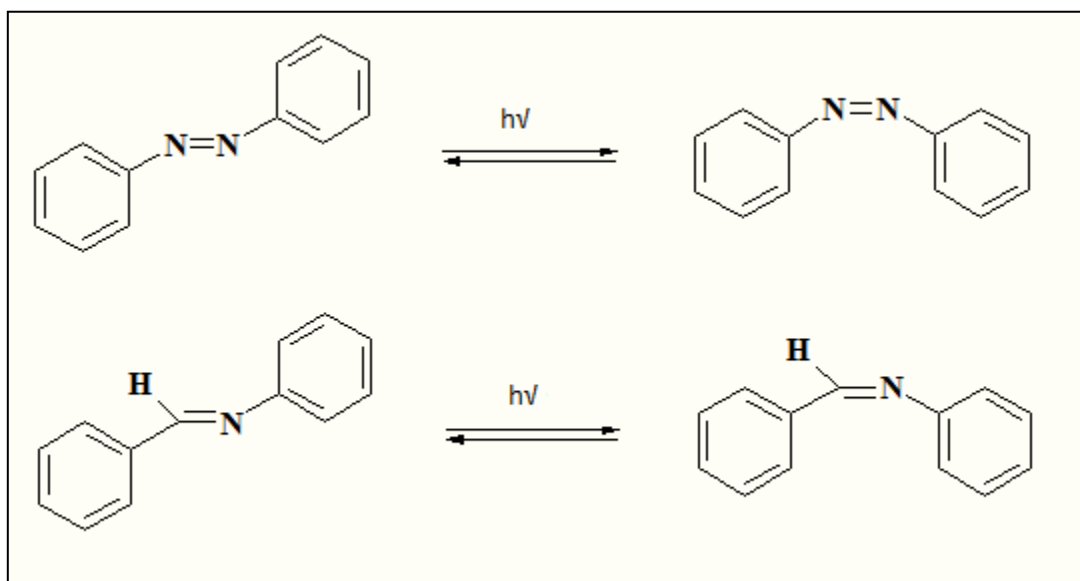


9. Photochemistry of Arenes and Benzene Derivatives

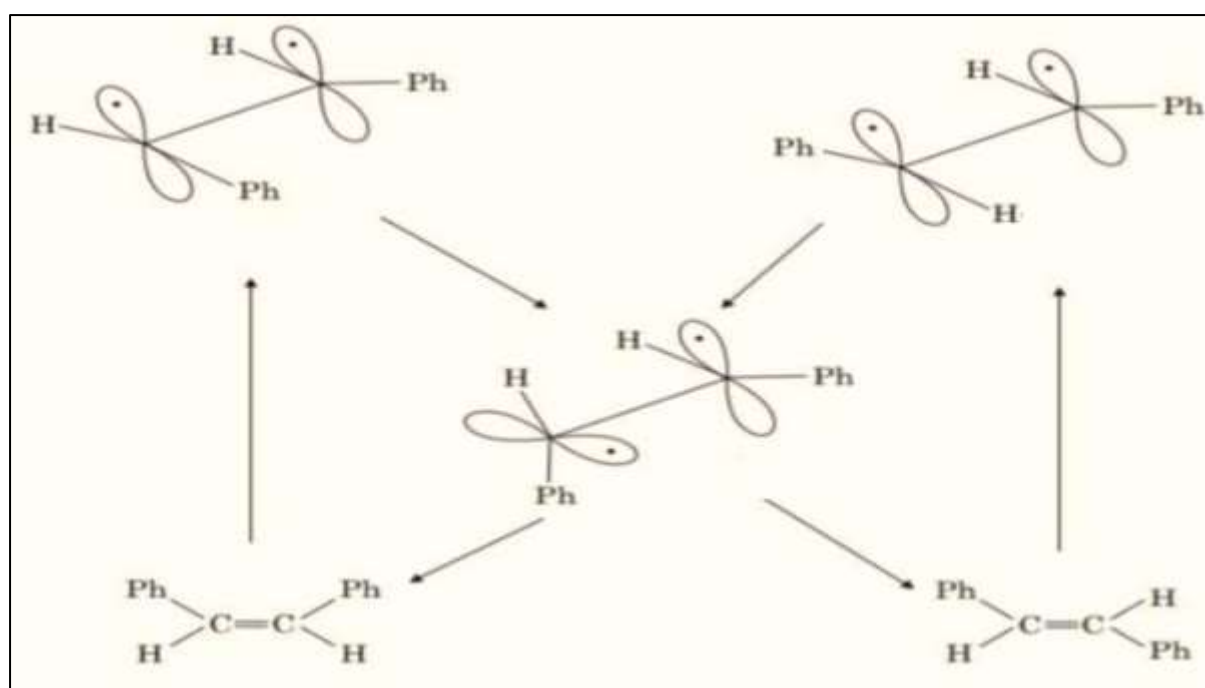
When Benzene is irradiated with light it undergoes photoisomerism to form different isomers namely Benzvalene, Dewar Benzene, Prismane etc through the zwitter ion formation.

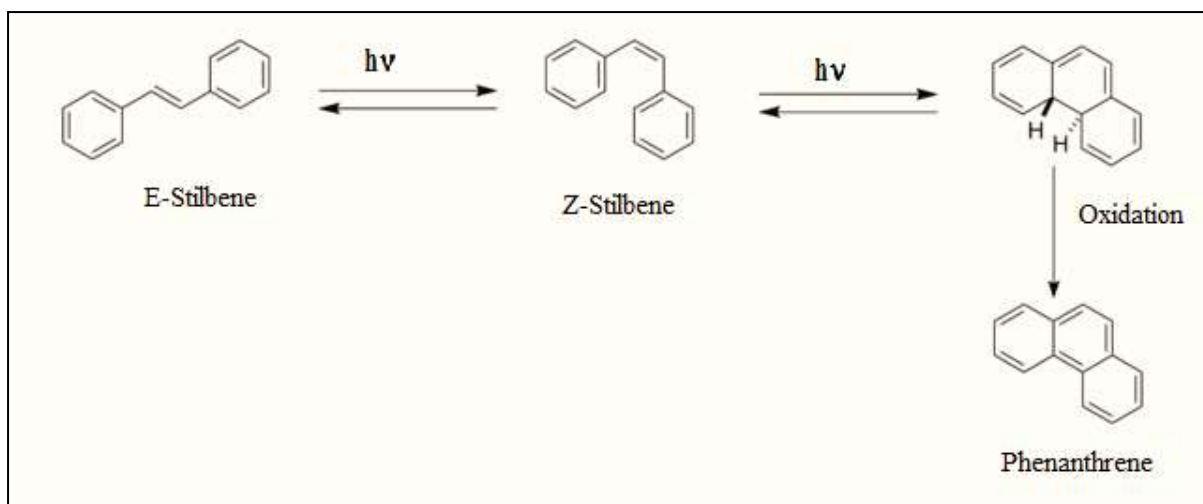


Similar to Benzene arene compounds also undergoes photoisomerism when irradiated with light. Mostly they undergo cis-trans isomerism or open-closed ring transitions. Equilibrium exists (photo stationary state). Absorption of light by both cis and trans is same ($h\nu$). Full conversion is not achieved. The trans isomer absorbs more light and has high ϵ_{max} . The conversion of trans to Cis is 95%. The ϵ_{max} of trans is $\epsilon_{\text{max}} = 16,300$ and that of Cis isomer is only $\epsilon_{\text{max}} = 2800$.



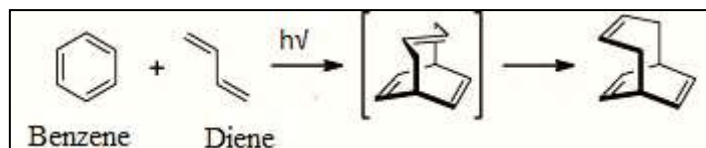
The *cis* and *trans* isomers convert from one form to another via the same intermediate.



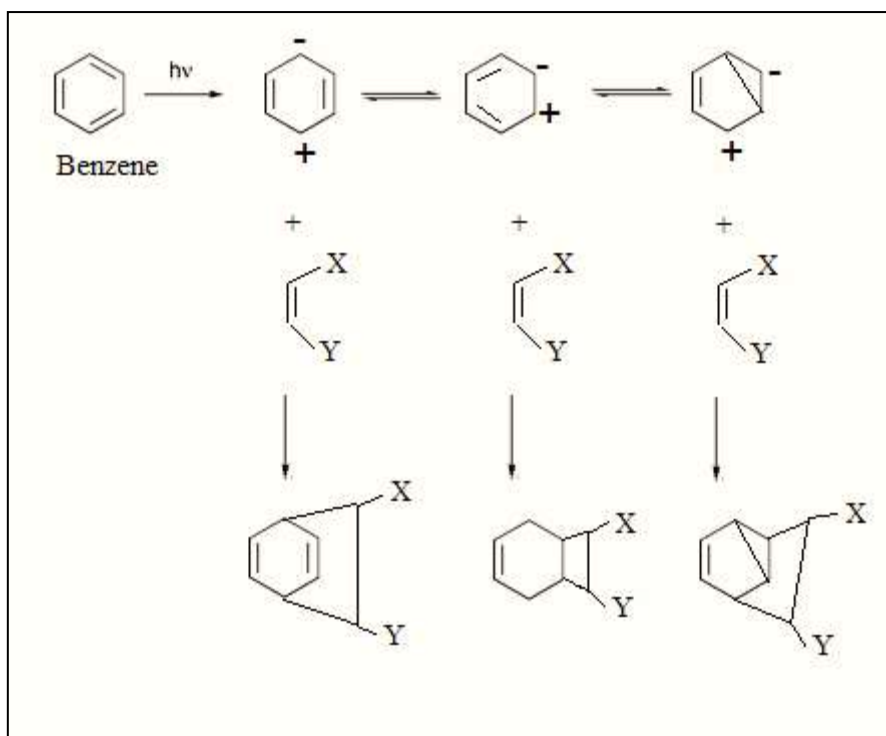


10. Photocycloaddition of Benzene to Olefins and Dienes

Benzene undergoes photocycloaddition with dienes in presence of light to various cycloadducts. Photo cycloaddition of 1,3- dienes to benzene was first reported for but a – 1, 3 – diene to yield the meta – cycloadduct together with Z and E- para – cycloadducts and a substitution product.



Benzene undergoes photocycloaddition with olefins in presence of light to various cycloadducts.



QUESTIONS

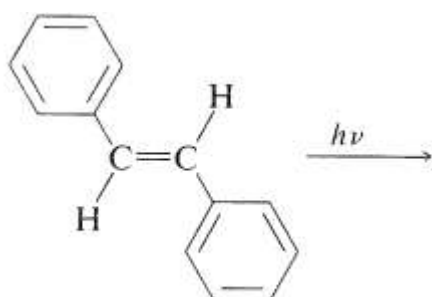
PART-A

1. Explain the mechanism of photo-Fries rearrangement with an example.
2. Explain the photoisomerism of Benzene.
3. Explain the cycloaddition of Benzene with alkenes and dienes.
4. Explain the direct and cross-over addition of alkenes.
5. With a suitable example explain the Di-pi- methane rearrangement.
6. Explain the Barton reaction with a suitable example.
7. Discuss the Cis – trans isomerisation of alkenes.

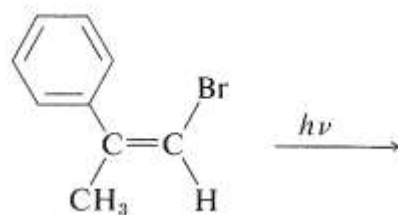
PART-B

1. Explain the photoreduction of carbonyl compounds and discuss the factors influencing photoreduction reaction.
2. Write short notes on Dimerization reactions of π - π^* reactivity of alkenes and conjugated dienes.
3. With a suitable example explain the Paterno-Buchi reaction. Explain the factors affecting stereospecificity and regioselectivity of substituent in alkenes in paterno-Buchi reaction.

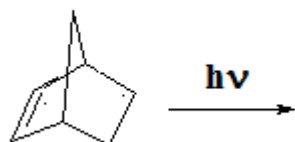
4. Predict the products



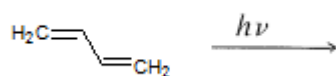
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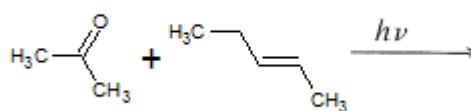
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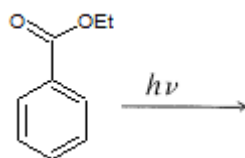
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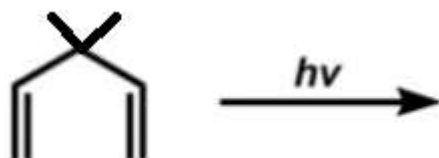
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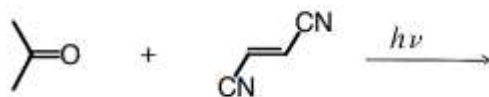
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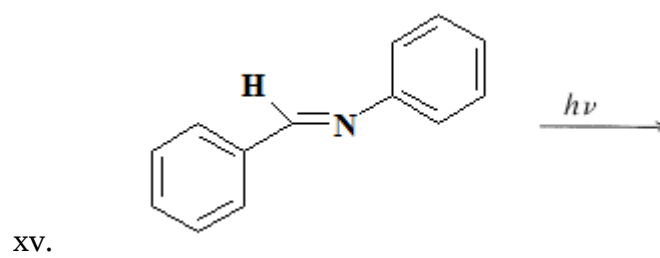
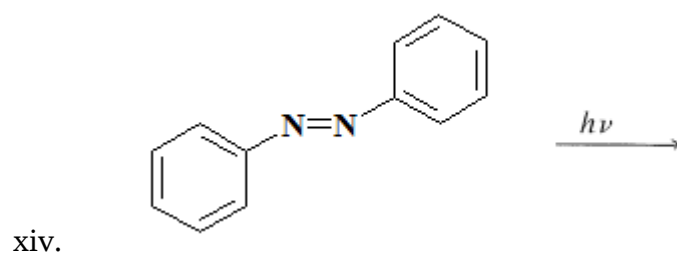
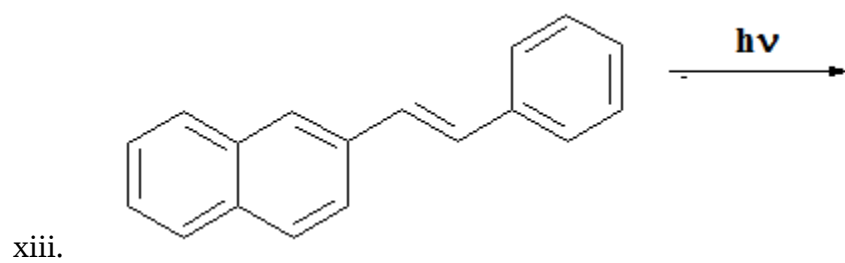
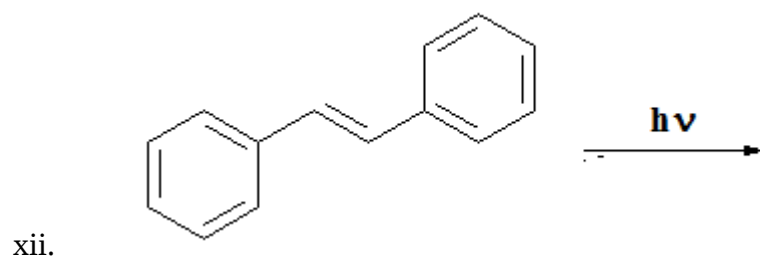
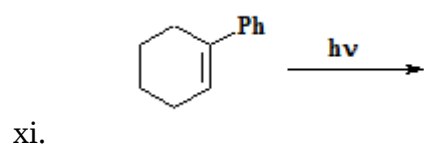
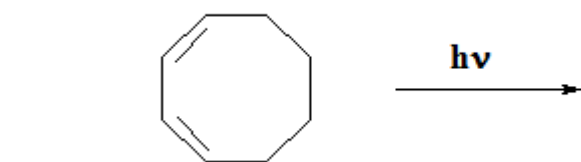
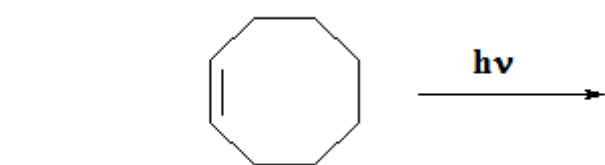
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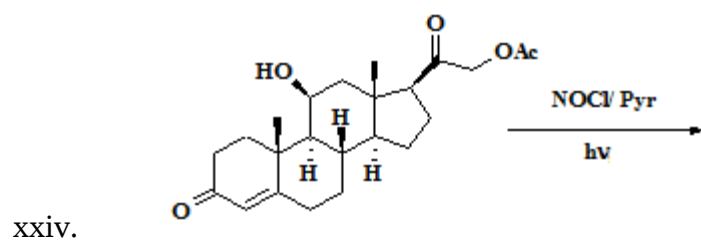
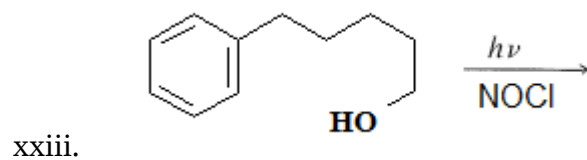
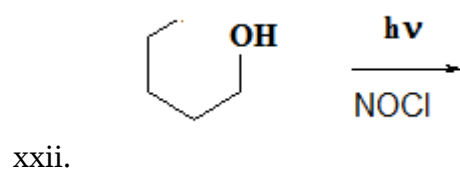
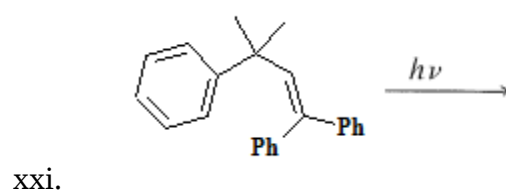
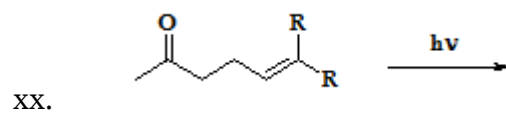
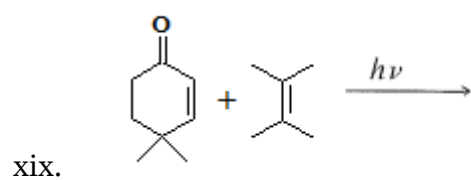
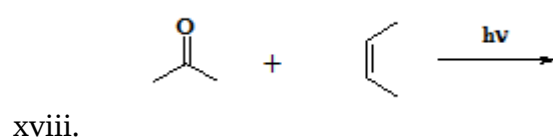
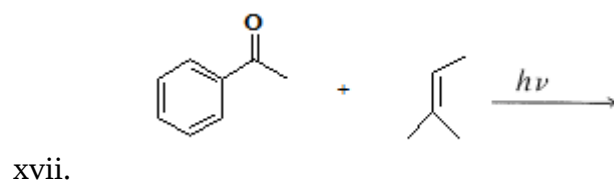
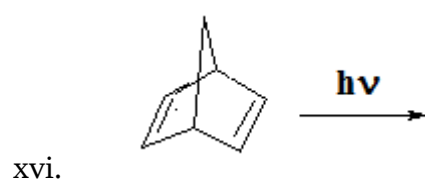


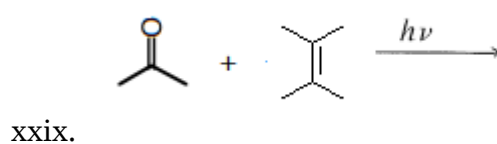
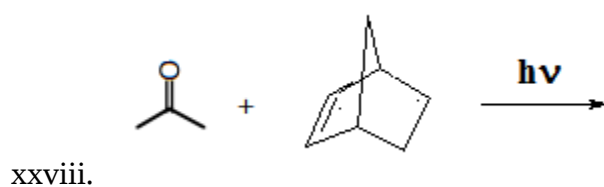
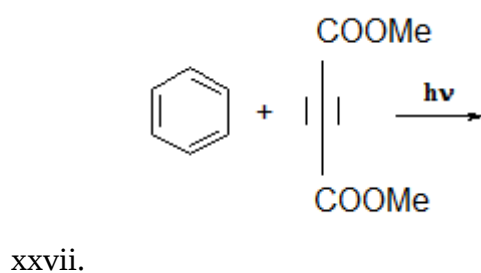
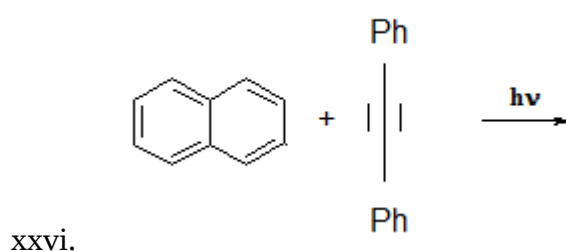
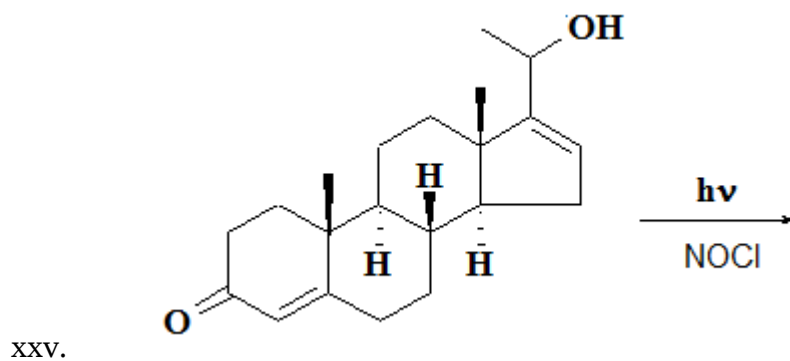
vii.



viii.







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