MSCCH-02

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ORGANIC CHEMISTRY

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MSCCH-02

ORGANIC CHEMISTRY

Unit-1: Delocalized Chemical Bonding

Structure of Unit:

1.1 Objectives

In this unit the students will be able to understand

- Delocalized chemical bonding
- Different types of delocalized systems.
- Concept of resonance effect and its types.
- The mechanism and orientation of substitution in reaction showing resonance type reactions.
- About the *ortho* and *para* directing groups.
- Concept of inductive effect and its types.

1.2 Introduction: Delocalized chemical bonding

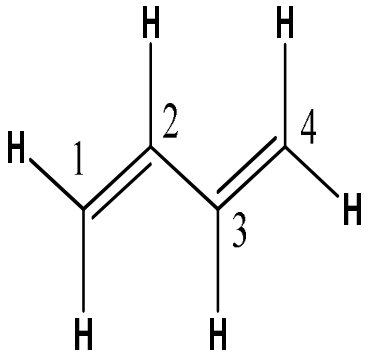
Bonding in many molecules can be adequately described by a single Lewis structure, but this is not sufficient for many other molecules. The molecules containing one or more bonding orbitals that are not restricted to two atoms, but are spread out over three or more atoms such bonding is said to be delocalized. On contrary localized

chemical bonding may be defined as bonding in which the orbital electrons are shared by two and only two nuclei.

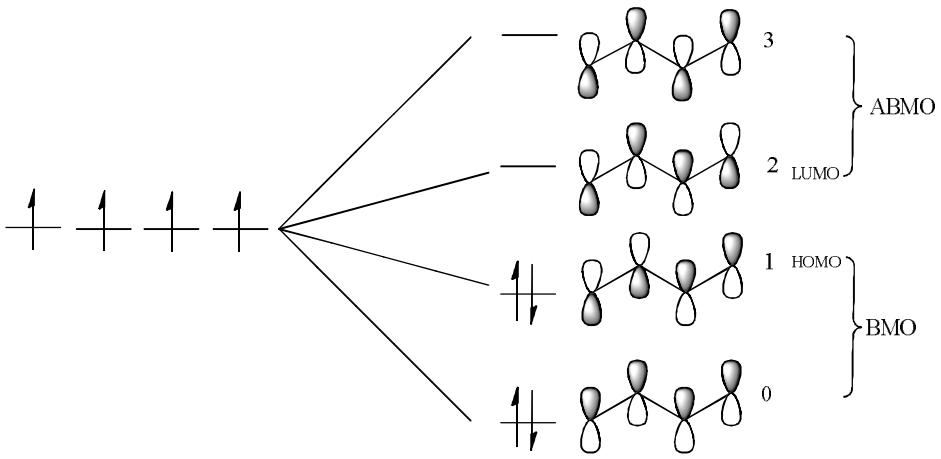
1.3 Conjugation

Presence of alternate double bonds in a molecule is considered as conjugation and molecule is said to be conjugated. Conjugated molecules have ΠΠ electrons that are not localized in individual double or triple bonds, but their ΠΠ electrons are delocalized throughout an extended ΠΠ system. e.g. dienes with two C=C bonds in which bonds are conjugated.

1,3-Butadiene is the simplest example of arrangement of C=C multiple bonds leading to conjugation and π electrons delocalization. In this example the resonance structure shows that the electrons can be "shared" or delocalized creating a cationic and anionic centers:



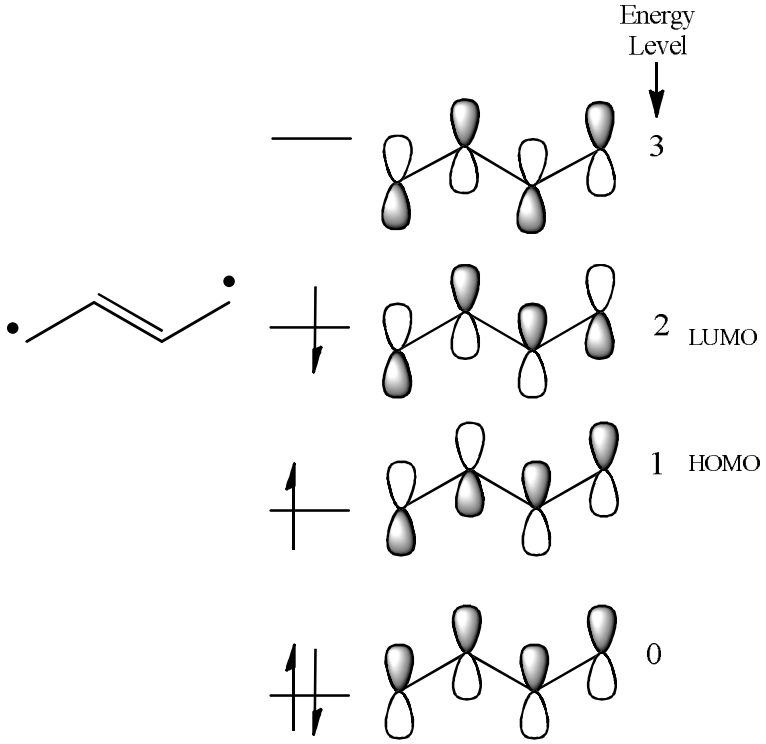
For linearly conjugated systems, it is quite straightforward to look at the molecular orbitals of the various energy levels in the molecule (fig. 1:1). There are certain rules for the conjugation to occur. Conjugation occurs whenever *p* orbital's can overlap on three or more adjacent atoms.



(Fig. 1:1)

(BMO- Bonding Molecular Orbitals, ABMO- Anti Bonding Molecular Orbitals, HOMO- Highest Occupied Molecular Orbitals, LUMO- Lowest Occupied Molecular Orbitals.)

The LUMO has its double-bond character in the center of the molecule, while the Highest anti-bonding orbital shows no interaction between any of the *p*-orbitals. Whenever molecule is in first excited state electron density shown in the LUMO diagram yields a diradical structure. (Fig. 1:2)



In 1, 3-Butadiene all carbon atoms are sp^2hybridised.Hence they all have a p-orbital each and they are parallel to each other. *P-orbitals* on adjacent atoms overlap permitting electron movement from one to the other. In 1, 3-Butadiene an electron from one end of the molecule can move to the other end through the π orbital pathway. This movement of electrons through the p-orbital pathway is one more way of describing conjugation.

Salient features of Conjugation:

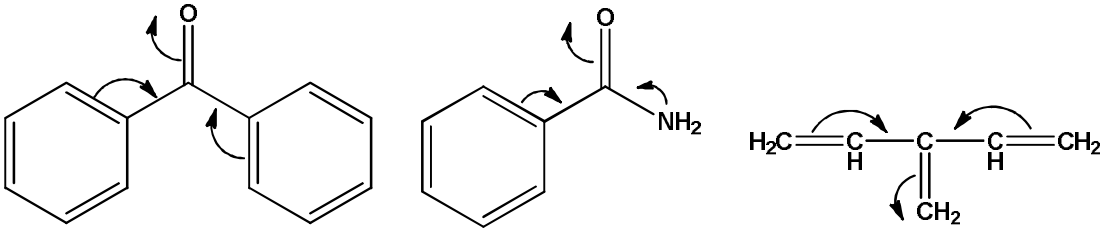
- A more conjugated compound absorbs light at higher λ_{max} in the UV-VIS range.
- As conjugation increases, λ_{max} increases, this is because, in a more conjugated compound the energy required for transition of the electron from Highest Occupied molecular Orbital (HOMO) to the Lowest

Unoccupied Molecular orbital (LUMO) decreases hence the wavelength of all absorption increases.

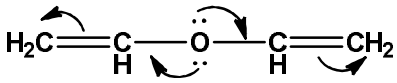
- More conjugated compound makes structure more stable as possibility of their number of resonance forms increases.

1.4 Cross Conjugation

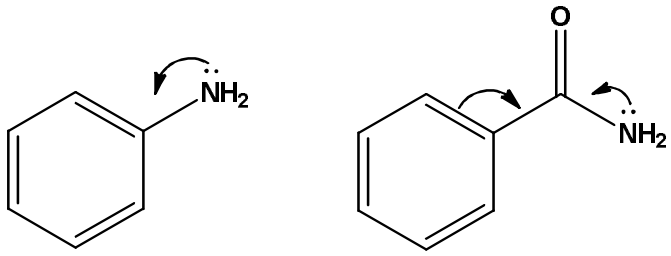
In a cross-conjugated compound, three groups are present, two of which are not conjugated with each other, although each is conjugated with the third. In other words, when conjugation is possible from either end of the molecule towards the center it is called cross conjugation.as shown below in three different molecules.



There is possibility that conjugation can start from the center of the molecule and moves towards either end.



Due to cross conjugation reactivity of molecules is greatly much affected which can be seen through following example.



(I) (II)

In aniline (I) the lone pair on nitrogen activates the ring at *ortho* as well as at *para* position, as a result bromination under ordinary conditions leads to tribromo aniline. While in the second case that is acetanilide. (II) due to cross conjugation the influence of the lone pair in activating the ring is less, hence bromination leads to mono substituted acetanilide (p-bromoacetanilide also $NH_2$is activating white CNH_2 is deactivating).

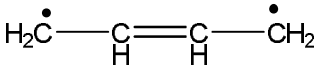
1.5 Resonance

The flow of electrons from one part of a conjugated π system to the other caused by phenomenon of delocalization is called resonance and the effect is called resonance effect or meoomeric effect. The re-distribution of electrons takes place in unsaturated and especially in conjugated systems via their π-orbitals.

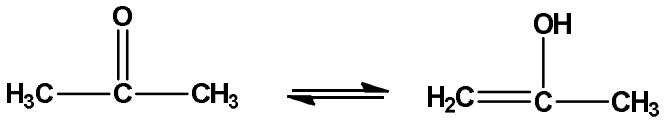
Different arrangement of electrons within conjugated π system but with identical of positions for atoms is called resonance structures or canonical forms. The resonance structures are imaginary and the actual structure of the molecule is considered as the hybrid (weighted average of contributing structure) of all the valid resonance structures. The energy of resonance hybrid is always less than the energy of any of the contributing structures. The delocalization of electrons is indicated by using curved arrows and structures are corrected by ⇨ arros.

Rules for resonance:

1. All resonance structures must be valid Lewis structures which obey octet rule i.e. carbon with five bonds is not allowed.
2. They should possess same number of electrons and equal net charge.
3. All canonical forms must have same number of electrons. e.g. Following structure for butadiene is not valid



4. The positions of atoms should be same in all the resonance structures. e.g. the following structures are not the resonance structures, since the position of one hydrogen atom is not same. Indeed, they are different molecules, which are in dynamic equilibrium with each other. These are called tautomers of each other.



keto enol

5. The bond order of two connecting atoms may vary between two different resonance structures.
6. The resonance structures may or may not be equivalent.

7. The atoms that are part of the delocalized system must be arranged in one plane or nearly so. The reason is to get maximum overlap between the orbitals.

There are two types resonance effects depending on their strength of electron withdrawing or electron releasing nature with respect to conjugated π system.

1) Positive resonance or mesomeric effect(+M) 2) Negative resonance or mesomeric effect(-M)

1) **Positive resonance or mesomeric effect (+R or +M)**: The electronal releasing groups show positive mesomeric effect when they release electrons to the rest of the molecule by delocalization. These groups are denoted by +M or +R. Due to this effect, the electron density on rest of the molecular entity is increased. Examples of el(-) denating groups are:-

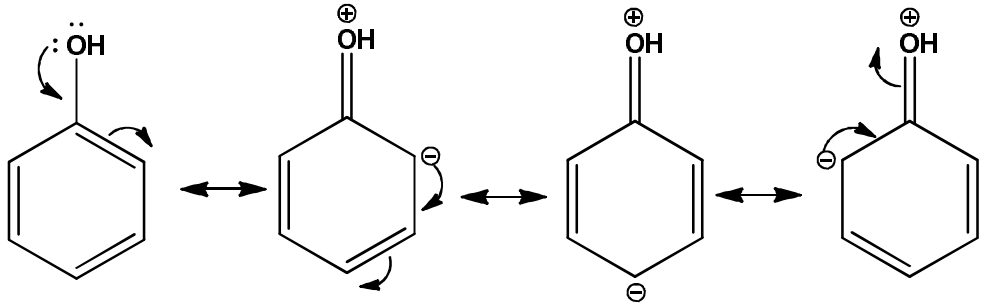
   E.g. -OH, -OR, -SH, -SR, $-NH_2$, $-NR_2$ etc.

2) **Negative resonance or mesomeric effect (-R or -M)**: It is shown by electron withdrawing substituents or groups that withdraw electrons by delocalization from rest of the molecule and are denoted by -M or -R. The electron density on rest of the molecular entity is decreased due to this effect. Examples of el(-)withdrawing groups are:-

   E.g. $-NO_2$, -C=O, -C≡N, -COOH, $-SO_3H$ etc.

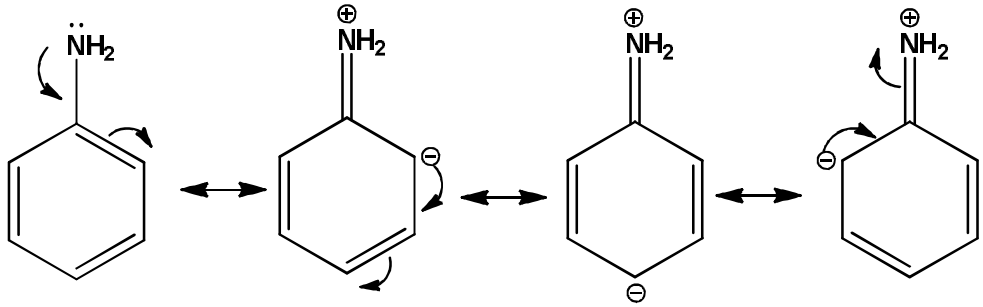
Applications of resonance:

1) The -OH group in phenol is showing positive resonance or mesomeric effect (+R or +M) effect due to delocalization of lone pair on oxygen atom towards the ring. Thus the electron density on benzene ring is increased particularly on ortho and para positions. Hence phenol is more reactive towards electrophilic substitution reactions. The substitution is favored more at ortho and para positions.

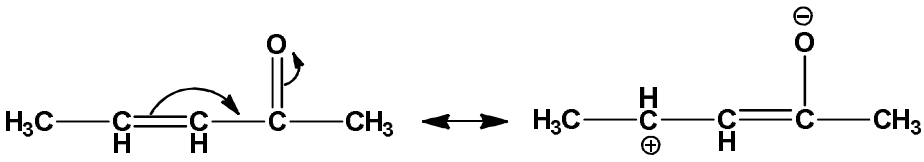


2) The $-NH_2$ group in aniline also exhibits +R effect. It releases electrons towards benzene ring through delocalization. As a result, the electron density

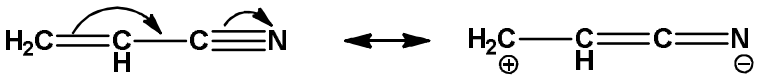
on benzene ring increases at ortho and para positions. Thus aniline activates the ring towards electrophilic substitution at ortho and para positions.



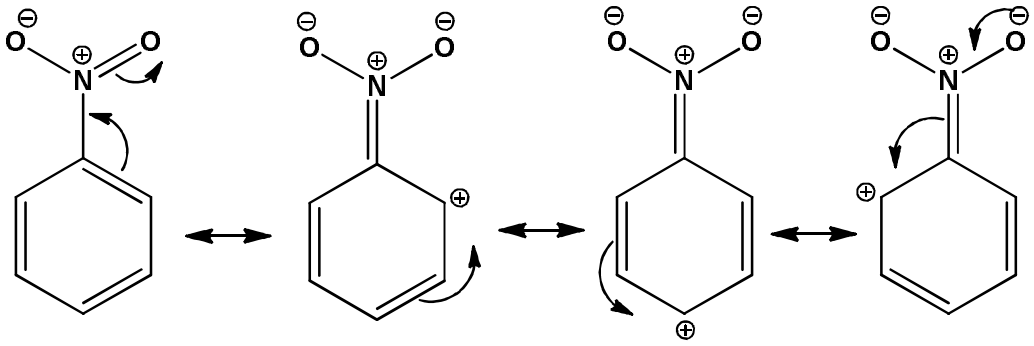
3) Carbonyl group are showing negative resonance effect (-R or -M). It withdraws electrons by delocalization of π electrons and reduces the electron density particularly on β- carbon as shown below.



4) Cyanide group in acrylonitrile is showing negative mesomeric effect (-R or -M) It withdraws electrons. The electron density on β- carbon decreases due to delocalization of π electrons towards cyanide group.



5) The nitro group, $-NO_2$, in nitrobenzene showing negative mesomeric effect (-R or -M) due to delocalization of conjugated π electrons. Hence nitro group deactivates the benzene ring towards electrophilic substitution reaction.



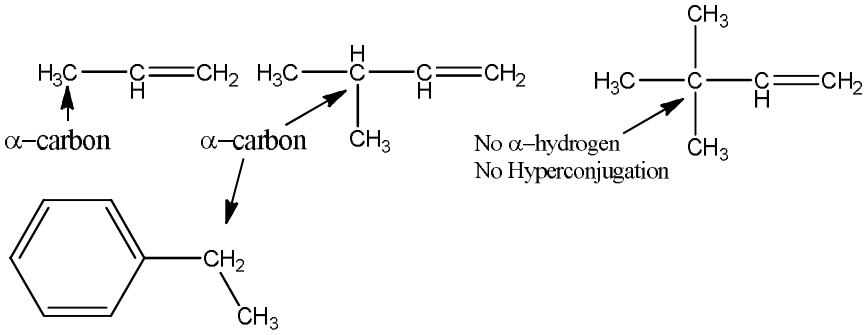
1.6 Hyperconjugation

Delocalization of electrons by the overlap of a (sigma) bond orbital with an empty *p* orbital is called hyperconjugation. Alkyl substituent's having α- hydrogen on α-carbon of a C=C (bond) acts and give rise to a hyperconjugation effect. Hyperconjugation occurs due to overlapping of σ-bonding orbital and the orbital containing a lone pair with adjacent π-orbital or p-orbital with proper orientation. .
Structural requirements for Hyperconjugation:

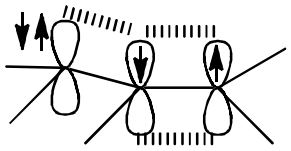
1. Compounds must possess sp^2 hybrid carbon of alkene, arene, carbocation or radical.
2. Presence of at least one α-hydrogen (sp^3carbon) adjacent to sp^2 hybrid carbon.

Hyperconjugation is of three types:

1. In alkynes and alkyl substituted aromatic compounds (α-π) as shown below in the examples (a) and (b).

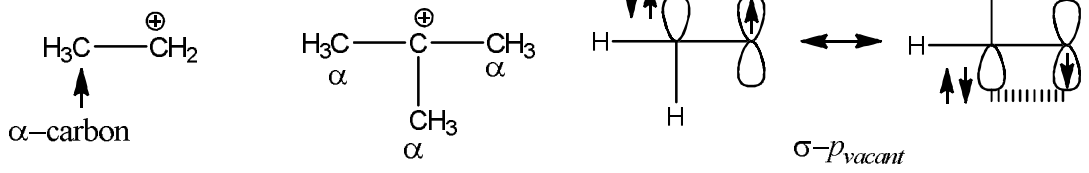


(a)



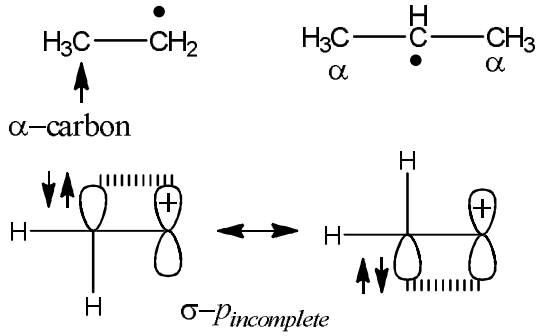
(b)

2. in carbocations (σ-p_{vacant}):



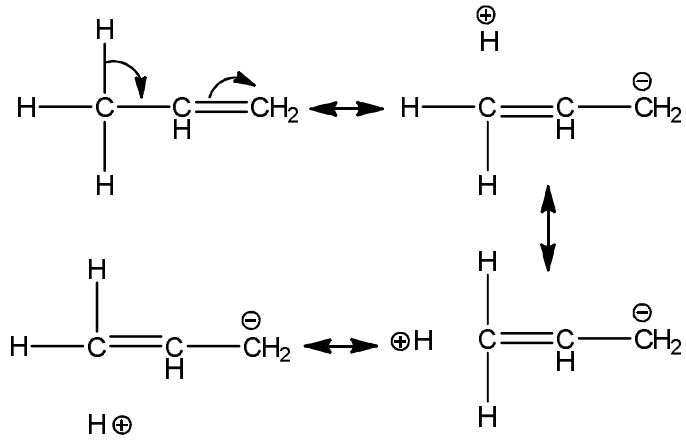
(a) (b)

3. in radicals (σ-$p_{incomplete}$):



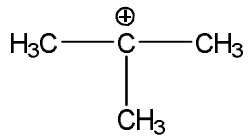
(a) (b)

Mechanism: Resonating structures involves hyperconjugation considered as 'no bond resonance' between α- carbon and hydrogen present on α- carbon. Since structure ∏ has no existence but only contributes to structure (I) via delocalization of ∏ bond electron through



Hence more the number of α- hydrogen increase in hyperconjugation resonance effect occurred listed in table.

Structure	Number of α hydrogen	Number of resonating structures
$H_3C—HC=CH_2$	3	4
$H_3C—\overset{\oplus}{C}H_2$	3	4
$H_3C—\overset{\oplus}{C}(CH_3)—C(H)=CH_2$	6	7

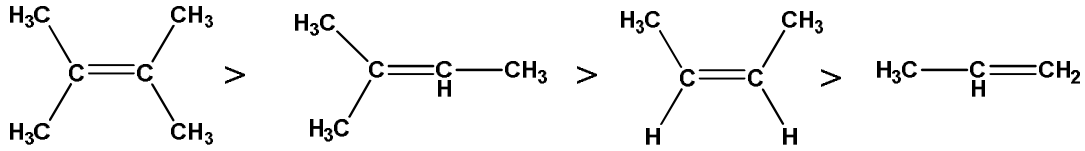
	9	10

Application of Hyperconjugation:

1) Stability of alkenes:

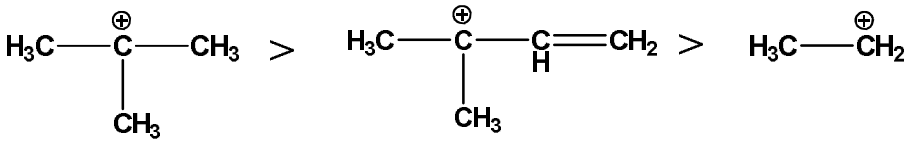
Stability of alkenes increases with increase in the number of alkyl groups (α- carbon) on the double bond. It is due to increase in the number of hyperconjugation resonance structures.

eg.



2) Stability of carbocation:

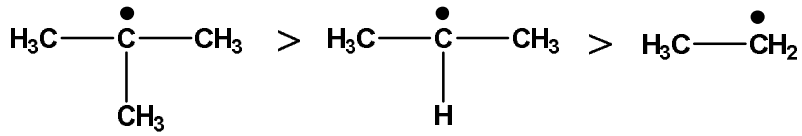
Stability of carbocation is increases with increase in the number of alkyl groups (containing α -hydrogen) due to increase in the number of contributing structures hyperconjugaing structures are shown below.



3^0 2^0 1^0

3) Stability of free radicals:

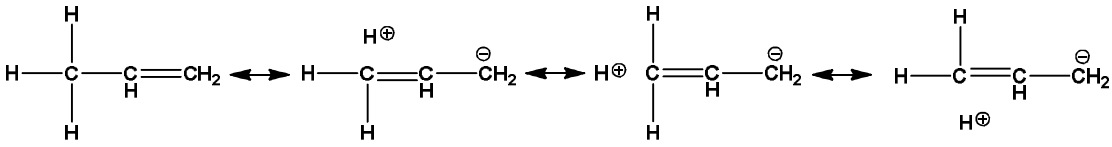
Stability of free radicals is influenced by hyperconjugation same like carbocations the order of stabilitis as follows:



4) Dipole moment and bond length:

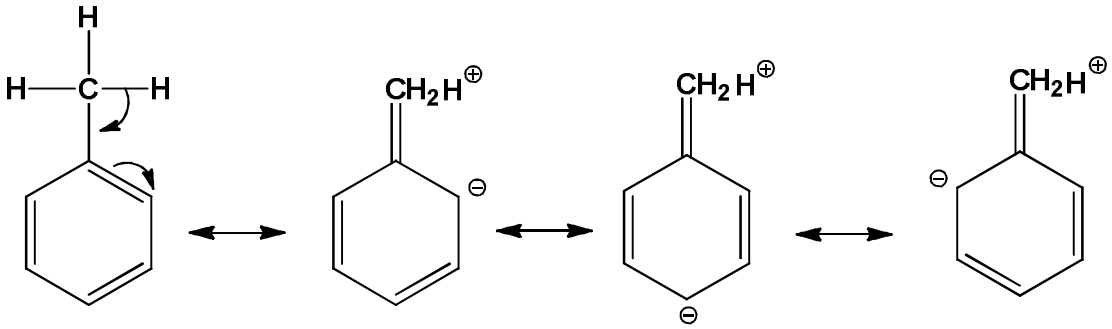
Due to hyperconjugation, dipole moment as well as bond lengths of the molecules is significantly affected since the contributing structures show considerable polarity. The single bond get partial double bond character and double bond gets a single bond character.

Eg.



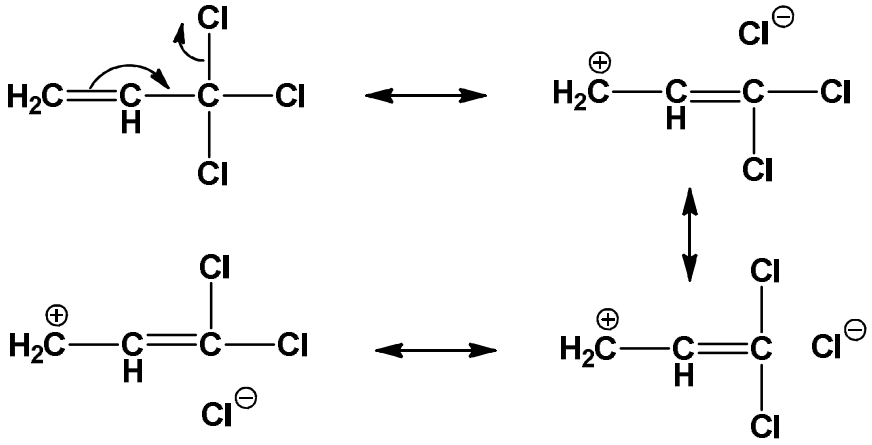
5) Reactivity and orientation of electrophilic substitution on benzene ring:

Due to hyperconjugation resonance, methyl group in toluene releases electrons towards the benzene ring. Alkyl group is ortho and para directing and hence It is an activating group for electrophilic substitution reactions of aromatic compounds.



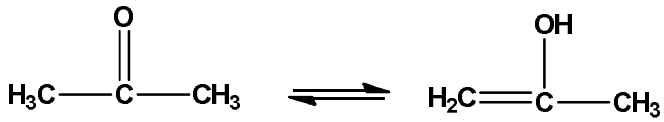
6) Reverse hyperconjugation:

In α-halo alkenes due to hyperconjugative effect delocalization of electrons occurs towards halogen. It is called as reverse hyperconjugation.



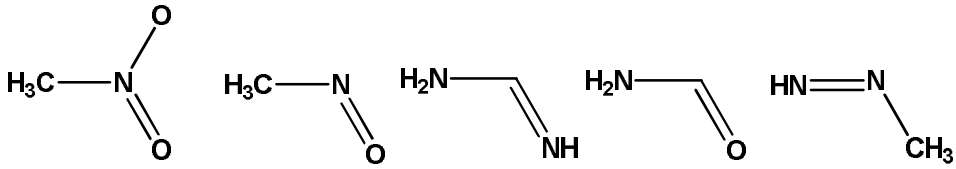
1.7 Tautomerism

Tautomers are isomers of a compound which differ only in the position of the protons and electrons. The overall carbon skeleton of the compound is unchanged. Tautomers are "isomers that are rapidly interconverable. The most important type of tautomerism in organic chemistry are keto-enol tautomers. Typically the 'keto' form of the compound is more stable, but in some instances the 'enol' form can be the more stable.

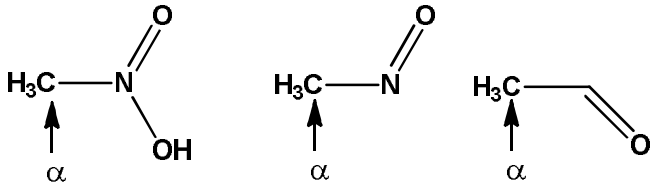


Condition for tautomerism:

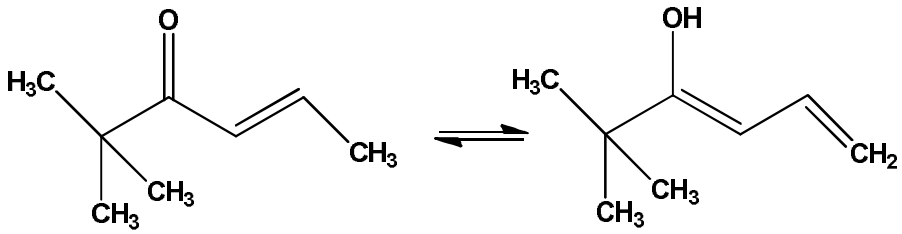
1. Compound should have at least one electronegative atom such as N, O etc. and it must be multiple bonded i.e. double or triple bonded.



2. Availability of at least one acidic hydrogen present at α-position of the molecule.



3. If α-carbon is double bonded, then hydrogen attached to it is not used for tautomerism.



Classification of tautomerism:

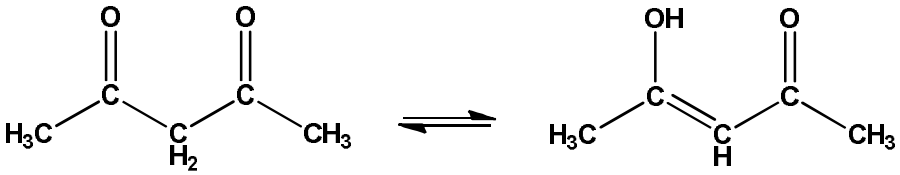
It is possible to classify all the compounds exhibiting tautomerism:

1. Open system tautomerism
2. Ring chain tautomerism
3. Valence tautomerism

1. Open system tautomerism:

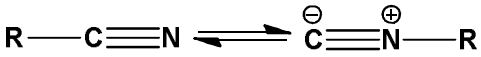
In open system tautomerism both tautomeric forms are open chain compounds and it is accelerated by due to migration of acidic hydrogen from alpha (α) carbon aom in the form of proton.

eg. 1-Keto-enol tautomerism

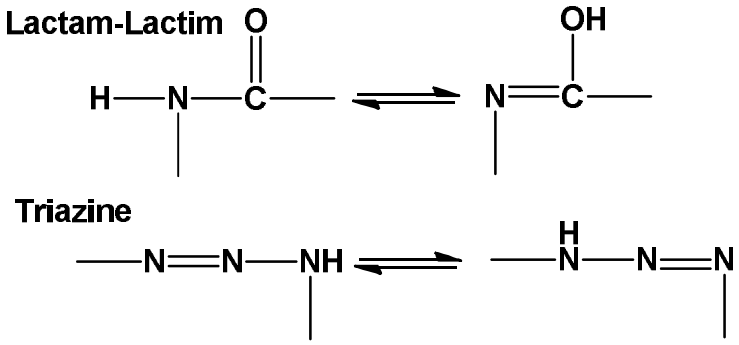


keto form enol form

2. Diad system:

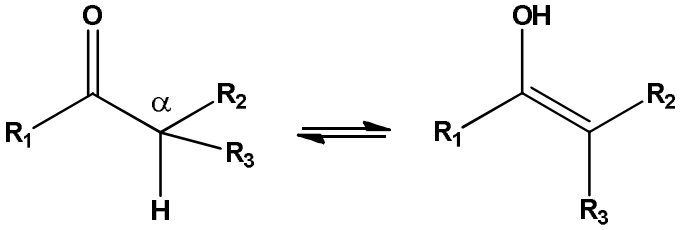


3. Triad system:



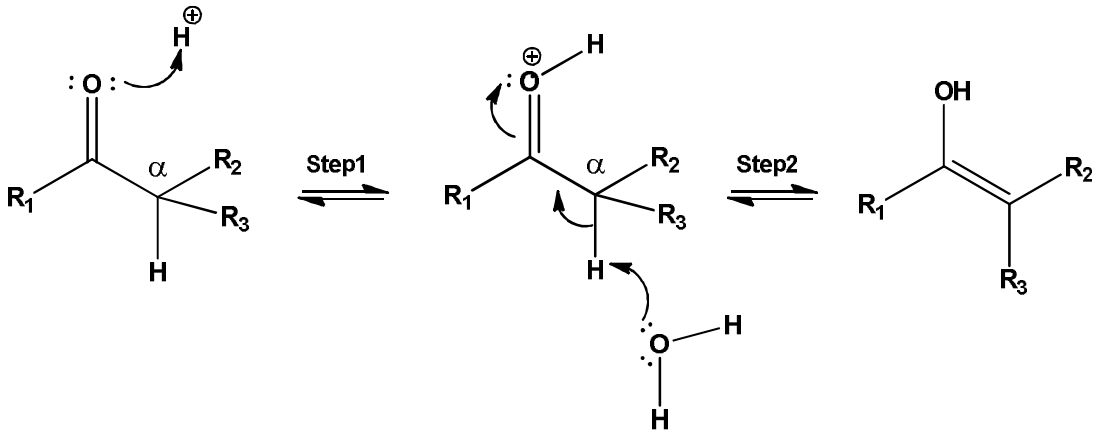
Keto-enol tautomerism

Ketones that have hydrogen atoms on their α-carbon are in equilibrium along with an isomeric structure as enol in which the α-hydrogen ends up on the oxygen in place of the carbon..

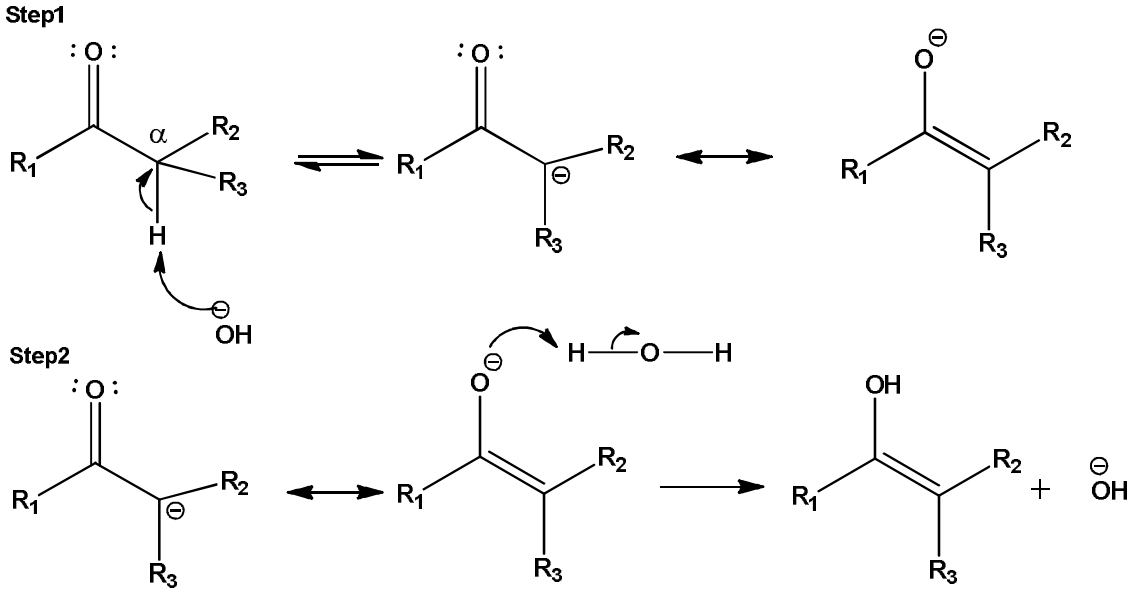


Tautomerism mechanism is catalyzed through acid or base. While catalyzed by acid, the carbonyl group works as a nucleophile with the oxygen by using a lone pair of electrons to create a bond with a proton.

Acid catalyzed mechanism:

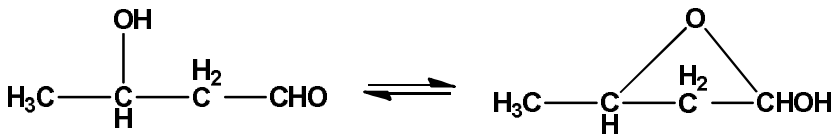


Base catalyzed mechanism:



2. Ring chain Tautomerism:

In some of the molecules, migration of hydrogen results into a ring formation. Thus ring chain tautomers are those which one of the isomer is in ring form and the other is in chain form.



3. Valence Tautomerism:

It is quite distinct from resonance, even through only electrons shift in it, The positions of the nuclei are not the same in two structures. Molecules that eschibit valance tautmerism are said to have fluxinal structures. eg. Bicyclo (5.1.0) Ociadience. Bullvalene.

1.8 Inductive Effect

Inductive effect is defined as permanent polarization due to electron withdrawing or electron donating effect of shared electron pair in a carbon chain towards more electronegative atom or group. Inductive effect occurres due to difference in electronegativities between two atoms forming an σ- bond. Its magnitude gets dismished with increase in distance.

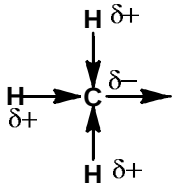
There are two types inductive effect depending on their strength of electron withdrawing or electron releasing nature with respect to hydrogen.

1) Positive Inductive effect, 2) Negative Inductive effect.

1) Positive inductive effect (+I):

Positive inductive effect is denoted by +I. Atoms or functional groups that show electron releasing nature may have a possitive inductive effect (+I). Following are the examples of groups in the decreasing order of their +I effect.

$-C(CH_3)_3 > -CH(CH_3)_2 > -CH_2CH_3 > -CH_3 > H$



2) Negative inductive effect (-I):

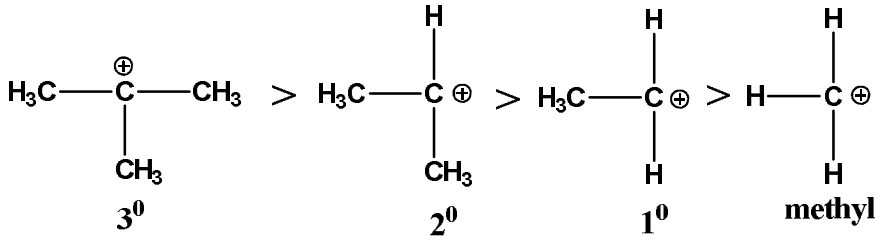
Negative inductive effect is denoted by -I. Atoms or functional groups that are electronegative relative to hydrogen such as the halogens, oxygen, nitrogen, etc. may have a negative inductive effect (-I), groups or atoms having decreasing order of –I effects is as follows.

$CN > CHO > CO > COOH > COCl > CONH_2 > F > Cl > Br > I > OH > NH_2 > H$

Applications of Inductive Effect:

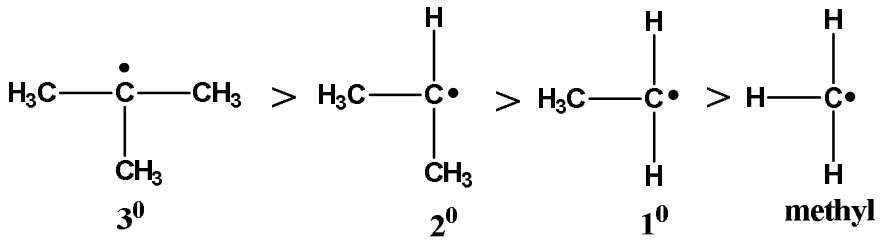
1. Stability of carbocation:

As number of alkyl substituent's increases the most stable carbocation is formed due to their +I effect. The alkyl groups release electrons to carbon through +I effect, bearing positive charge and thus stabilizes the ion. Hence tertiary carbocation is more stable than secondary than primary. The order of stability of carbocation or carboniuem ion is as follow:



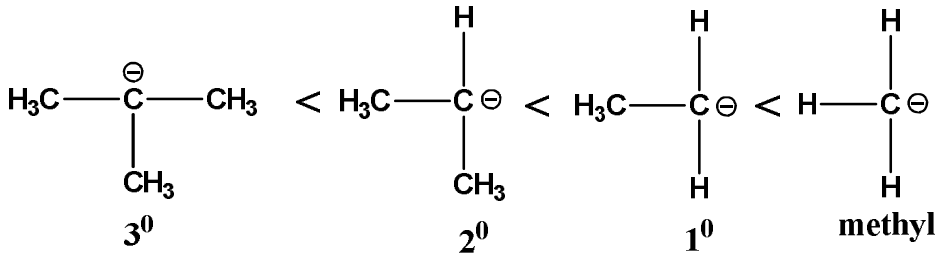
Stability of free radicals:

Stability of free radicals follows the same trend as that of carbocation hence stability increases with increase in the number of alkyl groups.



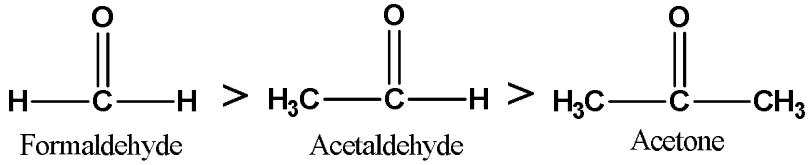
Stability of carbanions:

Stability of carbanions decreases with increase in the number of alkyl groups. Reason behind this is electron donating alkyl groups destabilize the carbanions as electron density is increased around it. The order of stability and reactivity of carbanions is:



Reactivity of carbonyl compounds:

The electron releasing groups increase the electron density (+I effect) at carbonyl carbon due to which their reactivity decreases towards nucleophile. Thus the order of reactivity follows:



The essential difference between the inductive and mesomeric effect

1. The inductive effect occurs essentially in saturated compounds while mesomeric effect in unsaturated and especially conjugated compounds.
2. The inductive effect involves the electrons in σ-bonds, while in the mesomeric effect electrons of π- bonds are inwowed.
3. Inductive effects are transmitted over only short distance in saturated chain whereas mesomeric effect may be transmitted from one end to the other of large molecules provided that conjugation is present though out the molecule.
4. Mesomeric effects are generally stronger than inductive effect.
5. +M group stabilizes an anion more effectively than a +I group.
6. The Inductive and Mesomeric effect influence:-
    - The strength of acids and bases.
    - Reactivity of alkyl halides.
    - Equilibria and rate of reaction.
    - Substitution in aromatic species.
    - Reactivity of Carbonyl compounds.

1.9 Summary

Delocalized chemical bonding involves resonance for which conjugation is must. The resonance depends upon the substituent's at aromatic system. Hyperconjugation increases the stability of intermediates i.e. Carbocation and free radicals. *Tautomers* are isomers of a compound which differ only in the position of the protons. Keto form is more stable than enol form. Tautomerism mechanism observed in acid as well as in basic medium. Due to difference in electronegativities between two atoms forming an σ- bond gives Inductive effect.

1.10 Glossary

- In a delocalized chemical bonding, one or more bonding orbitals that are not restricted to two atoms, but that are spread out over three or more atoms.

- Conjugated molecules have π electrons which are delocalized over double or triple bonds of molecules.
- Resonance can be used to delocalise both lone pairs of electrons and cationic charges which are adjacent to double bonds
- Delocalisation of positive and negative charges leads to relatively stable cations and anions, respectively.
- Due to resonance, *benzene ring becomes. ortho*, *para*-directing and activating groups are: O^-, NR_2, NH_2, OH, NHCOR, OCOR, SR, alkyl and aryl in aromatic compounds.
- Mesomeric effect in unsaturated and especially in aromatic compounds
- Hyperconjugation is the stabilizing interaction that results from the interaction of the electrons in a σ-bond (usually **C-H** or **C-C**) with an adjacent empty or partially filled p-orbital or a π-orbital to give an extended molecular orbital that increases the stability of the system.
- Alkyl substituent's having α- hydrogen on α- carbon with respect to sp^2 carbon is a must condition to give a hyperconjugation effect.
- In Tautomerism, isomers of a compound which differ only in the position of the protons and electrons and these isomers are rapidly interconvert.
- The inductive effect occurs in saturated compounds and is short range (unlike resonance effects).
- Alkyl groups give +I effect while other electronegative groups give –I effect.

1.11 Review questions / Comprehensive Questions

1. What is delocalized chemical bonding?
2. Explain the conjugation with example and its salient features.
3. What is cross conjugation? Explain with example.
4. What is resonance? Discuss its types with example.
5. Discuss the rules for resonance and orientation and reactivity in aromatic compounds.
6. Write a note on hyperconjugation and its applications.
7. What is tautomerism? Explain acid and base catalyzed keto-enol mechanism.
8. What is inductive effect? Discuss its types with example.
9. What is the difference between the inductive and mesomeric effect?

1.12 References and Suggested readings

1. A Guidebook to Mechanism in Organic Chemistry (6th ed.)- Peter Sykes (Longman Technical & Scientific) 1985.
2. Organic Chemistry- J. Clayden, Greeves, S. Warren and others (Oxford University Press) 2001.
3. March's Advanced Organic Chemistry (7^{th} ed.)- M. Smith and J. March (John Wiley & Sons, Inc., Hoboken, New Jersey) 2007.
4. Organic Reaction Mechanisms- V. K. Ahluwalia and R. K. *Para*shar (Narosa Publishing House) 2002.
5. Advanced Organic Chemistry- J. Singh and L. D. S. Yadav (Pragati Prakashan) 2005.

Unit-2 : Five And Six Membered Heterocycles Containing One Heteo Atom

Structure of Unit:

2.1 Objective

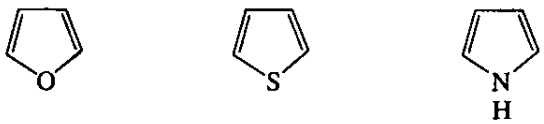
The study of heterocyclic compounds is of great interest from the theoretical as well as practical point of view. Heterocyclic compounds occur widely in natural as well as non-naturally occurring compounds. A large number of heterocyclic compounds are essential for life. Various compounds such as haemoglobin, alkaloids, vitamins, antibiotics, hormones and a large number of dyes and drugs contain heterocyclic ring systems. Knowledge of heterocyclic chemistry is useful in biosynthesis and metabolism of drug.

2.2 Introduction

Carbocyclic compounds in which one or more carbon atoms are replaced by hetero atoms, like oxygen, nitrogen and sulphur are known as heterocyclic compounds. Many important natural products such as alkaloids, chlorophyll, vitamins, drugs etc., are derivatives of simple five or six-membered nitrogen heterocycles.

2.3 Five membered heterocycles containing one hetero atom

Simple examples of this type of compounds are pyrrole, thiophene and furan containing respectively nitrogen, sulphur and oxygen as the hetero atom respectively. These are also referred to as azole, thiole and oxole respectively. Figre 2.1

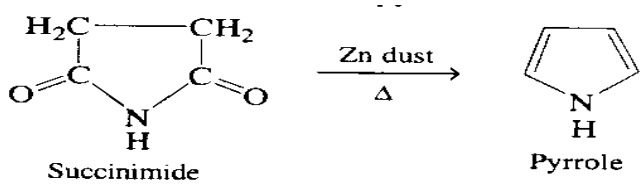


Furan (Oxole) Thiophene (Thiole) Pyrrole (Azole)

2.4 Pyrrole

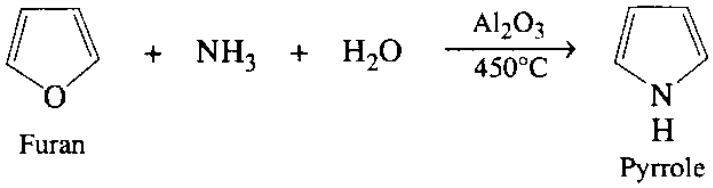
2.4.1 Methods of Preparation:

(i) From Succinimide:



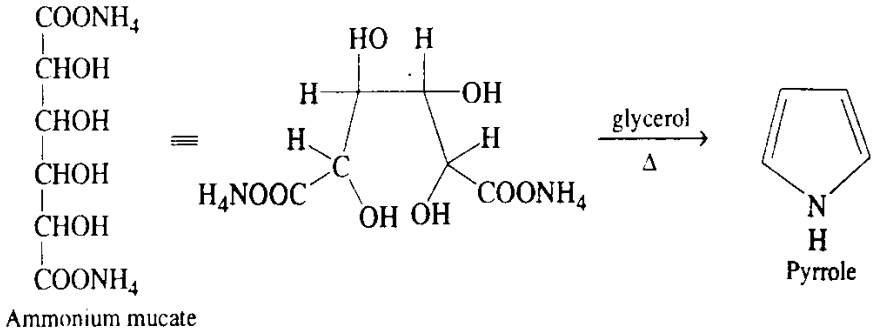
(Figure 2.2)

(ii) From Furan



(Figure 2.3)

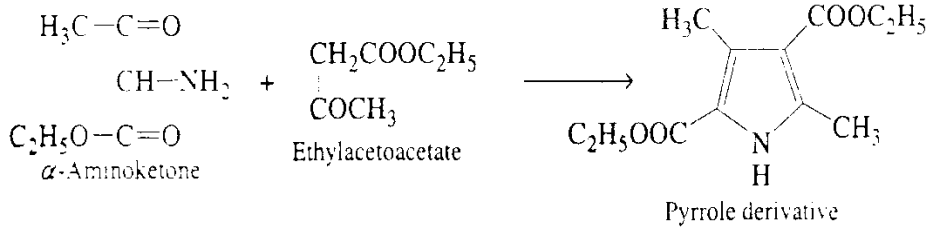
(iii) From Ammonium Mucate:



(Figure 2.4)

(iv) The Knorr Synthesis:

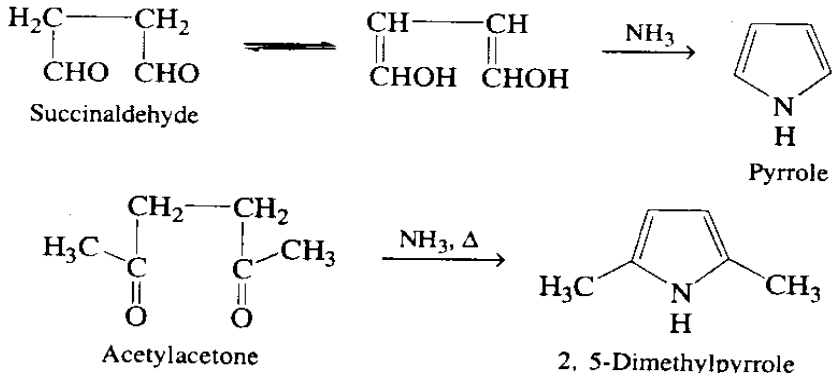
This method involves the condensation of an α-amino ketone or α-amino-β-keto ester with another dicarbonyl compound carrying an active methylene group in the presence of acetic acid.



(Figure 2.5)

(v) The Paal –Knorr Synthesis:

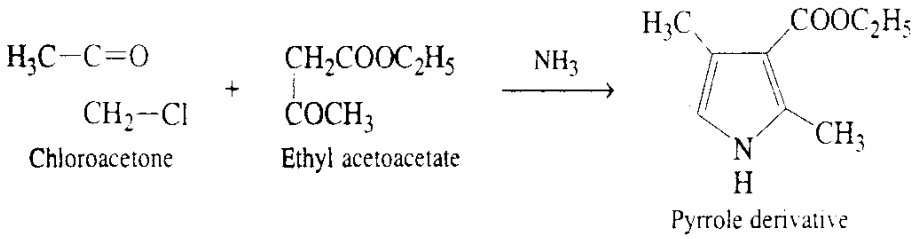
In this method condensation of a 1,4-diketone with ammonia or a primary amine yields pyrroles.



(Figure 2.6)

(vi) The Hantzsch Synthesis:

In this reaction condensation of an α-haloketone or aldehyde with a β-keto ester (or β-diketones) in the presence of a nitrogen containing base such as ammonia or an amine gives pyrrole derivatives.



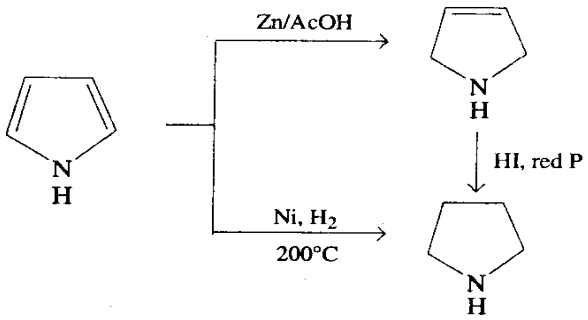
(Figure 2.7)

2.4.2 Physical Properties:

Pyrrole is a colourless liquid which has b.p. 131°C.It has an odour similar to that of chloroform. It is poorly soluble in water (around 5 %) but is completely miscible with most organic solvents.

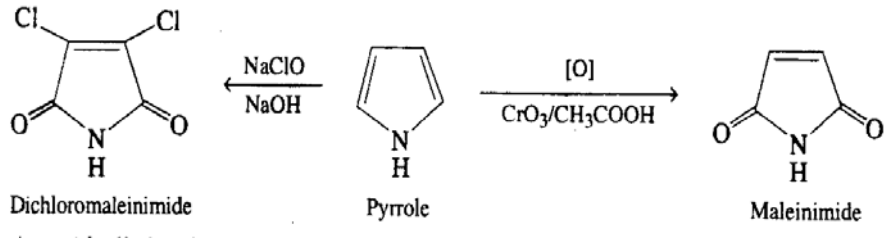
2.3.2 Chemical Reactions:

(i) Reduction:



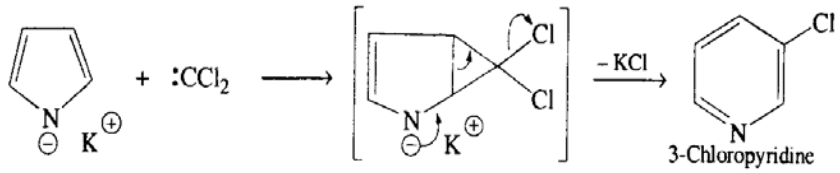
(Figure 2.8)

(ii) Oxidation:



(Figure 2.9)

(iii) Reaction with carbenes or Ring Expansion Reaction

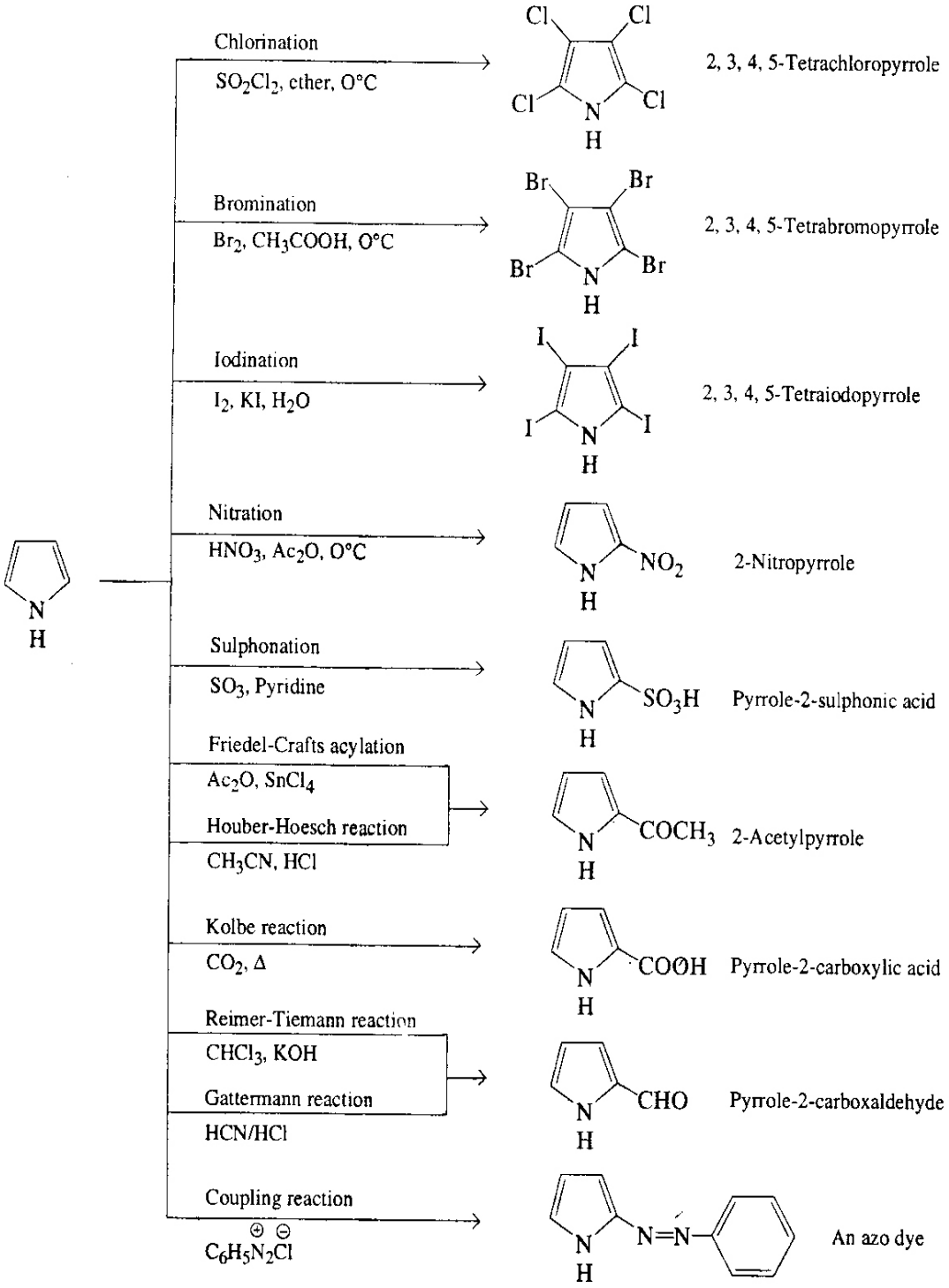


(Figure 2.10)

(iii) Electrophilic Substitution Reaction:

Five membered aromatic heteroeyclic compounds undergo electrophilic substitute reaction and are m ore reactive than bengene. Pyrrole undergoes electrophilic substitution predominantly at the 2-position rather than 3-position.

Pyrrole undergoes the following electrophilic substitution reactions:

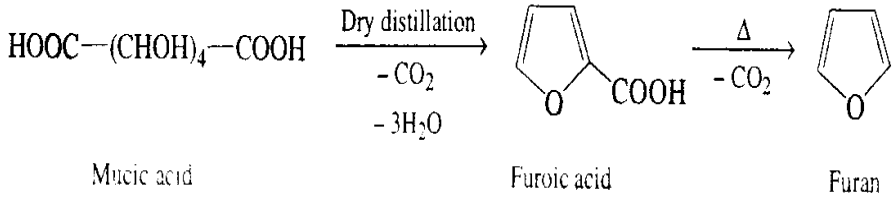

Chlorination
SO_2Cl_2, ether, 0°C
2, 3, 4, 5-Tetrachloropyrrole
Bromination
Br_2, CH_3COOH, 0°C
2, 3, 4, 5-Tetrabromopyrrole
Iodination
I_2, KI, H_2O
2, 3, 4, 5-Tetraiodopyrrole
Nitration
HNO_3, Ac_2O, 0°C
2-Nitropyrrole
Sulphonation
SO_3, Pyridine
Pyrrole-2-sulphonic acid
Friedel-Crafts acylation
Ac_2O, $SnCl_4$
Houber-Hoesch reaction
CH_3CN, HCl
2-Acetylpyrrole
Kolbe reaction
CO_2, Δ
Pyrrole-2-carboxylic acid
Reimer-Tiemann reaction
$CHCl_3$, KOH
Gattermann reaction
HCN/HCl
Pyrrole-2-carboxaldehyde
Coupling reaction
$C_6H_5N_2Cl$
An azo dye

(Figure 2.11)

2.5 Furan

2.5.1 Methods of Preparation:

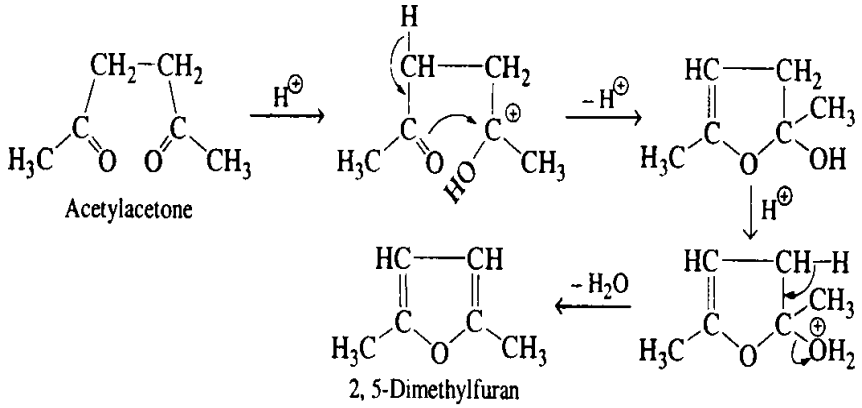
(i) From Mucic Acid:



(Figure 2.12)

(ii) The Paal-Knorr Synthesis:

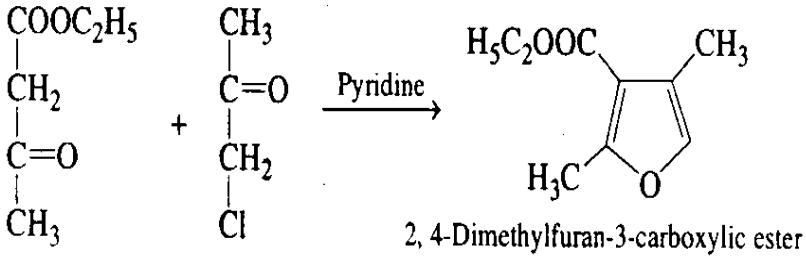
The cyclization of 1,4-diketones under acidic reagents results in furan formation.



(Figure 2.13)

(iii) The Fiest-Benary Synthesis:

In this method an aldol condensation of an α-haloketone or aldehyde is condesened with a,β-keto ester (or a β-diketone) in the presence of pyridine.



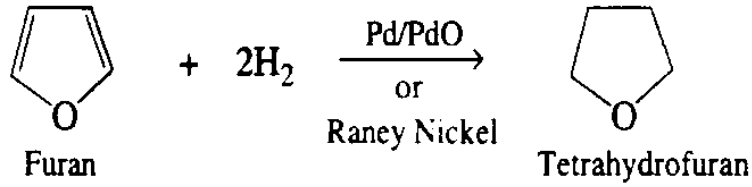
(Figure 2.14)

2.5.2 Physical Properties:

Furan is a colourless liquid of boiling point 32^0C.It is insoluble in water but is soluble in most organic solvents.

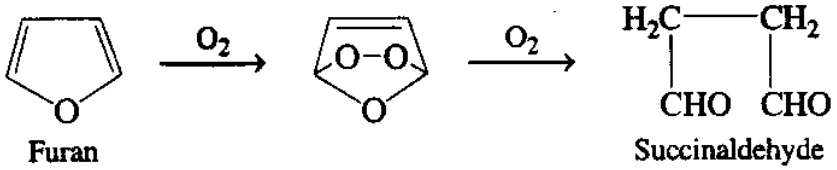
2.5.3 Chemical Reactions:

(i) Reduction:



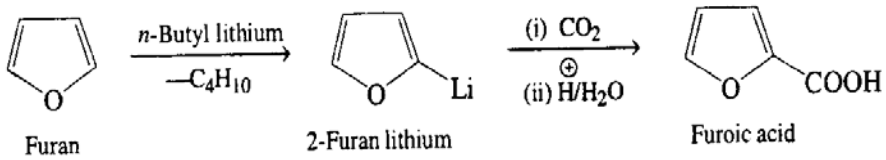
(Figure 2.15)

(ii) Oxidation:



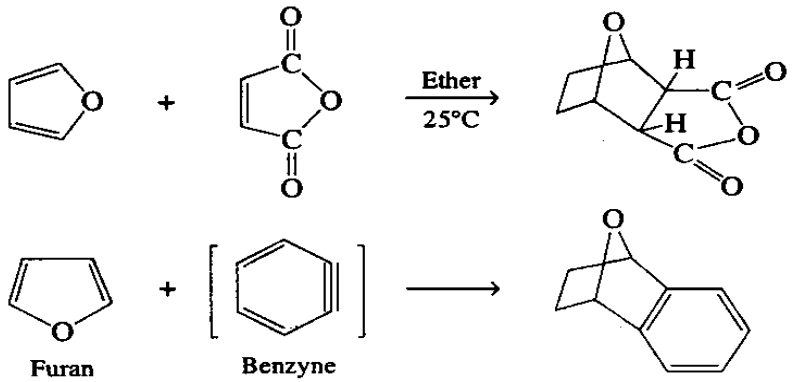
(Figure 2.16)

(iii) Reaction with n-Butyl lithium



(Figure 2.17)

(iv) Diels Alder Reaction:

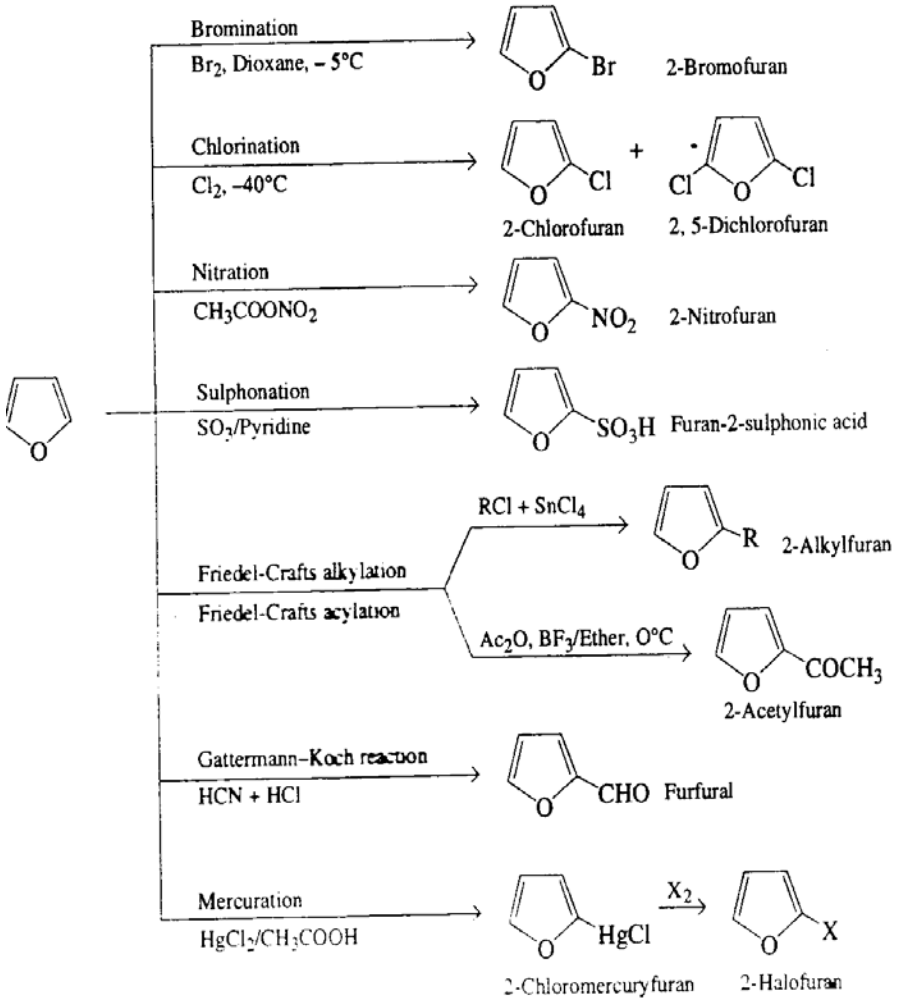


(Figure 2.18)

(vi) Electrophilic Substitution Reaction:

The 2-position of furan nucleus is much more reactive towards electrophilic substitution reaction than the 3-position.

Some electrophilic substitution reactions of furan are given below.

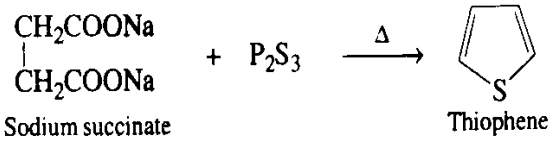


(Figure 2.19)

2.6 Thiophene

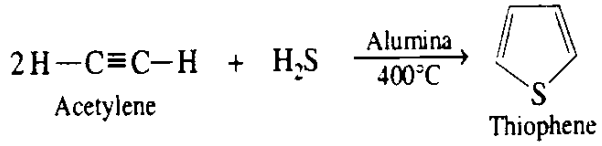
2.6.1 Methods of Preparation

(i) From Sodium Succinate:



(Figure 2.20)

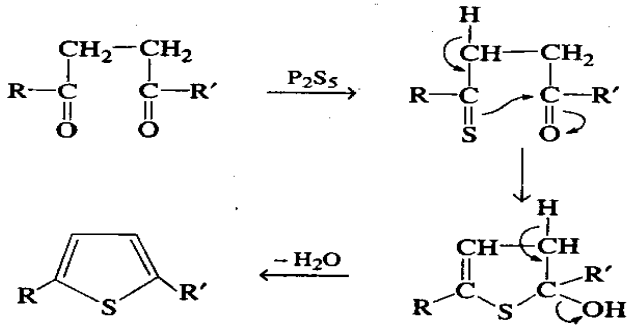
(iii) From Acetylene:



(Figure 2.21)

(ii) The Paal-Knorr Synthesis:

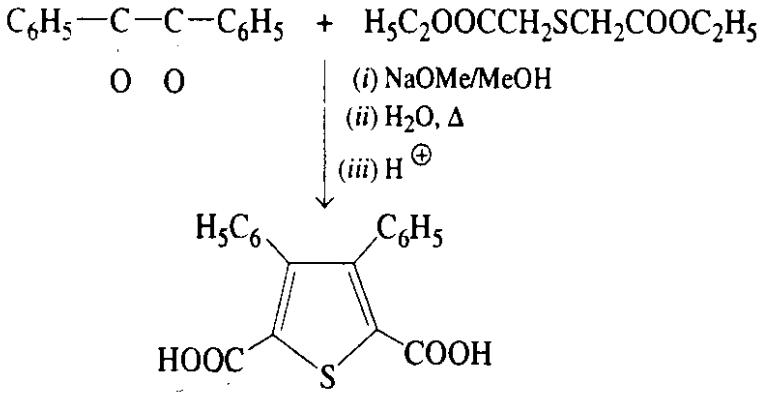
When enolizable 1, 4-diketone is heated with phosphorus pentasulfide to give rise to 2,5-disubstituted thiophenes.



(Figure 2.22)

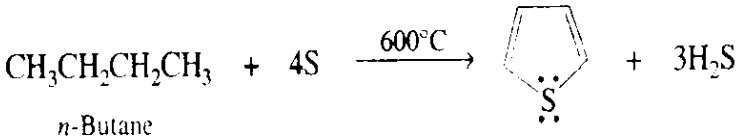
(iv)The Hinsberg Method:

This method involves the reaction between 1, 2 dicarbonyl compound and diethylthiodiacetate in the presence of strong base.



(Figure 2.23)

(v) From Butane:



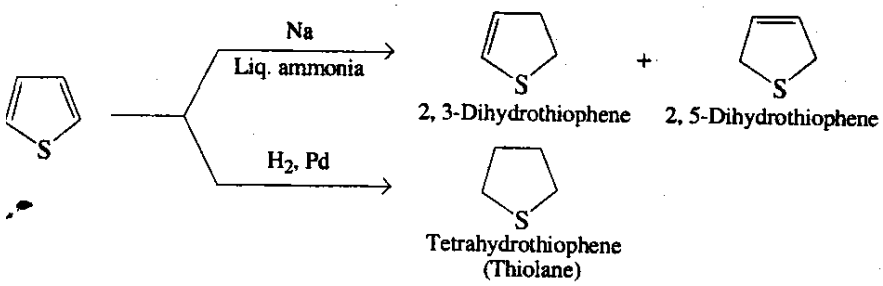
(Figure 2.24)

2.6.2 Physical Properties:

Thiophene is a colourless liquid, b.p. 80^0C and the freezing point is -38.3^0C.It is miscible with water but soluble in most organic solvents.

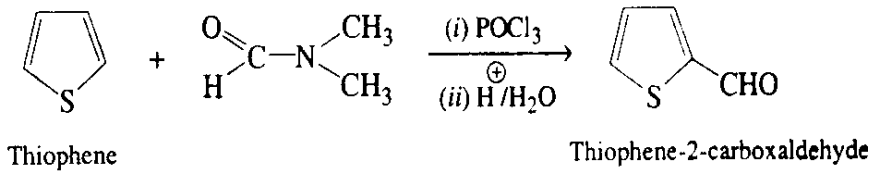
2.6.3 Chemical Reactions:

(i) Reduction:



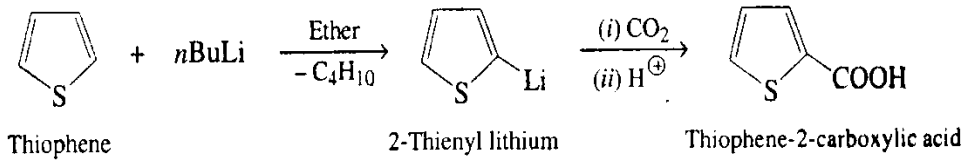
(Figure 2.25)

(ii) Vilsemeier Formylation Reaction:



(Figure 2.26)

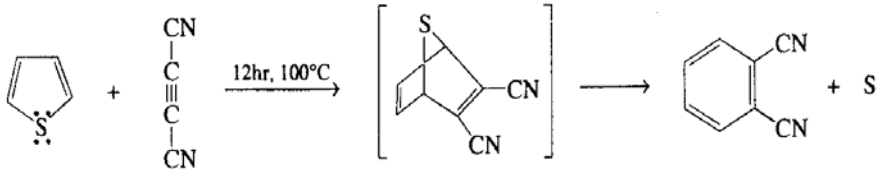
(iii) Reaction with n-Butyl lithium:



(Figure 2.27)

(iv) Diels-Alder Reaction:

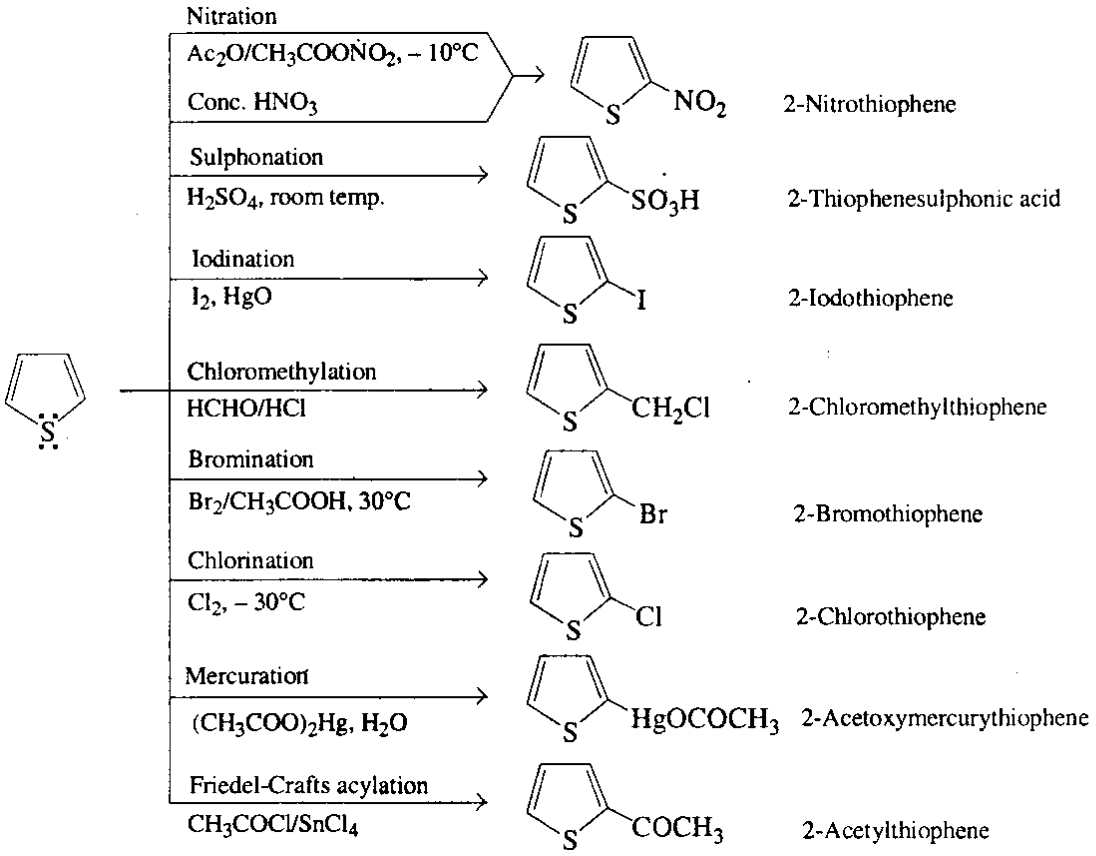
This phere does not undergo diels Aldus reactions under normal condition.



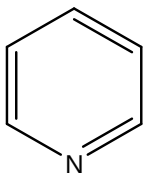
(Figure 2.28)

(v) Electrophilic Substitution Reaction:

As in the case of pyrrole and furan, electrophilic substitution reaction reactions of thiophene take place at position-2. Some of the common electrophilic substitution reaction reactions of thiophene are given below.

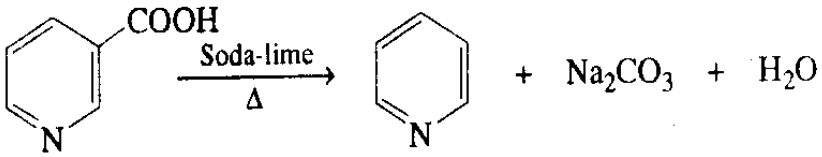


2.7 Pyridine



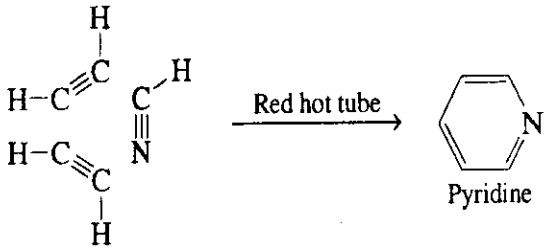
2.7.1 Methods of Preparation:

(i) From Nicotinic Acid:



(Figure 2.30)

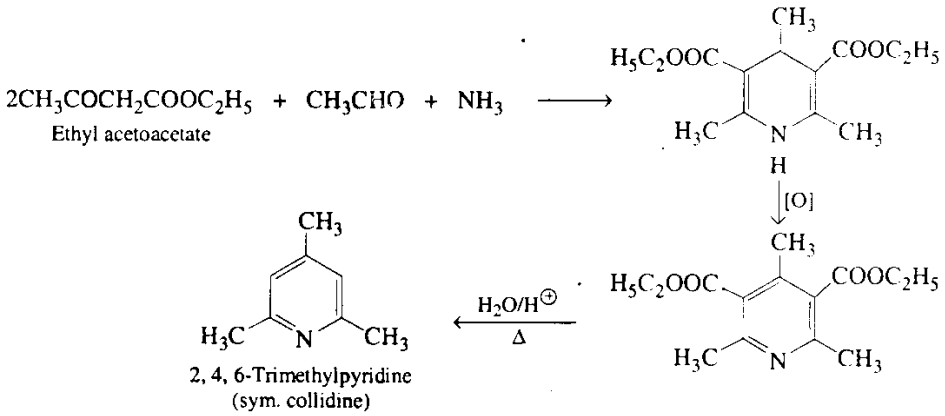
(ii) From Acetylene and Hydrogen Cyanide:



(Figure 2.31)

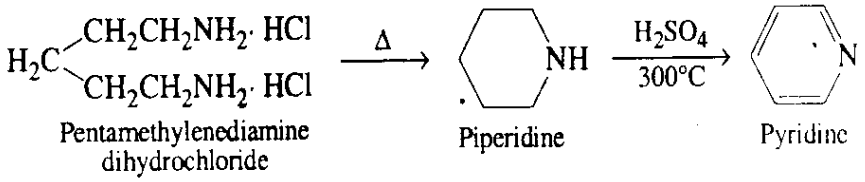
(iii) The Hantzsch Synthesis:

This is the most important synthesis of pyridine which involves the condensation of an aldehyde with two moles of a β-dicarbonyl compounds and ammonia.



(Figure 2.32)

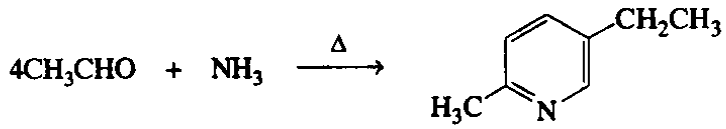
(iv) From pentamethylene diamine:



(Figure 2.33)

(v) Chichibabin Pyridine Synthesis:

The reaction of carbonyl compounds with ammonia or amines under pressure yield pyridine derivatives.



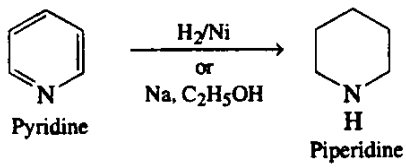
(Figure 2.34)

2.7.2 Physical Properties:

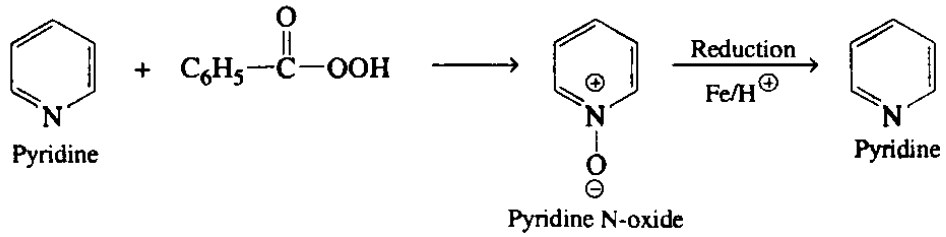
Pyridine is a colourless liquid, b.p. 115°C having a characteristic unpleasant odour. It is miscible with water due to the presence of H bonding between pyodine & water. Its dipole moment is 2.3 D.

2.7.3 Chemical Reactions:

(i) Reduction:



(ii)Oxidation:

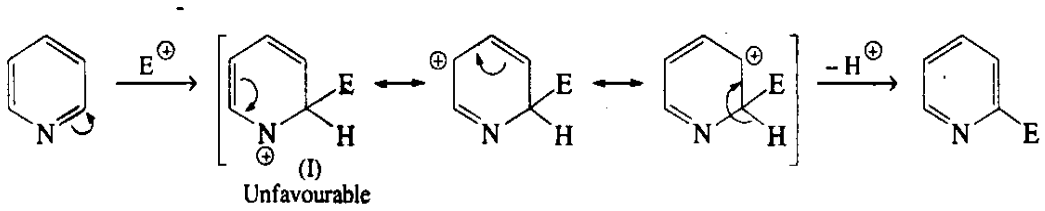


(Figure 2.35)

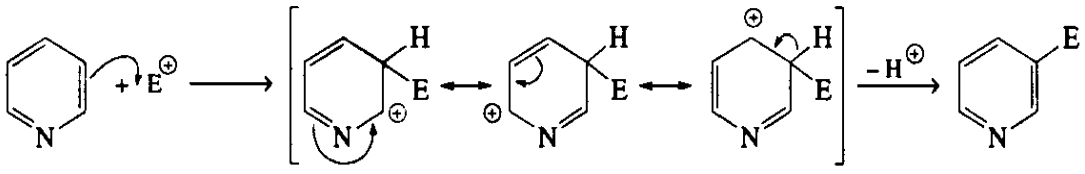
(iii) Electrophilic Substitution Reaction:

In pyridine, the nitrogen atom deactivates position 2 and 4 more than 3.So the electrophilic substitution takes place preferably at position 3.

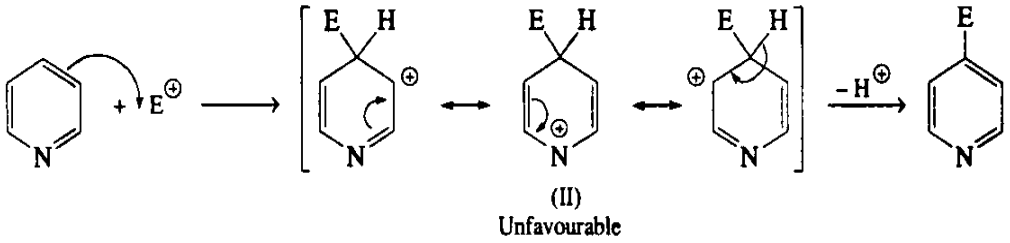
Substitution at position-2



Substitution at position-3



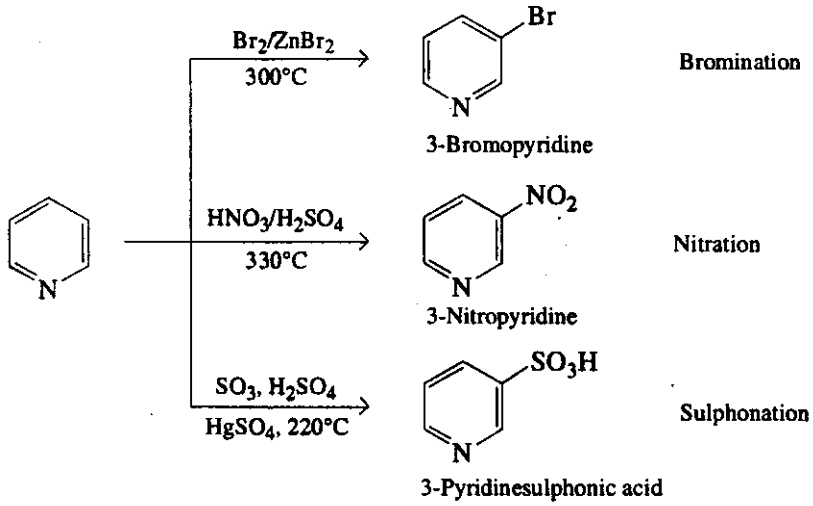
Substitution at position-4



(Figure 2.36)

The intermediate cations (I and II) formed during 2- and 4-substitution respectively are unstable and hence the attack at carbon 2 and 4 is unfavorable energetically. Therefore, the product with substitution at carbon 3, where no such situation arises, predominates and is favourable.

Some typical electrophilic substitution reactions of pyridine are given below.

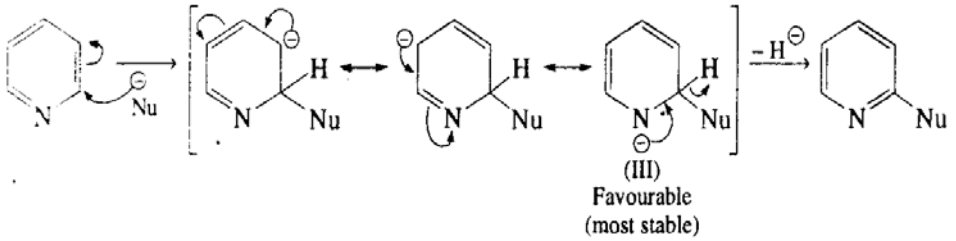


(Figure 2.37)

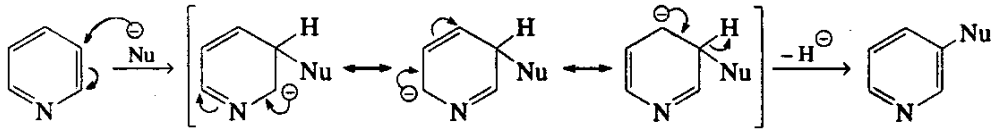
(iv) Nucleophilic Substitution Reaction:

Nucleophilic substitution in pyridine take place at position -2 and -4.This is clearly understood by considering the intermediates arising due to attack of nucleophilic on position -2,-3 and 4.Substitution does not take place at position-3.

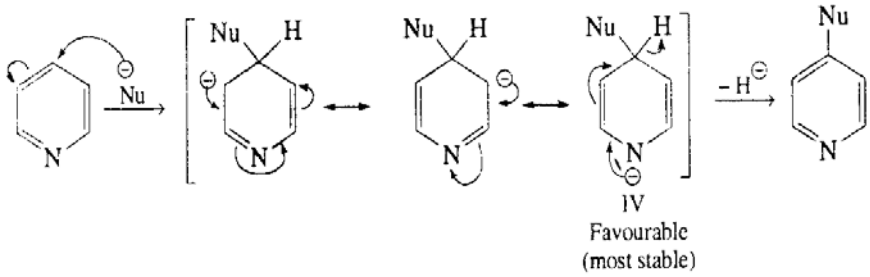
Substitution at position-2



Substitution at position-3



Substitution at position-4

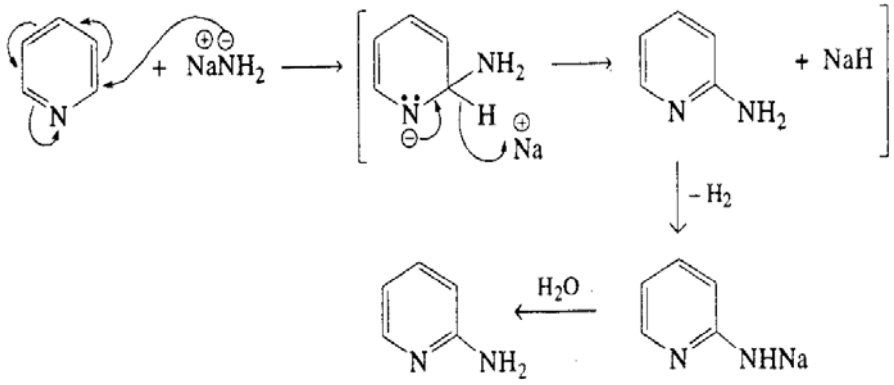


(Figure 2.38)

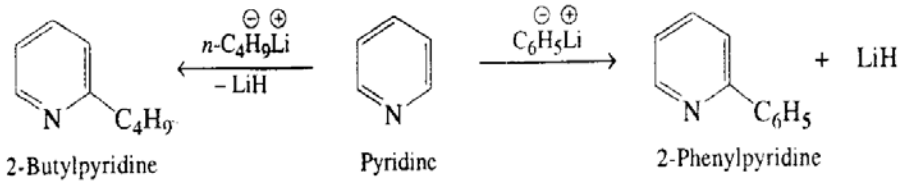
As it has been observerd that, one of the intermediate obtained due to attack at position -2 and -4 is having negative charge on N. There is no such structure arising due to attack at position-3.

Some important nucleophilic substitution reactions of pyridine are given below:

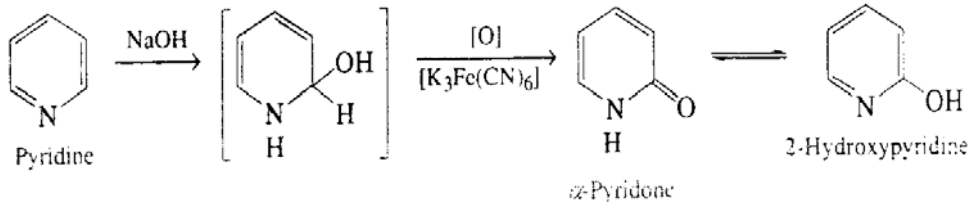
(a) Chichibabin reaction:



(b)Reaction with organolithium compounds:

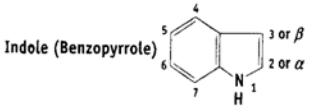


(c) Reaction with sodium hydroxide:



(d) Nucleophilic substitution of halogens at 2- or 4-positions in halopyridines:

2.8 Indole

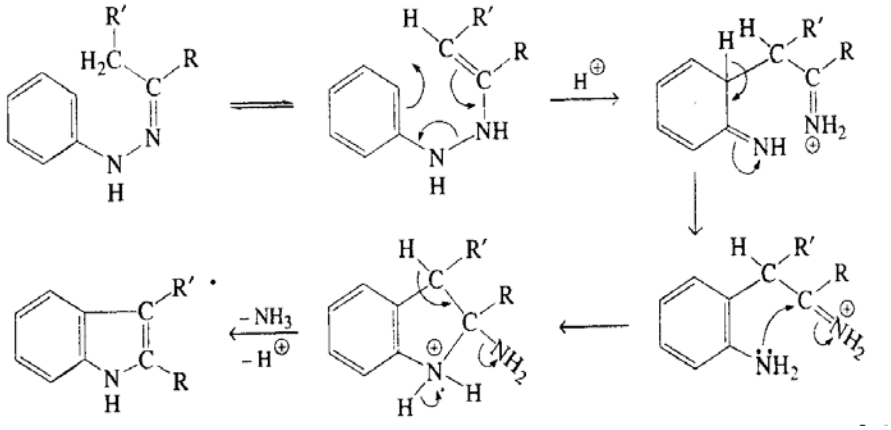


2.8.1 Methods of Preparation:

(i) The Fischer-Indole Synthesis:

This method involves an acid-catalyzed rearrangement of a phenylhydrazone of an aldehyde or ketone, with the elimination of a molecule of ammonia. Zinc chloride, polyphosphoric acid or a Lewis acid BF_3 are used as a catalyst in this method.

The probable mechanism is as follows:

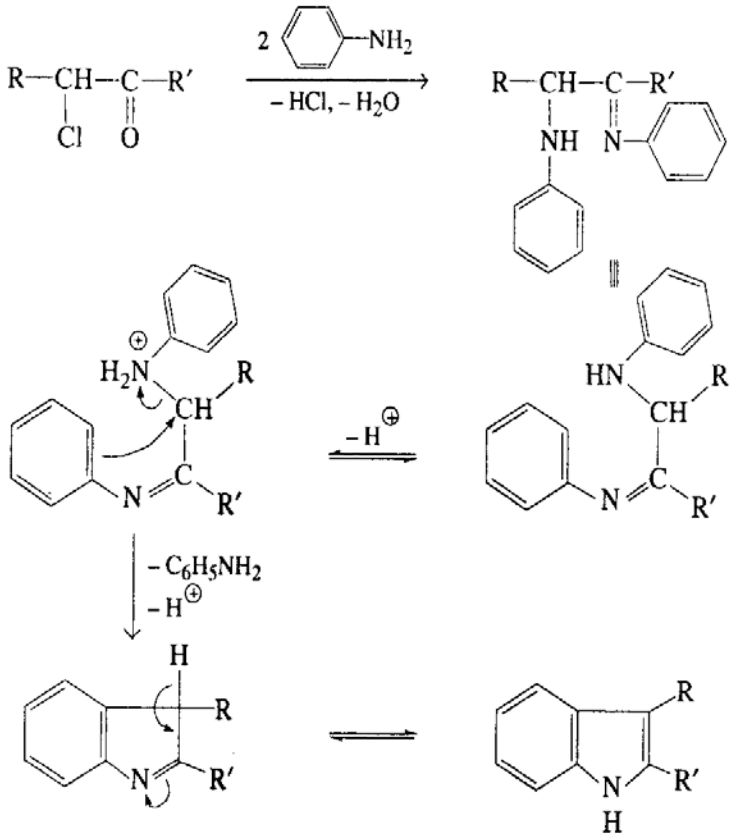


(Figure 2.40)

(ii) The Bischler Synthesis:

When α-arylaminoketone or aldehyde (prepared from α-halo ketone or aldehyde) is with heated an arylamine in the presence of zinc chloride or an acid, it forms an indole derivative.

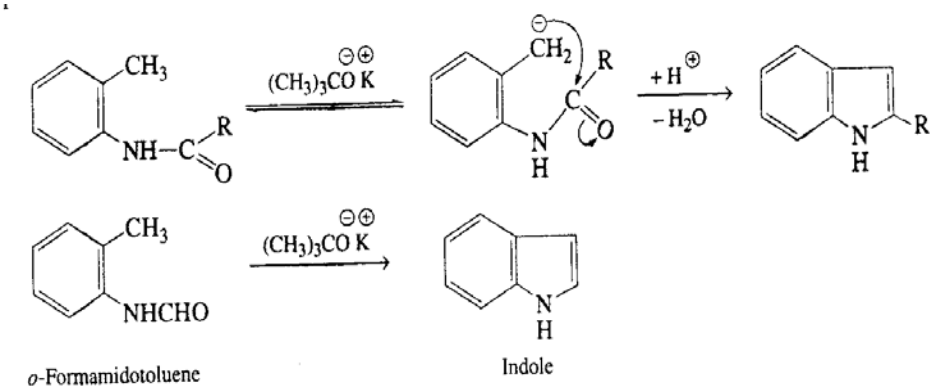
The probable mechanism is as follows:



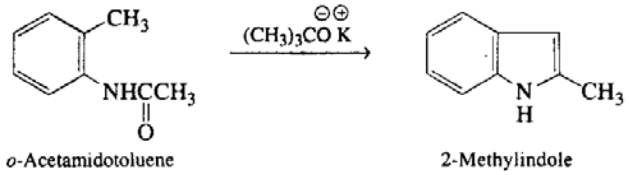
(Figure 2.41)

(iii) The Medelung Synthesis:

This method involves the dehydration and cycliasation of an of an o-acetamidotoluene in the presence of a strong base at high temperature.



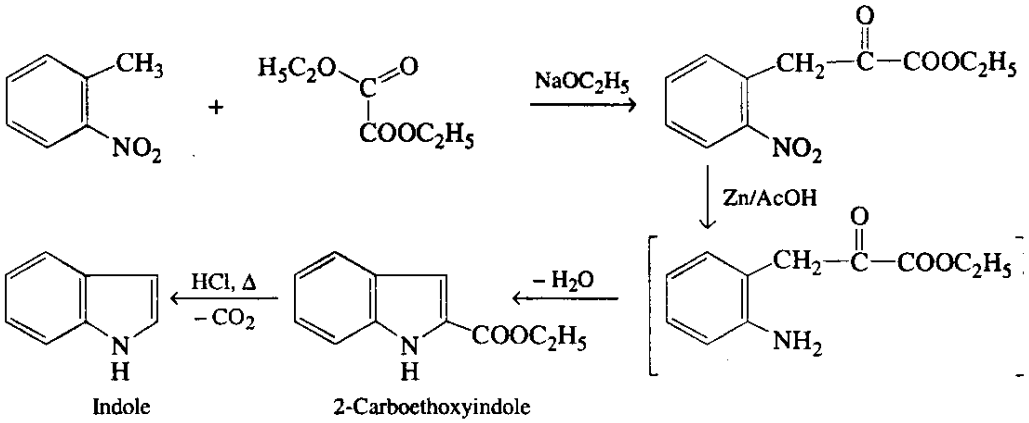
(Figure 2.42)



(Figure 2.43)

(iv) The Reissert Indole Synthesis:

It involves a base-catalyzed condensation of o-nitrotoluene with oxalic acid ester in the presence of sodium ethoxide.



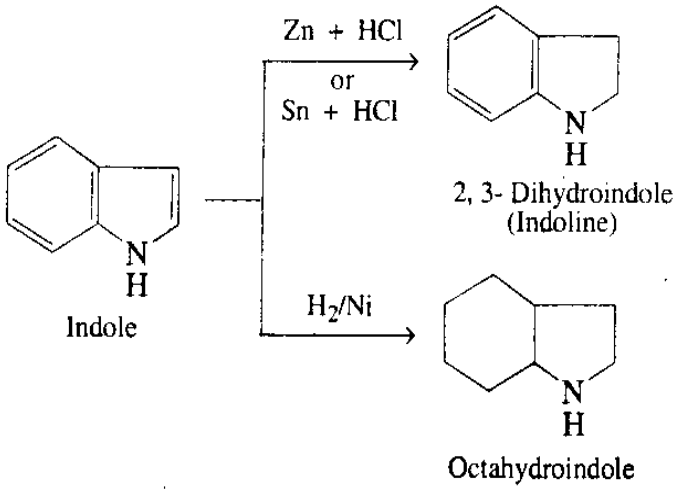
(Figure 2.44)

2.8.2 Physical Properties:

Indoles are colourless crystalline solids. Indole melts at 52^0C and boils at 254^0C.It is a soluble in most of organic solvents. Pure indole has a very pleasant smell and is used as a perfume base, impure indole has unpleasant odour.

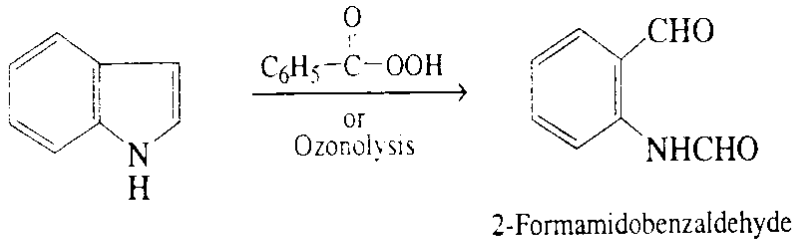
2.8.3 Chemical Reactions:

(i) Reduction:



(Figure 2.45)

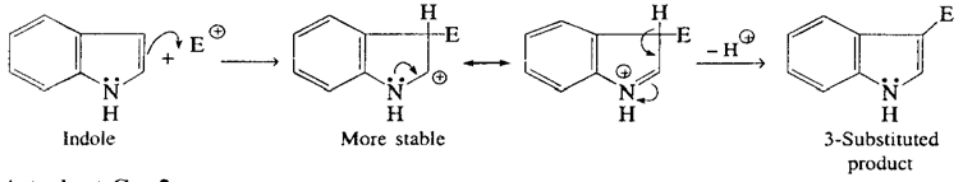
(ii) Oxidation:



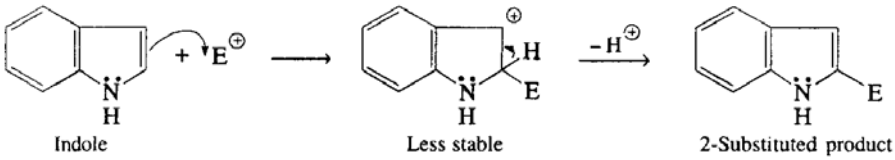
(Figure 2.46)

(iii) Electrophilic Substitution Reaction: Indole, isextremely susceptible to electrophilic substitutions and at position-3, pyrrole takes place at position-2.This is due to the fact that all ack at the position of indole ring intermediate C non benzendid streel in obtained which not preffer. Comparable stabilities of the transition states resulting due to the electrophilic attack at position -2 and -3.

Attack at position - 3

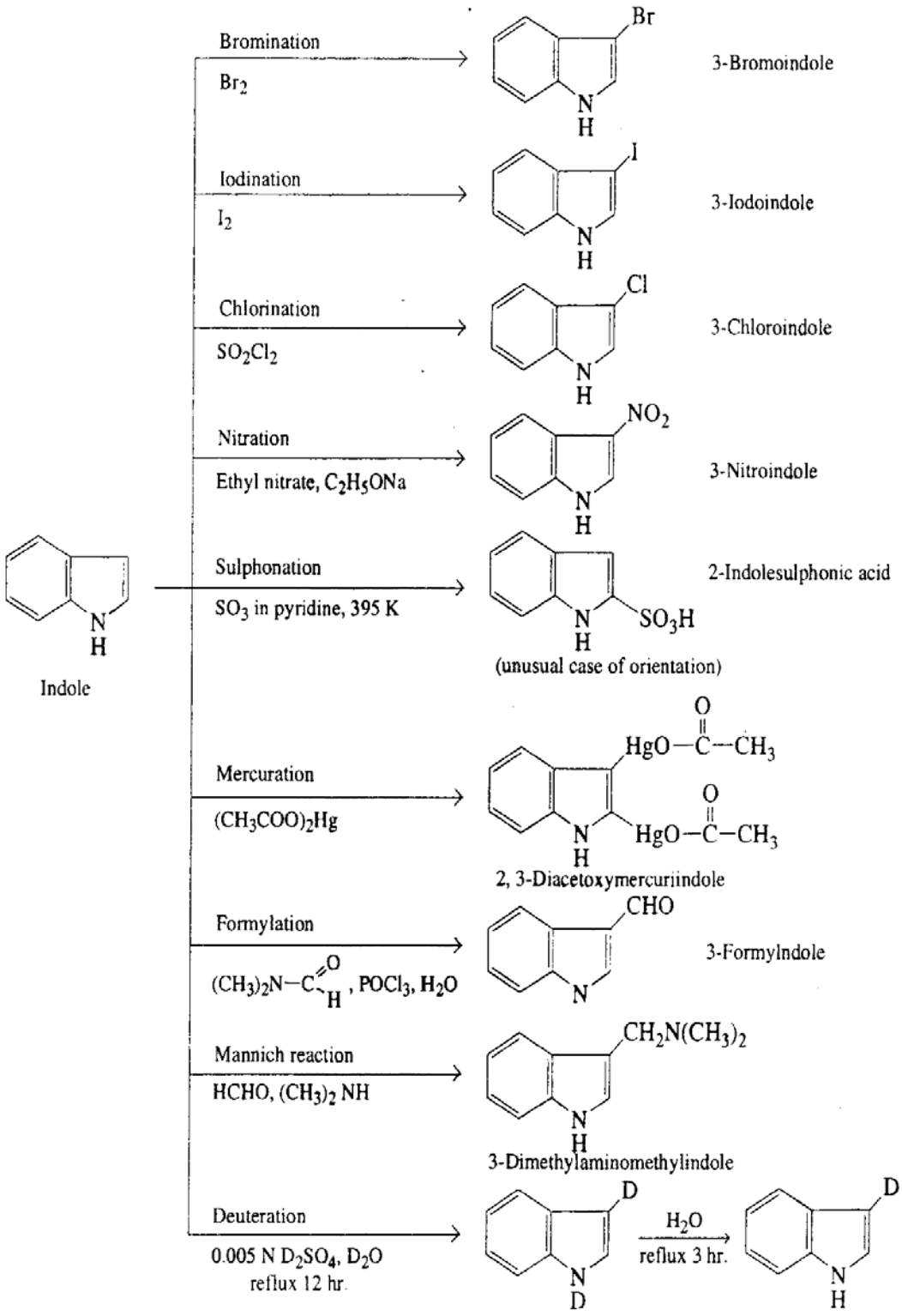


Attack at position - 2



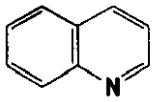
(Figure 2.47)

Some important electrophilic substitution reactions of indole are as follows.


Indole
Bromination
Br2
3-Bromoindole
Iodination
I2
3-Iodoindole
Chlorination
SO2Cl2
3-Chloroindole
Nitration
Ethyl nitrate, C2H5ONa
3-Nitroindole
Sulphonation
SO3 in pyridine, 395 K
2-Indolesulphonic acid
(unusual case of orientation)
Mercuration
(CH3COO)2Hg
2, 3-Diacetoxymercuriindole
Formylation
(CH3)2N—C(=O)H, POCl3, H2O
3-Formylndole
Mannich reaction
HCHO, (CH3)2 NH
3-Dimethylaminomethylindole
Deuteration
0.005 N D2SO4, D2O
reflux 12 hr.
H2O
reflux 3 hr.

(Figure 2.48)

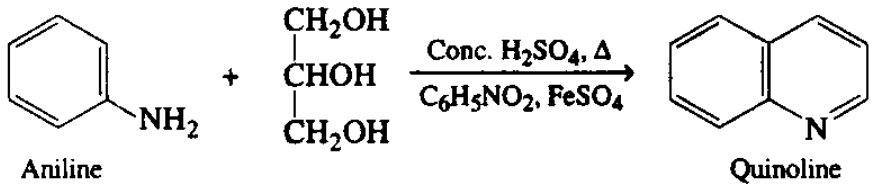
2.9 Quinoline



2.9.1 Methods of formation:

(i) The Skrup Synthesis:

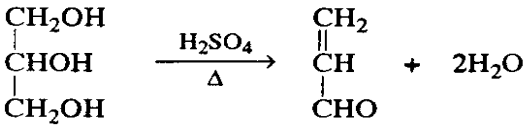
Quinoline can be prepared by heating aniline (containing at least one vacant ortho position) with glycerol in the presence of concentrated sulphuric acid and nitrobenzene as oxidizing agent.



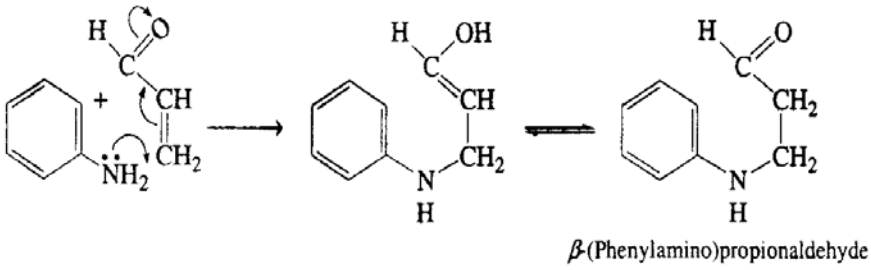
(Figure 2.49)

The mechanism of the reaction involves the following sequence of steps:

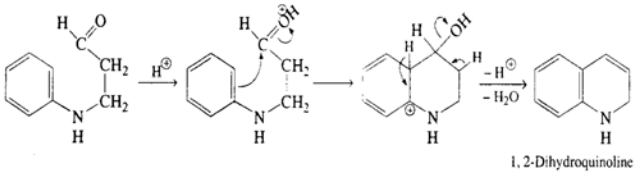
(a) Dehydration of glycerol to acrolein



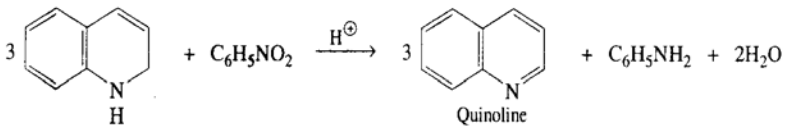
(b) Michael addition of aniline to acrolein yields, β- (phenylamino) propionaldehyde



c) Intramolecular electrophilic substitution upon the aromatic ring by protonated aldehyde followed by dehydration yields 1, 2-dihydroquinoline.



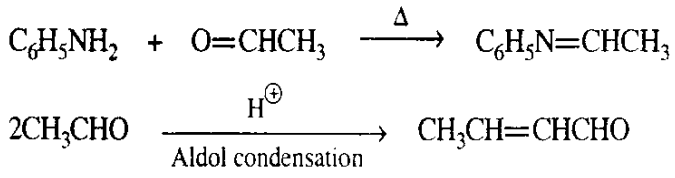
(d) Dehydrogenation of 1, 2-dihydroquinoline by nitrobenzene yields quinoline.

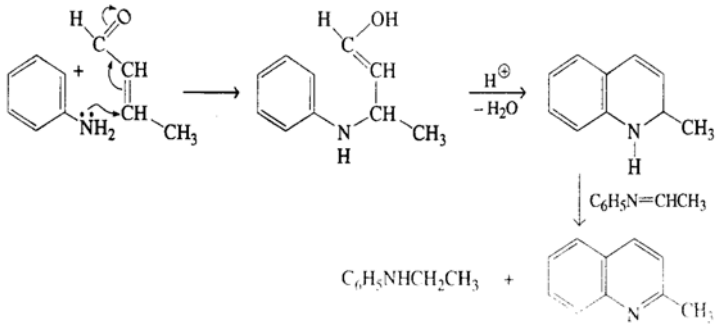


(Figure 2.50)

(ii) The Doebner-Miller Synthesis:

In this synthesis an aromatic amine (aniline) and an aldehyde (acetaldehyde) are heated in the presence of hydrochloric acid.





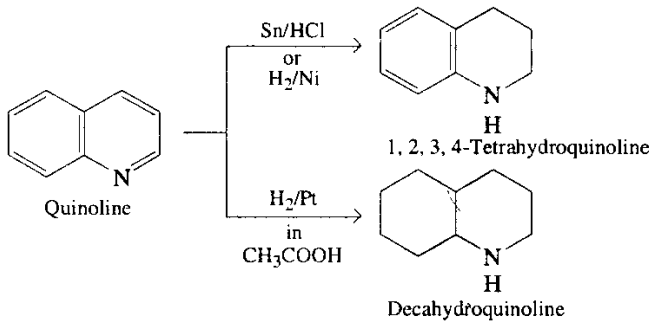
2.9.2 Physical Properties:

Quinoline is a colourless hygroscopic liquid; b.p. 237^0C.It has a characteristic smell resembling that of pyridine. On exposure of air it develops a yellow colour.

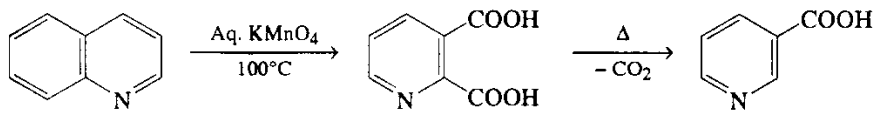
2.9.3 Chemical Reactions:

Quinoline exhibits the reactions of both pyridine and benzene. Some important reactions are as follows:

(i) Reduction:

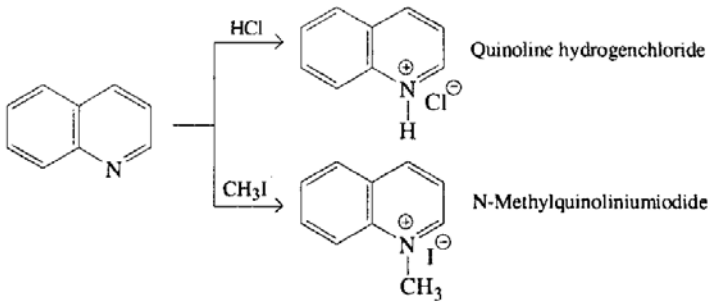


(ii) Oxidation:



Quinoline | Pyridine-2, 3-dicarboxylic acid | Nicotinic acid

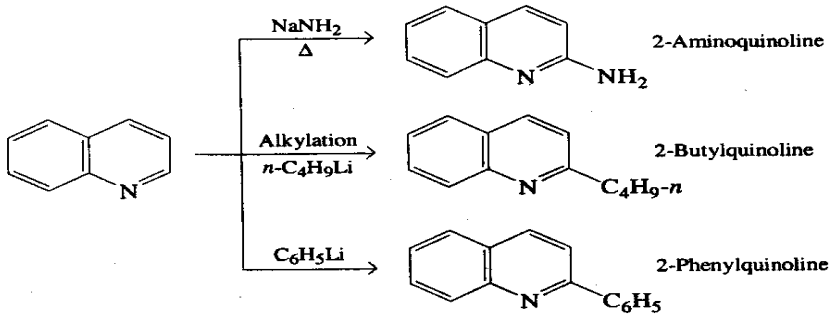
(iii) Basic Nature:



(Figure 2.52)

(iv) Nucleophilic Substitution Reaction:

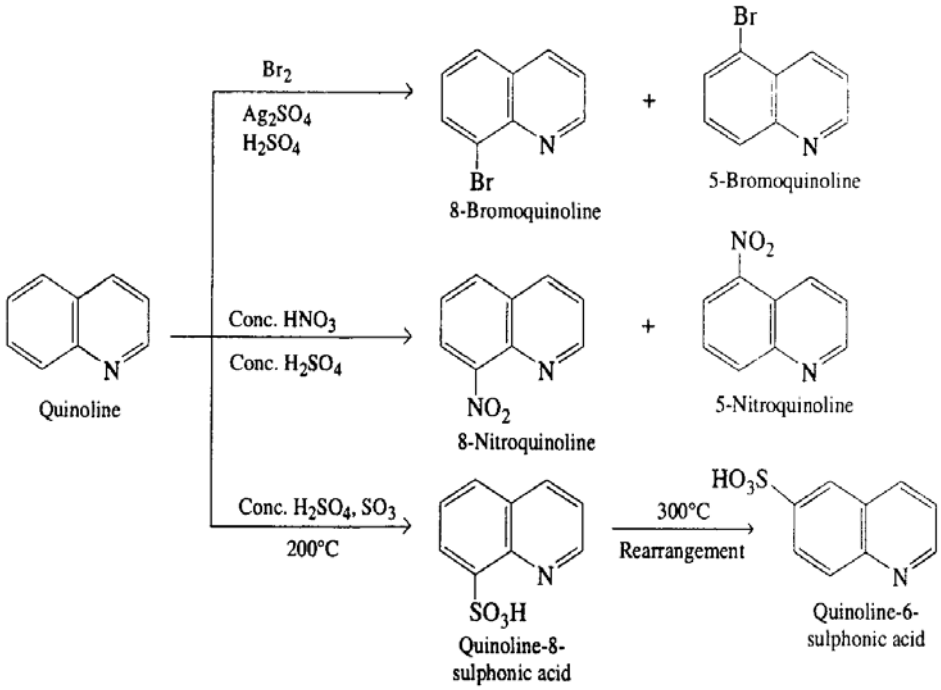
Attack by a nucleophile occurs in the pyridine ring of quinoline and position-2 is the preferred site for such an attack. If this position is occupied than attack may take place at the position-4.



(Figure 2.53)

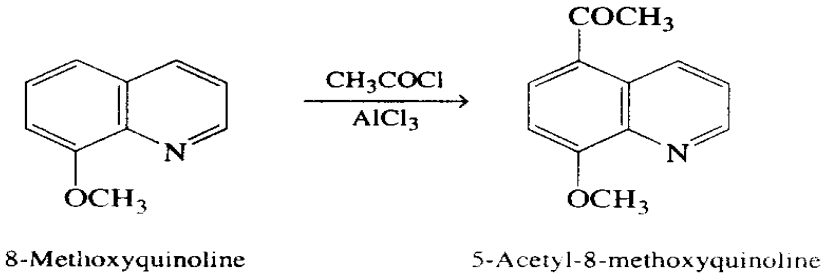
(v) Electrophilic Substitution Reactions:

The nitrogen atom has considerable deactivating effect on the ring towards electrophilic attack. Thus, electrophilic substitution occurs preferably at benzene half of the molecule. The reaction takes place preferably at 8-position in the benzenoid ring with small amounts of 5-substituted product.



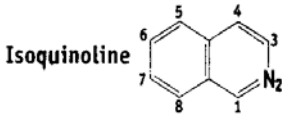
(Figure 2.54)

Quinoline bearing an activating group displays Friedel-Crafts acylation reaction. For example,



(Figure 2.55)

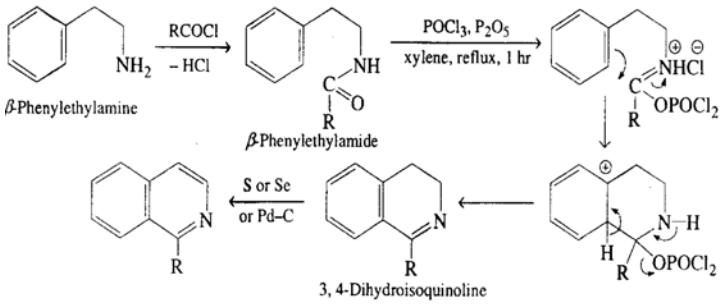
2.10 Iso-Quinoline



2.10.1 Methods of Preparation:

(i) The Bischler-Napieralski reaction:

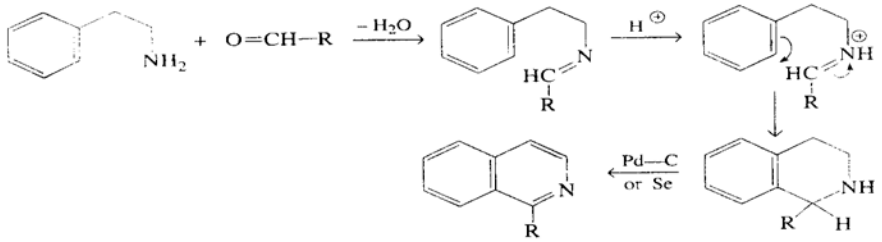
In this reaction, acyl derivatives of β-phenylethylamine undergo cyclodehydration by reacting with phosphoryl chloride to give dihydroisoquinoline. Subsequent oxidation of dihydroisoquinoline with Pd on charcoal yields corresponding isoquinolines.



(Figure 2.56)

(ii) The Pictet-Spengler Isoquinoline synthesis:

Isoquinolines can also prepared by condensingβ-phenylethylamine with aldehydes. Cyclization of the resulting Shifts bases in the presence of large excess of Hydrochloric acid leads to tetrahydroisoquinolines, which on oxidation give iso-quinolines.



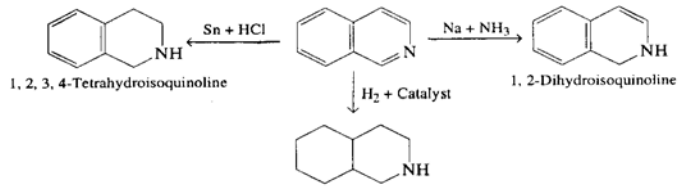
(Figure 2.57)

2.10.2 Physical Properties:

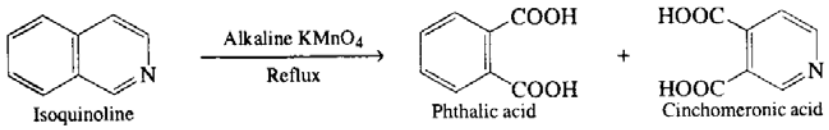
Isoquinoline is a colourless liquid, b.p. 243°C, sparingly soluble in water but miscible with alcohol and ether. It has a smell resembling that of benzaldehyde.

2.10.3 Chemical Reactions:

(i) Reduction:



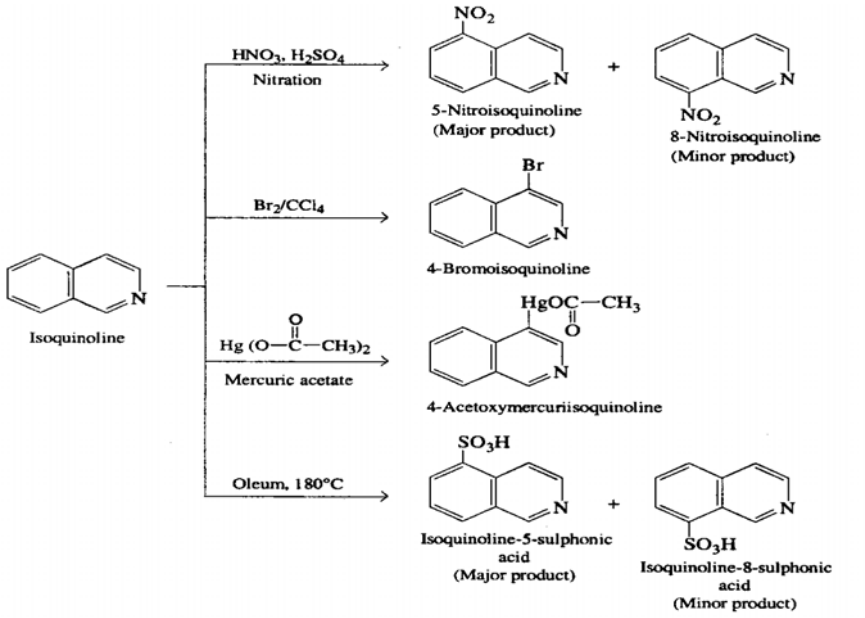
(ii) Oxidation:



(Figure 2.58)

(iii) Electrophilic Substitution Reaction:

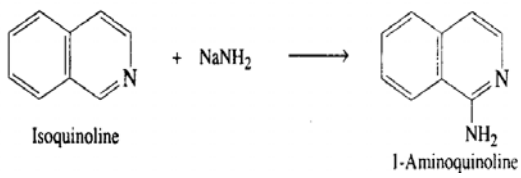
Analogous to quinoline, the electrophilic attack in isoquinoline takes place in the benzene ring due to the deactivation of the pyridine ring because of protonation. Electrophilic attack occurs mainly at 5-position though a small amount of 8-substituted product is also obtained. For example, nitration and sulphonation yield predominantly 5-substituted product. However, mercuration and brornination yield the 4-substituted product.



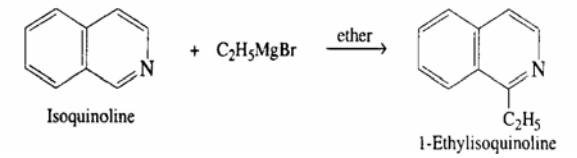
(Figure 2.59)

(iv) Nucleophilic Substitution Reaction:

Nucleophilic substitution in isoquinoline occurs mainly at position-1. Thus, l-amino isoquinoline is obtained on heating with sodamide (Chichibabin reaction)



Similarly, l-alkyl derivatives are obtained by treating isoquinoline with Grignard reagent.



(Figure 2.60)

2.11 Summary

- Pyrrole, Furan and Thiophene gives electrophilic substitution reaction at position-2.
- Pyrrole does not give Diels Alder Reaction.
- Furan and Thiophene gives Diels Alder Reaction.
- Pyridine is more basic than pyrrole.
- Pyridine gives nucleophilic substitution reaction at position -2 and -4.
- Pyridine gives electrophilic substitution reaction at position -3.
- Indole gives electrophilic substitution reaction at position-3.
- Quinoline gives nucleophilic substitution reaction at position-2.
- Quinoline gives electrophilic substitution reaction at position-8 of the benzene ring.
- Iso-Quinoline gives electrophilic substitution reaction at position-5of the benzene ring.
- Iso-Quinoline gives nucleophilic substitution reaction at position-1.

2.12 Review Question / Comprehensive Questions

1 How will you synthesize pyrrole by the following method

(a) The Paal-Knorr Synthesis (b) The Hantzsch Synthesis

2 Give the following reaction of pyrrole

(a) Nitration (b) Friedel Crafts-Acylation (c) Gattermann Reaction (iv)Reimer-Tiemann Reaction

3 How will you synthesize furan by the following method

(a) The Paal-Knorr Synthesis (b) The Fiest-Benary Synthesis

4 Give the following reaction of furan

(a) Sulphonation (b) Bromination (c) Mercuration (iv) Diels Alder Reaction

5 How will you synthesize thiophene by the following method:

(a) Hinsberg Method (b) From Acetylene (c) From Sodium Succinate (iv) From Butane

6 Give the following reaction of thiophene:

(a) Vilsemeier Formylation Reaction (b) Diels Alder Reaction (c) Reduction

7 Give any two Nucleophilic and Electrophilic substitution reaction of pyridine.

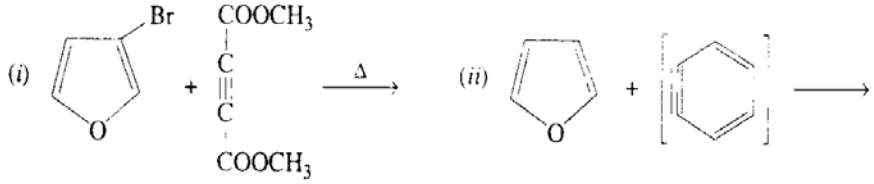
8 How will you synthesize indole by the following method:

(a) Fischer-Indole Synthesis (ii) Bischler Synthesis

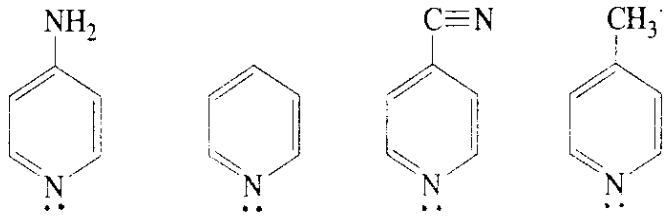
9 Explain the oxidation and reduction reactions of indole.

10 Give any four electrophilic substitution reaction of indole.

11. Write the structures of Diels-Alder adducts in the following reactions:



12 Arrange the following compounds in order of their increasing basicity:



13 How will you synthesize quinoline by the following method:

(a) Skrup Synthesis (ii) Doebner-Miller Synthesis

14 Give any two electrophilic and nucleophilic substitution reaction of quinoline.

15 How will you synthesize isoquinoline by the following method:

(a) Bischler-Napieralski Synthesis (ii) Pictet-Spengler Synthesis

14 Give any two electrophilic and nucleophilic substitution reaction of isoquinoline.

2.13 References and Suggested readings

1. Hetrocyclic Chemistry-II, R.R.Gupta, M.Kumar,V.Gupta, Springer,1998
2. Hetrocyclic Chemistry , Raj K.Bansal,New Age International Publishers,2010(Fifth Edition)
3. Hetrocyclic Chemistry , V.K.Ahluwalia, Narosa Publishing House,2012
4. Hetrocyclic Chemistry , Rakesh K.Parashar, Ane Books pvt. Ltd., 2010
5. Organic Chemistry-Vol.-3,Jag Mohan,R.Chand & CO.,New Delhi,2005
6. Organic Chemistry –Vol.1 , ELBS, Longman, lond on, (VI Edition) 1973

Unit – 3 : Aromaticity

Structure of Unit:

3.1 Objectives

At the end of the unit learner will be able

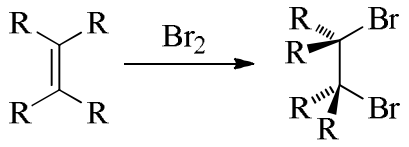
- To become familiar with Aromaticity.
- Understand the importance of Huckels (4n+2) rule.
- Differentiate between benzenoid and nonbenzenoid compounds.
- Differentiate between alternant and nonalternant hydrocarbon.

3.1 Introduction

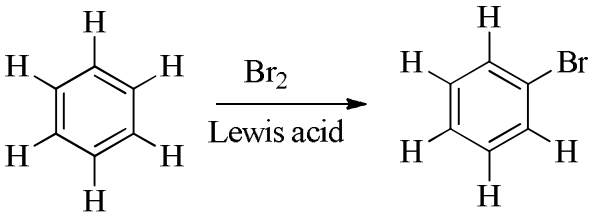
The original meanings of the words aliphatic and aromate no longer have any significance as new facts came to light , the term aromatic came to be associated with chemical stability rather than any aroma Hydrocarbons mainly form a basic scaffold in organic chemistry. In ancient time, hydrocarbons were mainly classified in to two types i.e. aliphatic and aromatic hydrocarbons. In this chapter we mainly deal with aromaticity of benzenoid and non-benzenoid compounds, alternant and non-alternant hydrocarbon, Huckel's rule and bonds which are weaker than covalent bonds addition compounds.

3.3 Aromaticity and Huckel's rule

Those organic compounds which are cyclic in nature posssess alternate single and double bond and also resemble benzene with unusually large resonance energies are called aromatic compound and phenomenton is called as amomanlcty is a simple example of aromatic compound. Benzene differs from other conjugated compound in the sense of reactivity. Alkenes, alkynes usually undergo addition reaction with bromine. Benzene does not undergo addition reaction but it gives substituted product with lewis acids only.



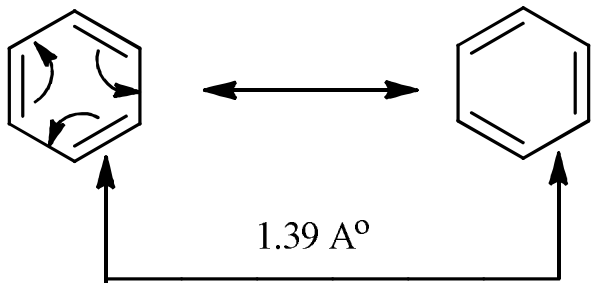
Simple alkene 1,2-dibromoalkene



Benzene monosubstituted benzene

Structure of Benzene:

Benzene is simple prototype aromatic hydrocarbon with molecular formula C_6H_6. It is a conjugated system with same length of all C-C bonds (1.39A^o). It is unsaturated planar, six membered ring with four degrees of unsaturation. Index of hydrogen deficiency equal to four.



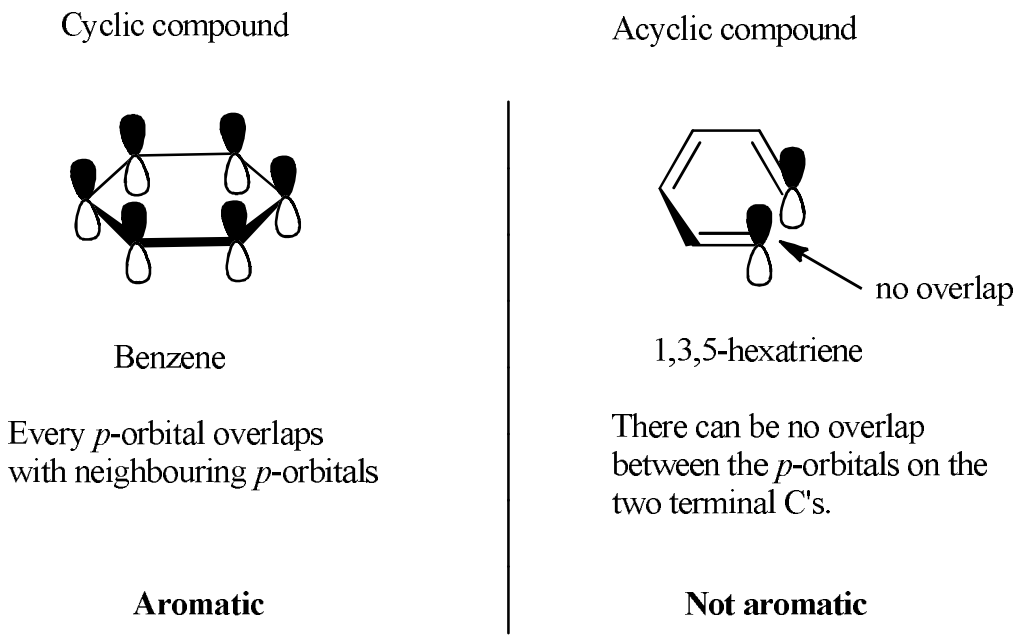
Benzene has equal C-C bonds length

(Figure 3.2)

Huckel's rule:

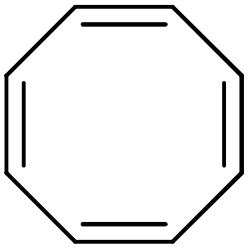
For a compound to be an aromatic it must fullfil following essential criteria:

1. **Compound should be cyclic one** which is helpful in *p*-orbital overlap of two adjacent atoms to give continuous ring of parallel orbital. Benzene has six p-orbital which are continuously overlaping, hence it is aromatic. On other hand 1,3,5-hexatriene also has six *p*-orbitals but it is not a cyclic. The two terminal carbons in 1,3,5-hexatriene are not overlap with each other, so it is not aromatic.



(Figure 3.3)

2. **It should be planar** to give delocalized π electron cloud. In benzene all p-orbitals are aligned with each other so π electron cloud is delocalized. Cyclooctatetraene has a cyclic structure with conjugated system which resembles like benzene. Cyclooctatetraene is not planar rather it is tub shaped , due to which adjacent P orbitals fail to overlap and hence Cyclooctatetraene is not Aromatic. Cyclooctatetraene gives similar reaction as alkenes.

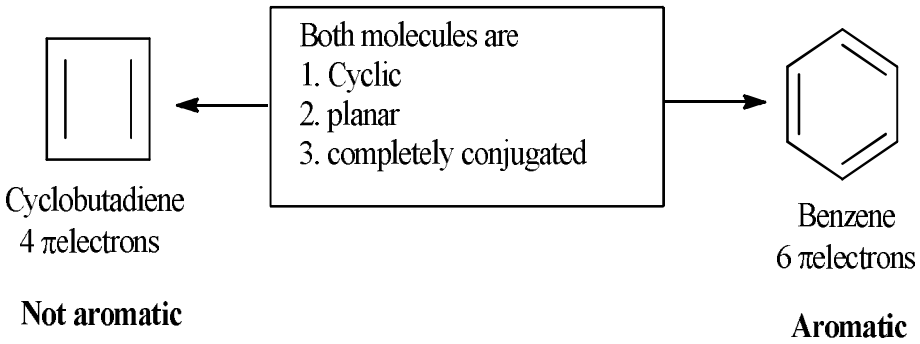


Cyclooctatetraene
Not planar

(Figure 3.4)

3. **Uninterrupted conjugation** of each sp^2 hybridized carbon atomsmust be there regard less of the number of carbon atoms. 1,3-cyclohexadiene and 1,3,5-cycloheptatriene are not completely conjugated, with lack of p-orbital on one carbon make them non aromatic.

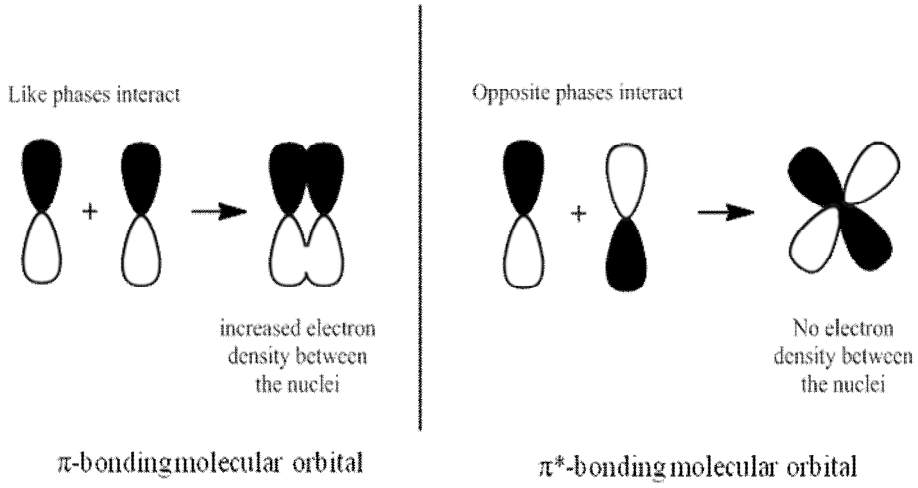
4. It must have total number of π electrons which satisfies **Huckel's (4n+2) rule**. Some compounds have all above three criteria for aromaticity, even though they are not aromatic. Cyclobutadiene is planar, cyclic compound with complete conjugation, but still not aromatic. According to Huckel's rule in addition to first three criteria, compound should have specific number of π electrons. For compounds to be an aromatic, it must contain (4n+2) π electrons hence it is not aromatic n= 0, 1, 2, 3,…… any positive integer. Cyclobutadiene contains 4 π electrons, where as benzene contains 6 π electrons thus, Huckels rule is mathematical way of saying that an aromatic compound must have an odd number of pairs of the electrons.



(Figure 3.5)

The basis of aromaticity can be also understood with the help of Molecular orbital (MO) theory. When two p (atomic) orbital combines, two molecular orbitals are formed one with lower energy and other than the and other with higher energy combining atomic orbitals. The lower energy molecular orbitals

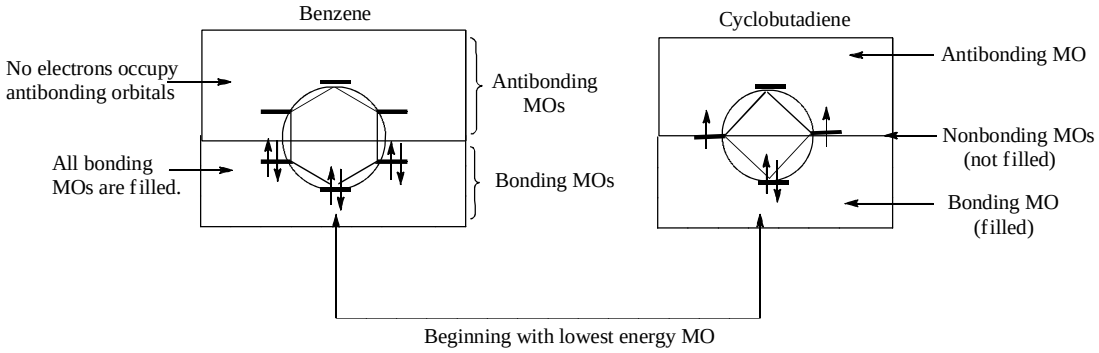
are formed by side-by-side overlap of two p orbitals of similar phase, giving rule to π bonding molecular orbital. When two p orbitals of opposite phase combines, it gives π* antibonding orbital with higher energy.



(Figure 3.6)

According to molecular orbital theory, every molecule (with odd or even number of atoms) contains one single molecular orbital lowest in energy than all others. All molecular orbitals come in degenerate pairs (with equal energy), except orbitals with lowest and highest energy. Lowest energy orbital holds two π electrons, and then successive degenerate pairs with equal energy forms four each, in a "closed shell". These degenerate pairs correspond to integer (n) in (4n+2) rule.

Cyclobutadiene has four Molecular orbitals (MOs), one bonding, two nonbonding and one antibonding. Therefore lowest energy bonding MO contains two π electrons whereas one electron is present in each of the two nonbonding MOs. As cyclobutadiene's nonbonding MOs are not completely filled it is not aromatic. In contrast, benzene has six π electrons which completely fills all bonding orbitals. Hence benzene is aromatic.



(Figure 3.7)

3.4 Aromaticity in benzenoid and nonbenzenoid compounds

Aromatic compounds are further divided in to two types on the basis of presence or absence of benzene nucleus in compound.

Benzenoid compound

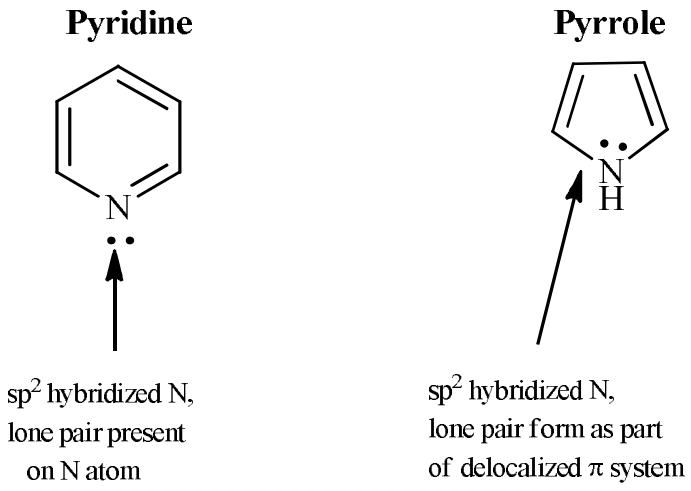
Aromatic compounds which contain benzene ring or having electronic structure resembling to that of benzene are called as benzenoid compounds. Benzenoid compounds are further classifieds into following types

3.4.1.1 Aromatic heterocycles

Atoms other than carbon having lone pair of electrons, can also be aromatic. For example oxygen, nitrogen and sulfur atoms have at least one lone pair of electrons. This lone pair of electrons is either localized on heteroatom or forms a part of delocalized π system in the ring. These two possibilities can be illustrated by pyridine and pyrrole.

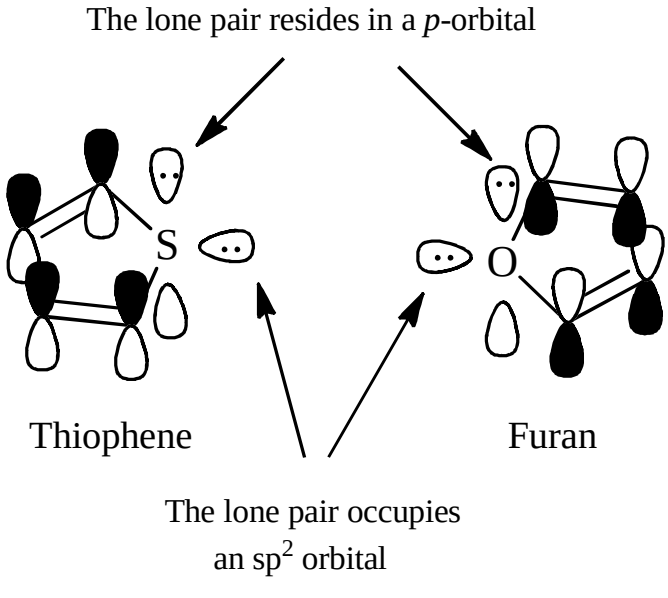
Pyridine is six membered nitrogen containing cyclic, planar heterocycle with complete conjugation**.** It has six π electrons and lone pair localized on N atom, not a part of delocalized π system. The N atom of pyridine is attached to two neighbouring carbon atoms and has a lone electron pair, making it sp^2 hybridized. It mainly leaves one unhybridized p orbital that overlaps with adjacent p orbitals. The lone pair on N atom is surrounded by a sp^2 hybridized state and it is perpendicular to the delocalized π electrons / cloud.

Pyrrole is a five membered cyclic planes compound with nitrogen as a heteroatom in the ring. Pyrrole mainly has four π electrons, two from each π bonds. Pyrrole has complete conjugated system of p orbital on every adjacent atom. In addition, it also has extra two π electrons which are originated from lone pair present on N atom. Hence lone pair mainly forms part of delocalized π system. Hence both pyridine and pyrrole are aromatic.



(Figure 3.8)

Another interesting examples of aromatic heterocycles are furan and thiophene which are having two lone pairs on O and S atom respectively. In both the heterocycles one of the lone pair form an integnal part of delocalized π system and another lone pair resides itself on heteroatom in sp^2 hybrid orbital.

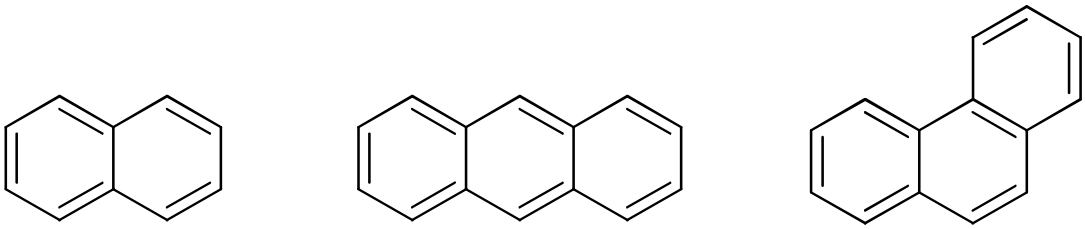


(Figure 3.9)

3.4.1.2 Aromatic compounds with more than one ring

Hucke's rule has limitation that it can be applied only for monocyclic compounds. There are many other compounds which having more than one benzene ring. For example, Naphthalene, phenanthrene and anthracene which consist of two, three, and three fused benzene ring respectively. These fused aromatic compounds have

alternate single, double bonds. Naphthalene has 10 π electrons, phenanthrene and anthracene contains 14 π electrons each.



Napthalene
10 π electrons

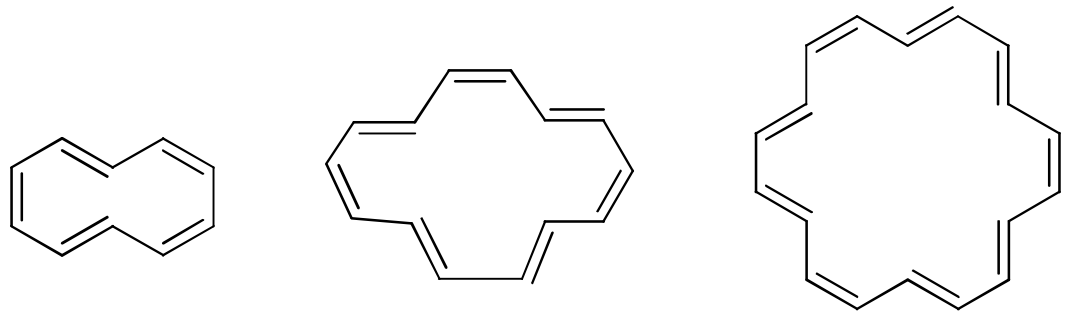
Anthracene
14 π electrons

Phenanthrene
14 π electrons

(Figure 3.10)

3.4.2 Nonbenzenoid compounds

Benzene is an aromatic compound with single ring. There are many other compounds which have single ring with alternating single and double bonds and called are as **annulenes**. It is mainly indicated by the number of atoms in the ring in square brackets and then the adds name annulene. Mostely annulenes have n= 10,12,14,16,18,20,24 out of which only [14] and [18] are aromatic. [14] and [18] annulenes are (4n+2) compounds, whereas others are only 4n compounds. [10] Annulene satisfy the Huckel's rule but it is not planar,hence not aromatic.



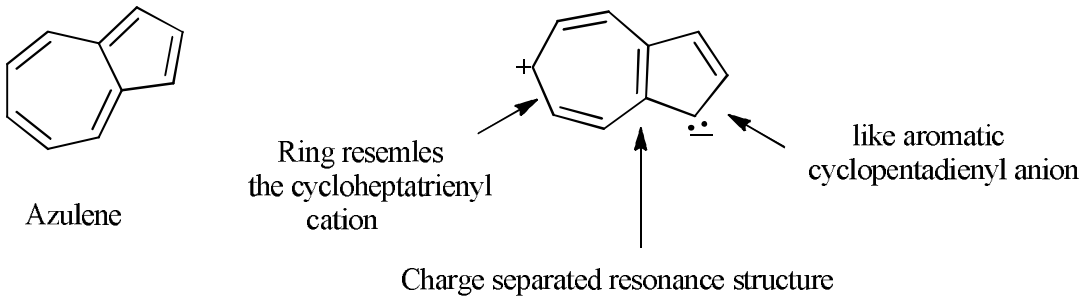
[10]-annulene

[14]-annulene

[18]-annulene

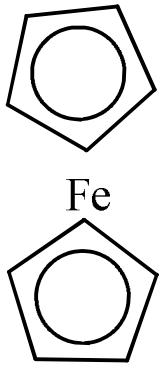
(Figure 3.11)

Another example of nonbenezoid compounds is **Azulene**. Azulene is hybrid of aromatic cyclopentadienyl anion and cycloheptatrienyl cation.



(Figure 3.12)

Ferrocene a highly stable nonbenzenoid aromatic compound which undergo many electrophilic substitution reactions**.** It seems like that ferrocene is mainly formed by p orbital overlap of the cyclopentadienyl anions and 3d orbital of the iron atoms**.**

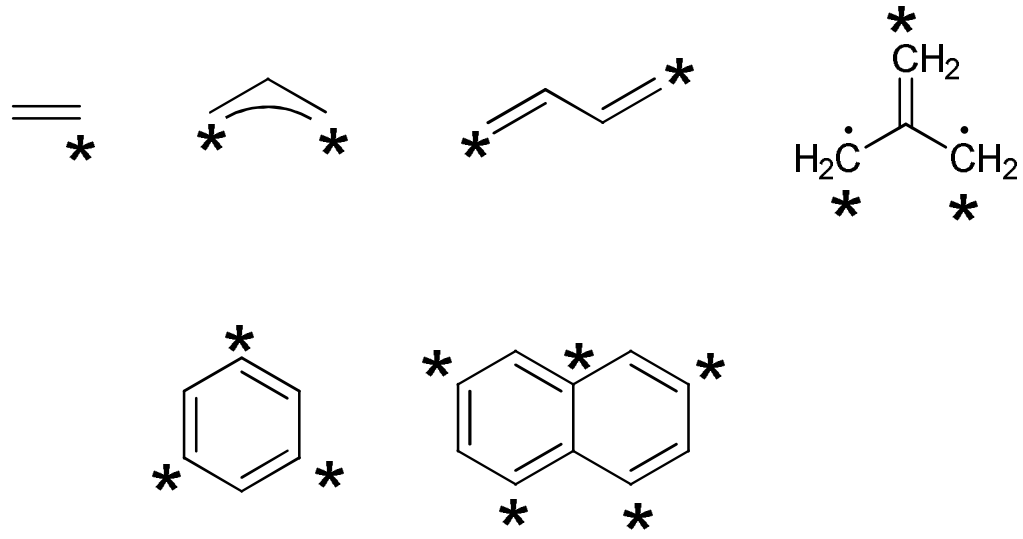


Ferrocene

(Figure 3.13)

3.5 Alternant and nonalternant hydrocarbon

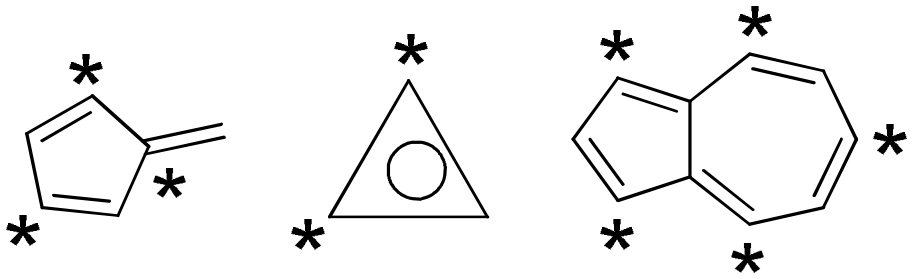
An easy method to describe conjugated hydrocarbon aystem which is also helpful in explaining their properties is alternant and non alternant conjugation. A conjugate hydrocarbon is alternant if stars (asterisks) can be placed on alternate π centre with no two stars adjacent. Alternant π system mainly has even number of π electron density in molecule with a net result of single π electron at each conjugated carbon atom. The π MO's are symmetrically distributed with zero energy.



Alternant hydrocarbons

(Figure 3.14)

It a conjugated system has unavoidable starred (asterisks) or unstarred π system on the adjacent atom, then such system is referred as nonalternant π system. Nonalternant π system mainly has larger dipole moments.



Nonalternant hydrocarbon

3.6 Bonds weaker than covalent-addition compounds

Molecule is mainly formed by aggregation of atoms in a distinct three dimensional arrangement which are held together by defferent bond. Depending upon the type of bond present, it mainly has bond energy in the range of 2-100 kcal mol^{-1}. It a reaction between two compounds is such that it heads to product formed in such reaction with mass of both the compounds; the product is called as addition product. In the addition compound, two or more molecules are held together by weak bonds.

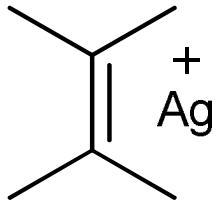
We can segregate them in to mainly four classes as: electron donor-acceptor complexes, complexes formed by crown ether inclusion compounds and catenanes.

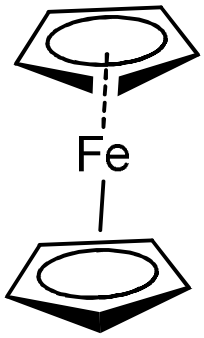
3.6.1 Electron donor-acceptor complexes

As name indicates these complexes are mainly formed by a donor and an acceptor molecule. Donor donates its unshaired pair of electron a π system of an alkenes or aromatic system. This complex usually contains 1:1 ratio of acceptor and donor. There are different types of acceptor molecules these are as follows:

3.6.1.1 Complexes in which acceptor is a metal ion and donor an alkene or an aromatic ring

Metal ions usually form stable complexes with alkene, alkynes, dienes and aromatic ring. For example, ethene forms stable η^2-complex with silver, where 2 indicates the number of atoms the ligand (ethene) uses to bond with metal (silver) (Fig, 3:1) Similarly, ferrocene forms η^5-complex with iron (Fig 3:2).





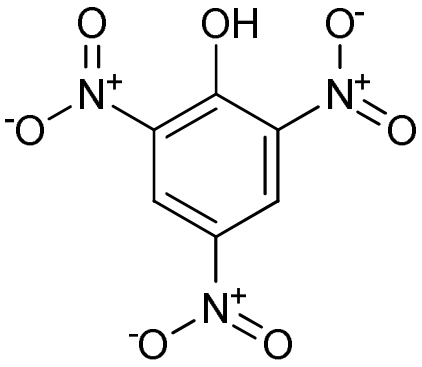
Ethene η^2complex **Ferrocene η^5complex**

(Figure 3.16)

3.6.1.2 Complexes in which the acceptor is an organic molecule

Many poly nitro containing compounds form solid complexes with aromatic hydrocarbons, aromatic amines and aliphatic amines. olefins and other compounds For example, picric acid forms addition product with above mentioned amines. They are called picrates, though they are not salts of Picric acid but addition compounds.

3.6.1.3 Complexes in which the acceptor is I_2, Br_2 or even Cl_2 Such complex are formed with amines aromatic hydrocarbon, ketones etc. Such molecules accept electorn from both nalonors and π doness presumnbly by the expanelion of the outer shell to hod 10 electrons.

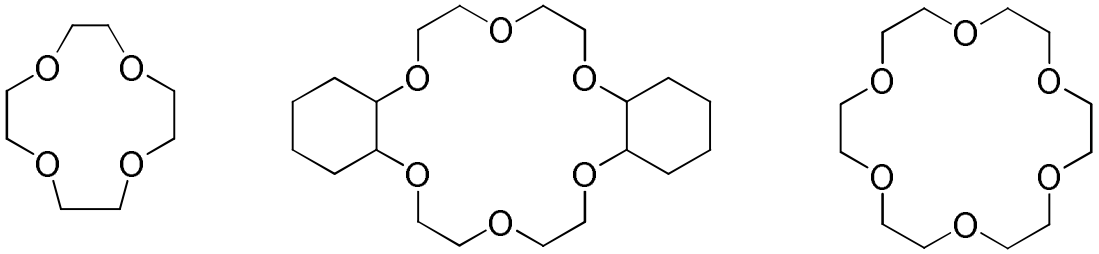


Picric acid

(Figure 3.17)

3.6.2 Crown-ether complexes

Crown-ethers are large cyclic compounds with number of oxygen atoms. usually in a regular pattern Crown-ethers mainly act as a host and forms complex with positive metallic ions (guest). Metallic ions are bind tightly in the center of cavity. Each crown-ether has different binding affinity depending upon the size of guest compound. For example, 12-crown-4 binds to Li^{+}, dicyclohexano-18-crown-6 binds to K^{+} and 15-crown-5 binds to Hg^{2+}.



12-crown-4 **Dicyclohexano-18-crown-6** **15-crown-5**

(Figure 3.18)

Crown-ethers also form complexes with amines, phenols, and other neutral compounds.

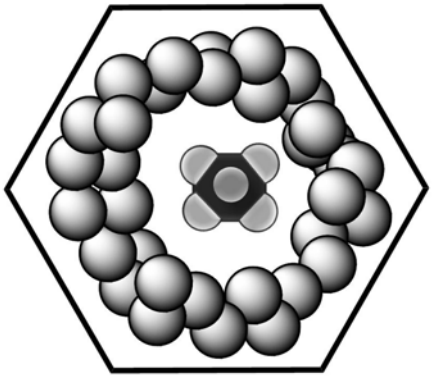
3.6.3 Inclusion compounds

Inclusion compounds have van der Waals forces between the host and the guest without any bonding. Host mainly forms a crystal lattice with enough spaces for the guest to fit inside. On the basis of the shape of space, the inclusion compounds are classifieds into two types: tunnels or channels inclusion compounds and Clathrate or cage inclusion compounds. In both the types of compounds, guest molecule with

only appropriate size tends to fit inside the crystal lattice, too large or too small guests are unable to go into the lattice and addition product will not form.

3.6.3.1 Tunnels or Channels inclusion compounds

These inclusion compounds have space of the shape like long tunnels or channels. For example, urea acts as one of the most important host molecule among the inclusion compounds. In the absence of guest molecule, urea crystallizes in a tetragonal lattice and in presence of guest molecule it lattice mainly crystallizes into hexagonal in presence of guest molecule. Channel diameter of urea is ~5 Å and selection of guest molecule is largely dependent on size irrespective of chemical and electronic effects. For example octane and 1-bromooctane both fits inside the crystal lattice of urea, but 2-bromooctane, 2-methylheptane and 2-methyloctane fails to fit. These types of complexes are used for separation of isomers.

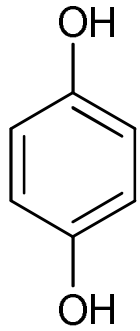


(Figure 3.19)

Crystal lattice of urea with guest molecule

3.6.3.2 Clathrate or cage inclusion compounds

These types of inclusion compound have completely enclosed spaces. In clathrate, three molecules are help together to form cage through hydrogen bonding. In the cage one molecule of host usually hydroquinone fits. Other guest molecules that fit into the cage are methanol, SO_2, CO_2, argon, water and inorganic sodium chloride. In the absence of guest molecule, urea crystlattges in telragenal lattice and in presence of guest moleculs it mainly crystalliges into hexanonal lattice.



Hydroquinone

(Figure 3.20)

Cyclodextrins are one of the hosts that can form both tunnels (e.g. α-cyclodextrin) and cage inclusion (β and σ-cyclodextrins) compounds.

3.6.4 Catenanes

Catenanes contains two or more non bonded (independent) portions without any valence forces, but they must remain linked. [n]-Catananes are formed by two or more rings which are held together as links in a chain, where 'n' corresponds to number of rings linked. Catenanes mainly has amide linkages.

[2]-Catenane [3]-Catenane

(Figure 3.21)

3.7 Summary

Aromaticity is mainly based on number of π electrons present in the compound. Some compound even satisfies Huckel's (4n+2) rule but still are not aromatic due to imbalance in other essential criteria for aromaticity. Huckel's rule is only applicable for monocyclic compound. On the basis of presence or absence of bengene ring, aromatic compounds are again classified into benzenoid and nonbenzenoids compounds.

3.8 Glossary

- Aromatic hydrocarbons mainly have pleasant odor, whereas aliphatic hydrocarbons are fats or oils.
- Aromaticity is an ability of compound to assist the induced ring current.
- Aromaticity of a compound mainly dependent upon number of π electrons present.
- According to Huckel's, rule aromatic compounds should posses (4n+2) π electrone.
- Benzene is a simplest prototype aromatic compound with same length of bonds.
- Benzene undergoes aromatic substitution reaction rather than addition reactions.
- Aromatic compounds with benzene ring are called as benzenoid hydrocarbon, whereas aromatic compound without benzene ring are called as nonbenzenoid hydrocarbons.
- Compoind with alternate starable (asterisks)π system are called.
- Compound alternate starrable(asterisks) π system are called as alternant hydrocarbon, whereas compound with adjacent starrable π system are called as nonalternant hydrocarbon.

3.9 Review questions / Comprehensive Question

1. What is Aromaticity? What are essential criteria for aromaticity?

2. Statehuckel's (4n+2) rule. Give significance of (n) in this rule.

3. Define benzenoid and nonbenzenoid compounds with suitable example.

4. Differentiate between channel and clathrate inclusion compounds.

5. What are crown-ether complexes?

6. What are alternate and nonalternate hydrocarbons?

3.10 References and Suggested readings

1. Organic chemistry, 3rd edition- Janice Gorzynski Smith (Mc Graw Hill publisher) 2011.
2. Organic chemistry- J Clayden, N Greeves, S Warren (Second edition, Oxford University press) 2012.
3. March's advanced organic chemistry reactions, mechanisms, and structures- M. B. smith and J. March (Sixth edition, Wiley-Interscience, a John Wiley & Sons, Inc., Publication) 2007.

Unit - 4 Complex Organic Molecules

Structure of Unit:

4.1 Objective

At the end of the unit learner will be able to

- Understand about organic complexes like crown ether complexes, cryptands, inclustion compounds etc.
- Earn knowledge about synthesis, properties, applications and structures of cycloderxtrins, catenanes, and rotaxanes.
- Understand the boding in fullerenes.

4.2 Introduction

This chapter deals with the complex organic molecules complexed with other hydrocarbons and inorganic this compounds like crown ether complexes, cryptands, inclustion compound etc. This chapter also describes the synthesis, properties, applications and structures of cyclodextrins, catenanes, rotaxanes and bonding in fullerenes.

4.3 Crown Ether Complexes and Cryptands

Crown ethers

Crown ethers are cyclic polyethere they are cyclic polymers of ethylene glycol, $(OCH_2CH_2)n$ and are named as x-crown y- where x is the total nujber of atms in the ring and y is the number of oxygens important members of this series are titromus (Y=4) Pentamers (y=5) and the hexamers (y=6) the crown ethers have the property complexes with positive ions the relationship between the crown ether and the ion that it solvate is called a host guest releationship the crown ither act as host and the coordinate cation as the guest the intesor of the complex containsthe oxygen solvated cations but he exterior has hydrocarbon properties (hgydrophobic) . As a result the completed ion is soluble in non-polar organic solvent. The ability of a host moluele to bind specific guests called molecular recognition this property renders crown ethers as potential phase transfer catalysts. The denticity of the polyether influences the affinity of the crown ether for various cations. For example, 18-crown-6 has high affinity for potassium cation, 15-crown-5 for sodium cation, and 12-crown-4 for lithium cation. Crown ethers are not the only macrocyclic ligands that have affinity for the potassium cation. Ionophores such as valinomycin also display a marked preference for the potassium cation over other cations.

Affinity for cations

Apart from its high affinity for potassium cations, 18-crown-6 can also bind to protonated amines and form very stable complexes in both solution the as well as gas phase. Some amino acids, such as lysine, contain a primary amine on their side chains. Those protonated amino groups can bind to the cavity of 18-crown-6 and form stable complexes in the gas phase. Hydrogen-bonds are formed between the three hydrogen atoms of protonated amines and three oxygen atoms of 18-crown-6. These hydrogen-bonds make the complex a stable adduct.

Azacrowns

Macrow cycles containing nitrogen and sulfer atoms have similar propertiesa s do these containing more that one kind of 21- and 18-membered diazacrown ether derivatives exhibit excellent calcium and magnesium selectivities and are widely used in ion-selective electrodes. Some or all of the oxygen atoms in crown ethers can be replaced by nitrogens to form cryptands. A well-known tetrazacrown is cyclen in which there are no oxygens.

Cryptands

Bicyclies and cycles of higher order are called cryptands and the complexes formed are called as cryplates suchy molecules can surround the enclosed ion in three demensions binding it even more tight than the monocyclic crouwn eithers the nobel prize. The Nobel Prize for Chemistry in 1987 was given to Donald J. Cram, Jean-Marie Lehn, and Charles J. Pedersen for their efforts in discovering and determining uses of cryptands and crown ethers, thus launching the now flourishing field of supramolecular chemistry. The term cryptand implies that this ligand binds substrates in a crypt, interring the guest as in a burial. These molecules are three-dimensional analogues of crown ethers but are more selective and complex the guest ions more strongly. The resulting complexes are lipophilic.

Structure

The most common and most important cryptand is $[CH_2CH_2OCH_2CH_2OCH_2CH_2]_3N$ the formal IUPAC (International Union of Pure and Applied Chemistry) name for this compound is 1,10-diaza-4,7,13,16,21,24-hexaoxabicyclo[8.8.8]hexacosane. This compound is termed as [2.2.2]cryptand where the numbers indicate the number of ether oxygen atoms (and hence binding sites) in each of the three bridges between the amine nitrogen "caps". Many cryptands are commercially available under the tradename "Kryptofix." All-amine cryptands exhibit particularly high affinity for alkali metal cations, thus preferring the isolation of salts of K^+.

Properties

The 3-dimensional interior cavity of a cryptand provides a binding site - or nook - for "guest" ions. The complex between the cationic guest and the cryptand is called a cryptate. Cryptands form complexes with many "hard cations" including NH_4^+, lanthanoids, alkali metals, and alkaline earth metals. In contrast to crown ethers, cryptands bind the guest ions using both nitrogen and oxygen donors. This three-dimensional encapsulation mode confers some size-selectivity, enabling discrimination among alkali metal cations (e.g. Na^+ vs. K^+).

Uses

Cryptands are more expensive and difficult to prepare, but offer much better selectivity and strength of binding than other complexing agents for alkali metals, such as crown ethers. They are able to bind otherwise insoluble salts into organic solvents. They can also be used as phase transfer catalysts by transferring ions from one phase to another. Cryptands enabled the synthesis of the alkalides and electrides. They have also been used in the crystallization of Zintl ions such as Sn_9^{4-}.

4.4 Inclusion Compounds

A clathrate is a chemical substance consisting of a lattice that traps or contains molecules. The word clathrate is derived from the Latin clatratus meaning with bars or a lattice. Traditionally, clathrate compounds are polymeric and completely envelop the guest molecule, but in modern usage clathrates also include host-guest complexes and inclusion compounds. According to IUPAC, clathrates are "Inclusion compounds in which the guest molecule is in a cage formed by the host molecule or by a lattice of host molecules."

Occurrence

Traditionally clathrate compounds refer to polymeric hosts containing molecular guests. More recently, the term refers to many molecular hosts, including calixarenes and cyclodextrins and even some inorganic polymers such as zeolites. Many clathrates are derived from an organic hydrogen-bonded frameworks. These frameworks are prepared from molecules that "self-associate" by multiple hydrogen-bonding interactions. The most famous clathrates are methane clathrates where the hydrogen-bonded framework is contributed by water and the guest molecules are methane. Large amounts of methane naturally frozen in this form exist both in permafrost formations and under the ocean sea-bed. Other hydrogen-bonded networks are derived from hydroquinone, urea, and thiourea. Photolytically-sensitive caged compounds have been examined as containers for releasing a drug or reagent. Inclusion compounds are often molecules, whereas clathrates are typically polymeric. Intercalation compounds, are not 3-dimensional, unlike clathrate compounds. In host-guest chemistry an inclusion compound is a complex in which one chemical compound (the "host") forms a cavity in which molecules of a second "guest" compound are located. The definition of inclusion compounds is very broad, extending to channels formed between molecules in a crystal lattice in which guest molecules can fit. If the spaces in the host lattice are enclosed on all sides so that the guest species is ‘trapped’ as in a cage, the compound is known as a clathrate. In

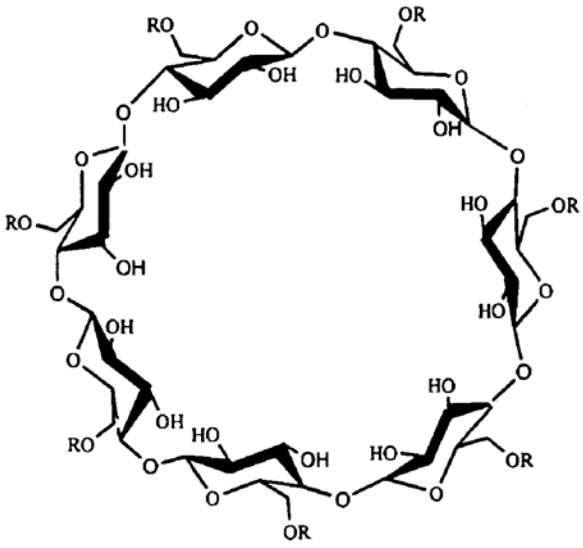
molecular encapsulation a guest molecule is actually trapped inside another molecule. Inclusion complexes are formed between cyclodextrins and ferrocene . When a solution of both compounds in a 2:1 ratio in water is boiled for 2 days and then allowed to rest for 10 hours at room temperature orange-yellow crystals are formed. X-ray diffraction analysis of these crystals reveals a 4:5 inclusion complex with 4 molecules of ferrocene included in the cavity of 4 cyclodextrine molecules and with the fifth ferrocene molecule sandwiched between two stacks of ferrocene - cyclodextrine dimers. Cyclodextrin also forms inclusion compounds with fragrance molecules . As a result the fragrance molecules have a reduced vapor pressure and are more stable towards exposure to light and air. When incorporated into textiles the fragrance lasts much longer due to the slow-release action.

4.5 Cyclodextrins

Cyclodextrins are a family of compounds made up of sugar molecules bound together in a ring (cyclic oligosaccharides). Cyclodextrins are produced from starch by means of enzymatic conversion. They are used in food, pharmaceutical, drug delivery and chemical industrial and also in agricultural and environmental engineering.

Structure

Typical cyclodextrins are constituted by 6-8 glucopyranoside units, can be topologically represented as toroids with the larger and the smaller openings of the toroid exposing to the solvent secondary and primary hydroxyl groups respectively. Because of this arrangement, the interior of the toroids is not hydrophobic, but considerably less hydrophilic than the aqueous environment and thus able to host other hydrophobic molecules. In contrast, the exterior is sufficiently hydrophilic to impart cyclodextrins (or their complexes) water solubility.



R = H; β–Cyclodextrin
R = 2-Hydroxypropyl;
2-Hydroxy propyl-
β–Cyclodextrin

Chemical structure of the cyclodextrins.

The formation of the inclusion compounds greatly modifies the physical and chemical properties of the guest molecule, mostly in terms of water solubility. This is the reason why cyclodextrins have attracted much interest in many fields, especially pharmaceutical applications: Because inclusion compounds of cyclodextrins with hydrophobic molecules are able to penetrate body tissues, these can be used to release biologically active compounds under specific conditions. In most cases the mechanism of controlled degradation of such complexes is based on pH change of water solutions, leading to the loss of hydrogen or ionic bonds between the host and the guest molecules. Alternative means for the disruption of the complexes take advantage of heating or action of enzymes which are able to cleave α-1,4 linkages between glucose monomers.

Synthesis

The production of cyclodextrins is relatively simple and involves treatment of ordinary starch with a set of easily available enzymes. Commonly cyclodextrin glycosyltransferase (CGTase) is employed along with α-amylase. First starch is liquified either by heat treatment or using α-amylase, then CGTase is added for the enzymatic conversion. CGTases can synthesize all forms of cyclodextrins, thus the product of the conversion results in a mixture of the three main types of cyclic molecules, in ratios that are strictly dependent on the enzyme used: each CGTase has

its own characteristic α:β:γ synthesis ratio. Purification of the three types of cyclodextrins is done by taking advantage of the different water solubility of the molecules: β-CD which is very poorly water soluble (18.5 g/l or 16.3mM) can be easily retrieved through crystallization while the more soluble α- and γ-CDs (145 and 232 g/l respectively) are usually purified by means of expensive and time consuming chromatography techniques. As an alternative method, a "complexing agent" can be added during the enzymatic conversion step: such agents (usually organic solvents like toluene, acetone or ethanol) form a complex with the desired cyclodextrin which subsequently precipitates. The complex formation drives the conversion of starch towards the synthesis of the precipitated cyclodextrin, thus enriching its content in the final mixture of products. Wacker Chemie AG uses dedicated enzymes, that can produce alpha-, beta- or gamma-cyclodextrin specifically. This is very valuable especially for the food industry, as only alpha- and gamma-cyclodextrin can be consumed without a daily intake limit.

Applications

Cyclodextrins are able to form host-guest complexes with hydrophobic molecules due to the unique nature imparted by their structure. As a result, these molecules have found a number of applications in a wide range of fields. One example is Sugammadex, a modified γ-cyclodextrin which reverses neuromuscular blockade by binding the drug rocuronium. Other than the above mentioned pharmaceutical applications, cyclodextrins can be employed in environmental protection: These molecules can effectively immobilise toxic compounds inside their rings, like trichloroethane or heavy metals, oralso they can form complexes with stable substances, like trichlorfon (an organophosphorus insecticide) or sewage sludge, enhancing their decomposition.

The ability of cyclodextrins to form complexes with hydrophobic molecules has led to their usage in supramolecular chemistry. In particular they have been used to synthesize certain mechanically-interlocked molecular architectures, such as rotaxanes and catenanes, by reacting the ends of the threaded guest. Based on the photodimer obtained, it is established that the halogen-halogen interactions, which play an interesting role in solid state, can be observed in solution. Existence of such interactions in solution has been proved for the first time by V.Ramamurthy's group by selective photodimerization of dichloro substituted stiblazoles in Cyclodextrin and Cucurbiturils.

The application of cyclodextrin as supramolecular carrier is also possible in organometallic reactions. The mechanism of action probably takes place in the

interfacial region. *Wipff* also demonstrated by computational study, that the reaction occurs in the interfacial layer. The application of cyclodextrins as supramolecular carrier is possible in various organometallic catalyle reactions.

Increasing bioavailability

Because cyclodextrins are hydrophobic inside and hydrophilic outside, they can form complexes with hydrophobic compounds. Thus they can enhance the solubility and bioavailability of such compounds. This is of high interest for pharmaceutical as well as dietary supplement applications in which hydrophobic compounds shall be delivered. Alpha-, beta-, and gamma-cyclodextrin are all generally recognized as safe by the FDA.

Cholesterol free products

In the food industry, cyclodextrins are employed for the preparation of cholesterol free products: the bulky and hydrophobic cholesterol molecule is easily lodged inside cyclodextrin rings which are then removed.

Multifunctional dietary fiber

α-Cyclodextrin has been authorized for use as a dietary fiber in the European Union since 2008. In 2013 the EU commission has verified a health claim for alpha-cyclodextrin. The EU assessment report confirms that consumption of alpha-cyclodextrin can reduce blood sugar peaks following a high-starch meal. Weight loss supplements are marketed prepared from alpha-cyclodextrin which claim to bind to fat and be an alternative to other anti-obesity medications.

Due to its surface-active properties, α-cyclodextrin can also be used as emulsifying fiber, for example in mayonnaise as well as a whipping aid, for example in desserts and confectionary applications.

Other food applications

Applications further include their ability to stabilize volatile or unstable compounds and the reduction of unwanted tastes and odour. Beta-cyclodextrin complexes with certain carotenoid food colorants and it has been shown to intensify color, increase water solubility and improve light stability of these colorants

The strong ability of forming complex withfragrances can also be used for another purpose: first dry, solid cyclodextrin microparticles are exposed to a controlled contact with fumes of active compounds, then they are added to fabric or paper products. Such devices are capable of releasing fragrances during ironing or when heated by human body. Such a device is commonly used as a typical 'dryer sheet'. The heat from a clothes dryer releases the fragrance into the clothing.

Aerosols

Aqueous cyclodextrin solutions can generate aerosols in particle size ranges which are suitable for pulmonary deposition. Large quantities of aerosol can be nebulized in acceptable nebulization times. The cyclodextrin concentration does not modify nebulization efficiency in the range tested.

4.6 Catenanes

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Crystal structure of a catenane

A catenane is a mechanically-interlocked molecular architecture consisting of two or more interlocked macrocycles. The interlocked rings cannot be separated without breaking the covalent bonds of the macrocycles. Catenane is derived from the Latin ***catena meaning "chain".*** They are conceptually related to other mechanically-interlocked molecular architectures, such as rotaxanes, molecular knots or molecular Borromean rings. Recently the terminology "mechanical bond" has been coined that describes the connection between the macrocycles of a catenane.

Synthesis

There are two primary approaches to the organic synthesis of catenanes. The first is to simply perform a ring-closing reaction with the hope that some of the rings will be form around other rings giving the desired catenane product. This so-called "statistical approach" led to the first successful synthesis of a catenane; however, the method is highly inefficient, requiring high dilution of the "closing" ring and a large excess of the pre-formed ring, and is rarely used. The second approach relies on supramolecular preorganization of the macrocyclic precursors utilizing hydrogen bonding, metal coordination, hydrophobic forces, or coulombic interactions. These non-covalent interactions offset some of the entropic cost of association and help in positioning the components to form the desired catenane upon the final ring-closing. This "template-directed" approach, together with the use of high-pressure conditions, can provide yields of over 90%, thus improving the potential of catenanes for applications. An example of this approach is used in bis-bipyridinium salts which form strong complexes threaded through crown ether bis(para-phenylene)-34-crown-10. Sanders has shown that dynamic combinatorial approaches using reversible

chemistry can be particularly successful in preparing new catenanes of unpredictable structure.

Properties and applications

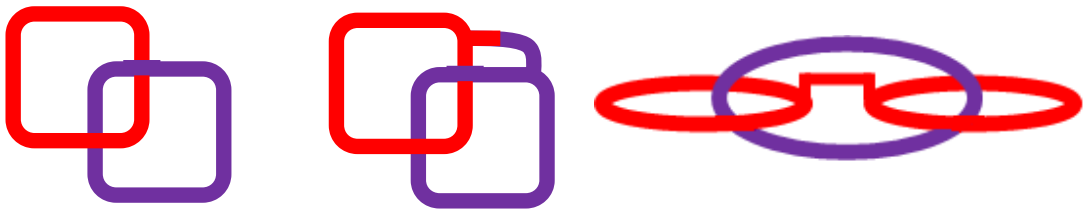
A particularly interesting property of many catenanes is the ability of the rings to rotate with respect to one another. This motion can often be detected and measured by NMR spectroscopy, among other methods. When molecular recognition motifs exist in the finished catenane (usually those that were used to synthesize the catenane), the catenane can have one or more thermodynamically preferred positions of the rings with respect to each other. In the case where one recognition site is a switchable moiety, a mechanical molecular switch results. When a catenane is synthesized by coordination of the macrocycles around a metal ion, then removal and re-insertion of the metal ion can switch on & switch off the free motion of the rings on and off. Catenanes have been synthesized incorporating many functional units, including redox-active groups (e.g. viologen, TTF=tetrathiafulvalene), photoisomerizable groups (e.g. azobenzene), fluorescent groups and chiral groups. Some such units have been used to create molecular switches as described above, as well as for the fabrication of molecular electronic devices and molecular sensors.

Families of catenanes

There are a number of distinct methods of holding the precursors together prior to the ultimate ring-closing reaction in a template-directed catenane synthesis. Each noncovalent approach to catenane formation results in what can be considered as different families of catenanes.

Another family of catenanes are called pretzelanes or bridged [2]catenanes after their likeness to pretzels with a spacer linking the two macrocycles. In one such system[1] one macrocycle is an electron deficient oligo Bis-bipyridinium ring and the other cycle is crown ether cyclophane based on para phenylene or naphthalene. X-ray diffraction shows that due to pi-pi interactions, the aromatic group of the cyclophane is held firmly inside the pyridinium ring. A limited number of (rapidly-interchanging) conformers exist for such type of compounds

Families of catenanes



Catenanes Pretzelanes Handcuff-shaped catenanes Nomenclature
In catenane nomenclature, a number in square brackets precedes the word "catenane" in order to indicate how many rings are involved.

4.7 Rotaxanes

A rotaxane is a mechanically-interlocked molecular architecture consisting of a "dumbbell shaped molecule" which is threaded through a "macrocycle" (see graphical representation). The name is derived from the Latin word rota which mean wheel the name of derived from the latin word rota which means wheel and axle which means axis. The two components of a rotaxane are kinetically trapped since the ends of the dumbbell (often called sdissociation disassociation (unthreading) of the components since this would require significant distortion of the covalent bonds. Much of the research work is going on concerning rotaxanes and other mechanically-interlocked molecular architectures such as catenanes,

Synthesis

The earliest reported synthesis of a rotaxane in 1967 relied on the statistical probability that if two halves of a dumbbell-shaped molecule were reacted in the presence of a macrocycle then some small percentage would connect through the ring. To obtain a reasonable quantity of rotaxane, the macrocycle was attached to a solid-phase support and treated with both halves of the dumbbell (in large excess) and then it was seprated apart from the support to give a 6% yield. However, the synthesis of rotaxanes has been advanced significantly and efficient yields can be obtained by preorganizing the components utilizing hydrogen bonding, metal coordination, hydrophobic forces, covalent bonds, or coulombic interactions. The three most common strategies to synthesize rotaxane are "capping", "clipping", and "slipping", though others do exist.

Capping

Synthesis via the capping method relies strongly upon a thermodynamically driven template effect; that is, the "thread" is held within the "macrocycle" by non-covalent interactions, for example rotaxinations with cyclodextrin macrocycles involve exploitation of the hydrophobic effect. **Clipping**

The clipping method is similar to the capping reaction except that in this case the dumbbell shaped molecule is complete and is bound to a partial macrocyle.

Slipping

The method of slipping is one which exploits the kinetic stability of the rotaxane. If the end groups of the dumbbell are of an appropriate size, it will be able to reversibly thread through the macrocycle at higher temperatures.

"Active template" methodology

Leigh and co-workers recently began to explore a strategy in which template ions could also play an active role in promoting the crucial final covalent bond forming reaction that captures the interlocked structure.

Nomenclature

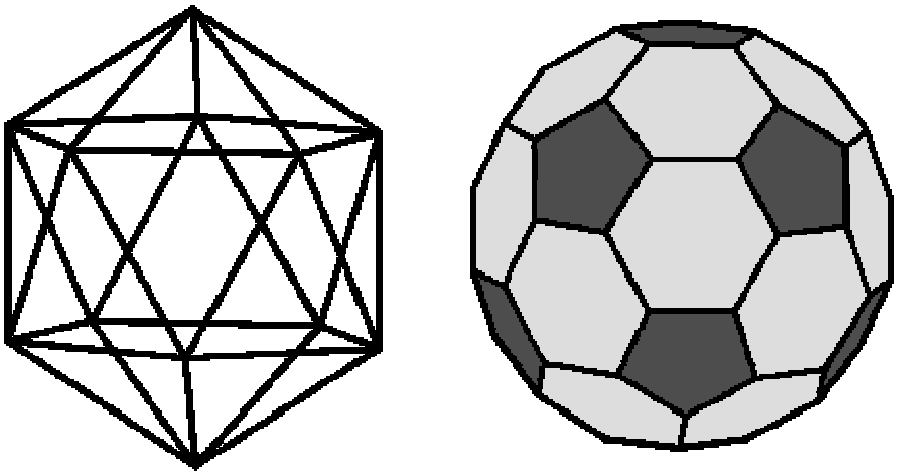
Accepted nomenclature is to designate the number of components of the rotaxane in brackets as a prefix. Therefore the graphical representation of rotaxane displayed above would be a rotaxane as it consists of a single dumbbell and a single macrocycle.

11.8 Bonding in Fullerences

A fullerene is any molecule composed entirely of carbon, in the form of a hollow sphere, ellipsoid, tube, and many other shapes. Spherical fullerenes are also called buckyballs, and they resemble the balls used in football (soccer). Cylindrical ones are called carbon nanotubes or buckytubes. Fullerenes are similar in structure to graphite, which is composed of stacked graphene sheets of linked hexagonal rings; but they may also contain pentagonal (or sometimes heptagonal) rings. The first fullerene molecule to be discovered, for family's namesake was buckminsterfullerene (C_{60}). In this chapter structure of C_{60}

The Truncated Icosahedron

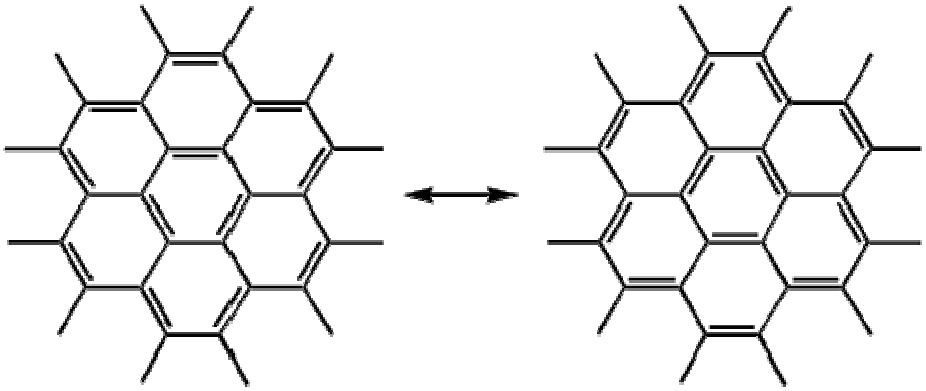
The proposed structure for C60, a "truncated icosahedron", is derived from an icosahedron by truncating or "snipping off" each of the twelve vertices Hence, each vertex is replaced by a five-membered ring - a pentagon. This snipping process also converts each of the twenty former triangular faces into six-membered rings - hexagons.



Icosahedron (left) and "truncated icosahedron" (right).

Bonding in C_{60}

In the proposed structure for C_{60}, each vertex of the truncated icosahedron is occupied by a carbon atom, and each carbon is then-connected to other three carbon atoms by one double bond and two single bonds. Carbon atoms with this kind of connectivity are usually referred to as "sp^2 carbons" because the orbitals used to sigma-bond the three adjacent carbons are hybrids of the 2s orbital and the two 2p orbitals ($2p^x$ and $2p^y$). The remaining 2p orbital ($2p^z$) is responsible for the pi-bond. Usually, an sp^2 carbon and its three neighboring atoms are all coplanar. This is the case, for example, in graphite where there are infinite planar sheets of sp^2 carbons arranged in edge-sharing hexagons. The p^z orbitals all lie parallel to each other and perpendicular to the graphite plane, generating a sea of π- electron density above and below the plane. In graphite, the C-C bonds are all equal in length and are intermediate between normal single and double bonds. This "delocalization" can be explained by noting that graphite has many different but equivalent "resonance structures". (The resonance structures differ only in the placement of the double bonds.)



Two resonance structures of a portion of graphite.

Clearly, the proposed structure for C^{60} is not planar! The angle between a p^z axis and a C-C bond vector, θ is 101.6° (as compared to 90° in planar graphite). The bowl-shape or concavity at each sp^2 carbon center introduces some strain into the molecule. However, the high symmetry distributes this strain evenly across the entire structure.

Other Fullerenes

The truncated icosahedron is not the only possible fullerene-type structure. There are, in fact, many other hollow cage structures that can be constructed using only pentagons and hexagons. Interestingly, each of these structures contains exactly twelve pentagons, while the number of hexagons is arbitrary. The pentagons are necessary for closure. (Recall that graphite, which consists only of fused hexagons, is essentially a planar sheet. While this sheet may warp and bend, it can never close.) The number of vertices in closed fullerene-type structures is necessarily even.

The smallest possible fullerene would be C^{20}, containing twelve pentagons and zero hexagons. However, such a structure would possess a great deal of strain, because the local topology at each carbon center would be highly non-planar. Other possible fullerenes include C^{28}, C^{32}, C^{50}, and C^{70}. Because the molecular strain tends to be concentrated in the five-membered rings that are responsible for closure, structures that avoid contiguous (edge-sharing) pentagons are particularly stable. It turns out that C_{60} and C_{70} are the smallest carbon clusters for which this can be achieved.

Other Possible Structures for C_{60}

While the truncated icosahedron structure for C_{60} is elegant and aesthetically-pleasing, it is important to bear in mind that when it was proposed, there was only one piece of supporting experimental evidence - an unusually large peak at 720 in the

mass spectrum. Other C60 cluster structures, including the following three,arealos possible.

Planar graphite fragments

The problem with this type of structure is that it contains many unsatisfied valences, and it is not clear why C_{60} should be any more stable than any other cluster size.

Cyclic polyalkynes.

In this structure, there are no unsatisfied valences but the stability of C_{60} vs. other cluster sizes is not easily rationalized.

Other fullerenes, i.e., other hollow cage structures with different atom arrangements.

These would necessarily be less highly symmetric than the truncated icosahedron and would less effectively distribute strain evenly around the molecule. Given these possible, albeit less attractive, alternatives, it was crucial to obtain additional experimental evidence for the structure of C60.

4.9 Summary

In this chapter main organic complex molecules (complexed with other hydrocarbon and inorganic compounds) like crown ether complexes, cryptands, inclustion compound etc. are described. This chapter also described the synthesis, properties, applications and structures of cyclodextrins, catenanes, rotaxanes and bonding in fullerenes.

4.10 Review Question / Comprehesive Questions.

1. What are clathrates?
2. Explain inclusion compounds.
3. Explain synthesis of Rotaxanes.
4. Describe structure and applications of cyclodextrines.
5. Explain bonding in fullerene with respect to $C_{60.}$

4.11 References and Suggested readings

1. Adv Organic Chemistry- J. March(Ed IV).
2. Organic Chemistry- Jonathan Claden (Oxford) 2012
3. Material from Internet.

Unit – 5 : Basic Introduction of Stereochemistry

Structure of Unit

5.1. Objectives

At the end of unit learner will be able to understand

- About three dimensional arrangements of atoms is molecule.
- Importance of Isomerism
- Differental ways of representing molecule
- About plane polarized light
- Change of physical properties due to isomerism

- Naming of different isomers
- About symmetry of the molecule
- Nomenclature of zeometrical Isomers

5.2 Introduction

This unit deals with the Stereochemistry is a subdiscipline of chemistry, Which involves the study of the relative spatial arrangement of atoms that form the structure of molecules and their manipulation. An important branch of stereochemistry is the study of chiral molecules.Stereochemistry is also known as 3D chemistry because the prefix "stereo-" means "three-dimensional".The study of stereochemistry focuses on stereoisomers and spans the entire spectrum of organic, inorganic, biological, physical and especially supramolecular chemistry. Stereochemistry includes methods for determining and describing these relationships; the effect on the physical or biological properties of these relationships impart upon the molecules in question, and the manner in which it influence the reactivity of the molecules in question (dynamic stereochemistry). In this unit basic terms of stereochemistry are described i.e. isomerism, chirality, optical Activity, nomenclature of stereo isomers.

5.3. Stereochemistry

The branch of chemistry which deals with three dimensional structure of molecules is known as stereochemistry.

5.4. Isomerism

Isomers are defend as compoiunds having the same molecular formula but different structure , or in other words different compounds having same molecular formula are called isomers and the phenomenon is called Isomerism.

5.5. Constitutional isomerism

The isomers which differ in the connectivity of their atoms in molecule are known as **constitutional isomers** and this phenomenon is known as **constitutional isomerism** The constitutional isomerium includes, chain isomerism, position isomerism, functional isomerism and metamerism.

5.6. Stereoisomerism

Isomers that have same constitution but different spatial arrangement of their atoms or group of atoms are known as stereoisomer's and this type of isomerismis known as stereoisomerism.

Their are two sub-types of stereo isomers:

- **Enantiomers: Stereoisomers which are non superimposable mirror images.**
- **Diastereoisomers: Stereoisomers which are not mirror images.**

The examples of cis- and trans-1,4-dimethylcyclohexane are of the latter type, that is , they are diastereoisomers. Cis- and trans-isomers in general are diastereoisomers. They have the same connectivity but are not mirror images of each other. Enantiomers are mirror image isomers. This is the very most subtle way in which two chemical compounds can differ:In an overal sense, then, **there are three types of isomers:**

(1) constitutional isomers

(2) diastereoisomers and

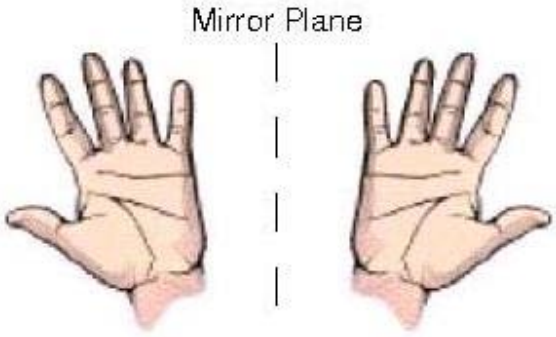
(3) enantiomers in order of increasing subtlety of difference. Since we have previously considered constitutional isomerism, and since the difference between diastereo isomers and enantiomers depends upon the concept of **mirror image isomerism**, we must now about mirror image of isomers.

5.7 Mirror Image Isomerism

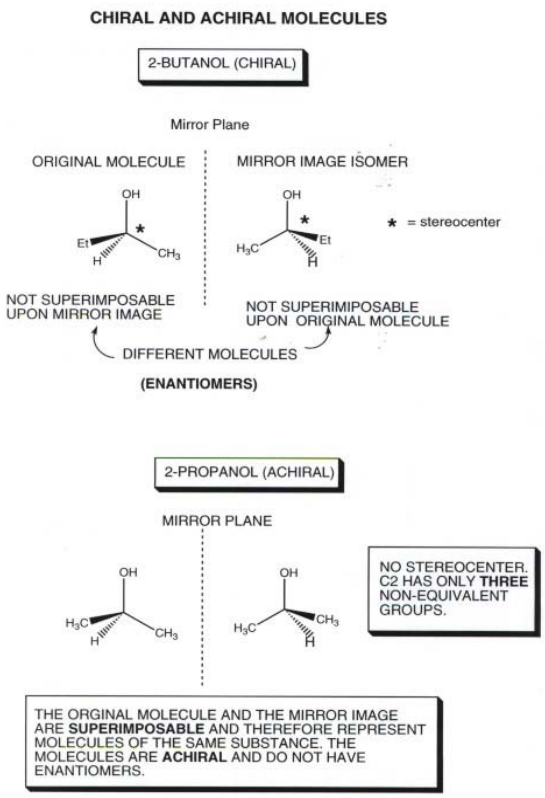
To be an isomer, molecules must not be identical. **The test for "identicality" is one of superimposability**. In a sample of butane, all of the molecules are identical because they can be superimposed upon one another in some conformation. The same is true of ethanol or propanol or 1-butanol, but in the case of 2-butanol there are two isomeric forms which can not be superimposed. They do not differ in connectivity, obviously, or they wouldn't both be called by the same name (2-butanol). They also don't have a cis or trans prefix, to indicate that they are diastereoisomers. They have a very specific, unique relationship to one another, the same relationship which exists between an object and its mirror image. A key aspect of this difference, as we all know, is that a mirror acts to interchange left and right hands.

5.8. Chirality

- A molecule or object which is not identical to (i.e., non-superimposable upon) its mirror image molecule or object is said to be **chiral**. This means it resembles a human hand in that the left and right hands are not superimposabile but can be readily distinguished (at least by some of us).



- In the similar manner, a molecule or any object is said to be **achiral** if it is identical to (superimposable upon) its mirror image molecule or object. Many molecules are achiral, but many are chiral, especially complex molecules such which are found in biological systems.How can we anticipate whether a molecule is chiral and therefore has an isomer (an enantiomer) or if it is achiral and has no enantiomer.
- Consider **2-butanol**, which is an example of a **chiral** molecule. The illustration below shows that the mirror image of 2-butanol isomer is **non-superimposable** upon the original molecule.
- Although 2-butanol is a chiral molecule and therefore has two enantiomers, the very similar molecule **2-propanol is achiral** and does not exist as an enantiomeric pair.

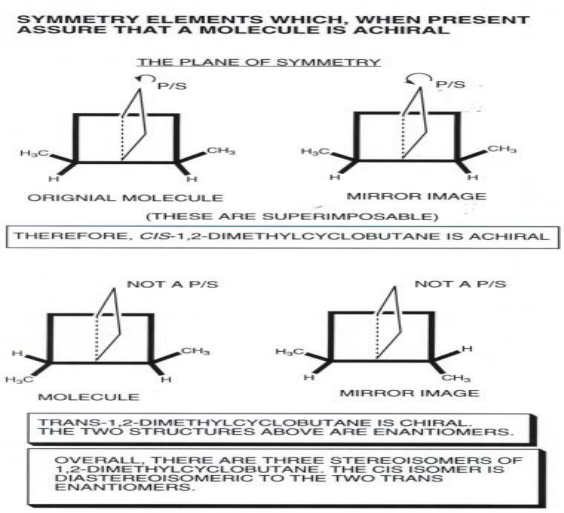


5.9. Stereogenic Centre

In 1874,Van't Hoff and Le Bell independentaly proposed that a molecule with a carbon atom having four different groups arranged tetrahedrally around it would be chiral and will exhibit optical activity aswell a enantiomerism.For example2-butanol (the one marked by an asterisk) is a stereogenic center, having H,OH,methyl, and ethyl groups attached. **Since it has just a single stereogenic center , it must be chiral.** On the other hand, **2-propanol has no stereogenic center and is achiral.** The corresponding carbon atom of 2-propanol has an OH,H, and two methyl groups attached. Of course, no methyl carbon atom or methylene carbon can be chiral since these groups automatically have at least two identical groups (H's) attached. We will see a little later what happens when we have more than one stereogenic center.

The second method, especially useful when there are more than one stereogenic center, is the use of **symmetry elements**.If the molecule or object has either a **plane of symmetry or a center of symmetry it is achiral**. The examples shown below refer to *cis*- and *trans*-1,2-dimethylcyclobutane, The former of which is achiral and the latter chiral. They both have two stereogenic centers, viz., the ring carbons which

have the methyl group and hydrogen attached, but one molecule is chiral and the other achiral. This emphasizes the point that a molecule or object is guaranteed to be chiral only if it has a single stereogenic center. If it has more than one stereogenic center, it may be either chiral or achiral. Note that in the *cis* isomer, the two methyds are on the same side of the ring and are equidistant from the plane of symmtery which runs through the center of the ring, perpendicular to the ring. In the *trans* isomer, the methyls are on opposite sides of the ring, so that where there is a methyl group on the right there is a H on the left.

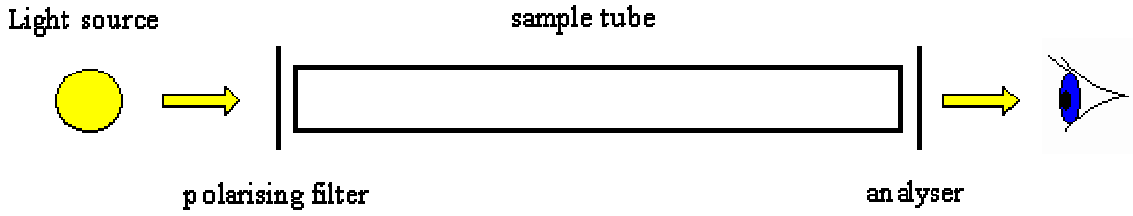


(Figure 5.3)

The *cis* and *trans* isomers of 1,2-dimethylcyclobutane are **diastereoisomers**, having the same connectivity but obviously not being mirror images of each other. To sum up, *there are three isomers of 2,3-dimethylcyclobutane, a single cis isomer, and two enantiomeric trans isomers*.

5.10. Optical Activity

Optical activity is the ability of a chiral molecule to rotate the plane of plane-polairsed light, which is measured using a **polarimeter**. A simple polarimeter consists of a light source, polarising lens, sample tube and analysing lens.



(Figure 5.4)

When light passes through a sample that can rotate plane polarised light, the light appears to be dim because it no longer passing in a straight through the polarising filters. The amount of rotation is quantified as the number of degrees that the analysing lens must be rotated by so that it appears as if no dimming of the light has occurred.

Measuring Optical Activity

When rotation is quantified using a polarimeter it is known as an **observed rotation,** because rotation is affected by path length (*l,* the time the light travels through a sample) and concentration (*c*, how much of the sample is present that will rotate the light). When these effects are eliminated a standard for comparison of all molecules is obtained and this is known as the **specific rotation, [α]**.

[α] = 100 α / *cl* when concentration is expressed as g sample /100ml solution and l is the length of sample tube in decimeter.

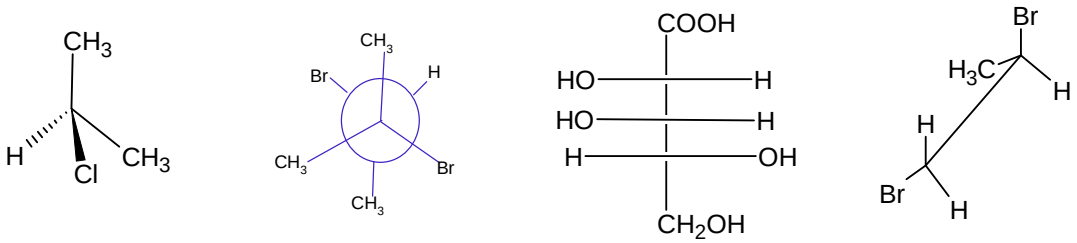
The plane polariesed light can be rotated either to left or to right termninology used to diffentivate the two is dextrorotary.

Dextrorotary designated as *d* or (+), clockwise rotation (to the right)
Levorotary designated as *l* or (-), anti-clockwise rotation (to the left)

If only one enantiomer is present a sample is considered to be **optically pure**. When a sample consists of a mixture of enantiomers, the effect of each enantiomer cancels out. For example, a 50:50 mixture of two enantiomers or a racemic mixture will not rotate plane polarised light and is **optically inactive**. A mixture that contains one enantiomer in excess, however, will display a net plane of polarisation in the direction characteristic of the enantiomer that is in excess.

5.11. Representation of three dimensional molecule.

Three-Dimensional Representations: Straight-Chain Structures



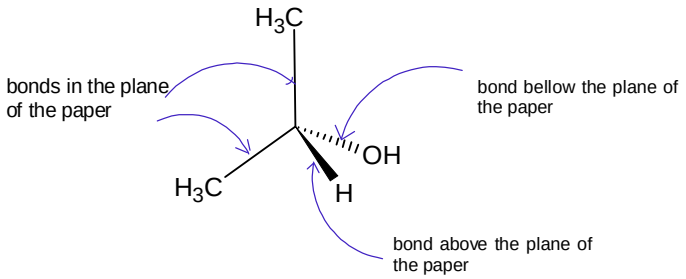
(Figure 5.5)

There are four main types of representations for straight-chain molecules, as shown

above. From left to right, these structures are the *Wedge-Dash,* the *Newman Projection, the Fisher Projection*, and the *Sawhorse Projection*…

Flying-Wedge or Wedge-Dash projections

The Flying-Wedge projection are the most common three-dimensional representation of a three dimensional molecule on a two dimensional surface (paper). This kind of representation is usually done for molecules containing chiral centre. In this representation, the ordinary lines represent bonds in the plane of the paper. A solid Wedge (—) represents a bond above the plane of the paper and a dashed wedge (……..) represents a bond below the plane of the paper. The Flying-Wedge projection formula of (R)- Lactic acid , for example, can be shown as follows…..



(R) - Lactic acid

(Figure 5.6)

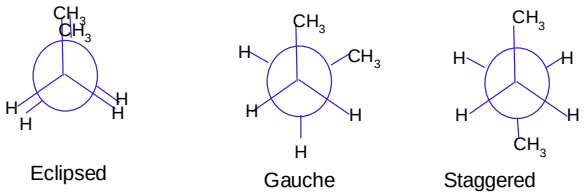
Newman Projections

Newman Projections are used mainly for determining conformational relationships. Recall that conformers are molecules that can be converted into one another by a rotation around a single bond. **Newman Projections** are also useful while studying a reaction involving prochiral molecules that have a double bond, in which the addition of a new group creates a new stereocenter.

In this notation, you are actually viewing a molecule by looking down a particular carbon-carbon bond. The front carbon of this bond is represented by a dot, and the back carbon is represented by a large circle. The three remaining bonds are drawn as *sticks* coming off the dot (or circle), separated by one another by 120 degrees. A **Newman Projection** can be drawn such that the groups on the front carbon are *staggered* (60 degrees apart) or *eclipsed* (directly overlapping) with the groups on the back carbon. Below are two **Newman Projections** of ethane, C_2H_6. The structure on the left is staggered, and the structure on the right is eclipsed. These are the simplest **Newman Projections** because they have only two carbons, and all of the groups on both carbons are identical.

(Figure 5.7)

Adding more carbons makes **Newman Projections** more complicated. For example, **Newman Projections** can be made for butane, such that it's *eclipsed*, *gauche*, and *anti* conformations can be seen. (Recall that these three forms of butane are conformational isomers of one another.) In this case, the front dot represents the second carbon in the butane chain, and the back circle represents the third carbon in the butane chain. The **Newman Projection** condenses the bond between these two carbons.



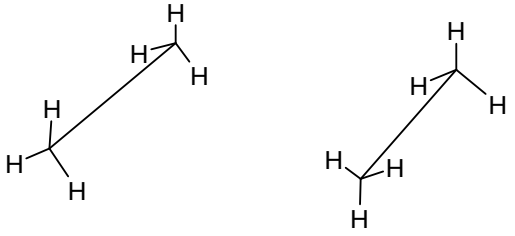
(Figure 5.8)

Sawhorse Projections

Sawhorse Projections are very similar to Newman Projections, but are used more often because the carbon-carbon bond that is compressed in a Newman Projection is fully drawn out in a **Sawhorse Projection**. When properly laid-out, **Sawhorse Projections** are useful for determining enantiomeric or diasteromeric relationships between two molecules, because the mirror image or superimposibility relationships are clearer.

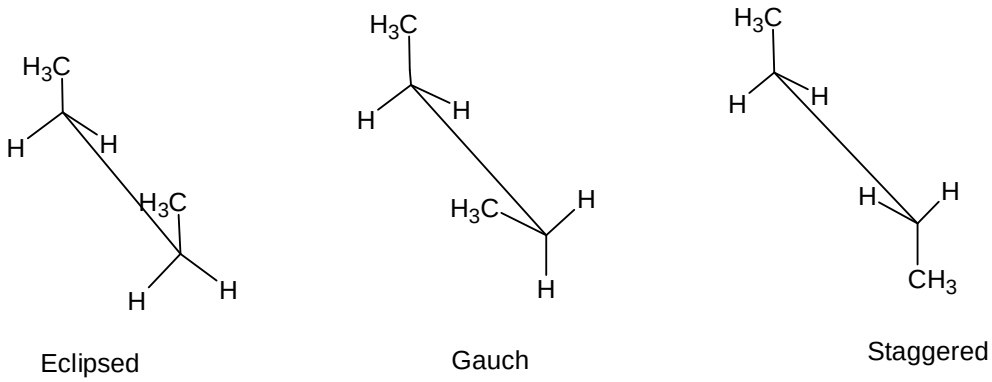
Like with Newman Projections, a **Sawhorse Projection** is a view of a molecule down a particular carbon-carbon bond, and groups connected to both the front and back carbons are drawn using *sticks* at 120 degree angles. **Sawhorse Projections** can also be drawn so that the groups on the front carbon are *staggered* (60 degrees apart) or *eclipsed* (directly overlapping) with the groups on the back carbon. Below are two **Sawhorse Projections** of ethane. The structure on the left is staggered, and the structure on the right is eclipsed. These are the simplest **Sawhorse**

Projections because they have only two carbons, and all of the groups on the front and back carbons are identical.



(Figure 5.9)

Adding more carbons makes **Sawhorse Projections** slightly more complicated. As with Newman Projections, **Sawhorse Projections** can be made for butane, such that it's *eclipsed*, *gauche*, and *anti* conformations can be seen. (Recall that these three forms of butane are conformational isomers of one another.) Notice that is much easier to determine the number of carbons in the longest chain using **Sawhorse Projections** than it is for Newman Projections because the carbon-carbon bond between the second and third carbons is drawn out.

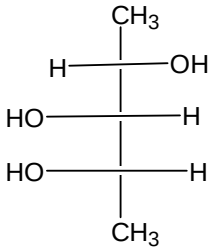


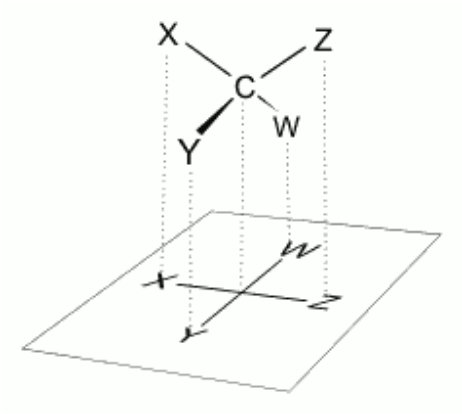
(Figure 5.10)

Fischer Projection

A simplifed representation of fisher projection formula is flying wedge representation in which all bonds are drawn as solid lines.

The use of Fischer projections in non-carbohydrates are discouraged, as such drawings are ambiguous and are confused with other types of drawing.





(Figure 5.11)

Fischer Projections are used often in drawing sugars and hydrocarbons, because the carbon backbone is drawn as a straight vertical line, making them very easy to draw. When properly laid-out, **Fischer Projections** are useful for determining enantiomeric or diasteromeric relationships between two molecules, because the mirror image relationship is very clear.

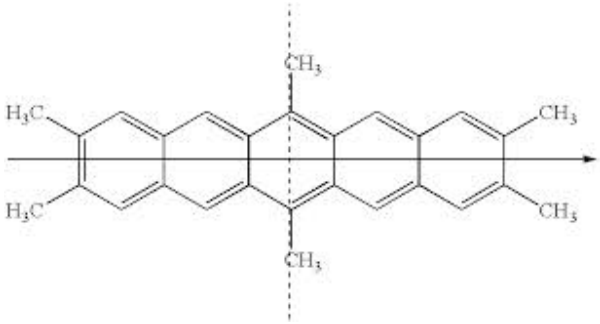
In a **Fischer Projection**, each place where the horizontal and vertical lines cross each other represents a carbon. The vertical lines are actually oriented away from you (similar to *dashes* in the Wedge-Dash Notation) and the horizontal lines are oriented toward you (similar to *wedges* in the Wedge-Dash Notation).

5.12. Element of Symmetry

All the optically of active molecules are chiral and they exhibit enantiomerism. Element of symmetry offer a simple device to decide whether a molecule is chiral or not. When a molecule has a plane of symmetry or a centre of symmetry or an n-fold alternating axis of symmetry ,it is superimposable on its mirror image and molecule is achiral.

Plane of symmetry

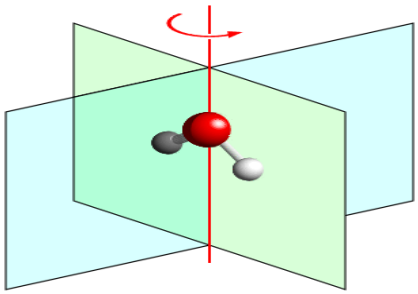
An imaginary plane which passes through atoms and bonds in a molecule such that it divides it into two halves each one a mirror image of the other.



(Figure 5.12)

Simple axis of symmetry

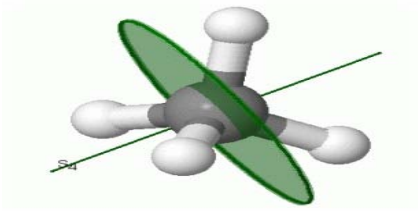
A "n" fold simple axis of symmetry is an axis passing through a molecule in such a way that rotation about this axis by an angle of 360/n degrees brings the molecule into a position indistinguishable from the original position.



(Figure 5.13)

Centre of symmetry

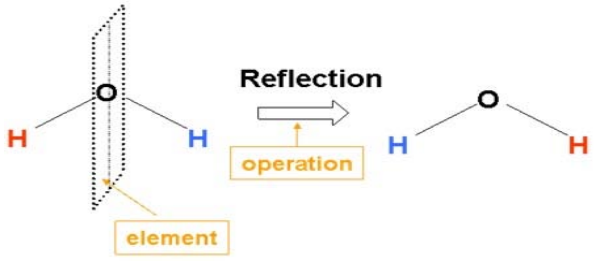
A point within the molecule such that if a straight line is drawn from any part of the molecule through it and extended on either side to an equal distance meets with similar environment. For a sphere the geometrical centre represents the centre of symmetry.



(Figure 5.14)

Alternating "n" fold axis of symmetry(Rotation-reflection symmetry)

The molecule containing such an axis is rotated by 360/n degrees about the axis and is followed by reflection across a plane at right angles to the axis a new molecule is obtained which is in distinguishable from the original one.



(Figure 5.15)

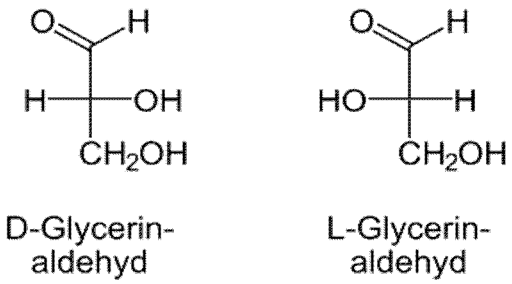
5.13. Nomenclature of stereo isomers

D.L. System of Nomenclature

The oldest system of nomenclature of enantiomers is DL system.In this system configuration of all compounds were designed with respect to glyceraldehydes(relative configuration), the configuration of which was taken as arbitory standard by Rosanoff(1906).

The compound glyceraldehyde, $HOCH_2CH(OH)CHO$, was chosen as the standard reference for defining configuration.

- Those enantiomer which rotates plane polarized light in clockwise (+) direction were arbitrarily as labeled D
- The other enantiomer which rotates plane polarized light in anlotock wise / directions become L.



(Figure 5.16)

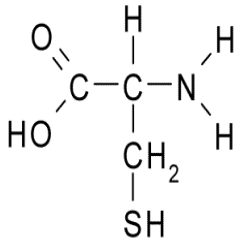
As shown, the assignments in modern notation are R and S, respectively. (Note: it will **not** always work out that D = R and L=S; this is an accident here.)

- The source of the D and L labels was the Latin words *dexter* (on the right)

  and *laevus* (on the left)

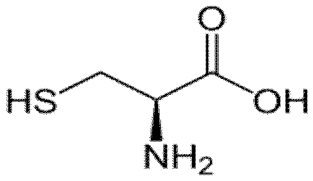
- R comes from *rectus* (right-handed) and S from *sinister* (left-handed)

  Any other molecule containing a single chiral center was to be assigned as D or L by imagining a resemblance between the ligands on its chiral center and those in glyceraldehyde
- The enantiomer having the "same or similar" groups in the same places as D-glyceraldehyde becomes D.
- Thus, for example, the naturally occuring form of the amino acid cysteine was labeled L.



L-Cystein

(Figure 5.17)

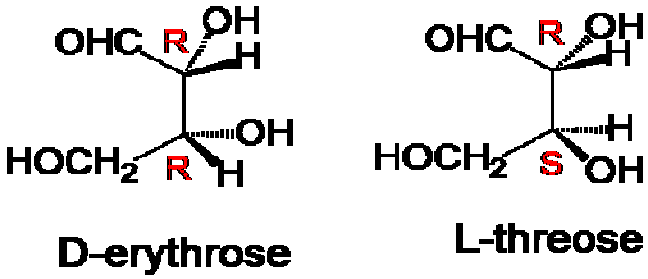


L-Cystein

(Figure 5.18)

When more than one chiral center is present, similarity is defined only by the arrangement of ligands on the highest numbered chiral center, and the assignment of D or L is made on the basis of that center only.

- The configuration at the other centers usually is specified by giving the diastereomeric molecules entirely different names.
- The student is expected simply to memorize which arrangement of ligands goes with which names.
- For example, look at the two aldotetroses below:



(Figure 5.19)

- The D and L were assigned on the basis of the arrangement at the lower of the two chiral centers.
- That the two sugars are diastereomers which is specified by giving them different names.

Clearly, this system is not possible to apply widely, and it requires extensive memorizing of structures, and is also seriously ambiguous.

5.14. R.S. System of nomenclature

Since two enantiomers are different compounds, we will need to have nomenclature which distinguishes them from each other. The convention which is used is called the (R,S) system because one enantiomer is assinged as the R enantiomer and the other as the S enantiomer. This nomenclature is govern by some rules.

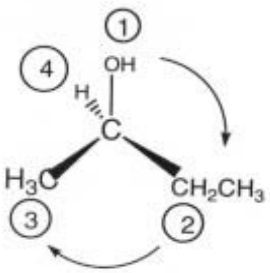
- Priorities are assigned to each of the four different groups attached to a given stereogenic center from to four, one being the group of highest priority). (It should be understood that each stereogenic center has to be treated separately.)
- Orient the molecule such that the group of the last (fourth) priority four (lowest priority) points away from the observer.
- Draw a circular arrow from the group of first priority to the group of second priority.
- If this circular motion is clockwise, the enantiomer is the R enantiomer. If it is counterclockwise, it is the S enantiomer.
- There is also a set of conventions (rules) which govern the setting of group priorities, which is a part of the R,S system of nomenclature.

- **Priority is based upon atomic number**, i.e., H has the lowest priority, O over C, F over O, and so on. **Priority assignment is based upon the four atoms directly attached to the stereogenic center**. For example, in 2-butanol, the example we considered previously, the four atoms are H,O, and two C's. Oxygen gets the first priority, and H the fourth. But the methyl and ethyl groups both are attached through carbon , so there is initially a tie for the second and third priorities.

- In this kind of tie situation, priority assignments proceed outward to the next atoms, which we will call the beta atoms.(The directly attached atoms are the alpha atoms). For the methyl group, the alpha atom is carbon and the beta atoms are three H's, while for the ethyl group the alpha atom is also carbon and the beta atoms are two H's and 1 carbon. This beta C of the ethyl group wins the priority competition because there is no beta atom on the methyl group which has an atomic number greater than 1 (all three beta atoms are H). In general, the competition continue from alpha to beta to gamma to delta atoms until a tie-breaker is found.

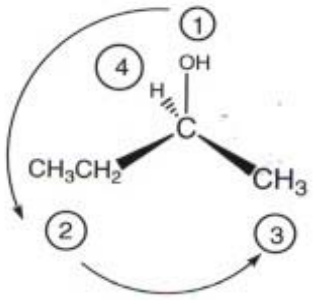
- Some additional conventions are necessary for handling multiple bonds and aromatic bonds, and these are a little tricky to learn. As an example, take the vinyl group. Each carbon of this double bond is considered to have two bonds to carbon, because of the double bond. In the case of a carbonyl group, the carbon is considered to be bonded to two oxygens, and the oxygen is considered to be bonded to two carbons. For this reason, a vinyl group has priority over an isopropyl group, as shown in the illustration.

R,S NOMENCLATURE FOR ENANTIOMERS



Clockwise arrow motion, therefore this is the R enantiomer of 2-butanol

(R)-2-butanol

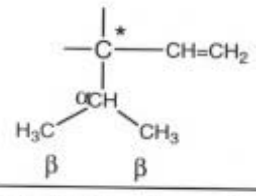


Counterclockwise motion, therefore this is the S enantiomer of 2-butanol

(S)-2-butanol

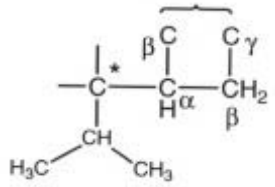
Priority Rating for C-C Multiple Bonds

Consider the following partial structure, where the star designates a stereocenter. The competition is between an isorpropyl group and a vinyl group. The latter requires special handling because of the C=C.



by convention is treated as:

supplied to simulate the double bond

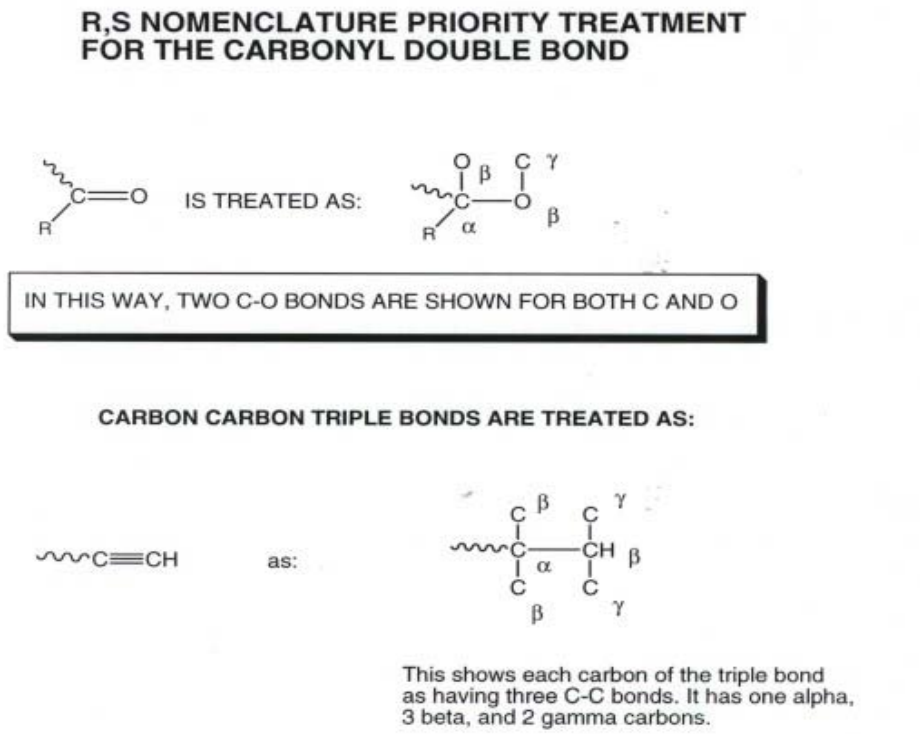


The isopropyl group has 1 alpha and 2 beta carbons

The Count is : α,β,β ⇦ Lower priority

The simulated doublel bond has a alpha and 2 beta carbons, like the isopropyl group, but it also has a gamma carbon

Count: α.β.β.γ ⇦ Higher priority



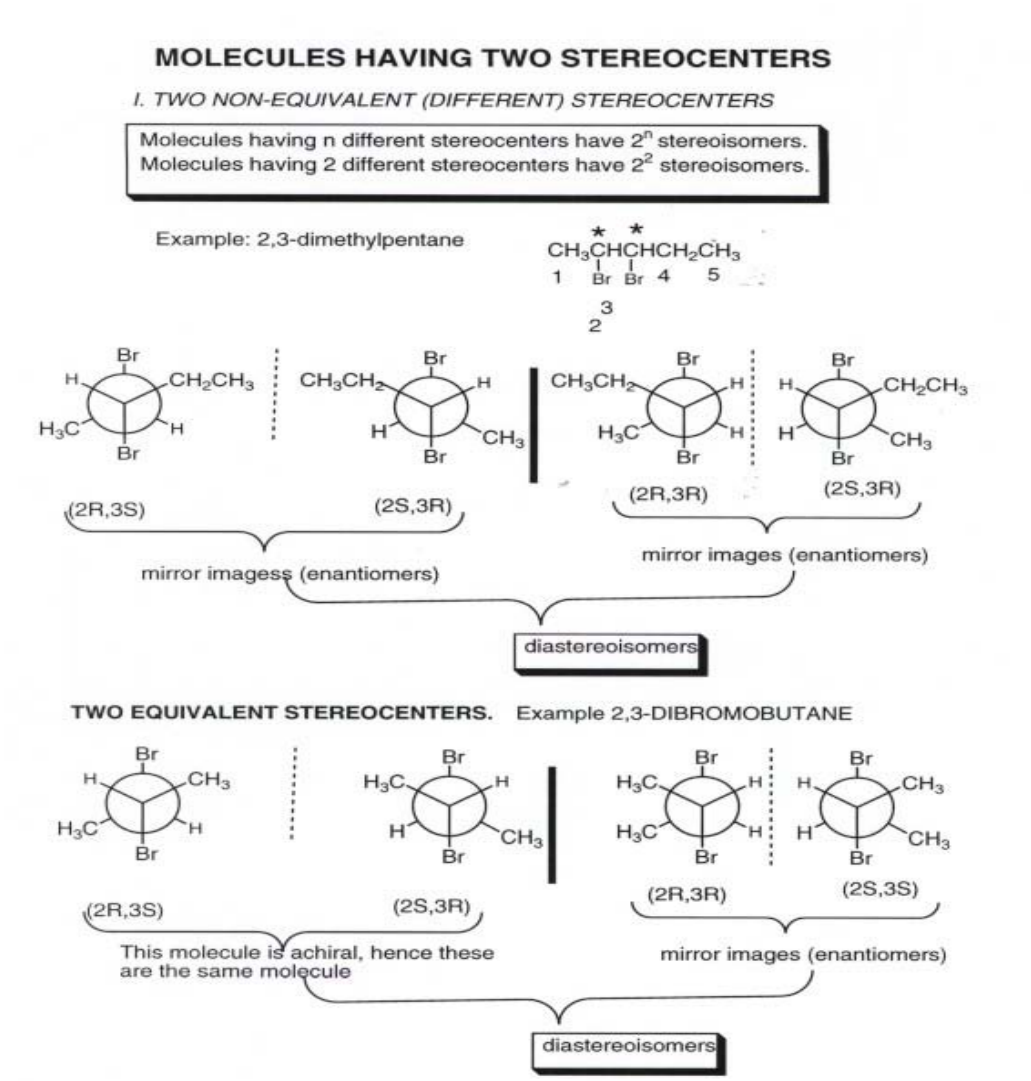
(Figure 5.22)

5.15.Two Stereogenic Centers

Non-Equivalent Stereogenic Centers

When a molecule has two stereogenic centers, each of them can be designated as R or S. Thus there are four possible stereoisomers. If we designate one stereocenter as "a" and the other as "b" just for labelling purposes, the four stereoisomers can be designated as R_aR_b,R_aS_b,S_aR_b, and S_aS_b These designations correspond to the cirucumstance possible for stereocenter "a" (It can have the R or S configuration ,and stereocenter "b" can have either configuration) In general, if there are n such stereogenic centers , there will be a maximum of 2^n stereoisomers. For example, with three stereogenic centers, there are eight possible stereoisomers. The maximum number of 2^n Stereiomers actually) occurs when there are all non-equivalent stereocenters. Stereogenic centers are equivalent when all four substituents attached to the both centers are identical. For example, in 2,3-dibromobutane, both stereogenic carbons have a H, a Br, a methyl, and a 1-bromoethyl substituent. The maximum of four stereoisomers is not observed here, as we observed before. In fact there are three stereoisomers, including one achiral stereoisomer. This is because the 2R,3S molecule is identical to the 2S,3R molecule, since carbons 2 and 3 are

equivalent.On the other hand, 2,3-dibromopentane has two non-equivalent stereogenic centers and there are four stereoisomers, consisting of two pairs of enantiomers. It should be noted that the relationship between one enantiomeric pair and the other pair of enantiomers is that they are diastereoisomers..



(Figure 5.23)

Two Equivalent Stereogenic Centers

- As noted above, when both stereogenic centers are equivalent, the number of stereoisomers is less than the maximum of 2^n, and fact it is n + 1. In the case of two stereogenic centers (n = 2), there are 3 stereoisomers, as we saw for 2,3-dibromobutane. There is, first of all , a pair of enantiomeers: these are the

(2R,3R) and (2S,3S) isomers. Note that the mirror image of 2R,3R is 2S,3S (i.e., the mirror image inverts the configuration at each stereocenter).

- There is also an achiral stereoisomer. A molecule which has stereocenters but is achiral is called a **meso compound.** We saw in an earlier diagram that this molecule has a point of symmetry in its most stable conformation.
- It should be noted carefully that the meso isomer is a **diastereoisomer** of the two enantiomers.

Comparative Properties of Enantiomers and Diastereoisomers.

Diastereoisomers.

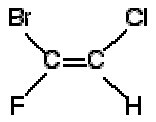
- Diastereoisomers are **not** mirror image isomers. They are essentially like any other pair of isomers (e.g., constitutional isomers) in that they have distinct chemical and physical properties. Since they have the same functional groups, however, they are usually rather similar to one another in their reactions and properties.
- Two diastereoisomers can usually be separated from one another by e.g., recrystallization, since they have different solubilities.
- Although their chemical properties(reactions) are similar, the **two diastereoisomers will typically react at different rates**.

Enantiomers

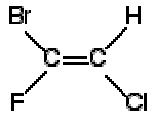
- Since two enantiomers are mirror images of each other, they are not distinguished by any physical or chemical means
- Therefore 2 enantiomers have exactly the same energy, solubility in typical achiral solvents, boiling and melting points, NMR and IR spectra, etc.
- Their chemical properties, including both the qualitative reactions and the quantitative rates of

5.16. E-Z Notation For Geometrical Isomers

Consider a simple case of geometrical isomerism. If the two groups with the higher priorities are on opposite sides of the double bond, then this is the (E)- isomer. and Z hands fdor German word zussaman maning together E comes from the German word entgegen which means opposite and of the two groups with higher priorites are on same side of the double bond then this is z isomer. So the two isomer are



(Z)-rest_of_name



(E)-rest_of_name

(E)- : the higher priority groups are on opposite sides of the double bond.

(Z)- : the higher priority groups are on the same side of the double bond

5.17 Summary

The above unit describes basic introduction of stereochemistry, which is a subdiscipline of chemistry, and it involves the study of the relative spatial arrangement of atoms that form the structure of molecules and their manipulations. Stereochemistry includes methods for determining and describing these relationships; the effect on the physical or biological properties these relationships impart upon the molecules in question, and the manner in which these relationships influence the reactivity of the molecules in question (dynamic stereochemistry). In this unit basic terms of stereochemistry are described i.e. isomerism, chirality, optical Activity, nomenclature of stereo isomers. The learner is able to understand about basics of stereochemistry in which learners can learn chiraly, optical activity, E,Z and R,S nomenclature of stereoisomers. Thus unit is enough to understand basics of stereochemistry of organic molecules.

5.18. Review Questions / Comprehensive Questions

1. Explain different type of symmetry elements present in a molecule.
2. What is optical activity? How you will obtain plane polarized light?
3. Define stereoisomerism. Explain Enantiomers and Diastereoisomers by getting suitable examples.
4. What is Chirality? Explain it by taking examples.
5. Explain Newmann projection and Sawhorse Projections formulas..
6. Explain R S System of nomenclature. How it is better than DL System?
7. Explain EZ System of nomenclature by taking example.
8. Draw the configuration and specify the R and S enantiomers of 2-Chloropentane.

9. Draw the Fischer projection for(R)-2-iodobutane and convert it to flying wedge formula.
10. Label the hydrogen atom in cis-1,2-dichlorocyclopropane as enantiotropic or diastereotopic

5.19.References and Suggested Readings

1. Advance Organic Chemistry, Jerry March, John Wiley.
2. Advanced Organic chemistry, F.A.Carey and Sundberg, Plenum
3. Structure and Mechanism in Organic Chemistry, C.K.Ingold, Comell University Press.
4. Organic Chemistry, R.T.Morrison and R.N.Boyed,Prentice-Hall.
5. Stereochemistry of Organic Compounds, D.Nasipuri,New Age International.
6. Stereochemistry of Organic Compounds, P.S.Kalsi,New Age International
7. research.cm.utexas.edu/nbauld/teach/stereo.html
8. www.chemeddl.org/resources/stereochem/**threed3**.htm
9. http://www.google.co.in/search?q=images+of+symmetry+of+molecule
10. Al-Hilalmission (An Educational, Cultural & Social Welfare Organization) Kadambagachhi, Barasat, Kolkata-7000125

Unit - 6 : Stereochemical Principles

Structure of Unit:

6.1 Objectives

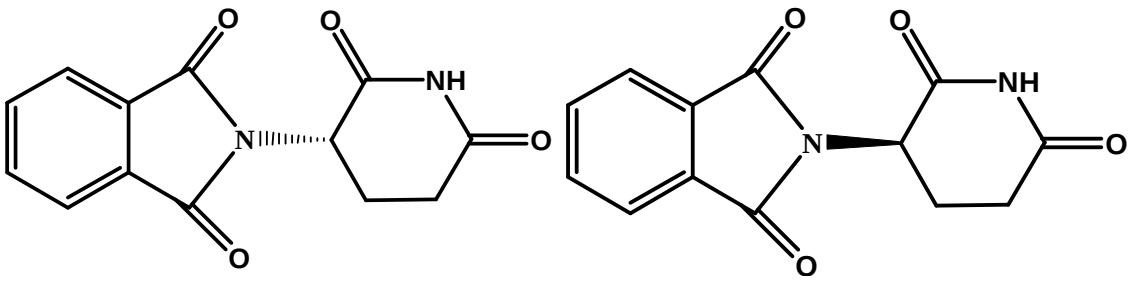
At the end of the unit learner will be able to understand

- What is stereochemistry.
- Enantiomeric and diastereomeric relationship of molecules.
- Nomenclature of different conformations.
- Prochirality, stereoselectivity and stereospecificity.

6.2 Introduction

Stereochemistry involves the study of the relative spatial arrangement of atoms constituting molecules and their manipulation. The study of chiral molecules is very important topic in stereochemistry. Stereochemistry is also known as 3D chemistry because the prefix "stereo-" means "three-dimensionality". The study of stereochemistry focuses on stereoisomers and spans the entire spectrum of organic, inorganic, biological, physical and especially supramolecular chemistry. Stereochemistry includes methods for determining and describing these relationships, the effect on the physical or biological properties these relationships impart upon the molecules in question, and the manner in which these relationships influence the reactivity of the molecules in question Louis Pasteur described as the first stereochemist, observed in 1849 that salts of tartaric acid collected from wine production vessels could rotate plane polarized light, but the salts from other sources could not. This property, the only physical property in which the two types of tartrate salts differed, is due to optical isomerism. In 1874, Jacobus Henricus van 't Hoff and Joseph Le Bel explained optical activity in terms of the tetrahedral arrangement of the atoms bound to carbon. Cahn-Ingold-Prelog priority rules are given for describing a molecule's stereochemistry. They rank the atoms around a stereocenter in a standard way, allowing the relative position of these atoms in the molecule to be described unambiguously. A Fischer projection is a simplified way to depict the stereochemistry around a stereocenter.

An offen used example of the importance of stereochemistry relates to the thalidomide disaster. Thalidomide is a drug, first prepared in 1957 in Germany, prescribed for treating morning sickness in pregnant women.



(Figure 6.1)

Thalidomide enantiomers

The drug was discovered to be teratogenic, causing serious genetic damage to early embryonic growth and development, leading to limb deformation in babies. Some of the several proposed mechanisms of teratogenecity involve a different biological interaction for the (R)- and the (S)-thalidomide enantiomers. In the human body however, thalidomide undergoes racemization: even if only one of the two enantiomers is administered as a drug, the other enantiomer is produced as a result of metabolism. Accordingly, it is incorrect to state that one of the stereoisomer is safe while the other is teratogenic.

Types of stereoisomerism

Atropisomerism- are stereoisomers resulting from hindered rotation about single bonds In such compounds the steric strain energy barrier to rotation is high enough to allow the isolation of the conformers.

Cis-trans isomerism- cis/trans isomerism is also known as geometrical isomerism and is a form of stereoisomerism which describes the relative orientation of functional groups within a molecule. In general, such isomers contain double bonds, which cannot rotate, but this can also arise from ring structures, wherein the rotation of bonds is greatly restricted. Cis and trans isomers occur both in organic molecules and in inorganic coordination complexes.

Conformational isomerism- Conformational isomerism is a form of stereoisomerism in which the isomers can be interconverted exclusively by rotations about single bonds. Such isomers are generally referred to as conformational isomers or conformers and, specifically, as rotamers. Rotations about single bonds are restricted by a rotational energy barrier which must be overcome to interconvert one conformer to another. Conformational isomerism arises when the rotation about a single bond is relatively unhindered. That is, the energy barrier must be small enough for the interconversion to occur. **Diastereomers**- Diastereomers are stereoisomers that are not enantiomers. Diastereomerism occurs when two or more stereoisomers of a compound have different configurations at one or more of the equivalent stereocenters but are not mirror images of each other. When two diastereoisomers differ from each other at only one stereocenter they are epimers. Each stereocenter gives rise to two different configurations and thus increases the number of stereoisomers by a factor of two. **Enantiomers**- An enantiomer is one of two stereoisomers that are mirror images of each other that are non-superposable, like one's left and right hands are the same except for opposite orientation. Organic compounds that contain a chiral carbon usually have two non-superposable

structures. These two structures are mirror images of each other and are, thus, commonly called enantiomorphs (enantio = opposite ; morph = form), and this structural property is now commonly referred to as enantiomerism. Enantiomers are offen show different chemical reactions with other substances what are also enantiomers. Since many molecules in the bodies of living beings are enantiomers themselves, there is sometimes a marked difference in the effects of two enantiomers on living beings. In drugs, for example, often only one of a drug's enantiomers is responsible for the desired physiologic effects, while the other enantiomer is less active, inactive, or sometimes even responsible for adverse effects.

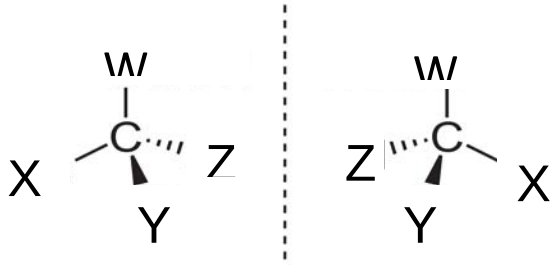
6.3 Enantiometric Relationships

Any compound that rotates the plane of polarized light is said to be optically active. If a pure compound is optically active, the molecule is nonsuperimposable on its mirror image. If a molecule is superimposable on its mirror image, the compound does not rotate the plane of polarized light; it is optically inactive. The property of nonsuperimposability of an object on its mirror image is called chirality. If a molecule is not superimposable on its mirror image, it is chiral. If it is superimposable on its mirror image, it is achiral. The relationship between optical activity and chirality is absolute. No exceptions are known, and many thousands of cases have been found in accord with it. The ultimate criterion, then, for optical activity is chirality (nonsuperimposability on the mirror image). This is both a necessary and a sufficient condition. This fact has been used as evidence for the structure determination of many compounds, and historically the tetrahedral nature of carbon was deduced from the hypothesis that the relationship might be true. Note that parity violation represents an essential property of particle and atomic handedness, and has been related to chirality. If a molecule is nonsuperimposable on its mirror image, the mirror image must be a different molecule, since superimposability is the same as identity. In each case of optical activity of a pure compound there are two and only two isomers, called enantiomers (sometimes enantiomorphs), which differ in structure only in the left and right handedness of their orientations.

Enantiomers have identical physical and chemical properties except in two important respects:

1. They rotate the plane of polarized light in opposite directions, although in equal amounts. The isomer that rotates the plane to the left (counterclockwise) is called the levo isomer and is designated as (-), while the one that rotates the plane to the right (clockwise) is called the dextro isomer and is designated

(+). Because they differ in this property they are often called optical antipodes.



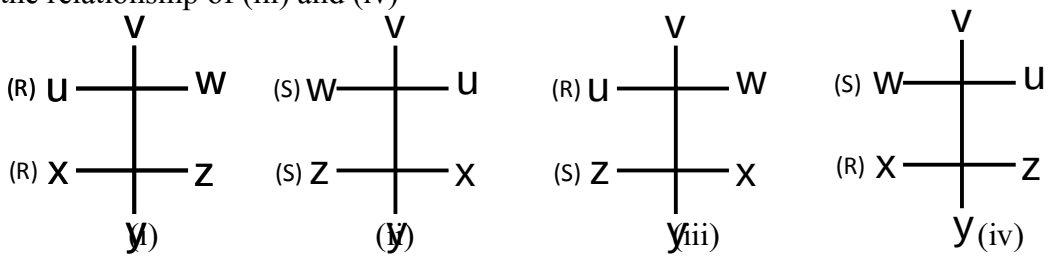
Enantiomers Figure 6.2

2. They react at different rates with other chiral compounds. These rates may be so close together that the distinction is practically useless, or they may be so far apart that one enantiomer undergoes the reaction at a convenient rate while the other does not react at all. This is the reason that many compounds are biologically active while their enantiomers are not. Enantiomers react at the same rate with achiral compounds.

In general, it may be said that enantiomers have identical properties in a symmetrical environment, but their properties may differ in an unsymmetrical environment. Besides the important differences previously noted, enantiomers may react at different rates with achiral molecules if an optically active catalyst is present; they may have different solubilities in an optically active solvent; they may have different indexes of refraction or absorption spectra when examined with circularly polarized light, and so on. In most cases, these differences are too small to be useful and are often too small to be measured. Although pure compounds are always optically active if they are composed of chiral molecules, mixtures of equal amounts of enantiomers are optically inactive since the equal and opposite rotations cancel. Such mixtures are called racemic mixtures or racemates. Their properties are not always the same as those of the individual enantiomers. The properties in the gaseous or liquid state or in solution usually are the same, since such a mixture is nearly ideal, but properties involving the solid state, such as melting points, solubilities, and heats of fusion, are often different. The separation of a racemic mixture into its two optically active components is called resolution. The presence of optical activity always shows that a given compound is chiral, but its absence does not shows that the compound is achiral. A compound that is optically inactive may be an achiral, or it may be a racemic mixture.

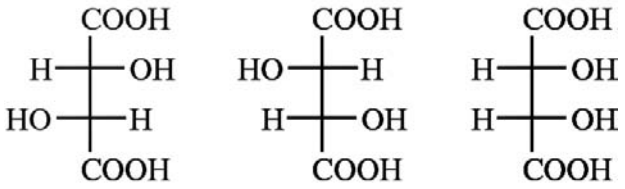
6.4 Diastereomeric Relationships

When a molecule has two stereogenic centers, each has its own configuration and can be classified (R) or (S) by the Cahn–Ingold–Prelog method. There are a total of four isomers, since the first center may be (R) or (S) and the same is with second. Since a molecule can have only one mirror image, only one of the other three can be the enantiomer of (i). This is (ii). Both (iii) and (iv) are a second pair of enantiomers and the relationship of (iii) and (iv)



(Figure 6.3)

to (i) and (ii) is designated by the term diastereomer. Diastereomers may be defined as stereoisomers that are not enantiomers. Since (iii) and (iv) are enantiomers, they must have identical properties, the same is true for (i) and (ii). However, the properties of (i) and (ii) are not identical with those of (iii) and (iv). They have different melting points, boiling points, solubilities, reactivity, and all other physical, chemical, and spectral properties. The properties are usually similar, but not alike. In particular, diastereomers have different specific rotations; indeed one diastereomer may be chiral and rotate the plane of polarized light while another may be achiral and not rotate at all. It is now possible to see why, as mentioned before, enantiomers react at different rates with other chiral molecules, but at the same rate with achiral molecules. In the latter case, the activated complex formed from the (R) enantiomer and the other molecule is the mirror image of the activated complex formed from the (S). Since the two activated complexes are enantiomeric, their energies are the same and the rates of the reactions in which they are formed must be the same. However, when an (R) enantiomer reacts with a chiral molecule that has, say, the (R) configuration, the activated complex has two chiral centers with configurations (R) and (R), while the activated complex formed from the (S) enantiomer has the configurations (S) and (R). The two activated complexes are diastereomeric and do not have the same energies, and consequently are formed at different rates.



***dl* Pair** **meso**

(Figure 6.4)

Although four is the maximum possible number of isomers when the compound has two stereogenic centers (chiral compounds without a chiral carbon, or with one chiral carbon and another type of stereogenic center), some compounds have fewer. When the three groups on one chiral atom are the same as those on the other, one of the isomers (called a meso form) has a plane of symmetry, and hence is optically inactive, even though it has two chiral carbons. Tartaric acid is a typical case. There are only three isomers of tartaric acid: a pair of enantiomers and an inactive meso form. For compounds that have two chiral atoms, meso forms are found only where the four groups on one of the chiral atoms are the same as those on the other chiral atom. In most cases with more than two stereogenic centers, the number of isomers can be calculated from the formula 2n, where n is the number of chiral centers, although in some cases the actual number is less than this, owing to meso forms. Two diastereomers that have a different configuration at only one chiral center are called epimers.

6.5 R and S, E and Z Nomenclature

The Cahn–Ingold–Prelog rule (CIP system of nomenclature)

The Cahn–Ingold–Prelog rules are distinctly different from those of other naming conventions, such as general IUPAC nomenclature, since they are designed for the specific task of naming stereoisomers rather than the general classification and description of compounds. This has replaced the DL system. In this system the four groups on an asymmetric carbon are ranked according to the set of priority rules.

The steps for naming molecules using the CIP system are often presented as:

1. Identification of stereocenters and double bonds
2. Assignment of priorities to the groups attached to each stereocenter or double-bonded atom
3. Assignment of R/S and E/Z descriptors

The details are as follows:

1. Substituents are listed in order of decreasing atomic number of the atom directly joined to the carbon.
2. Where two or more of the atoms connected to the asymmetric carbon are the same, the atomic number of the second atom determines the order. For example, in the molecule $(CH_3)_2CH\text{-}CHC_1\text{-}CH_2OH$, the CH_2OH group takes precedence over the Me_2CH group because oxygen has a higher atomic number than carbon. Note that this is so even although there are two carbons in Me_2CH and only one oxygen in CH_2OH. If two or more atoms connected to the second atom are the same, the third atom determines the precedence, and so on.
3. All atoms except hydrogen are formally given a valence of 4. Where the actual valence is less (as in nitrogen, oxygen, or a carbanion), phantom atoms (designated by a subscript 0) are used to bring the valence up to four. These phantom atoms are assigned an atomic number of zero and necessarily rank lowest. Thus the ligand $-HNHMe_2$ ranks higher than $-NMe_2$.
4. A tritium atom takes precedence over deuterium, which in turn takes precedence over ordinary hydrogen. Similarly, any higher isotope (e.g., 14C) takes precedence over any lower one.
5. Double and triple bonds are counted as if they were split into two or three single bonds, respectively, (note the treatment of the phenyl group). Note that in a C=C double bond, the two carbon atoms are each regarded as being connected to two carbon atoms and that one of the latter is counted as having three phantom substituents.

By application of the above rules, some groups in descending order of precedence are COOH, COPh, COMe, CHO, CH(OH)2, o-tolyl, m-tolyl, p-tolyl, phenyl, C=CH, tert-butyl, cyclohexyl, vinyl, isopropyl, benzyl, neopentyl, allyl, n-pentyl, ethyl, methyl, deuterium, and hydrogen. Thus the four groups of glyceraldehyde are arranged in the sequence: OH, CHO, CH_2OH, H.

Once the order is determined, the molecule is held so that the lowest group in the sequence is pointed away from the viewer. Then if the other groups, in the order listed, are oriented clockwise, the molecule is designated (R), and if counterclockwise, there is designated as (S).

Double bonds: E/Z

For alkenes and similar double bonded molecules, the same process assigning priorities is followed for the substituents. In this case, it is the placing of the two

highest priority substituents with respect to the double bond which matters. If both high priority substituents are on the same side of the double bond, i.e. in the cis configuration, then the stereoisomer is assigned as Z or Zusammen configuration. If, by contrast they are in a trans configuration, then the stereoisomer is assigned an E or Entgegen configuration. In this case the identifying letters are derived from German for 'together' and 'in opposition to', respectively.

6.6 Dynamic Stereochemistry

Dynamic stereochemistry includes the effect of stereochemistry on the rate of chemical reactions involving bond breaking or making or on conformational transformations involving of interconversion of conforms. It correlates the stereochemistry of starting materials and products in terms of transition states and intermediats

6.7 Prochiral Relationship

Prochiral molecules are those that can be converted from achiral to chiral in a single step. If two identical substituents are attached to a sp^3-hybridized atom, the descriptors pro-R and pro-S are used to distinguish between the two. Promoting the pro-R substituent to higher priority than the other identical substituent results in an R chirality center at the original sp3-hybridized atom, and analogously for the pro-S substituent. A trigonal planar sp^2-hybridized atom can be converted to a chiral center when a substituent is added to the re or si face of the molecule. A face is labeled re if, when looking at that face, the substituents at the trigonal atom are arranged in decreasing Cahn-Ingold-Prelog priority order in a clockwise order, and si if the priorities decrease in counter-clockwise order; but the designation of the resulting chiral center as S or R depends on the priority of the incoming group.

6.8 Stereoselective and Stereospecific Reactions

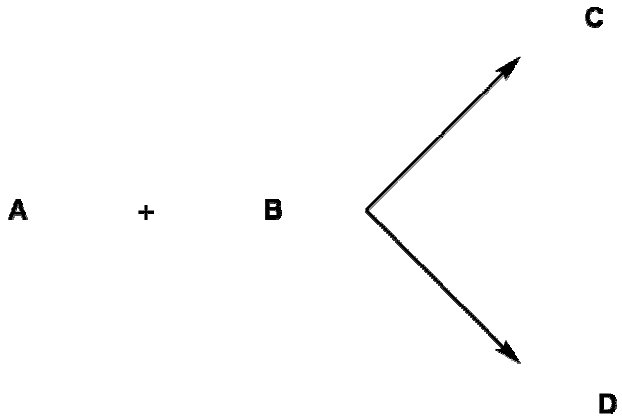
Stereoselective and stereospecific reactions

Stereoselective Reaction

Stereoselectivity is the property of a chemical reaction in which a single reactant forms an unequal mixture of stereoisomers during the non-stereospecific creation of a new stereocenter or during the non-stereospecific transformation of a pre-existing one. The selectivity arises from differences in steric effects and electronic effects in the mechanistic pathways leading to the different products. Stereoselectivity can vary in degree but it can never be total since the activation energy difference between the

two pathways is finite. However, in favorable cases, the minor stereoisomer may not be detectable by the analytic methods used. More simply define, If more than one reaction could occur between a set of reactants under the same conditions giving products that are stereoisomers and if one product forms in greater amounts than the others, the overall reaction is said to be stereoselective.

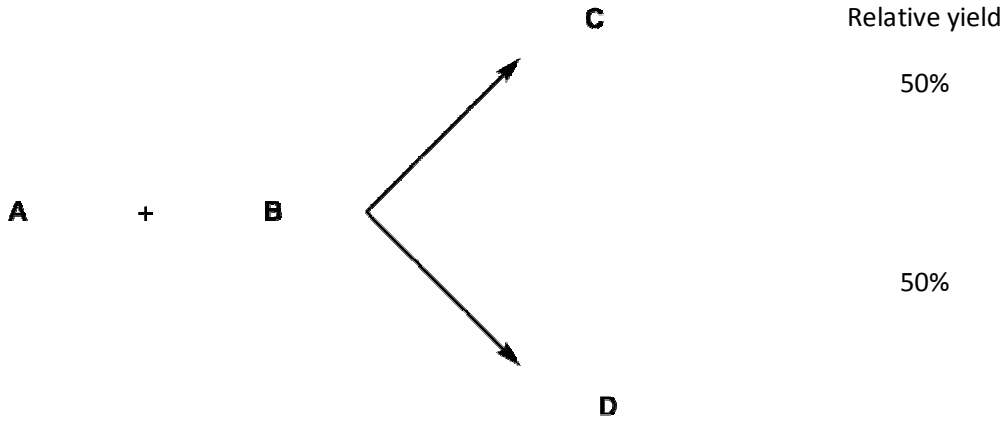
Suppose two reactions could occur between the hypothetical reactants **A** and **B** under the same conditions giving the stereoisomeric products **C** and **D**.



(Figure-6.5)

There are two possibilities:

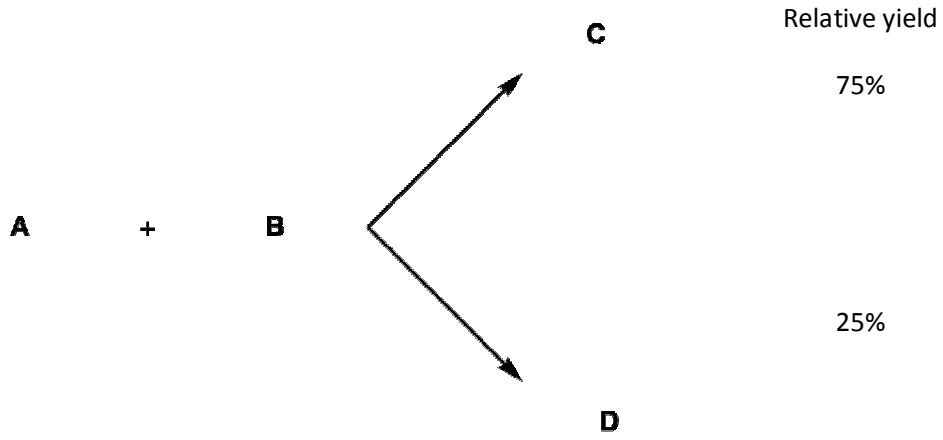
1. The two products form in equal amounts, i.e., the relative yield of each product is 50%.



(Figure-6.6)

The overall reaction between A and B is not stereoselective.

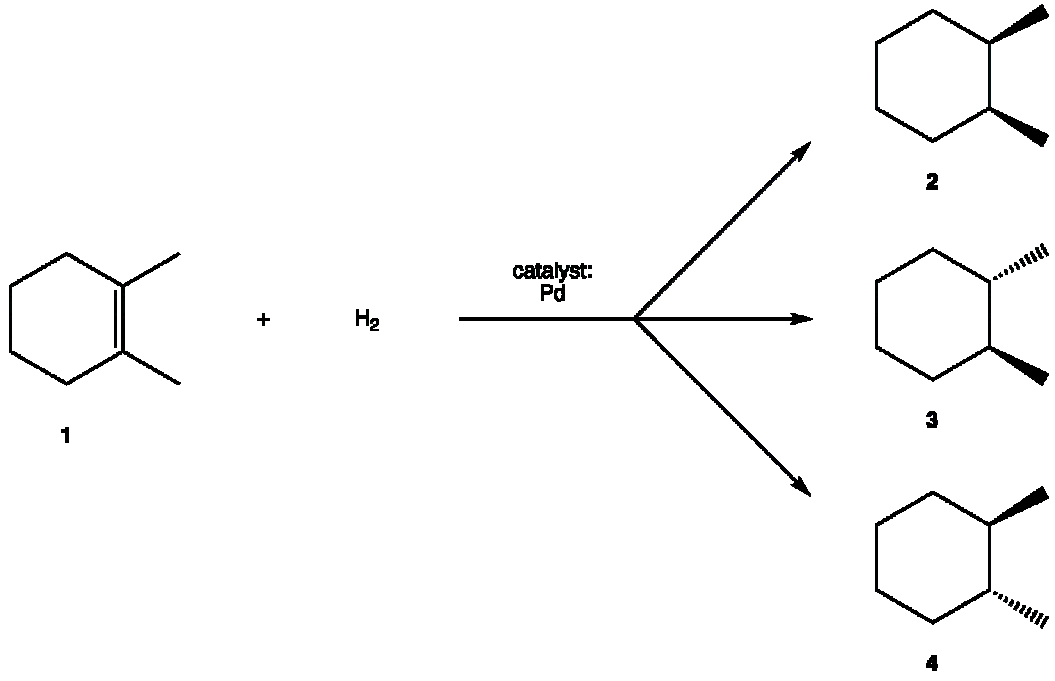
2. One product forms in greater amounts than the other. Say, for example, the relative yields of **C** and **D** are 75% and 25%, respectively.



The overall reaction between A and B is stereoselective.

(Figure-6.7)

For example:

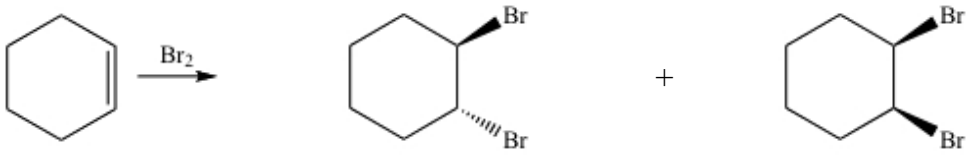


(Figure-6.8)

Experimentally, **2** is the major product. Thus, the overall reaction between **1** and H_2 is stereoselective toward **2**. The term "stereospecific" is sometimes used to mean

"100% stereoselective". However, the original definition of the term stereospecific is different, so it is best to avoid using the term stereospecific to mean 100% stereoselective.

Another example for stereoselective reaction



Trans-1,2-dibromocyclohexane
Observed product

Cis-1,2-dibromocyclohexane
None formed

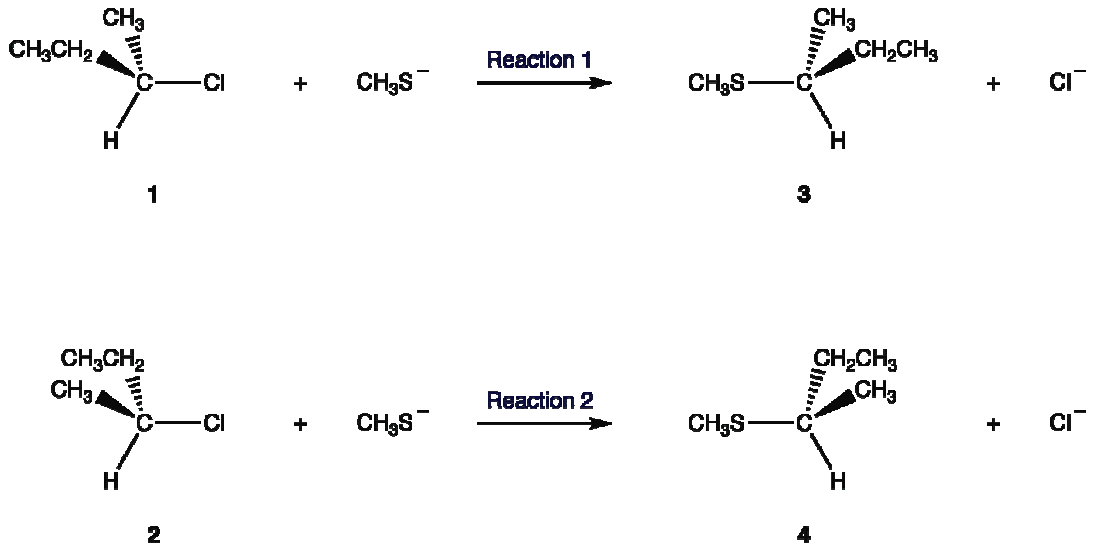
(Figure-6.9)

The addition of molecular bromine to cyclohexene is stereoselective because only the *trans*- dibromide is produced.

Stereospecific Reaction

If, in a reaction, stereoisomeric (see stereoisomers) reactants gives stereoisomeric products, the reaction is said to be stereospecific.

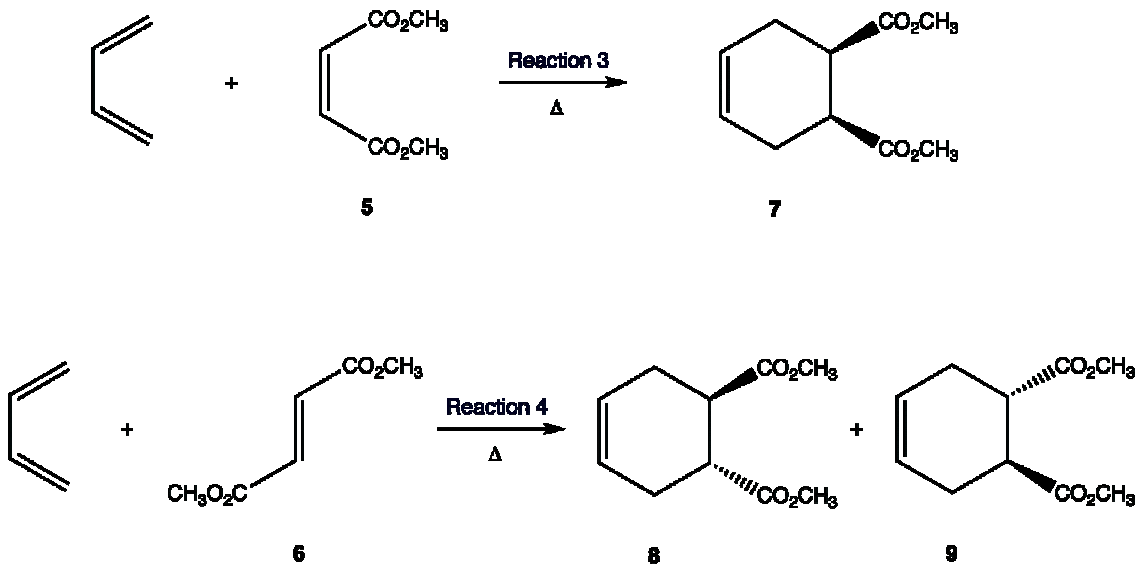
For example:



(Figure-6.10)

Reactions 1 and 2 are S_N2 reactions of stereoisomeric substrates **1** and **2** with the same nucleophile, leading to stereoisomericsubstitution products **3** and **4**, respectively. Thus, S_N2 reactions are stereospecific.

For example:



(Figure-6.11)

Reactions 3 and 4 are Diels-Alder addition reactions of stereoisomeric dienophiles **5** and **6** with the same diene, 1,3-butadiene. The products of the reaction of dienophile **5** is **7**; the products of the reaction of dienophile **6** are **8** and **9**. **7** and **8** are stereoisomers, so are **7** and **9**. Thus, Diels-Alder reactions are stereospecific.

For example:

The addition of molecular bromine to 2-butene is stereospecific: The addition of molecular bromine to (E)-2-butene or *trans*-2-butene gives meso-2,3-dibromobutane whereas addition of molecular bromine to (Z)-2-butene *cis*-2-butene gives a racemic mixture of (2S,3S)-2,3-dibromobutane plus (2R,3R)-2,3-dibromobutane.

* *

$CH_3CH=CHCH_3 + Br_2 \rightarrow CH_3CHCHCH_3$

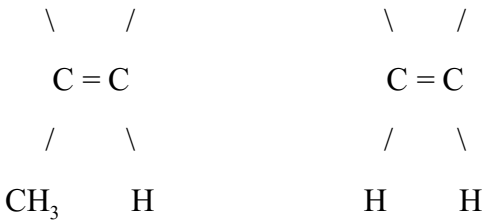
Br Br

2-butene 2,3-dibromobutane

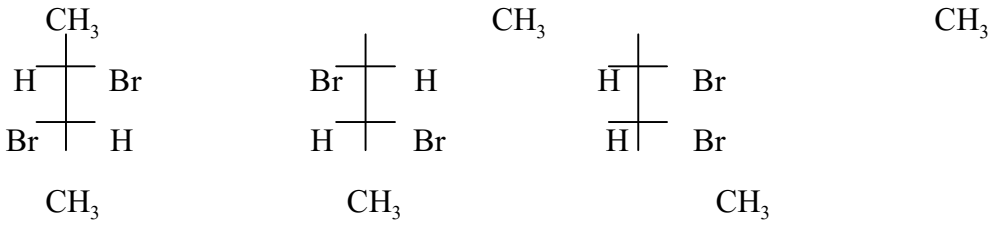
2 geometric isomers 3 stereoisomers

cis- and *trans*- (*S,S*)-, (*R,R*)-, and (*R,S*)- *meso*-

H CH_3 CH_3 CH_3

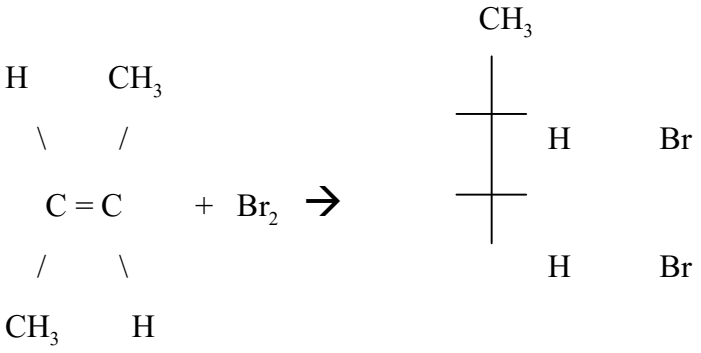


trans-2-butene *cis*-2-butene



(S,S) *(R,R)* *meso*

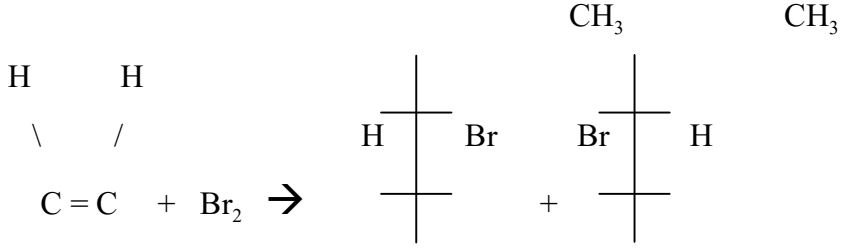
(Figure 6.12)



trans-2-butene *meso*-2,3-dibromobutane *only product*

(Figure-6.13)

A reaction that yields predominately one stereoisomer (or one pair of enantiomers) of several diastereomers is called a stereoselective reaction. In this case the *meso*-product is produced and not the other two diastereomers.



/ \ Br H H Br

CH_3 CH_3

CH_3 CH_3

cis-2-butene (*S,S*)- & (*R,R)*-2,3-dibromobutane

racemic modification only products

(Figure-6.14)

A reaction in which stereochemically different molecules react differently is called a stereospecific reaction. In this case the *cis*- and *trans*- stereoisomers give different products.

The fact that the addition of halogens to alkenes is both stereoselective and stereospecific gives us additional information about the stereochemistry of the addition and the mechanism for the reaction.

6.9 Summary

The chapter deals with the basic stereochemical principles in which enantiomeric and diastereomeric relationship of molecules, their nomenclature (R, S and E, Z) is described. Apart from these condition of prochiralty, stereoselective and stereospecific reactions are also described.

6.10 Review Questions

1. What is stereochemistry? Explain enantiomerism and diasteromerism with suitable examples.
2. Explain CIP system of nomenclature.
3. What are stereoselective reactions? Explain.
4. What are stereospecific reactions? Explain.
5. What is prochirality?

6.11 Reference and Suggested readings

1. AdvOrganic Chemistry- J. March(Ed IV).
2. Organic Chemistry- Jonathan Claden (Oxford) 2012.
3. http://en.wikipedia.org/wiki/stereochemistry.

Unit 7 Optical activity in the absence of chiral carbon

Structure of Unit

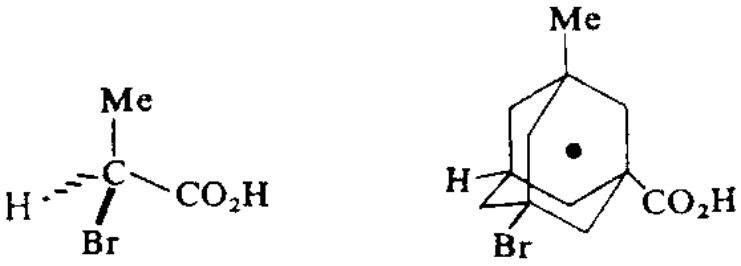
7.1 Objectives

At the end of this unit learner will be able to –

- Understand Optical Activity
- Stereoisomerism in Compounds without a stereogenic carbon-(axial chirality)

7.2 Introduction

The chiral compounds contain one or more stereogenic centers and have their chirality specified at one or more such centres. As an additional and a specific case of chirality one may consider the suitably substituted adamantanes with four different groups at the bridgehead positions which are chiral and therefore, display optical activity.



2-Bromopropionic acid 3-Methyl 5-bromoadamantance-carboxylic acid

Figure 7.1

The adamantane derivative has four bridgehead substituents and four stereocenters. It has however, only a (±) pair (due to high symmetry). A stereocentre thus may not always reside on an atom.

-Bromopropionic acid 3-Methyl 5-bromoadamantance-carboxylic acid has four nonequivalent stereocenters and due to highly symmetrical structure, however, it exists only as a (±) pair. In fact, the four substituents form a regular tetrahedral arrangement and the arrangement has a center of chirality (shown by a dot) in the unoccupied pace of the molecular frame- work of the adamantane. Two point come to light, firstly the center of chirality in a molecule may not always lie on an atom (as e.g., on carbon in the case of 2-bromopropioni acid). Secondly, the number of stereoisomers may be lesser than calculated from 2n.

However, in some compounds with non-superimposible mirror images it is not possible to identify a stereocenter and it then becomes necessary to focus our attentions on a larger portion of the molecule. In the same sense as we have spoken of chirality in the case of compounds with a stereocenter, we may speak of axial chirality, planar chirality and helicity other chiral compounds. As we have spoken of cherlity in the case of compounds ith a stereacenter we may also speak about accual cherality, planner cherlity and helicity in other cheral compounds.

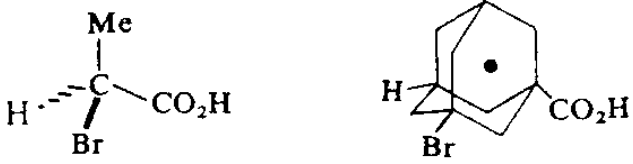
Whilst for models with a stereocenter all the four groups have to be different, for ones with an axis of chirality (stereoaxis) a smaller number of differences are sufficient. As one will see later on; for models with a plane of chirality (stereoplane), even one difference is enough.

Thus, the presence of a stereocenter is not a necessary and sufficient conditon for molecular dissymmetry. The overall chirality of a molecule can be factorized into three elements, stereocenters, stereoaxes, and chairality helicity. Several important classes of chiral compounds have one or more stereocenters. Thus, for example, a

stereocenter X can be detected in a molecule when the four different ligands *a, b, c* and d of a central atom *X* are located on corners of a tetrahedron. In case this center is replaced by a linear grouping e.g., C-C or C=C=C, the tetrahedron becomes elongated i.e., extended along the axis of the grouping. On speculative elongation of this tetrahedron the stereocenter is extended to produce a chiral axis (the stereoaxis). In this type of an extended tetrahedron on which axial chirality is based, the conditions for chirality are much less stringent when compared to a regular tetrahedron. Indeed a reference to such compound shows that an extended tetrahedron (with lesser symmetry) will be chiral if the pair of ligands at one end of the axis and the pair at other end constitute two different ligands, i. e., the minimum condition for chirality is that the ligand $a \neq b$.

7.3 Optical activity-stereoisomerism in compounds without a stereogenic carbon-(axial chirality)

The chiral compounds contain one or more stereocenters and have their chirality specified at one or more such centres. As an specific case of chirality one may consider the suitably substituted adamantanes with four different groups at the bridgehead positions which are chiral and therefore, display optical activity. The adamantane derivative (Figure 7.2) may be regarded as the formal analogue of 2-bromo- propionic acid and is completely asymmetric (belonging to C_1 point group).



2-Bromopropionic acid 3-Methyl 5-bromoadamantance-carboxylic acid

Figure 7.2

This has four nonequivalent stereocenters and due to highly symmetrical structure, however, it exists only as a (±) pair. In fact, the four substituents form a regular tetrahedral arrangement and the arrangement has a center of chirality (shown by a dot) in the unoccupieds pace of the molecular frame- work of the adamantane. Two

point are important here, firstly the center of chirality in a molecule may not always lie on an atom (as e.g., on carbon in the case of 2-bromopropioni acid). Secondly, the number of stereoisomers may be lesser than calculated from 2n.

However, in some compounds with non-superimposable mirror images it is not possible to identify a stereocenter and it then becomes necessary to focus our attentions on a larger portion of the molecule. In the similar sense as we have spoken of chirality in the case of compounds with a stereocenter, we may in the case of some other chiral compounds speak of axial chirality, planar chirality and helicity.

Whilst for models with a stereocenter all the four groups have to be different, for ones with an axis of chirality (stereoaxis) a smaller number of differences are sufficient. As one will see later on; for models with a plane of chirality (stereoplane), even one difference is enough.

Hence, the presence of a stereocenter is not a necessary and sufficient condition for molecular dissymmetry. The overall chirality of a molecule can be factorized into three elements, stereocenters, stereoaxes, and stereoplanes, there is still another element of chairality helicity.

Elongated tetrahedron approach can be applied to a variety of compounds e.g., allenes, spiranes, biphenyls etc. which are chiral not due to the presence of a stereocenter but a stereoaxis. The application of this approach to an allene (Figure 2) shows; that an allene e.g., 2,3-pentadiene will be chiral if (minimum) the two substitutents at each end are different i.e., a « b, (Figure 7.3).

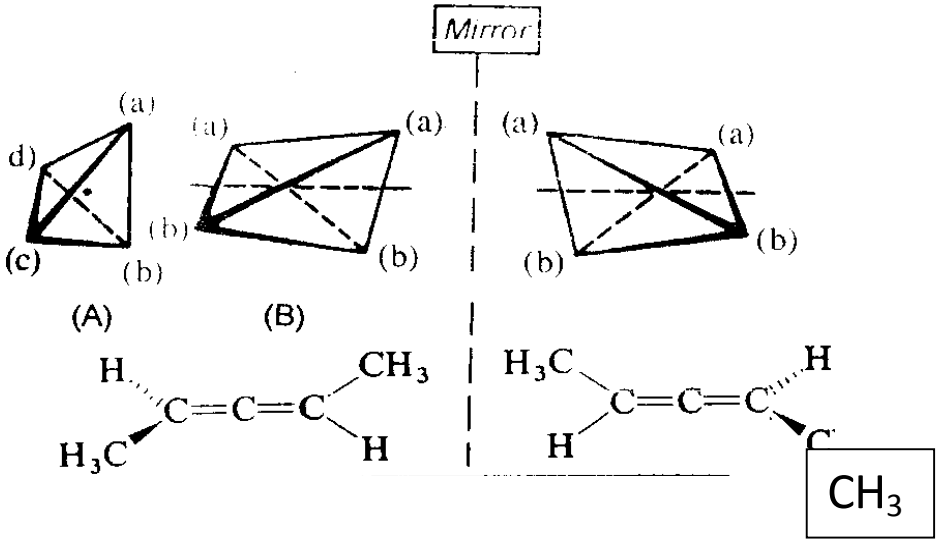


Figure 7.3

Several of these axially chiral compounds have a twofold axis of symmetry (C_2) and therefore, cannot be termed asymmetric. Because of these reasons the term asymmetric carbon has been replaced by stereogenic carbon i.e., a stereocenter. Interestingly, however, the term asymmetric synthesis still survives in a molecule with an axis of symmetry, but it cannot exist in a compound with a plane of symmetry, a center of symmetry or an alternating axis of symmetry.

A shrewd eye for symmetry will detect a C_2 axis e.g., in the substituted allene 1,3 - dichloropropa-1,2-diene in its Newman projection. This C_2 axis passes through the center of the molecule and rotation of the molecule about this axis by 180^0 gives an identical molecule. Thus it can be shown that (la and 1b, Figure 3) are enantiomers. The enantiomer (lb, Figure 3) has an equivalent representation in (Ic) and the later is obtained by simply ex- change of groups in (la) in left end carbon. Thus exchange of ligands at either of the terminal atoms across the stereoaxis reverses the chirality. The structure (lb) when rotated 90^o around C=C=C axis gives the equivalent structure (Ic, Figure 3).

The allenes have the general formula Cab = C = Cab and possess a C_2 axis and be-long to point group C_2. In case the three or four of the end groups of an allene are different the C_2 axis disappears and then the molecule becomes totally asymmetric belonging to C_1 point group.

7.4 Optical Isomerism of Allenes, Spiranes and Related Compounds (Axial Chirality)

In the geometric arrangement of the cumulative double bonds of allene, the four substitutents of the allene grouping are situated at the apexes of an imaginary tetrahedron, elongated.

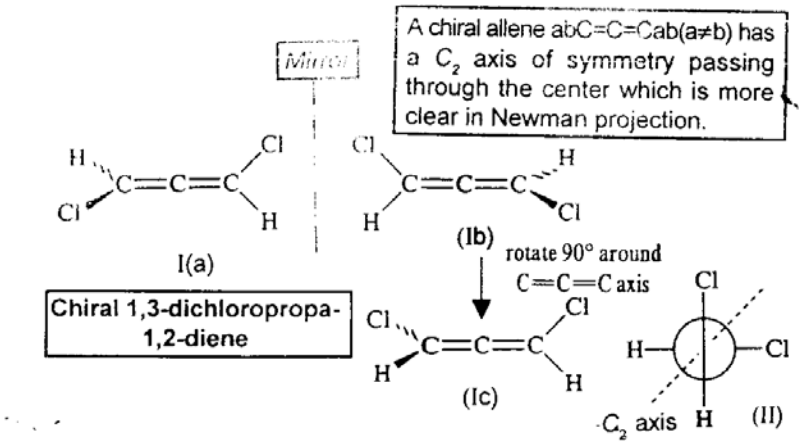


Figure 7.4

In order to generate chirality it is not necessary for all of the substituents to differ. It is sufficient to have each substituent different from its nearest neighbor.

Allenes have *sp* hybridized linear central carbon atom and, the two outer carbon atoms are sp^2 hybridized and trigonal. The central, sp hybrid carbon atom must therefore, use different p orbitals to form the pi bonds with the two outer carbon torus. The two unhybidized p orbitals on a sp hybrid carbon atom are perpendicular, so the two pi bonds must also be perpendicular.

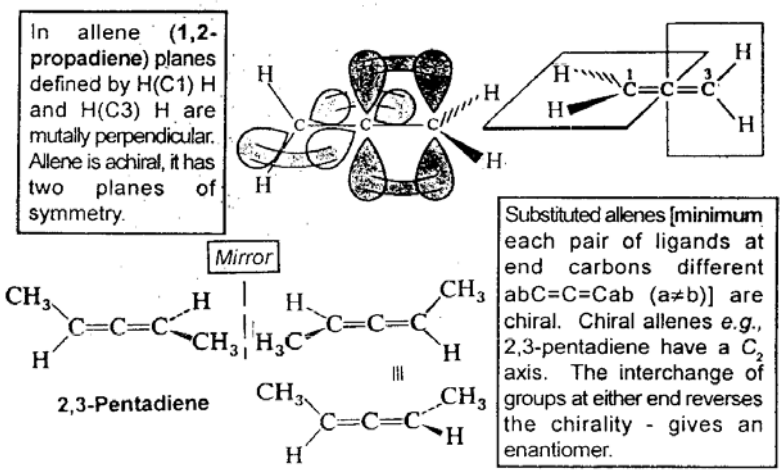


Figure 7.5

Hence, allenes of the type ABC = C = CAB (A ≠ B) as e.g., in 2,3-pentadiene are chiral, (not super imposable on their mirror images) and exist as enantiomers despite of the absence of a stereo center. Thus, in allenes one has a situation of restricted rotation giving rise to perpendicular dissymmetric planes. Summarily allene itself is achiral (it has two planes of symmetry) when some substitutents are added so that the pair of substitutents at both the end are each formed by two different substitutents, the substituted allene becomes chiral. This is so in chiral 2,3-pentadiene, substitutents at one end (H, CH_3; H ≠ CH_3) and at the other end (H, CH_3; H ≠ CH). Thus the cumulated bonding systems (compounds with two or more successive double bonds) of the type with an even number of double bonds do not have a plane of symmetry or a center of symmetry and therefore, must show optical isomerism and must be resolvable into enantiomers (Figure 7.6).

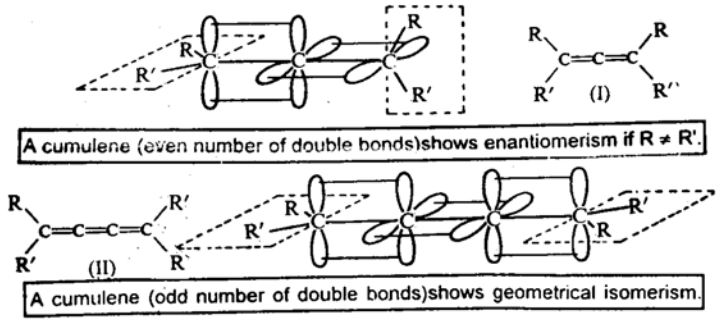


Figure 7.6

Interestingly the compounds with odd number of cumulated double bonds intend to display Z-E (geometrical) isomerism. When the allene chain of compound (Figure 5) is extended by one more double bond, one then gets a system (Figure 5) in which the substituted groups at the two ends of the cumulated chain now lie in the same plane and geometrical isomerism is shown. In Summary unsymmetrically substituted cumulates with even number of double bonds are chiral while with odd number show geometric (E-Z) isomerism. When one double bond is replaced by a ring in allene the it gives alkylidenecycloalkanes (sometimes referred to an hemispiranes) and it does not alter the basic geometry of the system of allenes and suitably substituted compounds, therefore, exist in optically active forms. Related compounds in which sp^2-carbon is replaced by nitrogen, e.g.. compound (Figure 7.7) has also been obtained as enantiomers.

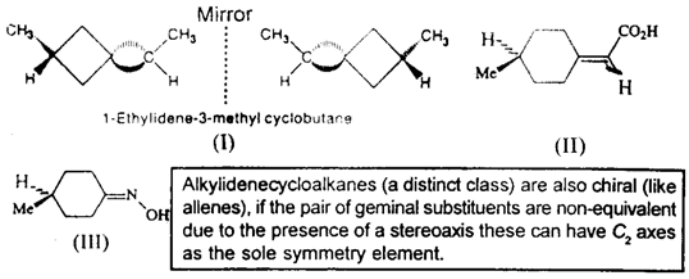


Figure 7.7

The replacement of both double bonds in an allene by ring systems gives a spirane; appropriately substituted compounds have been obtained in optically active forms, (Figure 7).

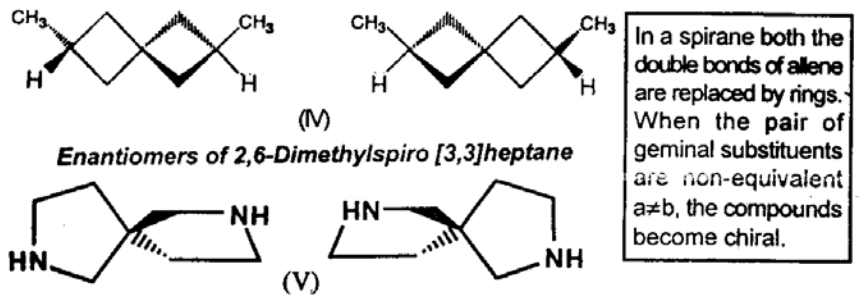


Figure 7.8

7.5 Optical Isomerism in Biphenyls (Atropisomerism)

7.5.1 Optically Active Biphenyl Derivatives

The two conformations of meso -2,3-dichlorobutane are nonsuperimposable mirror reflections of each other (Figure 7.9). However, It is not possible to separate the enantiomeric forms since rotation about the central C-C bond occurs very rapidly resulting in the interconversion of the two conformations.

When the barrier to rotation about a C-C exceeds about 80kJ per mole in some suitably substituted compounds, the rotation at room temperature is

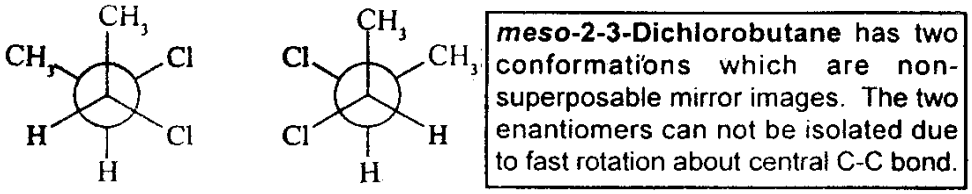


Figure 7.9

slow enough to allow isolation of the two optically active isomers. This case is observed in some biphenyls.

In the crystal, both benzene rings of biphenyl lie in the same plane. However, in solution and vapour phase 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 (Figure 7.10). These interaction effects are further enhanced by ortho substituents larger than hydrogen thus:

- The rotation about the bond linking the two phenyl rings does not occur due to steric hindrance between the bulky ortho substituents.

- The two rings lie in different planes which are perpendicular, to make it impossible for the molecule to achieve a symmetrical structure shown for example by the planar formula of *O, O'* difluorodiphenic acid.

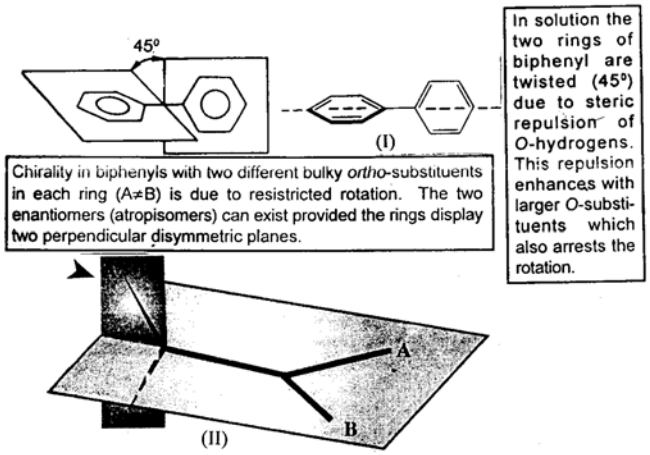


Figure7.10

Isolable stereisomers resulting from restricted rotation about single bonds are called atropisomers, while rotamers are stereo isomers obtained by rotation about a single bond.

In their structure, chiral atropisomers approach chiral allene derivatives and also display axial chirality (in the absence of stereocenters). Optical activity is generated if each aromatic ring is asymmetrically substituted with regard to the axis passing through the single bond between the phenyl groups and the para positions (I, Figure 9). Thus, 6,6' -dinitrobiphenyl-2,2' dicarboxylic acid (Figure 10) can be resolved into its enantiorners and each enantiomer is stable indefinitely. The nitro and carboxylic groups are so bulky that they cannot pass by each other. In case either or both the rings, are not asymmetrically substituted with regard to the axis shown in (Figure 7.11), then the molecule will have a plane (s) of symmetry and will be achiral.

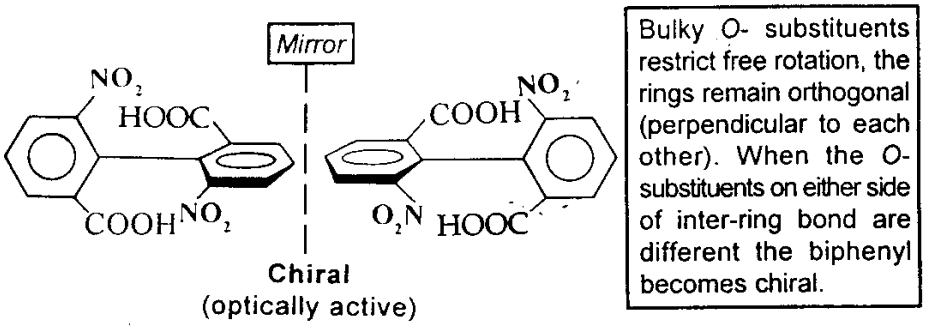


Figure 7.11

Thus in suitably substituted biphenyls in the artho-positions there may be restricted rotation which may place the two rings in perpendicular disymmetric planes (II, Figure 7.11). In chiral biphenyls either of the two perpendicular planes can be bisect d by a plane of symmetry. In case either of the plane could be so bisected the molecule would be superposable on its mirror image and becomes achiral since such a plane would be a plane of symmetry. The minimal conditions for chirality are:

• None of the rings should be symmetrically substituted, so that the molecule cannot have a plane of symmetry. Thus, the biphenyl (Figure 10) is chiral ($A \neq B$ in either pair, COOH: $\neq NO_2$ of the ortho substituents.substituents are defferent The biphenyl (Figure 7.12) is, however, achiral. In this case e.g., ring (II) is symmetrically substituted (A= B=COOH). A plane drawn perpendicular to ring (II, Figure 7.12) contains all the atoms and groups of ring (I) in it, hence it is a plane of symmetry and since it bisects the plane of ring B into two equal halves, thus the biphenyl (Figure 7.12) is achiral.

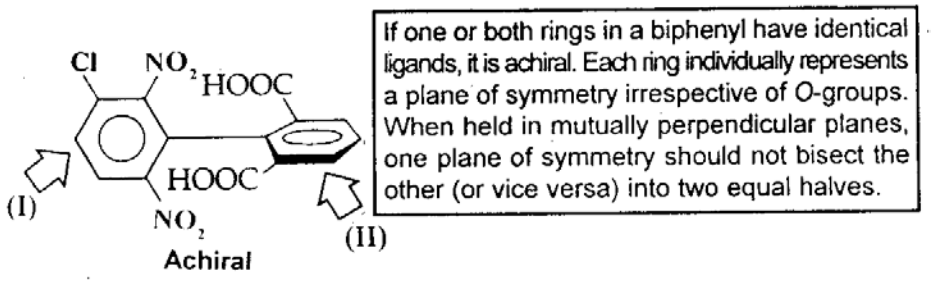


Figure 7.12

- In order to show optical activity the substitutents in the ortho position must be large enough to prevent the two rings from becoming coplanar (the rotational energy barrier must be high enough so that interconversion of enantiomeric conformers does not occur). Thus e.g., all attempts to resolve diphenic acid (Figure 7.13) have failed. The process of slipping a small hydrogen past the carboxylic acid group is very facile so that racemization of enantiomers occurs very rapidly through the planar form. Surprisingly the diamide (1, Figure 7.13) is optically active and is resolvable. The activity is lost on hydrolysis since the resulting dilactam (II, Figure 7.13) is forced to be planar and a point ofsym- metry can be easily detected in it.

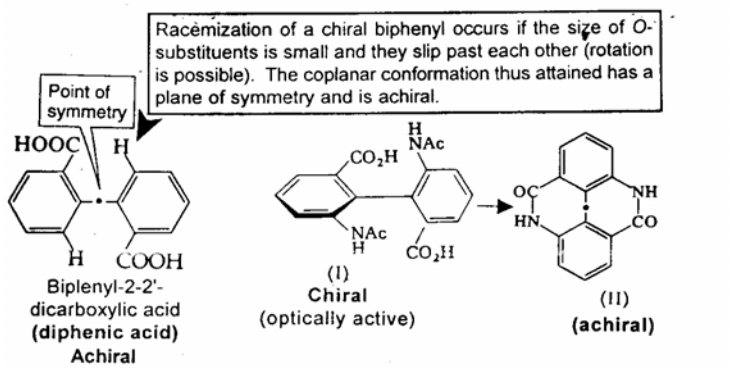


Figure 7.13

Compounds with a stereocenter, or in the case of allenes, one enantiomer may interconvert into the other only if a chemical bond is ruptured and formed again, i.e., by means of a chemical reaction. In the case of atropisomers, however, the other enantiomer may be formed if the substituent in one ortho-position is successful in "pushing through" the smaller ortho-substituent on the second ring. The constancy of the optical activity of atropisomers may thus serve as a measure of the size (effective volume) of the substituents. When the bulky nitro groups (Figure 7.14) are replaced by the smaller fluorine atoms the resulting compound, 6,6'-difluorobiphenyl- 2,2'-dicarboxylic acid can still display optical activity (Figure 7.14). How- ever, the compound racemizes readily, i.e., the enantiomers are readily inter- converted. The procedure involves squeezing fluorines past the adjacent carboxyl groups via the planar conformation. Once they reach the planar conformation the chirality is lost and racemization results. This transition state is congested and requires the bending of bonds. The process takes energy and is measurably slow.

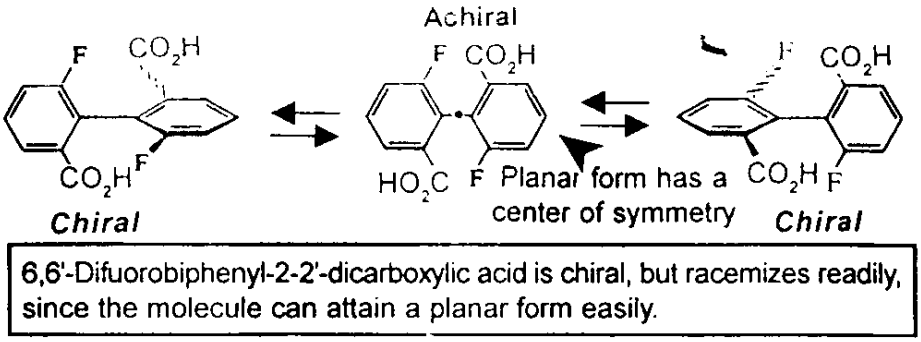


Figure 7.14

- Although the hydrogen atom is quite small, optically active compounds exist with two or even three ortho-positions of the biphenyl occupied by hydrpgen. In the second case the benzene ring that is unsubstituted in the ortho-positions must have a substituent in a meta-position. The meta.,substituent has no influence on rotation but it creates the necessary chirality of the molecule; 3-bromobiphenyl-2' -trimethylarsonium iodide (I, Figure 7.15) may serve as an example .

- In the case of (I, Figure 7.15) the rotation around the pivotal bond is only moderately restricted to allow interconversion between two enantiomeric atropisomers in solution and thus mono-*ortho*-substituted biphenyls in general are not resolvable, but demonstrate mutarotation when chiral additives are mixed. Thus the (+) camphorsulfonate of the arsonium salt (II, Figure 7.15) shows mutarotation in solution. Here the chiral counter ion (+) camphorsulfonate discriminates between the readily inter convertible atropiosomers of the biphenyl to give two unequally populated diastereomeric salts. Thus an inter conversion of diastereomers occurs in solution since the two diastereomers (i.e., diastereomeric salts) are not equally stable.

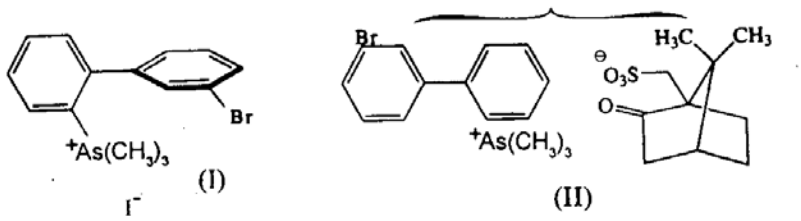
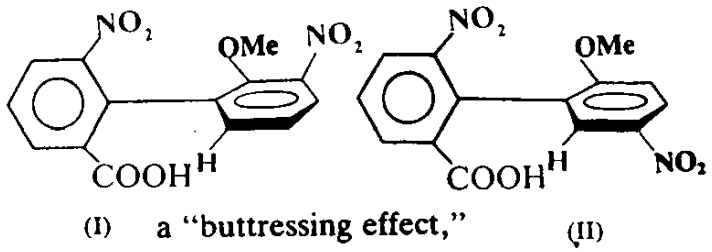


Figure 7.15

- "In addition to the bulk of the ortho substitutents, the substitutents in the meta-position tend to improve racemization barriers by what is called as "buttersing effect", i.e., by preventing the outward bending of an ortho substitutent, which would otherwise occur in the transition state (coplanar conformation) for racemization. This bending would allow the ortho substitutents to slip past each other more readily. Thus the rate of racemization of the 3-nitroderivative (I, Figure 7.16) is much lower compared with the 5' -nitro derivative (II, Figure 7.16).



(I) a "buttressing effect," (II)

Figure 7.16

The apparent order of steric hindrance produced by different groups (as gauged by racemization rates of differently ortho-substitutedbiphenyls) is Br > CH_3 > Cl > NO_2 > COOH > OCH_3 > F > H. This order roughly parallels van der Waals radii of atoms and groups.

7.5.2 Bridged Biphenyls

When a 2, 2'-bridge of the type revealed in (I, Figure 7.17) with n = 1 , one has a disubstituted fluorene, this being a planar molecule, is not resolvable. When n = 2, the compound is a disubstituted 9,10-dihydrophenanthrene. The nonplanar six membered ring can give rise to atropisomerism and the compound is resolvable, provided the other two ortho positions are substituted with bulkyl groups i.e., methyl (II, Figure 7.17), otherwise they slip through the plane readily (please consider models). In case n is larger than 2 the bridged biphenyls lead to atropisomers irrespective of the bulk of two ortho substituents. In such cases the non-planarity is maintained by the puckering of the rings which in planar configuration suffer from

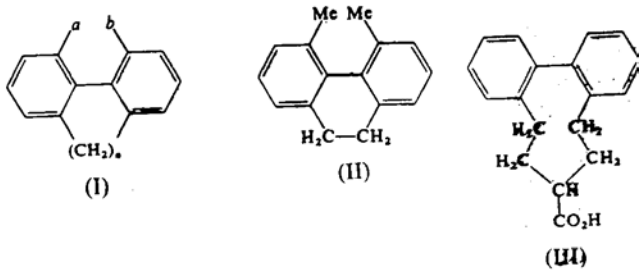


Figure 7.17

angle strain and non-bonded interactions. An example of such a compound is (III, Figure 7.17), however, these bridged biphenyls undergo easy racemization since the angle strain and steric interaction in medium rings is not very large.

7.6 Atropisomerism in Compounds Other Than Biphenyls

1,1' -Binaphthyl may be looked as a diorthosubstituted biphenyl and has been resolved. The 2,2' -binaphthol is a constituent of a useful chiral reagent BINAL -H.

The rotation around the pivotal bond is hindered due to steric factors. In 1,1' -binaphthyl itself e.g., the peri H's provide enough steric hindrance to keep the rings non-planar.

One or both of the phenyl groups may be replaced by other aromatic or heteroaromatic rings, appropriately substituted N-phenylpyrrole and N, N' -bipyrryl (Figure 7.18) are resolvable

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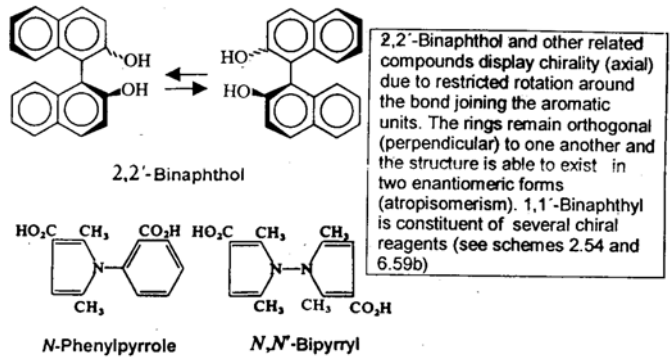


Figure 7.18

Optical isomerism also arises in suitably substituted polyphenyls, Morever, the stereochemistry is more complex since both meso from and geometrical isomerism are also possible. For example, consider the terphenyl drivatives (I and II, Figure 7.19), "where restricted rotation may arise around two pivotal bonds, consequently the two terminal phenyl groups are co-axial as well as coplanar. The terphenyl compounds of the type shown (Figure 7.19) exist in three stereoisomeric forms: a chiral cis isomer (exists as- an enantiomeric pair) while the trans isomer (in which the CH_3 groups on the end rings are on opposite sides) with a center of symmetry is an optically inactive *meso* form.

Atropisomers may also exist in compounds in which one benzene ring is

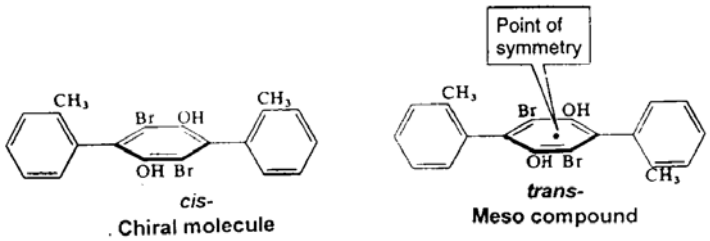


Figure 7.19

replaced by a substituted ethylene group or another substituted group i.e. situations with restricted rotation about single bonds.(Figure 19)

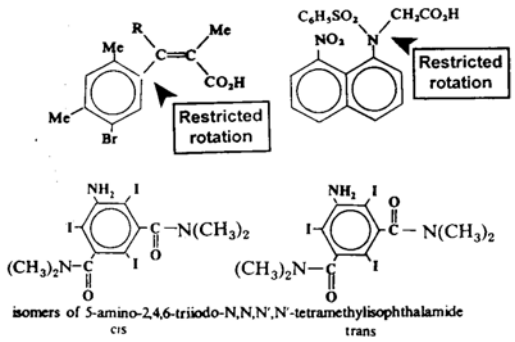


Figure 7.20

However , in the case of 5-amino-2,4,6-triodo-N,N,N, N-tetramethylisophthalamide, the *cis* and trans isomers have been synthesized. The $CONMe_2$ groupsare imprisoned between the two bulky iodine atoms and the situation, therefore, does not leave any room for these groups to rotate. The cis-isomer is a meso form, while the trans-isomer is chiral and has been resolved.

7.7 Nomenclature of Compounds with (Stereoaxis) Axial Chirality

Three ways may be employed for assigning R/S configuration to compounds with a stereoaxis. One may adopt any of these. The last third method is developed as a problem solving hint and is the easiest.

7.7.1 First method

(i) Allenes

For the assignment of configurational nomenclature to axially chiral molecules e.g., allenes, the orbital picture is projected to a Newman formula i.e. The following points have been kept into mind when the procedure is applied to (S)-2, 3-pentadiene.

• The molecule can be viewed from either end of the stereoaxis to give the same descriptor. The near groups are given priority over far groups.

• For better visualization it is suggested to put the groups nearest the view direction on a thick line (horizontal or vertical).

• Thus in the projection formula of (S)-2,3-pentadiene (Figure 7.21), the horizontally placed, (nearest the view direction) CH_3 and H are to be numbered 1 and 2 and the remaining vertically placed (rear) ligands are simply assigned priorities according to sequence rules i.e. CH_3 and H are numbered 3 and 4 respectively. The sequence $1 \rightarrow 2 \rightarrow 3$ gives the configurational descriptor S (anticlosckwise).

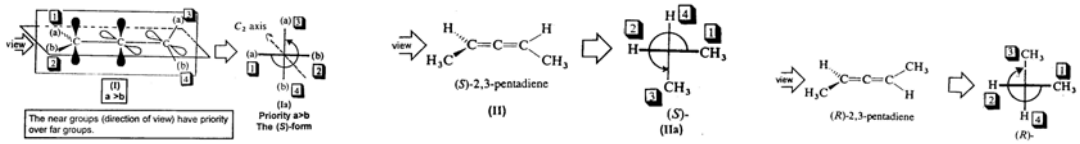


Figure 7.21

• Interchange of the two geminal groups at one end in these molecules gives the enantiomer, e.g., (R)-2,3-pentadiene is obtained from the (S)-enantiomer (Figure 7.21) and is properly named as shown.

• As mentioned earlier, it makes no difference which end the structure is viewed, the stereodescriptor will remain unchanged. Consider again (S)-2-,3-pentadiene now viewed from other direction (Figure 7.22) as compared to that in (Figure 7.22). Now the far groups (view, Figure 7.21) become the near groups And consequently get priority.

These are put on the thick vertical line and the configuration again comes out to be (S).

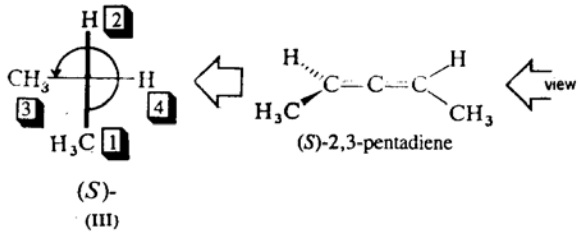


Figure 7.22

• For practice one may assign stereodescriptors to the two enantiomers of 2,3pentadiene drawn in different orientation (Figure 22).

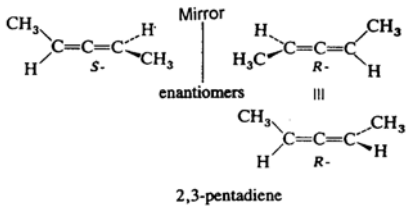


Figure 7.23

(ii) Spiranes and Alkylidene-Cycloalkanes

These compounds possessing axial chirality are assigned configurationally descriptors in the same way as discussed for allenes. Similar to allenes, the inter-change of the two germinal groups in these molecules also leads to enantio- mers (II compared to I, Figure 7.24).

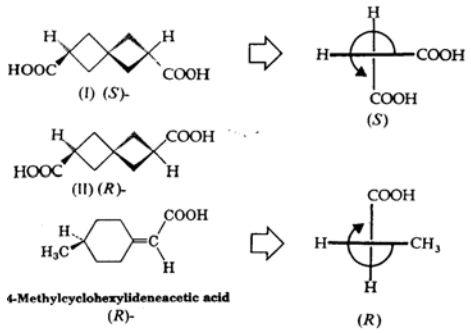


Figure 7.24

(iii) Biphenyls

In the case of biphenyls, however, it is important to remember that the four orthocarbons are sequenced properly according to CIP rules. Thus in the biphenyl (Figure 24) in the left ring the sequence is C-2 > C-6 > (OCH_3 > C-H) while in the other ring C2' > C6' (N > C) and therefore, configuration is S when the biphenyl (Figure 7.25) is viewed from either direction.

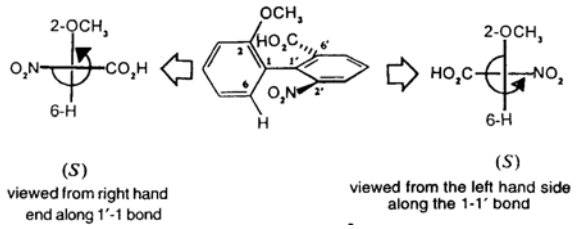


Figure 7.25

When in a biphenyl the C_2 and C_6 in a ring are attached to identical atoms, the priority order of the ortho carbon atoms is then determined through explo- ration around the ring or side chain. Thus in the biphenyl (Figure 7.26) the 2-H adjacent to 3-Br precedes 6-H.

Figure7.26

7.7.2 Second method

The following points may be noted:

- The molecule (I, Figure 7.27) considered as an elongated tetrahedron is viewed along the axis as in (II) with substituents at the vertices.
- In thecase of enantiomer of 1, 3-dibromo-allene (I, Figure 7.27), the top pair of groups are in the plane of paper (continuous lines) whereas the bottom pair of groups are perpendicular with the bromine at the back (dotted line) and the hydrogen is in the front (solid line).

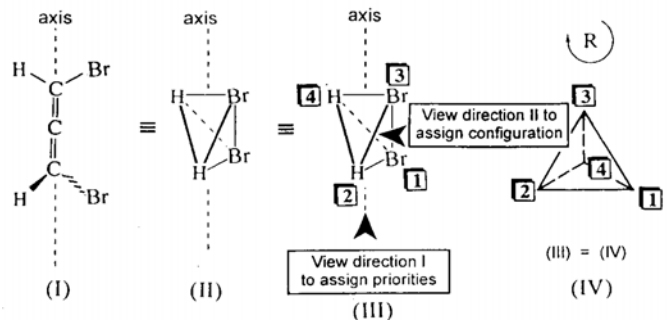


Figure 7.27

- The solid diagonal lines in (II, Figure 7.27) from H to H and H to Br depict connections in the front of the tetrahedron whereas the dashed lines shows at the rear and .
- The view direction (1) is simply used to allocate priorities to the pair of ligands. The pair of groups nearest the view direction (1) have precedence over the other pair of groups and. therefore. the priori ties are assigned if one looks to the allene from the bottom (III. Figure7.27).
- To assign R/S configuration the elongated tetrahedron must be viewed from reverse the least preferred ligand (4) which is view direction (2).
- Following this procedure in (Figure 7.27) one is having a trigonal face with the remaining three groups $1 \rightarrow 2 \rightarrow 3$ clockwise to show that the allene (I. Figure 7.27) has R configuration.
- The same results could be obtained by viewing this enantiomer of allene from the top and now the top groups take precedence over the bottom groups (Figure 7.28).
- To find out the order of $1 \rightarrow 2 \rightarrow 3$ clockwise or anticlockwise one must view the arrangement from the side opposite the least preferred group (4). Thus the

arrangement when viewed from the rear becomes (II), i. e., ligands 1 and 2 change places and the configuration reached is still R.

Similarly biphenyls, binaphthyls etc. can be assigned configurations using this method.

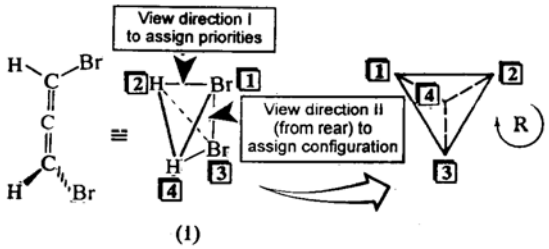


Figure7.28

7.7.3 Third method

A simple mental exercise to assign R/S configuration to compounds with axial chirality

This is the easiest exercise developed by P. S. Kalsi and can be used quickly to assign configuration to any compound with a stereoaxis and is used by adopting the following procedure:

- Turn the molecule to bring the groups in the plane of paper (continuous lines) at the top while the pair of groups which are perpendicular are put at the bottom (I-II, Figure 7.29).
- Always view the molecule from bottom, thus the bottom groups take precedence over the other pair at the top (II, Scheme 1.33c) and thus as- sign priorities to all the four groups.
- Draw a cross (III, Figure 7.29) and put the groups (as their priorities) on the top of (II) on the horizontal line as you see these in (II). Thus Br(3) is on the right hand side while CH_3(4) is on the left.

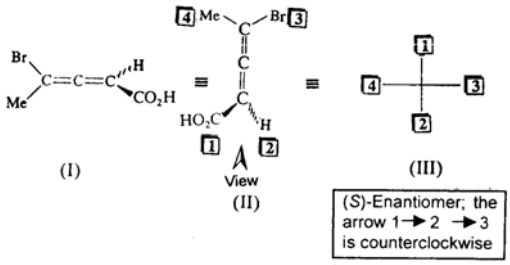


Figure 7.29

- Put the groups of the bottom pair (perpendicular to the plane of paper) on the vertical line of the cross with the group on the thick line (i.e. , the group at the front) at the top while the group at back (i.e., the group on dotted line) at the bottom. of the vertical line .
- The sequence 1 $\rightarrow$ 2 $\rightarrow$3 clockwise show R configuration while I $\rightarrow$ 2 $\rightarrow$3 anti clockwise shows S configuration.

Example 1. Consider (Figure 7.30) the enantiomer considered here. Thus if the orientation (1, Figure 7.30) is rotated clockwise around the axis defined by the three allenic carbons the COOH group and H on right occupy the plane of paper while Br and Me become perpendicular to give the same enantiomer (Figure 7.30).

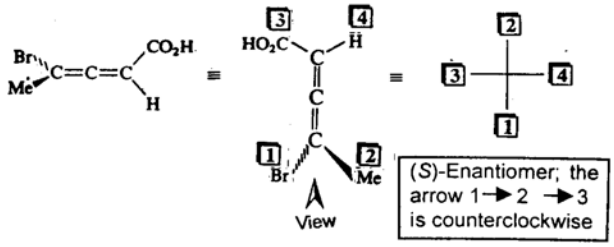


Figure 7.30

Example 2. Consider one of the enantiomers of a chiral biphenyl by considering the relevant ortho groups (Figure 7.31). One rotates the molecule so as to put the ring A (in the plane of paper) at top while ring B which is perpendicular to ring A at the bottom. Looking from bottom and assignment of priorities to the ortho groups shows that it is S enantiomer. The $N0_2$ group in ring B is on a thick portion of the molecule so it is at the top of vertical line

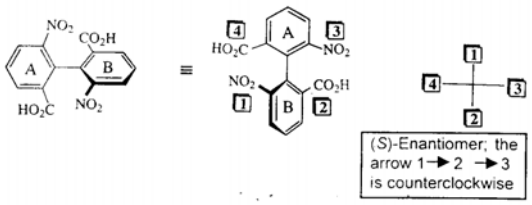


Figure 7.31

Example 3. The configuration of one of the enantiomers of 2,2' -binaphthol (1, Figure 7.32) is to be determined. This will be with reference to the carbons C_2, C_9 and $C_{2'}$ and $C_{9'}$. One looks along Cl and Cl' bond, by first turning the orientation so that as drawn the ring system A (in the plane of the paper) is at top while the ring system B perpendicular to it is at bottom (1 $\rightarrow$II, Figure 7.32). As in other cases the

molecule is viewed from bottom and priorities are assigned. The configuration comes out to be R.

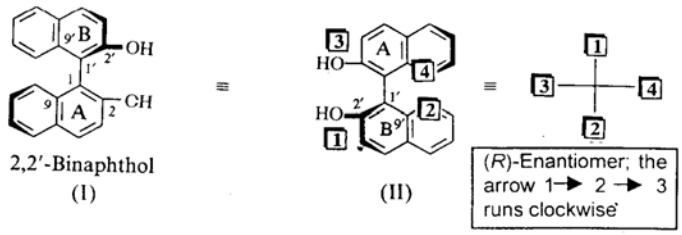
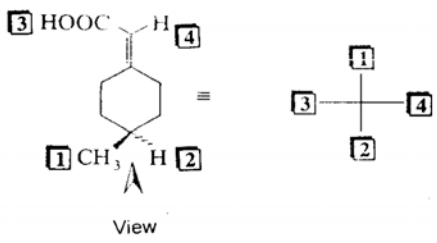


Figure 7.32

Example 4. A parallel procedure is applied to cyclic molecules with an exocyclic alkylidene moiety e.g., (Figure 7.33). This system has two different groups at C_4 of the cyclohexyl ring while two different groups are present at the ΤΤ bond. The cyclohexyl "arms" (ring residues) are in the plane of the π bond and COOH and H group along with the cyclohexyl arms are in the plane of paper and are already at the top. The CH_3 and H at C_4 of the cyclo- hexane ring are in a different plane and these constitute the bottom. The molecule when viewed from bottom with assigned priorities comes out to have R configuration.



Enantiomer, the arrow 1 → 2 →3 runs clockwise

Figure 7.33

(D) Helical Descriptors (M and P)for Molecules with Chiral Axes

The perpendicular segment of the substituents about the chiral axis (stereoaxis) means that such compounds like, allenes, biphenyls, alkylidene, cycloalkanes, etc. have very little helical segments and their configuration may be denoted as P or M (Similar to the compounds which are chiral due to helical structure). For assignment of helix descriptors only the groups of highest priority nearer to the view direction and the far are considered e.g., in (II, Figure 7.34) the considered, ligands are 1 and 3. In case the turn from priority front group 1 to priority rear group 3 is clockwise. The stereodescriptor is P, if anticlockwise it is M. Thus (S)-2,3-pentadiene (II, Figure 7.34) is S (chiral axis nomenclature) or P (helix nomenclature). The correspondence of R with M and as with P is general.

One has seen that the smallest carbocyclic ring that can incorporate a double bond with trans-geometry is eight membered. Similarly the smallest sized ring which can contain an allene has nine carbons. One enantiomer of this compound of cyclonona-l,2-diene (Figure 32) has the S configuration as arrived by adopting third method or P configuration as pert the (helix nomenclature).

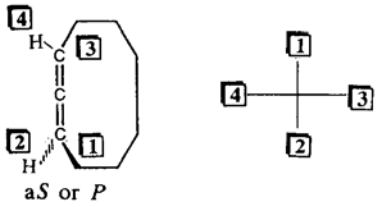


Figure 7.34

Cyclonona-1, 2-diene has as or Sa (chiral axis nomenclature) or P (helix nomenclature). For assigning M or P descriptors to compounds with . axial chirality, groups of highest priority from near view direction and the far are considered and the path 1 $\rightarrow$3 whether clockwise or anticlockwise determined.

7.8 Summary

In the above unit optical activity of compounds in the absence of chiral carbon is explained. The perpend-icular segment of the substituents about the - chiral axis (stereoaxis) means that such compounds like, allenes, biphenyls, alkylidene-cycloalkanes, etc. have very short helical segments and their configuration may be denoted as P or M (as for compounds which are chiral due to helical structure). For assignment of helix descriptors only the groups of highest pri- ority nearer to the view direction and the far are considered e.g., in (II, Figure 20) the considered, ligands are 1 and 3. In case the turn from priority front group 1 to priority rear group 3 is clockwise. The stereodescriptor is P, if anticlockwise it is M. Thus (S)-2,3-pentadiene (II, Figure 20) is as (chiral axis nomenclature) or P (helix nomenclature). The correspondence of aR with M and as with P is general.

One has seen that the smallest carbocyclic ring that can incorporate a double bond with trans-geometry is eight membered. Similarly the smallest sized ring which can contain an allene has nine carbons. One enantiomer of this compound of cyclonona-l,2-diene has the S configuration as arrived by adopting third method or P configuration (helix nomenclature).

7.9 Review Questions / Comprehensive Questions

1. What is optical activity?

2. Give the example of compounds which shows optical activity in absence of chiral carbon.
3. What is axial chirality?
4. Explain the nomenclature of compound having axial chirality.
5. Descuss optical activity in spiranes, allenes and biphenyles.

7.10 References and Suggested Readings

1. Stereochemistry of Organic Compounds, D.Nasipuri,New Age International.
2. Stereochemistry of Organic Compounds, P.S.Kalsi,New Age International
3. Advance Organic Chemistry, Jerry March, John Wiley.
4. Advanced Organic chemistry, F.A.Carey and Sundberg, Plenum
5. Structure and Mechanism in Organic Chemistry, C.K.Ingold, Comell University Press.
6. Organic Chemistry, R.T.Morrison and R.N.Boyed,Prentice-Hall.
7. research.cm.utexas.edu/nbauld/teach/stereo.html
8. www.chemeddl.org/resources/stereochem/**threed3**.htm
9. http://www.google.co.in/search?q=images+of+symmetry+of+molecul
10. Al-Hilalmission (An Educational, Cultural & Social Welfare Organization) Kadambagachhi, Barasat, Kolkata-7000125

Unit-8: Aliphatic Nucleophilic Substitution

Structure of Unit:

8.1 Objectives

In this unit the students will be able to understand

- Aliphatic nucleophilic substitution and its types.
- The synthetic aspects of these reactions
- The mechanism and stereochemistry in these reactions.
- About the classical and non-classical carbocation formation.
- Various organic reactions which involves the nucleophilic substitution.

8.2 Introduction: Aliphatic Nucleophilic Substitution

Nucleophiles are chemical species that react with centers of positive ionic character. When the center is an aliphatic carbon, the process is called aliphatic nucleophilic substitution. Chemical reactions of this type are extremely important for the synthesis

of new compounds and for understanding the mechanisms in organic chemistry. All nucleophilic substitution reactions may take several reaction courses, but all have similar appearances at the outset. All reactions have an attacking species, a **nucleophile** (Nu) that bears a pair of electrons either as an anion or as a neutral species. The organic compound known as the **substrate** has a structure that greatly influences the outcome of the reaction and it contains the **leaving group** (L) that is lost in the reaction. The **conditions** of the reaction, especially solvent and temperature are also important contributors to the process. In order to understand the products of the reaction and how they are formed, the reaction is studied from a mechanistic point of view .

8.3 S_N2 Reactions

S_N2 indicates a *substitution*, *nucleophilic*, *bimolecular* reaction, described by the IUPAC designation is A_NDN. Substitution: one species replaces another Nucleophilic: the substitution occurs as the result of attack by an electron-rich species Bimolecular: two species are involved in the rate-determining step (2 in S_N2 stands for bimolecular) and deals with the rate of the reaction. The rate of the reaction is dependent on the concentration of both the nucleophile [Nu] and that of the substrate [RX] undergoing substitution. Both of these species are involved in the rate-determining (slowest) step.

Hence rate equation would be: Rate = k [Nu][RX], where k is a constant based on what species are actually involved. The rate of the reaction is directly linked to the number of times these two species can collide to react together.

Eg.

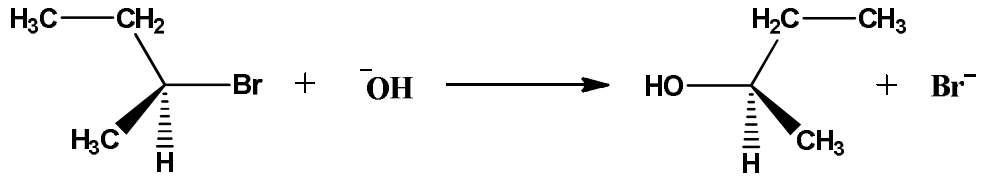


Figure 8.1

There are two possible ways by which the attack of hydroxide ion ie. Nucleophile can attack:

(i) Front side attack

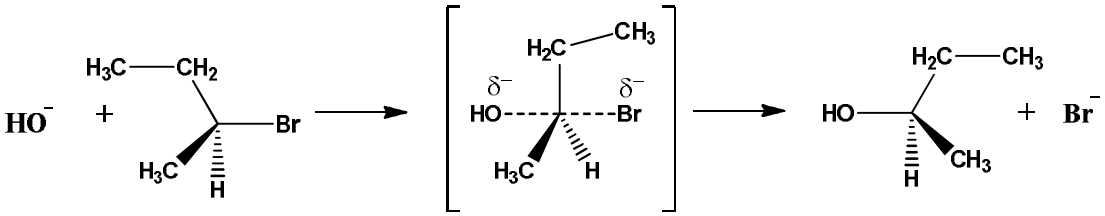
(ii) Back side attack

Figure 8.2

The attack from the frontside (the side the leaving group is on) is disfavored for two reasons. First, there's sterics – the nucleophile is trying to attack in the same space the leaving group is trying to leave. Second, due to electronics replusions – the nucleophile is trying to attack bearing a full negative charge and the leaving group is trying to leave with a full negative charge, and they will repel each other (electrostatic repulsions).

Attack from the backside, where the nucleophile comes in from the opposite side of the leaving group, alleviates both the electronic and steric issues seen in the frontside attack. This is a one step concerted (i.e. happens all at once) process where all the bond formations and breakages occur simultaneously. There aren't any intermediates formed (no anions, cations, etc) and it is surmised based on the results that the following is an accurate depiction of the transition state of the process:

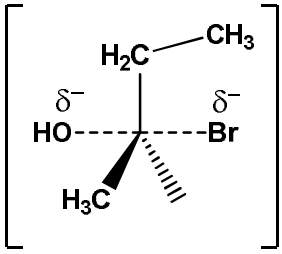
Mechanism:

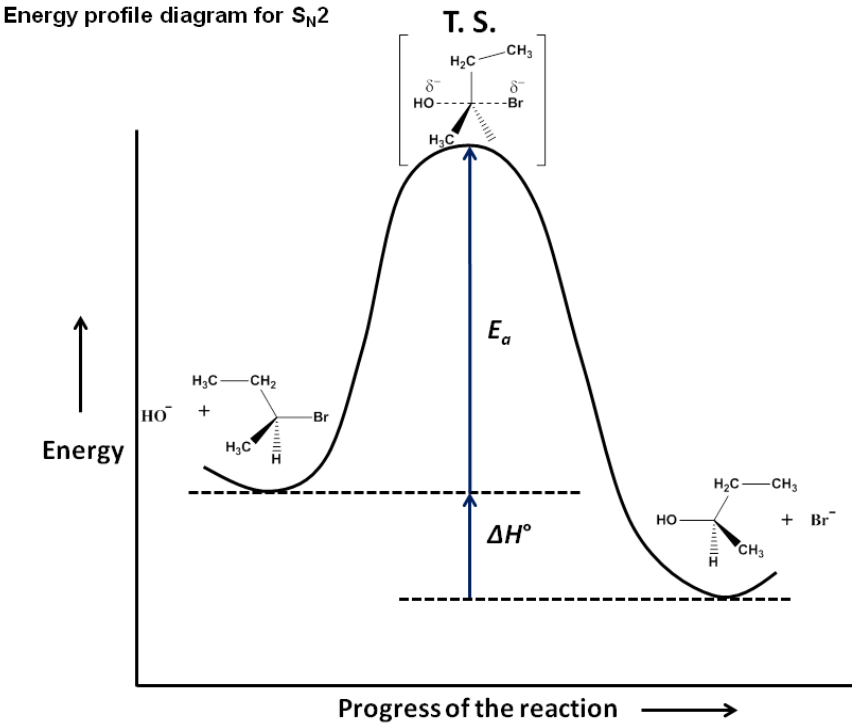


(Figure 8.3)

Any chiral center that was once perhaps the "*S*" configuration, as shown in the starting material here, winds up inverting its stereochemistry and becoming the "*R*" configuration. Centers that are not chiral cannot "show" this inversion but the inversion process is still occurring.

Transition State of S_N2: The original starting material was sp3 hybridized but note that the transition state resembles sp2 hybridization (turned on its side – with the nucleophile, OH, and the group that's leaving, Br, where the perpendicular p orbital might once sit). It is this planar geometry and the need to put the other groups through the inversion into this "planar"state that defines what alkyl halides can undergo the S_N2 reaction.





(Figure 8.4)

Factors that affect the S_N2:

1. Alkyl Halide: Steric hindrance around the carbon atom undergoing the inversion process will slow down the S_N2 reaction. Less hindrance = faster reaction!

$H_3C{-}X \;>\; R_2HC{-}X \;>>\; R_3C{-}X$

2. Leaving Group: The leaving group is almost always expelled with a full negative charge. As a result, the best leaving groups are those that can best stabilize an anion (i.e. a weak base).

Good Leaving Group $\bar{O}Ts > I^- > Br^- > Cl^- > F^-$ **Bad Leaving Group**

3. Solvent: The S_N2 reactions are forwarded by polar aprotic solvents – these are solvents such as acetone, DMSO, acetonitrile, or DMF that are polar enough to dissolve the substrate and nucleophile but do not participate in hydrogen bonding with the nucleophile. In case of protic solvents, solvation occurs with the nucleophile, where the protic solvent from hydrogen bonds to the anion which is

trying to attack the alkyl halide. This creates a shield around the nucleophile and slows down the reaction dramatically. Examples would include water or alcohols (ROH).

4. Nucleophiles:

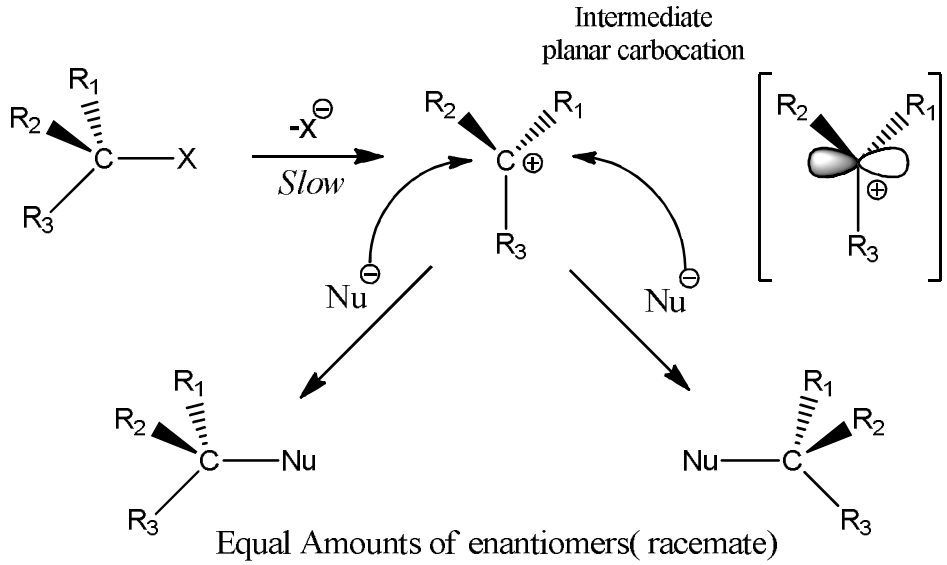
Strong bases are strong nucleophiles, and vice versa. Full negative charges are always more basic and also more nucleophilic (eg hydroxide and methoxide anion). The strength of a nucleophile is reduced by the presence of electron-withdrawing groups (EWG). The strength of a nucleophile increases for atoms down the column of the periodic table. Resonance stabilization results in spreading out the anion of the nucleophile, making it less concentrated, thus weaker.

8.4 S_N1 Reactions

S_N1 indicates a ***substitution***, ***nucleophilic***, ***unimolecular*** reaction, described by the **IUPAC designation is D_N+A_N.**

Unimolecular means: one species are involved in the rate-determining step (slow ionization of the species). The second is a rapid reaction between the intermediate carbocation and the nucleophile. The rate of any S_N1 reaction is directly proportional to the concentration only one species, the alkyl halide (RX) undergoing substitution and is rate-determining (slowest) step. The rate equation would be: Rate = k[RX], where It is a constant based on the species actually involved.

Eg.



(Figure 8.5)

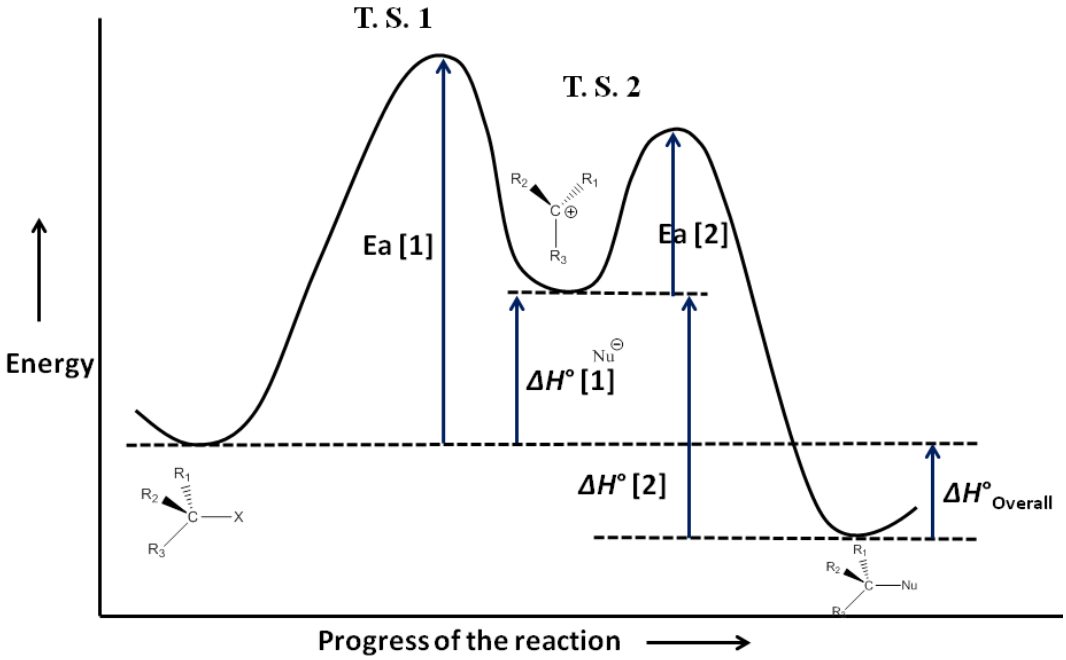
The reaction leads to the racemisation of a stereogenic centre in the starting material (i.e. an *R*-enantiomer will be converted to a 50:50 mixture of R- and S-enantiomers). This is because the nucleophile can equally attack either side of the planar

carbocation. The rate of reaction is dependent on the formation of a carbocation intermediate from the alkyl halide.

In the first step, a carbocation forms. This results in an empty p orbital that can be attacked by the nucleophile from either the right side or the left side. As a result, a mixture of two possible chiral centers occurs. Both retention and inversion of configuration is obtained. Hence when chiral compounds undergo S_N1 reaction, they form a racemic mixture of enantiomers.

Mechanism: In a two-step mechanism like the S_N1, the first step requires high activation energy. If the substrate has already reached this energy level there will be sufficient energy for the second step. Therefore the energy requirement of the first or slow step is the overall activation energy for the reaction.

Energy profile diagram for S_N1



(Figure 8.6)

Factors that affect the S_N1:

1. **Alkyl Halide**: more stable the carbocation, the faster it can form. The more stable carbocation intermediate has a lower activation barrier, so the SN^1 reaction occurs faster.Stability group

3^o carbocation > 2^o carbocation >> 1^o carbocation

2. **Leaving Group**: The leaving group is almost always expelled with a full negative charge. As

a result, the best leaving groups are those that can best stabilize an anion (i.e. a weak base).

Good Leaving Group $^{-}OTs > I^{-} > Br^{-} > Cl^{-} > F^{-}$ **Bad Leaving Group**

3. **Solvent**: Solvation of the carbocation allows the carbocation to be surrounded by more electron density, making positive charge more stable. The solvent can be protic or aprotic, but it must be polar.

4. **Nucleophiles**: Nucleophile undergoing SN^1 reactions are those that are weak, neutral molecules (ex. H_2O, ROH). Any nucleophile that is stronger than this is generally also a strong base and will result in elimination reactions instead.

8.5 Mixed SN^1 and SN^2 Reactions

Some reactions under a given set of conditions show Sn^2 mechanions while others proceeds via SN^1 Mechanism but in some cases it is not easy to determine the mechanistic patkway because such reactions neither follow Pure SN^1 nor Pure SN^2 Mechanisms various theoric have ocen prpoposed to explain the behavior of such reactions one such explaination was given by sneen in his intermediate ion pair mechanism thory according to it, all Sn^1 and Sn^2 reactions can be accomendated by one basumechaniosm (the ion pair mechanism)

In this mechanism formation of ion paisr (k^1) is rate determining in SN^1 mechanism and destruction of ion pair (k^2) is rate determining in Sn^2 . Boderline behavour Is found where the rate of formation is found where the rate of formation and destruction of ion pair are of same order of mangitutde such reaction are said to follow mixed or simillatnieous SN1 & SN2 mechanism.

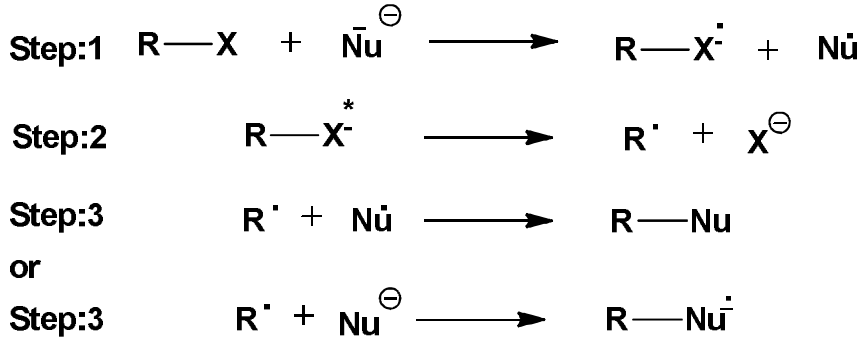
Comparison of S_N1 and S_N2 reactions		
	S_N1	**S_N2**
Rate Law	Unimolecular (substrate only)	Bimolecular (Substrate & nucleophile)
Big Barrier	Carbocation Stability	Steric hindrance
Nucleophile	Weak	Strong
Alkyl halide	$3^o > 2^o >> 1^o$	$1^o > 2^o >> 3^o$

Solvent	Polar protic or aprotic	Polar Aprotic
Stereochemistry	Retention and inversion	Inversion

(Figure 8.7)

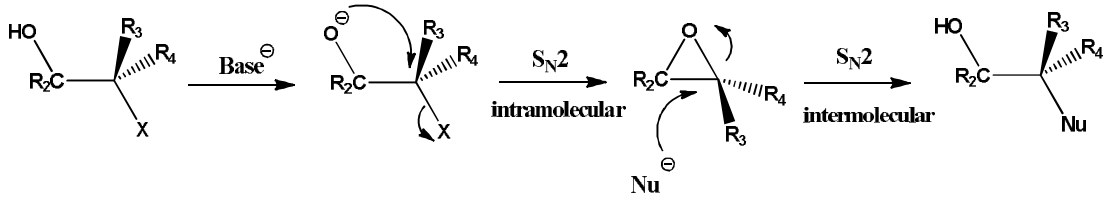
8.6 SET Mechanism

In some of the nucleophilic substitutions reactions, radicals and/or radical ions are involved. The first step in these types of reaction includes an electron transfer from the nucleophile to the substrate to form a radical anion. Mechanism in which such type electron transfer occurred called as SET (single electron transfer) mechanisms. In second step this radical ion cleaves and can formed products with Nu* or with the nucleophilic ion Nu^-.



8.7 Neighboring group participation (or anchimeric assistance)

Two consecutive (successive/ repeated) S_N2 reactions will lead to retention of configuration at chiral centre. This is possible only when a neighboring group acts as one of the nucleophile in two S_N2 reactions. The first S_N2 reaction is within the same molecule (i.e. intramolecular reaction) while second S_N2 reaction is a reaction between two different molecules (i.e. intermolecular reaction).



(Figure 8.8)

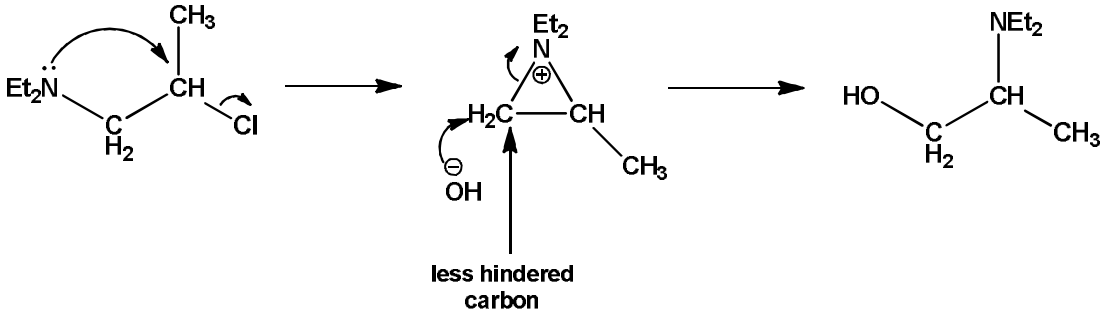
Hence neighboring group is acting as nucleophile and it present in the same molecule which is readily available for this favorable attack. Such types of reaction are much faster than intermolecular nucleophilic substitution reactions. Hence such types of reactions are called as anchimeric assistance and such reactions are called as anchimerically assisted reactions. Such types of reactions follow first order rate laws reactions i.e. Rate= *k*[substrate].

Sometimes formed cyclic intermediates are not symmetrical which create possibility of rearrangements and substitutions product are forms together.

When NGP is in operation: 1) It is normal for the reaction rate to be increased. 2) It is also possible for the stereochemistry of the reaction to be abnormal (or unexpected) when compared with a normal reaction.

There is different heteroatom which acts neighboring group such as oxygen in above example.

Nitrogen as a neighboring group (**aza-Payne rearrangements)**:

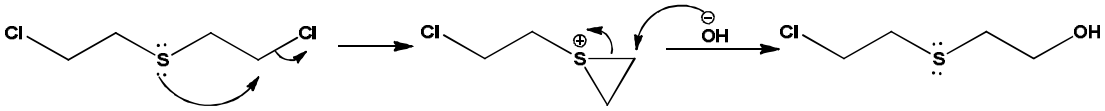


(Figure 8.9)

Here nitrogen acts as a neighboring group. The hydroxide ion attacked on carbon which is less hindered hence rearranged product is favored in this case.

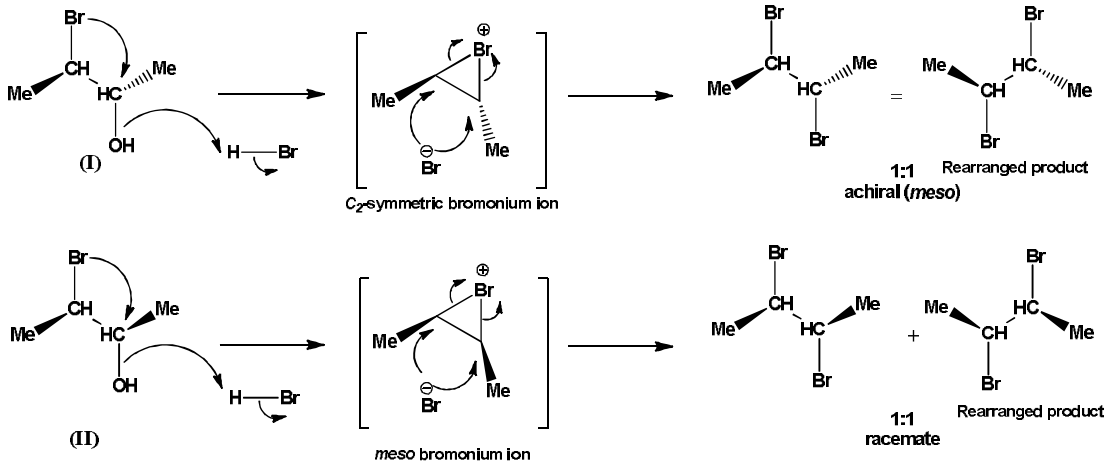
Sulphur as a neighboring group:

In base catalyzed hydrolysis of mustard gas sulphur participate as a neighboring group.



(Figure 8.10)

Halogens as a neighboring group (Bromonium ion rearrangements):



(Figure 8.11)

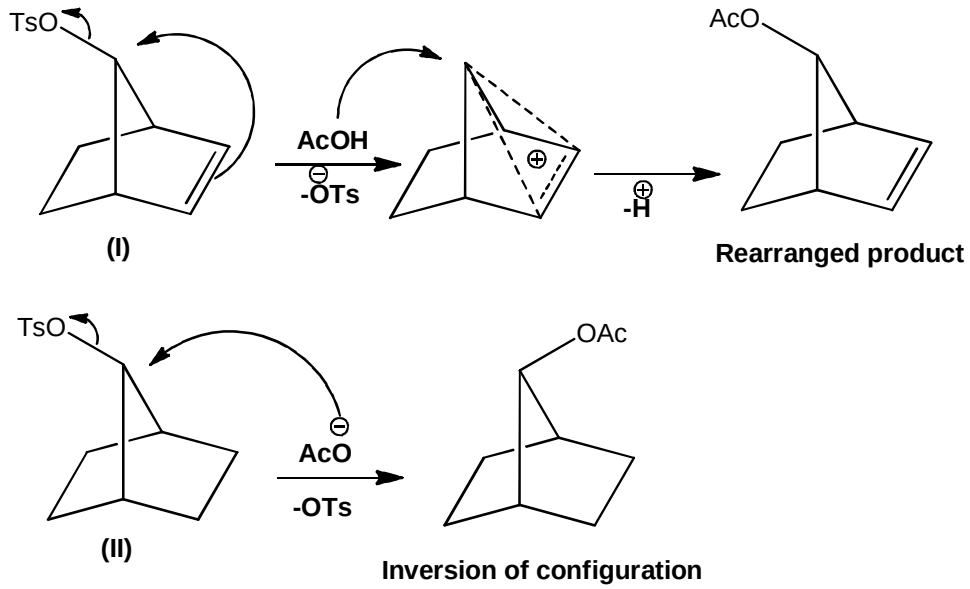
Optically active *erythro*-3 bromo-2- butanol (I) reacts with HBr with retention of configuration to give meso-product while *threo*-3 bromo-2-butanol (II) give an equimolar mixture of *R,R* and *S,S* enantiomers i.e. racemic mixture.

8.8 Neighboring group participation by π and σ Bonds

1. C=C (π) as a neighboring group:

Reaction rate of acetolysis of 7-norbornenyl tosylate(I) is much higher than its saturated analogue 7-norbornyl tosylate(II). The product formed is with retention of configuration form I while II give product with inversion of configuration. This confirms the role of C=C ie. π bonds.

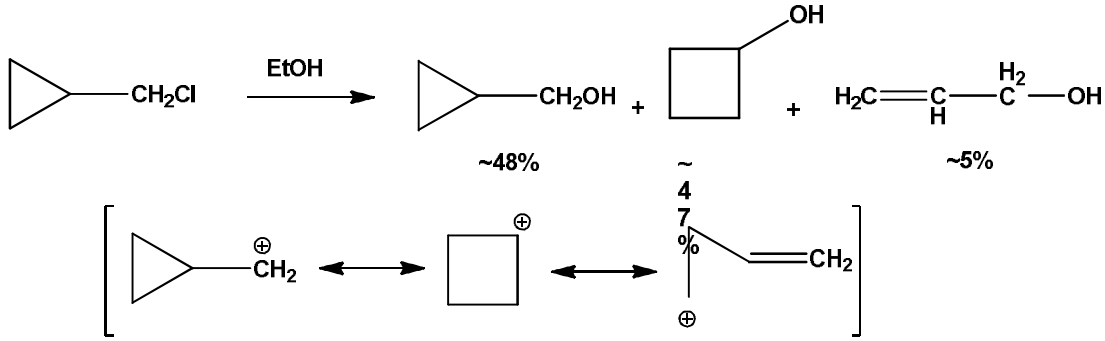
Here C=C group attached to a carbon atom which is adjacent to carbon atom where nucleophile substitution can occur and during the course of the reaction becomes bonded of partially bonded to the reaction centre to form a non-classical carbocation or bridged ion.



(Figure 8.12)

2. Neighboring group participation by σ bonds:

Reaction rate of solvolysis reaction of cyclopropyl methyl system is higher due to participation of σ bond. Formed cation is symmetrical and is stabilized by both sides. Hence possibility of formation of different product increased as rearrangement might took place.



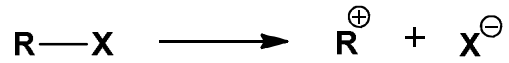
(Figure 8.13)

The products often include not only unrearranged cyclpropylmethyl but also cyclobutyl and a homoallyl compound confirms the participation of σ bond.

8.9 Classical Carbocation

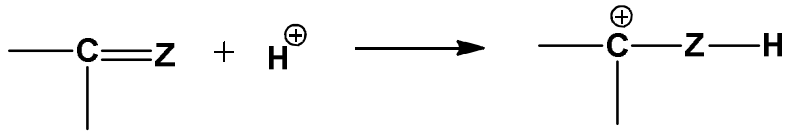
The classical carbocation is the one other in which the positive charge islocalized on one carbon atom or delocalized by resonance or a double or triples bond in the allylic positions. There are different ways of generation of carbocations:

1. By direct ionization: Alky halides generate carbocation on direct ionization by loss of halide in the presence of metals ions such as Ag^{+}.

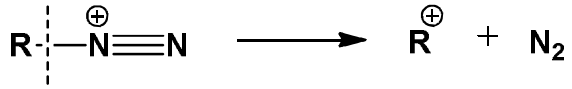


X- Cl, Br, I)

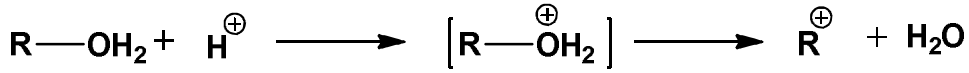
2.From alkene: Proton adds to one atom of unsaturated system which generates a carbocation on adjacent carbon atom



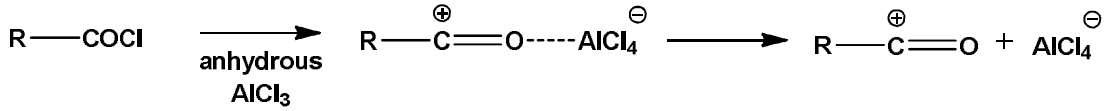
3.From alkyl diazonium ion: decomposition of alkyl diazonium ion generates a carbocation.



4.From protonation of alcohols: protonation of alcohols generates a carbocation on decomposition.

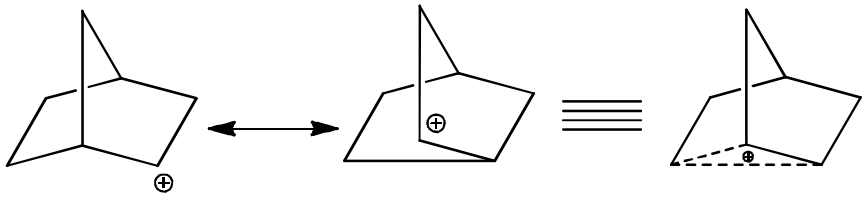


5.From acyl halides: In Friedel Crafts acylation carbocation generated in presence of $AlCl_3$.

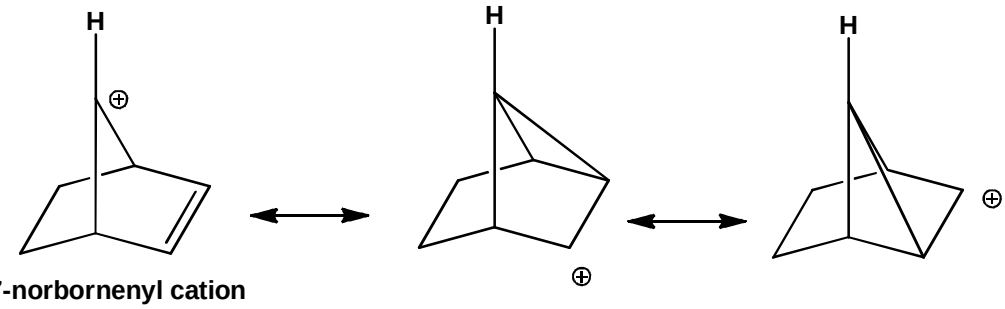


8.10 Non-classical Carbocation or Bridged Carbocation

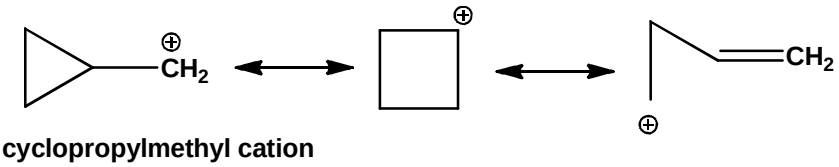
In contract to classical carbonation On converse in a non-classical carbocation, positive charged is delocalized either by double or triple bond which is not in the allylic position or by a single bond. These carbocation may cyclic, bridged ions and possess a three centre bond in which three atoms share two electrons. The non-classical carbocations can be generated if proper substrate is chosen. The examples are 7-norbornenyl cation, norbornyl cation and cyclopropylmethyl cation.



norbornyl cation



7-norbornenyl cation



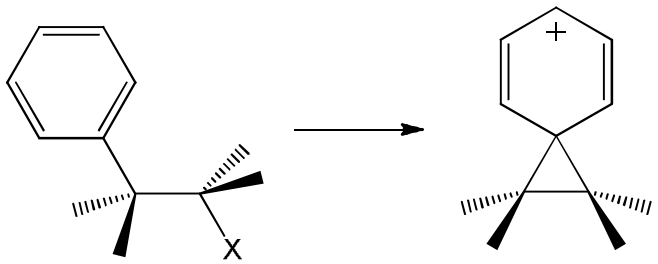
cyclopropylmethyl cation

(Figure 8.14)

One of the reasons behind formation of non classical carbocation is that when several intermediates are possible, the most stable one is likely to be formed. Since charge is most diffuse in the bridged ion than in the classical ion, the bridged structure would be expected to be more stable than the classical structure.

1. Phenonium ion:

A 'phenonium' ions system is thoroughly checked for the participation of aromatic electron i.e. participation by a β-phenyl group. Because the neighboring phenyl ring can make a π electron pair available, a phenonium ion intermediate is formed.



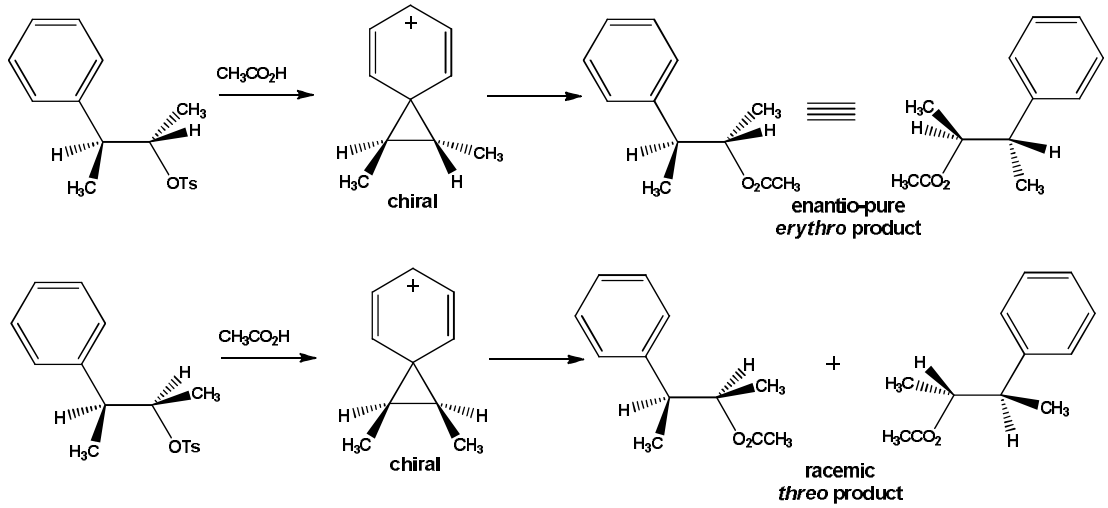
phenonium ion

(Figure 8.15)

Phenonium ions lead to a bridged carbocation with the positive charge which delocalized over the aromatic ring.

Phenonium ions evidence was first obtained by a study on the stereochemistry of solvolysis of compound 3-phenyl-2-butyl tosylates. The *erythro* isomer gave largely

retention of configuration via abridged ion intermediate. The *threo* isomer, where participation leads to an achiral intermediate, gave racemic threo product.

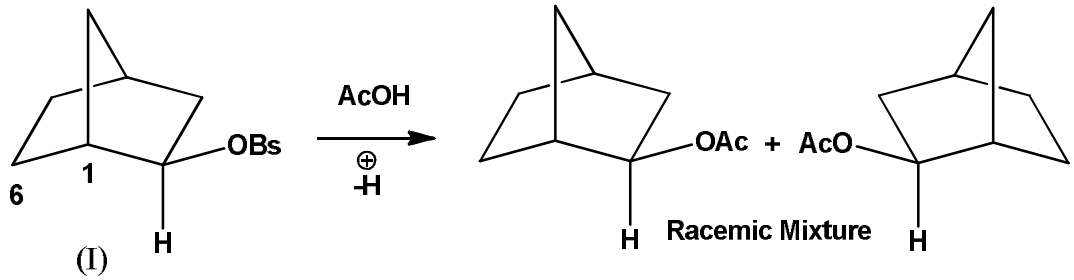


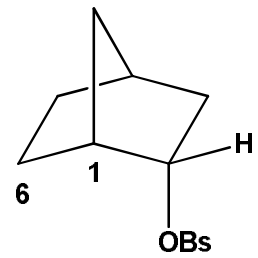
(Figure 8.16)

Participation of the β-phenyl group is highly dependent on the solvent. Solvents with good nucleophilicity (e.g., ethanol), the normal solvent displacement mechanism makes a larger contribution. As solvent nucleophilicity decreases, the relative extent of aryl participation increases. It is thus clear that β-phenyl group can function as neighboring groups.

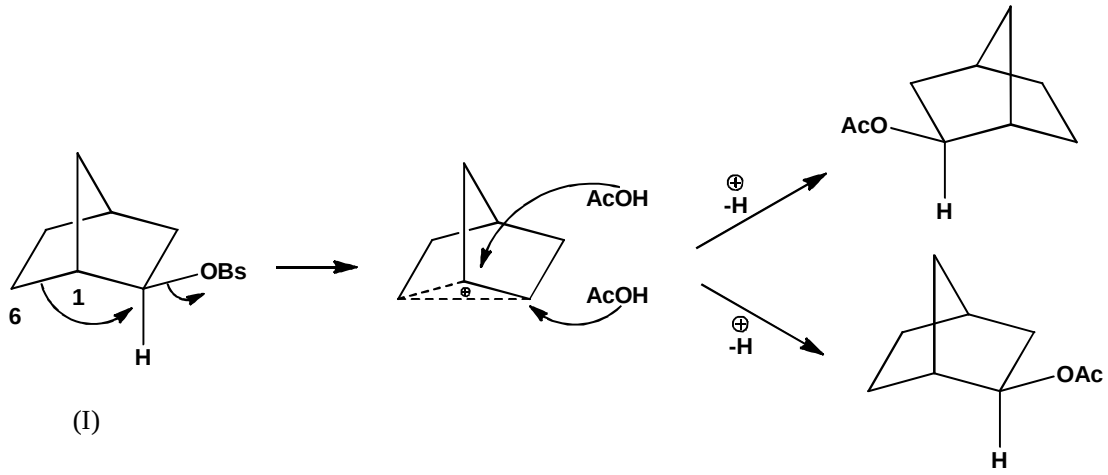
2. 2-norbornyl system

Acetolysis of optically active *exo*-2-norbornyl brosylate (I) gave racemic mixture of two *exo* acetates while no *endo* isomer was formed. The *exo* (I) solvolyzed 350 times times faster than its *endo*(II) isomer. These observations were first reported by Winstein and Trifan as 1.6 bond assist in the departure of –OBs group and nonclassical carbocation as an intermediate is involved.





Mechanism:



(I)

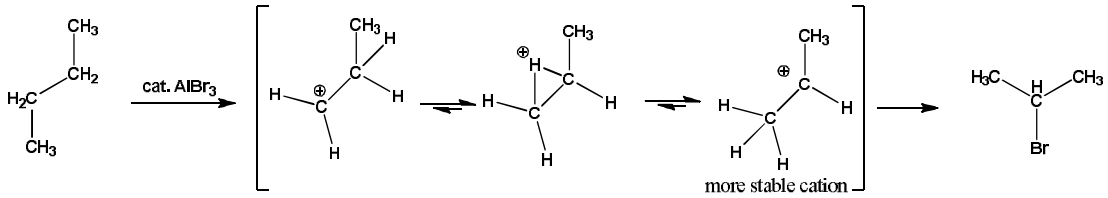
(Figure 8.17)

Solvolysis of II is not assisted by 1,6 bond as backside attack is not favorable. Hence solvolysis of *endo*- II takes place at normal rate are compare to *exo*- I. Therefore higher rate of *exo*-I is explain on the basis of anchimeric assistance and formation of nonclassical carbocation.

8.11 Application of neighboring group participation in carbocation rearrangements

Wagner-Meerwein Shifts:

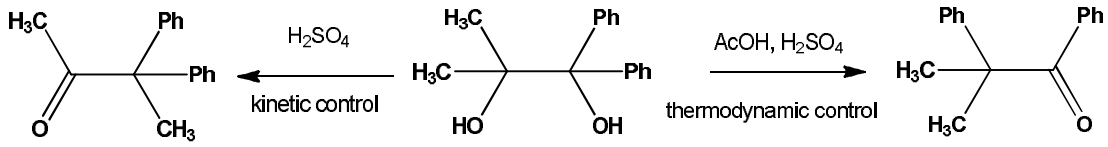
These 1, 2-hydride shifts occur if it leads to the new carbocation being more stabilized than the original. This is usually the case if the carbon adjacent to the positively charged centre is secondary or tertiary. Subsequent elimination will then occur.



(Figure 8.18)

Pinacol Rearrangement:

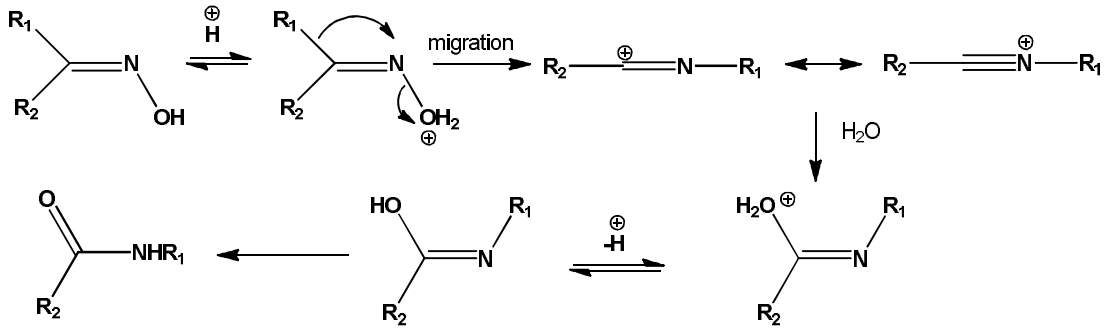
Treatment of 1,2 diols with acid, which converts them to carbonyls. The reaction can also occur on β-aminoalcohols, halohydrins, epoxides and allylic alcohols. It proceeds via a 1,2 alkyl shift, and the overall reaction is:



(Figure 8.19)

Beckmann Rearrangement:

The most important point to remember here is that the R_1 group *anti* to the oxime N-O bond is the one that migrates (i.e. R_1 in the above), regardless of migratory aptitudes.



(Figure 8.20)

8.12 Summary

Aliphatic nucleophilic substitution reactions precede either by $S_N1$and by $S_N2$mechanism. The rate of aliphatic nucleophilic substitution is depending on the type of mechanism involved. In neighboring group participation, different heteroatom's can acts as nucleophiles and reaction follows first order i.e. Rate= *k*[substrate]. Neighboring group participation by π and σ bonds occurred in 7-norbornenyl tosylate and cyclopropyl methyl system. Phenonium ion and 2-norbornyl system involves formation of Non-classical Carbocation or Bridged Carbocation.

8.13 Glossary

- In a **nucleophilic aliphatic substitution reaction**, a nucleophile substitutes for a leaving group of a compound.

- S_N2 reactions take place by the one-step mechanism and the rate of the reaction is dependent on both the concentration of the nucleophile [Nu] and that of the substrate [RX] undergoing substitution.
- S_N1 reactions take place by the two-step mechanism.
- In S_N1 reactions, the first step is rate determining step of the reaction while second step is fast reaction leading to give substituted product.
- In S_N2 reactions inversion take place at chiral center while in S_N1 reactions both i.e. inverted as well retention products are formed.
- SET mechanism involves electron transfer.
- In neighboring group participation two consecutive S_N2 reactions will lead to retention of configuration at chiral centre.
- Heteroatom's as well as halogens can acts as neighboring group in reaction.
- Neighboring group participation also assisted by π and σ Bonds.
- Phenonium ions lead to a bridged carbocation with the positive charge which delocalized over the aromatic ring.
- In 2-norbornyl system 1, 6 sigma bond assist in the departure of –OBs group and generate non-classical carbocation.

8.14 Review questions/ Conprehensive Questions

1. What is aliphatic nucleophilic substitution?
2. Explain S_N^2 and S_N^1 reaction and their mechanism.
3. Write a note on factors affecting S_N1 and S_N2 reactions.
4. Write a short note on SET mechanism.
5. What is neighboring group participation? Explain with example.
6. Discuss with examples of neighboring group participation by π and σ Bonds.
7. Write a note on classical carbocation and non-classical carbocation.
8. Discuss applications of neighboring group participation in carbocation rearrangements.

8.15 References and Suggested readings

1. A Guidebook to Mechanism in Organic Chemistry (6the ed.)- Peter Sykes (Longman Technical & Scientific) 1985.
2. Organic Chemistry- J. Clayden, Greeves, S. Warren and W others (Oxford University Press) 2001

3. March's Advanced Organic Chemistry (7^{th} ed.)- M. Smith and J. March (John Wiley & Sons, Inc., Hoboken, New Jersey) 2007.
4. Organic Reaction Mechanisms- V. K. Ahluwalia and R. K. *Para*shar (Narosa Publishing House) 2002.
5. Advanced Organic Chemistry- J. Singh and L. D. S. Yadav (Pragati Prakashan) 2005.

Unit – 9 The SN^i Mechanism

Structure of Unit:

9.1 Objectives

At the end of the unit learner will be able to

- Understand with nucleophilic substitution reaction
- Learn brief idea about mechanism of S_ni reaction
- Understand exact differences between attacking nucleophile and ambident nucleophile
- Importance of Phase transfer catalyst
- Understand the term “Regioselectivity”

9.2 Introduction

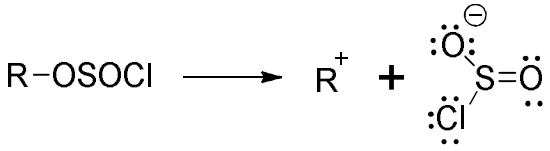
In this unit mainly deal with nucleophilic substitution reactions at an allylic, aliphatic trigonal, vinylic carbon along with brief mechanism for S_N1 reaction. This unit also covers reactivity effects of structure along with different attacking nucleophile, leaving groups, reaction medium phase transfer catalyst, ambient nucleophile and regioselectivity.

9.3 S_Ni mechanism

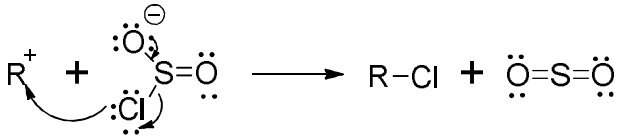
There are mainly two possible nucleophilic substitution mechanisms as per as alkyl halides are concerned i.e. S_N1 and S_N2. These represent the extreme mechanisms of nucleophilic substitution, and some reactions involve mechanisms which lie somewhere in between the two. In both the reactions mechanisms mainly proceeds with the loss of halide anion from alkyl halides. S_N1 reaction mainly proceeds with racemization whereas S_N2 reaction gives product with inversion of configuration, on the basis of attack of nucleophile. There are few reactions which mainly proceed with retention of configuration without the effect of neighboring group e.g. S_Ni reaction. In S_Ni reaction, substrate is attacked by part of leaving group which gives product with inversion of configuration. This reaction is mainly proceeds with two steps.

Mechanism:

Step-I: Formation of intermediate carbocation by heterolysis of C-O bond.



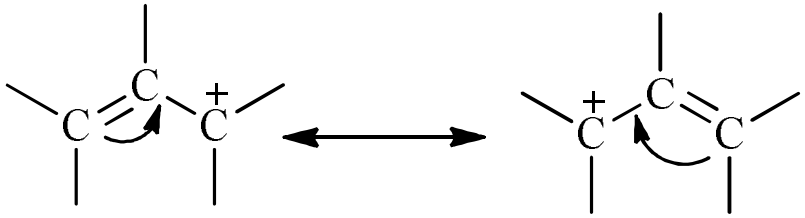
Step-II: Substrate is attacked by part of leaving group and formation of product with retention of configuration.



The best example of S_Ni mechanism is reaction between alcohols and thionyl chloride to give alkyl halides.

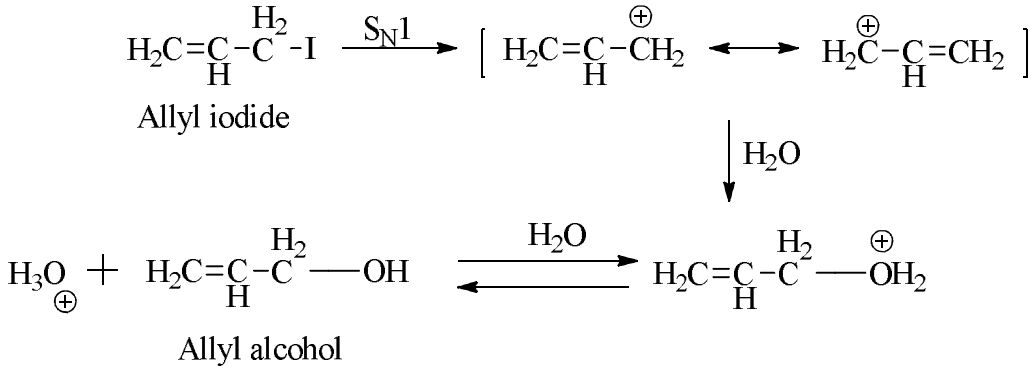
9.4 Nucleophilie Substitution at an allylic carbon

Allyl halides are more reactive than the saturated halides towards the nucleophilic substitution reaction. Allyl halides are generally reactive under S_N1 reaction conditions due to the resonance stabilization of intermediate allyl carbocation.



Resonance stabilization of allyl carbocation

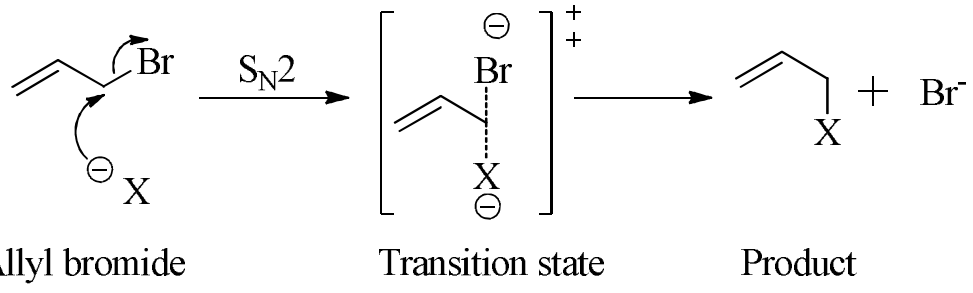
Resonance stabilization of intermediate allyl carbocation has an acceleration effect on the ionization of allyl halides. For example, solvolysis of ally iodide in water proceeds much faster than the solvolysis of propyl iodide.



Allyl iodide

Allyl alcohol

Allyl halides also have much faster reaction rate than simple alkyl halides in S_N2 reaction. For example, allyl bromide is about 100 times much reactive than simple alkyl bromide or other alkyl halides. The double bond mainly stabilizes the S_N2 transitions by conjugation with p orbital at the carbon atom under attack.

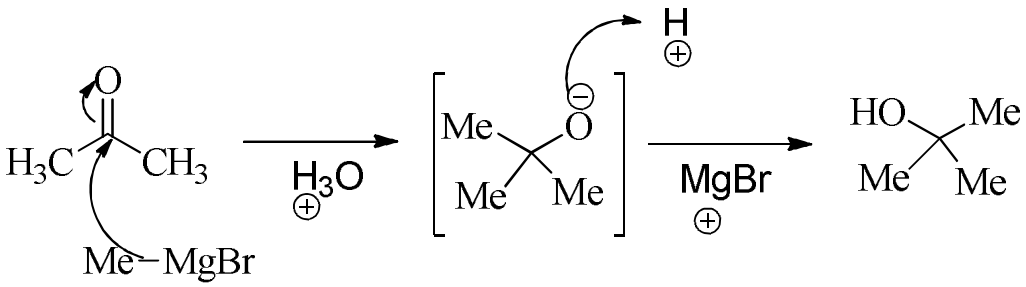


Allyl bromide Transition state Product

9.5 Nucleophilie Substitution at an aliphatic trigonal carbon

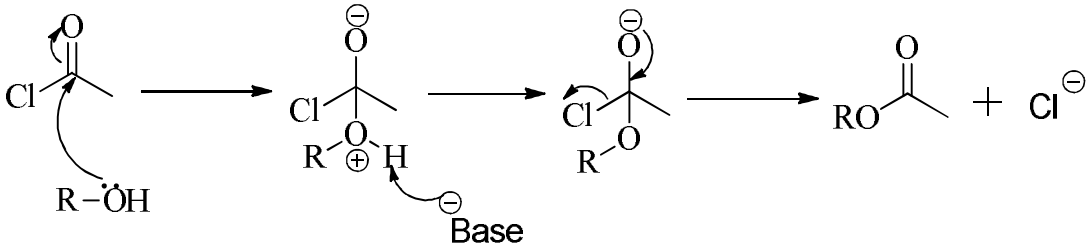
Aldehydes and ketones mainly contains trigonal carbon atom. Nucleophiles react with this carbonyl carbon atom which acts as a good electrophile, to give products

containing hydroxyl groups. Addition of alkyl magnesium halide to a carbonyl carbon of aldehydes or ketones gives stable alkoxide which will be protonated to an alcohol.



ketone Intermediate Tertiary alcohol

Acid chlorides and acid anhydride reacts with alcohols to give esters. In the reaction of acyl chloride with alcohol the first step is addition of nucleophilic alcohol to the electrophilic carbonyl carbon. The abstraction of proton from alcohol by base is a key step for the formation of unstable intermediate. This unstable intermediate collapse through an elimination reaction (with loss of chloride) ion, to form an ester.

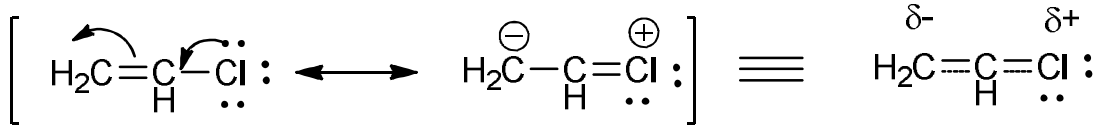


Acyl chloride Unstable intermediate Ester

9.6 Nucleophilic Substitution at an vinylic carbon

This reaction mainly involves the interaction of two nucleophiles. Halogen attached to doubly bonded carbon nucleus is usually quite unreactive due to the short and stronger bond between Carbon-halogen. For example, vinyl chloride has a bond length of 1.69 A^{o}, as compared to alkyl chlorides which has a bond length of 1.77-1.80 A^{o}. In vinyl chloride the carbon atom attached to halogen is sp^2 hybridized and less willing to release electron to halogen due to more electronegativity than sp^3 hybridized carbon atom. Hence formed vinyl carbocation are thermodynamically less stable than alkyl carbocations which prevents S_N1 mechanism. Another reason for there unreactivity is overlaping of p-orbital of halogen with π-orbital of the double bond which mainly forms delocalized cloud of the π-electrons. Thus the carbon-halogen bond shows partial double bond character with high strength which is

difficult to break. These effects mainly inhibit nucleophilic substitution reactions of either the S_N1 or S_N2 type, thus net reactivity of the molecule is considerably less than that of saturated alkyl halides.



Delocalization of electrons by resonance in vinyl chloride

9.7 Structural effectson Reactivity

In S_N1 reaction formation of carbocation is a rate determining step. Therefore, order of reactivity of organic substrate is mainly depends on stability of carbocation formed after ionization of substrate. Hence order of stability of alky halides carbocation is:

$$R_3X > R_2X > R_1X$$

Substitution of hydrogen atom attached to positive carbon of a carbocation by methyl group, stabilize the ion by 15 to 30 kcal/mol. In most cases the substituents which having positive inductive and positive hyperconjugation effects mainly stabilizes the carbocation.

Relatively stable carbocation such as, allylic, benzylic, and tert-carbocations mainly react by S_N1 mechanism.

3^o > allyl ~ benzyl > 2^o > 1^o > CH_3

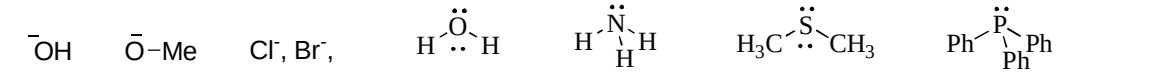
The transition state of S_N2 reaction is mainly bonded to five atoms of groups; therefore, this steric hindrance around carbon site makes huge difference in rate of S_N2 reaction. The more crowded the transition state relative to substrate, the higher its energy will be, and the slower it will be formed. As a result increasing alkyl substituent's on carbon atom results in steric hindrance. Hence the order of reactivity of alkyl halides in S_N2 reaction is:

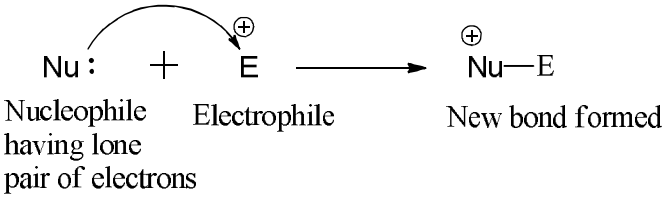
CH_3X > 1^o > 2^o > 3^o

9.8 Attacking Nucleophile

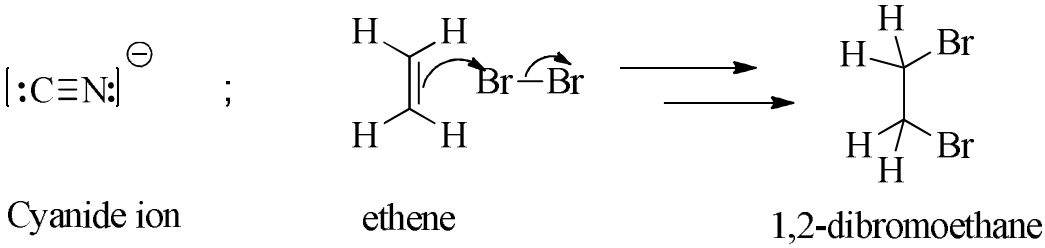
As name indicates nucleohiles are nucleus loving species. Nucleophiles are negatively charged (hydroxide, halide, alkoxide ions) or neutral species (water,

ammonia, alcohols, dimethylsulfide and triphenylphosphine) with nonbonding lone pairs of electrons in the high energy filled orbital which can be donated to electrophiles.

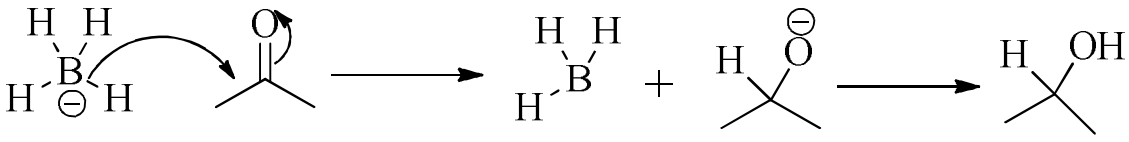




Cyanide ion is a rare example of carbon nucleophiles with lone pairs of electrons. Although there are few example of neutral carbon electrophiles usually have a π bond which mainly acts as the nucleophilic portion of the molecule. When there are no lone pair electrons to supplied by high-energy nonbonding orbitals, the next best is the lower-energy filled π orbitals rather than the even lower-energy σ bonds. Simple alkenes are weakly nucleophilic and react with strong electrophiles such as bromine.



In some cases it is also possible that σ bonds act as nucleophiles such as borohydride anion, BH_4^-. It mainly has a nucleophilic B–H bond and can donate those electrons into the π* orbital of a carbonyl compound breaking that bond and eventually giving an alcohol as product.



Increasing electron density mainly increases the necleophilicity of a given atom; therefore nucleophile with a negative charge is stronger than its conjugate acid. For example alkoxide and hydroxide ions are more nucleophilic than their respective

conjugate acids i.e. alcohol and water. Following is the decrasing orders of nucleophic behaviours.

$$R_3C^- > R_2N^- > RO^- > F^-$$

In Periodic table withim a period Within a period of periodic table, necleophilicity mainly decreases with increasing atomic number and within a group, in contrast, necleophilicity increases with increasing atomic number.

9.9 Leaving group

Leaving group is mainly the functional group which is eliminated in a chemical reaction with electrons of the σ bond. The nature of leaving group mainly influence the rate of both S_N1 and S_N2 reaction as better the leaving group, faster is the reaction. The relative leaving ability of leaving group (Y) is mainly influenced by considering: (i) the strength of the R-Y bond; (ii) the polarizability of R-Y bond; (iii) the stability of formed Y^- group (iv) the degree of stabilization of formed Y^- by solvation. In general good leaving groups are mainly large in size with low electronegativity and low necleophilicity. Thus in case of halides the order of leaving gropu ability is: $I^- > Br^- > Cl^- >> F^-$

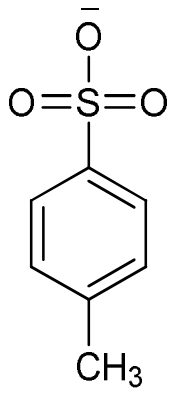
The iodide ion (I^-) is larger in size with high polarizability and is better solvated by solvent, therefore, it is better leaving group than fluoride ion. The stability of halide ions can be measured by using the pKa values of respective acids (HX). The strength of C-X bonds can also be related to pKa values as represented in following table.

Halogen (X)	Strenghth of C-X bond (kJ mol^{-1})	pKa of HX
Fluorine	118	+3
Chlorine	81	-7
Bromine	67	-9
Iodine	54	-1

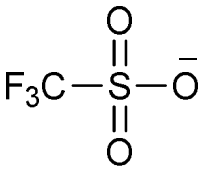
It is clear from table that iodide ion is better leaving group than the other halides as it has low bond strength with low pKa values.

Usually charged species has better leaving ability as compared to the neutral species. The respective conjugate bases of strong oxygen acids such as tosylate, triflate and

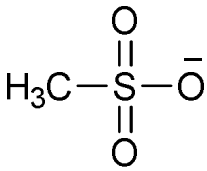
mesylate anions are good leaving groups due to weak strength of C-O (sulfonate) bond, and stabilization of leaving group by resonance.



Tosylate



Triflate



Mesylate

The strong bases such as OH^-, RO^-, and NH_2^- are bad leaving groups. However protonation of strong bases which converts them to very weak bases which are much better leaving groups. For example OH^- cannot be directly displaced by Br^-, but can be displaced if it is protonated first.

9.10 Reaction Medium

In S_N1 reaction, the choice of solvent polarity mainly depends upon whether the substrate is neutral or positively charged. Solvents polarity has direct effect on rate of reaction. When substrate is neutral, more polar solvent is of great choice which mainly reduces energy of ionic transition state and increases rate of reaction. In contrast, when substrate is positively charged, less polar solvents are used to increase rate of reaction. S_N1 reaction proceeds in polar protic solvent and S_N2 reaction in polar aprotic solvent. Water, alcohols, and carboxylic acids are polar protic solvents, whereas acetone, dimethyl-sulfoxide (DMSO), dimethylformamide (DMF), acetonitrile, and sulfur dioxide are polar aprotic solvents. Size of attacking anion also affects rate of reaction in protic and aprotic solvent. Protic solvents have developed structure; therefore are best fitted in it. In case of aprotic solvents, they are loosely held and large anions can be easily fitted in it. Hence on changing solvents from protic to aprotic one, small anions are greatly affected.

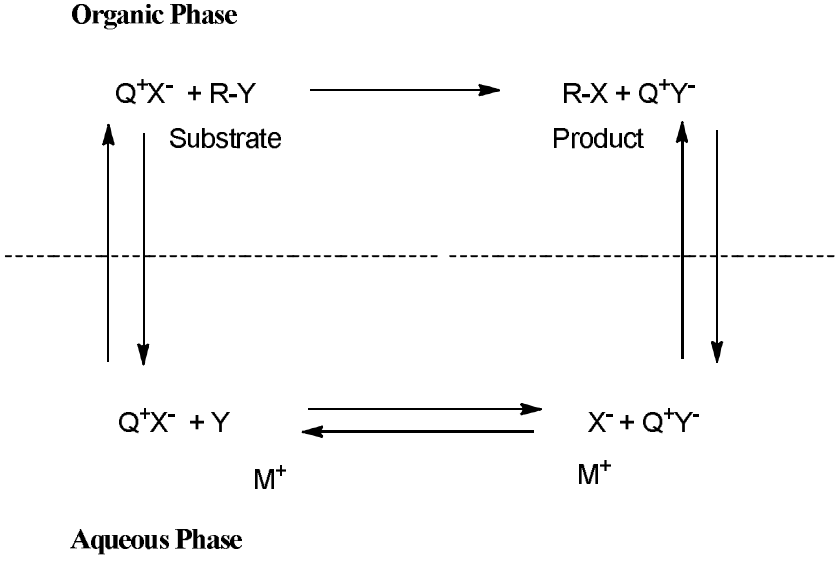
9.11 Phase Transfer catalysts

There are many desirable reactions which cannot be proceeds due to hindrance in reactants to react with each other. This difficulty is mainly due to solubility of reactants in different phases. For example, in S_N2 reaction medium: the gas phase,

where the anion is completely impediment and highly reactive. The purpose of solvent is to combine the reactants. The organic reactant can be dissolve in aprotic solvent such as benzene and Dichloromethane but solubility of ionic reactant in such solvent is problematic one. This difficulty can be overcome by using phase transfer catalysts (PTC). Phase-Transfer Catalysis (PTC) is a well-known method of promoting reactions between reagents with opposite solubility preferences. In such systems each reactant is dissolved in the appropriate solvent. Commonly, the two solvents are immiscible to one another, and then a phase-transfer catalyst is added to facilitate the transport of one reactant into the other phase. By means of the catalytic step, the enhanced reactivity between the ionic species leads to increase of the rate of the desired reaction.

Types of Phase-Transfer Catalysts: There are many types of PTC such as Quaternary ammonium amd Phosphonium salts, crown ethers, Polyethylene glycols, etc. among these Quaternary ammonium salts is most widely used. Typical phase transfer catalysts used are benzyltrimethylammonium chloride and hexadecyltributylphosphonium bromide.

Mechanism of PTC: When a quaternary ammonium halide dissolved in the aqueous phase, ionization of (Q^+X^-) takes place and formed anion were exchanged with anion of reactant in the aqueous solution. The ion-pair formed (Q^+X^-) is lipophilic and easily crosses the liquid-liquid interface and diffuses into the organic phase, this step being the phase-transfer. In the organic phase, nucleophilic anion of ion-pair undergoes a nucleophilic substitution reaction with the organic reagent forming the desired product (RY). The catalyst subsequently returns to the aqueous phase and the cycle continues.



Other mechanisms that can be considered as phase-transfer catalytic are process:

PTC of neutral species: Transfer of neutral protic species or metal salts into the organic medium.

Electron-transfer catalysis for Redox systems.

Metal ion-transfer: transfer from aqueous solutions into water immiscible ionic liquids. ***Pyrolytic alkylation process***, formation of volatile alkyl derivative through thermal decomposition of a quaternary ammonium salt.

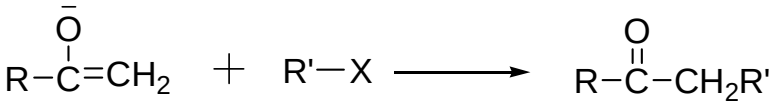
9.12 Ambident nucleophile

The nucleophiles with more than one reactive atom are known as ambident nucleophiles. Cyanide, isothiocynate, nitrite and enolate ions are some example of ambident nucleophiles, since they have more than one reactive sites. DMSO is also an ambident nucleophile with two reactive atoms i.e. O and S with unshared pairs of electrons.

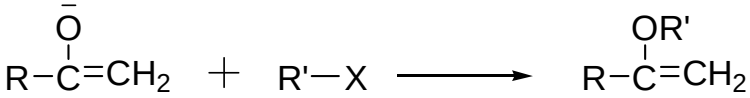
Cyanide ion Isothiocyanate ion Nitrite ion Enolate ion

Alkylation of enolate can either occur at C or O. since most negative charge of an enolate is on the Oxygen atom, the O-alkylated product is dominated.

C-alkylation



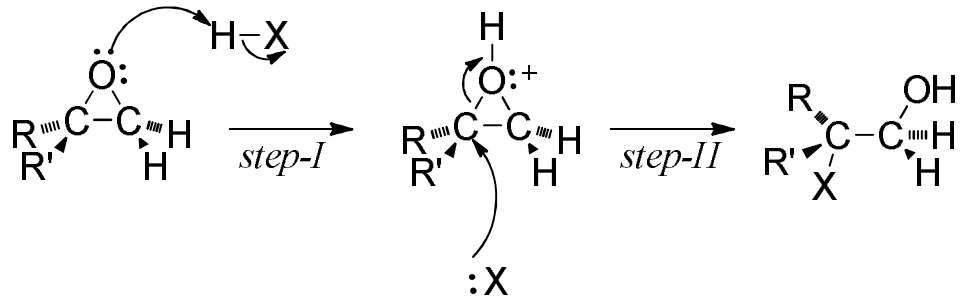
O-alkylation



9.13 Regioselectivity

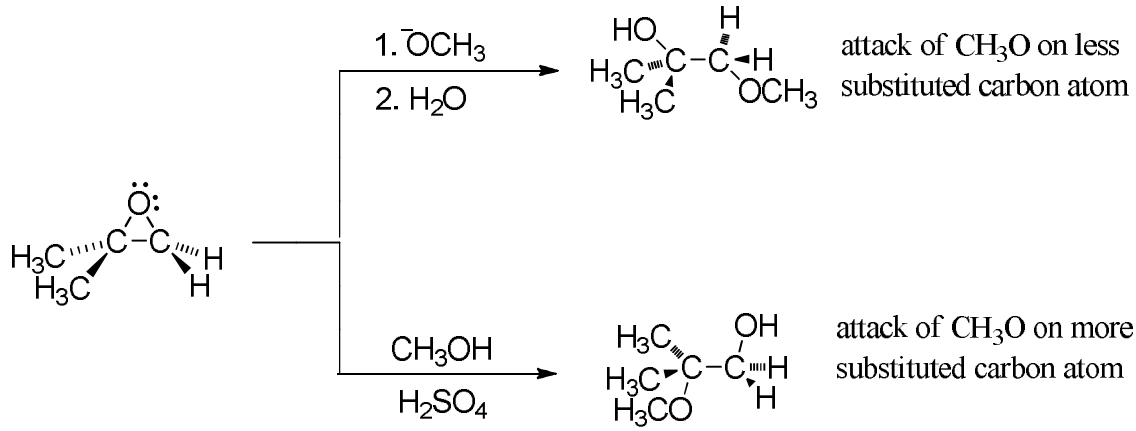
When a reaction takes place preferontioally at a particular position then such reactions is preferential site known as regioselective reaction. In simple way, we can say that regioselectivity is where the nucleophile is going to attack. Regioselectivity of nucleophilic substitution reaction can easily be understood using an example of epoxides opening. Acid (HX) containing a nucleophile (X^-) opens epoxide ring mainly in teo steps. In first step formation of good leaving group (OH) takes place by protonation of epoxide oxygen with acid. This step also results in formation of good nucleophile (X^-). In second step, nucleophile (X^-) attack from backside to open

protonated epoxide ring which forms trans 1,2-disubstituted cycloalkane as a major product.



Epoxide Intermediate trans-1,2-disubstituted cycloalkanes

Mechanism of nucleophile attack is thought to be in between S_N1 and S_N2 mechanism. Attack of nucleophile from backside mainly suggests S_N2 mechanism, where as attacks on more substituted carbon atom suggests S_N1 mechanism. Acid or strong nucleophilic catalysed opening of epoxide ring is regioselective with one of constitutional isomer as a major product.



9.14 Summary

Nucleophilic substitution reaction mainly takes place by either S_N1 or S_N2 mechanism. Tertiary halides, weak nucleophile and polar protic solvent are key points for S_N1 reaction. Attacking nucleophiles mainly contain atleast one reactive atom which attacks on electrophiles. In contrast to attacking nucleophiles, ambident nucleophile contains more than one reactive atom. This unit also covers key notes on leaving groups, Phase transfer catalyst and regioselectivity.

9.15 Glossary

- S_Ni reaction mainly proceeds with inversion of configuration without the assistance neighboring group.
- In S_Ni reaction, part of leaving group mainly attacks on substrate to give final product.
- Allyl halides mainly follow S_N1 mechanism
- Nucleophilic substitution reaction at an vinylic carbon involves interaction between two nucleophiles.
- Order of reactivity for S_N1 reaction is: $R_3X > R_2X > R_1X$ and for S_N2 reaction is: $R_1X > R_2X > R_3X$.
- Necleophilicity increases with increasing electron cloud.
- Ambient nucleophile contains more than one reactive species.
- A good nucleophile is small in size with low electronegativity and low necleophilicity.
- The choice of polarity is depends on nature of substrate.
- Phase transfer catalyst (PTC) mainly used for promoting reaction between reagents with opposite solubility preferences.
- When a reaction takes place proferecmially at a particular position then such reaction is called as regioselective reaction

9.16 Review Questions / Comprehensive Questions

1. Why S_N1 reaction proceeds with racemization?
2. What is ambient nucleophile?
3. Explain the term PTC.
4. Nucleophilic substitution reaction at vinylic carbon does not take place! Explain.
5. Discuss the order of reactivity of defferent alkychalide towards for S_N1 and S_N2 reaction mechanism.

9.17 References and Suggested readings

1. Organic chemistry- Janice Gorzynski Smith (Third edition, Mc Graw Hill publications)

2. Organic chemistry- J Clayden, N Greeves, S Warren (Second edition, Oxford University press) 2012.
3. March's Advanced Organic Chemistry (7^{th} ed.)- M. Smith and J. March (John Wiley & Sons, Inc., Hoboken, New Jersey) 2007.
4. Advanced Organic Chemistry- J. Singh and L. D. S. Yadav (Pragati Prakashan) 2005.

Unit-10 : Addition to Carbon-Carbon Multiple Bonds

Structure of Unit

10.1 Objectives

At the end of this unit, learner will be able to understand the-

- Electrophilic addition reactions
- Regioselectivity During Electrophilic Additions
- Nucleophilic Additions of Alkenes and Alkynes
- Free Radical Addition
- Orientation and Reactivity
- Michael reaction

10.2 Introduction

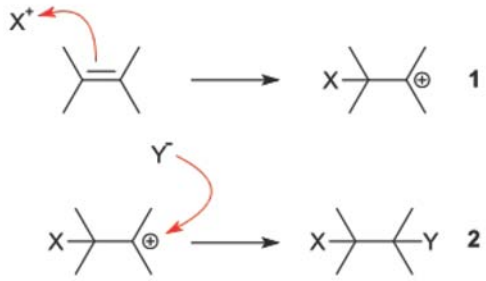
The unit deals with the reactions and mechanism of addition reactions to the C-C multiple bonds. The study reveals that there are four fundamental ways in which addition to a double or triple bond can take place. Three of these are two-step processes, with initial attack by a nucleophile, or by an electrophile or a free radical. The second step consists of combination of the resulting intermediate with, a

positive species, a negative species, or a free radical entity respectively. In the fourth type of mechanism, attack at the two carbon atoms of the double or triple bond is simultaneous (concerted). Which of the four mechanisms is operating in any given case is determined by the nature of the substrate, the reagent, and the reaction conditions. Some of the reactions in this chapter can take place by all four above mentioned mechanism.

Electrophilic Addition

An electrophilic addition reaction is an addition reaction where, in a chemical compound, a π bond is broken intialy by an electronic and two new σ bonds are formed. The substrate of an electrophilic addition reaction must have a double bond or triple bond.

The driving force for this reaction is the formation of an electrophile X^+ which forms a covalent bond with an electron-rich centre of unsaturated C=C bond. During the formation of C-x bond, the positive charge on x+ is transferred to carbon carbon bond , this forming a corboation.



I step 2 of an electrophilic addition, the positively charged intermediate combines with (Y) which is electron-rich and usually an anion to form the second covalent bond.

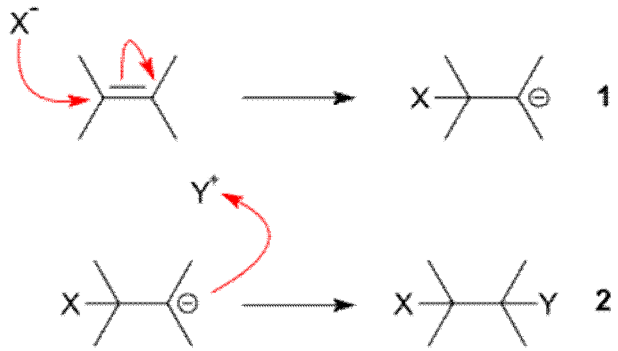
Step 2 is same as nucleophilic attack process found in an S_N1 reaction. The exact nature of the electrophile and the nature of the positively charged intermediate are not always clear and depend on reactants and reaction conditions.

In all asymmetric addition reactions to carbon, carbon multiple bonds regioselectivity is important and often determined by Markovnikov's rule. Organoborane compounds give *anti*-Markovnikov additions. Electrophilic attack to an aromatic system results in electrophilic aromatic substitution rather than an addition reaction.

Nucleophilic addition

A nucleophilic addition reaction is an addition reaction where (a chemical compound with an electron deficient or electrophilic double or triple bond) a π bond reacts with

electron rich reactant, termed a nucleophile, with disappearance of the double bond and creation of two new single, or σ, bonds. These reactions are of prime importance to an orgainic chemist as these are involved in biological syntehesis of compounds informetafolusm opf every using organism used by chemists in acodimes and also in pharmaceutical industries to prepare new and existing complex organic chemicals. Addition reactions require the presence of groups with multiple-bondes in the electrophile: carbon–heteroatom multiple bonds as in carbonyls, imines, and nitriles, or carbon–carbon double or triple bonds.



The driving force for the addition to alkenes is the formation of a nucleophile X^- that forms a covalent bond with an electron-poor unsaturated system -C=C- (step 1). The negative charge on X is transferred to the carbon – carbon bond. step 2 the negatively charged carbanion combines with (Y) that is electron-poor to form the second covalent bond. Ordinary alkenes are not susceptible to a nucleophilic attack (apolar bond).

Free-radical addition

Free-radical addition is an addition reaction in organic chemistry involving free radicals. The addition may occur between a radical and a non-radical, or between two radicals.

The basic steps with examples of the free-radical addition (also known as radical chain mechanism) are:

Initiation by a radical initiator: A radical is created from a non-radical precursor.

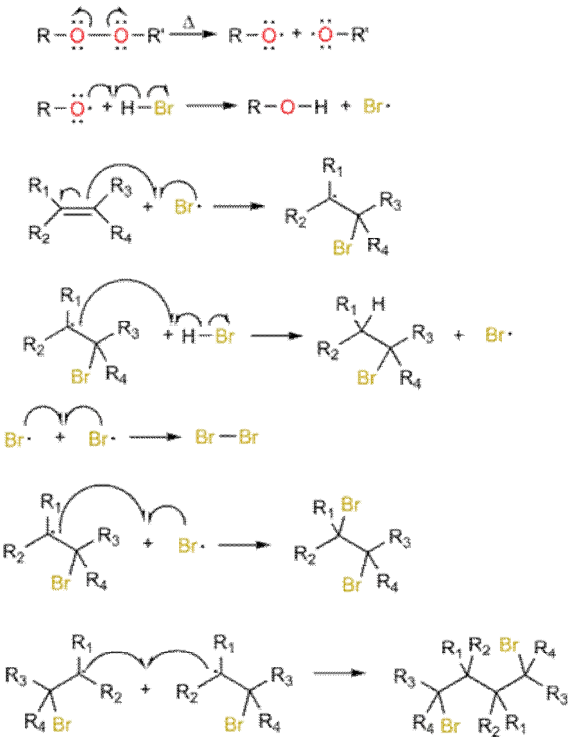
Chain propagation: A radical reacts with a non-radical to produce a new radical species

Chain termination: Two radicals react with each other to create a non-radical species

Free-radical reactions depend on a reagent having a (relatively) weak bond, allowing it to homolyse to form radicals (often with heat or light). Reagents without such a weak bond would likely to react via a different mechanism. An example of an addition reaction involving aryl radicals is the Meerweins arylation.

Addition of mineral acid to an alkene

Consider the alkoxy radical-catalyzed, *anti*-Markovnikov addition reaction of hydrogen bromide to an alkene. In this reaction, a catalytic amount of organic peroxide is needed to abstract the acidic proton from HBr and generate the bromine radical, however a full molar equivalent of alkene and acid is required for completion.



Note that the radical will be on the more substituted carbon. Free-radical addition does not occur with the molecules HCl or HI. Both reactions are extremely endothermic and are not chemically favoured.

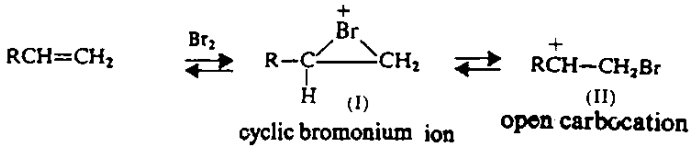
In this unit discussion will further focus on addition reactions which proceed via polar or ionic mechanisms and other related processes.

10.3 Electrophilic addition reaction

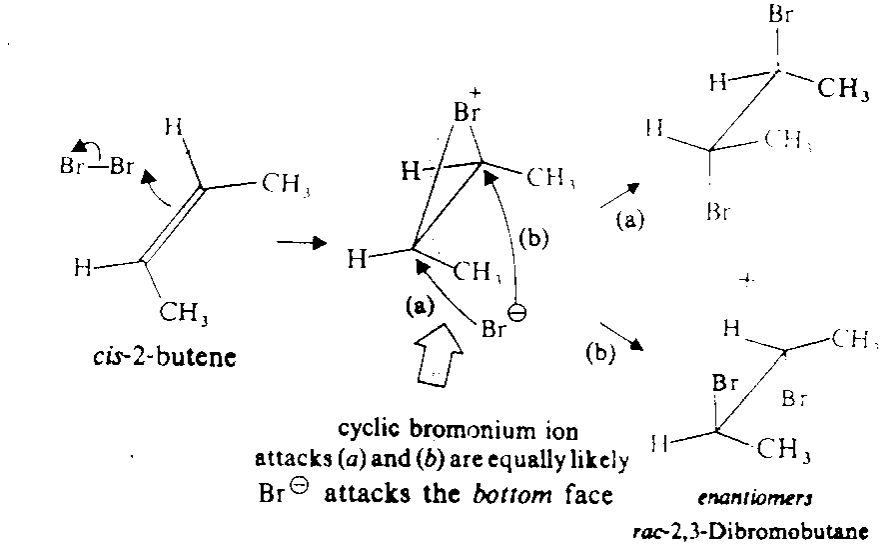
Halogens Addition

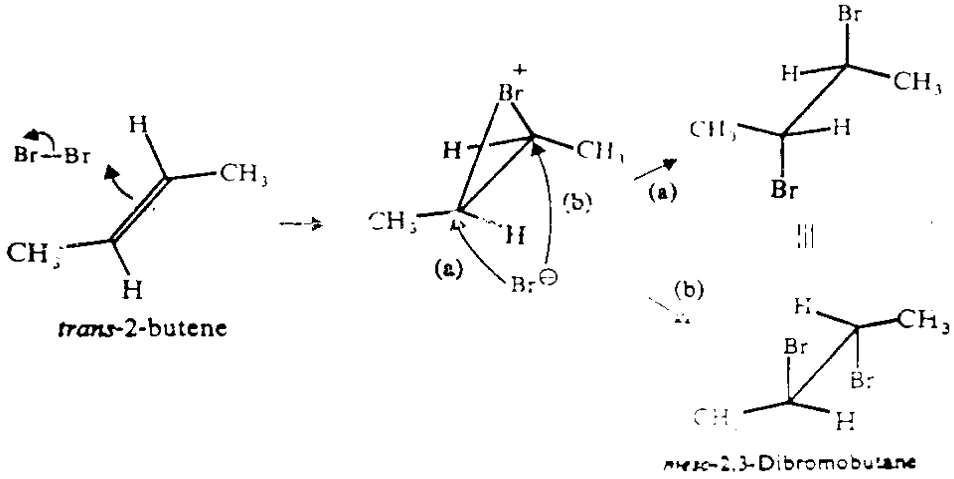
Brominations and chlorinations of alkenes are widely studied reactions. These are electrophilic additions and proceed through a discrete positively charged inter-

mediate which may be a bridged cyclic halonium ion (e.g., bromonium ion 1. Scheme 10.1) or a carbocation (II). This discrete positively charged intermediate is formed after the addition of Br^+ to the alkene.



Scheme 10.1





Scheme 10.2

The *anti*-addition of bromine is observed for alkenes which do not have substituent groups that would strongly stabilize a carbocation intermediate (II, Scheme 10.1).

Thus, addition of bromine to *cis*- and *trans*-2-butene is stereo specific (Scheme 10.2). The first step is the formation of a bridged cation and in the second step the

nucleophile, Br^- adds to the face away from the bridging group to give the overall *anti* addition.

When the alkene is with an aryl group attached to the double bond, the selectivity becomes less and both *anti* and *syn* adducts are formed. This is so, because now the positive charge in the intermediate is delocalized on the aromatic ring. The presence of a phenyl group, therefore, provides sufficient stabilization to allow carbocation formation of the type (II, Scheme 10.1). This situation reduces the effectiveness of bridging and allows rotation to occur. The freely rotating open carbocation would be expected to yield both the *syn* as well as *anti* addition products.

Chlorine being a weaker bridging group (it is less polarizable and more reluctant to become positively charged), it is thus found that although *anti* addition is dominant during bromination *syn* addition is slightly preferred for chlorination.

In various situations bromonium ions have been observed. Under superacid conditions l-bromo-2-fluoropropane gives a cation, which in fact is a bromonium ion related to propene as shown by NMR spectroscopy. The highly hindered alkene adamantylideneadamantane gives a bromonium ion. An X-ray crystal structure determination of its derivative has shown the cyclic nature of the bromonium ion, In this case the bromonium ion is not attacked by Br^-, the attack is completely prevented by the steric hindrance offered to the backside approach of the bromide ion by the extremely bulky cage like structure.

Whether the intermediate is a holomium ion of the type (I Scheme 10.1) or an open carbocation (II. Scheme 10.1), the mechanism is termed Ad_E2 i.e. electrophilic addition, bimolecular. The kinetics of brominations reactions are often complex and a third order reaction (Ad_E3) has been proposed namely, the attack of a halide ion on the initially formed alkene-halogen π-complex. The π-complex may collapse to an ion-pair which then gives the product. The cationic intermediate may have the bromonium ion structure .

Other mechanisms for the reactions which are over all third-order and second-order with respect to bromine have been proposed). One may recall that allylic bromination (instead of addition) of an alkene is a reaction on treatment with NBS in CCI_4 in the presence of peroxides or light. In summary, in a non-polar solvent and with a very low concentration of bromine, the reaction is not addition of bromine but it reacts to substitute an allylic hydrogen atom. NBS provides a very concentration of bromine by reacting with HBr. To understand the reason for allyic substitution at high temperature over addition a consideration of entropy change is important. Addition of bromine combines two molecules into one, thus the reaction has a substantial

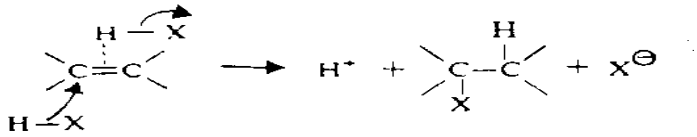
negative entropy change. However, at low temperature the $T\Delta S^*$ term in $\Delta G = T\Delta S^*$ is now not large to offset the favourable ΔH^* term. At higher temperatures, the $T\Delta S^*$ term gains more significance, consequently ΔG^* becomes more positive and the equilibrium becomes more unfavourable. (In the addition of bromine. the bromonium ion formation is a reversible step).

Addition of Hydrogen Halides to Alkenes

The first aspect of mechanism of addition of hydrogen halides to alkenes was observed and the regioselectivity was shown to be controlled by Markovnikov's rule i.e., the relative ability of the carbon atoms to accept positive charge. One has seen that regioselectivity of addition of HBr can be complicated when a free radical chain addition occurs (formation of *anti*-Markovnikov addition product) in competition with the ionic addition.

One may note that unlike, carbocations are not formed in all cases. An unsymmetrical alkene will however, follow the Markovnikov rule during addition of hydrogen halides, since the partial positive charge, which develops will reside primarily at the carbon which is most able to accommodate the electron deficiency i.e., the more substituted of the unsaturated carbons. Hydrogen halides and other acids do not form bridged ions with alkenes.

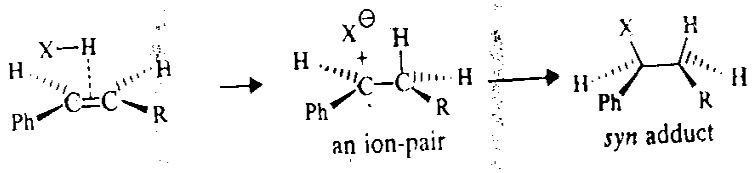
The contribution of a particular structure i.e., a complex may be therefore shown in the mechanistic pathway. Mechanistic details of the addition of hydrogen halides to alkenes are further supported by studening the kinetics and stereochemistry of the reaction. Some of the typical additions of HBr and HCl to alkenes follow a third order rate expression and the stereochemistry of addition to unconjugated alkenes is predominantly *anti*. These observations of rate expression and stereochemistry are consistent with the formalation of a complex (I, Scheme 1 to 3) the *anti* product is being formed by the backside attack on the complex, i.e., the transition state involves proton transfer to the alkene from one hydrogen halide molecule and capture of the halide ion from the second (Scheme 10.3).



Scheme 10.3

However. when the double bond is conjugated with an aryl group the syn adduct predominates. As in the case of bridging, the stabilization of the carbocation intermediate by the aryl group reduces the effectiveness of the complex formation

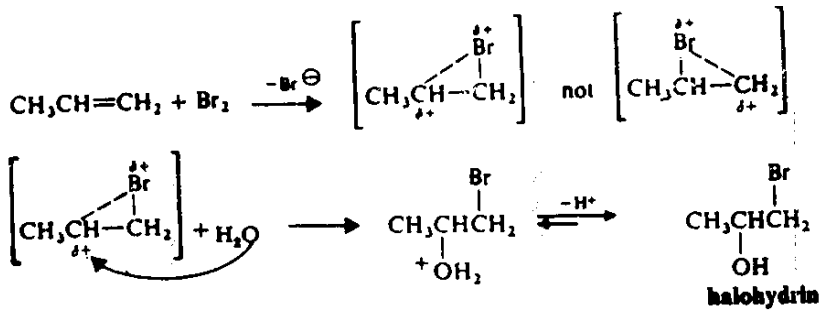
and the ion pair is the key intermediate (Scheme 10.4). If the ion-pair (formed by the initial alkene protonation), collapses to the product faster than the rotation, the result would be *syn* addition. This is so since the proton and the halide ion initially remain on the same side of the molecule:



Scheme 10.4

10.4 Regioselectivity During Electrophilic Additions

1. Strong bridging ensures that the *anti* product will be the major product of additionl(see. Scheme, 10.1). However, as far as regioselectivity is concerned the intermediate ion would be the one which is the more stable of the two possible cations. The addition of bromine to propylene in water follows the course (Scheme 10.5). Thus halonium ion opening is regioselective, the more highly substituted carbon is being attacked preferentially by the incoming nucleophile. In the halonium ion the nucleophile attacks the more highly substituted carbon of the ring, because this carbon is more positively polarized than the other. In summary the bridged halonium ions are subject to stereospecific and regioselective ring opening in a manner which is mechanistically very similar to the nucleophilic opening of the epoxides .



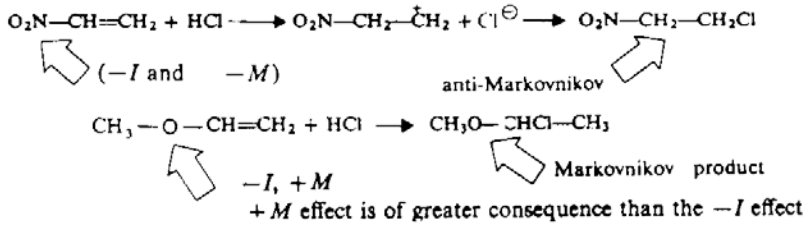
Scheme 10.5

2. The hydrogen in halogen acids HX also adds largely to the less substituted carbon atom of the alkene according to Markovnikov's rule .

3. Alkenes undergo stereoland regioselective addition reactions with reagents of the type A-B, in which A acts as an electrophile and B as nucleophile. In additions to an alkene, the more electronegative moiety acts as-the nucleophile and less electronegative part as the electrophile. Thus, Brll is polarized in the sense $Br^{\delta+}CI^{\delta-}$ and contains an electrophilic bromine.

Similarly polarization of ICI is $I^{\delta+}$, $CI^{\delta-}$ and RSCI is $RS^{\delta+}$'$C1^{\delta-}$ Polarization of A-B is also affected by hybridization and the relative electronegativity of other attached atoms. In the case of cyanogen bromide. polarization is $B^{\delta+}$ $CN^{\delta-}$, even though the difference in electronegativity between bromine (3.0) and carbon (2.6) there is minimized as the carbon is sp-hybridized and the nitrogen (electronegativity 3.0) attached to carbon is also relatively electron attracting.

4. When the alkene contains substituents of electron attracting type i.e of -I and/or -M not only the rate of electrophilic addition is retarded (these groups destabilize carbocations) but the regioselectivity is also reversed (eq I. Scheme 10. 6),



Scheme 10.6

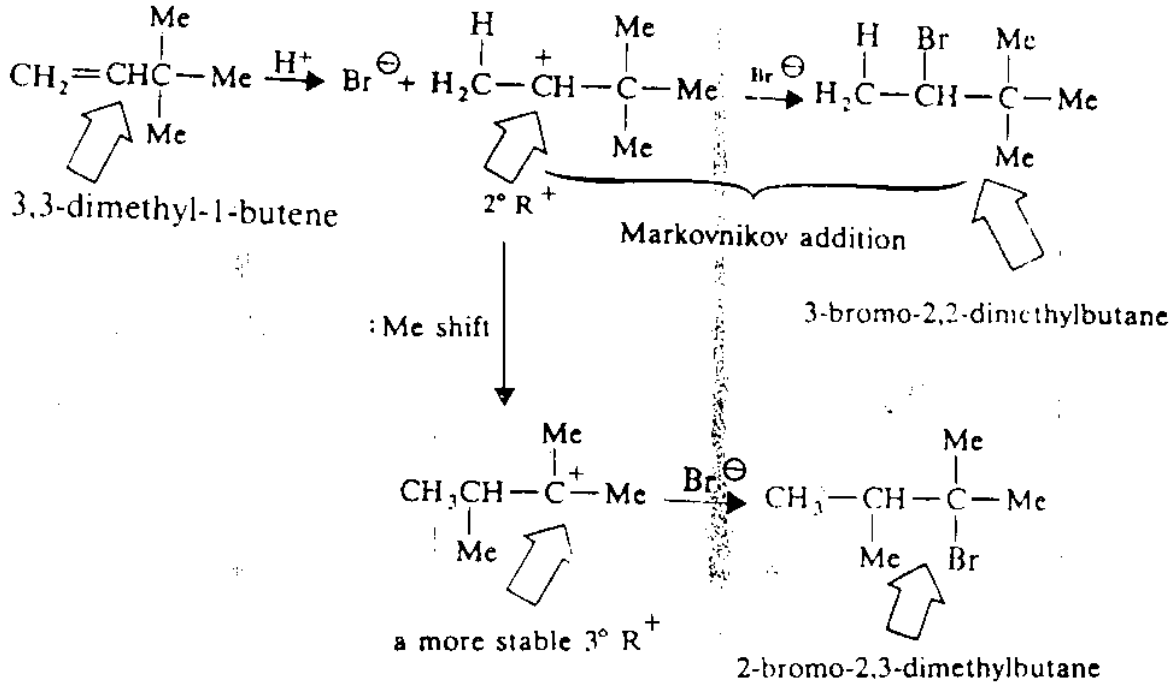
With several other substituents e.g alkoxyl and amino, the +M effect is much larger than -I effect. In these cases e.g., methyl vinyl ether, the reaction is both rapid (compared to unsubstituted alkene) and in accordance with Markovnikovs rule (eq. II. Scheme 10.6).

5. The cation can undergo a molecular rearrangement, particularly when the new corbocation is more stable (Scheme 10.7), Thus when HBr adds to 3, 3-dimethyl-I-butene. in addition to the predicted product of addition 3-bromo-2, 2-dimethylbutane (Markovkinov rule), 2-bromo-2, 3-dimethylbutane is also formed.

6. The proton loss from the intermediate cation can take place in preference to reaction with a nucleophile particularly when the addition is sterically hindered.

7. The enol ethers react with halids in the presence of water differently than in the absence of water (See. Scheme 10.6).

8. The addition of hydrogen halides to dienes can give 1,2- or 1, 4-addition .



Scheme 10.7

9, Benzene and its simple derivatives react with electrophiles via substitution rather than addition, since on addition there would be loss of the aromatic stabilization energy.

Addition of electrophiles to aromatic carbon-carbon double bonds is however observed provided obtained provided the product of addition is itself strongly stabilized.

Electrophilic Additions Involving Metal Ions

Several metal cations are capable of electrophilic attack on alkenes for e.g., $Hg^{+}OAc$ obtained from a solution of mercuric acetate $Hg(OAc)_2$ in water or tetrahydrofuran. The mercuration products are stable and the usual nucleophile is the solvent either water or an alcohol. The term oxymercuration is used to refer to these reactions where water or alcohols act as nucleophiles. The final step of this synthesis is demercuration which is normally achieved by using sodium borohydride. This sequence of reactions is generally both *anti* sterospecific and is also regioselective (Markovnikov hydration of the starting material). This hydration procedure is superior to acid catalyzed hydration of most alkenes. In cases where acid- catalyzed hydration gives poor yields or rearranged products, the oxymercuration-demercuration gives high yields of Markovnikov alcohols. The rearrangement of carbon skeleton rarely occurs during oxymercuration-demercuration. Thus unlike the acid catalysed hydration of 3, 3-dimethyl-1-butene, which is accompanied by

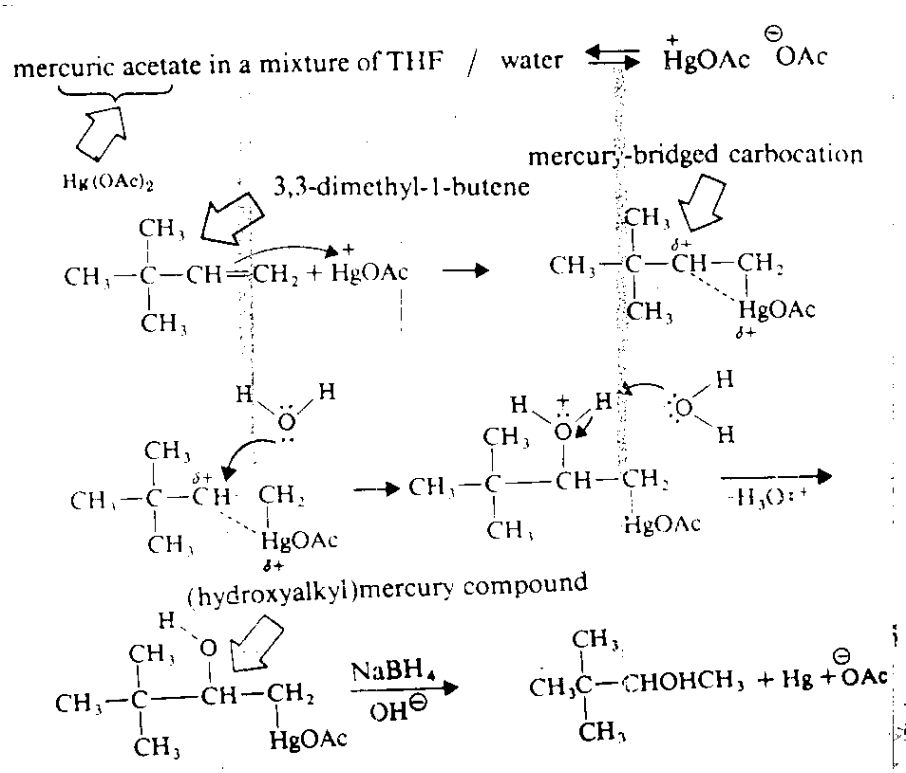
rearrangement (eq. I. Scheme 10.7). oxymercuration-demercuration (eq. II. Scheme 10.8) sequence does not involve any rearrangement.

A mechanism which explains *anti* stereospecifity and precludes rearrangement is depicted (in Scheme 10.8.). The first step is the electrophilic attack of Hg^{+} (OAc) species at the less substituted carbon of the double bond to form a cyclic (bridged) mercurinium ion. Water (nucleophile) attacks this ion at the more substituted carbon atom to give a (hydroxy alkyl) mercury compound. The mercurinium ion in the present reaction is infact called mercury-bridged carbocation. Much of the positive charge here is accommodated by the mercury moiety while only fractional positive charge is present on the more substituted carbon atom. This charge though enough to bring about Markovnikov orientation, is not sufficient (as in the case of fully developed carbocations) to bring about a rearrangement. Similarly addition of bromine to 3, 3-dimethyl-1-butene gives only 1, 2-dibromo-3, 3-dimethylbutane because of the formation of cyclic bromoniurn ion and not 1, 3-dibromo-2, 3-dimiethylbutane as would be expected if an open cation would have been involved.

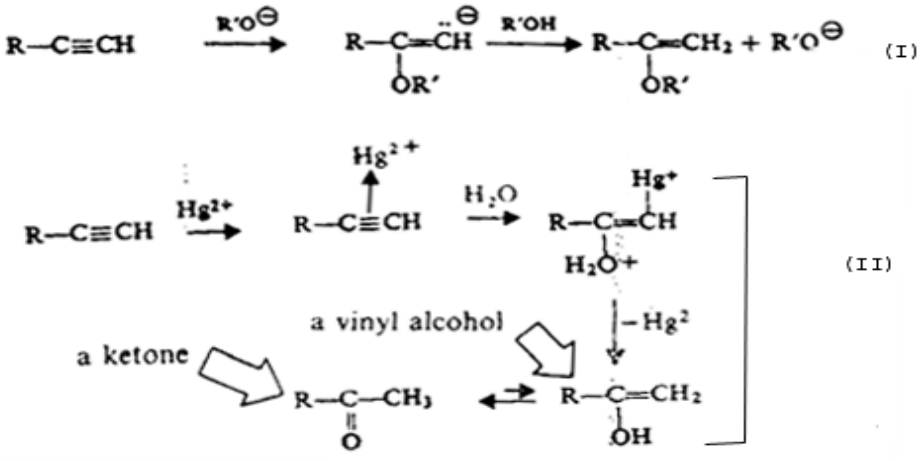
10.5 Nucleophilic Additions of Alkenes and Alkyanes

Nucleophiles do not attack alkenes, however, if the carbon-carbon double bond is conjugated to a group having effect-M type. they readily attack the alkene. Examples of this are seen during Michael additions and epoxidation of α,β-unsaturated aldehydes and ketones with alkaline hydrogen peroxide.

Powerful nucleophiles e.g., an alkoxide ion (in an alcoholic solution) react with alkynes (eq. I, scheme 10.9), however, with less powerful nucleophiles a catalyst like mercury (II) ion is needed. This ion complexes and consequently draws electrons from the triple bond. Thus water adds to an alkyne in the presence of mercury (II) sulfate and dilute sulfuric acid to initially give an enol which tautomerizes to a ketone (eq. II Scheme10.9)



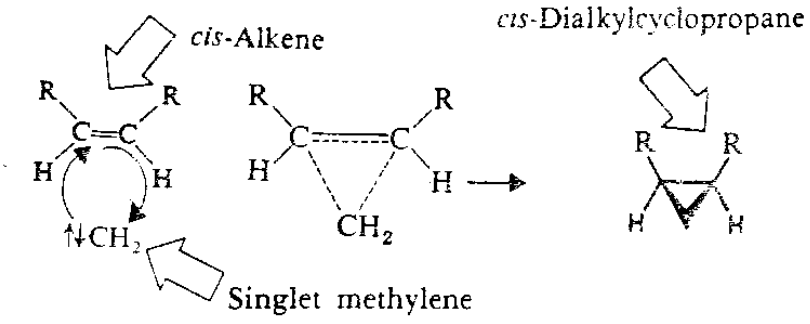
Scheme 10.8



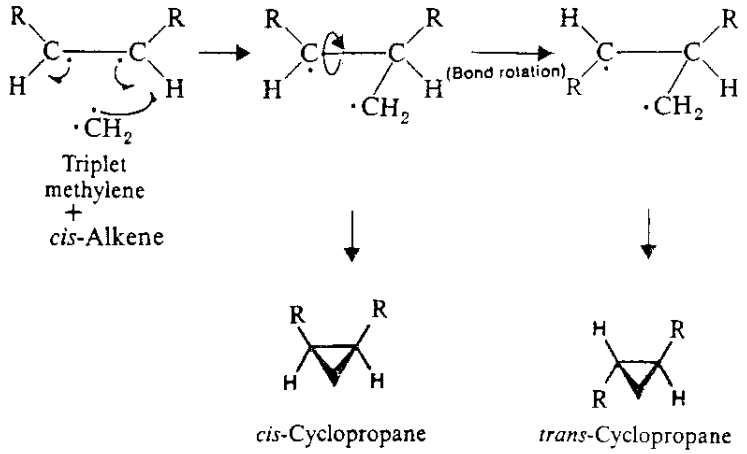
Scheme 10.9

10.6 Free Radical Addition

Carbenes add to alkenes to give cyclopropane derivatives. Singlet methylene, reacts with an alkene stereospecifically, the addition occurs in one step and the sterochemisrry of the alkene is preserved in the product (Scheme 10.10). The electrons in the triplet methylene are not paired and consequently it reacts with an alkene in a stepwise process (Scheme 10.11). The initial reaction is the formation of a biradical, and this has sufficient lifetime to allow rotation. The addition is therefore, non stereospecific.



Scheme 10.10



Scheme 10.11

Carbene addition to a double bond is complicated due to too many side products. The Simmons Smith procedure is superior and leads to same results. The process involves reaction of a compound having double bond with di-iodoemethane (CH_2I_2) and a Zn-Cu couple, the attacking species involved are an organozinc intermediate (CH_2ZnI), a carbene like species called a carbenoid

10.7 Orientation and Reactivity

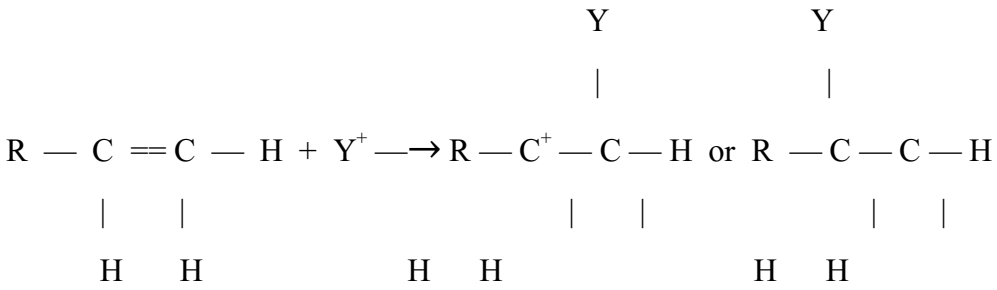
As according to electrophilic aromatic substitution, the electron donating groups increase the reactivity of a double bond toward electrophilic addition and electron withdrawing groups decreases it. The electrophilic addition of a group increases in olefins –

$$CCl_3CH == CH_2 < Cl_2CHCH == CH_2 < ClCH_2 - CH == CH_2 < CH_3CH_2 == CH_2$$

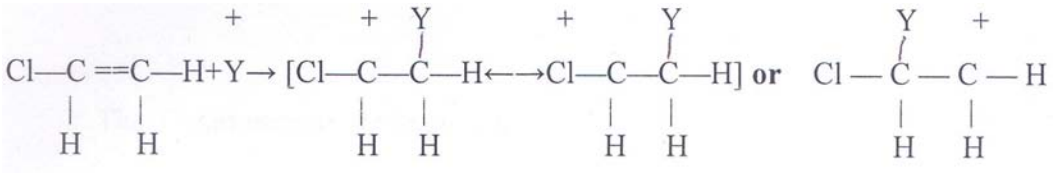
for nucleophilic addition the situation is reversed.

Electron withdrawing groups enhances nuclophilic addition and inhibit electrophilic addition because they lower the electron density of the double bond.

In the Markonikov's rule, the positive portion of the reagent goes to the side of the double or triple bond having more The secondary carbocation are more stable than primary.



More stable



More stable

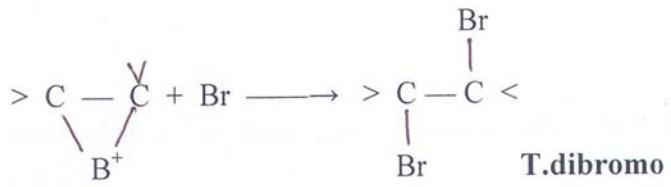
In **Electrophilic Addition**, the reaction of olefins take place in polar medium and are supposed to take stepwise as – Bromine molecule is polarized due to proximity of –

$$< C == C <$$

$$CH_2 == CH_2 \qquad Br - Br \longrightarrow Br^{8+}\ B^{5-}$$

π complex

electrons of π bond of alkane. The polarized Br_2 forms less stable complex with π cloud of the alkene. Nucleophilic attack of bromide ion, alkene gives rise dibromotrans compound.



Free Radical

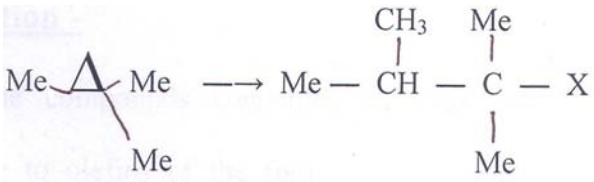
When reactants are in vapour phase in sunlight and in the presence of peroxides and non-polar solvents, the reaction. The free radical reactions are inhibited by presence of oxygen.

A reaction to give two or more structural isomers but actually produces e.g. Nucleophilic NCO usually given only isocyanate RNCO and not isomeric cynates ROCN or RNCO. In Chemo-selectivity – a reducing agent usually depends on what other functional groups are present; each reducing agent reduces certain groups and not others, known as Chemo-selectivity. Ketons can be chemo-selectively reduced in the presence of oldehydes with NaBH in aquous EtOH in presence of ceriumtrichloride at 15º C.

Addition to Cyclopropane Ring

The Cyclopropane undergo addition reaction like double bond containing compounds resulting in the opening of the three membered rings, having electrophilic attack and also follows Markonikove's rule eg. reaction of 1,1,2 trimethyc ayclo propane is as follows propane with HX

$$\Delta + HBr \longrightarrow CH_3CH_2Br$$



10.8 Michael reaction

The compounds containing electron arthdrawing groups add, in the presence of bases to olegfins to form C=C-Z this is called Michael Reaction and it involues conjugate addition many different nucephioles can add to , B unsaturated cabonye compounds . in micalcl reaction the nucleophile taken actually is enolate, and the enolates that work best in Mechacl reaction are those that are hanked by two electron withdrawing group enolates of B dikelonk P-dioctes ketoesox and keto nitribes etc .All therse reactions take place by the same mechanism. A base removes a proton from the carbon of the carbon and. the enolate add to the b carbon of an x b unsaturxted carbonys compoiund and the x carbon obtain a roton pomthe & owent.

10.9 Summary

This unit deseribes triple bond. these mechanisms are related to……alkynes and free radical additions after this orientation and reactivity of reaclants and products are deserbed.

10.10 Review Questions / Comprehensive Questions.

1. What do you understand by addition reaction of carbon-carbon multiple bond? Describe their mechanism.
2. Describe electrophilic addition.
3. Describe nucleophilic addition.
4. Discuss free radiacal addition and Michael addition.
5. Discuss orientation and reactivity of addition reactions.

10.11 References and Suggested readings

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Unit-11: Aromatic Electrophilic Substitution

Structure of Unit:

11.1 Objectives

In this unit the students will be able to understand

- The electrophilic substitution reactions in aromatic systems.
- The synthetic aspects of these reactions
- The mechanism and orientation in these reactions.
- About the *ortho* and *para* directing groups and ipso attack.
- Various organic reactions which involves the electrophilic substitution.

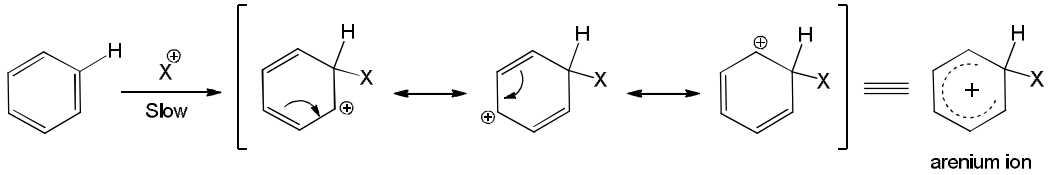
11.2 Introduction

Majority of the substitution reactions of aliphatic carbon are nucleophilic substitution reactions. However, in the aromatic systems the condition is reversed. The aromatic ring acts as a Lewis base due to due to delocatesation of TT-Electrons above and

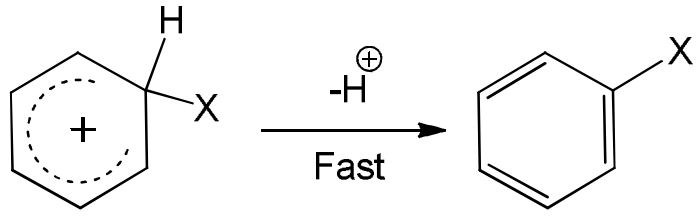
below the plane of ring and tends to give electrophilic substitution reactions. In these reactions a positive ion or the posive end of a dipole is attacked by the aromatic ring. In aromatic electrophilic substitution reactions, the leaving group depart without electrons.

11.3 Arenium ion mechanism

The aromatic electrophilic substitution reactions proceed by only one mechanism that is known as *arenium ion mechanism*. In this mechanism an electrophile must be produced from the reagent (reaction mixture) to initiate the aromatic substitution. The electrophile is attacked by the π-electrons of the aromatic ring in the first step. This reaction leads to formation of a new C-X bond where x is an electrophile and a new sp^3 carbon. This positively charged intermediate called an arenium ion, The positively charged intermediate species (the arenium ion) is stabilized by resonance. In the second step the sp^3 carbon adjacent to a positively charged carbon in arenium ion, losses a proton and regains its aromaticity and leasds to the formation of areomatic substitution product.



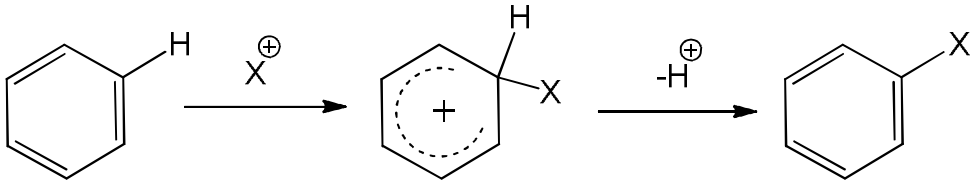
The electrophile is attacked by a pair of electrons from the aromatic sextet to give carbocation intermediate. This intermediate is resonance hybride and this type of ion is called Wheland intermediate, σ-complex or arenium ions. The arenium ion is highly reactive species. The reaction proceeds with loss of the proton and the aromatic sextet is restored in the final product.



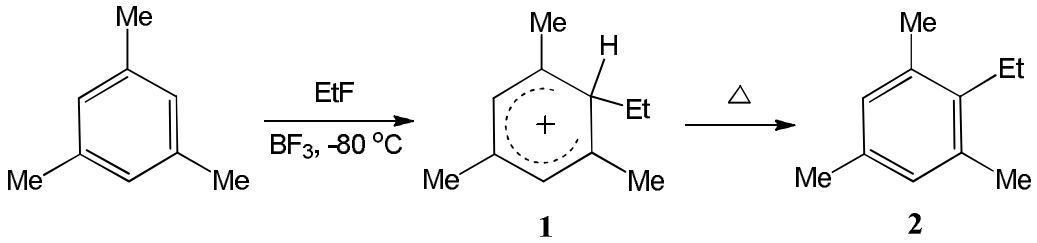
There are mainly two evidences for the arenium ion mechanism.

1. **Isotope effects:** It the proton departs before the arrival of the electrophile (S_E1 mechanism) or if the arrival and departure are simultaneous, there should be a substantial isotope effect (i.e., deuterated substrates should undergo substitution more slowly than non-deuterated compounds) because, in each case, the C-H bond is broken in the rate determining step. But, in the arenium

ion mechanism, the C-H bond is not broken in the rate determining step, so no isotope effect should be observed. As expected in many cases no isotope effect was observed especially in the nitration reactions. It is clear that the aromatic electrophilic substitutions involve two-steps and the loss of hydrogen is not the rate determining step. For the case where hydrogen is the leaving group, the arenium ion mechanism can be summarized as given below:-



2. Isolation of Arenium Ion Intermediates: A very strong evidence for the arenium ion mechanism comes from the isolation of arenium ions in a number of cases. For example, the arenium ion **1** was isolated as a solid (m.p. -15 °C) in the reaction given below and when it was heated, the normal substitution product **2** was obtained.

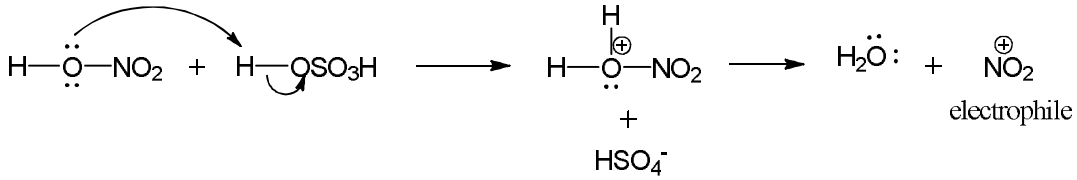


1 **2**

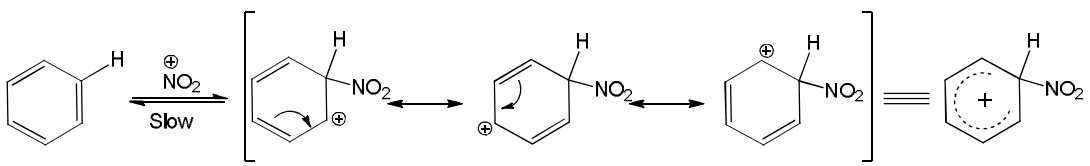
Some typical aromatic electrophilic substitution reactions:

Nitration:

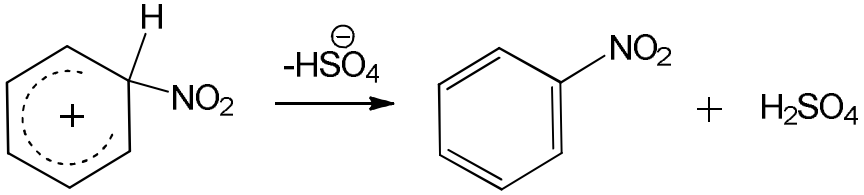
Nitration is carried out with a mixture of concentrated nitric acid and sulfuric acid (called nitrating mixture). Nitration is an especially useful reaction because a nitro group can then be reduced to an NH_2 group.



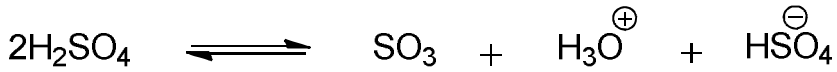
The attack of nitronium ion as an electrophile no the benzene ring takes place to give arenium ion, which is stabilized by the resonance.



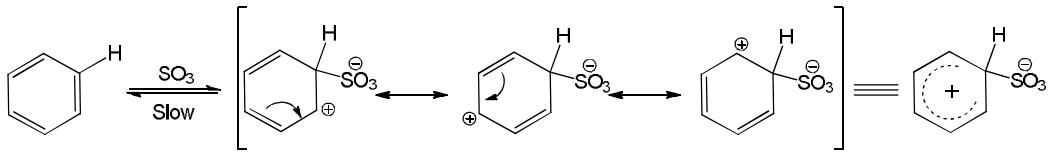
Finally, the proton gets removed to form substituted product.



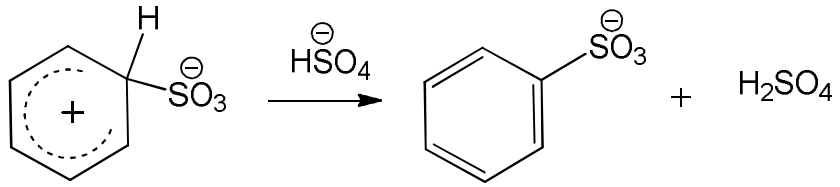
Sulfonation: Sulfonation is carried out with fuming sulfuric acid (i.e. oleum) or concentrated sulfuric acid.



SO_3 (electrophile) attacks on the aromatic ring to give arenium ion, which is stabilized by the resonance.

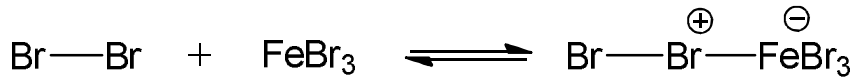


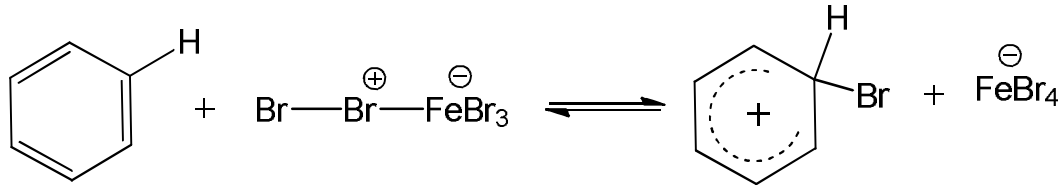
Finally, the proton gets removed to form substituted product.



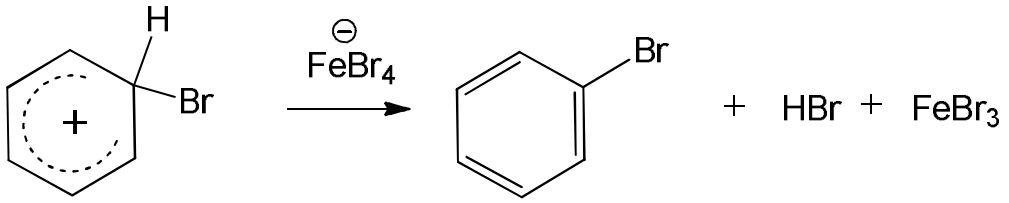
Halogenation:

Aromatic compounds can be halogenated with chlorine and bromine in the presence of a Lewis acid catalysts like $FeCl_3$, $FeBr_3$, $AlCl_3$ etc.



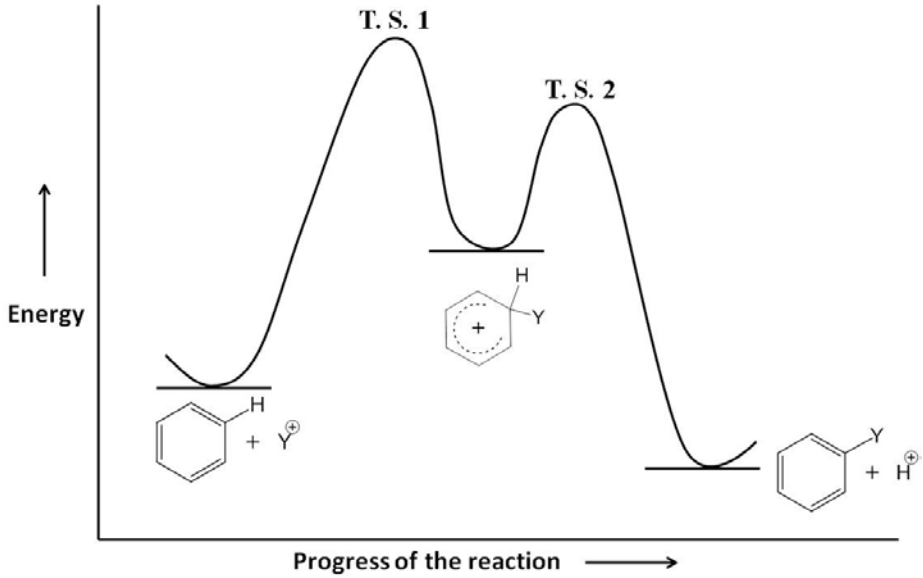


Finally, a proton is removed from the arenium ion by a base to give the halogenated product.



11.4 Energy profile diagram for aromatic electrophilic substitution

A detail picture of arenium ion mechanism is illustrated in its energy profile diagram. The formation of transition state (T.S. 1) is immediately preceding the arenium ion.

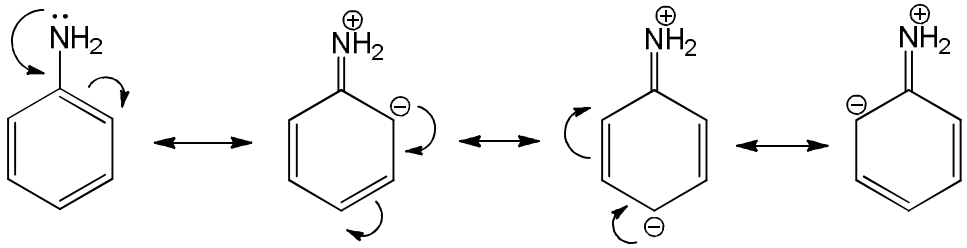


11.5 Orientation and reactivity

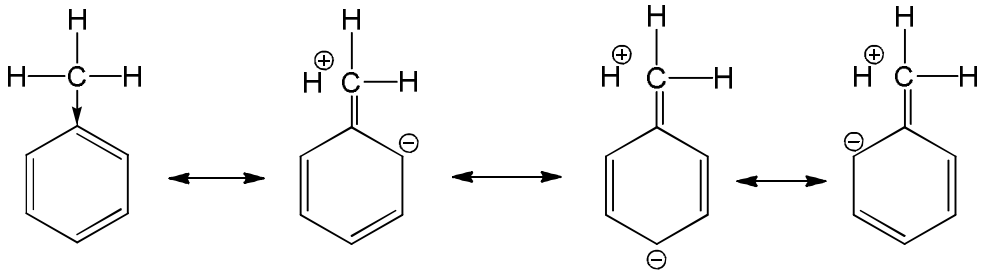
When an electrophilic substitution reaction is performed on a monosubstituted benzene, the position taken up by the incoming group (the orientation) and the rate of reaction are determined by the substituent which is already present in the benzene ring. Groups that increase the reaction rate are called *activating* and those which slows the reaction rate are called as *deactivating*. These substituents can be divided into three categories:

1. ***Ortho*, *para*-directing and activating groups:** If a group of this type is present in the benzene ring then the new group (incoming group) will be attached to the *ortho* and *para* positions. The presence of this type of groups on the benzene ring increases the reactivity towards electrophilic substitution (i.e. through $+I$ or $+R$ or $+M$ effect). The following under groups come in this category are: O^-, NR_2, NHR, NH_2, OH, OR, NHCOR, OCOR, SR, alkyl and aryl.

For example, if NH_2 is present on the benzene ring, the electron density on *ortho* and *para* positions increases through conjugation. Thus, the incoming electrophile will get attached to the *ortho* and *para* positions.

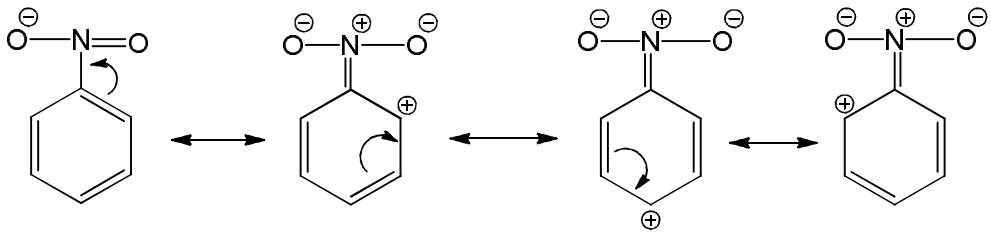


In case of alkyl groups due to hyperconjugation the electron density increases on *ortho* and *para* positions.

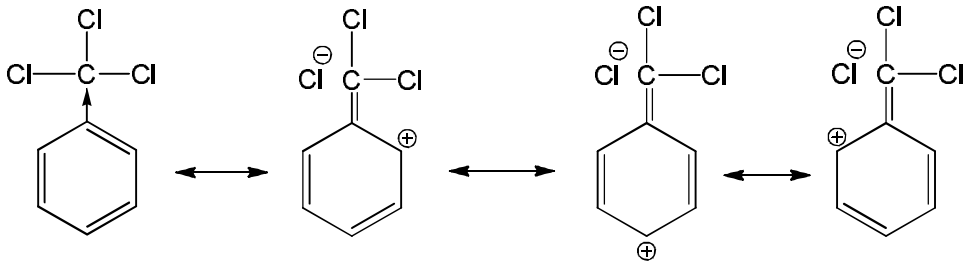


2. ***Meta* directing and deactivating groups:** The groups that have a positive charge on the atom connected to the ring or lack of an unshared pair of electrons on the ring connected atom, are *meta* directing groups (i.e. *–I* or *-R* or *-M* effect). The groups falling under in this category are: NR_3^+, NO_2, CF_3, CN, SO_3H, CHO, COR, COOH, COOR, $CONH_2$, CCl_3, NH_3^+.

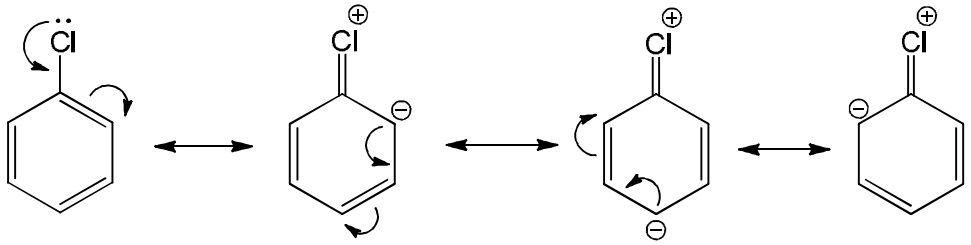
   For example, if NO_2 is present on the benzene ring, it attracts electrons from *ortho* and *para* positions through conjugation. Thus, electron density on *meta* position is relatively high. Therefore, the incoming nucleophile is attached to *meta* position.



In case of CCl_3 group, electron attraction from the *ortho* and *para* position is through hyperconjugation effect as well as *-I* effect.

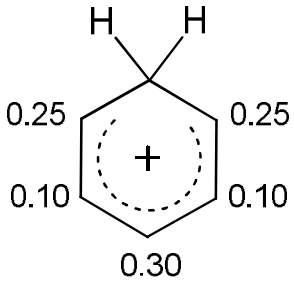


3. ***Ortho*, *para* directing and deactivating groups:** Halogens are *ortho* and *para* directing, but they decrease the reactivity of the benzene ring for electrophilic substitution, thus, they are deactivating groups. The reason for this is due to two opposite effects +*R* (or +*M*) and –*I* effect.



11.6 The *ortho*/*para* ratio

When an *ortho-para*-directing group is present on a benzene ring, mainly *ortho* and *para* substituted products are formed. But, it is difficult to predict that how much of the product will be the *ortho* isomer and how much of the product will be *para* isomer. The *ortho/para* ratio depends greatly on the reaction conditions. Numerous factors such as steric hindrance, solvent effect, polar effect of the substituent, temperature, etc. affect the *ortho/para* ratio in the products. For example, chlorination of toluene results an *ortho*/*para* ratio from 62:38 to 34:66. On the statistical basis there would be 67% *ortho* and 33% *para*. Since there are two *ortho* positions and only one *para* position, it is expected that the *ortho* and *para* ratio should be 2:1. But, in actual practice this ratio is less. The phenonium ion which is generated by the protonation of benzene, has the approximate charge distribution as shown below:

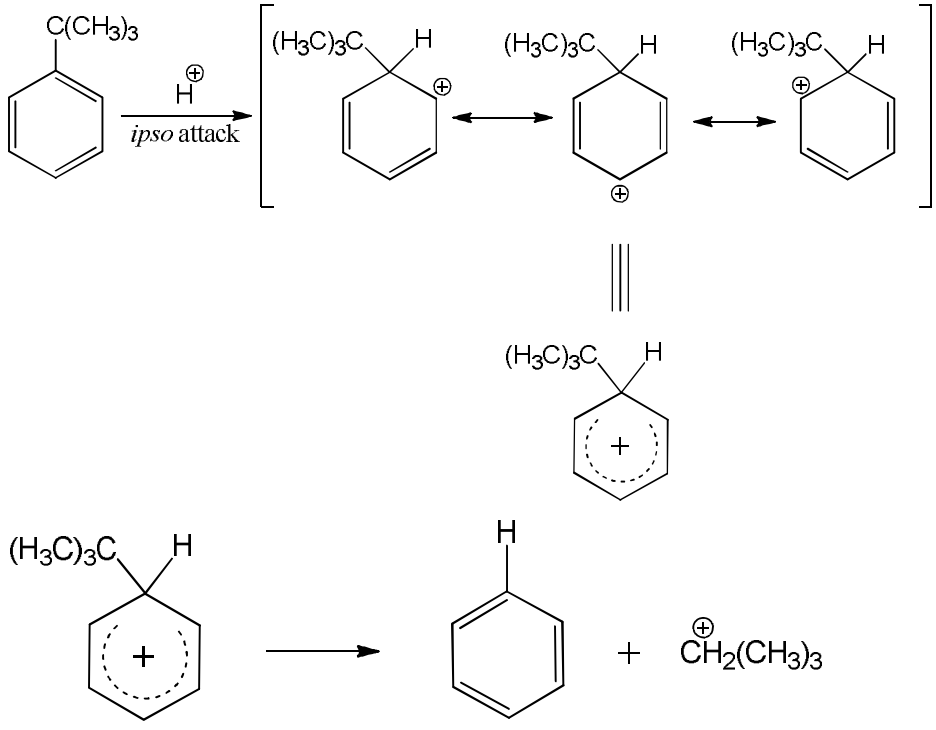


In this model of arenium ion, in aromatic substitution, *para* substituent should have a greater stabilizing effect on the adjacent carbon as compare to *ortho* substituent. If other effects are absent than >33% *para* and <67% *ortho* would be obtain.

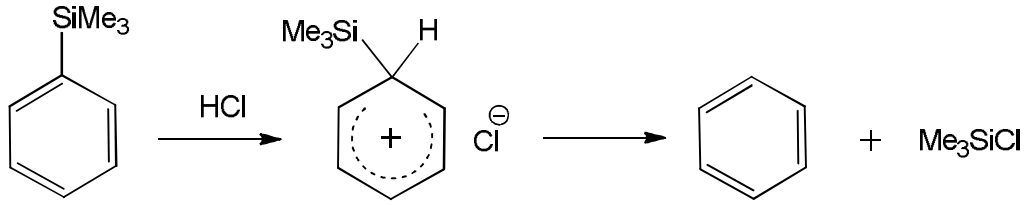
Another important factor is the steric effect, if the group present on the benzene ring is large or the group on the electrophile is large, the proportion of *para* isomer increases. For example, on the nitration of toluene and *tert*-butylbenzene under the same condition, toluene gave 58% of the *ortho* compound and 37% of the *para* compound, while more bulky *tert*-butylbenzene gave 16% of the *ortho* compound and 73% of the *para* compound.

11.7 *Ipso* attack

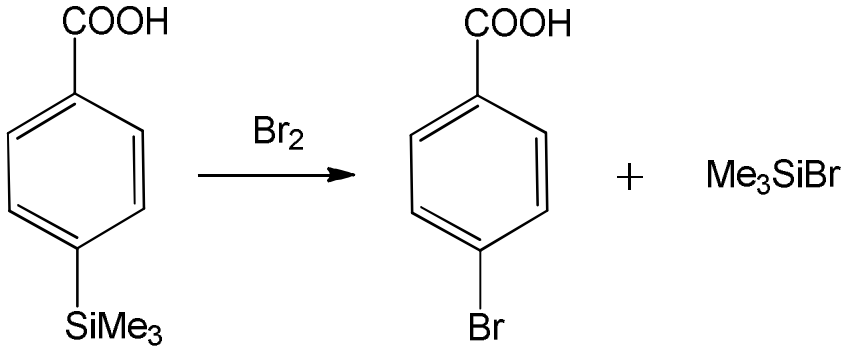
The position bearing the non-hydrogen substituent in an aromatic ring is called *ipso* position and the attack on this position is called *ipso* attack. Replacement of the substituent which was already present, is called *ipso* substitution.



Protodesilylation:

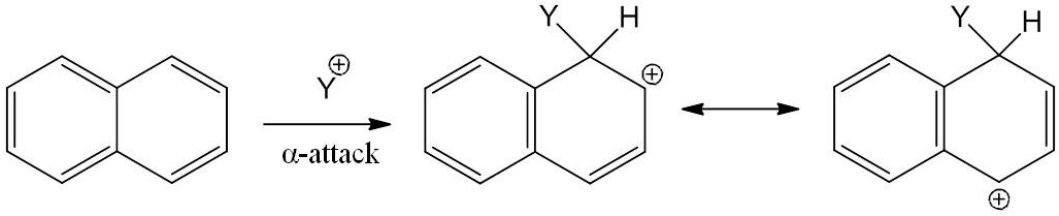


Bromodesilylation:

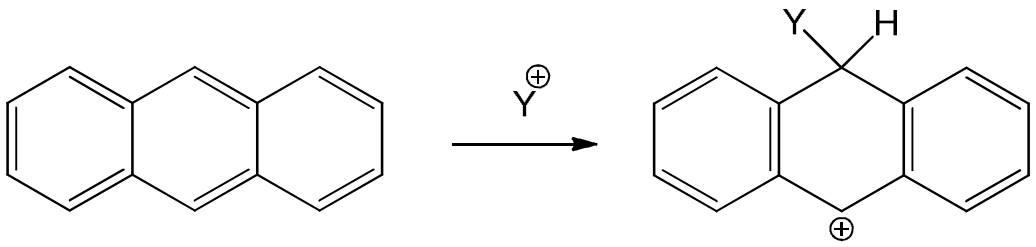


11.8 Orientation in other ring systems

In fused ring systems (such as naphthalene, anthracene etc.), the positions are not equal and there is typically a preferred orientation, even in the unsubstituted hydrocarbons. For example, the α-position is the preferred site of attachment in the naphthalene. Because it is possible to draw more canonical forms for the arenium ion formed after the attack of electrophile. Due to the more extensive delocalization of charges in the corresponding arenium ions, naphthalene is more reactive than benzene and substitution is faster at both positions. Similarly, due to the delocalization of charges anthracene and other fused polycyclic aromatic hydrocarbons are also more reactive than benzene in electrophilic substitutions.



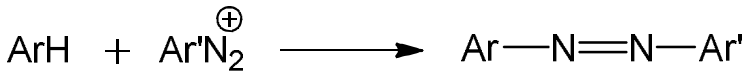
The preferred site for electrophilic attack in anthracene is on the center ring, because the intermediate carbocation generated from the attack on the center ring has two benzene rings intact.

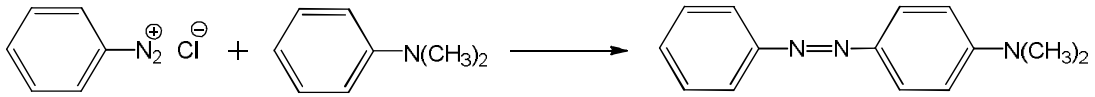


The orientation in the polycyclic aromatic hydrocarbons can also be predicted and explained on the basis of the stability of the carbocations (arenium ions) generated by the attack of an electrophile.

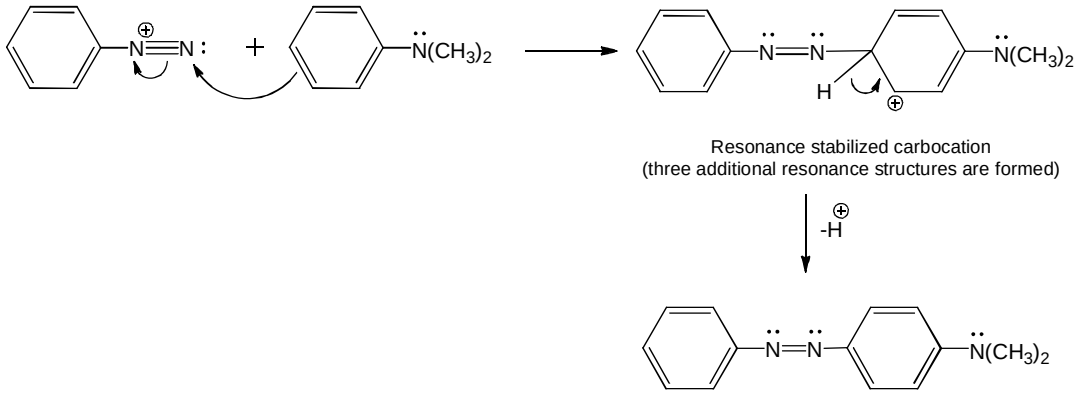
11.9 Diazonium coupling

When a diazonium salt is treated with an aromatic compound that containing a strong electron-donor group, the two rings join together to form an azo compound, a compound with a nitrogen–nitrogen double bond. This reaction is known as diazonium coupling or coupling reaction.



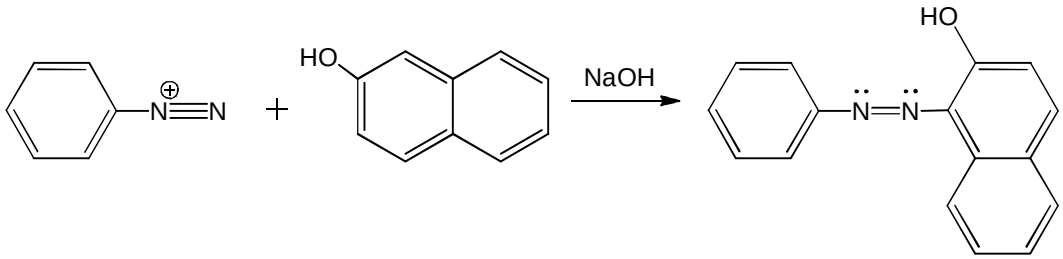


This reaction is an example of electrophilic aromatic substitution, with the diazonium salt acting as the electrophile. Like all electrophilic substitutions, the mechanism has two steps: addition of the electrophile (the diazonium ion) to form a resonance-stabilized carbocation, followed by deprotonation.



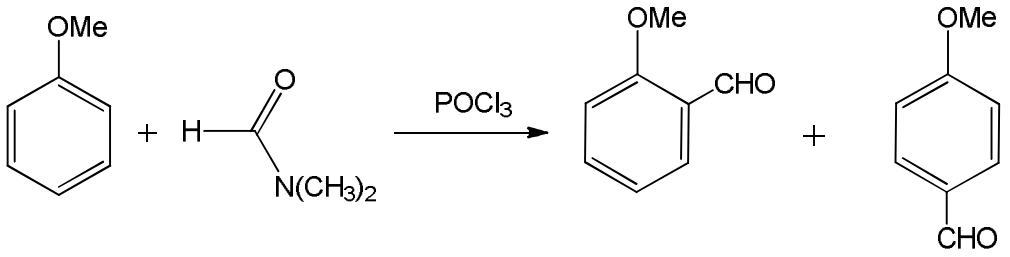
Because a diazonium salt is weakly electrophilic, the reaction occurs only when the benzene ring has a strong electron-donor group such as: NH_2, NHR, NR_2 or OH. Although these groups activate both the *ortho* and *para* positions, *para* substitution occurs unless the *para* position already has another substituent present.

Diazonium salts couples with 2-naphthol in alkaline solution to give 1-phenylazo-2-naphthol. This reaction is applied to test primary amines.

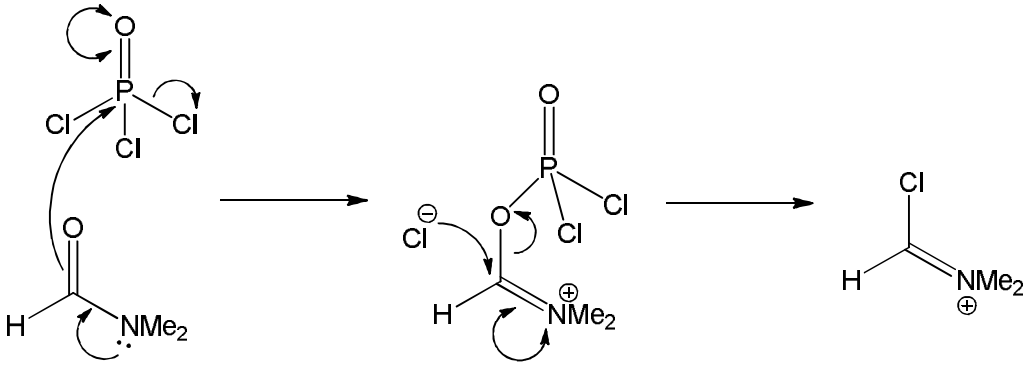


11.10 Vilsmeier reaction

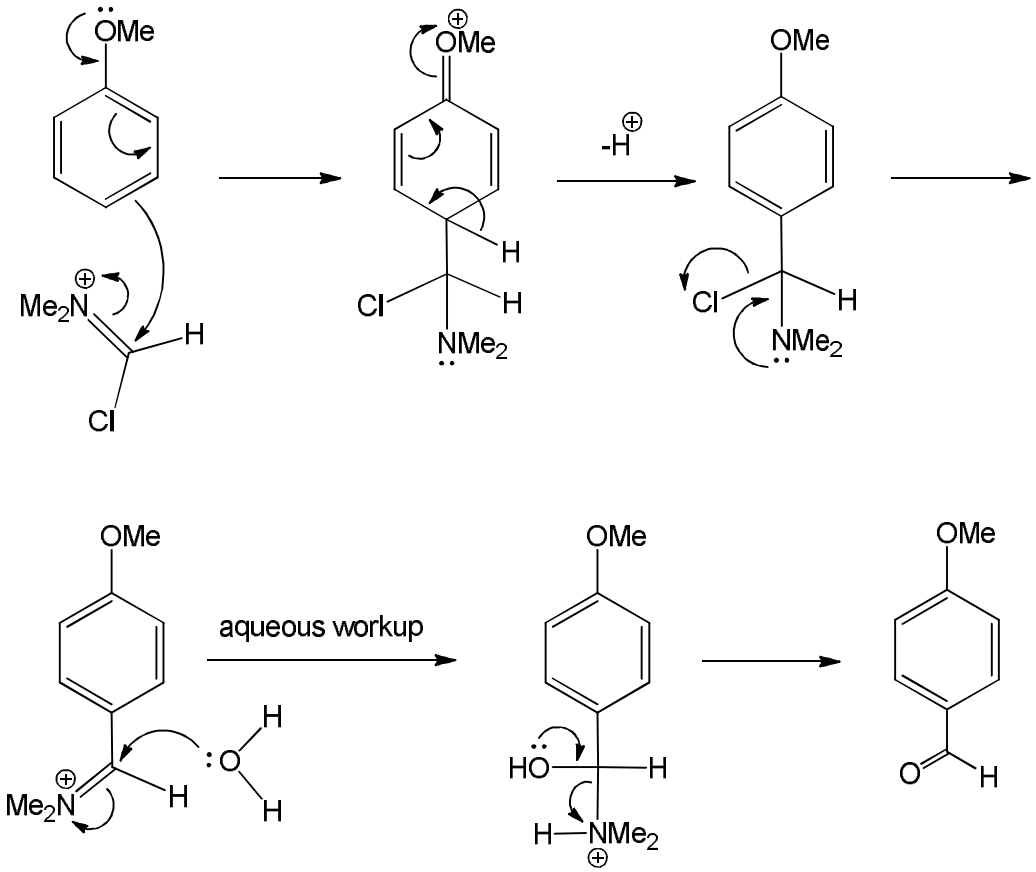
The reaction of electron-rich aromatic compounds with N,N-dimethylformamide and phosphorus oxychloride to yield an aromatic aldehydes is called the *Vilsmeier reaction*. or sometimes the *Vilsmeier–Haack reaction*.



In the first step, the reactive formylating agent is formed from, N,N-dimethyl formamide (DMF) and phosphorus oxychloride. The formylating agent is likely to be a chloromethyl iminium salt also called the Vilsmeier reagent. This iminium cation acts as an electrophile in an electrophilic substitution reaction with the aromatic substrate.



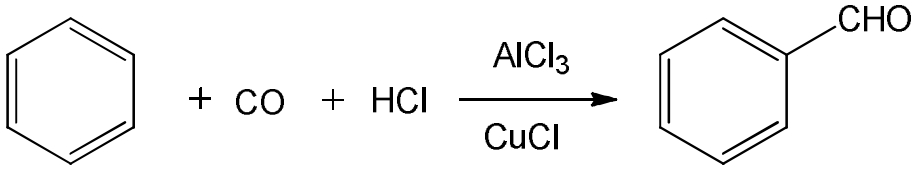
The iminium cation reacts with the electron rich aromatic compound to form more stable iminium salt. This iminium salt is hydrolysed to give aromatic aldehydes as the final reaction product.



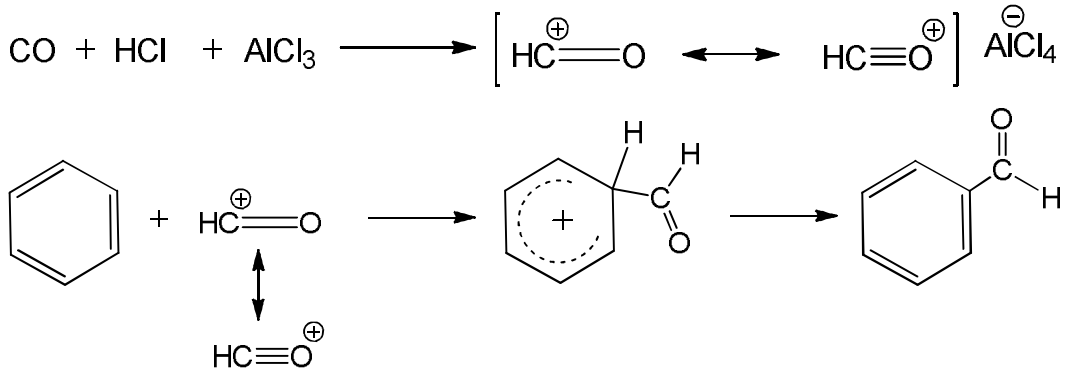
The reaction can be carried out with disubstitued amines, other than formamide to give ketones. Other reagents such as $SOCl_2$ and $COCl_2$ have also been used instead of $POCl_3$.

11.11 Gattermann-Koch reaction

The introduction of a formyl group into electron rich aromatic rings by applying CO and HCl in the presence of a Lewis acid catalyst (AlX_3, FeX_3, where X = Cl, Br, I) to synthesize aromatic aldehydes is known as the Gattermann-Koch reaction. The reaction is usually limited to benzene and alkylbenzenes. Deactivated aromatic compounds (having *meta*-directing substituents) cannot be formylated with this. The formylation takes place mostly at the *para* position. A carrier/activator (such as $CuCl_2$, $TiCl_4$ or $NiCl_2$) for the catalyst is necessary at atmospheric pressure. However, no activator is needed at high pressure.



The mechanisms of the Gattermann and Gattermann-Koch formylation belong to the electrophilic aromatic substitution but are not known in detail. When carbon monoxide is used, the electrophilic species is believed to be the formyl cation, which is attacked by the aromatic ring to form a complex. This complex is then converted to the aromatic aldehyde by losing a proton.



11.12 Summary

Aromatic electrophilic substitution reactions proceed by arenium ion mechanism. Benzene's aromaticity causes it to undergo **electrophilic aromatic substitution reactions**. The most common electrophilic aromatic substitution reactions are halogenation, nitration, sulfonation, and Friedel–Crafts acylation and alkylation. The rate of electrophilic aromatic substitution is increased by electron-donating substituents and decreased by electron-withdrawing substituents. Substituents can donate or withdraw electrons inductively or by resonance.

11.13 Glossary

- In an **electrophilic aromatic substitution reaction**, an electrophile substitutes for a hydrogen of an aromatic compound.
- All the electrophilic aromatic substitution reactions take place by the two-step mechanism.
- In the first step, aromatic compound reacts with an electrophile forming a carbocation intermediate.(arenium ion)
- In the second step, loss of a proton takes place to give substituted product.
- The proton is always removed from the carbon that has formed the new bond with the electrophile.
- Nitration, Sulfonation and halogenation of benzene belong to aromatic electrophilic substitution, Which proceds via arenium ion mechanism.

- The orientation in electrophilic substitution reactions of monosubstituted benzene is determined by the group which is already present on the benzene ring.

4. *Ortho*, *para*-directing and activating groups are: O^-, NR_2, NHR, NH_2, OH, OR, NHCOR, OCOR, SR, alkyl and aryl.

- *Meta*-directing and deactivating groups are: NR_3^+, NO_2, CF_3, CN, SO_3H, CHO, COR, COOH, COOR, $CONH_2$, CCl_3, NH_3^+.
- Halogens are *ortho*, *para* directing and deactivating groups.
- In case of naphthalene electrophilic substitution reaction take place at α-position.
- In case of anthracene electrophilic substitution reaction take place on the center ring.
- The position bearing the non-hydrogen substituent in an aromatic ring is called *ipso* position and the attack on this position is called *ipso* attack.

11.14 Review Questions /Comprehensive Questions

1. What do you understand by aromatic electrophilic substitution? Discuss the arenium ion mechanism.
2. Explain with mechanism the Nitration, Sulfonation and Halogenation reactions of aromatic ring.
3. What is ipso substitution? Explain with example.
4. Discuss the orientation and reactivity in aromatic electrophilic substitution.
5. Write a note on Vilsmeier r formylation reaction.
6. Discuss diazonium coupling and Gattermann-Koch reaction.
7. Explain the orientation of naphthalene and anthracene in aromatic electrophilic substitution reactions.

11.15 References and suggested readings

1. March's Advanced Organic Chemistry (7^{th} ed.)- M. Smith and J. March (John Wiley & Sons, Inc., Hoboken, New Jersey) 2007.
2. A Guidebook to Mechanism in Organic Chemistry (6the ed.)- Peter Sykes (Longman Technical & Scientific) 1985.
3. Organic Reaction Mechanisms- V. K. Ahluwalia and R. K. *Para*shar (Narosa Publishing House) 2002.

4. Organic Chemistry- J. Clayden, Greeves, S. Warren and others (Oxford University Press) 2001.
5. Advanced Organic Chemistry- J. Singh and L. D. S. Yadav (Pragati Prakashan) 2005.

Unit-12: Aromatic Nucleophilic Substitution

Structure of Unit:

12.1 Objectives

The objective of this unit is to provide knowledge of aromatic nucleophilic substitution reactions to the students. In this unit the students will be able understand the various mechanisms such as S_NAr mechanism, S_N1 mechanism and $S_{RN}1$ mechanisms involved in the aromatic nucleophilic substitution reactions. This unit also explains the effect of substrate structure, leaving goup and attacking nucleophile on the reactivity of these reactions.

12.2 Introduction

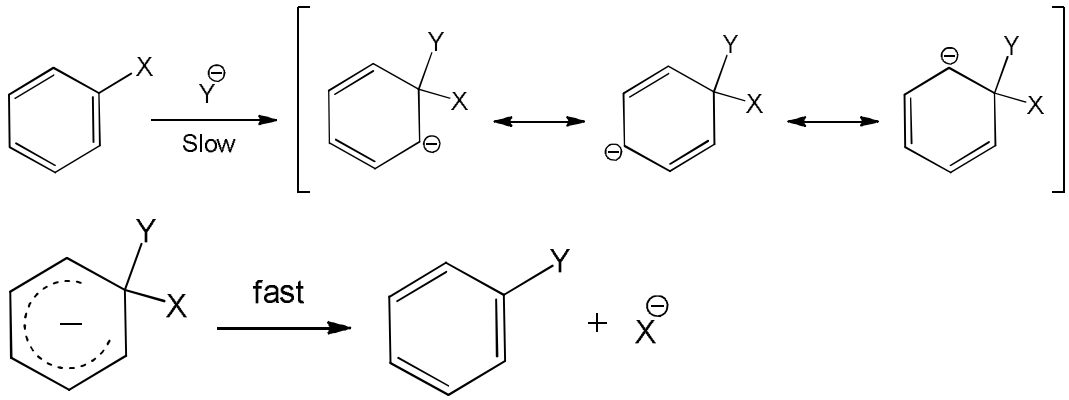
In aromatic nucleophilic substitution reactions, a hydrogen or a substituent on an aromatic ring is replaced by a nucleophile. The reaction of a nucleophile with a benzene ring is very rare. Aromatic nucleophilic substitution may take place in the presence of a catalyst or under drastic conditions, i.e. under high pressure or high temperature or both. Moreover, the reaction can occur when strongly electron-withdrawing substituents (e.g. NO_2) are at the *ortho*/*para* position of an aryl halide. The electron-withdrawing groups decreases the electron density (by *–R* or *–I* effect) on the aromatic ring and activate it for nucleophilic substitution reactions.

There are four types of mechanisms shwon for the promatic nucleophilic substitution reactions:

1. S_NAr mechanism
2. S_N1 mechanism
3. Benzyne mechanism
4. $S_{RN}1$ mechanism

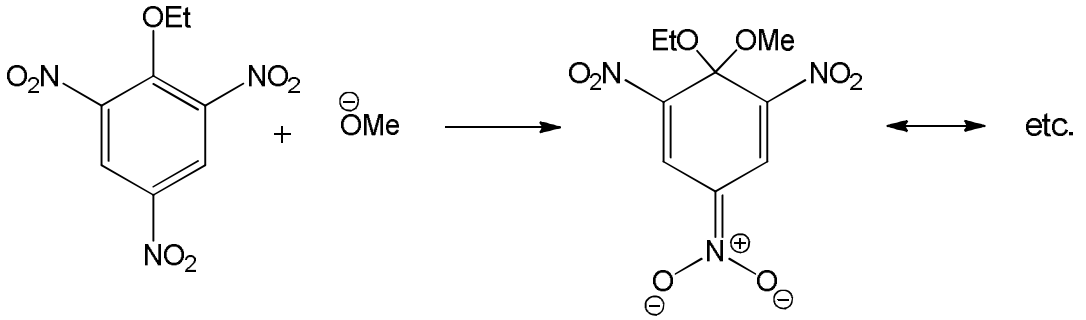
12.3 S_NAr mechanism

The most important mechanism for aromatic nucleophilic substitution consists of two steps. The first step involves the attack of the nucleophilic species at the ipso carbon of the aromatic ring to generate a carbanion, which is stabilized by resonance. In the second step removal of the leaving group takes place to regenerate the aromatic ring.



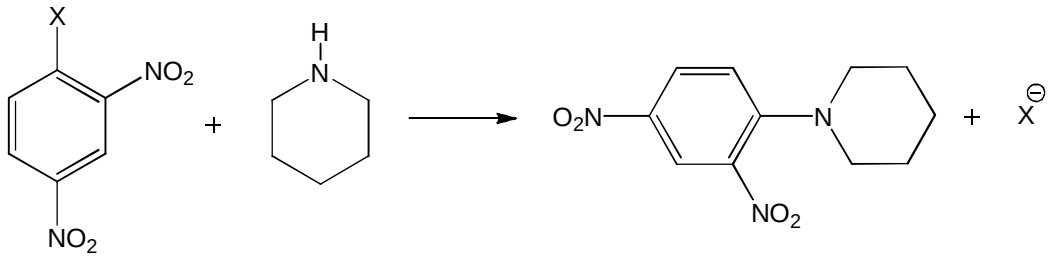
Evidences in support of the S_NAr mechanism:

1. The most convincing evidence for this mechanism is the isolation of the intermediate species. In the reaction between Ethyl picrate and methoxide ion the intermediate (called Meisenheimer or Meisenheimer–Jackson salts) have been isolated.



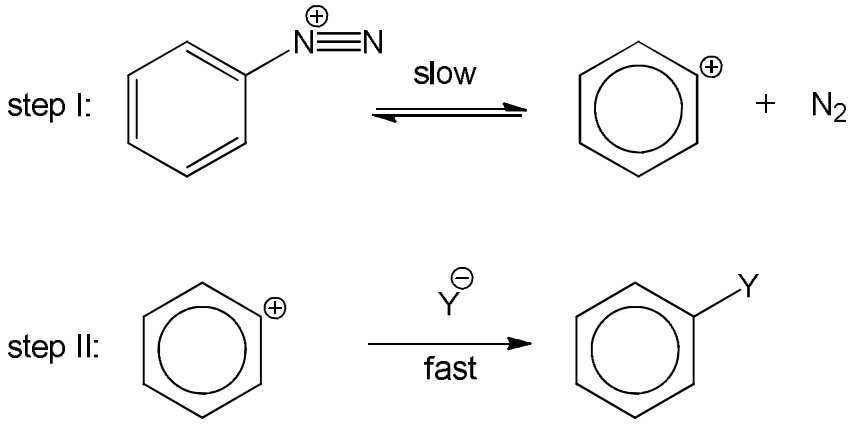
2. In the reaction of dinitro compound with piperidine, when X was Cl, Br, I, SOPh, SO_2Ph or *para*-nitrophenoxy, the rates differed only by a factor of about 5. This would not be expected in a reaction in which the Ar–X bond is broken in the rate-determining step. We do not expect the rates to be identical,

because the nature of X, affects the rate at which nucleophile Y attacks. When X = F, the relative rate was 3300 (competed with 1, when X = I). The fluoro is the best leaving group among the halogens in most aromatic nucleophilic substitutions. It is good evidence that is mechanism is different from the S_N1 and S_N2 mechanisms, because in S_N1 and S_N2 mechanisms fluoro is the poorest leaving group.



12.4 S_N1 mechanism

S_N1 mechanism for aryl halides and sulfonates is very rare. This mechanism has only been observed for the aryl triflates in which both *ortho* positions contain bulky groups such as *tert*-butyl or SiR_3. In the reactions with aromatic diazonium salts the mechanism is very important.



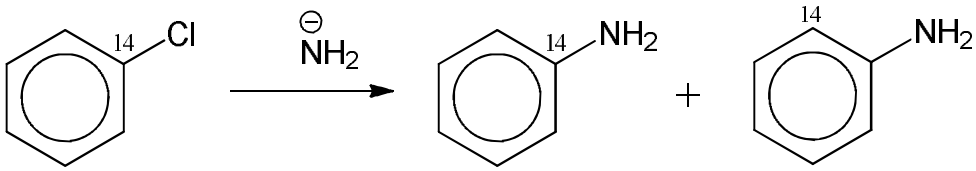
Evidences in support of the S_N1 mechanism:

1. The reaction rate is first order in diazonium salt and independent of the concentration of nucleophile (Y).
2. When high concentrations of halide salts are added, the product is an aryl halide but the rate is independent of the concentration of the added salts.
3. The effects of ring substituents on the rate are consistent with a unimolecular rate-determining cleavage.

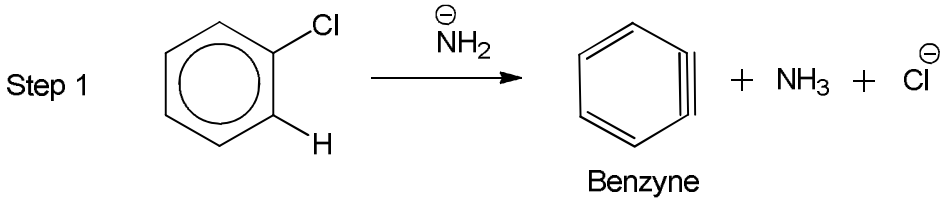
4. The first step is reversible cleavage. It was observed that when $Ar^{15}N{\equiv}N$ was the reaction species, recovered starting material contained not only $Ar^{15}N{\equiv}N$, but also $ArN{\equiv}N$. This is possible only if the nitrogen breaks away from the ring and then returns.

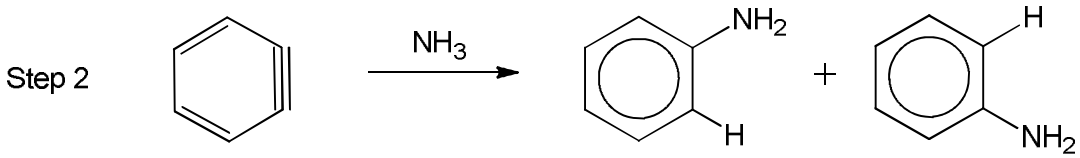
12.5 Benzyne mechanism

Aryl holides having no activating groups show some aromatic nucleophi9dic substitutions in the presence of a very strong base like KNH_2 or $NaNH_2$ in liquid ammonia.



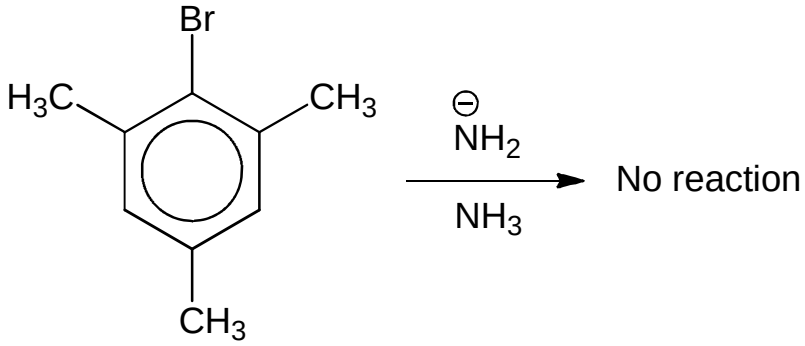
The most interesting feature of these reactions is that the incoming group does not always take the position vacated by the leaving group. This reaction involves the generation of a symmetrical intermediate benzyne and the mechanism is called benzyne mechanism.



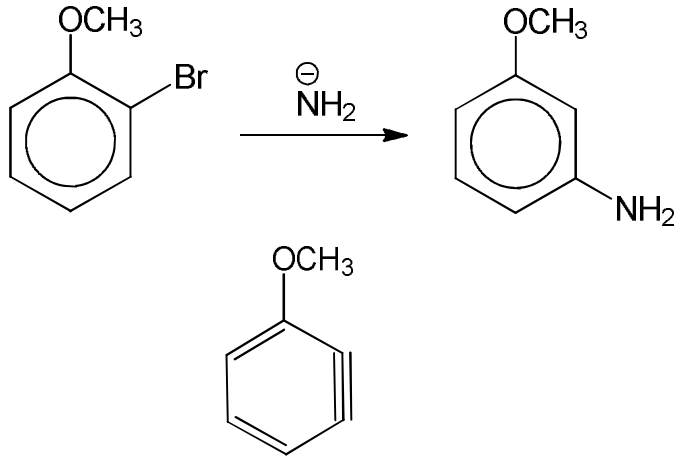


Evidences in support of the benzyne mechanism:

1. Aryl halides containing no hydrogen at *ortho* position to the halogen do not react in the similar conditions.



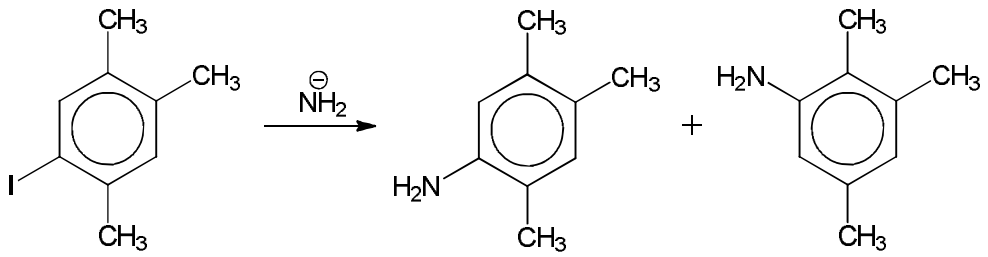
2. The reaction of 14_C-chlorobenzene under similar conditions produce almost equal amount of 14_C-1-aniline and 14C-2-aniline. The formation of these two products is possible only if the reaction is proceeding *via* a symmetrical intermediate.
3. The aromatic nucleophilic substitution reactions occasionally resulting in substitution at a different position is called *cine substitution*. In the conversion of *ortho*-bromoanisole to *meta*-aminoanisole, only *meta* isomer is formed. Because the benzyne intermediate formed is not symmetrical and the methoxy group directs the incoming group to *meta* position.



Unsymmetrical benzyne intermediate

12.6 The $S_{RN}1$ mechanism

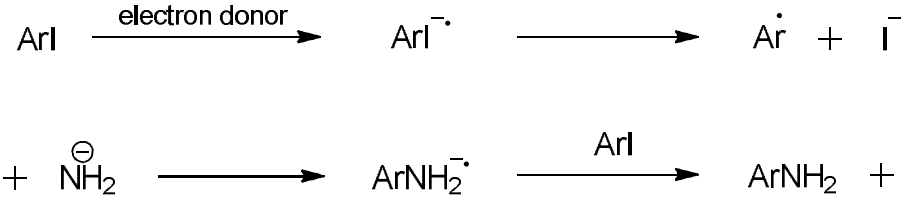
5-iodo-1,2,4-trimethylbenzene **1** on treatment with KNH_2 in NH_3 produces **2** and **3** in the ratio 0.63:1. The presence of an unactivated substrate, a strong base, and the occurrence of *cine substitution* along with normal substitutions, strongly indicates that the reaction proceeds *via* a benzyne mechanism.



1 **2** **3**

If the benzyne mechanism is operating then 6-iodo isomer of **1** should also give the same ratio, but in this case ratios is 5.9:1 (the chloro and bromo analogs give the same ratio 1.46:1 showing that benzyne mechanism may be taking place).

To explain the result obtained by the reaction of 5. iodo isomer it has been proposed that besides the benzyne mechanism, the following free radical mechanism is also operating here:



This is called SR_n^1 Mechanicsm The last step of the mechanism produces ArI^- radical ions, so the process is a chain mechanism. An electron donor is required to initiate the reaction. In the case above it was solvated electrons obtains from KNH_2 in NH_3.

Evidences in support of the $S_{RN}1$ mechanism:

1. The addition of potassium *meta*l (a good producer of solvated electrons in ammonia) completely suppressed the cine substitution.
2. The addition of radical scavengers (which would suppress a free radical mechanism) led to 9:10 ratios much closer to 1.46:1.
3. Some 1,2,4-trimethylbenzene was found among the products. This could easily be formed by abstraction of H by $Ar^{\bullet}$ from the solvent NH_3.

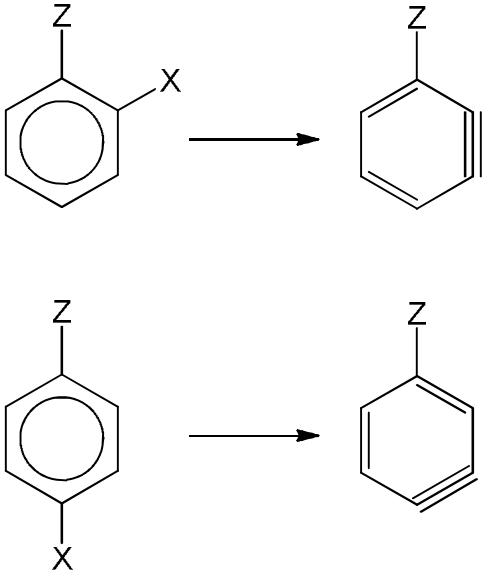
12.7 Effect of substrate structure, Leaving group and attacking nucleophile on the reactivity

The effect of substrate structure:

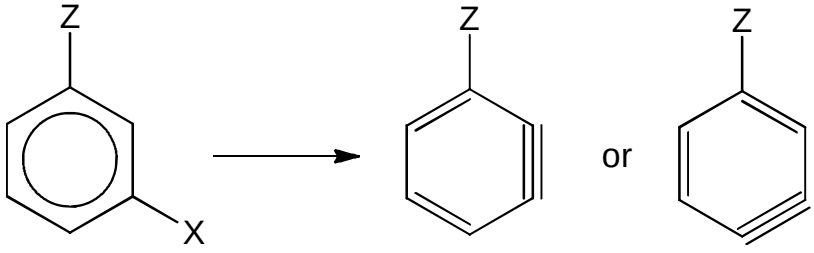
The substrate structure has an important effect on the reactivity because in a typical substitution there are four or five hydrogens that could serve as leaving groups.

Aeromatic nucleophilic substitutions involving S_NAr mechanism are accelerated by electron-withdrawing groups, especially in positions *ortho* and *para* to the leaving group and hindered by electron-attracting groups. Nitrogen atoms are also strongly activating (especially to the α and γ positions) and are even more so when quaternized. A detail table containing a list of groups arranged in order of activating or deactivating ability can be found in the *March's Advanced Organic Chemistry* (Authors: M. Smith and J. March). The highly activating group N_2^+ is rarely used to activate a reaction. The most common activating group is the nitro group and the most common substrates are 2,4-dinitrophenyl halides and 2,4,6-trinitrophenyl halides. Benzene rings that do not have activating substituents are generally not useful substrates for the S_NAr mechanism.

In reactions involving aryne intermediate these are two factors which affect the position of the incoming group. First one is the direction in which aryne forms. when there are groups orthoor para to the leaving group , these is no choice.

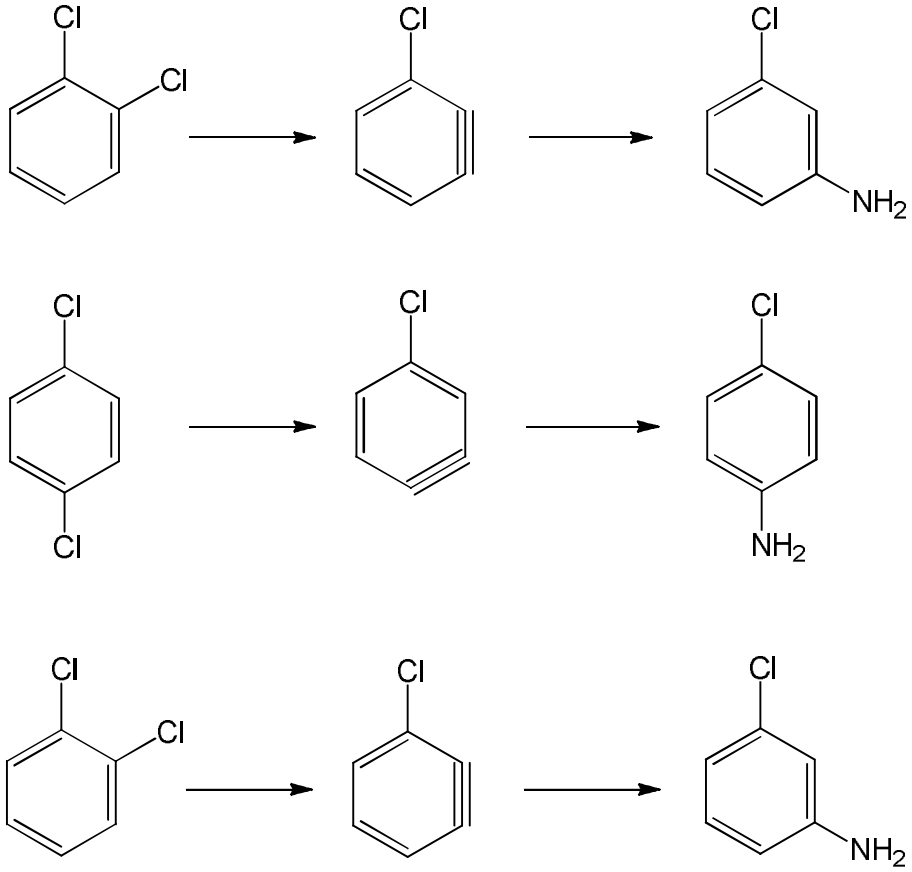


When a *meta* group is present, the aryne can form in two different ways:



In such cases, the more acidic hydrogen is removed. If Z is an electron-attracting group it favours removal of the *ortho* hydrogen while an electron-donating group (Z) favours removal of the *para* hydrogen.

The second factor is that the aryne, once formed, can be attacked at two positions. The most favoured position for nucleophilic attack is the one that leads to the more stable carbanion intermediate. It can be illustrated by the reaction of the three dichlorobenzenes with alkali-*meta*l amides to give the predicted products as shown below.



In each case, the predicted product was the one mainly formed.

The Effect of the Leaving Group:

The common leaving groups in aliphatic nucleophilic substitution such as halides, sulfate, sulfonate, NR_3^+ etc. are also common in aromatic nucleophilic substitution reactions. The groups such as NO_2, OR, OAr, SO_2R and SR, which are not generally lost in aliphatic substitution, are good leaving groups in aromatic substitutions. Interestingly, NO_2 is a good leaving group for aromatic substitution. The order of leaving group ability is:

$F > NO_2 > OTs > SOPh > Cl, Br, I > N_3 > NR_3^+ > OAr > OR > SR > NH_2$

The order of leaving group depends greatly on the nature of nucleophile.

The Effect of the Attacking Nucleophile:

Nucleophilicity order depends on the nature of substrate and different reaction conditions. Thus, it is not possible to construct a nucleophilicity order, but an over all approximate order is:

$^{-}NH_2$ O> Ph_3C^{-} > $PhNH^{-}$ (aryne mechanism) > ArS^{-} > RO > R_2NH > ArO^{-} > OH^{-} > $ArNH_2$ > NH_3 > I^{-} > Br^{-} > Cl^{-} > H_2O > ROH

12.8 Summary

In aromatic nucleophilic substitution reactions the nucleophile forms a resonance stabilized carbanion intermediate, and then the leaving group departs, re-establishing the aromaticity of the ring. The incoming nucleophile must be a stronger base than the substituent being replaced. A substituent that deactivates a benzene ring toward electrophilic substitution activates it toward nucleophilic substitution.

12.9 Glossary

- In Aromatic nucleophilic substitution reactions a hydrogen or a substituent is replaced of by a nucleophile.
- Strong electron-withdrawing substituents activate the aromatic ring for the nucleophilic substitution reactions.
- Aromatic nucleophilic substitution reactions proceed by S_NAr, S_N1, Benzyne and $S_{RN}1$ mechanisms.
- NO_2 is a good leaving group for the Aromatic nucleophilic substitution reactions.
- Meisenheimer or Meisenheimer–Jackson salts is the intermediate isolated in the reaction of Ethyl piorate and methoxide ion.

12.10 Review questions / Comprehensive Questions

1. Discuss the aromatic nucleophilic substitution reactions.
2. Explain the benzyne mechanism for aromatic nucleophilic substitution reactions.
3. Write a note on $S_{RN}1$ mechanism.
4. Discuss the effect of substrate structure, Leaving group and attacking nucleophile on the reactivity of aromatic nucleophilic substitution reactions.
5. Explain S_NAr and S_N1 mechanisms.

12.11 References and Suggested readings

1. March's Advanced Organic Chemistry (7^{th} ed.)- M. Smith and J. March (John Wiley & Sons, Inc., Hoboken, New Jersey) 2007.
2. Organic Chemistry- J. Clayden, Greeves, S. Warren and others (Oxford University Press) 2001.
3. Advanced Organic Chemistry- J. Singh and L. D. S. Yadav (Pragati Prakashan) 2005.

Unit-13: Elimination Reactions

Structure of Unit:

13.1 Objectives

In this unit the students will learn

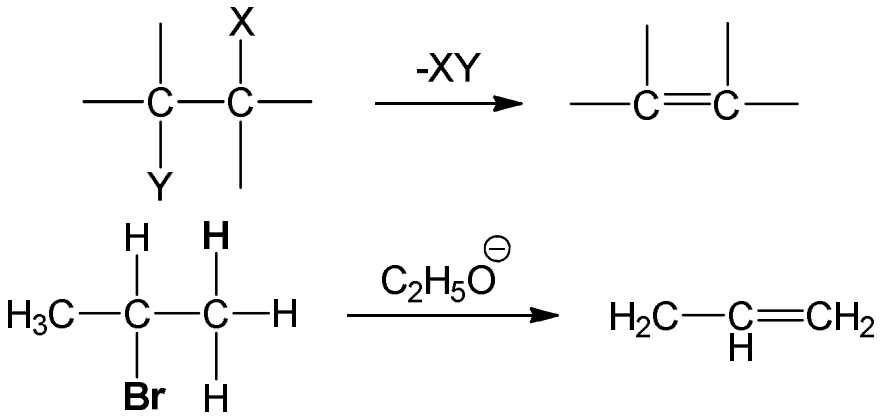
- The elimination reactions and their types.
- The stereochemistry of elimination reactions
- The differences and similarities between elimination and substitution reactions.
- *Anti* and *Syn* elimination reactions.

13.2 Introduction

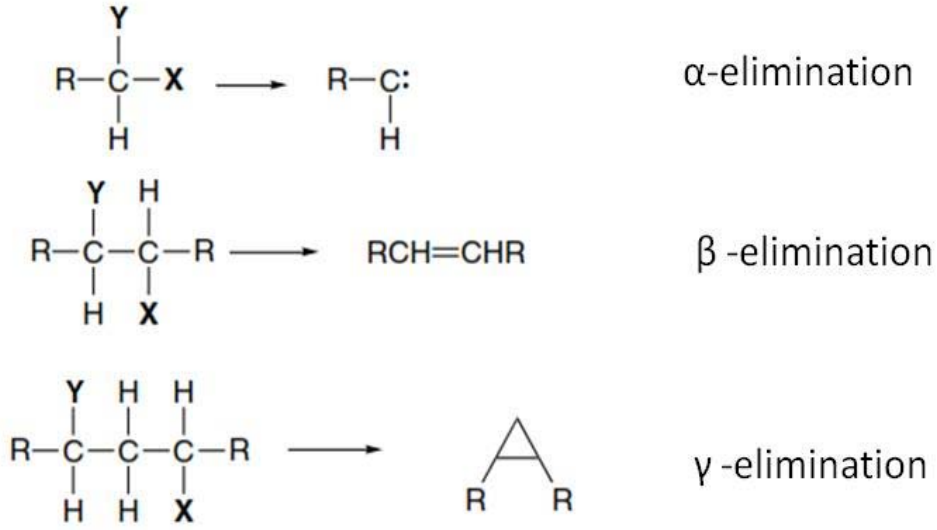
The elimination reactions which are an important part of organic reactions and their mechanisms have been discussed in the present chapter. This chapter focuses on the mechanistic details of elimination reactions, various types of elimination reactions and the stereochemistry of elimination reactions. A competition between substitution and elimination reactions has also been included in this chapter.

13.3 Elimination reactions

Reactions in which two atoms or atoms group of X and Y are removed from a compound, are referred as **elimination reactions**. For example, when an alkyl halide undergoes an elimination reaction, the halogen (X) is removed from one carbon and a proton is removed from an adjacent carbon. A double bond is formed between the two carbons from which the atoms are eliminated. Therefore, the product of an elimination reaction is an alkene. The elimination reactions are reverse of addition reactions.



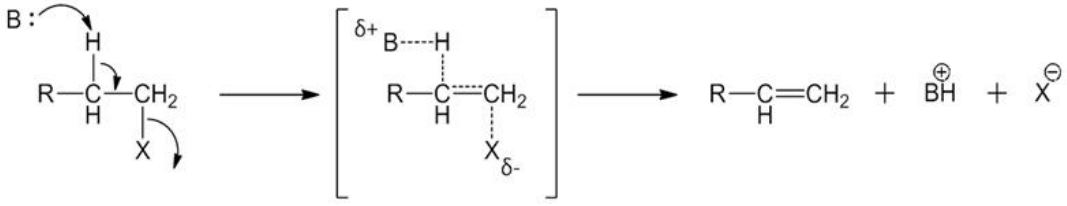
Elimination reactions can be classified according to the structural relationship between the proton and the leaving group. The products of α-eliminations are unstable divalent carbon species called carbenes. The β-elimination reactions lead to the formation of carbon-carbon double bonds. Elimination reactions involving γ- and elimination higher leaving groups result in cyclization; mechanistically they are intramolecular nucleophilic displacements.



In γ-elimination a new sigma-bond is produced instead of a pi-bond. The elimination reactions are given by those compounds which are having nucleophilic group as a leaving group. In general on the basis of mechanisms involved the elimination reactions are subdivided into three types.

13.4 Bimolecular elimination reaction (E2)

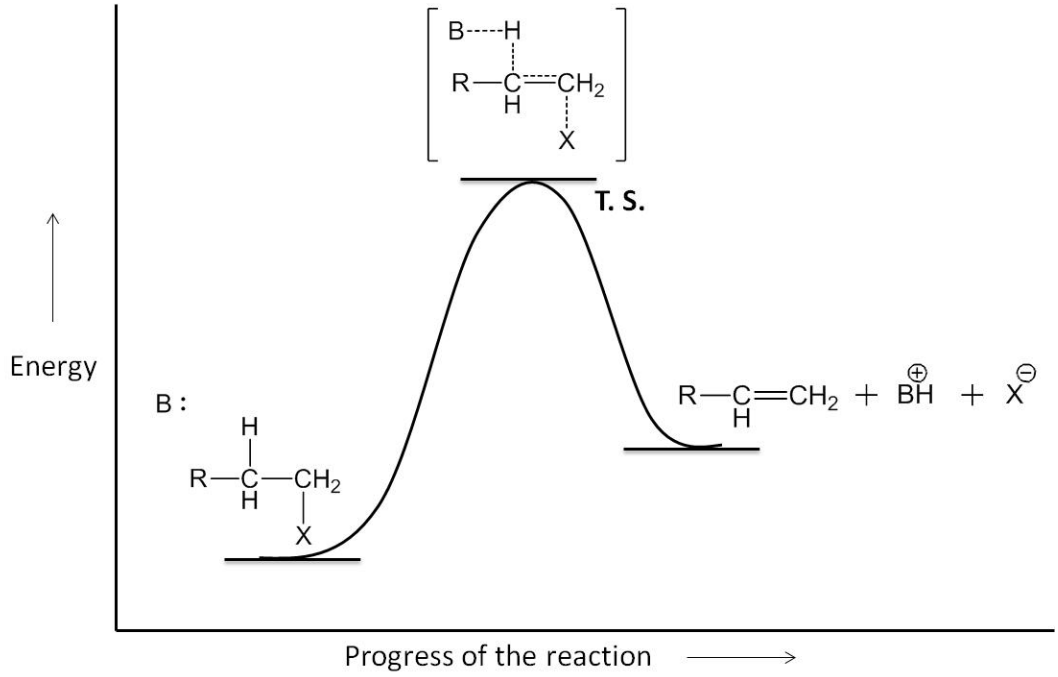
Bimolecular elimination reactions are represented as E2. In these elimination reactions, "E" stands for *elimination* and "2" stands for *bimolecular*. The E2 reaction is the most effective for the synthesis of alkenes from alkyl halides and can be used on primary, secondary, and tertiary alkyl halides. The rate of elimination depends on the concentration of the substrate and the nucleophile and the reaction is of second order. Similar to S_N2 reaction, the E2 reaction is also one step process. The mechanism thus takes place in one step and kinetically it is of second order: first order in respect to substrate and first order with respect to base.



The E2 reaction is a concerted, i.e. a one step process. The proton and the bromide ion are removed in the same step, i.e. in the rate determining step. For example, in the base induced elimination of HBr from the halide RCH_2CH_2Br, the rate law:

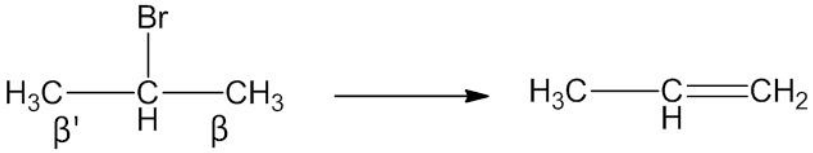
Rate = $k[RCH_2CH_2Br][B]$

The experimental evidence which is helpful in determining the mechanism of a reaction is a kinetic isotope effect. The reactions display considerable hydrogen-deuterium isotope effect. When eliminations are carried out by replacing hydrogen with deuterium, the reaction rates decreasels. Breaking a carbon-deuterium bond is slower than cleaving a similar carbon-hydrogen bond (kinetic isotope effect). Therefore, these results are consistent with a mechanism which involves carbon-hydrogen bond cleavage in the transition state.

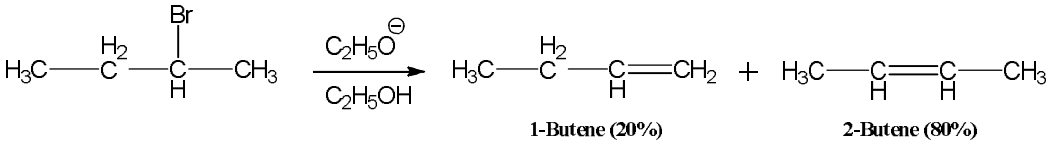


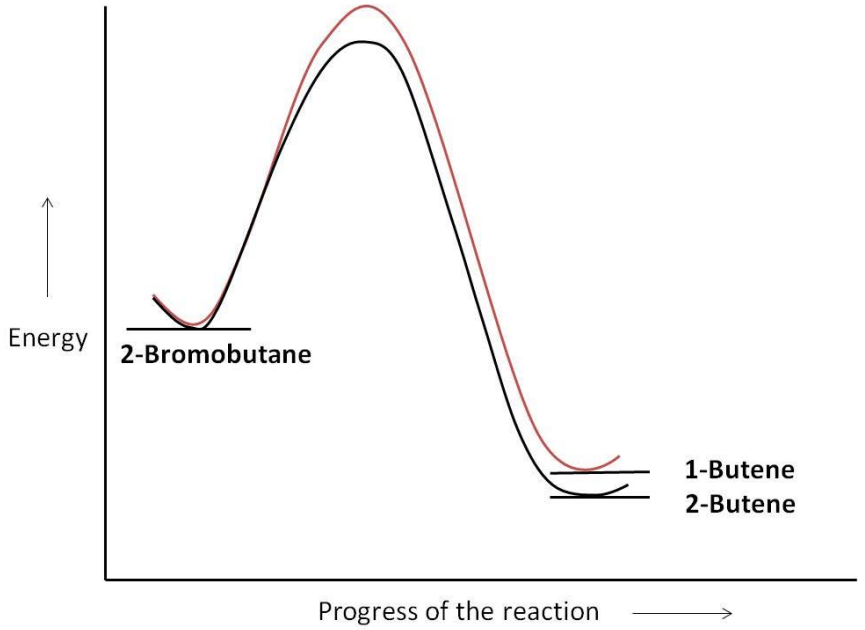
13.5 Orientation in E2 elimination reaction

An alkyl halide such as 2-bromopropane has two β-carbons from which a proton can be removed in an E2 reaction. Because the two carbons are identical, the proton can be removed with equal ease from either side. The product of this elimination reaction is propene.

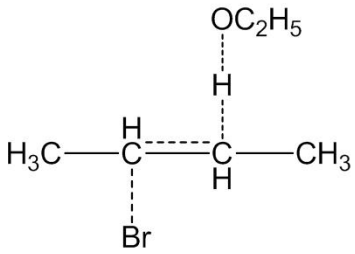


In contrast, 2-bromobutane has two structurally different β-carbons from which a proton can be removed. So when 2-bromobutane reacts with a base, two elimination products are formed: 2-butene and 1-butene. This E2 reaction is *regioselective* because one constitutional isomer is formed in large quantity compaired to the other.

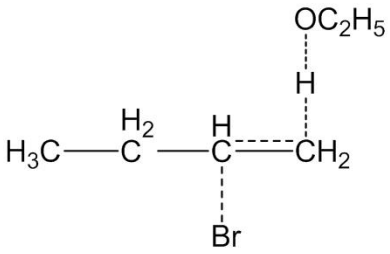




In the transition state leading to an alkene, the bonds are partially broken and the double bond is partially formed, giving the transition state an alkene-like structure. The difference in the rate of formation of the two alkenes is not very great. Consequently, both products are formed, but the *more stable* of the two alkenes will be the major product of the reaction.



Transition state
leading to
2-Butene
(More stable)

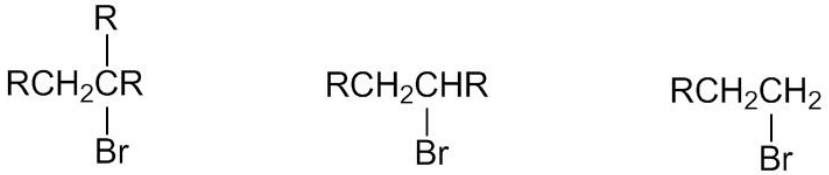


Transition state
leading to
1-Butene
(Less stable)

The stability of an alkene depends on the number of alkyl substituents bonded to its carbons: The greater the number of substituents, the more stable is the alkene. Therefore, 2-butene, with a total of two methyl substituents bonded to its carbons, is more stable than 1-butene, with one ethyl substituent.

The orientation of the reaction is determined by Saytzeff's and Hofmann's rule. According to the Saytzeff rule, the more substituted alkene is obtained when a proton is removed from the β-carbon. Thus the hydrogen is eliminated preferentially from the carbon atom which has less number of hydrogen atoms and highly substituted alkene is the major product.

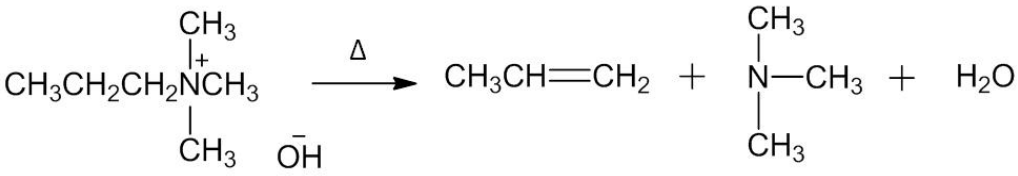
The relative reactivities of alkyl halides in an E2 reaction are as shown below this is so because elimination from a tertiary alkyl halide typically leads to a more highly substituted alkene than elimination from a secondary alkyl halide, and elimination from a secondary alkyl halide leads to a more highly substituted alkene than elimination from a primary alkyl halide.



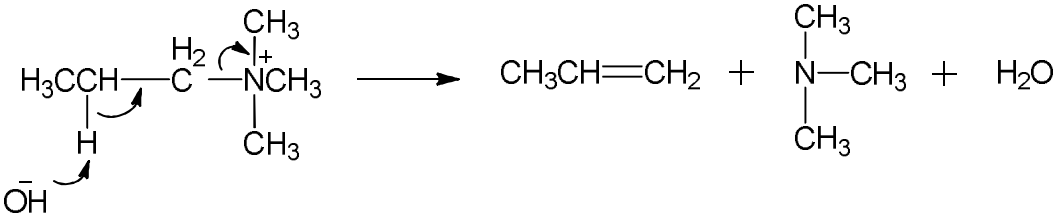
Tertiary alkyl halides > secondary alkyl halides > primary alkyl halides

The major product of an E2 reaction is the more stable alkene. However, the more substituted alkene is not always the more stable alkene. In some reactions the major alkene product is the least substituted alkene. The elimination reaction in which least substituted alkene is the major product is known as Hofmann's elimination reaction and the rule is known as Hofmann is rule.

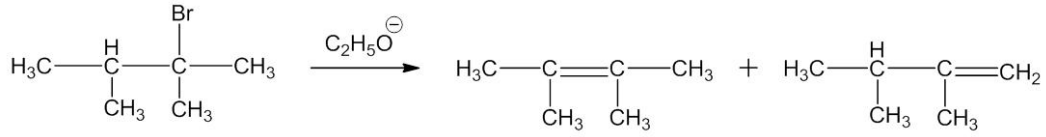
The reaction of a quaternary ammonium ion with hydroxide ion is known as a Hofmann elimination reaction. The leaving group in a Hofmann elimination reaction is a tertiary amine. Because a tertiary amine is only a moderately good leaving group, the reaction requires heat.

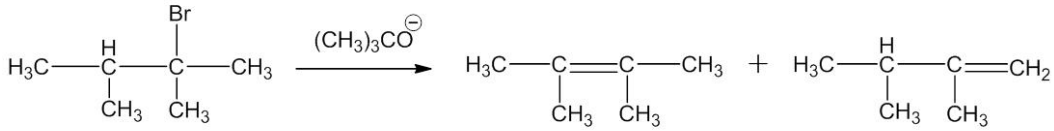


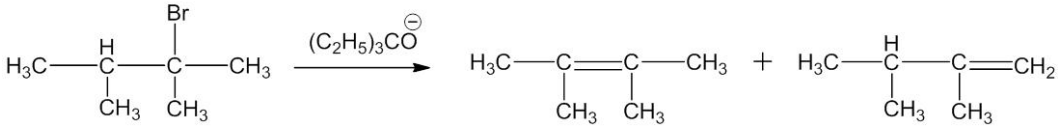
A Hofmann reaction is an E2 reaction, thus, it is concerted, one step reaction. The proton and the tertiary amine are removed in the same step.



When a highly branched base like $(CH_3)_3CO$ is used, alkyl halides give Hofmann elimination rather than Saytzeff elimination.

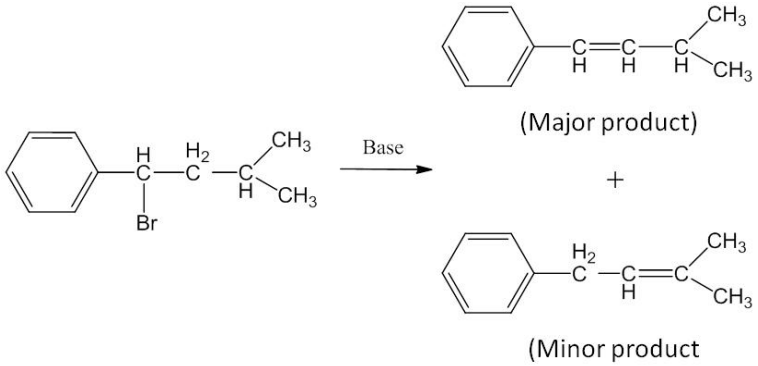






A highly branched base preferentially attacks on the least sterically hindered hydrogen to form stable transition state. In this case Hofmann product is formed and transition state depends on steric hindrance and not on the alkene character.

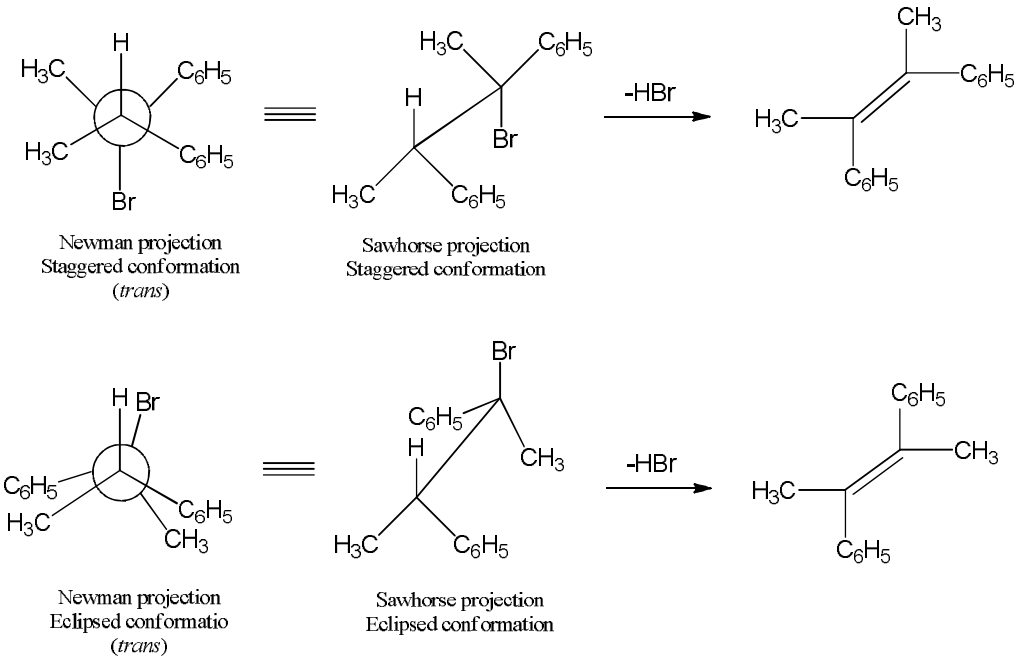
We know that the conjugated alkenes are more stable than the nonconjugated alkenes. Thus, the major product of the elimination reactions for those compounds having at least one double bond at γ-position to the alkyl halide is conjugated diene. These compounds do not follow Saytzeff's rule. Hydrogen always removes from that β-carbon which gives conjugated system.



13.6 Stereochemistry of E2 reactions

The E2 reactions involve the removal of two substituents (e.g. H and X) and it is an *anti*-elimination. The reaction is facile when both the leaving groups and the carbon bearing them are in the same plane, because the sp^3 hybrid orbital of the carbon

bonded to hydrogen and the sp^3 hybrid orbital of the carbon bonded to X become overlapping *p*-orbitals in the alkene. Thus, orbitals must overlap in the transition state. When the two leaving groups are in the same plane the C—H and C—L bonds can either be parallel to one another on the same side of the molecule (*syn*-coplanar) or on the opposite side of the molecule (*anti*-coplanar). If an elimination reaction removes two substituents from the same side of the molecule, the reaction is *syn*-elimination. If the substituents are removed from opposite sides of the molecule, the reaction is termed as *anti*-elimination. For example E2-elimination from threo-2-bromo-2,3-diphenylbutane, may be depicted as.

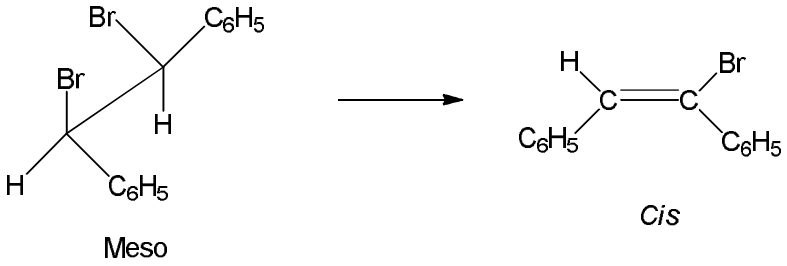


From the Newman and Sawhorse projections of the staggered (*trans*) and eclipsed (*syn*) conformations, we could observe that the elimination is more facile from the staggered conformation. There are several reasons for this. In staggered (*trans*) conformation the base approaches from the farthest side of the leaving group while in eclipsed (*syn*) conformation the base attacks from the same side of the leaving group, which causes repulsion.

Another reason is because the transition state leading to the elimination from the staggered conformation is more stable than the transition state leading to the elimination from the eclipsed conformation.

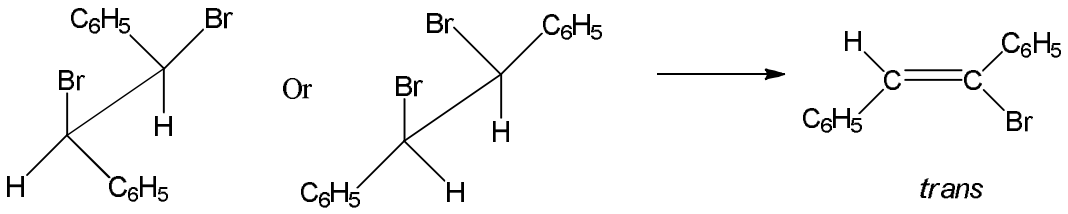
The E2 reaction is an *anti*-elimination is supported by the following examples:

(i) Elimination of HBr from meso-1,2-dibromo-1,2-diphenylethane gave cis-bromostilbene, while the (+) or (-) isomer gave the trans alkene.



Meso

Cis

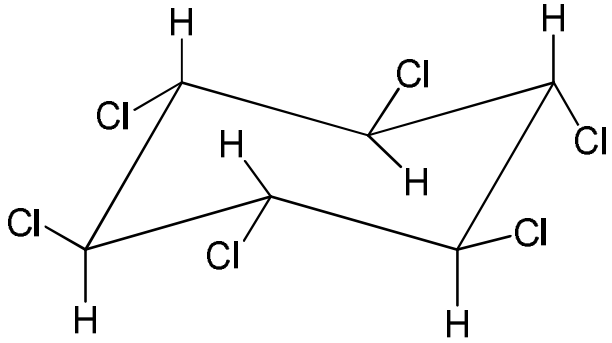


dl pair

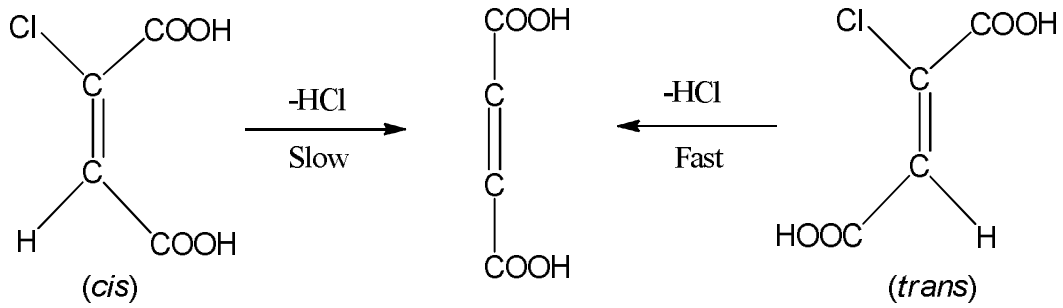
trans

This stereospecific results shows that in this case elimination is *anti*-elimination.

(ii) In open-chain systems, the molecule can generally adopt that conformation in which H and X are anti-periplanar. However, in cyclic systems this is not always possible. 1,2,3,4,5,6-hexachlorocyclohexane can exist in seven meso forms and a dl pair. When four of the meso compounds and the dl pair were subjected to elimination of HCl, only one of these isomeric forms loses HCl, 7000 times slowly than the others. This is because this isomer has no chlorine *trans* to an hydrogen. All the six chlorine are in equatorial positions and are *trans* to each other. Thus, no hydrogen is available in *trans* position.

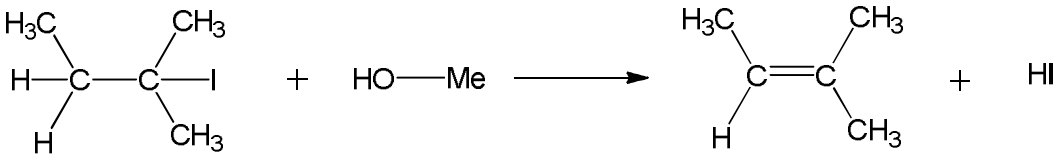


(iii) The elimination from *cis*- and *trans*-HOOC-CH=C(Cl)COOH shows that *anti*-elimination also leads to in the formation of triple bonds. In this elimination, the products are same in the both cases, but the *trans* isomer reacts 50 times faster than the *cis* isomer.



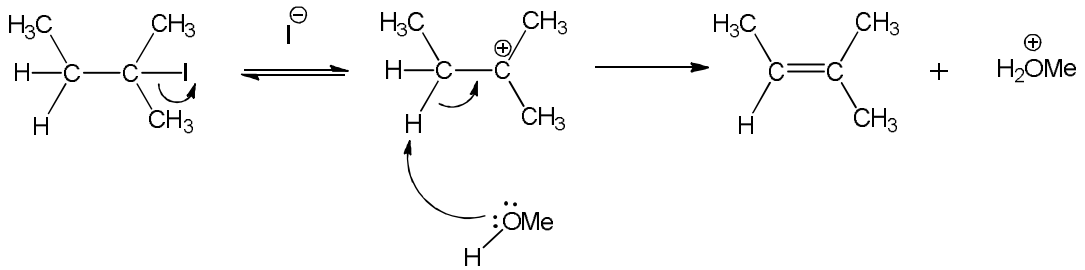
13.7 Unimolecular elimination reactions (E1)

The E1 mechanism is a two-step process in which the rate-determining step is ionization of the substrate to give a carbocation that rapidly loses a proton to a base (nucleophile), generally the solvent. In these reactions the rate of elimination is dependent only on the concentration of the substrate and is independent of the concentration of the nucleophile and the reaction is of the first order, (E1). The E1 reactions are two-step process like S_N1 reactions. The first step is the slow ionization of alkyl halide to generate the carbocation. The second step is the fast abstraction of a proton from the adjacent β-carbon atom to produce an alkene.



2-Iodo-2-methyl-butane

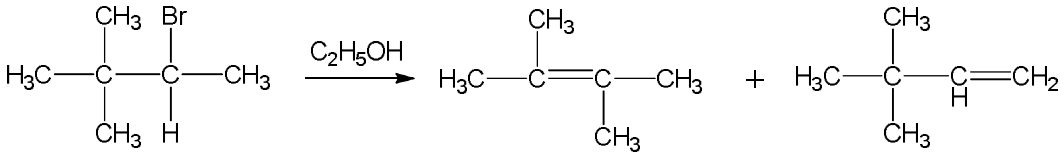
Mechanism:



There are two steps in this mechanism. The first step is exactly the same process described for the S_N1 mechanism and that is cleavage of the C–X bond to form a planar carbocation intermediate where the positive charge is stabilized by the three alkyl groups surrounding it. In the second stage, the methanol forms a bond to the susceptible proton on the β-carbon. The C–H bond breaks and both electrons are used to form a pi-bond to the neighboring carbocation. The first step of the reaction mechanism is the rate-determining step and since this is only dependent on the

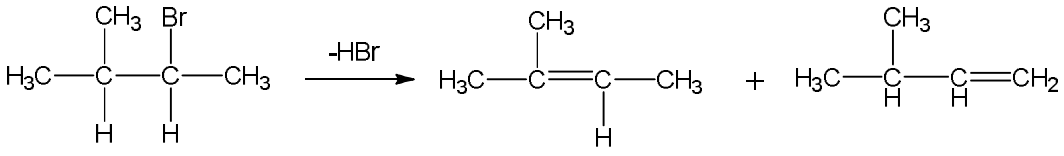
concentration of the alkyl halide, thus, the reaction is first order (El elimination unimolecular). There is no stereospecificity involved in this reaction and a mixture of isomers may be obtained with the more stable (more substituted) alkene being favored.

In the E1 mechanism the rate of reaction is determined by the rate of formation of the carbocation, which depends on the stability of carbocation. These may undergo rearrangements due to the formation of carbocation.



13.8 Orientation in E1 reactions

In the case of E2 reactions the orientation is determined by Saytzeff's fule (i.e. for alkyl halide, the product is highly substituted alkene) and by Hofmann's rule (i.e. for quaternary ammonium salts, the product is less substituted alkene). But, in case of E1 reaction same orientation is found for an alkyl halide substrate and for a quaternary ammonium salt because the same carbocation would arise from the ionization of alkyl halide or a quaternary ammonium salt. It has been experimentally verified that E1 reactin of both alkyl halide and quaternary ammonium salts produce the same products.



2-Bromo-3-methylbutane

2-Methyl-2-butene
(Major product)

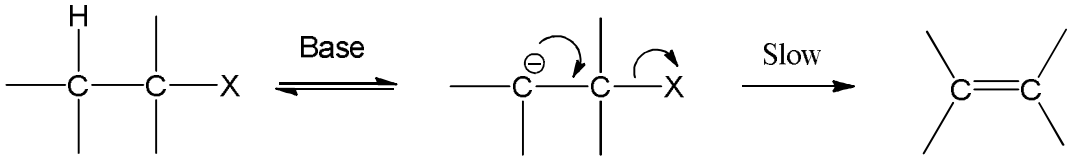
3-Methyl-1-butene
(Minor product)

Thus if a substrate is such that there is a possibility of more than, that one alkenes can be formed, the alkene will predominate which has higher number of alkyl groups on the double bonded carbon as per the Saytzeff's rule.

13.9 E1cB mechanism

In E1 mechanism the leaving group goes first, and proton removal follows in a second step. In E2 reactions, the two events happen at the same time thus, the proton is removed as the leaving group leaves. In E1cB mechanism the reaction begins with the loss of proton to generate a stabilized carbanion followed by the removal of leaving group. The elimination is unimolecular, and so is E1 reaction. The leaving group is not lost from the starting molecule, but from the conjugate base of the

starting molecule, so this sort of elimination, which starts with a deprotonation, is called E1cB (cB for conjugate Base).



Conjugated base of the substrate

The E1cB reaction is of first order in base and first order in substrate similar to the E2 reaction. But the reaction is unimolecular reaction because the reaction rate depends only on the concentration of the conjugate base of the substrate.

Rate = K [alkyl halide][base]

The E1cB reaction competes with the E2 reactions. But, the E1cb reactions are less common than the E2 reactions due to the instability of carbanions. Only some of the elimination reactions follow this pathway.

13.10 Effect of the substrate structure and leaving group on the E2 reactions

Substrate structure

The steric effects are of great value for the E2 reactions. The branching at α and β-carbons increases the rate of reaction of E2 because the branching on the carbon atoms of the developing double bonds increases the stability of the transition state.

The E1 reactions involves the formation of carbocation, thus, the rate of reaction of E1 depends on the stability of carbocation. Therefore the order of the reactivity of alkyl halides is as follows.

3° alkyl halide > 2° alkyl halide > 1° alkyl halide

Table 13.1 Effect of branching at α and β-carbons on E2 elimination

Substrate	Alkene %	Rate of reaction
CH_3CH_2Br	0.9	1.6×10^5
$(CH_3)_2CHBr$	80.3	0.237×10^5
$(CH_3)_3CBr$	97	4.17×10^5
$CH_3CH_2CH_2Br$	8.9	5.3×10^5

$(CH_3)_2CHCH_2Br$	59.5	8.5×10^5

Nature of the leaving group

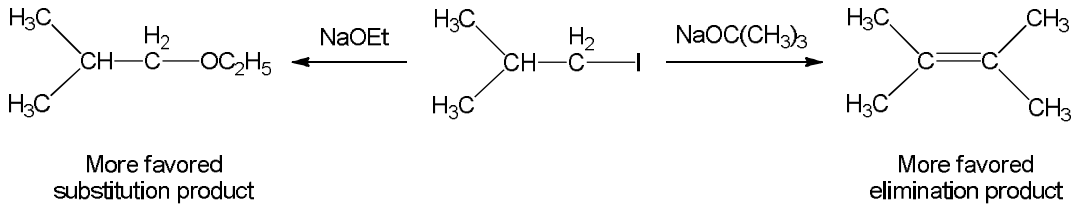
The reactivity of the substrate depends greatly on the nature of the leaving group. The rate of reaction of elimination reactions increases with the leaving power of the halogen atom. Thus, the order of the reactivity of the leaving group is:

$$F^{\ominus} < Cl^{\ominus} < Br^{\ominus} < I^{\ominus}$$

13.11 Competition between substitution and elimination

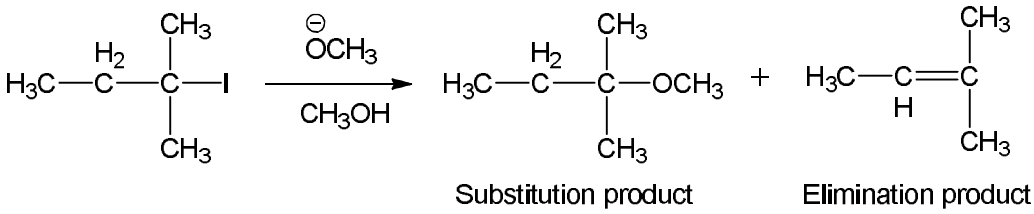
Alkyl halides can undergo elimination as well as substitution reactions and we may find both substitution and elimination products in the reactions. The ratio of the products obtained depends on the nature of the alkyl halide, the nature of the nucleophile and the reaction conditions.

Primary alkyl halides undergo the S_N2 reaction with a wide range of nucleophiles (such as I^-, CN^-, RS^-, Br^-) in polar aprotic solvents like hexamethylphosphoramide (HMPA). However, the E2 elimination reactions are also possible to occur. The substitution reactions are usually favoured over elimination reactions, even in the presence of strong bases. The use of a strong bulky base [$(CH_3)_3CO^-$] is desired for the E2 elimination reactions of primary halides. Primary halides do not give S_N1 and E1 reactions.



Secondary alkyl halides also undergo S_N2 and E2 reactions and give mixture of products. When a weak base is used in polar aprotic solvent substitution reaction is favored. If a strong base is used in polar protic solvent, the elimination reaction favored instead of substitution. On increasing the temperature elimination reaction is favorable.

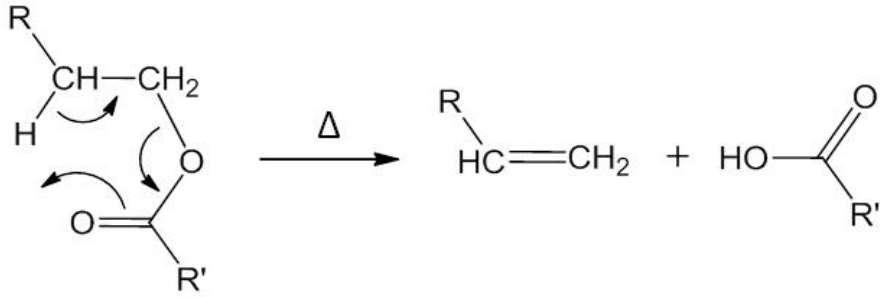
When tertiary alkyl halides are treated with a strong base in a protic solvent E2 reaction occurs. In a protic solvent under nonbasic conditions, E1 elimination and S_N1 substitution both take place.



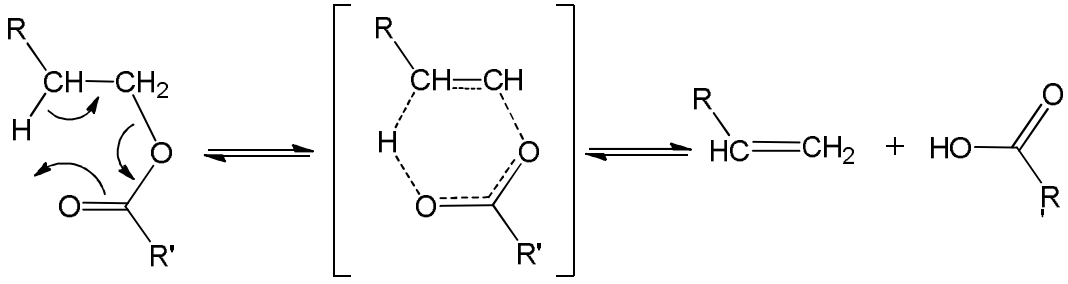
In the above reaction, in presence of a strong base the alkene would be expected to be the major product.

13.12 *Syn* or Pyrolytic elimination

Syn or pyrolytic elimination reactions often occurs in the gas phase, without the addition of another reagent. This type of reaction are different from those elimination reactions that we have already studied, because all of the other types required a base in one of the step, be it an additional external base or the solvent. If carboxylate esters are heated, they readily form an alkene and a carboxylic acid.



The mechanism involves a six-membered transition state. There is a requirement for a cis-β-hydrogen in order for this reaction to proceed. The kinetics is first order, so only one molecule of the substrate is involved in these reactions. These reactions are also known as intramolecular elimination reactions which involves five or six-membered cyclic transition state. The reaction is designated as Ei reactions. The Ei reactions are pericyclic elimination reactions. The mechanism of the reaction can be shown as follows:



Six-membered cyclic transition state

13.13 Summary

In an **elimination reaction**, groups are eliminated from a reactant. A double bond is formed between the two carbons from which the atoms are eliminated. There are three important elimination reactions, E1, E2 and E1cB. An E2 reaction is a concerted, one-step reaction. In an E1 reaction, the alkyl halide dissociates, forming a carbocation. In a second step, a base removes a proton from a carbon that is adjacent to the positively charged carbon. In E1cB reaction, a proton is abstracted by a base to generate a carbanion (conjugated base of sutstrate). In a second step, leaving group departs to givean sybstrate alkene.

13.14 Glossary

- Reactions in which two atoms or atom group of are removed from a compound are known as **elimination reactions**.
- The elimination reactions are reverse of addition reactions.
- The E2 reactions are concerted reactions (i.e. proceed in one step), where E stands for elimination and 2 stands for bimolecular.
- Saytzeff's rule: the hydrogen is eliminated preferentially from the carbon atom which has less number of hydrogen atoms and highly substituted alkene is the major product.
- The elimination reaction in which least substituted alkene is the major product is known as Hofmann's elimination reaction and the rule is known as Hofmann's rule.
- E2 elimination is an *anti*-elimination and the reaction proceed when both the leaving group and carbon bearing them are in the same plane.
- The E1 reactions are a two-step process, where E stands for elimination and 1 stands for unimolecular.
- E1 elimination involves the generation of carbocation in the first-step.
- E1cB reactions are also two-step process, where E stands for elimination, 1 stands for unimolecular and cB stands for conjugated base.
- E1 elimination involves the generation of carbanion in the first-step.
- Alkyl halides give both the elimination and the substitution reactions.

- The product of the reaction depends on the nature of the alkyl halide, nucleophile and the reaction conditions.
- *Syn* elimination reactions also occur and often proceed in gas phase.

13.15 Review questions / Comprehensive Questions

1. Discuss the stereochemistry of E2 elimination reactions.
2. What is Saytzeff rule? Exlain the orientation in elimination reactions.
3. What are elimination reactions? Differentiate E2, E1 and E1cB eliminations.
4. Write a note on E1 elimination reactions.
5. What is syn elimination? Explain with example.
6. Discuss the competition between elimination and substitution reactions.
7. Discuss E1cB elimination reactions.

13.16 References and Suggested readings

1. March's Advanced Organic Chemistry (7^{th} ed.)- M. Smith and J. March (John Wiley & Sons, Inc., Hoboken, New Jersey) 2007.
2. A Guidebook to Mechanism in Organic Chemistry (6^{th} ed.)- Peter Sykes (Longman Technical & Scientific) 1985.
3. Organic Reaction Mechanisms- V. K. Ahluwalia and R. K. Parashar (Narosa Publishing House) 2002.
4. Organic Chemistry- J. Clayden, Greeves, S. Warren and others (Oxford University Press) 2001.
5. Advanced Organic Chemistry- J. Singh and L. D. S. Yadav (Pragati Prakashan) 2005

Unit - 14 Oxidation And Reduction

Structure of Unit:

14.1 Objectives

At the end of the unit learner will be able to

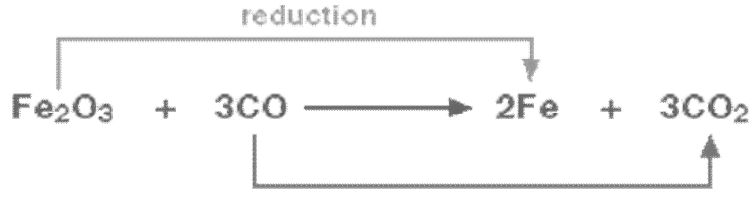
- Familiariese with oxidation and reduction.
- Learn the different reagents used for redox reactions.
- Understand the mechanistic details of working of different reagents..
- Increase knowledge about catalysts and their applications.

14.2 Introduction

The Chapter deals with increasing the knowledge of learner about oxidation and reduction and their mechanism, their synthesis, reactions, applications and structure. This chapter also explain brief about different reagents with is a matter of recent research. Along with these chapter also highlights the different catalysts used in redox reaction.

14.3 Definitions

- Oxidation is gain of oxygen.
- Reduction is loss of oxygen. For example, in the extraction of iron from



its

Because both **red**uction and **ox**idation are going on side-by-side, this is known as a **redox** reaction.

Oxidising and reducing agents an oxidising agent is substance which itself reduces and oxideses others else. In the above example, the iron(III) oxide is the oxidising agent.A reducing agent oxidisesitsey and deduces also. In the above equation, the carbon monoxide is the reducing agent.

- Oxidising agents give oxygen to another substance.
- Reducing agents remove oxygen from another substance.

14.4 Different Reagents:

Differnet reagents are used in Organic Synthasis there reagents are very specific in their mode of action many reagents of symthgtic importance are listed here.

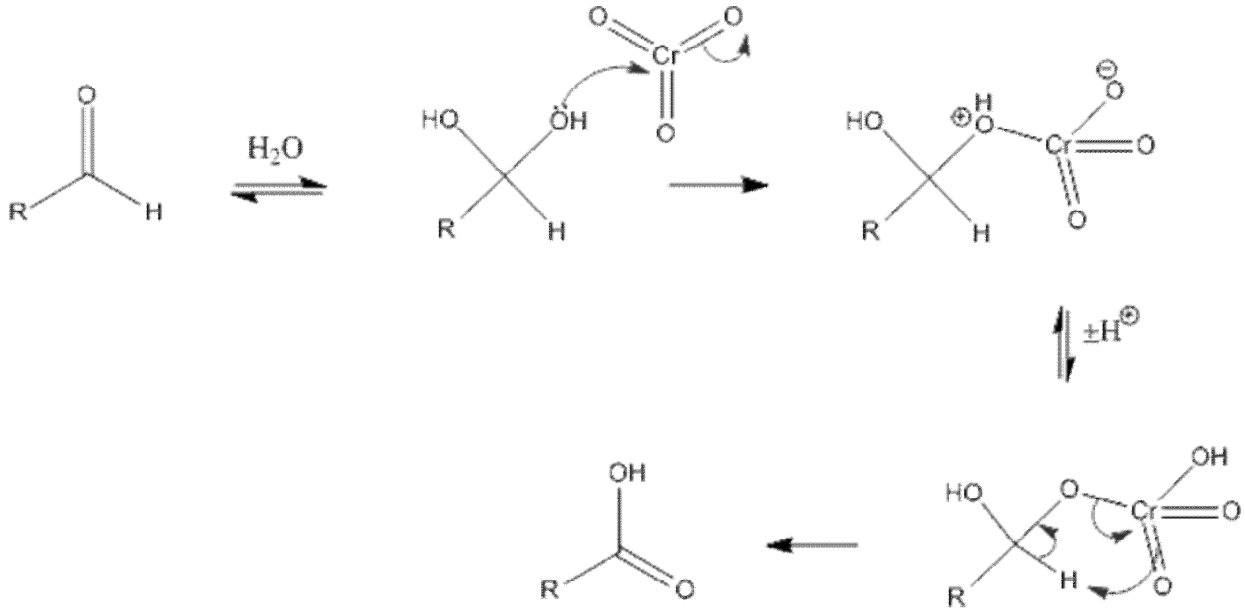
JONES REAGENT

The Jones Reagent is a solution of chromium trioxide(CrO_3) in concreted sulfuric acid and water that can be used safely for oxidations of organic substrates in acetone. The reagent can also be prepared from sodium dichromate and sulfuiric acid dichromate. Jones Reagent is especially suitable for the oxidation of secondary alcohols to ketones and of primary alcohols to carboxylic acids and in a few cases to aldehydes (Jones Oxidation). Some alternative chromium reagents allow the selective preparation of aldehydes, such as PCC and PDC.

Jones Oxidation

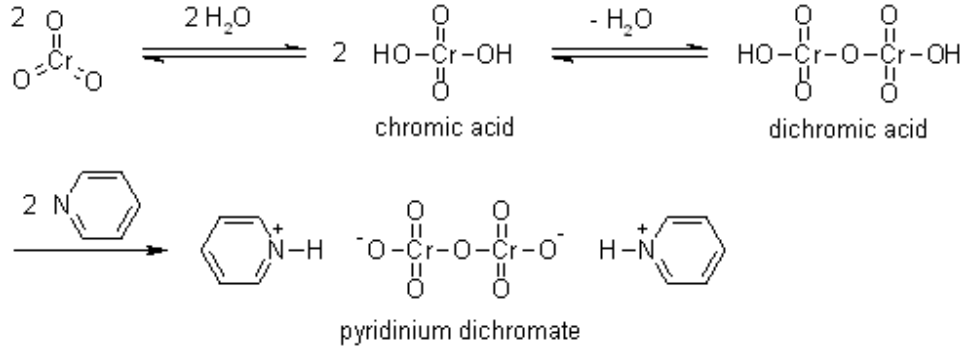
Jones Oxidation

Oxidation of Aldehyde to carboxylic acid using CrO_3



Pyridinium Dichromate (PDC)

Pyridinium dichromate is the pyridinium salt of dichromate that can be obtained by addition of pyridine to a solution of chromium trioxide(CrO_3) in



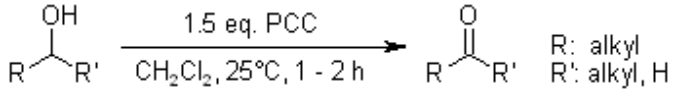
Pyridinium Dichromate (PDC) is orange coloured salt which is commercially available and can by conveniently handled and stored; it is non-hygroscopic and soluble in many organic solvents. A similar salt is Pyridinium Chlorochromate (PCC), which shares the same properties. Both PDC and PCC can convert alcohols into aldehydes and ketones, especially in dichloromethane at room temperature. PDC is less acidic than PCC and is therefore more suitable for the oxidation of acid-sensitive substrates.

Pyridinium Chlorochromate (PCC)
Corey-Suggs Reagent

Chlorochromic acid can by prepared by the dissolution of chromium trioxide in 6 M aq. hydrochloric acid. Addition of pyridine gives pyridinium to this solution chlorochromate as orange crystals.

The properties of PCC can be compared with those of PDC: it is not particularly hygroscopic, is stable, commercial available and can be stored. PCC is soluble in many organic solvents, and especially a solution of dichloromethane at room temperature has been used in most cases, on the other hand DMF promotes the over-oxidation of primary alcohols into carboxylic acids.

PCC is more acidic than PDC, but acid-labile compounds can be oxidized in the presence of sodium acetate or other buffers such as carbonates. Another drawback is the formation of viscous materials that complicates product isolation.



Pyridinium chlorochromate is a readily available, stable reagent that oxidizes a wide variety of alcohols to carbonyl compounds with high efficiency.

Potassium permanganate($KMnO_4$)

Potassium permanganate is an inorganic chemical compound with the formula $KMnO_4$. It is a salt consisting of K^+ and MnO_4^- ions. Formerly known as permanganate of potash or Condy's crystals, it is a strong oxidizing agent. It dissolves in water to give intensely pink or purple solutions, the evaporation of which leaves prismatic purplish-black glistening crystals. In this compound, manganese is in the +7 oxidation state.

Potassium permanganate is produced industrially from manganese dioxide which also occurs as the mineral pyrolusite. The MnO_2 is fused with potassium hydroxide and heated in air or with a source of oxygen, like potassium nitrate or chlorate. This process gives potassium mangante which upon electrolytic oxidation in alkaline media, or by boiling the manganate solution in the presence of carbon dioxide until all the green color is discharged, gives potassium permanganate.

$$2\ MnO_2 + 4\ KOH + O_2 \rightarrow 2\ K_2MnO_4 + 2\ H_2O$$

$$2\ MnO_4^{2-} + Cl_2 \rightarrow 2\ MnO_4^{-} + 2\ Cl^{-}$$

or: $3\ K_2MnO_4 + 2\ CO_2 \rightarrow 2\ KMnO_4 + 2\ K_2CO_3 + MnO_2$

Reactions

Dilute solutions of $KMnO_4$ convert alkenes into diols (glycols). This behaviour is also used as a qualitative test for the presence of double or triple bonds in a molecule, since the reaction decolorizes the initially purple permanganate solution and generates a brown precipitate (MnO_2). It is sometimes referred to as Baeyer's reagent. Under acidic conditions, the alkene double bond is cleaved to give the appropriate carboxylic acid.

$CH_3(CH_2)_{17}CH{=}CH_2 + 2\ KMnO_4 + 3\ H_2SO_4 \rightarrow CH_3(CH_2)_{17}COOH + CO_2 + 4\ H_2O + K_2SO_4 + 2\ MnSO_4$

Potassium permanganate oxidizes aldehydes to carboxylic acids, such as the conversion of *n*-heptanal to heptanoic acid.

$$5\ C_6H_{13}CHO + 2\ KMnO_4 + 3\ H_2SO_4 \rightarrow 5\ C_6H_{13}COOH + 3\ H_2O + K_2SO_4 + 2\ MnSO_4$$

Glycols and polyols are highly reactive toward $KMnO_4$. For example, addition of potassium permanganate to an aqueous solution of sugar and sodium hydroxide produces the "chemical chameleon" reaction, which involves dramatic color changes associated with the various oxidation states of manganese.

Reaction with acids

Concentrated sulfuric acid reacts with $KMnO_4$ to giveMn_2O_7, which can be explosive. Its reaction with concentrated hydrochloric acid gives chlorine. The Mn-containing products obtain from redox reaction depend on the pH, Acidic solutions of permanganate are reduced to the faintly pink manganese(II) ion (Mn^{2+}) and water. In neutral solution, permanganate is only reduced by three electrons to give MnO_2, wherein Mn is in a +4 oxidation state. Ones skin gents stain when one handles $KMNnO_4$ when handling $KMnO_4$. $KMnO_4$ spontaneously reduces in an alkaline solution to green K_2MnO_4, wherein manganese is in the +6 oxidation state.

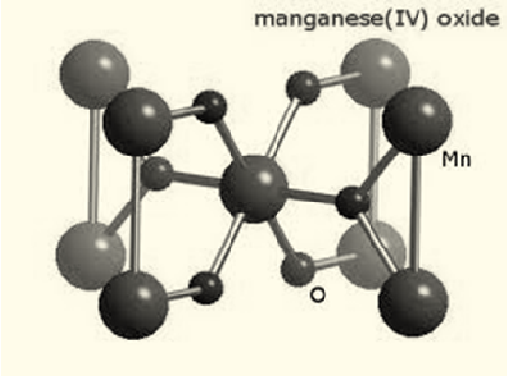
Potassium permanganate decomposes when exposed to light:

$$2\ KMnO_4 \rightarrow K_2MnO_4 + MnO_2(s) + O_2$$

Manganese(IV) oxide (MnO_2)

Manganese(IV) oxide is the inorganic compound with the formula MnO_2. This blackish or brown solid occurs naturally as the mineral pyrolusite, which is the main ore of manganese and a component of manganese nodules.The principal use for

MnO_2 is for dry-cell batteries, such as the alkaline battery and the Zinc –carbon battery. MnO_2 is also used as a pigment and as a precursor to other manganese compounds, such as $KMnO_4$. It is used as a reagent in organic synthesis, for example, for the oxidation of allylic alcohol.



The important reactions of MnO_2 are associated with its redox, both oxidation and reduction properties.

Reduction

MnO_2 is the principal precursor to ferromanganese and related alloys, which are widely used in the steel industry. The conversions involve carbothermal reduction using coke:

$$MnO_2 + 2\ C \rightarrow Mn + 2\ CO$$

Hot concentrated sulfuric acid reduces the MnO_2 to manganese (II) sulfate.

$$2\ MnO_2 + 2\ H_2SO_4 \rightarrow 2\ MnSO_4 + O_2 + 2\ H_2O$$

The reaction of hydrogen chloride with MnO_2 was used by Carl Wilhelm Scheele in the original isolation of chlorine gas in 1774:

$$MnO_2 + 4\ HCl \rightarrow MnCl_2 + Cl_2 + 2\ H_2O$$

Oxidation

Heating a mixture of KOH and MnO_2 in air gives green potassium manganate:

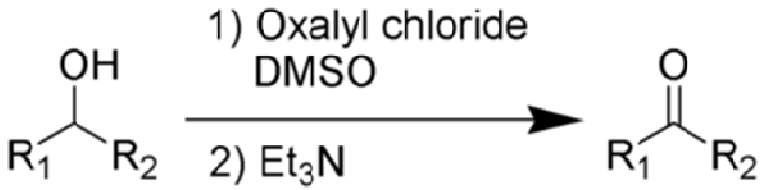
$$2\ MnO_2 + 4\ KOH + O_2 \rightarrow 2\ K_2MnO_4 + 2\ H_2O$$

Potassium manganate is the precursor to potassium permanganate, a common oxidant.

Swern Oxidation

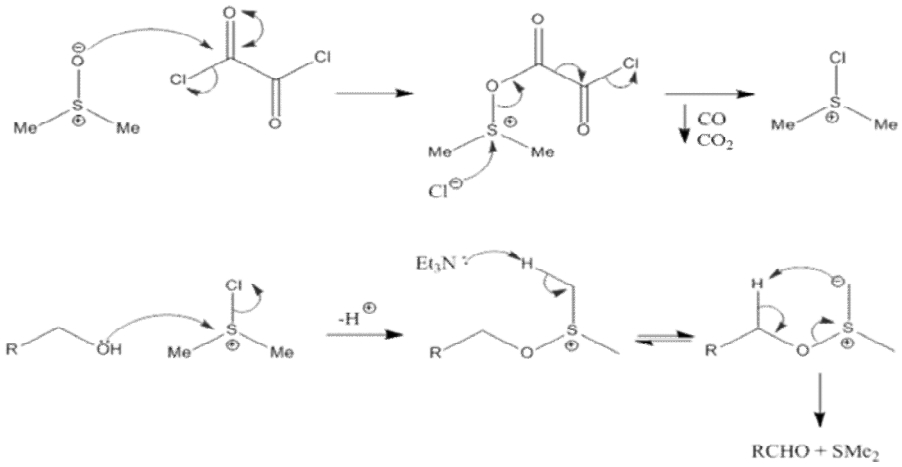
The Swern oxidation, named afterDaniel Swern , is a chemical reaction whereby a primary or secondary alcohol is oxidized to an aldehyde or ketone using oxalyl

chloride, dimethyl sulfoxide (DMSO) and an organic base, such as triethylamine The reaction is known for its mild character and wide tolerance of functional groups.



The by-products are dimethyl sulfide (Me_2S), carbon monoxide (CO), carbon dioxide (CO_2) and — when triethylamine is used as base — triethylammonium chloride (Et_3NHCl).

Oxidation of alcohol to carbonyl- Swern Oxidation



Selenium dioxide(SeO_2)

Selenium dioxide is the chemical compound with the formula SeO_2. It is also commonly known as the compound selenonyl. This colorless solid is one of the most frequently encountered compounds of selenium.

SeO_2 is considered an acidic oxide: it dissolves in water to form selenous acid. It reacts with base to form selenite salts containing the $SeO^2{}_3$ anion. For example, reaction with sodium hydroxide produces sodium selenite:

$$SeO_2 + 2\ NaOH \rightarrow Na_2SeO_3 + H_2O$$

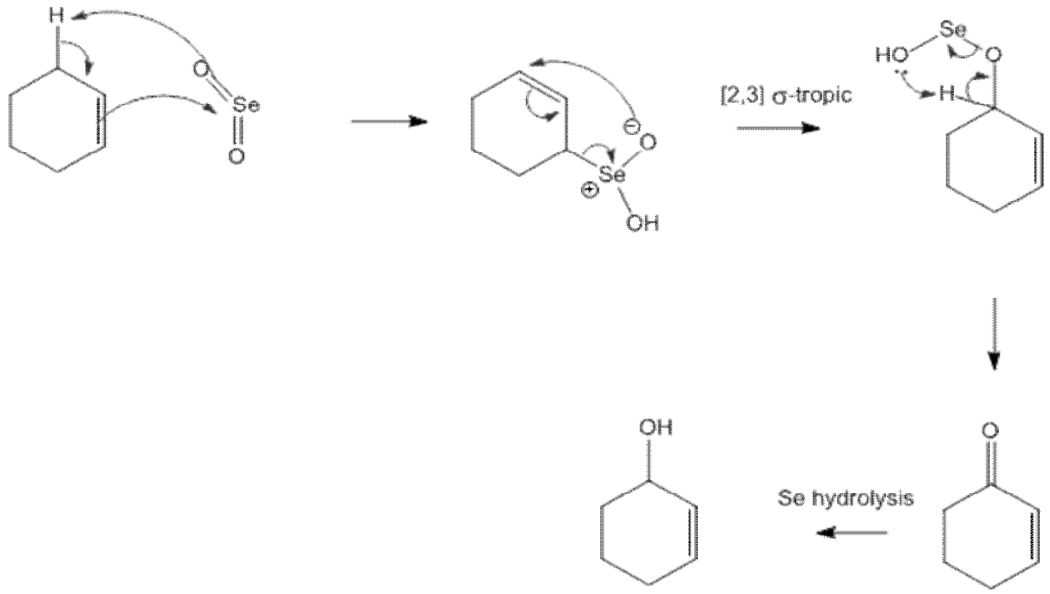
SeO_2 is an important reagent in organic synthesis. Oxidation of paraldehyde (acetaldehyde trimer) with SeO_2 gives glyoxal and the oxidation of cyclohxanone gives cyclohexane-1,2-dione. The starting material reagent used is reduced to

selenium, and precipitates as a red amorphous solid which can easily be filtered off. This type of reaction is called a Riley oxidation. It is also renowned as a reagent for "allylic" oxidation a reaction that entails the conversion as shown below;

$$R_2C=CR'-CHR''_2 + [O] \rightarrow R_2C=CR'-C(OH)R''_2$$

(where R, R', R'' are alkyl or aryl).

Oxidation of alkenes using SeO_2 to form allylic alcohol



Lead(IV) acetate

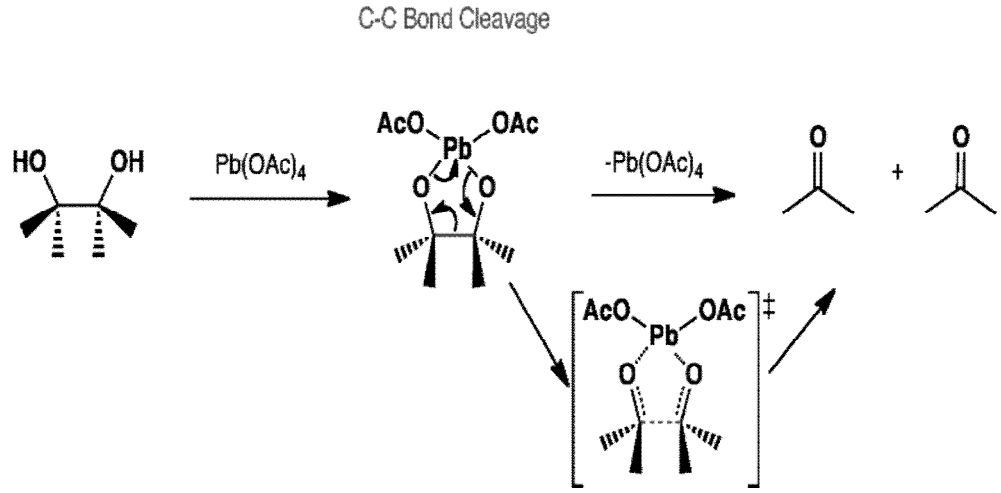
Lead(IV) acetate or lead tetraacetate is a chemical compound with chemical formula $Pb(C_2H_3O_2)_4$ and is a lead salt of acetic acid. It is commercially available often stabilized with acetic acid.

Lead tetraacetate is a strong oxidizing agent, a source of acetyloxy groups and a general reagent used for the introduction of lead into organolead compounds. Some of its uses in organic chemistry are:

- an alternative reagent to bromine in Hofmann rearrangement
- oxidation of hydrazones to diazo compounds for example that of hexafluoroacetone hydrazone to bis(trifluoromethyl)diazomethane
- oxidation of alcohols carrying a δ-proton to cyclic ethers.
- Oxidative cleavage of certain allyl alcohols in conjunction with ozone.

Oxidation of alkene using $Pb(OAc)_4$

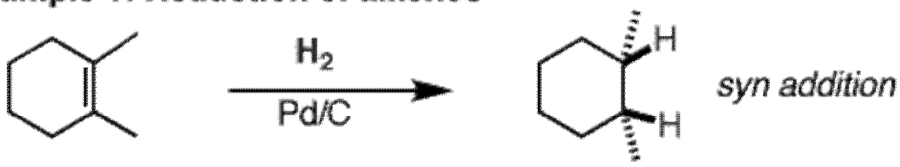
In this example lead tetraacetate is used cleave a carbon-carbon bond in a *vicinal* diol (glycol). This reaction is useful in the formation of ketones and aldehydes and involves a favourable five membered cyclic intermediate.



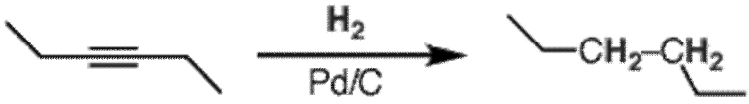
Pd/C

Palladium on carbon, often referred to as Pd/C, is a form of palladium used for catalysis. It is usually used for catalytic hydrogenations in organic chemistry. When the metal is distributed over finely-divided carbon catalyst support, the surface area become larger and the catalyst is more reactive. Palladium-on-carbon has also been used as the palladium(0) catalyst in the Suzuki reaction, Stille reaction, and related reactions. Reduction of Alken First of all Pd/C will reduce alkenes to alkanes when hydrogen is also present. It's important to note that the addition of hydrogens from the alkene are delivered syn (i.e. the same face of the alkene).

Example 1: Reduction of alkenes



Example 2: Reduction of alkynes



Pd/C and hydrogen will reduce alkynes all the way to alkanes – that is, two equivalents of H2 are added. Contrast that to Lindlar's catalyst, which only adds one equivalent of H2 (but also in syn fashion).

Pd/C and hydrogen will also reduce other multiple bonds, such as NO_2 (nitro groups), CN (nitriles) and C=NR (imines).

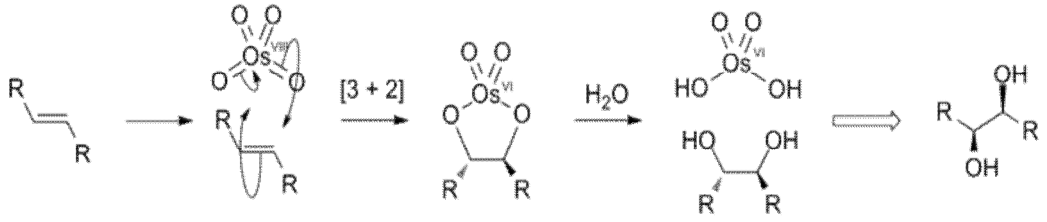
Finally, if enough heat and pressure is added, Pd/C and hydrogen gas will also reduce aromatic groups such as benzene. Note that this reaction is considerably more difficult than reducing a "normal" double bond due to the greater stability of the aromatic benzene.

Osmium(VIII) oxide

Osmium(VIII) oxide (also called osmium tetroxide) is the chemical compound with the formula OsO_4. The compound is noteworthy for its many uses, despite of the rarity of osmium. It also has a number of interesting properties, one being that the solid is volatile. The compound is colourless, but most samples appear yellow. This is most likely due to the presence of the impurity OsO_2 which is yellowish brown in colour.

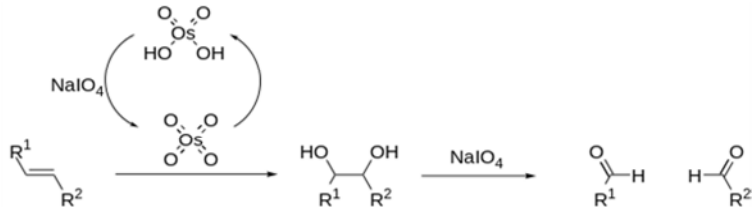
Oxidation of alkenes

Alkenes add to OsO_4 to give diolate species that hydrolyze to cis-diols. The net process is called dihydroxylation. This proceeds via a [3 + 2] cycloaddition reaction between the OsO_4 and alkene to form an intermediate osmate ester which rapidly hydrolyses to yield the vicinal diol. As the oxygen atoms are added in a concerted step the resulting stereochemistry is cis.



OsO_4 is expensive and highly toxic, making it an unappealing reagent to use in stoichiometric amounts. However its reactions are made catalytic by adding reagents to reoxidise the Os(VI) by-product back to Os(VIII). Typical reagents include H_2O_2, N-methylmorpholine N-oxide (NMO) and $K_3Fe(CN)_6$, as these will not react with the alkenes on their own. Other osmium compounds can be used as catalysts, including osmate(VI) salts ($[OsO_2(OH)_4]^{2-}$, and osmium trichloride hydrate ($OsCl_3 \cdot xH_2O$).

These species oxidise to osmium(VIII) in the presence of above mentioned oxidants. Lewis bases such as tertiary amines and pyridines increase the rate of dihydroxylation.. This process can be extended prepare to aldehydes in the Lemieux-Johnson oxidation, which uses periodate to achieve diol cleavage and to regenerate the catalytic loading of OsO_4. This process is equivalent to that of ozonolysis.



***meta*-Chloroperoxybenzoic acid**

meta-Chloroperoxybenzoic acid (mCPBA) is a peroxycarboxylic acid used widely as an oxidant in organic synthesis. mCPBA is often preferred to other peroxy acids because of its relative ease of handling. The main areas of use are the conversion of ketones to esters (Baeyer Villiger Oxidation), epoxidation of alkenes (villigers Reaction), conversion of silyl enol ethers to silyl α- hydroxyl ketones(Rubottom Oxidation), oxidation of sulfides to sulfoxides and sulfones , and oxidation of amines to produce amine oxides. mCPBA is a strong oxidizing agent that may cause fire upon contact with flammable material.

mCPBA is a strong oxidizing agent, which is comparable with other peracids. Advantages of 3-chloroperbenzoic acid is its handling, because it is present as powder, which can be kept in the refrigerator.

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Named Reactions

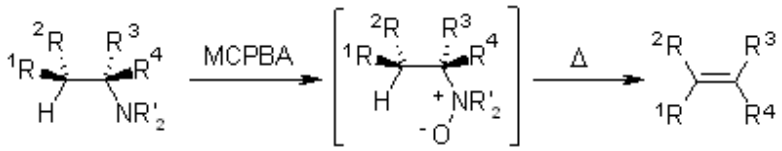
Baeyer-Villiger Oxidation

The Baeyer-Villiger Oxidation is the oxidative cleavage of a carbon-carbon bond adjacent to a carbonyl, which converts ketones to esters and cyclic ketones to

lactones. The Baeyer-Villiger can be carried out with peracids, such as MCBPA or with hydrogen peroxide and a Lewis acid.

Mechanism of the Baeyer-Villiger Oxidation

Cope Elimination Reaction



Priles chaiev Reaction

Rubottom Oxidation Reaction

Some more examples:

Ozone (O_3)

Ozone or trioxygen, is an inorganic molecule with the chemical formula O3(μ-O). It is a pale blue gas with a distinctively pungent smell. It is an allotrope of oxygen that is much less stable than the diatomic allotrope O2, breaking down in the lower atmosphere to normal dioxygen. Ozone is formed from dioxygen by the action of ultraviolet light and also atmospheric electrical discharges, and is present in low concentrations throughout the Earth's atmosphere. In total, ozone makes up only 0.6 ppm of the atmosphere.

Ozone is a powerful oxidizing agent, far stronger than O_2. It is also unstable at high concentrations, decaying to ordinary diatomic oxygen.

$$2\ O_3 \rightarrow 3\ O_2$$

This reaction proceeds more rapidly with increasing temperature and increased pressure. Deflagration of ozone can be triggered by a spark, and can occur in ozone concentrations of 10 wt% or higher.

With metals some commen reactions involving O_3

Ozone will oxidize most metals (except gold, platinum, and iridum) to oxides of the metals in their highest oxidation state. For example:

$$2\ Cu^{+} + 2\ H_3O^{+} + O_3 \rightarrow 2\ Cu^{2+} + 3\ H_2O + O_2$$

With nitrogen and carbon compounds

Ozone also oxidizes nitric oxide to nitrogen dioxide:

$$NO + O_3 \rightarrow NO_2 + O_2$$

This reaction is accompanied by chemiluminescence. The NO2 can be further oxidized:

$$NO_2 + O_3 \rightarrow NO_3 + O_2$$

The NO3 formed can react with NO_2 to form N_2O_5:

Solid nitronium perchlorate can be made from NO_2, ClO_2, and O_3 gases:

$$2\ NO_2 + 2\ ClO_2 + 2\ O_3 \rightarrow 2\ NO_2ClO_4 + O_2$$

Ozone does not react with ammonium salts, but it oxidizes ammonia to ammonium nitrate:

$$2\ NH_3 + 4\ O_3 \rightarrow NH_4NO_3 + 4\ O_2 + H_2O$$

Ozone reacts with carbon to form carbon dioxide, even at room temperature:

$$C + 2\ O_3 \rightarrow CO_2 + 2\ O_2$$

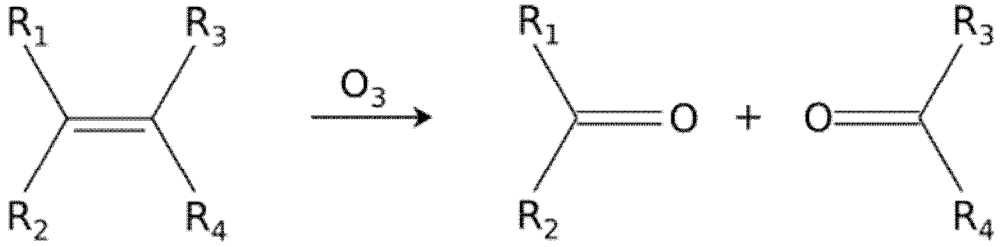
With sulfur compounds

Ozone oxidizes sulfides to sulfates. For example, lead (II) sulfide is oxidised to lead (II) sulfate.

$$PbS + 4\ O_3 \rightarrow PbSO_4 + 4\ O_2$$

With alkenes and alkynes

Ozonolysis: Alkenes can be oxidatively cleaved by ozone, in a process called ozonolysis, giving alcohols, aldehydes, ketones, and carboxylic acids, depending on the second step of the workup.



Usually ozonolysis is carried out in a solution of dichloromethane, at a temperature of −78°C. After a sequence of cleavage and rearrangement, an organic ozonide is formed.

Reduction of Ozone

Reduction of ozone gives the ozonide anion, O^{-3}. Derivatives of this anion are explosive and must be stored at cryogenic temperatures. Ozonides for all the alkali metals are known. KO_3, RbO_3, and CsO_3 can be prepared from their respective superoxides:

$$KO_2 + O_3 \rightarrow KO_3 + O_2$$

A solution of calcium in ammonia reacts with ozone to give ammonium ozonide and not calcium ozonide:

`3 Ca + 10 NH_3 + 6 O3 → Ca·6NH_3 + $Ca(OH)_2$ + $Ca(NO_3)_2$ + 2 NH_4O_3 + 2 O_2 + H_2

Applications

Ozone can be used to remove manganese from water, forming a precipitate, which can be filtered:

$$2\ Mn^{2+} + 2\ O_3 + 4\ H_2O \rightarrow 2\ MnO(OH)_2\ (s) + 2\ O_2 + 4\ H^+$$

Ozone will also detoxify cyanides by converting them to cyanates, which are a thousand times less toxic.

$$CN^- + O_3 \rightarrow CNO^- + O_2$$

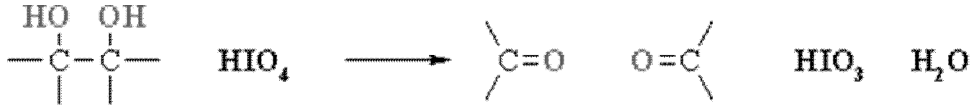
Ozone will also completely decompose urea:

$$(NH_2)_2CO + O_3 \rightarrow N_2 + CO_2 + 2\ H_2O$$

Periodic acid

Periodic acid, or iodic(VII) acid is an oxoacid of iodine having chemical formula HIO_4 or, in the more common hydrated form, H_5IO_6. "Periodic acid" is not derived from "period", but from "iodine"

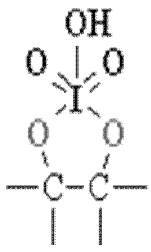
Oxidative Cleavage of Diols



Reaction type: Oxidation-reduction

Summary

- 1,2- or vicinal diols are cleaved by periodic acid, HIO_4, into two carbonyl compounds.
- The reaction is selective for 1,2-diols.
- The reaction occurs via the formation of a cyclic periodate ester (see right).
- This can be used as a functional group test for 1,2-diols.
- The products are determined by the substituents on the diol.



Tributyltin hydride

Tributyltin hydride is an organotin compound with the formula $(C_4H_9)_3SnH$. It is a colorless liquid that is soluble in organic solvents. The compound is used as a source of hydrogen atoms in organic synthesis.

The compound is produced by reduction of tributylin oxide with polymethylhydrosiloxane

$$2"(MeSiH)" + (Bu_3Sn)_2O \rightarrow "(Me_2Si_2O" + 2\ Bu_3SnH(Bu = CH_3CH_2CH_2CH_2):$$

$$(Bu_3Sn)_2O + 2/n\ (MeSi(H)O)_n \rightarrow 2\ Bu_3SnH + 1/n\ [(MeSiO)_2O]_n$$

The hydride is a distillable liquid that is mildly sensitive to air, decomposing to $(Bu_3Sn)_2O$. Its IR spectrum exhibits a strong band at 1814 cm^{-1} for ν_{Sn-H}.

Borane

Borane (also systematically named trihydridoboron), also called borine, is an inorganic compound with the chemical formula BH_3 (also written $[BH_3]$). It is a colourless gas that only persists at elevated temperatures or in dilution. Borane is the simplest member of the boranes

One example where molecular BH_3 is believed to be a reaction intermediate is in the pyrolysis of diborane to produce higher boranes.

$$B_2H_6 \rightleftharpoons 2BH_3$$

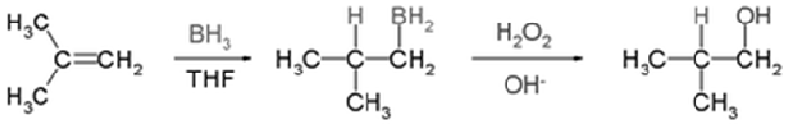
$$BH_3 + B_2H_6 \rightarrow B_3H_7 + H_2 \text{ (rate determining step)}$$

$$BH_3 + B_3H_7 \rightleftharpoons B_4H_{10}$$

$$B_2H_6 + B_3H_7 \rightarrow BH_3 + B_4H_{10} \rightleftharpoons B_5H_{11} + H_2$$

Further steps give rise to successively higher boranes, with $B_{10}H_{14}$ as the most stable end product contaminated with polymeric materials, and a little $B_{20}H_{26}$.

The general form of the reaction is as follows:

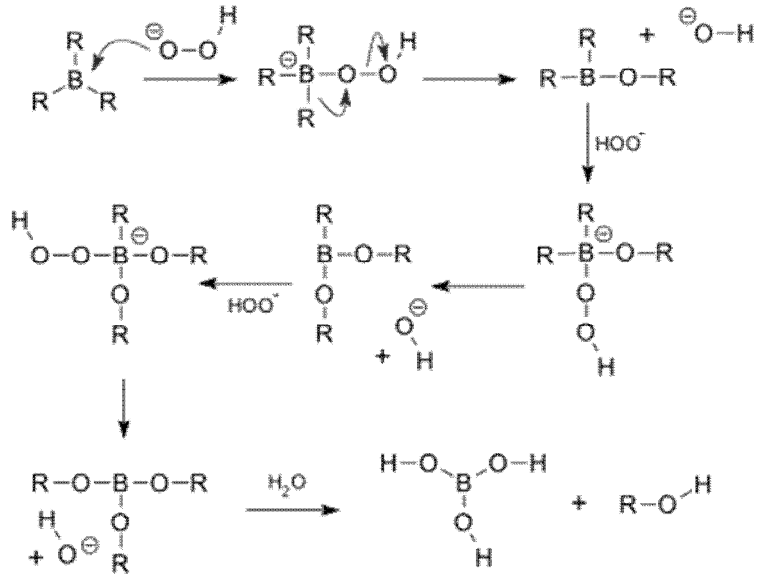


Tetrahydrofuran (THF) is the archetypal solvent used for hydroborations.

Oxidation step

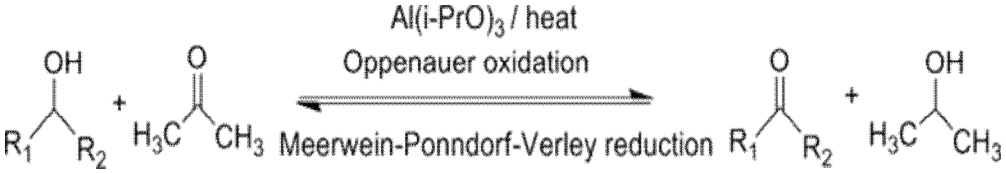
In the oxidation step of the reaction sequence, the nucleophilic hydroperoxide anion attacks the boron atom. Alkyl migration to oxygen gives the alkyl borane with

retention of stereochemistry (in reality, the reaction occurs via the trialkyl borate $B(OR)_3$, rather than the monoalkyl borinic ester BH_2OR).



Meerwein-Ponndorf-Verley Reduction

The Meerwein–Ponndorf–Verley (MPV) reduction in organic chemistry is the reduction of ketones and aldehydes to their corresponding alcohols utilizing aluminium alkoxide catalysis in the presence of a sacrificial alcohol. The beauty in the MPV reduction lies in its high chemoselectivity, and its use of a cheap environmentally friendly metal catalyst.



(Exchange of carbonyl oxidation states in the presence of aluminium isopropoxide)

The MPV reduction was discovered by Meerwein and Schmidt, and separately by Verley in 1925. They found that a mixture of aluminium ethoxide and ethanol could reduce aldehydes to their alcohols. Ponndorf applied the reaction to ketones and upgraded the catalyst to aluminum isopropoxide in isopropanol.

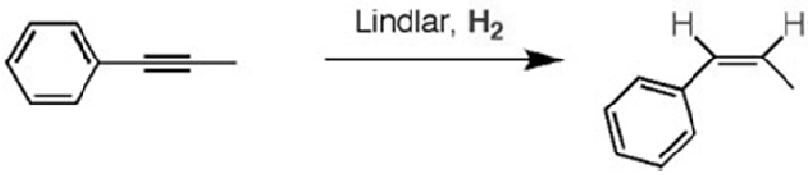
The aluminium-catalyzed hydride shift from the a-carbon of an alcohol component to the carbonyl carbon of a second component, which proceeds via a six-membered transition state, is referred to as the Meerwein-Ponndorf-Verley Reduction (MPV) or

the oppenauer oxidation depending on which component is the desired product. If the alcohol is the desired product, the reaction is viewed as the Meerwein-Ponndorf-Verley Reduction.

H_2/ CATALYST

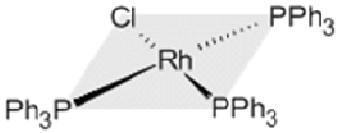
Lindlar's catalyst is a palladium catalyst poisoned with traces of lead and quinoline, that reduce its activity such that it can only reduce alkynes, not alkenes. It always gives the *cis*-alkene, in contrast to Na/NH_3, which gives the *trans* alkenes. Lindlar's catalyst doesn't really have a "structure". Like Raney nickel, it's basically a metal that has been modified in a very particular way to provide a certain desirable set of properties.

Examples: Reduction of alkynes to cis-alkenes



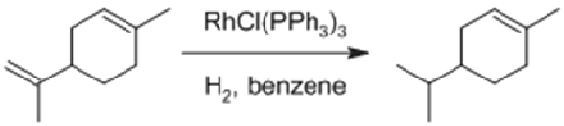
WILKINSON'S CATALYST

$RhCl(PPh_3)_3$ - Chlorotris(triphenylphosphine)rhodium(I), is known as Wilkinson's catalyst. It is used as a homogeneous hydrogenation catalyst. It is a square planar 16-electron complex. The oxidation state of Rhodium in it is +1.

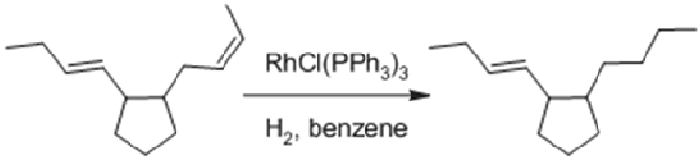


Wilkinson's catalyst can be used to achieve selective hydrogenations.

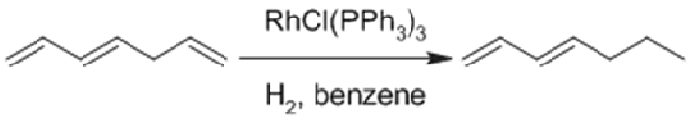
* Less substituted and sterically less hindered double bonds are selectively hydrogenated.



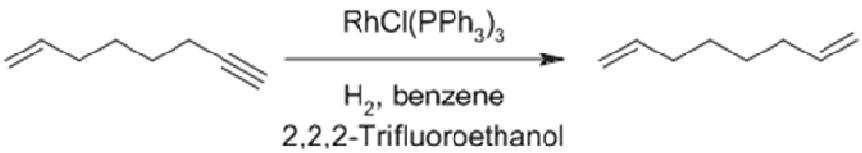
* Cis alkenes are reduced rapidly than trans alkenes.



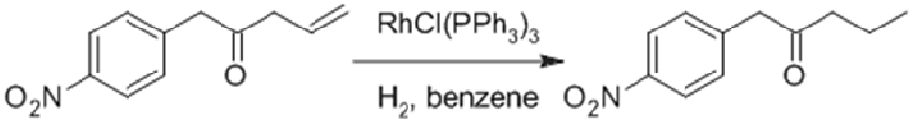
* Isolated double bonds are rapidly hydrogenated over conjugated dienes.



* Terminal alkynes are hydrogenated more rapidly than terminal alkenes. The selectivity can be enhanced by using acidic alcoholic co-solvents.



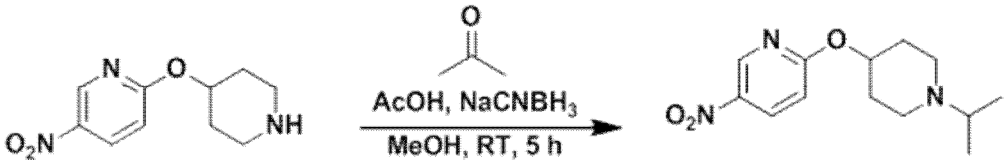
* Functional groups like C=O, C=N, NO_2, Aryl, CO_2R etc., are unaffected. The compatibility of Wilkinson's catalyst with polar multiple bonds indicates the metal hydride bond is primarily covalent in character.



Sodium cyanoborohydride

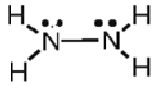
Sodium cyanoborohydride is the chemical compound with the formula (Na CN BH_3). It is a colourless salt, but commercial samples can appear tan. It is widely used in organic synthesis for the reduction of imines. The salt tolerates aqueous conditions.

Reducdtive Animation Examples:



It is especially favored for reductive amination, wherein aldehydes or ketones are treated with an amine in the presence of this reagent:

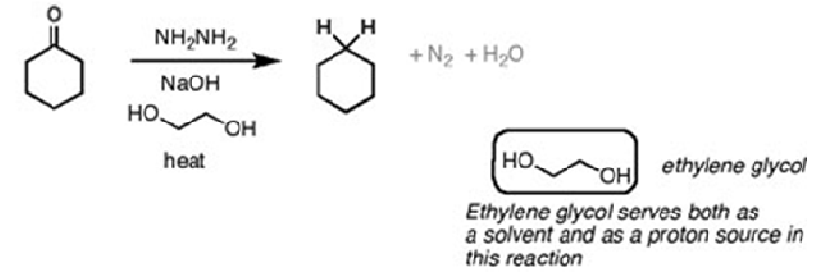
$$R_2CO + R'NH_2 + NaBH_3CN + CH_3OH \rightarrow R_2CH\text{-}NHR' + \text{"}NaCH_3OBH_2CN\text{"}$$



Hydrazine

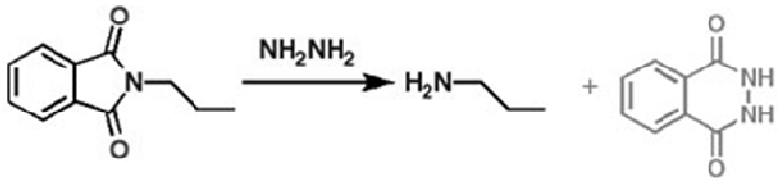
Hydrazine is dangerous. Not only is it toxic, but it is also potentially explosive. As a common component of rocket fuel, it can literally take you to the moon. See, every molecule of hydrazine yearns in its soul to one day shed its hydrogens so that it can become elemental nitrogen, N2, which makes it a powerful reducing agent it given the right conditions.

Example 1: The Wolff-Kishner reaction



Hydrazine is also used in the second step of the Gabriel synthesis, for liberating the new amine from the phthalyl group.

Example 2: In the Gabriel Synthesis

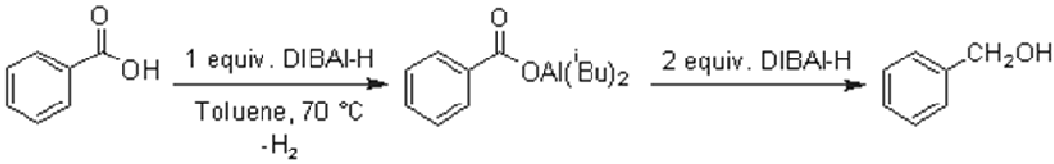


DIBAL-H, Diisobutylaluminium hydride

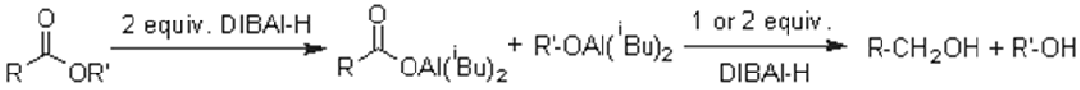
Diisobutylaluminium hydride **(**DIBALH**,** DIBAL**,** DIBAL-H or DIBAH**)** is a reducing agent with the formula $(i\text{-}Bu_2AlH)_2$, where *i*-Bu represents isobutyl (-$CH_2CH(CH_3)_2$). This organo aluminium was investigated originally as a co-catalyst for the polymerization of alkene.

Carboxylic acids require 3 moles of DIBAL-H for their conversion into alcohols at higher temperatures. One equivalent is consumed for the formation of salt of carboxylic acid. The rest for the conversion into alcohol.

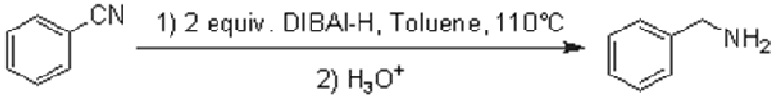
E.g. Benzoic acid requires 3 equivalents of DIBAL-H for its conversion into benzyl alcohol.



But in case of esters, 3 to 4 equivalents of DIBAL-H are required at ordinary temperatures. It may be due to formation of two alkoxyalumino intermediates, which then give corresponding alcohols.



E.g. Benzonitrile is reduced to Benzylamine when 2 equivalents of DIBAL-H are used at 110°C.



14.4 Summery

The Chapter deals with increasing the knowledge of learner about oxidation and reduction and their mechanism, their synthesis, reactions, applications and structure. This chapter also explain brief about different reagents with is a matter of recent research. Along with these chapter also highlights the different catalysts used in redox reaction.

14.5 Review Question / Comprehensive Questions

1. Define oxidation and reduction with by using jones reagent as a catalyst.
2. Write a note on Wilkinsons catalyst.
3. Give detail study and mechanism of reactions of Boranes nad hydroboranes.
4. Expalin the mechanism of workingP_b $(OAc)_4$
5. Give the oxidation and reduction reactions of O_3.

14.6 References and Suggested readings

1. J. Lee, T. Ryu, S. Park, P. H. Lee, *J. Org. Chem.*, **2012**, *77*, 4821-4825
2. M. M. Mojtahedi, E. Akbarzadeh, R. Sharifi, M. S. Abaee, *Org. Lett.*, **2007**, *9*, 2791-2793
3. N. K. Jana, J. G. Verkade, *Org. Lett.,* **2003**, *5*, 3787-3790

Unit-15 : Reactive Intermediates

Structure of Unit:

15.1 Objectives

In this unit the students will be able to

- Understand the chemistry of different intermediates involved in organic reactions.
- Get knowledge about the stability of the intermediate radicals and ions.
- Learn the mechanism of the reactions in which the intermediate species are formed and these species react to form products.
- Understand the difference between carbocation, cabanion and carbenes.

15.2 Introduction

The chemistry of reactive intermediates is central to a modern mechanistic and quantitative understanding of organic chemistry. The knowledge of intermediates formed during the reaction is necessary for treating the mechanisms of important classes of organic reactions. The primary focus of the unit is on the five types of intermediate species formed in organic reactions. The five types of species are carbocations, carbanions, carbenes, nitrenes and free radicals. Each of the five types is discussed in a separate part, which in each case includes short summaries of the ways in which these species are formed and react.

15.3 Carbocations

A species containing a positively charged carbon atom is called a **carbocation or carbenium.** ion Carbocations were formerly called carbonium ions and you can see this term in older chemical literature. Carbocations have only six electrons in their valence shell making them electron deficient. Thus, they are unstable electrophiles and will react very quickly with nucleophiles to form new bonds. Because of their high reactivity towards heteroatoms, carbocations are very useful intermediates in many common organic reactions.

Nomenclature

In 1902 Gomberg suggested that the word carbonium was inappropriate for such species because "onium" signifies a covalency greater than that of the neutral atom. But the nomenclature went on as it was well established until about 1964 when George Olah and his coworkers found evidence for the existence of a positively charged intermediate, the CH_5^+ ion. It was supposed to have been formed by the attack of H+ on C—H bond to give the species CH_5^+ which was also called the methanonium ion. This cation shares eight electrons among five bonds and has a full outer shell like that of the ammonium ion NH_4^+. Olah also proposed the term ''carbocation'' to include both types and International Union of Pure and Applied Chemistry (IUPAC) has accepted these definitions.

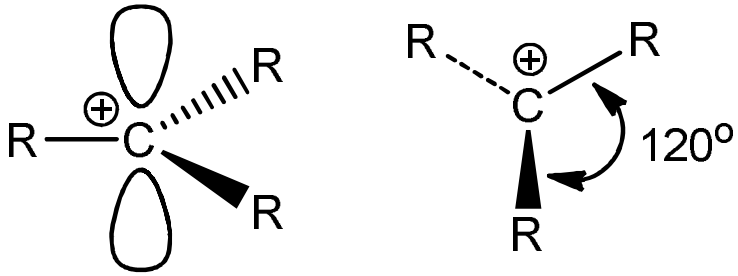
Although pentacovalent ions of carbon are much rarer than other positively charged ions, the general word carbocation is used to avoid confusions. The difference between carbenium and carbonium ions is summarized in the Table 1.

Property	**Carbenium ions**	**Carbonium ions**
Number of covalent bonds with C^+	**3**	**5**
Number of electrons in outer shell	**6**	**8**
Electron deficiency	**Electron deficient**	**Not electron deficient**
Empty orbital	**One p orbital**	**No p orbital**

The simplest example of a carbenium ion is CH_3^+, the methyl cation, and it would be planar with an empty p orbital. The CH_3^+ cation is so unstable that it is rarely formed even in the gas phase.

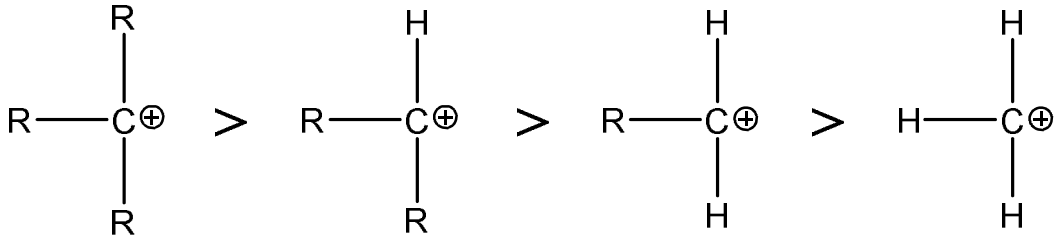
Structure and stability of carbocation

The orbitals of carbocations are generally sp^2 hybridized and it uses its all three hybridized orbitals for the formation of bonds with other atoms. The remaining p orbital is empty and perpendicular to the plane of the other three bonds. The empty p orbital will readily accept a pair of electrons from another atom. Because of the symmetry of this geometric arrangement, nucleophilic attack is equally favorable above or below the plane formed by the field Sp^2 hybrid orbitals. A carbocation is planar (or trigonal coplanar) with the bond angle of 120°.



Carbocation

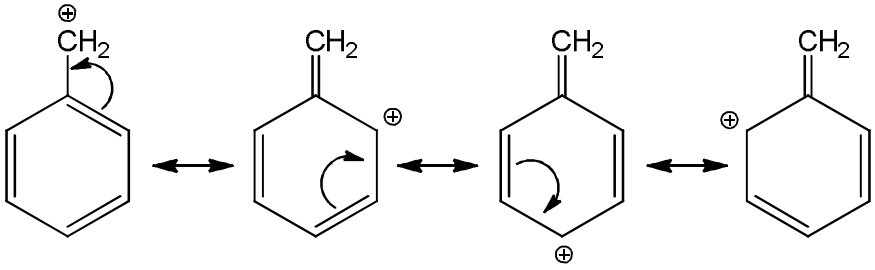
Carbocations are usually unstable and comparatively difficult to form. They generally cannot be isolated from a reaction as they will react immediately to fill their empty p orbital. Because they are electron deficient, if an electron donating group (such as alkyl groups) is present adjacent to the carbon atom bearing positive charge, then the stability of the carbocation increases. This is the reason that a tertiary carbocation is more stable than a secondary carbocation which sequentially is more stable than a primary carbocation. Therefore an ethyl carbocation ($CH_3CH_2^+$) is more stable than methyl carbocation (CH_3^+)



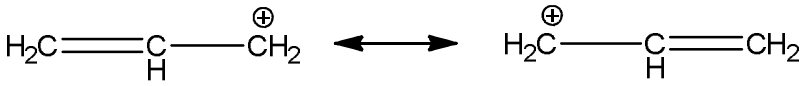
There are two main factors which affect the stability of the carbocations. The first is the inductive effect of electron donating alkyl groups, the more alkyl groups attached to the carbon atom; the greater is the stability of carbocation. The second factor is the hyperconjugation, during hyperconjugation some charge delocalization occurs between the p orbital of the positively charged carbon and the σ bonding orbital of the β C-H. the stability of the carbocations decreases in the presence of electron

withdrawing gropus (such as nitro, carbonyl etc.) adjacent to the carbon atom having positive charge.

The stability of a carbocation can also be explained by resonance. An increase in the canonical forms for a carbocation, increases the stability of it. Due to resonance the positive charge gets dispersed over other carbon atoms and increases the stability of the carbocation.



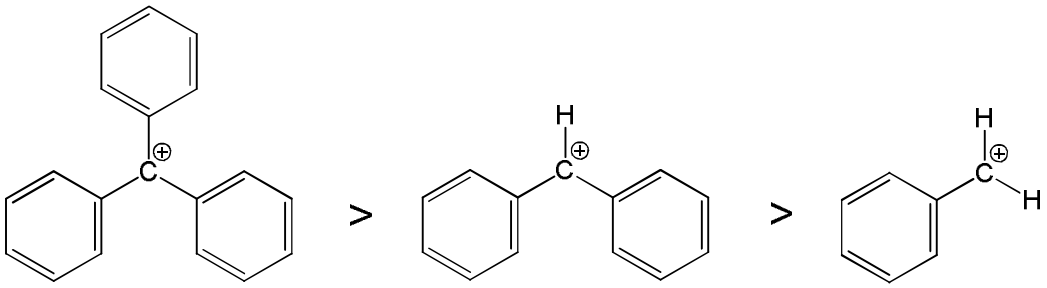
Benzyl carbocation (four canonical structures)



Allyl carbocation (two canonical structures)

Thus, the order of stability is:

Triphenylmethyl carbocations are so stable because the positive charge on the carbon is distributed equally over a number of structures.

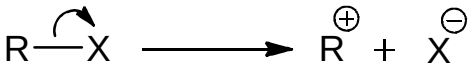


The salts of both triphenylmethyl and diphenylmethyl carbocations can be isolated and stored.

Generation of carbocations

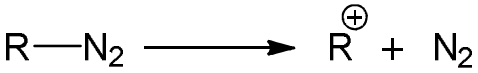
Numerous methods are available to generate carbocations.

1. The direct ionization of alkyl halides produces carbocations.

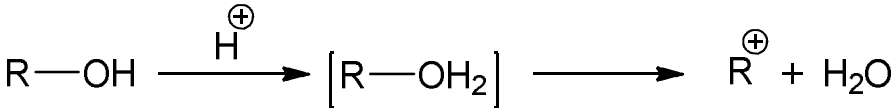


X = Cl, Br, I

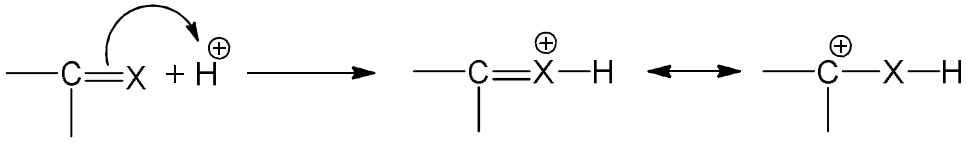
2. Decomposition of alkyl diazonium ion generates carbocation.



3. The protonated alcohols upon decomposition produce carbocations.



4. A positively charged species adds to one atom of an unsaturated system (C=X) leaving a positive charge on the adjacent carbon.



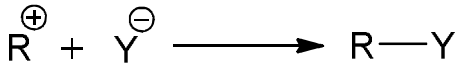
X = O, S, N

Reactions of carbocations

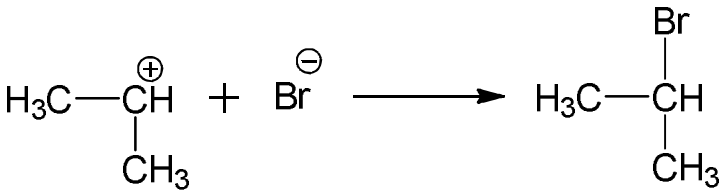
The carbocations are highly reactive species and undergoes following reactions to provide stable products:

1. **Reaction with nucleophiles**

   Carbocations will react with even mild nucleophiles (e.g. water) to form a new bond.

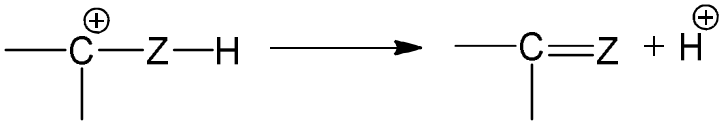


Y = OH-, halide ion or a neutral species.



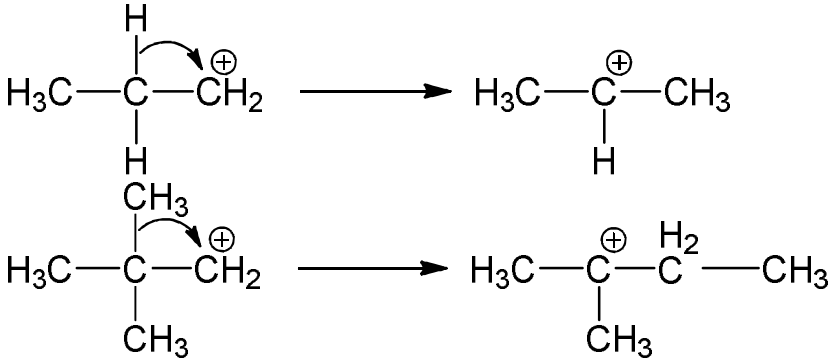
2. **Elimination of a proton**

   The carbon adjacent to the carbocation often loses a proton to form a double bond (or, in some cases triple bond) with the carbocation.



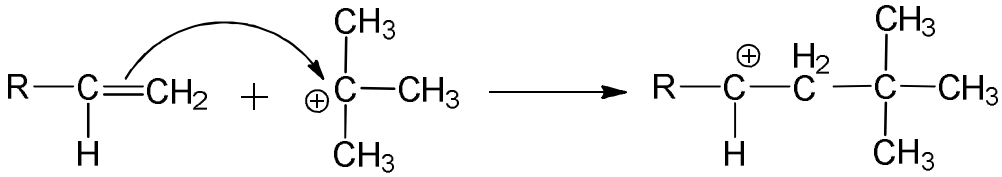
3. **Rearrangement**

Rearrangement involves the migration of an alkyl or aryl group or a hydrogen (sometimes another group) with its electron pair to the positive center, leaving another positive charge behind. The migration of hydrogen with its pair of electron is called **hydride shift** and the migration of alkyl group with its pair of electron is called **alkyl shift**.



4. **Addition**

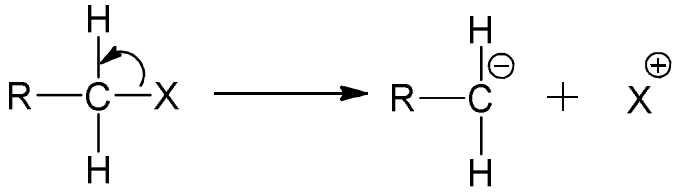
A carbocation may add to a double bond producing a positive charge at a new position. The new carbocation reacts further with a nucleophile or losses a proton to stabilize itself.



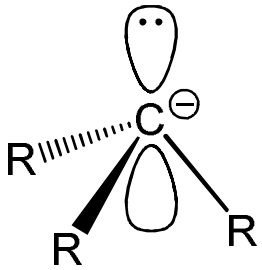
Numerous reactions have been explained on the basis of generation of carbocations e.g. Friedel-Craft alkylation and arylation, Beckmanns rearrangement, Wagner-Merweins rearrangement etc.

15.4 Carbanions

A species containing a negatively charged carbon atom is called a **carbanion**. The carbanions are generally formed by the heterolytic cleavage of C-X bond.

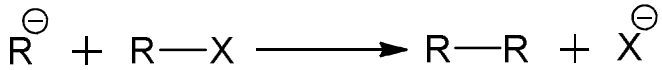


Carbanion is a tricovalent carbon with a pair of electrons and found to have a pyramidal geometry. The negatively charged carbon is in sp^3 hybridization, but when it is stabilized by delocalization, the hybridization changes to sp^2.

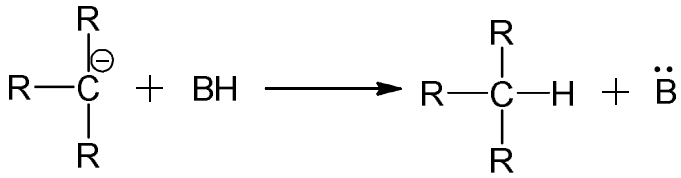


Stability of carbanions

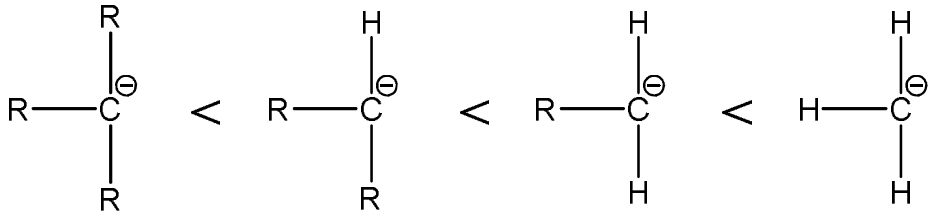
Carbanion is an electron-rich and highly reactive intermediate species involved in many important reactions in organic synthesis. Carbanions can be stabilize by combining with a variety of electrophiles and form compounds having carbon-carbon bonds in high yield.



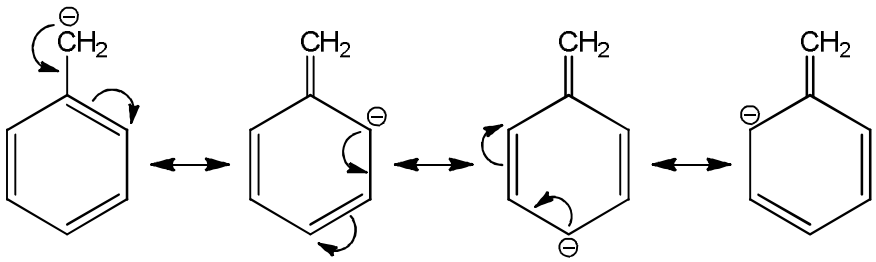
Due to the presence of an unshared pair of electron carbanion can function as a base and can abstract a proton to form a conjugate acid.



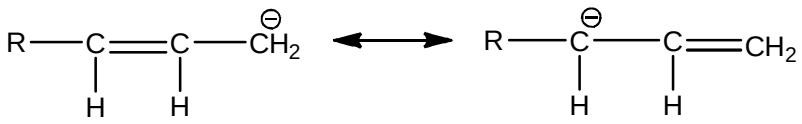
Carbanions can be stabilised by electron-withdrawing groups. The order of the stability of carbanions is as follows:



Like carbocations, the carbanions are also stabilized by resonance. The benzyl carbanion has been found to be most stable due to the delocalization of the negative charge over the various resonating structures.

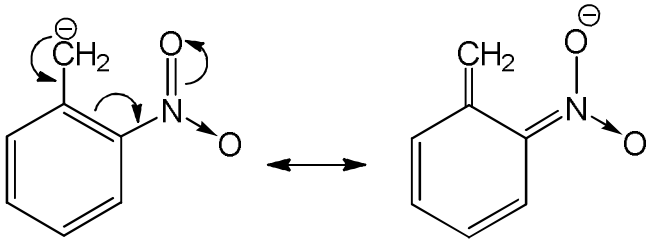


Benzyl carbanion (four canonical structures)



Allylic carbanion (two canonical structures)

The stability of carbanions increases due to the presence of electron withdrawing groups such as NO_2, -CN or carbonyl groups in the molecule.



The stability of the carbanion in presence of a functional group, in the α-position is of the order:

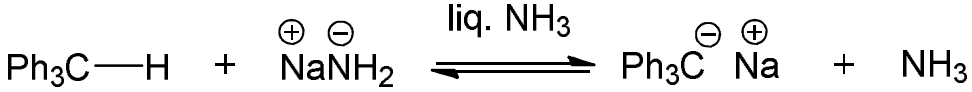
$NO_2 > RCO > COOR > SO_2 > CN = CONH_2 >$ halogens $> H > R$

Generation of carbanions

In a large number of organic reactions carbanions have been generated as reactive intermediates. Following methods are available to generate carbanions.

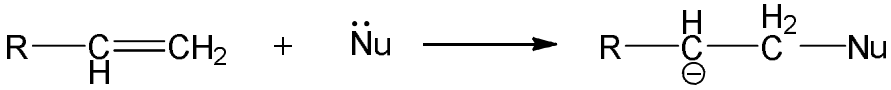
1. **Abstraction of hydrogen by a base**

   In the presence of a suitable base an organic substrate having a C-H bond results in the abstraction of hydrogen to generate carbanion. A simple example is the formation of triphenylmethyl carbanion by $NaNH_2$ in presence of liquid ammonia.



2. **From unsaturated compounds**

   The carbanions can be generated by the addition of a nucleophile to an unsaturated C-C bond.

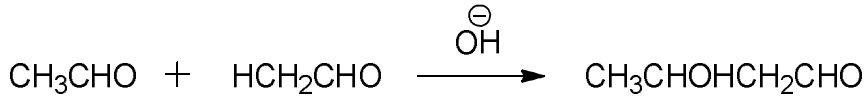


Reactions of carbanions

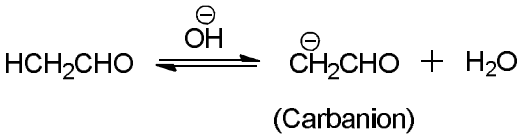
Carbanions are highly reactive and undergo reaction as soon as they are formed. Carbanions take part in the general types of reactions such as addition, elimination, substitution, rearrangement etc.

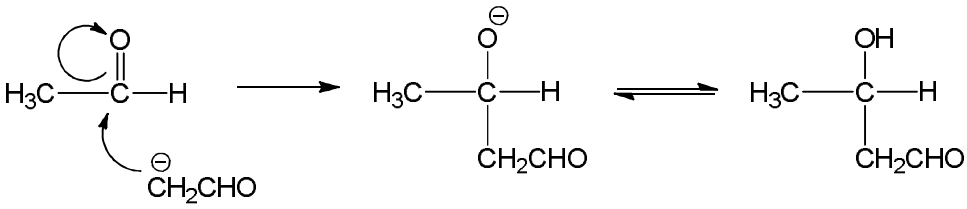
1. **Addition reactions**

The carbanions act as a nucleophile and add to the carbonyl group of aldehydes or ketones (e.g. **aldol condensation**).



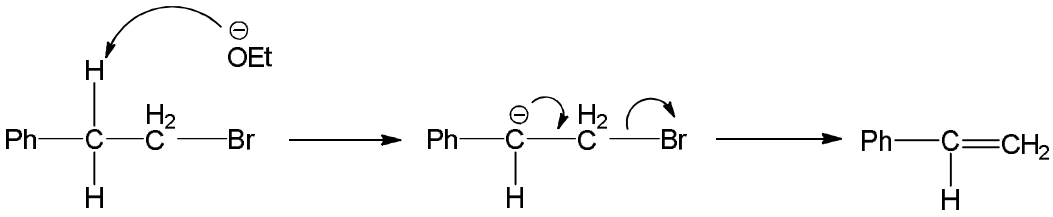
Mechanism:





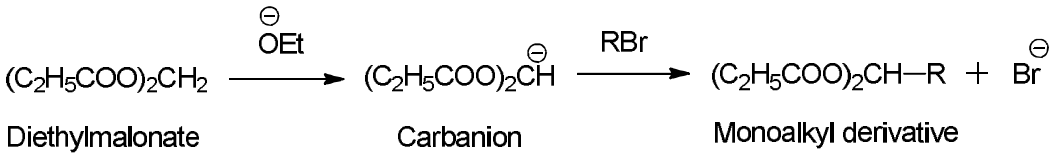
2. Elimination reactions

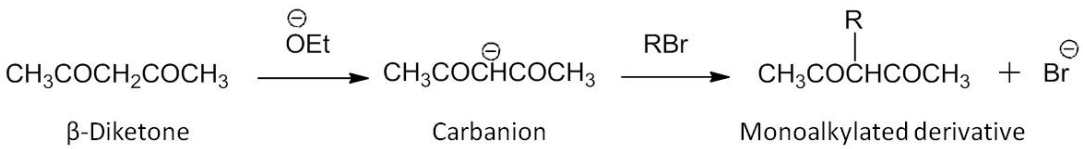
Carbanions are also involved as intermediates in elimination reactions. For example, when β-phenylethyl bromide is treated with a suitable base (like NaOEt) first a carbanion is formed by the loss of a proton followed by the loss of a halide ion and simultaneous formation of a double bond.



3. Substitution reactions

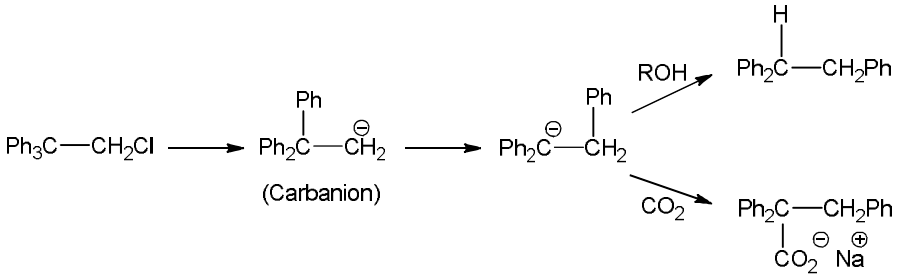
The carbanions are involved in numerous substitution reactions.





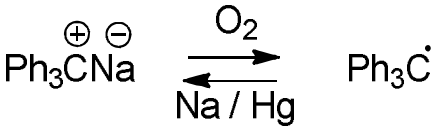
4. Rearrangement reactions

The rearrangement reactions of the carbanions are less common in comparison to the carbocations. As in the example below the carbanion formed undergoes rearrangement and may react with an alcohol or carbon dioxide to give the final products.

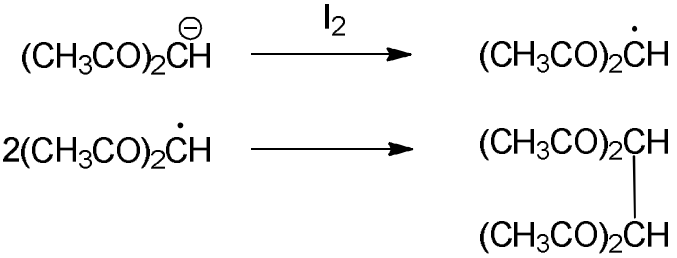


5. Oxidation

The carbanions can be oxidized under suitable conditions. The triphenylmethyl carbanion is oxidized slowly by air and the resulted radical can be reduced back to the carbanion by shaking with sodium amalgam.



In suitable cases, the carbanion can be oxidized with one-electron oxidizing agents (e.g., iodine),

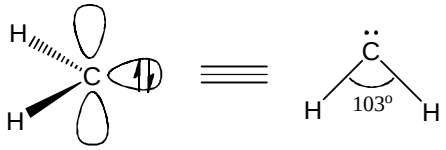


15.5 Carbenes

Carbenes are highly reactive species having lifetimes considerably less than one second. The parent species **:**CH_2 is usually called *methylene*, although derivatives are more often named by the carbene nomenclature. For example, **:**CCl_2 is generally known as dichlorocarbene. However, it can also be called dichloromethylene.

Carbenes are electron deficient species having six electrons analogous to carbocation. As carbenes are electron deficient, they can act as powerful electrophiles. As the same time, they can also be thought of acting as nucleophiles, because they contain an unshared pair of electrons. The two nonbonded electrons of a carbene can be either paired or unpaired. If both the electrons are paired (antiparallel spin), the

carbene is in *singlet* state, while if the two electrons are unpaired (parallel spin), the carbene is in *triplet* state.



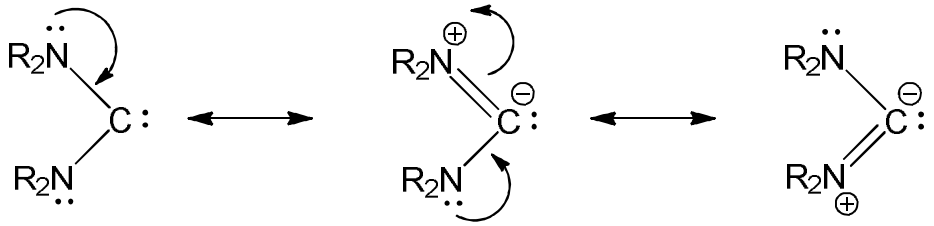
Singlet state of carbene

Triplet state of carbene

In singlet state, the carbon atom is sp^2 hybridized. The two sp^2 hybridized orbitals are bonded to two hydrogen atoms and the third contains a lone pair of electrons, thus, a singlet carbene is diamagnetic. The bond angle is 103° and C-H bond length is 1.12 Å.

In triple state, the carbon atom is sp hybridized. The two sp hybridized orbitals are bonded to two hydrogen atoms and the two unhybridized p-orbitals contain one electron each, thus, a triplet carbene is paramagnetic. The bond angle is 136° and C-H bond length is 1.03 Å. Since the triplet carbene is paramagnetic, it is has been investigated by the electron paramagnetic resonance spectroscopy.

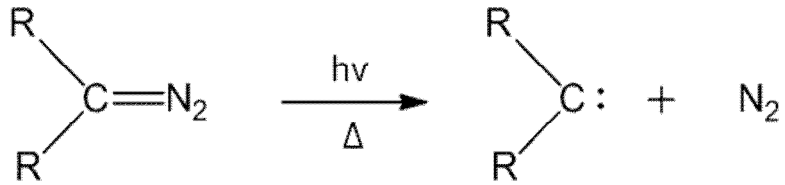
The carbrnes in which the carbon atom is attached to two atoms, each bearing a lone pair of electrons, are more stable because of resonance.



Generation of carbenes

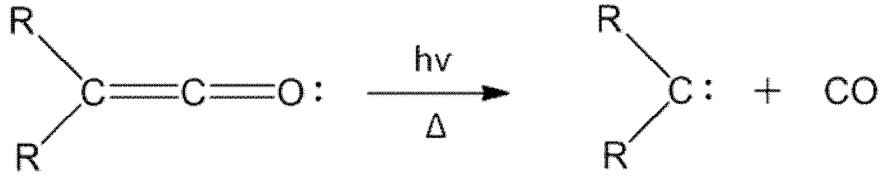
1. **From aliphatic diazo compounds**

   Aliphatic diazo decomposes photolytically or thermally to generate carbenes.



2. **From ketenes**

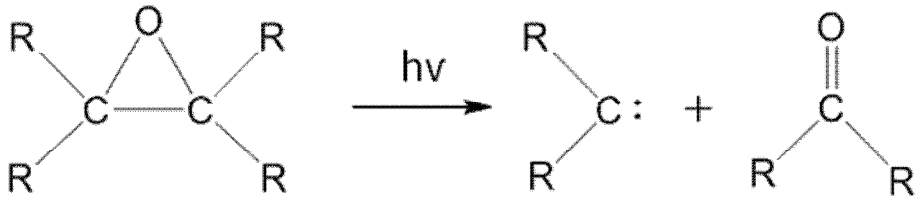
   Ketenes can be decomposed photolytically or thermally to generate carbenes.



   The ketenes can be obtained by the pyrolysis of acetone or from diazoketones.

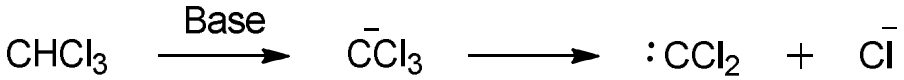
3. **From epoxides**

Photolytic decomposition of epoxides generate carbenes.



4. From alkyl halides

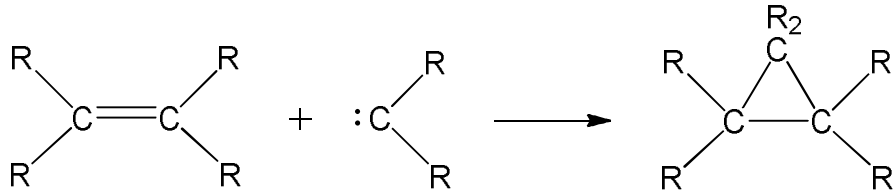
This method is usually used for the generation of chlorocarbenes.



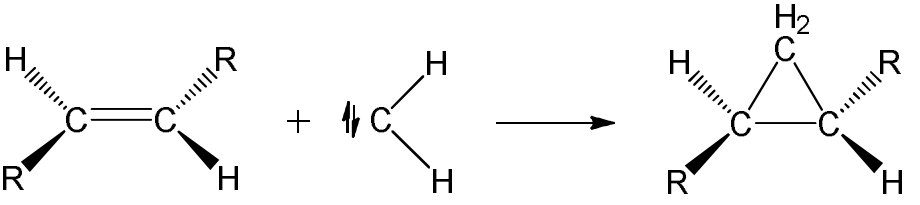
Reactions of carbenes

1. Cycloadditions

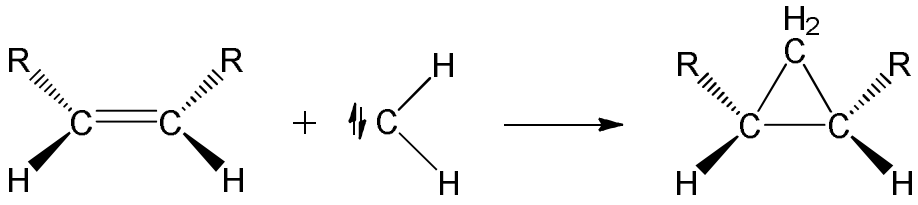
Addition of carbenes to an olefinic double bond produces a cyclopropane derivative.



In a liquid medium singlet carbene is generated, which adds in a stereospecific manner. For example, cis-alkene gives cis-cyclopropane and trans-alkene gives trans-cyclopropane.

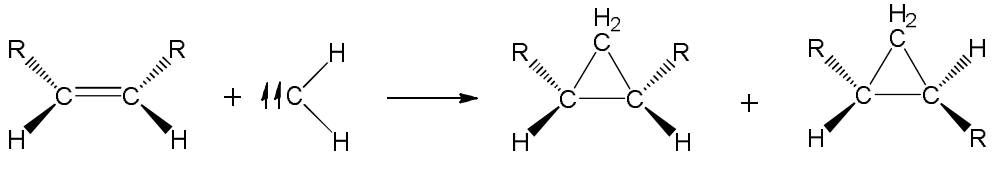


trans-alkene singlet carbene *trans*-cyclopropane



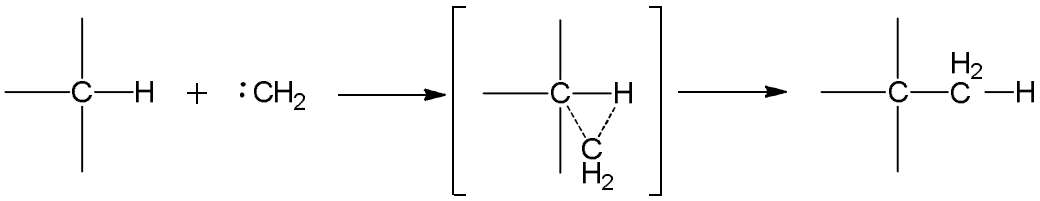
cis-alkene singlet carbene *cis*-cyclopropane

In gaseous medium triplet carbene is generated, which does not add stereospecifically.

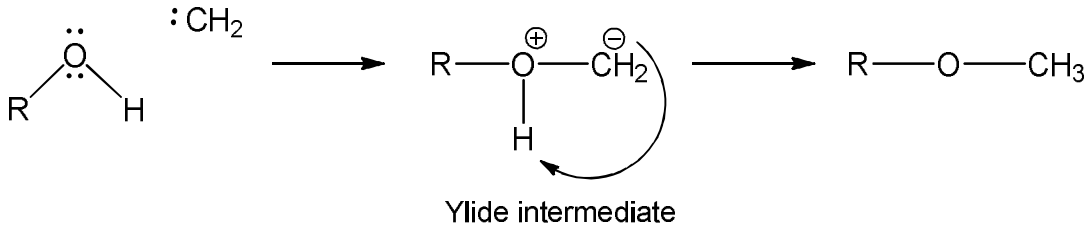


2. Insertion reactions

The carbene can insert into a C-H bond and forms a new C-C bond.

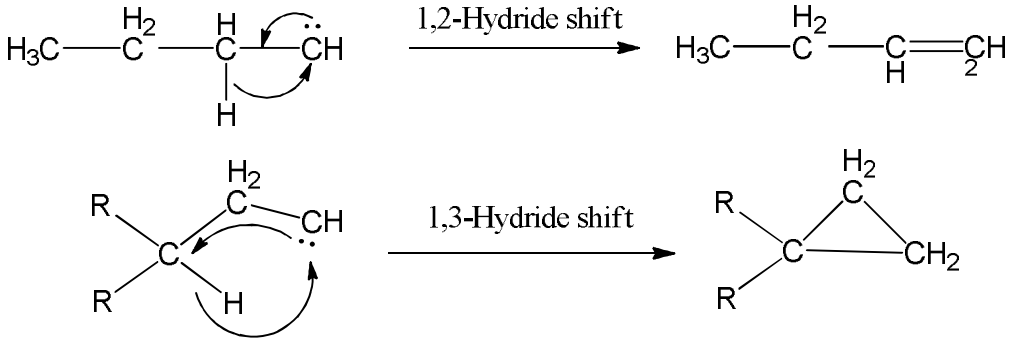


Carbenes can also insert into other single bonds (such as O-H and N-H bonds).



3. Rearrangements

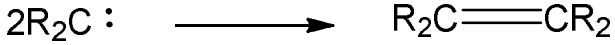
Carbenes can undergo facile rearrangement in which an atom or group on the adjacent carbon migrates to electron deficient carbon with simultaneous formation of a new C-C double bond (1,2-shifts).



Skattebol rearrangement and rearrangements also involve carbene rearrangement.

4. Dimerization

Carbene can couple with another carbene to form alkenes.



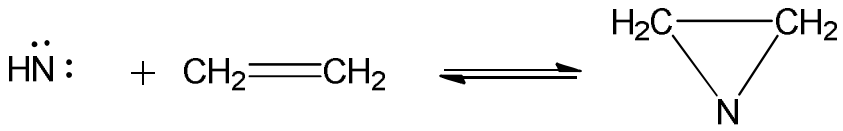
15.6 Nitrenes

Nitrenes are the nitrogen analogues of carbenes. Nitrenes are electron deficient monovalent nitrogen intermediates. Nitrogen atom in nitrenes has a sextet of electrons. Like carbenes, nitrenes can exist in singlet and triplet states.

Singlet Triplet

Nitrenes are highly reactive intermediates and cannot be isolated. However, a nitrene can be trapped by its reaction with carbon monoxide to produce an isocyanate.

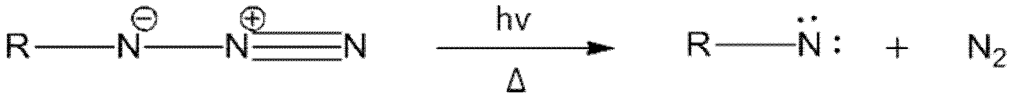
Nitrenes can also be trapped by ethylene.



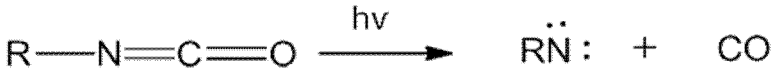
Generation of nitrenes

1. **From azides**

   Photolytic or thermal decomposition of azides generate nitrenes.

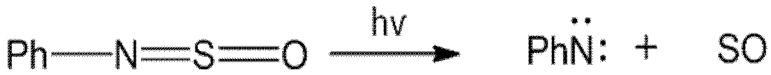


   Photolysis of acyl azides and isocyanates produces acyl and alkyl nitrenes.



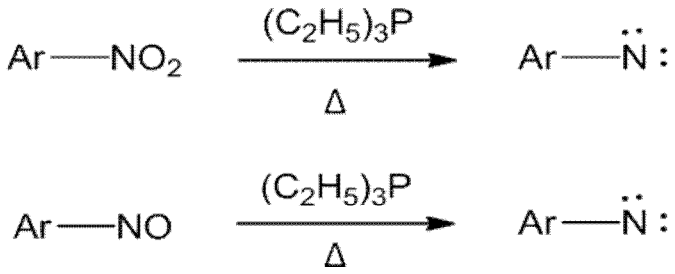
2. **From sulfinylamines**

   Nitrenes can be obtained by the pyrolysis of sulfinylamines.



3. **From nitro and nitroso compounds**

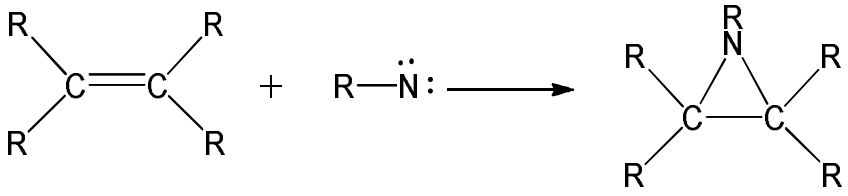
   Nitrenes can be generated by the deoxygenation of nitro and nitroso compounds. Various reagents have been used for the deoxygenation but the best results were obtained with triethylphosphite.



Reactions of nitrenes

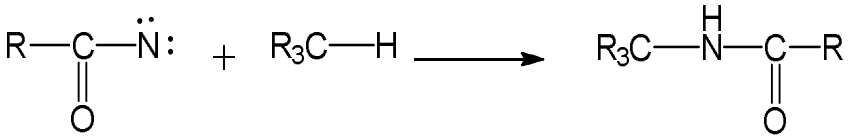
1. **Addition to alkenes**

   Alkenes are electron rich (nucleophile) and nitrenes are electron deficient (electrophile), thus addition reaction takes place between alkene and nitrene. Stereochemistry of the product depends on the spin state of nitrene. The addition is stereospecific with singlet and non-stereospecific with triplet nitrenes.



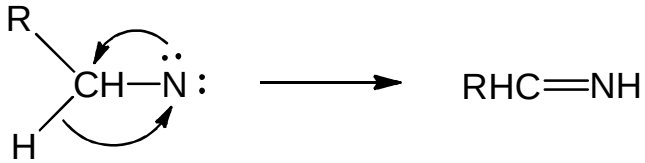
2. **Insertion reactions**

   Nitrenes, especially acyl and sulfonyl nitrenes, undergo insertion reactions into C-H bonds. Insertion reaction of nitrenes is an usful way of converting hydrocarbons into amine derivatives.



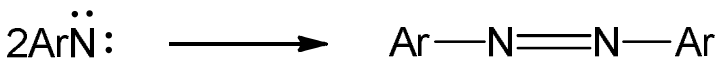
3. **Rearrangement reactions**

   Alkyl nitrenes generally do not give addition or insertion reactions because rearrangement is more rapid.



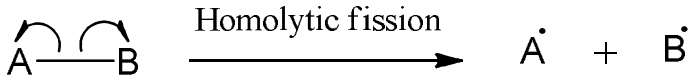
4. **Dimerization**

   The dimerization of aryl nitriles give azobenzene.



15.7 Free radicals

A free radical may be defined as a species that contains one or more unpaired electrons. Free radicals are generated by the homolytic fission of a covalent bond. The two departing atoms take one electron of the bonding pair of electrons and carry an odd electron each. The term free radical is used for any species which possess an unpaired electron (single nonbonding electron). These radicals react with other radicals or molecules by gaining one more electron to form stable bonding pair.



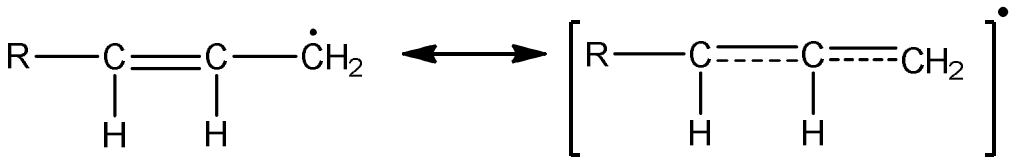
A free radical is a paramagnetic species and can be detected by electron paramagnetic resonance spectroscopy. For simple free radicals two structures are possible. One is a planar sp^2 hybridized radical, similar to carbocation and the other one is a pyramidal sp^3 hybridized radical, similar to a carbanion.

Planar (sp^2) Pyramidal (sp^3)

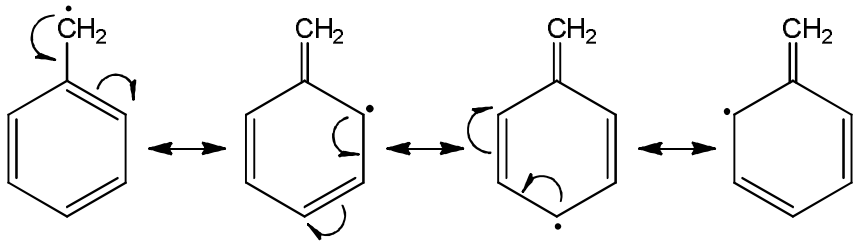
The structure of the carbon radical is difficult to predict. The geometry of the radials depends upon the groups and atoms attached to the carbon atom having the odd electron. For example methyl free radical is planar, while trifluoromethyl free radical is pyramidal.

Stability of free radicals

The stability order of free radicals is: tertiary > secondary > primary. This stability order can be explain on the basis of hyperconjugation similar to carbocations. The stability of the free radicals also depends on the resonance possibilities. Due to resonance allylic and benzylic free radicals are more stable and less reactive in comparison to the simple alkyl radicals.

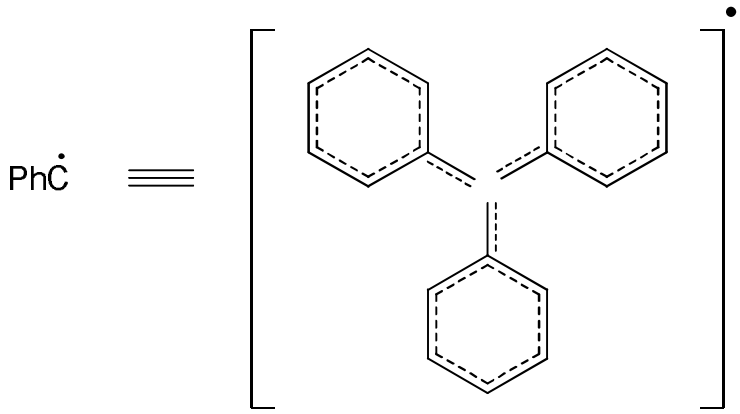


Allylic free radical (two canonical structures)



Benzyl free radical (four canonical structures)

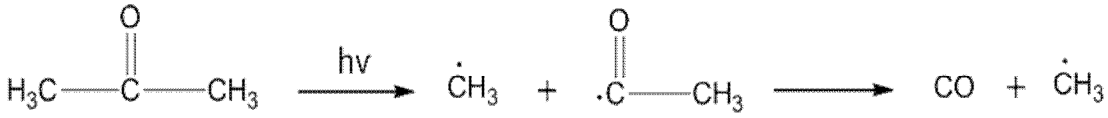
The stability of a radical increase as the extent of potential delocalization increases. Thus, $Ph_3C^{\bullet}$ is more stable in comparison to $Ph_2CH^{\bullet}$ and $PhCH_2^{\bullet}$ radicals. The extent of delocalization is maximum in $Ph_3C^{\bullet}$ than in $Ph_2CH^{\bullet}$ and in $PhCH_2^{\bullet}$. Triphenylmethyl free radical was the first known stable free radical. Steric hindrance is also the major cause of the stability of triphenylmethyl-type radicals.



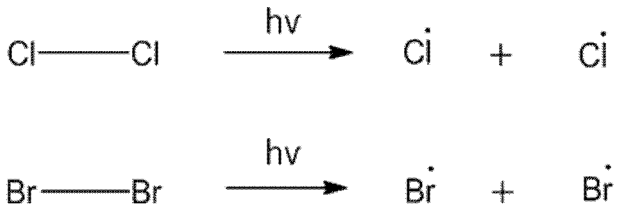
Generation of free radicals

1. **By photochemical cleavage**

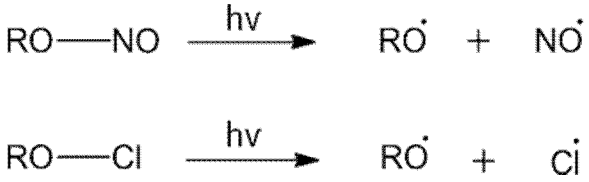
   A suitable organic molecule is subjected to UV radiation and the molecule absorbs the radiation in the ultra-violet or visible range. The cleavage of the molecule into two parts occurs and this process is known as photolysis. For example, acetone in vapour phase is decomposed by light having a wave length of about 320 nm to generate two molecules of methyl free radicals.



   The photochemical cleavage of halogen molecules is also very well known.

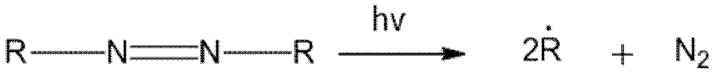


Some other species such as alkyl nitrites and alkyl hypochlorites can easily undergo photolysis.

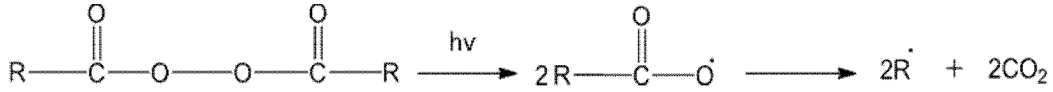


For the generation of free radicals the photolysis method has following advantages over the thermolysis method.

(a) Photolysis can cleave strong bonds which are difficult to cleave by thermolysis.

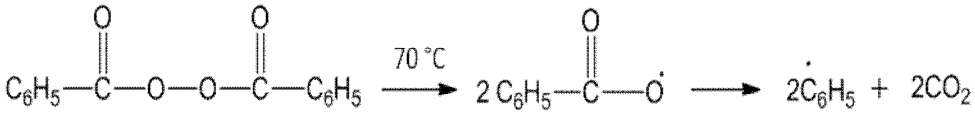


(b) In photolytic cleavage energy of only one particular wavelength is transferred to molecule and in this way photolysis is a specific method for homolytic fission than thermolysis.

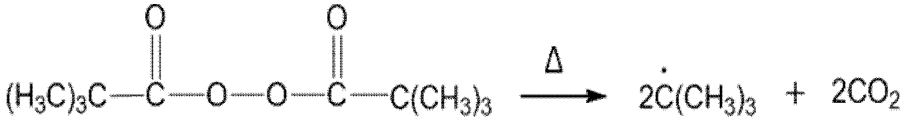


2. By thermolysis

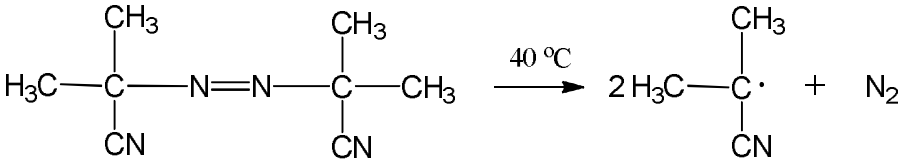
In thermolysis, the organic substrate is heated at suitable temperature to generate free radicals.



Benzoyl peroxide



Di-t-Butyl peroxide

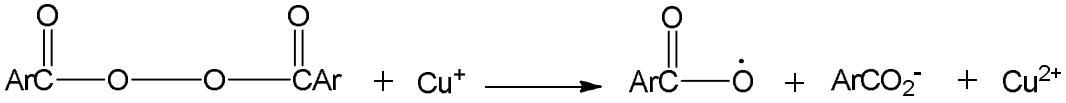


Azobisisobutyronitrile(AIBN)

Benzoyl peroxide and azobisisobutyronitrile (AIBN) are used as a free radical initiator in a number of organic reactions. The free radical initiators are responsible for the propagation of the reactions.

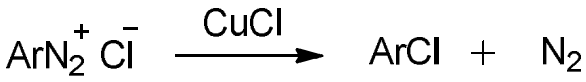
3. **By redox reactions**

   Redox reactions involve one-electron transfer to generate the free radicals. The source of one-electron transfer is the metal ion (e.g. Cu^{+}, Fe^{2+} etc.).

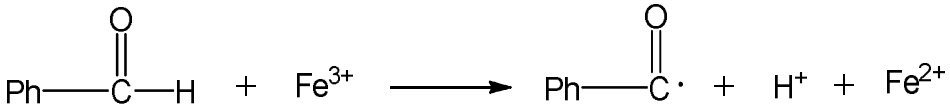


   This is a suitable method for the generation of $ArCOO^{\bullet}$ radicals because in thermolysis this radical further decomposes to generate $Ar^{\bullet}$ radical.

   Sandmeyer reaction also involves Cu^{+} for the decomposition of diaazonium salts. In this reaction the free radical $Ar^{\bullet}$ is generated as an intermediate.



   The autoxidation of benzaldehyde is also catalysed by metal ions.

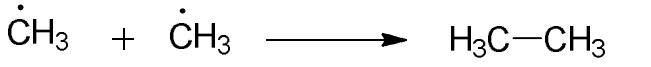


Reactions of free radicals

Free radicals are highly reactive intermediates and their half-life period is very short. Since free radicals have a odd electron, these have the natural tendency to pair their odd electron. A free radical may couple with other free radical or attack on a electrically neutral molecule to generate a new free radical. Free radicals have the following reactions:

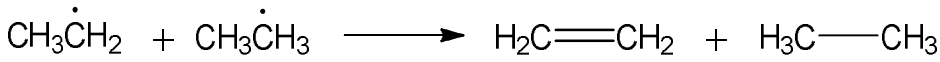
1. **Recombination**

   The free radicals may recombine to give hydrocarbons.



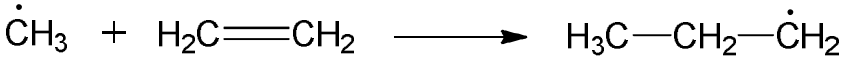
2. **Disproportionation**

   Alkyl radical may undergo disproportionation at higher temperature. The ethyl radical takes up hydrogen from another free radical to provide ethylene and ethane.

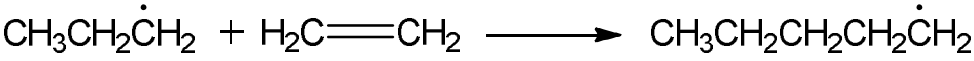


3. **Reactions with olefins**

   The alkyl radicals react with olefins to generate new free radicals.



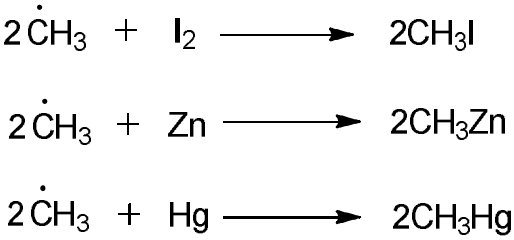
   This newly formed radical further attack on another olefin molecule.



The reactions continues till the formed radical couples with another free radical and termination of the reaction takes place.

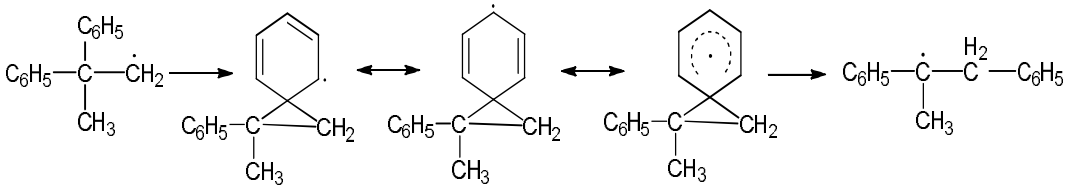
4. **Reactions with iodine and metals**

   The alkyl radicals may combine with iodine or other elements to form alkyl derivatives.



5. **Rearrangement**

   The free radicals undergo rearrangements involving 1,2-shifts of aryl group *via* bridgehead intermediate.



15.8 Summary

Four types of organic species are there in which the valency of carbon atom is either 2 or 3. These species are carbocation, carbanion, carbene and free radical. These species are highly reactive and mostly exist as intermediates in the reactions. Besides these species there is one more species called nitrene which is the nitrogen analog of carbene. In this unit we have discussed the structure, stability, generation and reactions of these reaction intermediates.

- A species containing a positively charged carbon atom is called a **carbocation or carbenium.**

- The orbitals of a carbocation are sp^2 hybridized and the geometry is planar (or trigonal coplanar).
- The order of the stability of carbocations is:
  tertiary carbocation > secondary carbocation > primary carbocation
- A species containing a negatively charged carbon atom is called a **carbanion**.
- The orbitals of a carbanion are sp^3 hybridized and the geometry is pyramidal (such as amine).
- The order of the stability of carbanions is:
  primary carbanion > secondary carbanion > tertiary carbanion
- Carbenes are electron deficient species contain an unshared pair of electron.
- If both the electrons are paired (antiparallel spin), the carbene is in *singlet* state, while if the two electrons are unpaired (parallel spin), the carbene is in *triplet* state.
- In singlet state, the carbon atom is sp^2 hybridized
- In triple state, the carbon atom is sp hybridized
- Nitrenes are the nitrogen analogues of carbenes and can also exist in singlet and triplet states.
- Free radicals are generated by the homolytic fission of a covalent bond and contain an unshared electron.
- A free radical is a paramagnetic species and can be detected by electron paramagnetic resonance spectroscopy.
- A free radical can have planar (sp^2) geometry, similar to carbocation or pyramidal (sp^3), similar to a carbanion.
- The stability order of free radicals is:
  tertiary radical > secondary radical > primary radical

15.9 Review questions / Comprehensive Questions

1. What are carbenes? Discuss their structure and generation.
2. Write a note on the stability of carbocation and carbanion.
3. Discuss the generation and reactions of nitrenes.
4. What are free radicals? Write the methods of generation of free radicals.
5. Write a detail note on the carbocations.
6. Discuss the structure, stability and reactions of carbanions.

15.10 References and Suggested readings

1. March's Advanced Organic Chemistry (7^{th} ed.)- M. Smith and J. March (John Wiley & Sons, Inc., Hoboken, New Jersey) 2007.
2. A Guidebook to Mechanism in Organic Chemistry (6th ed.)- Peter Sykes (Longman Technical & Scientific) 1985.
3. Organic Reaction Mechanisms- V. K. Ahluwalia and R. K. Parashar (Narosa Publishing House) 2002.
4. Organic Chemistry- J. Clayden, Greeves, S. Warren and others (Oxford University Press) 2001

Unit-16 : Molecular Rearrangements

Structure of Unit

16.1 Objectives

At the end of the unit learner will be able to

- Understand the molecular rearrangement
- Understand that how rearrangements take place in different reactions

16.2 Introduction

As we have observed in the previous chapters, in majority of organic reactions the structural changes take place in the functional groups of the substrate without affecting the carbon skeleton of the molecule. However, a number of organic reactions are known in which position of atoms (hydrogen), alkyl, aryl, double bonds or a functional group changes within the molecule. All such kind of reactions is known as rearrangement reactions or molecular rearrangements. Thus, molecular rearrangement may be defined as the reaction in which modification of the sequence of atoms or groups takes place within the molecule by breakage and formation of sigma and pi bonds resulting is structural reorganization of the paent molecule.

Rearrangement reactions are divided into following types:

(i) **Nucleophiclic Rearrangements by Migration to C- deficiant atoms-** Those rearrangement reactions in which migrating group moves with its bonding pair of electrons to the electron deficient centre. The migrating group may be hydrogen, carbon, nitrogen, oxygen, sulphur or halogens. This rearrangement is also known as nucleophilic rearrangement.

(ii) **Electrophilic Rearrangemtns by migration to e rich atoms.** Those rearrangement reactions in which migrating group moves without its electron pair to the electron rich centre. It is also known as electrophilic rearrangement.

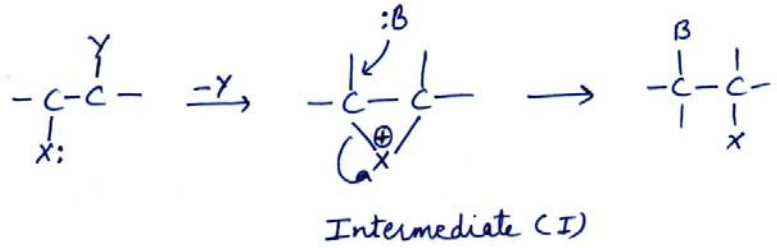
(iii) **Free-radical rearrangements:** Those rearrangement reactions in which the migrating group moves to a free-radical centre.

(iv) **Aromatic rearrangements:** Those rearrangement reactions which involve the migration of a group to the aromatic nucleus.

The first three types of rearrangement reactions comes under the category of intramolecular, while the aromatic rearrangement may be intramolecular, intermolecular or both. When the rearrangement takes place within the same molecule, are known as intramolecular rearrangement. In this type of rearrangements, the migrating group does not become completely detached from the system in which rearrangement is occurring and one step process while Intermolecular rearrangements are those in which the migrating group is first detached and then reattached at another site, thus making.

16.3 Nucleophilic Rearrangements by migration to e- deficient atoms.

In this rearrangement the migrating group moves with its bonding pair of electrons to the adjacent electron deficient atom. The electron deficiency arises by the loss of some electronegative group (:Y) with its bonding electrons during the reaction. The migrating nucleophilic species (X) may be carbon, hydrogen, a hetero atom or halogen which either detach from the migration origin and form bond with electron deficient atom also known as migration terminus or the migrating group remains partly bonded to both migration origin and migration terminus. In such case, formation of the intermediate takes place (I). The general 1,2- shift mechanism is given below.



Intermediate (I)

On the basis of migrating terminus this rearrangement reactions are divided into following three types.

(i) Rearrangements by migration to electron deficient carbon
(ii) Rearrangements by migration to electron deficient nitrogen, and
(iii) Rearrangements by migration to electron deficient oxygen

16.3a Rearrangements to Electron Deficient Carbon (Carbonium ion Rearrangements)

Since in this class the electron deficient atom is carbon, the intermediate is known as carbonium ion or carbocation and hence, the rearrangements of this class are known as carbonium ion rearrangements. Carbonium ions or carbocations are generated during substitution, elimination reactions, protonation of alcohol, ethers etc. If this carbonium ion is unstable then rearrangement occurs to get a more stable carbonium ion ($3^0 > 2^0 > 1^0$) by 1, 2 shift.

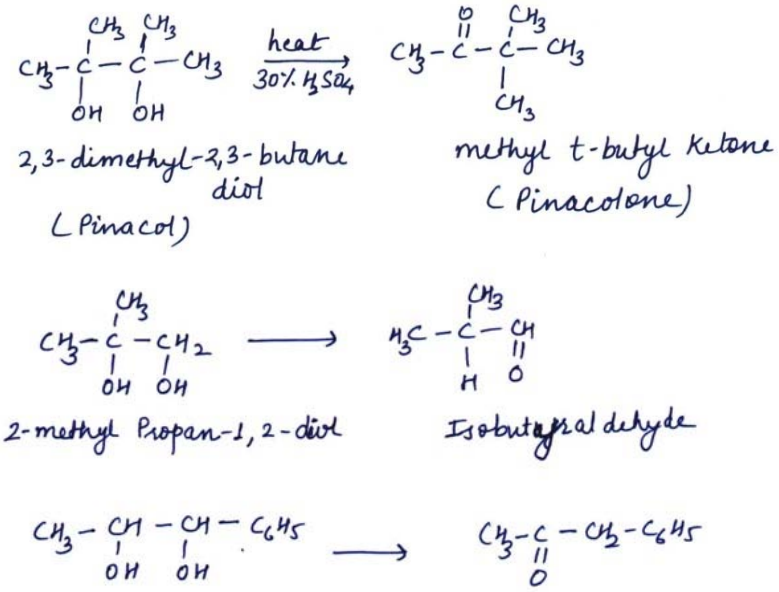
These rearrangements can further be divided into two classes

(i) Those in which carbocation rearrangement takes place with change in carbon skeleton
(ii) Those in which carbocation rearrangement takes place withou change in carbon skeleton

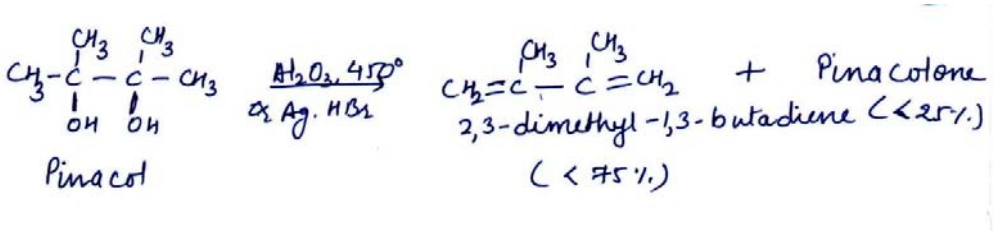
(A) Carbonium ion rearrangements with change in carbon skeleton:

The important examples of this group are described below.

1. **Pinacol-Pinacolone Rearrangement** – On treatment with dilute e/ modernatcon acids the pinacol (1,2- diol) is converted into ketones or aldehydes (pinacolone) with the elimination of water, this rearrangement is known as pinacol-pinacolone rearrangement.

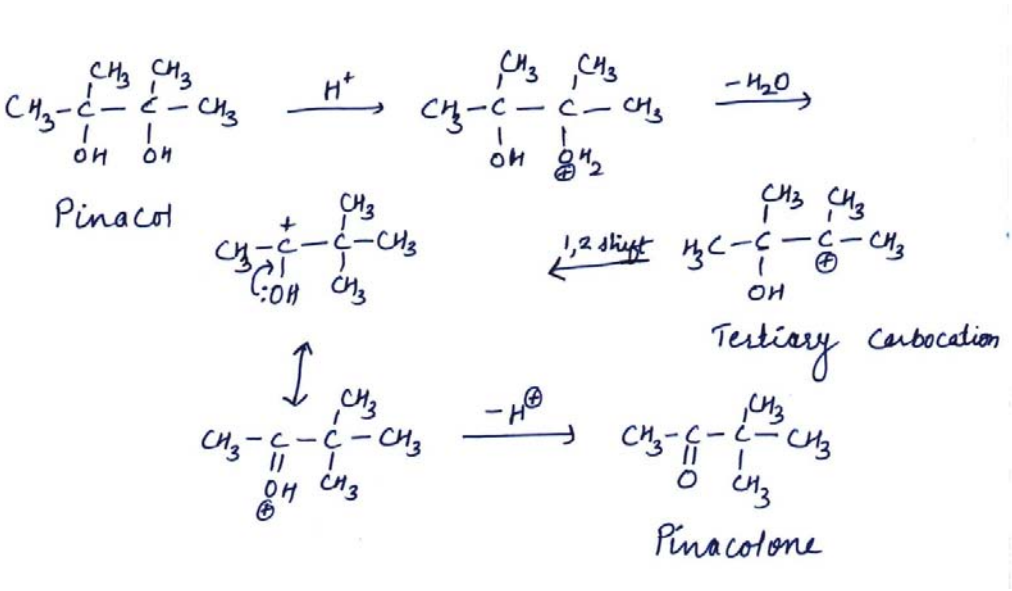


Pinacols under drastic conditions i.e., at higher temperature with Al_2O_3 or by distilling the mixture of pinacol and aqueous HBr gives olefin. This elimination takes place without rearrangement.

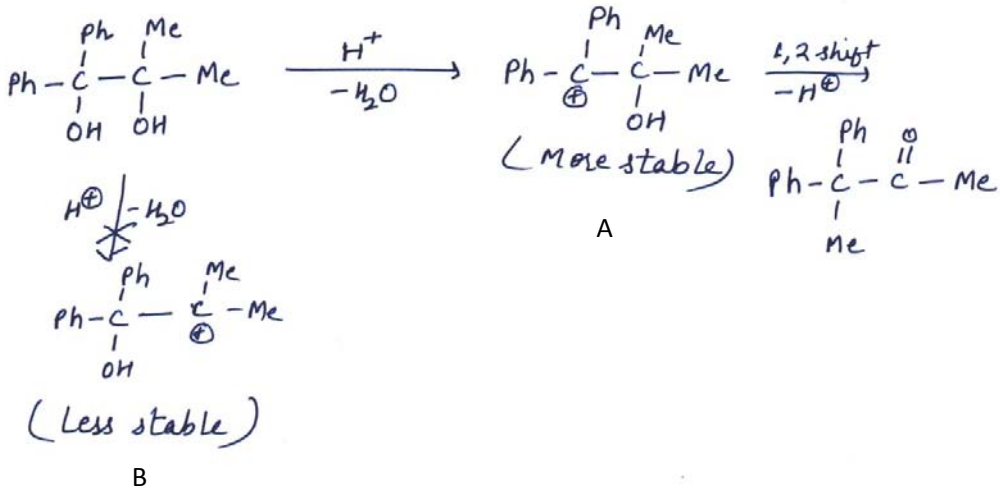


Mechanism - The reaction involves four steps.

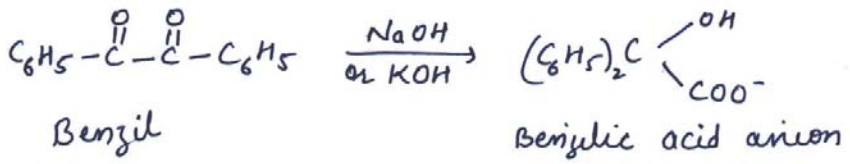
1. The reaction starts with protonation of the hydroxyl group
2. Elimination of water to form more stable carbocation
3. 1, 2 shift of -H, -R or -Ar to form carbocation.
4. Loss of proton to form carbonyl compound



It is important to note that first carbocation is tertiary but it prefers to form rearranged product (oxonium ion) for its resonance stability. The resonance stabilization is undoubtedly an important driving force for the rearrangement. It can be more understood with the help of following example. In 1,1-dimethyl-2,2-diphenyl glycol the resonance stabilized carbocation (A) is formed instead of (B) because of the resonance stabilization.

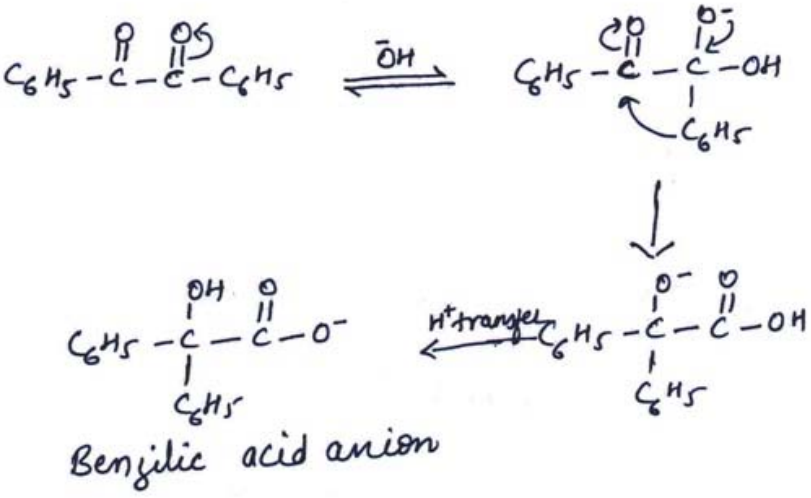


2**. Its an example of rearrangement due to migration to e deficint oxygen.** Rearrangement of α-diketones into α-hydroxy acid with strong base is known as benzilic acid rearrangement. The best known example is the conversion of benzil into benzilic acid.



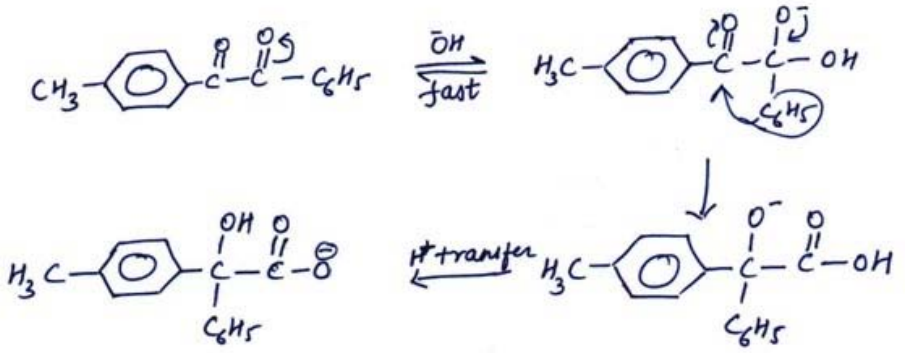
Mechanism-

1. The first step involves the nucleophilic attack of hydroxide ion to the carbonyl carbon atom. This step is found to be reversible as shown by the fact that the benzil exchanges O^{18} in basic solution faster than it rearranges.
2. The second step involves the migration of the phenyl group. This is the slow step hence is the rate determining step.
3. The next step is the rapid transfer of proton.



Note that the mechanism of benzilic acid rearrangement is similar to the intramolecular Cannizzaro reaction of glyoxal.

In the benzilic acid rearrangement when carbonyl groups are attached with two different aryl groups, then the carbonyl group attached to less electron releasing group is relatively more positively charged hence easily attacked by OH^-. Thus the less electron releasing group will preferentially migrate because the more electron releasing aryl group will tend to neutralize the positive charge on the carbonyl carbon atom to which it is attached by supplying the electrons.



p-tolyl group is more electron releasing than phenyl group.

16.3b Rearrangements to Electron Deficient Nitrogen Atoms

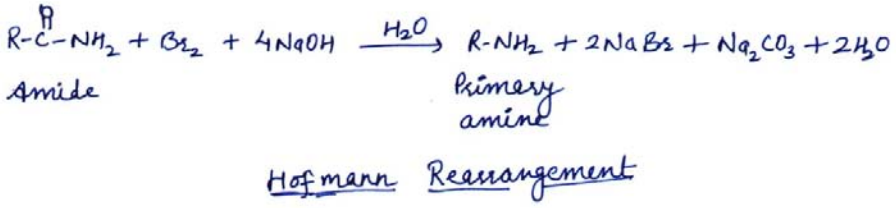
This group of rearrangements involves the migration of an alkyl or aryl group with its bonding pair of electrons from carbon to the adjacent nitrogen atom. The general mechanism for this type of rearrangement may be written as below.

Some well known important reactions of this class of rearrangements are Hofmann, Curtius, Schmidt, Lossen and Beckmann rearrangements. All the rearrangements except Backmann, involves conversion of acid into amine. All these rearrangements are closely related where migrating group moving from carbon to adjacent electron deficient nitrogen with the formation of isocyanate except that the leaving groups are different. In Hofmann reaction, -X is = -Br, in Curtius and Schmidt, -X is = $-N_2$ in Lossen, -X = -OCOR and in Beckmann -X is -OH or -OX.

If the migrating group in these rearrangements is asymmetric, it retains its configuration indicating that the migrating group never becomes free in the solution and therefore the rearrangements are intramolecular.

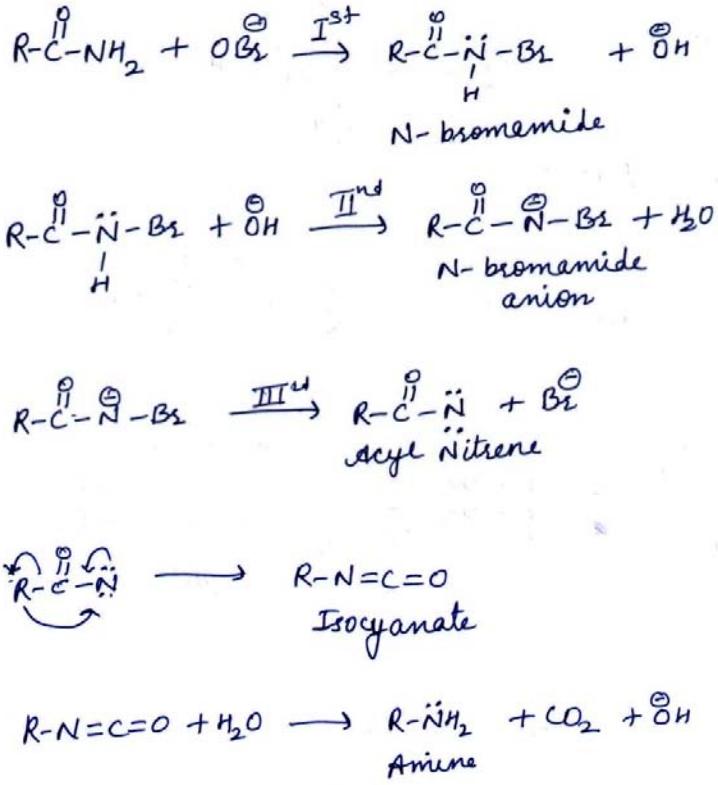
A. Hoffmann Rearrangement

Aminder having no tubstitment on nitrogen undergo a rearrangement by reacting with solution of alkaline hypohatite ($NaOH + Br^2Orcl^2$) to give 1^0 aminer is known as Hoffmann Rearrnagment.

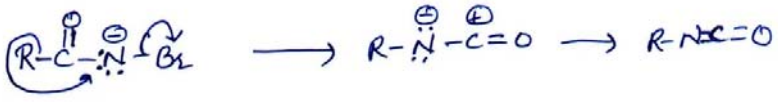


Mechanism: The mechanism involves following steps:

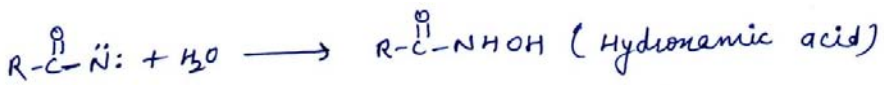
1. In the first step *N*-bromamide is formed on treatment of hypobromite on amide.
2. In the second step the base abstracts a proton from the nitrogen to give a bromamide anion.
3. In the third step loss of bromide ion gives a highly reactive intermediate i.e., acylnitrene.
4. In the fourth step migration of R group takes place which gives isocyanate on rearrangement.
5. Lastly the isocyanate undergoes hydrolysis to give carbamic acid which eliminates CO_2 to yield the amine.



The loss of bromide ion and the migration of R take place simultaneously, i.e., it is a concerted mechanism,

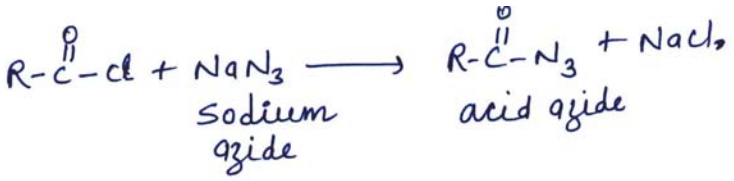


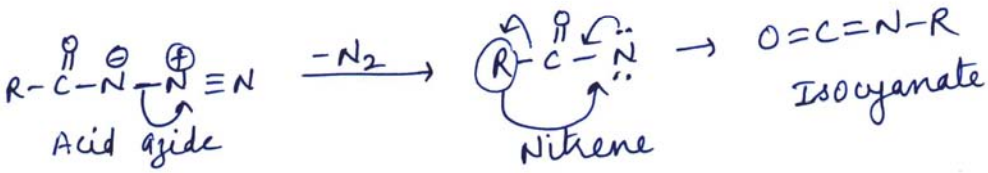
If it is not a concerted mechanism then acylnitrene is formed and it would react with water to form hydroxamic acid.



B. Curtius Rearrangements

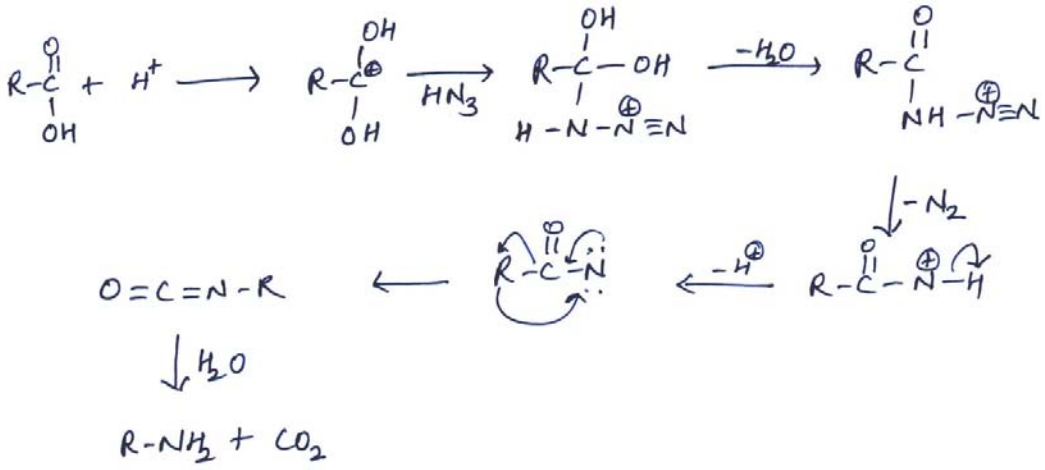
Curtius rearrangement is a thermal or photo chemical rarrangement of ocyl oridwes to isolyanites. Acid chlorides on treatment with sodium azide, gives acyl azides. Mechanism is similar to Hoffmann rearrangement. Acyl azide eliminates nitrogen molecule on heating and forms electron deficient nitrene which on rearrangement gives isocyanates.





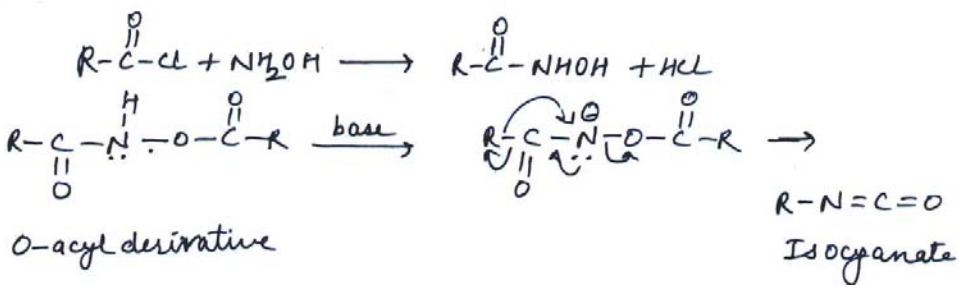
C. Schmidt Rearrangement

In this rearrangement in the presence of concentrated sulphuric acid when carboxylic acid reacts with hydrazoic acid and gives isocyanates which on hydrolysis gives amines. The mechanism involves the formation of protonated acyl azides which eliminates nitrogen molecule without heating and form isocyanates on rearrangement.which shows the unimole under acid catalysed delygration of carboxylic acid.



D. Lossen Rearrangement

Thermal, acid or base catalyzed convas on of hydrocramic acid and their O acyl or O alsoyl deriravtives to isocyanate. Hydroxamic acid is prepared by the action of hydroxylamine on acid chloride.



E. The Beckmann Rearrangement

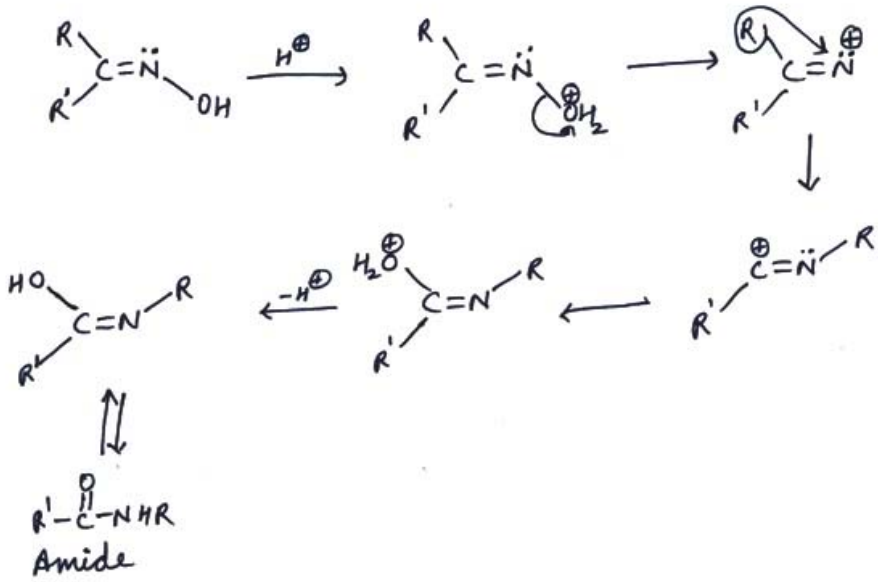
The acid catalyzed rearrangement of ketoximes to substituted amides is known as Beckmann rearrangement. In this rearrangement migrating group moves from carbon to electron deficient nitrogen.

RR'C=NOH RCONHR' or R'CONHR

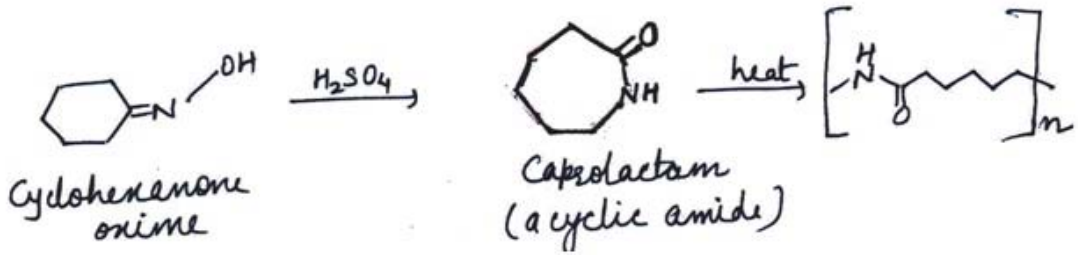
In this rearrangement the migration of the group depends on the position of the group with respect to the hydroxyl group. Group which is anti to the hydroxyl group migrates. Thus the reaction is stereospecific. This method is often used to determine the configuration of the oxime.

Mechanism: The mechanism involves following steps:

1. The function of the acidic regents is to convert the hydroxyl group to a better leaving group. First step involves the protonation of OH group.
2. Second step involves loss of water
3. Third step involves migration of R group to the electron deficient nitrogen, to give carbocation.
4. Next steps involve attack of water molecule followed by removal of H^+.



This reaction has applications in synthesis of isoquinoline and caprolactam. Caprolactam is prepared by ring enlargement of oximes of cyclic ketone. Caprolacam is used in the preparation of nylon.



16.3c Rearrangements to Electron Deficient Oxygen

Baeyer-Villiger Rearrangement

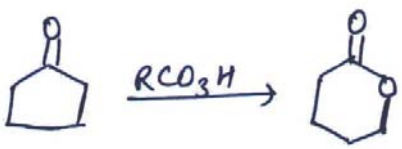
The reaction consists of oxidation of both an aldehyde and a ketone into an ester by means of a peracid such as trifluoroperacetic, peracetic, perbenzoic, permonosulphuric acid, etc.

1- $R_2CO + R'COOOH \rightarrow RCOOR + R'COOH$

2- R-C-H

This oxidation involves 1,2, migration to an electron deficient oxygen.

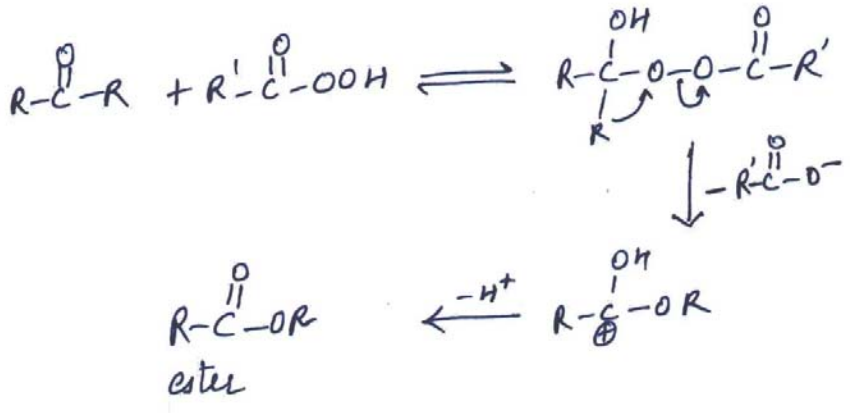
Bayer-Villiger rearrangement is an example of rearrangement of a group to the electron efficient oxygen. Cyclic ketones give lactones.



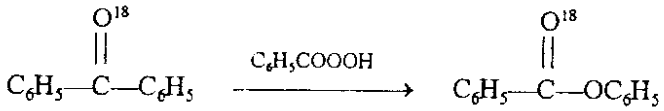
The overall reaction is an insertion of oxygen atom between the carbonyl group and the adjacent carbon in ketone.

Mechanism: the mechanism occurs in following steps:

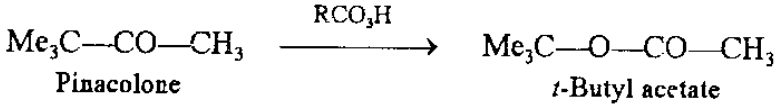
1. In the first step nucleophilic attack of per acid to the ketonic carbonyl group occurs to form an intermediate peroxide,
2. Second step involves the removal of carboxylate ion followed by migration of an alkyl group to an electron-deficient oxygen atom.
3. Third step involves the loss of proton to give ester.



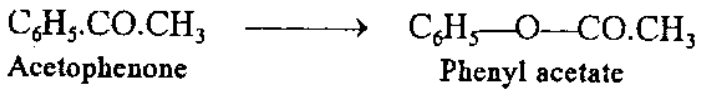
The reaction is catalysed by acids and electron-releasing groups in the ketone and electron with drawing groups in the peracid accelerates the reaction rate. The mechanism is also supported by the fact that the oxygen atom of the carbonyl group of the ester comes from the carbonyl group of the ketone. It was clearly demonstrated by the following reaction in which isotopically labelled oxygen (O^{18}) is taken in the molecule.



In an unsymmetrical ketone that group migrates having good electron releasing capacity. Among the alkyl groups the migratory aptitude is 3°>2°>1°>methyl. Among the aryl groups the migratory aptitude is *p*-anisyl>*p*-tolyl>-phenyl> *p*-chlorophenyl>*p*-nitrophenyl> p-aminophenyl etc. During the mechanism it is observed that an alkyl group migrates from carbon to oxygen; the order of this migratory aptitude in the alkyl series is tertiary> secondary> primary e.g.



When aryl and alkyl, both groups, are present, the migratory aptitude of various groups is: 3^{o} alkyl> 2^{o} alkyl> phenyl> 1^{o} alkyl> methyl. Thus in acetophenone, phenyl group migrates in preference to the methyl.

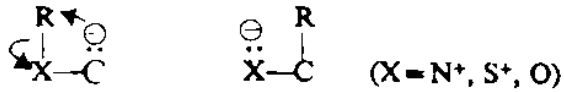


Acetophenone **Phenyl acetate**

The intramolecular nature of the reaction must be noted and thus the migrating group retains its configuration. This reaction has valuable synthetic applications in synthesis of esters which are difficult to synthesized as well as in synthesis of anhydrides from 1,2-diketones and *o*-quinone.

16.4 Rearrangement to Electron Rich Carbon

These include reactions which are initiated by the formation of an anion and are usually referred to as anionic rearrangements, Most anionic reaction begin with the removal of a proton by a strong base and these rearrangements may proceed by ionic or free-radical pathways.



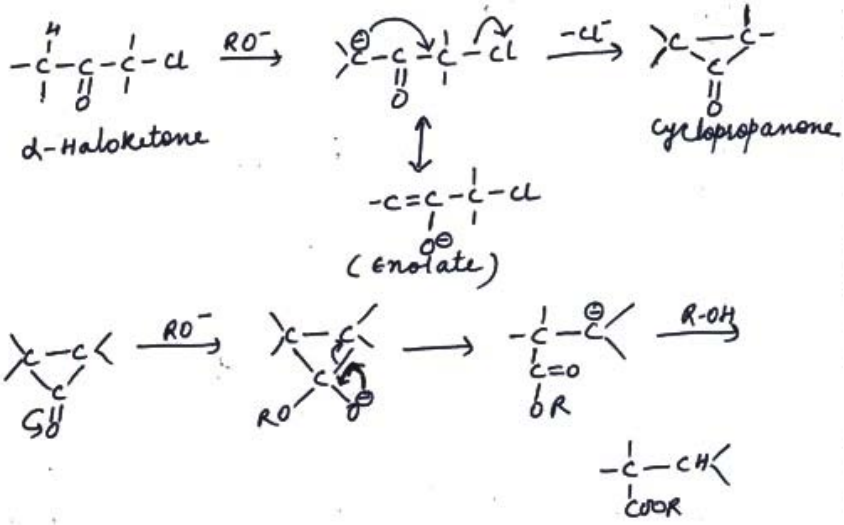
R migrates without its bonding-pair

A. Favorskii Rearrangement

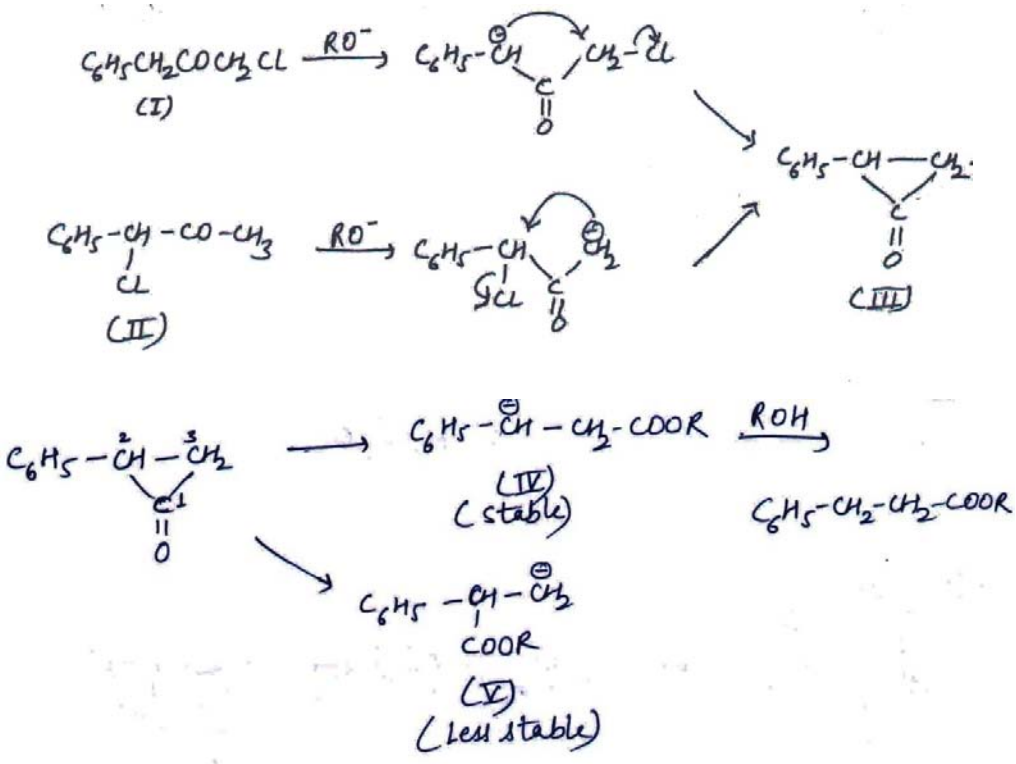
The reaction which consists of the conversion of α-haloketones to esters in presence of alkoxide is known as Favorskii rearrangement (use of hydroxide ions instead of alkoxide ions give the free acid).

Mechanism:

1. First step involves the formation of enolates via abstraction of proton through alkoxide ion.
2. This enolate on rearrangement gives esters via cyclopropanone intermediate.
3. In the next step alkoxide ion attacks on positively charged carbon of carbonyl group. So the cyclopropanone intermediate opens in such a way so as to give the more stable of the two possible carbanions.



In case of unsymmetrical ketone, the unsymmetrical cyclopropanone is formed which opens up to give the most stable carbanions. For example both the isomeric compounds (I and II) give the same cyclopropanone intermediate (III). Ring opening occurs on either sides of the carbonyl group to give the (IV and V) carbanions. Aryl group stabilize the negative charge by delocalization as compared to alkyl group so IV carbanion is more stable than V and on protonation gives corresponding ester.

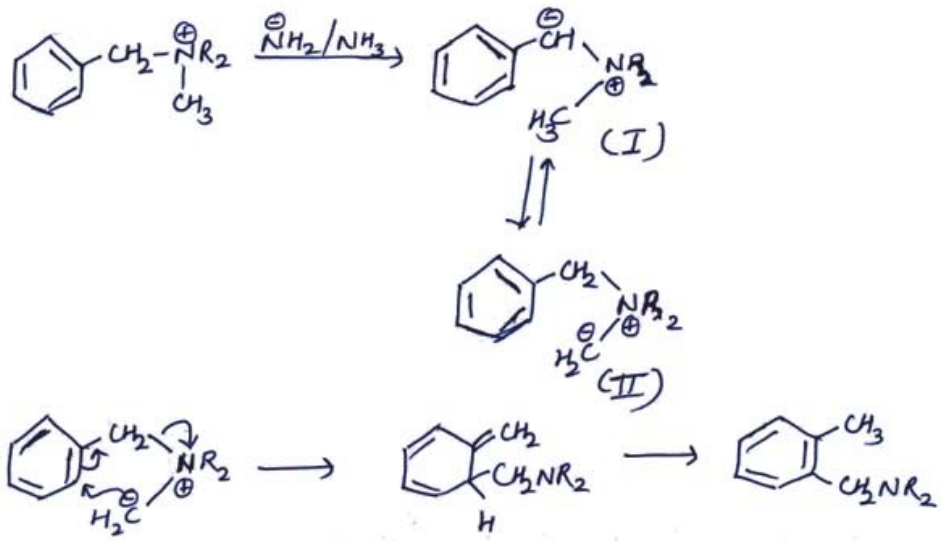


E. The Sommelet Hauser Rearrangement

This rearrangement is typical of benzyl quaternary ammonium salts, which on reaction with alkali metal amides give benzyl tertiary amines. In comparison of

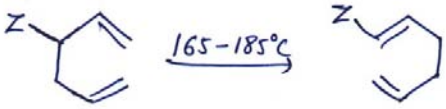
Stevens rearrangement, in Sommelet Hauser rearrangement, a strongly electron withdrawing group is absent. The α-hydrogen is too weakly acidic for the rearrangement to be induced by hydroxide ion. Thus stronger base is required to procede the reaction.

The Sommelet Hauser rearrangement is a [3,2] sigmatropic rearrangement. The benzyl hydrogen is most acidic and it is easily converted into ylide (I) after proton removal. This ylide on rearrangement gives II, after reprotovation which gives final product by [3,2] sigmatropic rearrangement.



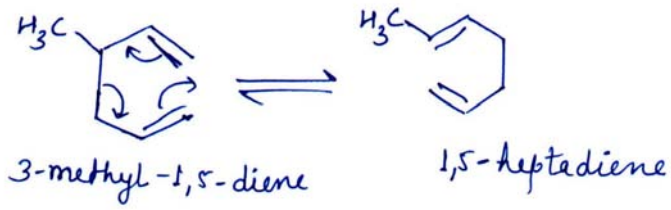
C. The Cope Rearrangement

When 1,5 dienes are heated it get isomerized in a [3,3] sigmatropic rearrangements known as Cope rearrangement.

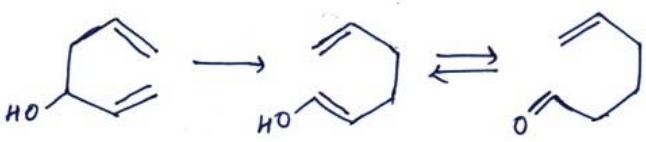


When the dienes are symmetrical about the 3,4 bond, in that case a product is obtained which is symmetrical to starting material.

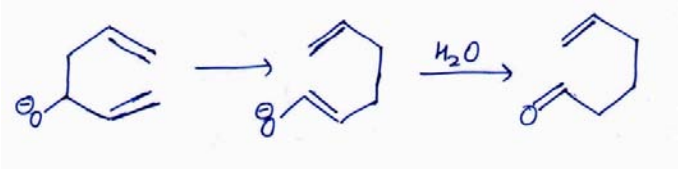
Therefore the cope rearrangement occurs when the diene is unsymmetrical about this bond. Any 1,5- diene gives the rearrangement, for example 3-methyl-1,5- diene when heated at higher temperature (300^{o}C) it is rearranged into 1,5-heptadiene.



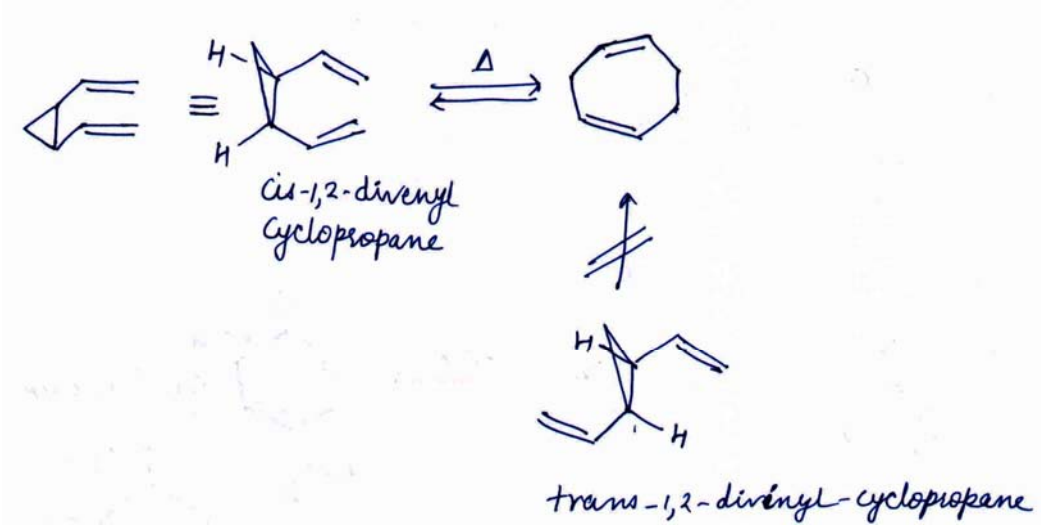
However the reaction takes place more easily even at low temperature when the group present on 3 or 4 carbon is such that, it produces an equilibrium mixture of two 1,5-dienes which is richer in the thermodynamically more stable isomer. For example in case of 3- hydroxyl-1,5-diene gives product which tautomerizes to the carbonyl compound, these two isomeric products are present in equilibrium.



The reaction of 3-hydroxy-1,5-dienes is called the oxy cope rearrangement, and are highly useful in synthesis. If alkoxide is used in place of hydroxyl group then this rearrangement is known as anionic oxy-cope rearrangement.

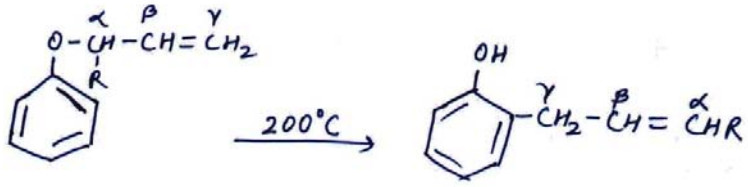


Cis-Divinylcyclopropane rapidly undergoes Cope rearrangement to 1,4-cycloheptadiene. Due to unfavorable molecular geometry, but the rearrangement of trans-isomer to cycloheptadiene cannot be possible because the ends of the molecule where bonding must occur are too far apart. This cis orientation not only provides a favorable geometry for interaction of the diene termini so that the loss in entropy in going to the transition state is smaller than for an acyclic diene, but the bond being broken is strained and this reduces the enthalpy of activation.

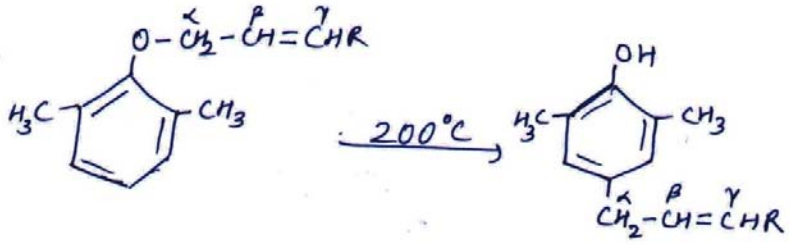


D. The Claisen Rearrangement

This rearrangement involves the shift of a group from oxygen to carbon. It involves [3, 3] sigmatropic pathway like Cope rearrangement. Example of Claisen rearrangement is the thermal conversion of aryl allyl ether to *o*-allylphenols. on heating at about 200 C this rearrangement is carried out either in the absence of solvent or in inert high b.p. solvent.

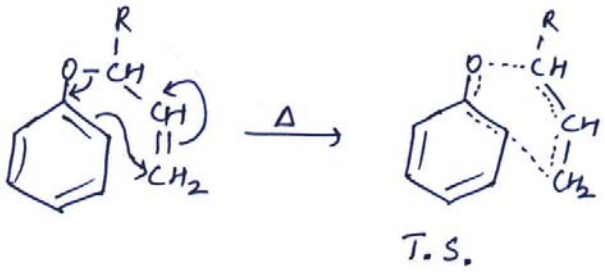


The group migrates to the ortho position. When both the ortho positions are occupied then para compound is formed. When both the ortho positions and para positions are occupied then mata product has not been observed. When ortho migration takes place then carbon atom α to the oxygen becomes γ to the ring at the end of the reaction as shown in above example. However when para migration occurs there is no change in the attachment of allyl group.

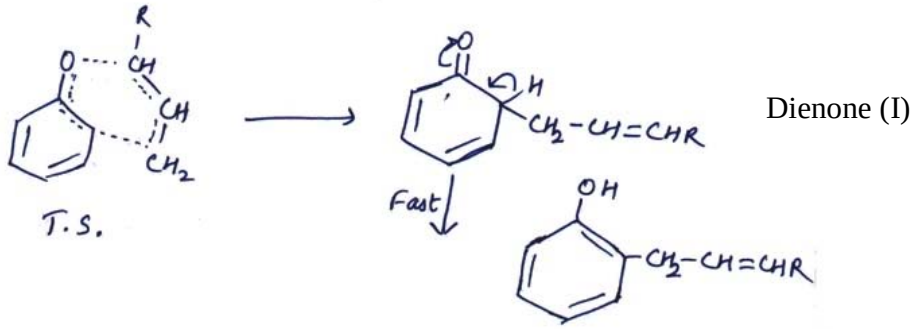


Mechanism: The following mechanism has been proposed:

The reaction proceeds through a cyclic six membered transition state in which the breaking of oxygen-carbon bond and making of carbon carbon bond takes place simultaneously, so it is a concerted mechanism. This transition state has aromatic character with six electrons.

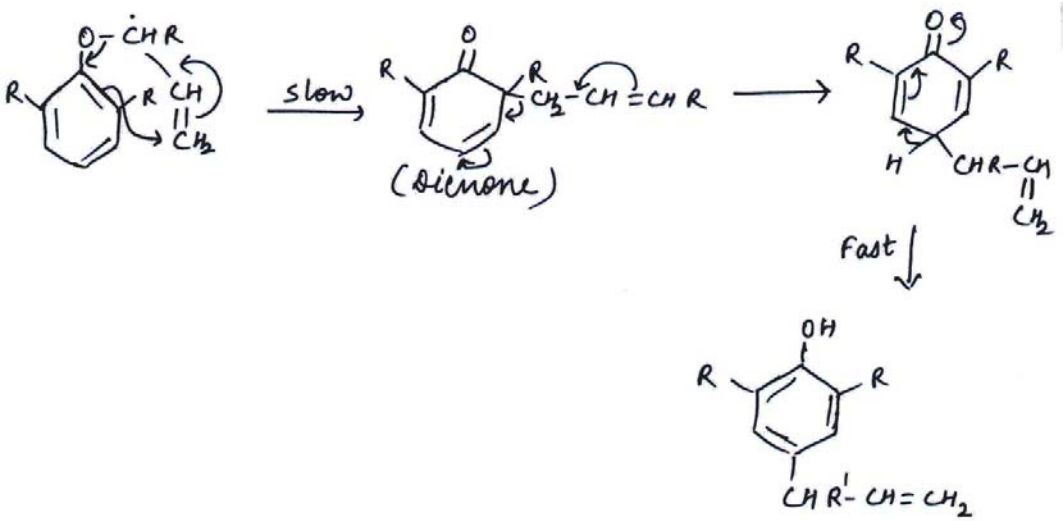


This six membered transition state is converted into dienone (I) intermediate, which rapidly converted into phenol.



Dienone (I)

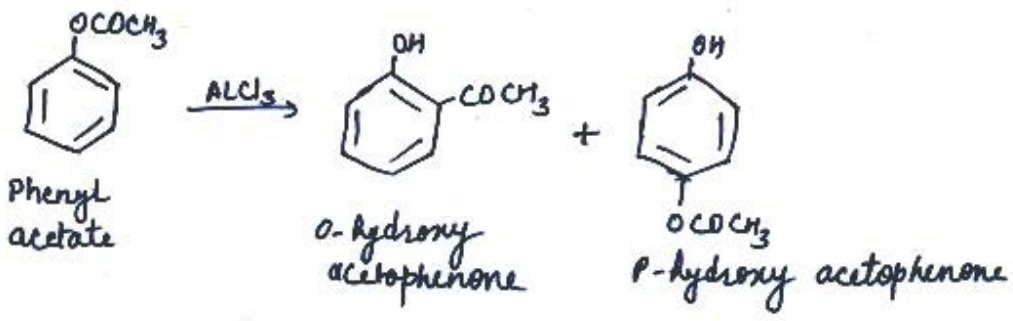
When the ortho positions are substituted, the migration will still occur at ortho position. But due to absence of hydrogen the enolization would not possible, so second migration occurs at para position.



16.5 Mixed Type of Aromatic Rearrangements

The only common rearmament of this type is the Fries rearrangement.

1. **Fries rearrangement:** This rearrangement involves the conversion of aryl esters to ortho and para hydroxy ketones on heating with lewis acids. This reaction is known as Fries rearrangement.

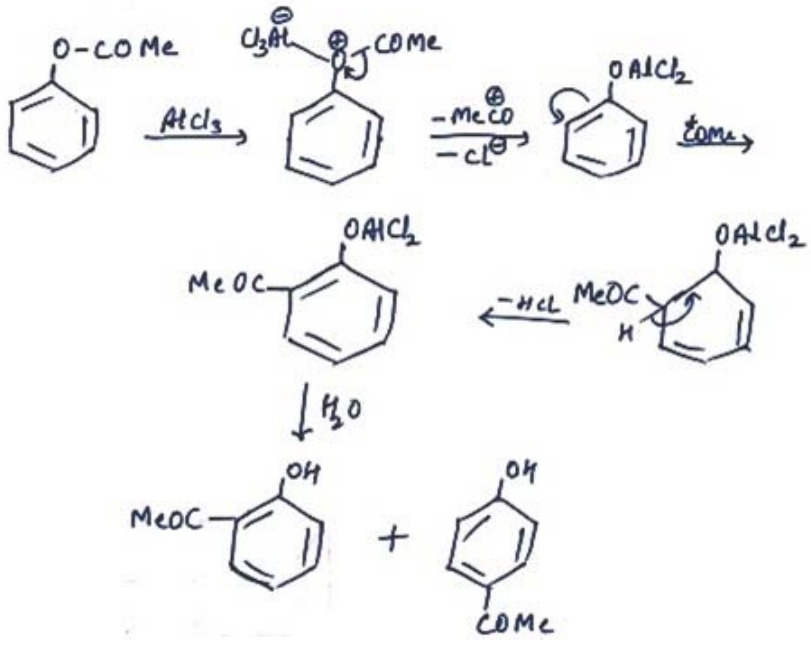


Mechanism: Two mechanisms have been proposed for the Fries rearrangement. There is evidence for both the intermolecular (Baltzly et al. 1948) as well as intramolecular mechanisms.

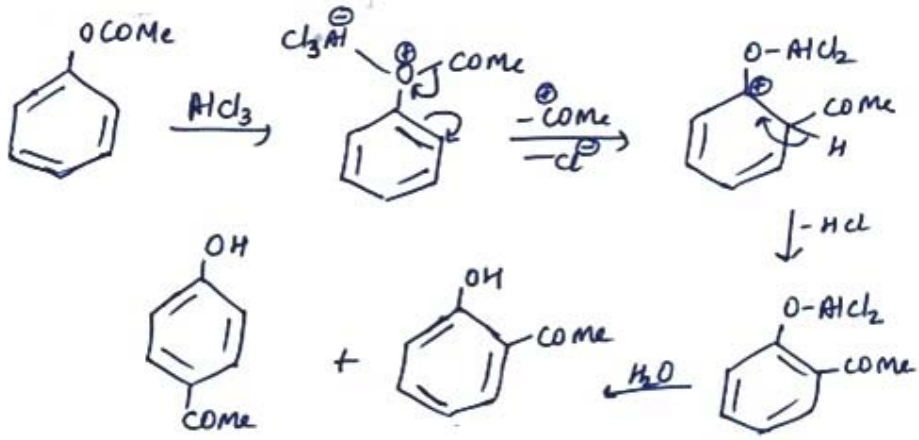
Intermolecular mechanism (Two step process)

It may be taken as a type of Friedel-Craft acylation with the acyl group already a part of the starting material.

The lewis acid ($AlCl_3$) complexes with the ester and eliminates an acyliym ion which attack on benzene ring at ortho and para positions, as in Friedel Craft's acylation.



Intramolecular mechanism (one-step process)



In both the mechanisms, ortho and para both the products are obtained. Formation of isomers depend on temperature, solvent and amount of catalyst. At high temperature ortho isomer is formed and at low temperature para isomer is formed as a major product.

16.6 Summary

In this chapter we have seen different molecular rearrangement reactions in which position of atoms (hydrogen), alkyl, aryl, double bonds or a functional group changes within the molecule, proceeds through the migration of a group to electron deficient carbon, nitrogen, oxygen, rearrangement to electron rich carbon and rearrangement to aromatic nucleus. These different rearrangement reactions have valuable synthetic applications.

16.7 Review Questions / Comprehensive Questions.

1 What are molecular rearrangement reactions? Classify them.

2 What is cope rearrangement? Give a suitable example.

3 Write down the mechanism of Pinacol-Pinacolone rearrangement.

4 What is Fries rearrangement reaction? Explain its two step mechanism.

5 Write a short note on following

a) Claisen Rearrangement
b) Beckmann rearrangement
c) Hofmann rearrangement
d) Baeyer-Villiger rearrangement

16.8 References and Suggested Readings

1. Organic Reactions and their Mechanism- P.S.Kalsi (New Age International Publishers) 2005.
2. Reactions, Rearrangements and Reagents – S.N. Sanyal (Bharati Bhawan, Publishers and Distributors) 2011
3. Advanced Organic Chemistry, 6th Edition –Michael B. Smith and Jerry March (John Wiley & Sons) 2012

Unit -17 : Phosphorus Nitrogen and Sulphur Ylides and Stereochemistry of compounds containig Phosphorus Sulphur and Nitrogen

Structure of Unit

17.1 Objectives

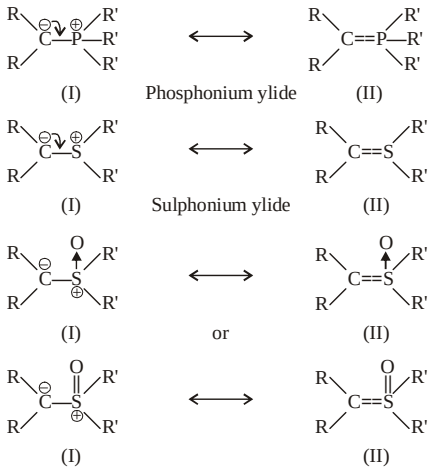
At the end of the unit learner will be able to

- Explain Ylide's structure.
- Understand structure and preparation of phosphorus ylides.
- Understand the importance of sulphur ylides as synthetic agent.
- Explain mechanism of synthesis of nigrogen ylides.
- Understand the stereochemistry of compounds containing phosphorus, sulphurs and nitrogen.

17.2 Introduction of Ylides

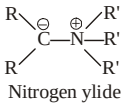
Ylides are defined as 'Compounds, in which positively charged heteroatom (*e.g.*, N, S, P, As, Se) is connected to a carbon carrying a negative charge'Which is a neutral dipolar moleule. They are also referred as vicinal ionic intermediates. There are three main type of ylides: Nitrogen, Phosphorus and Sulphur ylides.

Phosphorus and sulphur ylides can be represented by two resonating structures.



Structure (I) is known as ylide structure. This resonating structure has opposite charges on adjacent atoms in which both atoms have octels of electrons. The non-polar structure (II) is known as ylene. The nonpolar ylene resoance structures have ten electrons at phosphorus or, sulphur atom, these structures imply participation of d-orbitals on the heteroatom. Such structures are not possible for ammonium ylides. Structural studies indicate that the dipolar ylide structure is the main contributor.

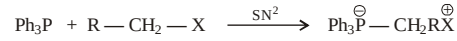
Phosphorus ylides are much more stable than the nitrogen ylides. Sulphur ylides have a low stability.



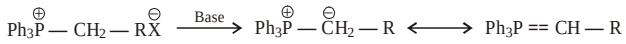
Most of ylides are strong nucleophiles or bases and are very important in organic synthesis.

17.3 Phosphorus Ylides

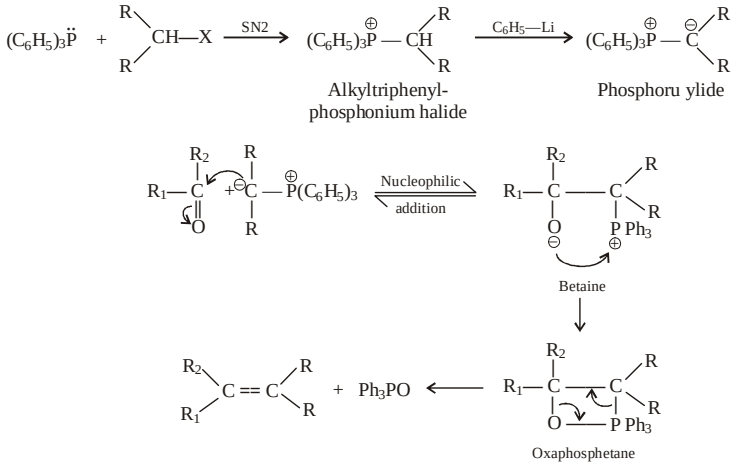
Phosphorus ylides are prepared by deprotonation of phosphonium salts. The phosphonium salts most oftenly used are alkyltriphenyl-phosphonium halides, which can be prepared by the reaction of triphenylphosphine and an alkyl halide (which has at least one hydrogen).



The alkyl halide must be one that is reactive for SN^2 reactions. Alkyltriphenylphosphonium halides are weakly acidic in nature therefore, strong base must be used for deprotonation. The strong base may be organolithium, sodium salt of DMSO, amide ion or substituted amide anions.



The phosphorus ylides have tremendous synthetic applications. The most well known reactions of phosphorus ylides (or the phosphoranes) are their reaction with carbonyl compounds to give olefins. The reaction is known as *Wittig reaction*. The wiltig reaction is a chemical reaction of an oldghde or retone with triphenyl phorphonium cylide also called with g regent to give an alkene & ri phency phospheme. The reaction take place as follow:

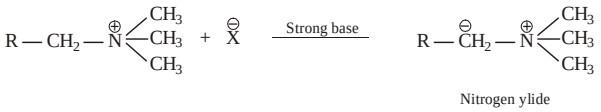


The Wittig reaction is applicable to a wide variety of compounds and although a mixture of (E) and (Z) alkenes may result, the Wittig reaction gives a great advantage over most other alkene synthesis in that no ambiguity exists as to the location of the double bond in the product. This is in contrast to elimination reaction of alkyl halides whch gives multiple alkene products either by rearrangement or by carbons.

Stability: The stability of the resulting neutral species is increased by substituent groups that can help to stabilize the electron rich carbon. Electron-withdrawing substitutents present on electron rich carbon increases stability of ylides.

17.4 Nitrogen Ylides

Nitrogen ylides are prepared by treating a tetraalkylammonium salt with a strong base. In most of the cases out of four alkyl groups, three are methyl and one is alkyl group having at least one hydrogen on carbon with respect to nitrogen.

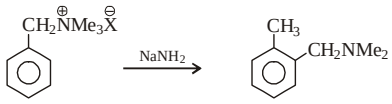


This nitrogen ylide will be stable if R is phenyl group or strong–I group.

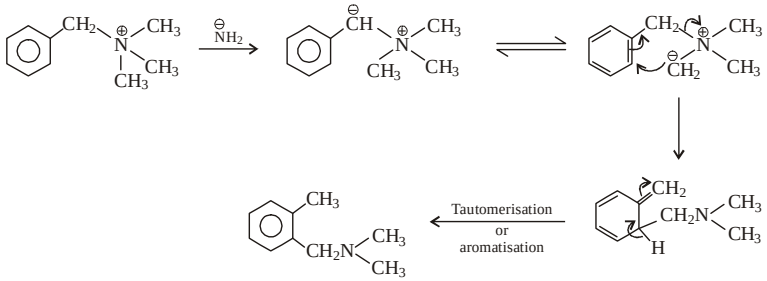
The nitrogen ylides are formed as reaction intermediate in the *Sommelet rearrangement* and *Stevens rearrangement.*

Sommelet-Hauser Rearrangement

When benzylic quaternary ammonium salts are treated with alkali-metal amides in presence of lig undergo a rearrangement called *Sommelet-Hauser rearrangement.* Since, the product is a benzylic tertiary amine, it can be further alkylated and the product again subjected to the rearrangement. This process can be continued around the ring until an ortho position is blocked.

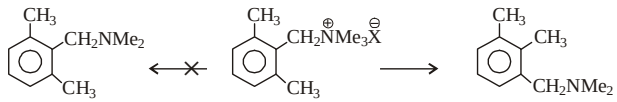


Mechanism:



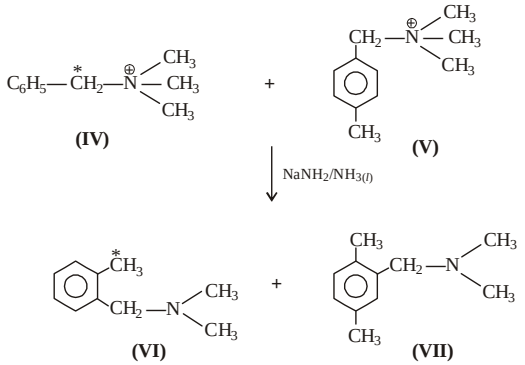
The reaction is most oftenly carried out with three methyl groups on nitrogen, but other groups can also be used. However, if a hydrogen is present, *Hofmann elimination* often competes. This mechanism is an example of [2,3] signmatropic rearrangement.

A mechanism in which a methyl group is detached from the nitrogen and then attaches itself to the ring is not acceptable. This is because in the following reaction **II** is not formed from **I**, but **III** is formed as expected from the first mechanism.

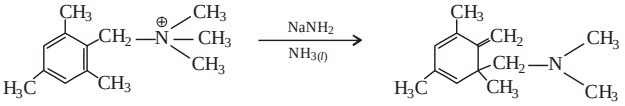


(II) **(I)** **(III)**

Crossover experiment showed that the Sommelet rearrangement is intramolecular in nature. This has been confirmed by isotopic labelling experiments. When **IV** and **V** are rearranged together, no radioactivity at all could be found in the product **VII**.

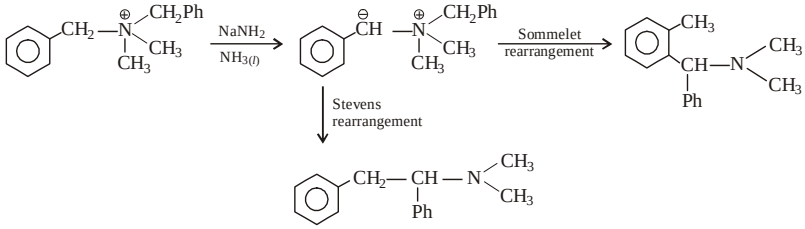


Exomethylene derivative **VIII** has been isolated. This clearly indicates the formation of the ylide B in the above mechanism.



(VIII)

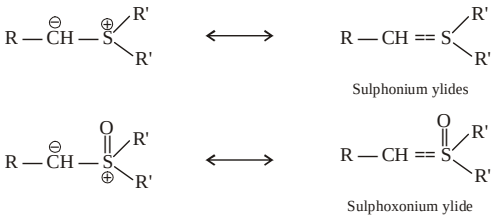
The main drawback of *Sommelet rearrangement* is that it is accompanied by *Stevens rearrangement* in present of base.



17.5 Sulphur Ylides

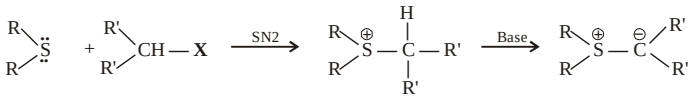
Sulphur ylides are next to phosphorus ylides in importance as synthetic reagents. These ylides are considered as *Zwitter* ions in which a carbanion is stabilized by interaction with an adjacent sulphonium centre.

The most widely used sulphur ylides are sulphonium ylides and sulphoxonium ylides.

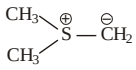


The additional electronegative oxygen atom in the sulphoxonium ylide stabilises these ylides considerably, relative to the sulphonium ylides.

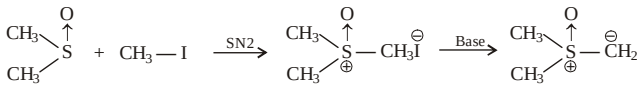
Sulphonium ylides are obtained by the deprotonation of sulphonium salts.



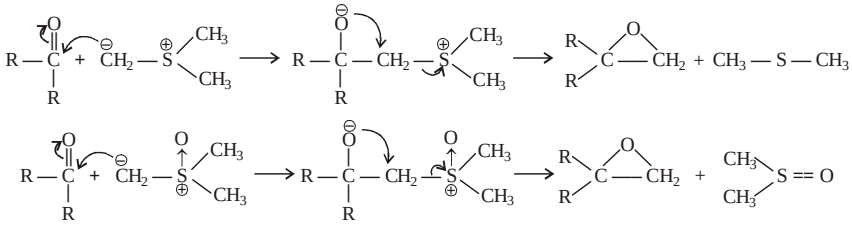
The most important sulphonium ylide is the dimethylsulphonium methylide.



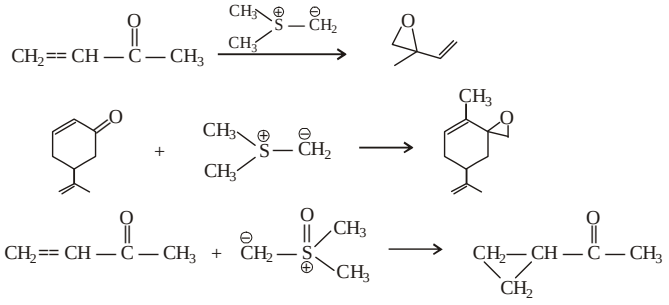
Similarly the most important sulphoxonium ylide is the dimethylsulphoxonium methylide which can be prepared as follow:

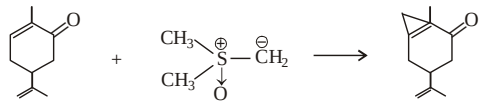


Sulphur ylides behave differently than the phosphorus ylides towards carbonyl compounds. Sulphur ylides react with carbonyl compounds to yield epoxides instead of alkenes. Instead of four center elimination the adduct formed from the sulphur ylides undergo intramolecular substitution reaction. An initial betaine formation, no doubt, takes place but the sulphur atom has less affinity for oxygen than phosphorus so that an internal attack occurs with the resultant displacement of sulphur substituents by oxygen. This results in epoxide formation.

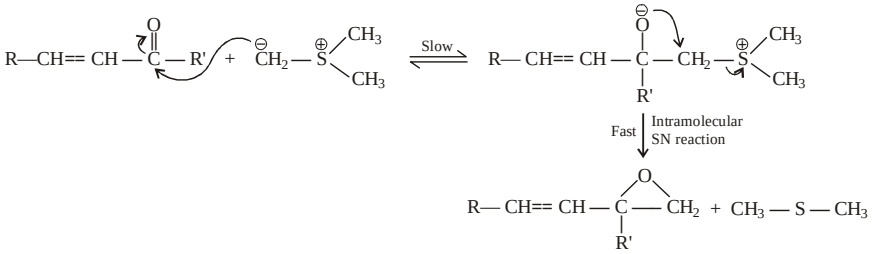


Dimethylsulphonium methylide is both more reactive and less stable than dimethylsuphoxonium methylide. Dimethylsulphonium methylide and dimethylsulphoxonium methylide differ in their reaction towards a, □-unsaturated carbonyl compounds. Dimethylsulphonium methylide gives epoxides whereas dimethylsulphoxonium methylide gives cyclopropane by a *Micheal addition* to the carbon-carbon double bond.

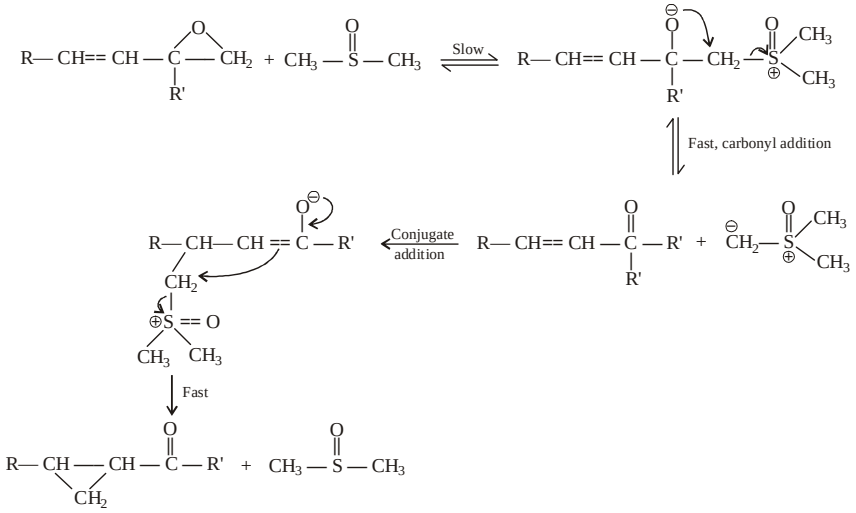




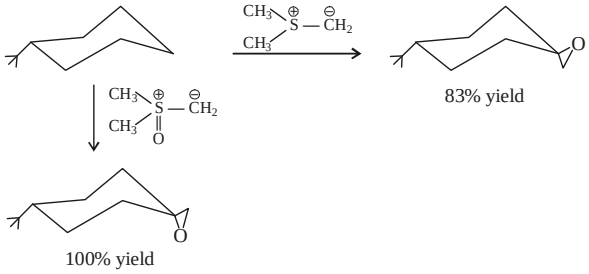
Dimethylsulphonium methylide give nucleophilic addition reaction with carbonyl compounds. The adduct undergoes intramolecular substitution reaction to give epoxide. The reaction take place as follows:



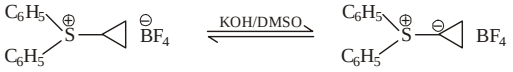
Dimethylsulphoxonium methylide also gives nucleophilic addition reaction, but this reaction is very fast and reversible. In this case product formation takes place by conjugate addition.



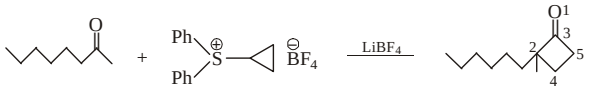
Another difference between these two reagents is the stereoselectivity in formation of epoxides from cyclohexanone. Dimethylsulphonium methylide usually adds from the axial direction whereas dimethylsulphoxonium methylide adds from the equatorial direction.



Another class of useful sulphonium ylides is diphenylsulphonium ylides, e.g., diphenylsulphonium cyclopropylide. They are generated in situ during a reaction by the action of sodium or potassium hydroxide on cyclopropyldiphenylsulphonium fluoroborate.



This ylide reacts with carbonyl compounds to form oxiranes which on rearrangement in the presence of $LiBF_4$ give cyclobutanone derivaties.



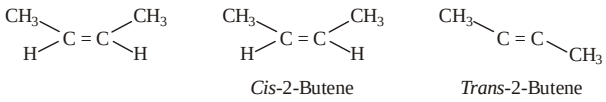
The cyclobutanones are also important intermediates.

17.6 Sterochemistry: An Introduction

In the study of organic chemistry, very often we come across different organic compounds which have same molecular formula. For example *dimethyl ether* (CH_3—O—CH_3) and *ethyl alcohol* (C_2H_5OH) have same molecular formula, C_2H_6O but their properties are quite different. Such compounds are called **isomers** and the phenomenon is referred to as **isomerism** (*iso* means same and *merros* means parts). Isomerism may thus, be defined as the *phenomenon by virtue of which different organic compounds can be represented by same molecular formula.* Isomerism can broadly be classified into two categories, namely; *Structural isomerism and stereoisomerism.*

(a) **Structural isomerism of constitutional isomerism.** In this type of isomerism, the isomers differ from one another in their structural arrangements. In other words, the structural isomers do have same molecular formula but they differ in the way in which the atoms are bonded to each other. For example in dimethyl ether (CH_3—O—CH_3)**.** Oxygen atom is bonded to two carbon atoms whereas in ethyl alcohol (C_2H_5–OH), the oxygen atom is bonded to carbon and hydrogen atoms.

(b) **Stereoisomerism.** In this type of isomerism, the isomers have same structural arrangement, *i.e.,* they have same way in which the atoms are bonded to one another, but, the spatial orientations of various atoms/groups are different. For example, in both the geometrical isomers of 2-butene, the double bonded carbon atoms are bonded to CH_3–group and H–atoms but the orientations of —CH_3 and H atoms in the two isomers are different.



Cis-2-Butene *Trans*-2-Butene

The branch of chemistry which deals with the study of molecular structures in three dimensional space is called stereochemistry**.** In the present unit we shall focus mainly stereochemistry of compounds containing phosphorus, sulphur and nitrogen.

The stereoisomerism can be broadly divided into two categories.

17.6.1 Conformational isomerism and Configurational isomerism

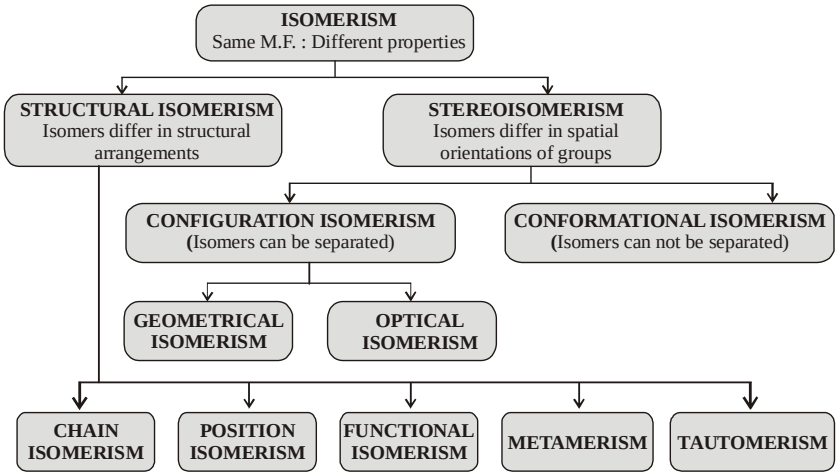
In **conformational isomerism**, the isomers go on changing into one another rapidly because of rotation about the single covalent bond and cannot be separated.

In **configurational isomerism**, the isomers do not change into one another automatically. They can get converted into another only if some bonds are broken and then re-established after rearrangement. Such isomers can be separated by suitable means. The stereoisomers can be re-established further divided into two types which are:

(i) *Geometrical isomers* and (ii) *Optical isomers*.

The details about geometrical isomers and optical isomerism will be discussed in the following sections.

The flowsheet of various categories of isomerism is given below.



17.6.2 Conformations

Conformations are different spatial arrangements of atoms or groups attached to carbon atoms bonded by single bond which arise due to rotation about the single bond. These arrangements are also called conformational isomers or conformers.

Out of infinite number of possible conformations of ethane, two conformations represent the extremes. These are called **staggered conformation** (a) and **eclipsed conformation** (b).

(a) In staggered conformation, the hydrogen atoms of the two carbon atoms are oriented in such way that they lie far apart from one another. In other words, they are staggered away with respect to one another.

(b) In eclipsed conformation, the hydrogen atoms of one carbon are lying directly behind the hydrogen atoms of the other. In other words, hydrogen atoms of one carbon atom are eclipsing the hydrogen atoms of the other.

The *Sawhorse projection formulae* of the two extreme conformers of ethane are shown in Fig. 17.1

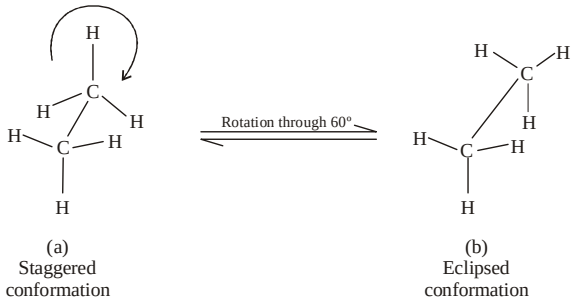


Fig. 17.1. Staggered and Eclipsed conformations of ethane.

Newman proposed simpler formulae for representing the conformations. They are called *Newman projection formulae*. In Newman projection, the two carbon atoms forming the bond are represented by two circles, one behind the other, so that only the front carbon is seen. The hydrogen atoms attached to the front carbon are represented by C–H bonds from the center of the circle. The C–H bonds of the back carbon are drawn form the circumference of the circle.

17.6.3 Some Important Terms and Concepts

Stereochemistry: It is branch of chemistry which deals with the study of molecular structures in three dimensional space.

Isomerism: The phenomenon by virtue of which different organic compounds can be represented by same molecular formula.

Structural Isomerism: The isomerism in which the isomers differ in their structural arrangements of atoms.

Stereoisomerism: The isomerism in which the isomers differ from one another in the spatial arrangements of atoms or groups with respect to one another.

Conformations: The different spatial arrangement of atoms or groups around the carbon–carbon single bond which can be converted into one another by rotation about C–C bond.

Geometrical Isomers: The isomers which differ from one another in the spatial arrangement of atoms or group bonded to carbon atoms carrying double bond.

Conformations cannot be separated from one another.

Plane Polarized Light: Light having oscillations of waves in a single plane.

Optically Active Substances: The substances which rotate the plane of polarised light.

Dextrorotatory Substances: Chemical substances which can rotate the plane of polarized light towards right.

Laevorotatory Substances: Chemical substances which can rotate the plane of polarized light towards lift.

Chiral Centre: A carbon atom in a molecule which is linked to four different atoms or groups.

Chiral Molecule: A molecular structure which possess plane of symmetry. A chiral molecule is nonsuperimposable on its mirror image.

Achiral Molecule: A molecular structure which possess plane of symmetry.

Enantiomers: These are pair of molecules which bear object image relationship but are nonidentical. Enantiomers rotate the plane of polarised light in opposite directions but to equal extent.

Diastereomers: These are the configurational isomers which are not enantiomers. In fact, they are stereoisomers which are neither mirror images of each other nor identical.

Meso Compound: These are the achiral molecules which possess chirality centres. They are optically inactive due to internal compensation.

Racemic Mixture: A mixture of equal parts of two enantiomeric forms of the substance. Racemic mixture is also called Racemic modification and is optically inactive due to external compensation.

Resolution: It is a process of separation of enantiomeric forms from the racemic mixture.

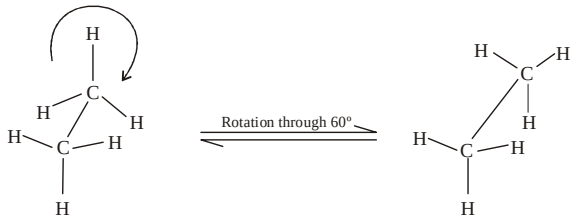
17.7 Stereochemistry of Compounds Containing Phosphorus

Phosphorus and arsenic compounds can exhibit covalencies of 3, 4, 5and 6; they give rise to more possible configurations than nitrogen. In tercovalent compounds the valency disposition is tetrahedral (sp^3); one orbital being occupied by a lone-pair of electrons, in quinquevalent compounds the valency disposal is trigonal bipyramidal

(sp^3d) and in quadricovalent unielectrovalent compounds one electron is transferred from phosphorus or arsenic atom to the anion and thus the valency disposition is again tetrahedral (sp^3).

1. Tercovalent phosphorus compounds. Unlike tertiary amines, certain trivalent phosphorus compounds (phosphines) have been resolved. The resolution is because of the slower frequency of oscillation of phosphorus (*e.g.*, the value in phosphine is 5×10^6) in phosphines as compared with that of nitrogen (2.3×10^{10}) in a tertiary amine. By increasing the weight of the groups attached to phosphorus in a phosphine the oscillation can further be slowed down, *e.g.*, replacement of the three hydrogen atoms by deuterium atoms decreases the oscillation frequency and hence can be resolved. In practice Horner *et al*. (1961) resolved (C_2H_5) (CH_3) C_6H_5P, $(CH_3)C_6H_7P$, etc.

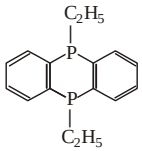
Horner also deternined the configuration of pheny methy-propyl phosphine (II) by reducing (+) benzylphenylmethylpropyl phosphonium bromide (I) electrolytically to the former and since the product can be reconverted into phosphonium bromide by means of benzylbromide, the configuration of the two compounds must be same. Now since the absolute configuration of the bromide has been shown to be (+), the phosphine must also be (+)-phosphine.



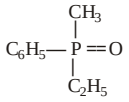
(a) Staggered conformation (b) Eclipsed conformation

Optically active phosphines are fairly optically stable and racemises on heating through oscillation.

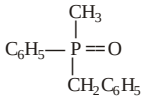
Mann *et al*, (1962) isolated the two geometrical isomers of the compound 5, 10-diethyl-5, 10-dihydrophosphanthrene.



2. Quinquevalent phosphorus compounds. Phosphine oxides were the earliest phosporus compounds to be resolved (Meisenheimer, *et al*. 1911). *e.g*.,

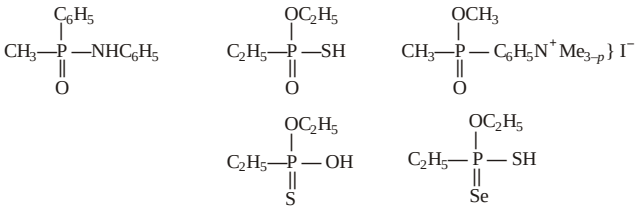


ethylmethylphenyl phosphine oxide

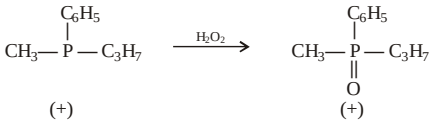


benzylmethylphenyl phosphine oxide

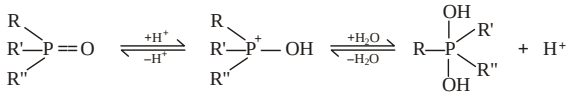
After the above two quinquevalent phosphorus compounds, several other compounds of the type $R_3 P = X$ have been resolved.



Optically active phosphine oxides (and sulphides) have been prepared from phosphines and hydrogen peroxide (and sulphur) with retention of configuration, *e.g.*,

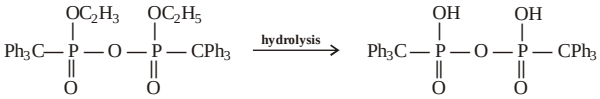


Phosphine oxides, when treated with acids, undergo racemisation, the possible mechanism being:

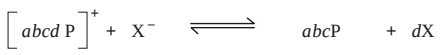


The above mechanism is supported by *tracer technique* (Denney *et al.*;1964).

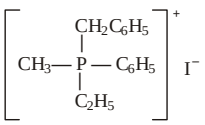
Hatt (1923) studied optical activity in compounds containing two similar asymmetric phosphorus atoms and obtained the meso and racemic modification foms of ethyl triphenylmethylpyrophosphate. Both the forms give same acid on hydrolysis.



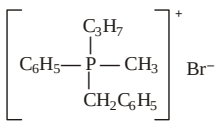
3. Quaternary phosphonium compounds. Although generally phosphonium salts containing alkyl groups tend to racemise in solution due to follwing type of dissociation,



compounds I and II have been resolved.

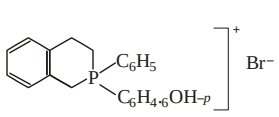


Benzylethylmethylphenyl phsophonium iodide, (I)

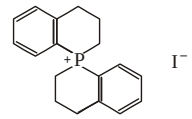


(II)

On the other hand, phosphonium salts containing phosphorus atom in the ring are much more optically stable and can be easily resolved *i.e*., they do not lose their optical activity in solution at room temperature. Thus Hollimann and Mann in 1947 and Mann in 1955 prepared and resolved compounds III and IV respectively.

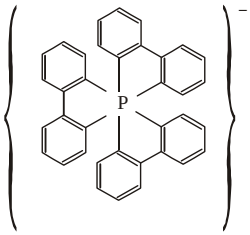


2-*p*-hydroxyphenyl-2-phenyl-1,2,3,4 tetrahydro isophosphinolianium bromide, (III)



p-spirobis-1,2,3,4-tetrahydro phosphinolinium iodide, (IV)

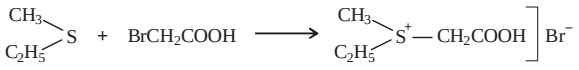
Hellwinkel (1965) resolved the salts of the hexavalent phosphrous compound, (V).



17.8 Stereochemistry of Compounds Containing Sulphur

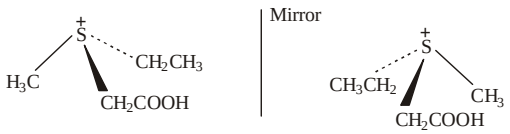
Several types of sulphur compounds have also been resolved and thus have been found to exhibit the optical isomerism. These sulphur compounds belong to sulphonium salts, sulphoxides, sulphinic esters, sulphidimines or sulphines.

1. Sulphonium salts (Sulphoniumion). The success of Peachey in resolving a substituted ammonium salt gave a great impetus to the investigation of compounds containing asymmetric sulphur atom. Pope and Peachey in 1900 prepared* carboxymethylethylmethyl sulphonium bromide (I) by treating ethyl methyl sulphide with bromoacetic acid. Since sulphur in sulphonium salts is tercovalent electrovalent



I

(sp^3 hybridisation), these salts are comparable to the quaternary ammonium salts. Several asymmetric sulphonium salts of the type, $[S^+R'R'']X^-$, have been resolved into optical enantiomers, and it is considered that four valencies are tetrahedral. Thus the two enantiomers of carboxymethylethylmethyl sulphonium salts can be represented as below.



Enantiomers of carboxymethylethylmethylsulphonium bromide

It seems quite surprising that these salts are resolvable while the tertiary amines are non-resolvable (explanation given in the end).

The practical existence of these two isomers was evidenced by the following two points.

(i) The synthetic carbo methyl ethyl methyl sulphonium bromide was treated with silver (+) – camphorsulphonate and the product was fractionally crystallised from ethanol – ether mixture. The less soluble fraction was found to possess M_D of + 68º and now since the rotation of (+)– camphorsulphonate ion is only about + 52º, the balance of rotation *i.e.*, + 68º– (+52–) = + 16º of the (+)– sulphonium camphorsulphonate must be the contribution of the sulphonium ion.

(ii) The camphorsulphonate ion of the (+) sulphonium camphorsulphonate when replaced by the platinichloride ion, the product $[CH_3(C_2H_5)SCH_2COOHH]_2^+PtCl_6^{2-}$ is found to possess an of + 4.5º in water.

In addition to the above sulphonium salt, the following two sulphonium salts have also been resolved.

ethylmethylphenacylsuphonium picrate (Smiles in 1900)
Specific rotation being +8.1º and –9.2º

[Mann and Holliman in 1946]

It is important to note that the optical activity of the sulphonium salt is not destroyed by the ionisation of the anion in aqueous or alcoholic solution and is thus concerned with the trisubstituted sulphonium ion (*cf* tertiary amines of the type NRR'R" which have no activity, although identical with sulphonium ions in the arrangement of valency electrons around the central atom).The resolvability of the sulphonium salts (sulphonium ions) is owing to the configurational stability of the sulphur atom in these compounds and thus failure of pyramidal inversion.

---

* Optically active sulphonium salts have also been obtained form the optically active sulphoxides in the following way (Anderson, 1971).

2. Sulphinic esters. The sulphinic esters of the type RSO_2R' were resolved by Phillips in 1925, by means of kinetic method of resolution. In practice, racemic modification of ethyl *p*-toluenesulphinate is heated with (–) –menthyl or (–) *sec*-octylalcohol (*alcoholysis*). Now since the two optical isomers react at different rates [in the present example (+)– ester reacts faster than the (–)–ester] with the optically

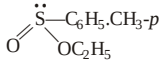
active alcohol, the product will be consisting of one diastereoisomer more than the other and thus the partial resolution has occurred.

$$(\pm)\,\text{Ester}\,(-)-\text{Alcohol} \rightarrow (+)-\text{Ester}\,(-)- \quad \text{Alcohol} + \,(-)-\text{Ester}(-)-\text{Alcohol}$$

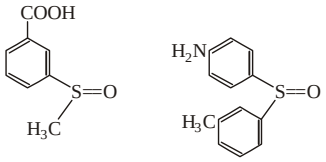
(Major) (Minor)

The products [mainly consisting of (+) – ester derivative] and reactants [mainly consisting of (–) ester] are separated from each other by means of fractional distillation: the reactants i.e., the unchanged ester will be distilled first on account of its lower boiling point. The product containing mainly (+) – ester derivative is then heated with excess of alcohol [alcoholysis; the (–)- menthy or (–) - *sec*-octy alcohol is replaced] to give back the original ethy *p*-toluenesulphinate containing more of the (+) –isomer.

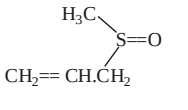
The optical isomerism sulphinates is explained on the basis of the following structure in which sulphur atom is sp^3 hybridised.



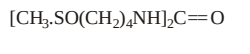
3. Sulphoxides: Sulphoxides of the type RSOR' have also been resolved, some of the important examples are:



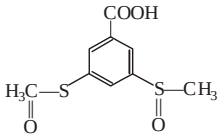
m-carboxyphenyl methyl sulphoxide



4 amino-4 methyldiphenyl sulphoxide



(Sulphoraphene, a naturally occurring optically active sulpoxide)

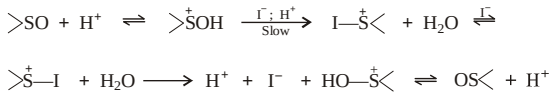


Bell and Bennett

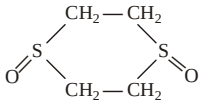
Optically active sulphoxides have also been obtained by the oxidation of unsymmetrically substituted sulphides, RSR', by means of optically active peroxy-acids (asymmetric synthesis). For example, Savige *et al*.(1965) prepared optically active disulphoxide monoxides (thiosulphinates) of the type ArSOSAr by oxidising diaryl disulphides with peroxycamphoric acid. Montanari *et al*. (1968) oxidised racermic alkyl aryl sulphoxides with optically active peroxy acids to racemic alkyl aryl sulphones and optically active sulphoxides (perferential oxidation of one of the sulphoxide enantiomers).

Cram *et al*. (1963) prepared the diastereomeric sulphoxides by the oxidation of (–)-2-octyl phenyl sulphide with *t*-butyl hydroperoxide (an asymmetric reagent).

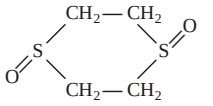
The phenomenon of racemisstion has been observed in sulphoxides (Henbest, 1964). For example, (+)-benzylp-tolyl sulphoxide is racemised on heating in decalin at about 162ºC. Optically active sulphoxides are also racemised at room temperature by means of hydrogen chloride in organic solvents, viz. benzene, dioxan, etc. The mechanism proposed for the racemisatrox of sulphoxides is:



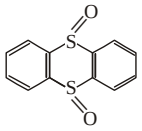
Disulphoxides also exhibit the phenomenon of geometrical isomerism. For example, the following disulphoxides exist in the *cis* and *trans*-forms.



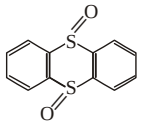
cis-Diethylene-disulphoxide



trans-Diethylene-disulphoxide



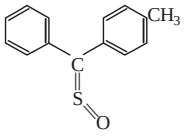
α-(*cis*)-thianthrene dioxide



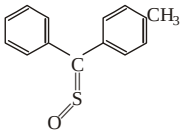
β-(*trans*)-thianthrene dioxide

Optical activity in sulphones of the type RSO_2R' has also beeb observed provided the two oxygen atoms are differnt. Thus Stirling (1963) synthesised (–)-benzyl-p-tolyl[^{16}O O^{18}] sulphone having the specific rotation of–0.16º. This was the first example of isotopic asymmetry* for a central atom other than carbon.

4. Sulphines: The NMR spectroscopic studies revealed the fact that the C=S=O system in sulphines is rigid and thus sulphines msy exist in two geometrical isomeric form. Mangini *et al*. (1969) observed that the sulphine prepared by the oxidation of the thioketone with peroxy acid may exist in the following isomeric forms.



syn



anti

17.9 Stereochemistry of Compounds Containing Nitrogen

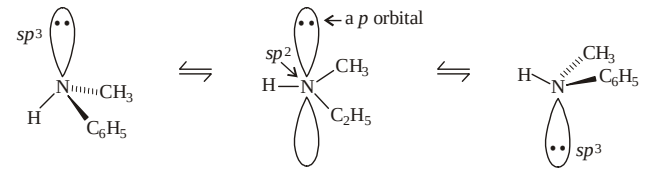
Like the carbon compounds, the nitrogen compounds also exhibit both the types of stereoisomerism, i.*e.,* the enantiomerism and geometrical isomerism.

The tetrahedral concept of carbon has also been successfully applied to nitrogen. The only difference from carbon is that one of the sp^3 orbitals of nitrogen usually contains a lone pair of electrons which is not involved in bonding. Thus, nitrogen generally has three ligands, and one lone pair in the sp^3 orbital. In terms of a chiral centre, nitrogen is analogous to carbon. Thus, tertiary amines of the type shown in

diagram I have a chiral nitrogen but do not exhibit optical activity. This is because the groups on the nitrogen atom undergo rapid interconversion involving movement of the lone pair from one face of the molecule to the other resulting in rapid racemisation.

--

* The example of isotopic asymmetry around carbon atom was first of all observed by Eliel in 1949 who prepared optically active phenylmethyldeuteromethane, $CH_3CHDC_6H_5$, by reducing optically active phenyl methyl chloride (phenylethyl chloride), $CH_3CHClC_6H_5$, with lithium aluminium hydride.



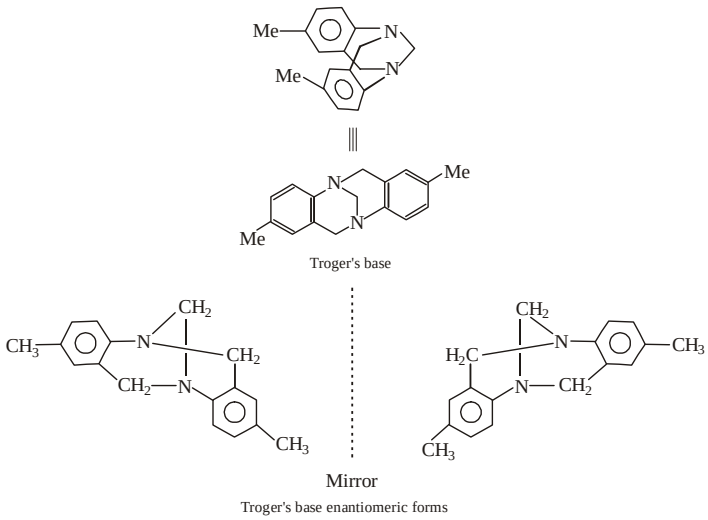
R–ethylmethylamine Transition state is planar *S*–ethylmethylamine

the lone pair moves from one face of the molecule to the other

(I)

Actually, no bonds are broken in the above interconversion, however, the configuration assignment is applied because the interconversion can be described as an inversion (turning inside-out of an umbrella) and to avoid confusion, such enantiomers are termed *invertormers*.

When the nitrogen atom is present at a ring junction in bridged ring systems, the pyramidal inversion is not possible without bond breaking. Thus, with proper substitution the tricoordinate nitrogen becomes a stable centre of chirality as in *Troger'd base*. Which has been resolved (Prelog and Wieland, 1944) by chromatography on powdered (+)- lactose.

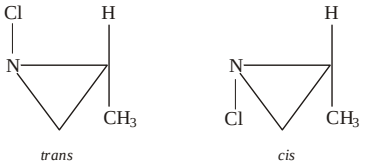


Troger's base

Mirror

Troger's base enantiomeric forms

Various N-substituted aziridines have been resolved into stable enantiomers but at temperatures below –50ºC. The rate of inversion in *N*-substituted aziridines depends on the nature of the *N*–substituent and the presence of substituents attached to the ring carbons. For example, the two invertomers of 1-chloro-2-methylaziridine have been separated, and they do not interconvert at room temperature.

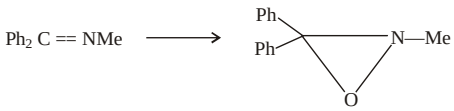


trans *cis*

1–Chloro-2-methylaziridines

Thus, a nitrogen atom in a three-membered ring and connected to another atom with an unshared pair invert particularly slowly. Consequently. *e.g.*, such a compound **III**

(2-methyl-3, 3-diphenyloxairidine) has been obtained by an asymmetric synthesis involving the oxidation of N-diphenylmethylene methylamine **II** with (1S)-(+)-peroxycamphoric acid.

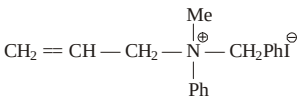


II (–) III

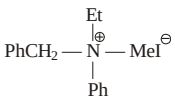
It is important to note that the tertiaing amines of the type $ArNr^1R^2$, where Ar is an aromatic nucleus containing at least one *ortho* ligand and R^1 and R^2 are different groups, have been resolved. The optical activity of these compounds is due to the chirality of the molecule as a whole which is due to the restricted roation about the N—C (aryl) bond.

When the lone pair is involed in bonding with a ligand giving the species, the rapid interconversion is prevented. Thus, tetraalkylammonium salts (Quaternary ammonium salts) with four different ligands exhibit optical activity. *Various quartunary ammonium salts have been resolved into their enantiomeric forms*, e.g., allylbenzylmethylpheny ammonium iodide **IV** and benzylethlmethylphenyl ammonium iodide **V**.

Optically active ammonium salts are very readily racemised as compared to that of carbon compounds. This is because of their decomposition into amines which then rapidly racemise. Now, the racemic amine recombines with dissociated product *dX* to form the racemised quaternary salt.

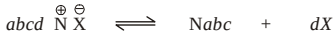


IV Resolved

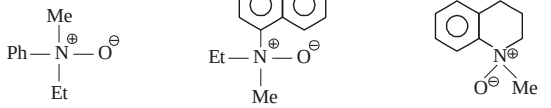


V Resolved

Optically active ammonium salts are very readily racemised as compared to that of carbon compounds. This is because of their decomposition into amines which then rapidly racemise. now, the racemic amine recombines with dissociated product *dX* to form the racemised quaternary salt.



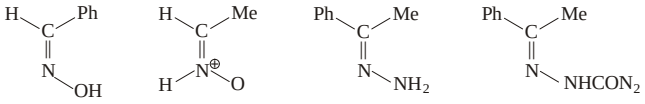
Like quaternary ammonium salts of the type abce , tertiary amine oxides of the type are resolvable, *e.g.,* the following amine oxides have been resolved:



Ethylmethylphenylamine oxide | Ethylmethyl-1-naphthylamine oxide | Kairoline oxide

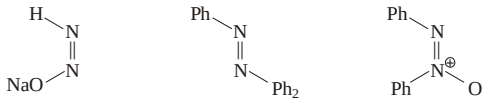
Geometrical Isomerism of Oximes

Nitrogen compounds containing >C=N— as well as —N = N— bond exhibit geometrical isomerism. The important classes of compounds exhibiting geometrical isomerism due to >C=N— bond are: (i) oximes (ii) nitrones (iii) hydrazones and semicarbazones



anti (Z) (Benzaldoxime) | (*E*) (Nitrone) | (*E*) (Hydrazone) | (*E*) (Semicarbazone)

Examples of compounds exhibiting geometrical isomerism due to —N==N— bond are:



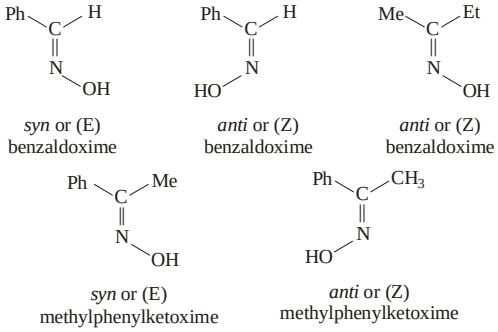
syn (Z) Diazoate | *anti* (E) Azobenzene | *syn* (E) Azoxybenzene

Oximes are the most common compounds and we will discuss their geometrical isomerism in detail.

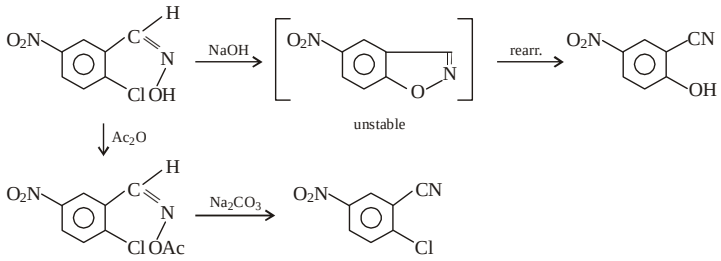
Both the carbon and nitrogen atoms in oximes are sp^2 hybridised. The C=N bond in oximes consists of one and one bond. There is no free rotation about C=N, hence oximes of aldehydes and unsymmetrical ketones exhibit geometrical isomerism.

Nomenclature: The prefixes *syn* and *anti* are used instead of *cis* and *trans*. In the syn oxime the hydroxyl group on nitrogen, and hydrogen or the first-named of the two groups on the carbon are on the same side, while in the anit-isomer they are on the opposite sides. The E-Z system of nomenclature is also applied to oximes and it is more convenient. If the group with greater priority and the hydroxyl group are on the

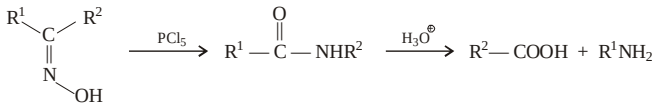
same side of the double bond, the configuration is Z, if on the opposite sides it is E. For example.



Determination of the configuration of oximes: The configurations of geometrical isomers of **aldoximes** are dertermined by their relative ease of dehydration. For example, the *anti*-aldoxime **I** (*anti*-2-chloro-5-nitrobenzaldoxime) readily undergoes cyclisation, hence this form is *anti*-isomer. This isomer gives cyanide on treatment with acetic anhydride follwed by aqueous sodium carbonate. Thus, *anti*-elimination must have occurred. On the other hand, the *syn*-aldoxime does not give cyanide. Hence using *anti*-elimination as the criterion for these reactions, the configurations of *syn*-and *anti*-forms can be determined.

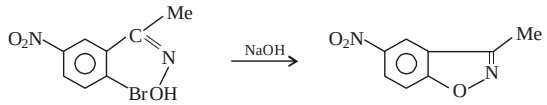


The configuration of **ketoximes** have been determined by *Beckmann rearrangement*. When treated with acidic reagents such as H_2SO_4, acid chlorides, acid anhydride, PCl_5, P_2O_5, etc. Ketoximes undergo Beckmann rearrangement to give a substituted amide by migration of the group which is anti to the hydroxyl group.

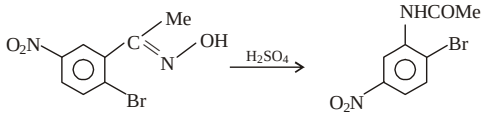


The structure of the amide obtained is determined by their hydrolysis to the corresponding carboxylic acid and amine which indicates the configuration of the parent oxime, because the group R incorporated in the amine must be *anti* to the hydroxyl group int the oxime.

That the group *anti* to the hydroxyl group actually migrates, was shown by the following reaction:



2-bromo-5-nitroacetophenone oxime



2-bromo-5-nitroacetophenone oxime

Out of the two isomeric ketoximes of 2-bromo-5 nitroacetophenone, one undergoes cyclisation with NaOH, hence it must be *syn*-methyl isomer. The othor isomer is unaffected by NaOH, but on treatment with H_2SO_4 it undergoes Beckmann rearrangement to give *N*-substituted acetamide: thus group *anti* to the hydroxyl group migrates.

17.10 Summary

In this unit we have discussed structure of different types of ylides, their synthesis and structures. Phosphorus ylides, Sulphur ylides and Nitrogen ylides were explained in detail.

Also, stereochemistry of compounds containing phosphorus, sulphur, nitrogen were explained.

17.11 Comprehensive Questions.

1. What is 'Ylide'?
2. Discuss the following with examples

   (i) Phosphorus ylides (ii) Nitrogen ylides (iii) Sulphur ylides.
3. Write short notes on :

   (i) Stereoisomerism (ii) Structural isomerism.
4. With suitable examples, discuss briefly the stereochemistry of phosphorus, sulphur and nitrogen compounds.

17.12 References and Suggested Reading

1. Morrison Boyd– Organic Reactions Mechanisms.
2. O.P. Agarwal– Reaction Mechanism.
3. Jerry March, Organic Chemistry.
4. Jagdamba Singh and LDS Yadav– Advanced Organic Chemistry.

Unit–18: Addition to Carbon Hetero Multiple bonds, addition of Grignard Reagent, Organozinc, organocopper and organolithium reagent to carbonyl and unsaturated carbonyl compounds

Structure of Unit

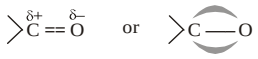
18.1 Objectives

At the end of the unit learner will be able to identify.

- Structure and reactivity of carbonyl compounds.
- How G.R. react with carbonyl compound.
- Mechanism of addition of organozinc to carbonyl compounds.
- Mechanism of addition of organolithium to carbonyl compounds
- Mechanism of addition of organocopper to carbonyl compounds.

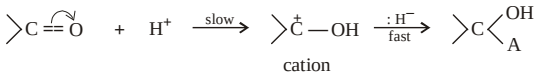
18.2 Introduction

Owing to different electronegativity of carbon and oxygen, the eletrons of the carbon-oxygen double bonds are shifted to the more electronegative oxygen and thus, such bonds are strongly polarised (difference from carbon-carbon double bonds).



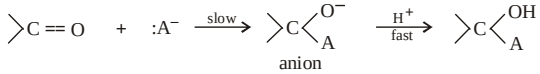
Thus, the carbonyl group has two active centres, *viz*. a positive centre (electrophilic or cationoid) on the carbon atom which can be attacked by nucleophilic reagents, and a negative centre (nucleophilic or anionoid) on the oxygen which can be attacked by electrophilic reagents. Thus, the addition reactions on carbonyl group can theoretically proceed via two mechanisms.

Mechanism I



cation

Mechanism II

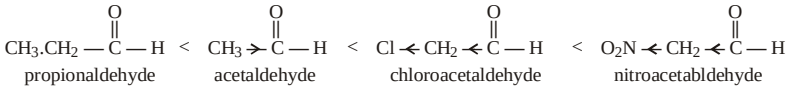


anion

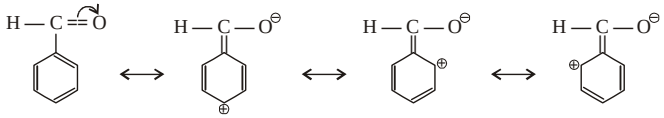
But since anion is more stable than cation, the addition to carbonyl group should proceed via mechanism II which is further proved in the addition of HCN to carbonyl group.

Structure and reactivity of carbonyl compounds: Since the rate determining step in the common mechanism II is the attack of nucleophilic reagent at the positively charged carbon atom of the carbonyl group, the reactivity of the carbonyl group towards the addition reactions depends upon the magnitude of the positive charge in the carbonyl carbon atom. Thus, any substituent or factor in the carbonyl compound that increases the positive charge on the carbonyl carbon atom must increase its reactivity towards addition reactions and vice versa. In practice also it is found to be so, e.g., the introduction of alkyl group or any other electron donating factor on the carbonyl group decreases its reactivity and thus, formaldehyde is more reactive that other aldehydes which in turn are more reactive than ketones.

On the other hand, introduction of electron attracting group in the carbonyl compound increases the positive character of the carbonyl carbon atom and hence increases its reactivity which is evident from the following examples.

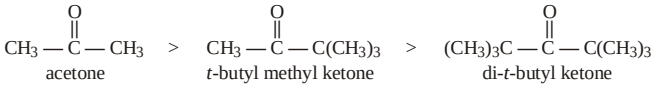


Since the positive charge on the carbonyl carbon atom can delocalized over the benzene nucleus in aromatic aldehydes, the latter are less reactive than aliphatic aldehydes.



Furthermore, as in aliphatic aldehydes the reactivity of aromatic aldehydes is further decreased by the presence of electron-donating group (*e.g.,* —OH) in the benzene nucleus; and increased by the presence of electron attracting group (*e.g.,* —OH_2) in the nucleus.

Lastly, it is also important to note the presence of bulky groups in the vicinity of the carbonyl group also retards the addition reactions which is evident from the following order of reactivity–



After studying the effect of various groups on the carbonyl group towards addition reactions, let us study some imporatant addition reactions individually.

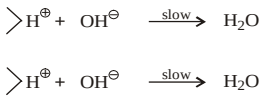
(i) Addition of hydrogen cyanide: Hydrogen cyanide forms addition compounds (cyanohydrins) with aldehydes and simple ketones; thus reaction is found to be catalyzed by bases or salts of weak acids, retarded by acids and unaffected by neutral compounds. These observations led to the following important conclusions:–

(a) Hydrogen cyanide does not add as a molecule but adds as H^+ and CN^- ions in two different steps.

(b) As the reaction is retarded by acids, the rate determining step does not involve the addition of H^+ and thus must involve the addition of CN^- (nucleophilic reagent) and therefore, cyanohydration is an example of nucleophilic addition.

(c) The addition of CN^- as the rate determnining step is evident from the fact that the reaction is accelerated by bases which shifts the equilibrium of ionization of HCN to right $(HCN \rightleftharpoons H^+ + CN^-)$ by fixing the H^+ ions with the OH^- ions as unionisable water:

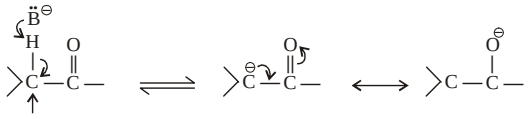
* It is important to note that the carbonyl compounds, other than aldehydes or ketones, viz. amides, esters, carboxylic acids, etc. do not readily undergo addition reactions because resonance of the carbonyl group with the neighbouring lone pair of electrons diminishes the group's polarity.



Therefore, the reaction proceeds with nucleophilic attack by cyanide ion, followed by protonation from HCN or H_2O.

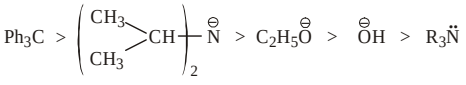
Carbon-carbon bond formation is the basis for the construction of the molecular frame work of organic molecules by synthesis. One of the fundamental processes for carbon-bond formation is a reaction between a nucleophilic carbon an electrophilic one.

A very important means of generating carbon nucleophiles involve removal of a proton from a carbon by a base. The anions produced are carbanions. Both the rate of deprotonation and the stability of the resulting carbanion are enhanced by the presence of substituent groups that can stabilize negative charge. A carbonyl group bonded directly to the anionic carbon can delocalize the negative charge by resonance and carbonyl compounds are especially important in carbanion chemistry. The anions formed by deprotonation of -hydrogen bear most of their negative charge on oxygen and are referred to as enolates. Enolates although resonance stabilised, are nevertheless high energy species which react with electron defficient carbonly carbon to form carbon-carbon bond.

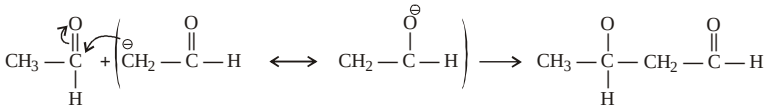


Formation of enolate ion.

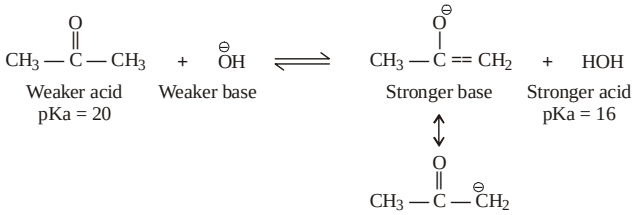
The commonly used bases for the formation of enolate ions, in order of decreasing base-strength are:



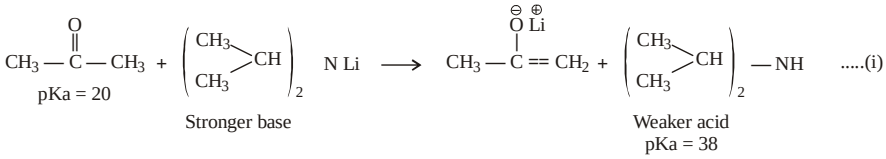
Most base-catalysed deprotonation reactions were carried out with an oxy-anion bases. However, for mono activated compounds where pKa of the carbonyl compound is in the range of 10–20, the concentration of enolate is very small.



Formation of carbon-carbon bond between -carbon of one molecule and carbonyl carbon of the other molecule



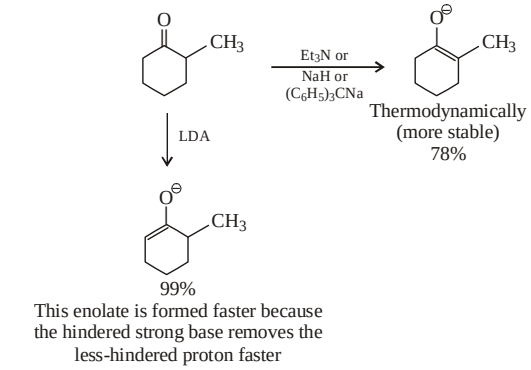
It has therefore become common practice to employ a base whose conjugate acid is sufficiently stronger than the enolate forming compound. For example, if the pKa of the bases of conjugate acids is 4 units greater than that of the carbonyl compound, formation of the enolate is 99.99%. One very useful strong base for converting ketones to enolate is lithium di-isopropylamide (LDA).



Regioselective Formation of Enolate Anions

An unsymmetrical ketone such as 2-methylcyclohexanone can form two possible enolates. Just which enolate is formed predominantly depends on the base used and also on the reaction conditions employed. The enolate with the more highly substituted double bond is the thermodynamically more stable enolate. This enolate is known as thermodynamic enolate. Thermodynamic enolate is formd in the presence of weak base and polar protic solvent.

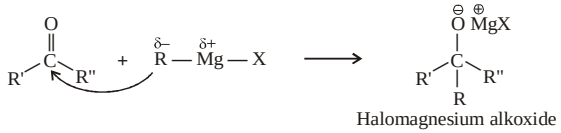
The enolate with the less substituted double bond is known as kinetic enolate. Ideal condition for kinetic control of enolate formation are those in which deprotonation is rapid, quantitative and irreversible. This idea is approached experimentally by using a very strong base in an aprotic solvent in the absence of excess of ketone. The best known strong base for this purpose is LDA. This strong sterically hindred base rapidally removes the proton from the less substituted alpha carbon of the ketone.



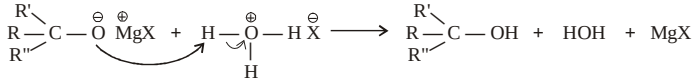
Enolates serve as carbon nucleophiles in carbonyl addition reactions. The addition reaction of enolates with carbonyl compounds is of very broad scope and is of great synthetic importance. The most common reactions of this category are *Aldol*, *Claisen*, *Knoevenagel*, *Perkin*, *Stobbe* and other related reactions.

18.3 Additon of Grignard Reagent to Carbonyl Compounds

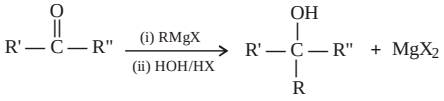
Grignard reagents react with carbonyl compounds (aldehydes and ketones) in the following way:



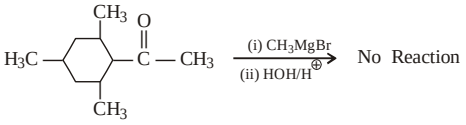
Halomagnesium alkoxide reacts with water in the presence of mineral acid (HX) to give alcohol. If the alcohol is teriary, it will be susceptible to acid-catalysed Grignard reagents always reacts in presence of on either in Halomanenisuim halie manaemeum las two positive changes. Mg+ dehydration. In this case, a solution of NH_4Cl in H_2O is often used because it is acidic enough to convert ROMgX to ROH without causing dehydration.

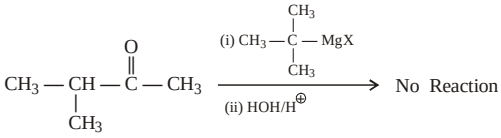


Thus the overall reaction is as follows:

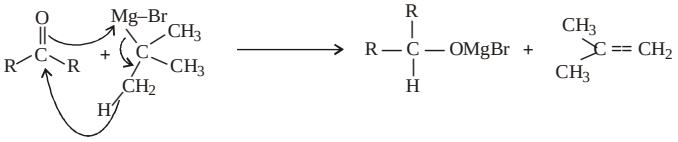


Effect of steric hindrance: Grignard additions are influenced by the presence of bulky groups around the keto group or in Grignard reagent or both.

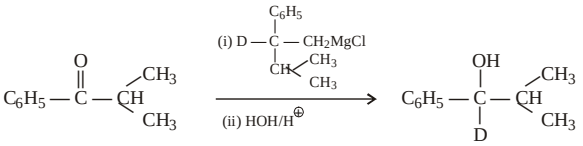




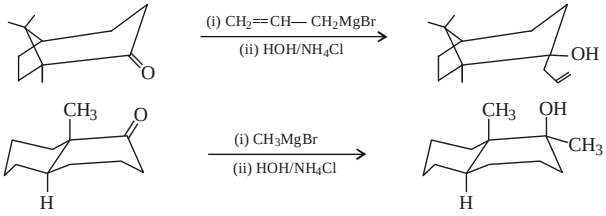
If the bulky group of the Grignard reagent has □-hydrogen then with some hindered ketones reduction of the carbonyl group via hydride ion transfer is observed.



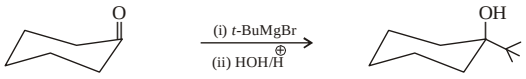
Optically active Grignard reagents having a hydrogen ie. T-Bumgx effectively transfer chirality to the substrate in the reduction of hindered unsymmetrical ketone. This result confirms that the hydride ion transfer takes place by the formation of six membered transition state.



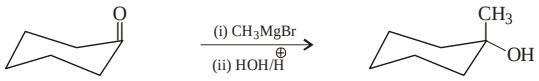
In cyclic ketones the less hindered face of the carbonyl group is attacked by the nucleophile.



Nature of the products also depends on the nature of Grignard reagents. If R of Grignard reagent is bulky then the OH group is situated at axial position, as the Grignard reagent approaches the keto group from the less hindered side due to steric repulsion.

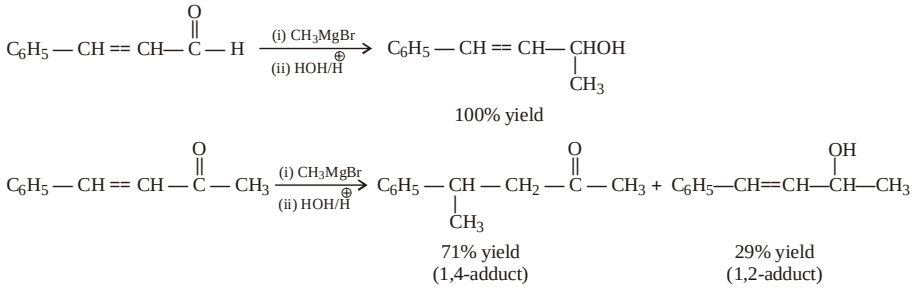


If R of the Grignard reagent is not bulky then —OH group is generally situated at equatorial position.

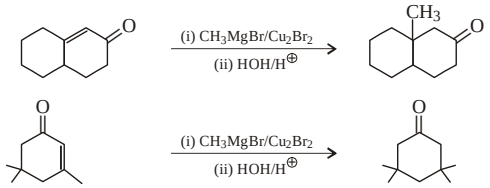


Grignard reagent readily add to unsaturated aldehydes and ketones. In such reactions both 1,2 and 1, 4 addition products are formed. In general, unsaturated aldehydes

give predominatly 1,2-addition product while ketones give 1,4-addition product as the major product.

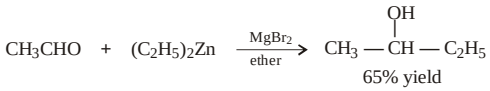


If addition of □,□-unsaturated ketones is carried out in the presence of Cu_2Br_2 then only I, 4-addition takes place.

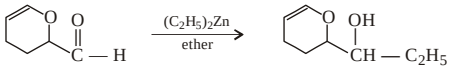


18.4 Addition of Orgonozinc to Carbonyl Compounds

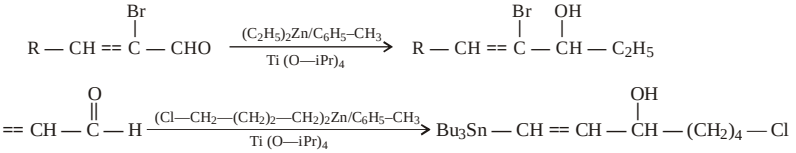
Diethylzinc reagents react slowly with carbonly compounds. Reactivity of lower dialkylzinc is more than the higher dialkylzinc reagents. Acetaldehyde reacts with diethylzinc in few hours. The reaction with higher homologues requires several days. Allylic zinc compounds are more reactive than simple dialky zinc reagents. Addition reaction of dialkylzinc compounds are promoted by Lewis acid metal halides.



The presence of a heteroatom at the alpha position to the carbonyl group accelerates the addition reaction.

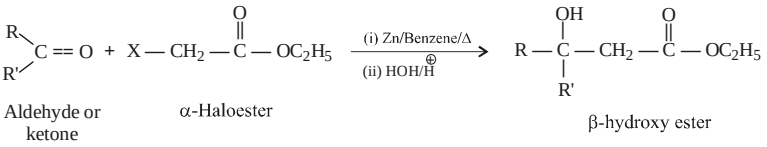


Very reactive titanium catalyst [$TiCl_4$, $Ti(O–iPr)_4$] increases reactivity of higher dialkylzinc reagents. The excellent functional groups tolerance allows the use of many functionalized aldehydes.



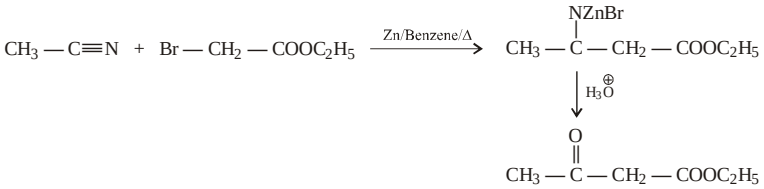
Reformatsky Reaction

Condensation reaction of carbonyl compound with *alpha*–halo ester in the presence of zinc metal leading to B- hyderoy ester is known as *Reformatsky reaction*. The solvent most often used in this reaction is benzene, ether or benzene-ether mixture. The product of the reaction after acidification is □-hydroxy ester.

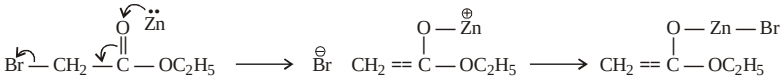


The halo ester in most of the cases is bromoester or its vinylogue, *e.g.*, R–CHBr–CH=CH–$COOC_2H_5$. However, the reaction may be carried out with halonitriles or halo N, N-disubstituted amides. Similar reaction also takes place between nitriles and halo ester.

In this case a □-keto ester is obtained.

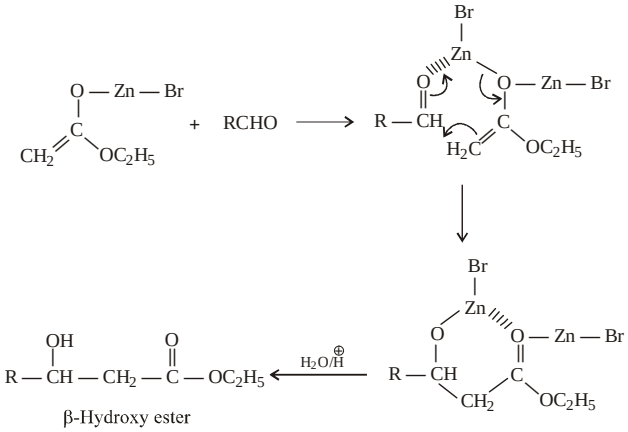


Mechanism: Zinc is a two electron donor and likes to be oxidized from Zn(0) to Zn(II). Zinc reacts with □-halo ester to form zinc enolate as follows:



Zinc enolate is often called the **Reformatsky reagent.**

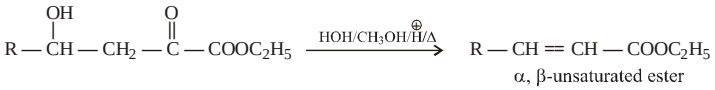
Zinc enolate react clearly with aldehydes and ketones to give zinc alkoxides which on hydrolysis give hydroxy ester.



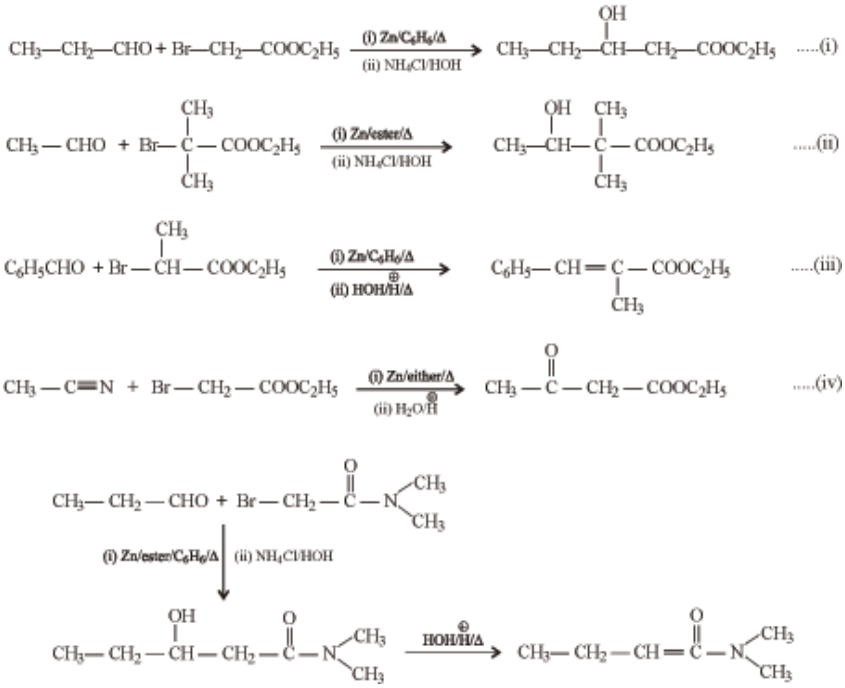
Mechanism of Reformatsky reaction

Zinc enolates do not react with esters. Hence there is no danger of self condensation between ester and ester in the presence of zinc metal. Therefore, use of zinc enolates is special to esters. Zinc does not form zinc enolate from a bromoaldehyde or an bromoketone. Thus there is not self condensation reaction between aldehyde or ketone.

The hydroxyester produced in this reaction is easily dehydrated to unsaturated ester because dehydration yields conjugated system which is stable due to the delocalisation.



Examples:



18.5 Addition of Organocopper to Corbonyl Compounds

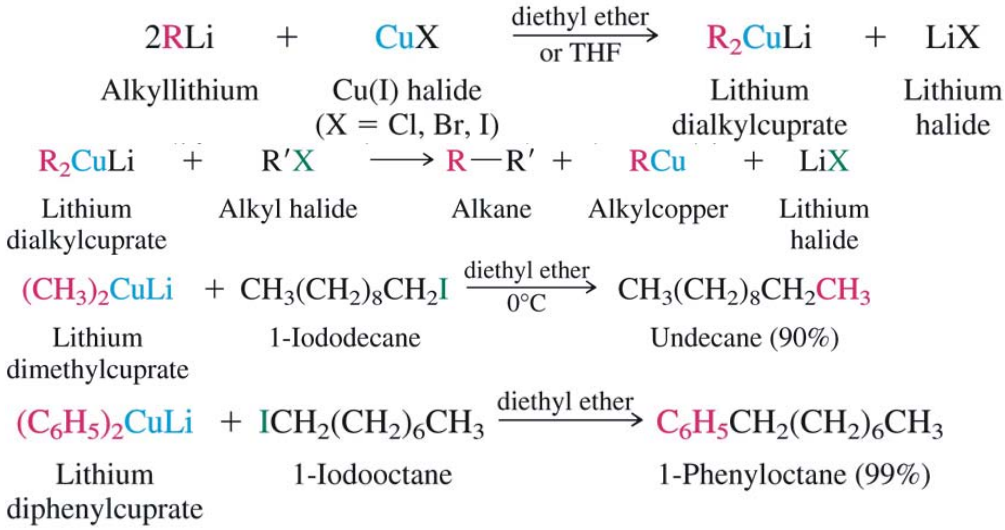
Among the various types of organo opper regrents most seen example lithium dialkys cuprate $[(R)_2Cu]^- Li^+$

Cuprates are less reactive than organolithium

- R acts as a Nucleophile
- Oxidation state of copper is Cu(I).
- Nucleophile “R” will attack various organic electrophiles.

- Organocuprates are used in cross-coupling reactions to form higher alkanes.
- Cross-Coupling Reaction: coupling of two different alkyls R and R' to yield a new alkane (R–R'). This type of reaction is used to make new C—C between alkyl groups.

Organocopper Reagents (Gilman Reagent)



Gilman Limitations

- Methyl and primary alkyliodides work well
  - elimination occurs with 2º and 3º R—X
  - seems to follow SN^2 conditions
- Also works for vinyl and aryl halides
- Use of organocopper reagents offers a very efficient method for coupling of two different carbon moieties.
- Cu is less electropositive than Li and Mg, the C—Cu bond is less polarized than the C—Li and C—Mg bonds. This difference produces three useful changes in reactivity:

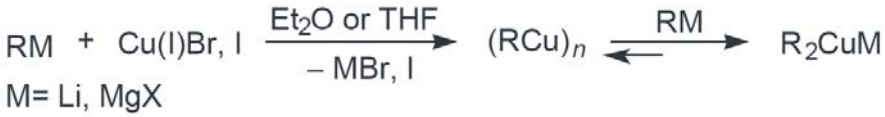
- organocopper reagents react with alkyl–, alkenyl–, and aryl halides to give alkylated products.
- organocopper reagents: more selective and can be acylated with acid chlorides without concomitant attack on ketones, alkyl halides, and esters.
- Relative reactivity: RCOCl > RCHO > tosylates, iodides > epoxides > bromides >> ketones > esters > nitriles.

- In reactions with unsaturated carbonyl compounds, the organocopper reagents prefer 1,4–addition over 1,2–addition.

Preparations

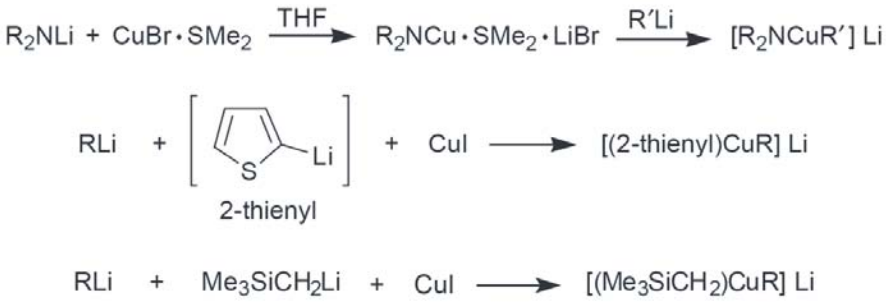
Homocuprate reagent (Gilman reagent: R_2CuLi, R_2CuMgX)

- Widely used organocopper reagents.
- Prepared by reaction of copper(I) bromide or preferably copper(I) iodide with 2 equivalents of appropriate lithium or Grignard reagents in ether or THF
- The initially formed **$(RCu)_n$** are polymeric and insoluble in Et_2O and THF but dissolve on addition of a second equivalent of RLi or RMgX.
- The resultant organocuprates are thermally labile and thus are prepared at low temperatures.



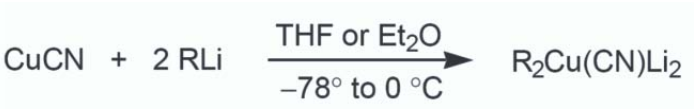
Preparations : Heterocuprate Reagent

- Since only one of the organic groups of homocuprates is usually utilized, a non-transferable group bonded to copper, such as RCC, 2-thienyl, PhS, *t*-BuO, R_2N, Ph_2P, or Me_3SiCH_2, is employed for the preparation of heterocuprate reagents.
- These cuprates are usually thermally more stable (less prone toward elimination of Cu–H), and a smaller excess of the reagent may be used.



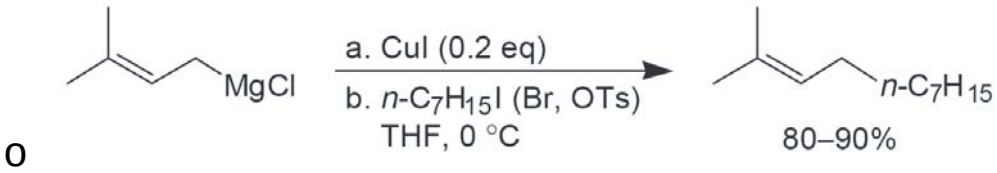
Preparations : Higher-order organocuprate reagents (Lipshutz reagents)

- Cyanocuprates exhibit the reactivity of homocuprates and the thermal stability of heterocuprates.
- Readily available by the reaction of CuCNwith 2 equivalents of RLi. The cyanocuprates are especially useful for substitution reactions of secondary halides and epoxides.



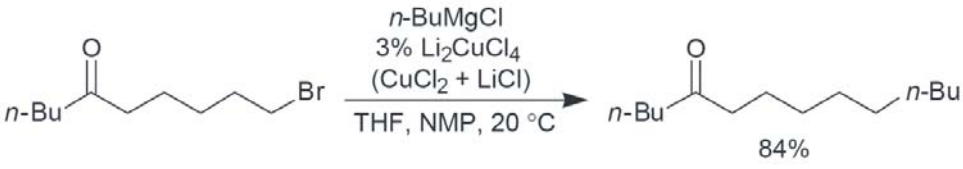
Preparations : Grignard-Copper(I) reagents

- Copper-catalyzed reactions of RMgX reagents are attractive when compatible with the functionality present in the starting material.
- Use of Grignard reagents is often the method of choice since they are readily available and only catalytic amounts of Cu(I) halides are required.



O

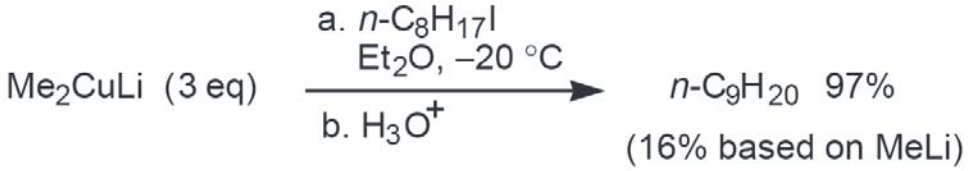
- Cu-catalyzed alkylation of organomagnesium reagents by RBr and RI in the presence of NMP (*N*-methylpyrrolidinone, a nontoxic, polar, aprotic solvent) represents an attractive alternative to the classical cuprate alkylation reaction.
- Only a slight excess of the Grignard reagent is required, and the reaction tolerates keto, ester, amide and nitrile groups. This method is especially suited for large-scale preparations.

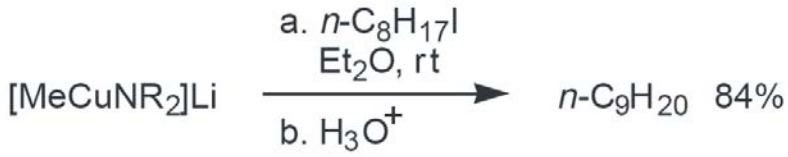


Reaction of Organocuprates

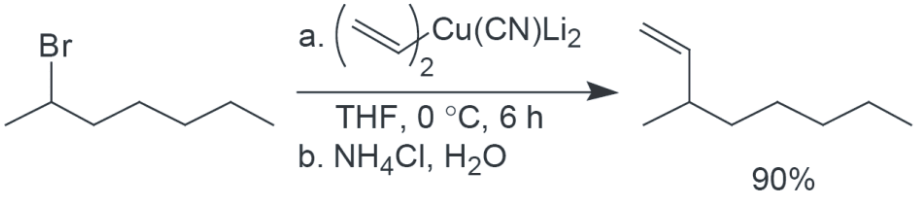
Substitution of alkyl halides

- Coupling of a ***primary alkyl iodide*** with an organocuprate is more economical when using a heterocuprate than a homocuprate.

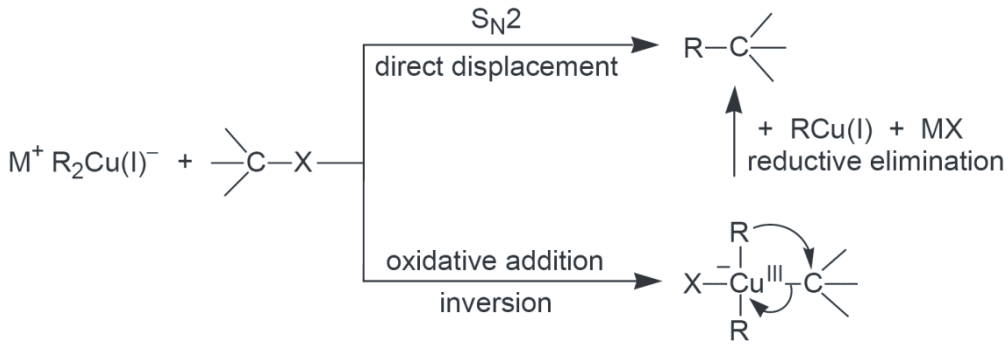




- While homocuprates readily undergo substitution reactions at primary positions, they do not couple well with unactivated secondary halides.
- However, cyanocuprates undergo substitution reactions even at unactivated secondary carbon centers.

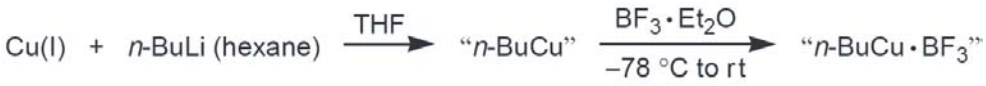


- Mechanism for the substitution reaction is complex, depending on nature of cuprate reagent, substrate, and solvent used.
- Reaction may proceed via an SN_2 displacement or via an oxidative addition followed by reductive elimination.

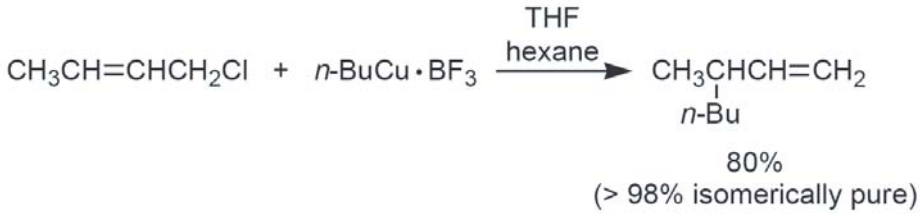


Substitution of allylic halides

- Alkylation of allylic halides with organocuprates usually produces mixtures of products due to competing SN_2 and SN_2, reactions.

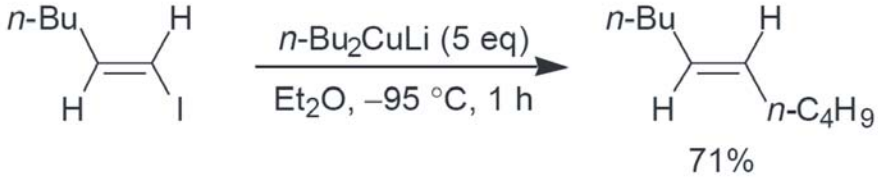


- Substitution with complete allylic rearrangement (SN_2 reaction) is observed with $RCu–BF_3$ as the alkylating agent.



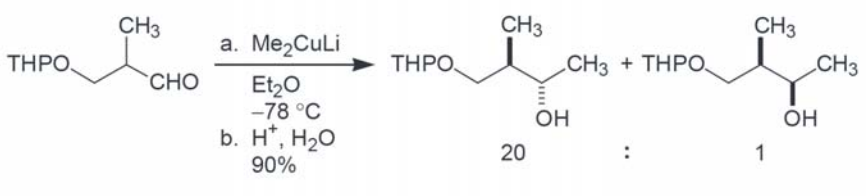
Reaction of vinyl halides

- Coupling of alkenyl bromides or iodides with organocuprates proceeds with high stereoselectivity.



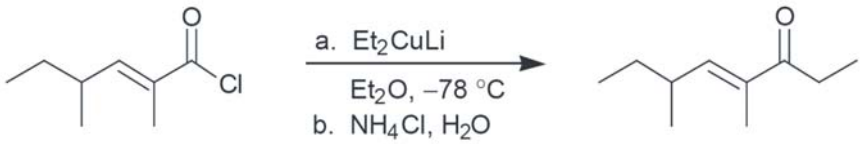
1,2-Addition to aldehydes and ketones

- Organocuprates undergo 1,2-additions to aldehydes, ketones, and imines. Reactions are often highly diastereoselective.

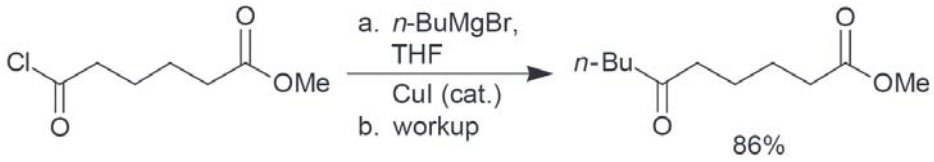


Acylation

- Reaction of organocopper reagents with acid chlorides affords corresponding ketones in high yields. Retrosynthetically, the reaction amounts to an alkylation of a carboxylic acid.



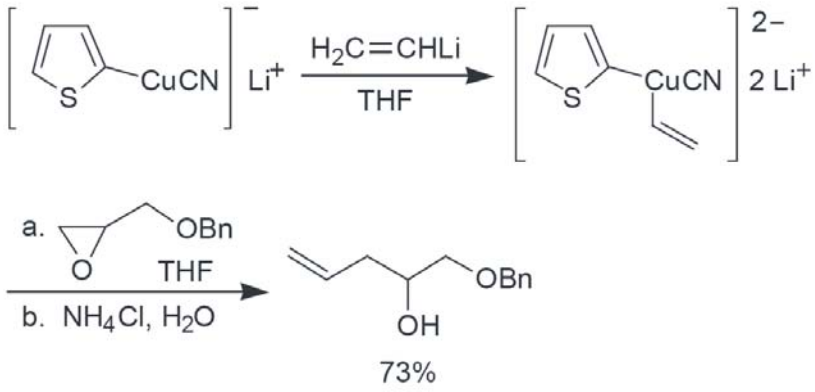
- In the presence of a catalytic amount of CuI, Grignard reagents convert acid chlorides chemoselectively to the corresponding ketones via a transiently formed cuprate reagent, which reacts competitively with the initial Grignard



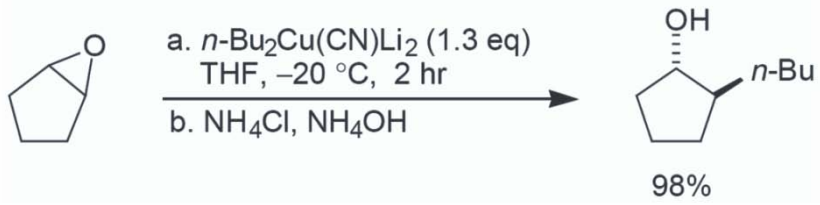
Epoxide cleavage reactions

- $R_2Cu(CN)Li_2$ reagents: among the mildest and most efficient reagents available for generating C–C bonds by way of epoxide cleavage using organocopper chemistry.

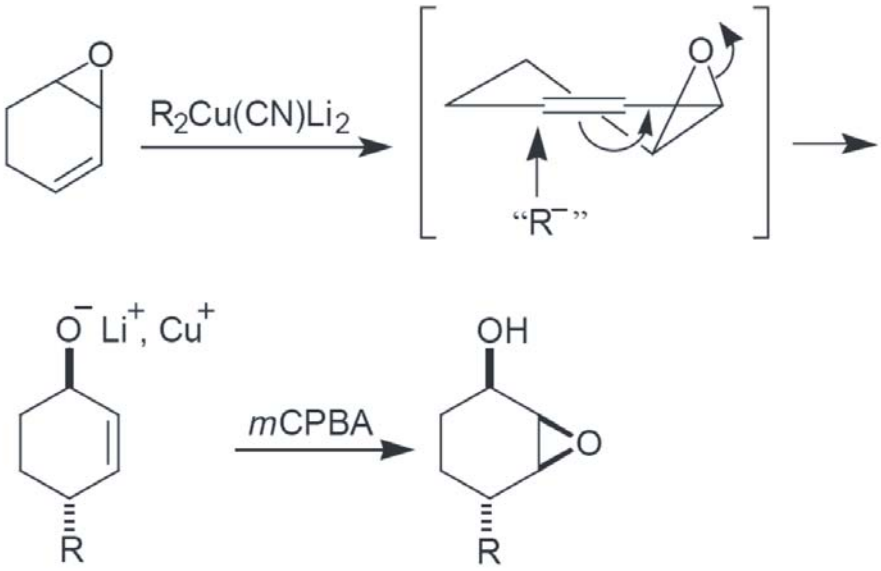
- Nucleophilic addition occurs at the less sterically hindered carbon of the oxirane ring



- Stereospecific SN_2 opening of cyclic epoxides with cyanocuprates furnishes, after workup, the *trans*-2-hydroxyalkylated products.



- However, the unsaturated epoxide reacts with cyanocuprates via an *anti*-SN_2-type mechanism. Directed epoxidation of the resultant allylic alcoholate produces a hydroxy epoxide containing 4 stereodefined carbon centers.



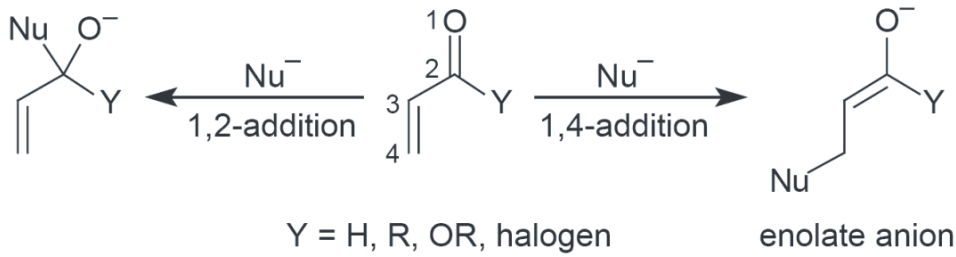
Conjugate Addition

- Conjugate addition is an important C–C bond formation
- Organometallic reagents may add in a 1,2- or 1,4-manner to unsaturated carbonyl compounds.

Table : Regioselectivity in Addition of RLi, RMgX, and Organocopper Reagents to unsaturated Carbonyl Compounds

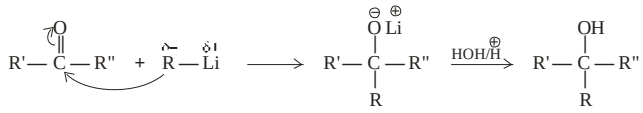
Nucleophile	1,2-Addition	1,4-Addition
RLi	+	–
RMgX	+	–
R_2CuLi	–	+
RMgX • CuX	–	+

- 1,4-Addition (conjugate addition) is most successful with "**soft**" (relatively nonbasic) nucleophiles such as –CN , RNH_2, RNH, RSH, enolates derived from □–dicarbonyl compounds, and organocuprates.
- 1,2-Addition is most successful with "**hard**" (relatively basic) nucleophiles such as hydride, organolithiums, and Grignard reagent.



18.6 Addition of Organolithium to Corbonyl Compounds

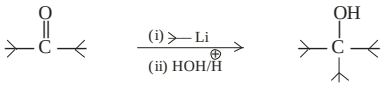
Carbonyl compounds react with organolithium to form lithium alkoxide which on hydrolysis gives hydroxy compounds.



Nucleophillc addition reaction of carbonyl compound with organolithlum

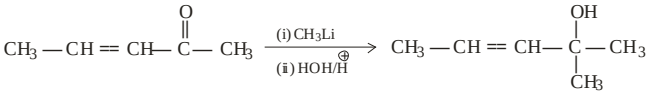
In some cases a major side reaction is deprotonation of alpha to the carbonyl group because organolithium is a strong base.

Organolithium has advantage over Grignard reagents. While the Grignard reagents fail to react with highly hindered carbonyl group, the organolithium react with such compounds to giving normal product.



Tritertiary butyl-carbinol

Organolithium compounds do not give conjugate addition reactions, they give only 1,2-addition reaction.



(only product)

18.7 Summary

In this unit structure of carbonyl group, effect of various groups on the carbonyl group towards addition reaction are studied.

Various addition reactions such as addition of HCN, addition of G.R., addition of organozinc, to carbonyl compounds are studied.

All these reaction occur by nucleophilic addition reaction mechanism and some of these reactions are found to be catalysed by base or weak acid.

18.8 Review of Questions

1. Write notes on Reformatsky reaction.

2. Write notes on Witting reaction.

3. Explain addition of Grignard Reagent to carbonyl compounds.

4. Explain addition to carbon hetero multiple bonds of organozinc to carbonyl compounds.

18.9 References and Suggested Reading

1. Morrison Boyd– Organic Reactions Mechanisms.
2. O.P. Agarwal– Reaction Mechanism.
3. Jerry March, Organic Chemistry.
4. Jagdamba Singh and LDS Yadav– Advanced Organic Chemistry.

Unit-19 : Conformational analysis of Acyclic Molecules

Structure of Unit

19.1 Objectives

At the end of unit learner will be able to understand

- Conformational Analysis
- Conformations of Acyclic Systems
- Conformations of Cycloalkanes
- Conformations of Sugars
- Conformations of Fused rings : DECALINS
- Effect of Conformation on Reactivity

19.2 Introduction

All molecule exhibit intramolecular motions such as deformation of bond angles, bond stretching and compression and rotation around one or more single bonds. This shows that a compound hardly have a fixed geometry but it exist in a dynamic equilibrium with a number of continuously changing temporal dimension to the molecular geometry.This is the reason that compound donot have fixed geometry

instead it exist in dynamic equilibrium with a continuously changing energy preferred conformations. Therefore the study of physical and chemical properties of a compound with respect to conformation of molecule is known as conformation analysis.

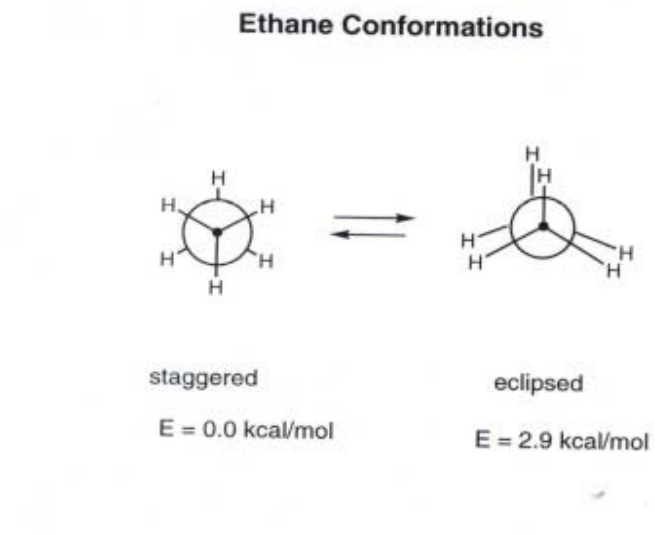
19.3 Conformational Analysis

The different spatial arrangements of atoms in a molecule which are readily interconvertible by rotation about single bonds are called conformations; configuration. Conformations, represent conformers which are readily interconvertible and thus, nonseparable. The terms conformation and configuration are related to energy barrier for inteconversions of different spatial arrangements of atoms in a molecule. If the energy barrier for conversion of different spatial arrangements is between >0.6 and < 16 kcal/mole they are conformations (i.e. conformers), and if it is $\geq$ 16 kcals/mole, they are configurations (i.e., stereoisomers). If the energy barrier is 0.6 kcal/mole or less at room temperature , the rotation would be free because this amount of energy can be readily provided by the thermal energy of the molecule. The study of the existence of preferred conformations in molecules and relating physical and chemical properties of a molecule to its preferred conformation is known as conformational analysis.

19.4 Conformations of Acyclic Systems

19.4.1 Conformations of Ethane

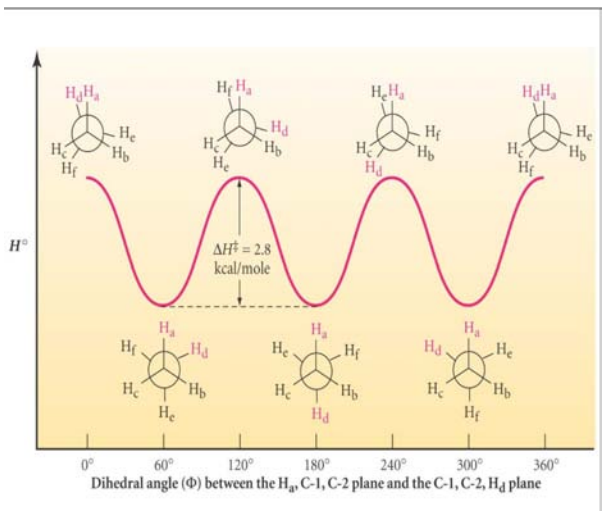
When an ethane molecule rotates about its carbon single bond, two extreme conformations can result: the staggered conformation and the eclipsed conformation. An infinite number of conformations between these two extreme conformations is also possible. There are various ways to represent the three dimensional conformations on the paper (as discussed in section 2.3, representation of three dimensional molecules) Here we will use newman projections to discuss the conformations of acyclic compounds. The newman projections for staggered and eclipsed conformation of ethane are given below.



Staggered conformation: A conformation with a 60^0 dihedral (torsional) angle is atoms known as staggered conformation. The angle between the stoms attached to the front and the rear carbon atoms is called the torsional angle.

Eclipsed conformation : A conformation with a 0^0 torsional angle is known as eclipsed conformation.

In staggered conformation the distance between the hydrogen nuclei is 2.55 A, but they are only 2.29 A apart in the eclipsed conformation. The rotational energy barrier in ethane is 2.9 kca/mole. This rotational barrier can be described in terms of the change in potential energy of the molecule as a function of the change in torsional angle as shown in Fig. 1.

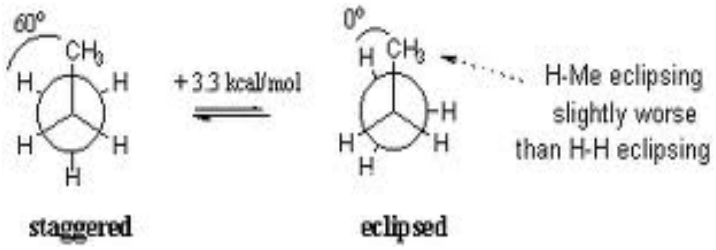


The extra energy of the eclipsed conformation is called torsional strain. Torsional strain is the name given to the repulsion felt by bonding electrons of one substituent as they pass close the bonding electrons of another substitutent.

The energy barrier between staggered and eclipsed conformation in ethane molecule is 2.9 kcal/mole. This barrier is more than energy for free rotation at room temreature (0.6k cal/ more) and less than energy barrier for complete restricted rotation ie. frozen rotation (16.20 Kcal/ more).Thus the rotation about the carbon-carbon single bond is neither completely free nor frozen (completely restricted) but only restricted by 2.8 kcal/mole.

19.4.2 Conformation of propane.

Similar to ethane, propane also has the following two extreme conformations:

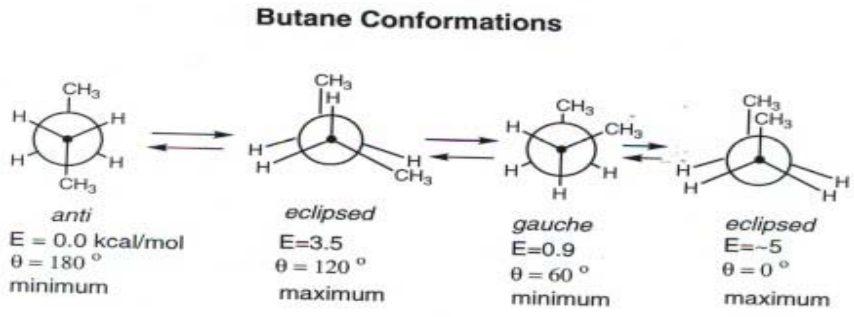


www.sparknotes.com

19.4.3 Conformations of n-butane

Butane has three carbons single bond and the molecule can rotate about each of them.

CH_3 - CH_2-CH_2-CH_3 If the rotation will be about C_2 and C_3 bond then conformations will be symmetrical. For conformational analysis butane may be treated as the derivative of ethane where one hydrogen on each carbon is replaced by a methyl group. Different conformations of butane can be obtained by rotation about its middle carbon-carbon bond (i.e. between C_2 and C_3 bond) as shown below:



http://research.cm.utexas.edu/nbauld/teach/butane.html

Butane has more then one staggered conformers . Conformer , in which the two methyl groups are as far apart as possible is more stable than the other staggered conformers . The most stable of the staggered conformers is called the anti conformer and the other staggered conformers are called gauche conformers (anti is Greek for "opposite of", gauche is French for "left"

The eclipsed conformer in which the two methyl groups are closest to each other is less stable than the other eclipsed conformers . All these eclipsed conformers have both torsional and steric strain. Torsional strain is due to bond repulsion and steric strain is due to the closeness of the eclipsing groups. In general, steric strain in the molecule is directly proportional to the size of the eclipsing groups.. The energy diagram for rotation about the $C_2 - C_3$ bond of butane is shown in Fig. 19:2 below:-

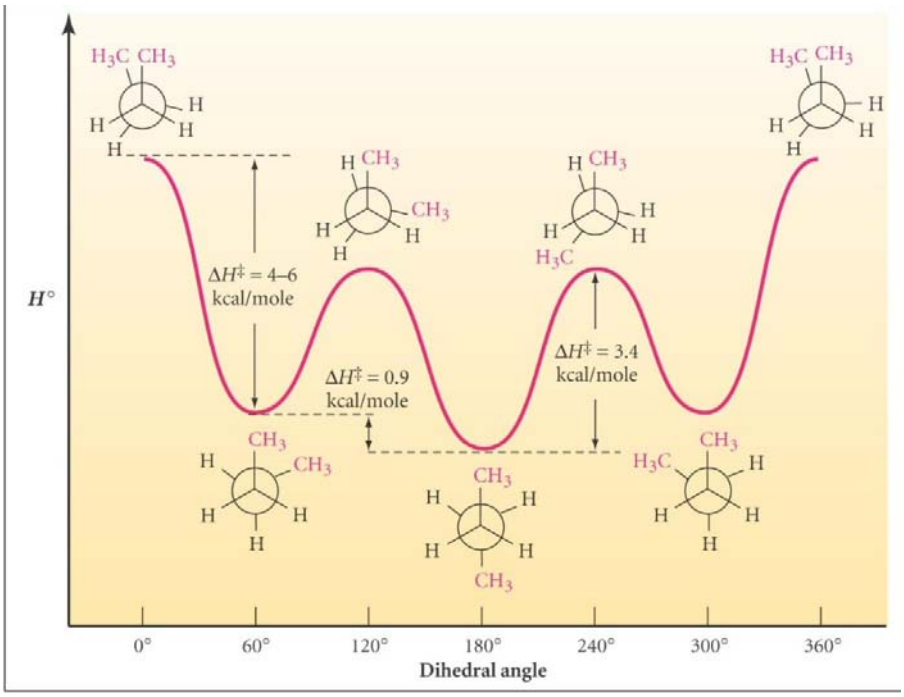


Figure 19:2

Thus the relative stabilities of the six different conformers of n-butane in decreasing order is as follows:

Anti > Gauche>Eclipsed>Fully eclipsed

Molecule with carbon-carbon single bonds have many interconvertible conformers. Conformers cannot be separated because they rapidly inrerconvert.

19.5 Conformations of Cycloalkanes

19.5.1 Stability of Cycloalkanes

conformational analysis is the study of the energical of different conformations. Compounds with three and four membered rings are not as stable as compounds with five and six membered rings. The German chemist Baeyer (1985) was the first to suggest that the instability of these small ring compounds was due to angle strain. This theory is known as Baeyer strain theory.The greater the ring strain the lower the stability of the cycloalkanl and vice versa the internal bond angle of cyclo alkane can be calculated by the following formula.

180 (n-2) (n= no. of carbon atoms)

for example for cyclopentant n= 5

Hence deviation is guesn as

Assuming that the rings are planar, the angle strain in various cycloalkanes can be expressed in terms of angle of deviation (distortion), d, i.e. deviation from 109.50 for one bond.

$$d=\frac{1}{2}\left[109.5-\frac{2(n-2}{n}x90\right]$$

$$d=\frac{1}{2}(109.5-\alpha)$$

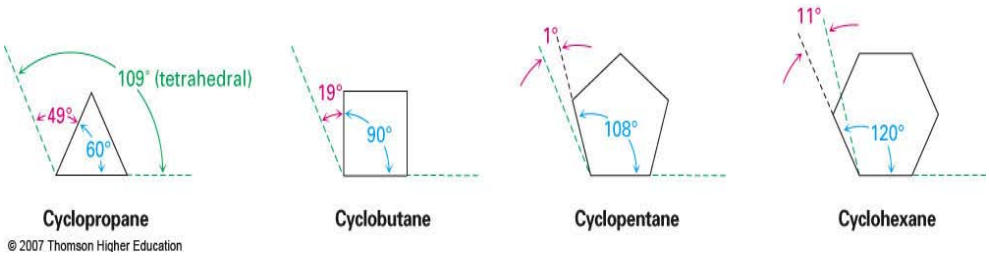
or

α = inner bond angle in the cycloalkane ring

angle strain α d

stability $\alpha \frac{1}{d}$

the factor of $\frac{1}{2}$ is put in because the strain is spread over two bonds. For example, for cyclopropane ring the inner angle α is 600, hence $d=\frac{1}{d}(109.5 - 60) = 24.750$. similarly the angle strain can be calculated for rings of different sizes. E.g. d= 9.750 for cyclobutane; 0.750 for cyclopentane; -5.250 for cyclohexane; -9.50 for cyclopheptane and –12.750 for cyclooctane. The positive values of seviation mean that the bond angles are compressed, while negative values mean expansion of the bond angle from the tetrahedral angle. In both the situations the molecule would be strained.(Table 19:1)



Put these figure below Fig. 19:3

(Based on McMurry's *Organic Chemistry*, 7th edition)

Cyclic compounds twist and bend in order to achieve a final structure which minimizes the following three kinds of strain that can destabilize a cyclic compound:

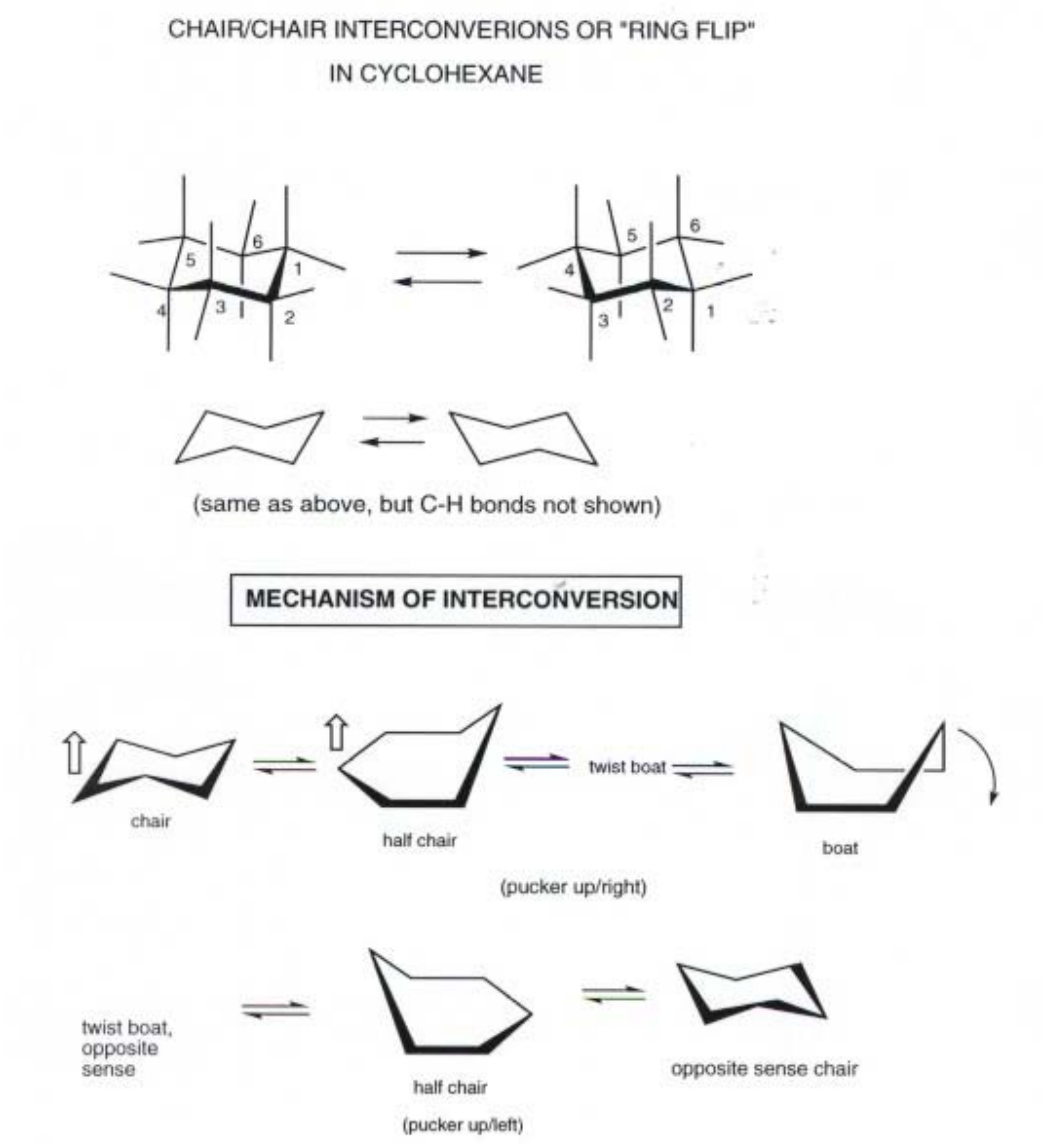
1. Angle strain (Beeyer strain): this results when the bond angle is different from the desired tetrahedral bond angle of 109.50. Torsional strain(Pitzer strain): this is caused by repulsion of the bonding electrons or one substituent with bonding electrons of another substituent on the adjacent atom.

2. steric strain (van der waals strain): this is caused by atoms or groups approaching each other too closely.

19.5.2 Conformations of cyclohexane

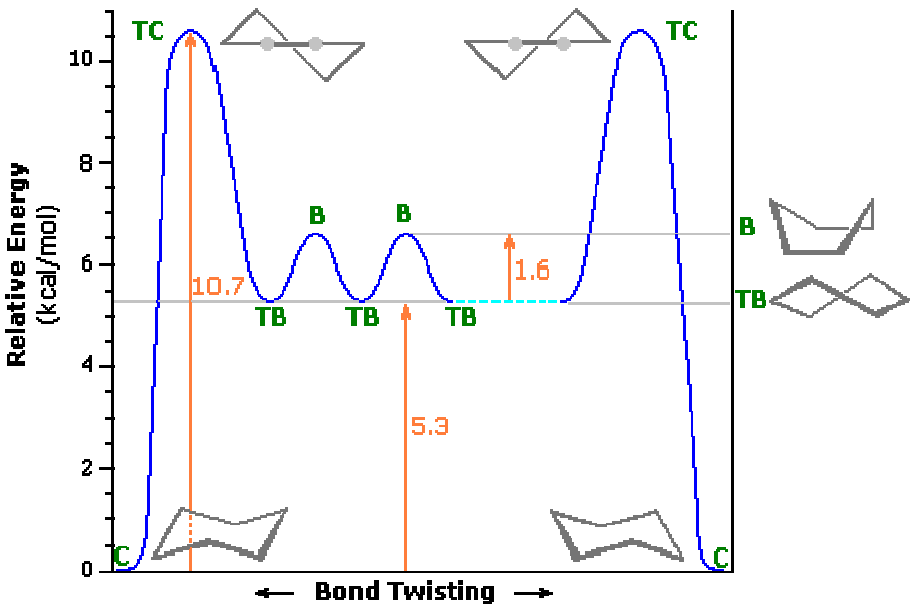
Sachse (1890) proposed that cyclohexane and larger rings are not planar but they are puckered in which all the angles are tetrahedral, and thus, the rings are strainless. According to sachse cyclohexane exists in two forms which are called the chair and boat conformations. Mohr (1931) suggested the possibility of existence of two forms which readily undergo interconversion by rotation about single bonds. This theory is known as Sachs-Mohr theory of strainless rings.

Both the chair and the boat forms are free from angle strain. In the boat conformation the C-H bonds at C2, C3 and C5, C6 are eclipsed resulting in torsional strain, while in the chair conformation all the C-H bonds on adjacent carbons are staggered.



The chair conformation is rigid because when it is changed to the boat conformation. some angular deformation is necessary. The energy barrier for this transformation os 10.7 kcal/mole.

The boat conformation is flexible and can be readily distorted into many shapes in which the eclipsing of C-H bonds is reduced. In an modified boat conformation, known as the twist boat, the torsional and steric strains are minimized (figure below 19:4).



www2.chemistry.msu.edu.

Fig:19:4

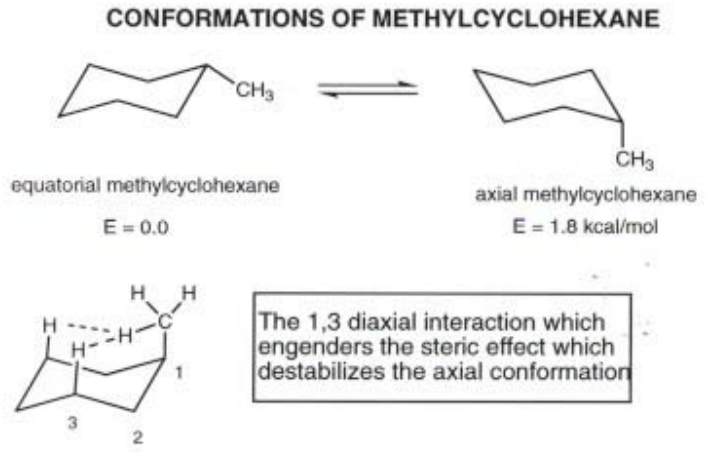
The twist boat is about 1.5 kcal/mole lower in energy than the boat form at 25^0C. At room temperature, most of cyclohexane molecules (99.9%) exist in the most stable chair conformation. The twist form occurs as an intermediate stage in the conversion of one chair form to another since the boat from is preferred conformation only in a few cases, we shall confine our attention to the chair form.

Axial and Equational bonds in cyclohexane: In the chair conformation of cyclohexane, there are two kinds of positions occupied by the hydrogen atoms. Six hydrogens are held by bonds which are perpendicular to the average plane of the ring; these are called axial (a) bonds. The other six bonds holding hydrogens in the average plane of the ring are called equatorial (e) bonds. In the chair conformation each carbon has one axial and one equatorial bond :

At room temperature cyclohexane rapidly interconverts (flips) to mirror image chair conformations. On flipping all the equatorial hydrogens become axial and all the axial hydrogens become equatorial. This interconversion is so rapid at room temperature that all hydrogens on cyclohexane can be considered equivalent.

19.5.3 Conformations of monosubstituted cyclohexanes.

When one hydrogen in cyclohexane is replaced by a larger atom or group, crowding occurs. Thus a monosubstituted cyclohexane will assume the chair conformation in which the substituent occupies an equatorial position. For example there are two possible chair conformations for methylcyclohexane, one with methyl group -me in an axial position and the other with – Me in an equatorial position as shown below. Due to 1,3-diaxial interaction of the methyl group with hydrogens at C3 and C5. the e-Me conformation is more stable than the α - Me by about 1.8 kcal/mole. Furthermore, an axial substituent experiences gauche interactions with C3 and C5. when the substituent is present in equatorial position. It becomes anti to C3 and C5. at room temperature most molecules (~95%) exist in the uncrowded equatorial Me conformation.



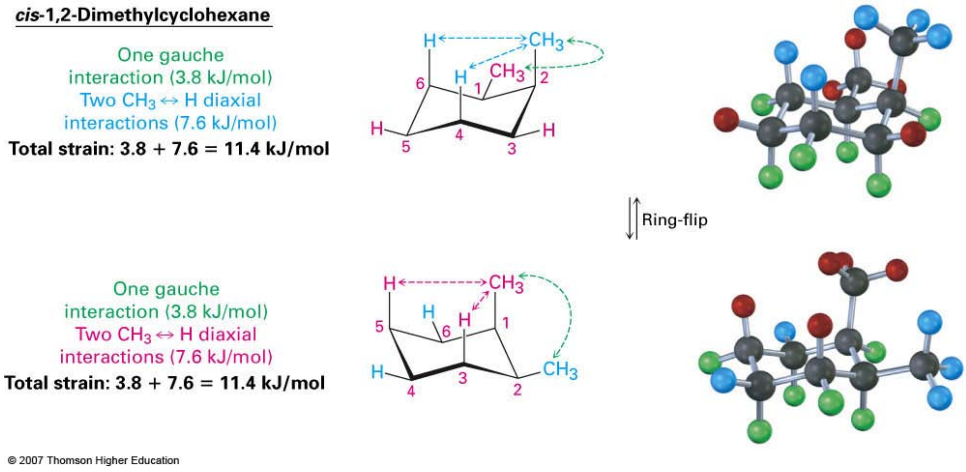
www.research.cm.utexas.edu.

In conclusion, in monosubstituted cyclohexanes chair conformation is more stable than the boat conformation, and out of the two chair conformations, the conformation with an equatorial substituent is more stable than that with an axial substituent.

19.5.4 Conformations of disbustituted cyclohexanes

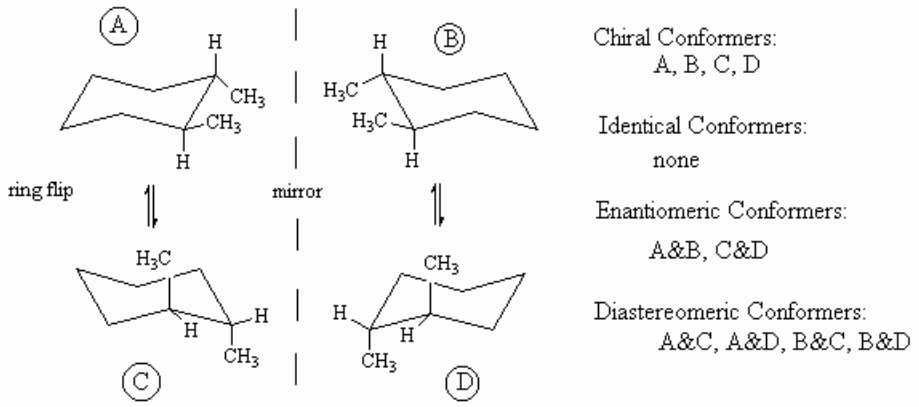
When two substituents are present on a cyclohexane ring, one has to consider whether they are cis or trans to each other and whether they are 1,2-; 1,3- or 1,4- with respect to each other. In general in disbustituted cyclohexanes the chair conformation containing both the substituents in equatorial positions will be the preferred conformation or when this is not possible, the conformation with bulkier substituent in an equatorial position will be the preffered conformation. Let us take some specific examples.

1,2-Dimethylcyclohexane: For 1,2-dimethylcyclohexane, two forms are possible, cis and trans. The conformation of the cis configuration must have one axial and one equatorial substituent (i.e. 1a, 2e or 1e, 2a). the trans configuration can exist in two different conformation 1a, 2a and 1e, 2e. in cis-1,2-dimenthylcyclohexane there is one axial group methyl group which causes two 1,3-diaxial methyl-hydrogen interactions (Me/H 1,3-diequatorial trans 1,2-dimethylcyclohexane, there is no axial methyl group, hence there is no 1,3-diaxial interaction causing strain. Thus, ee-1,2-dimehylcyclohexane is more stable than ae (or ea)-1,2-dimethyl cyclohexane. In the case of aa-1,2-dimethylcyclohexane, there are two axial methyl groups which cause four Me/H 1,3-diaxial interactions resulting in greater strain and lesser stability than that of ae-1,2-dimethylcyclohexane the order of stability of these conformations is: ee>ae>aa; and the preferred conformation (most stable conformation) is ee-1,2-dimethylcyclohexane.



Enantiomerism in 1,2-dimethylcyclohexane :

1,2-dimethylcyclohexane has two chiral centers, hence can have no more than four stereoisomers (22=4), but actually it has only three. The cis-1,2-dimethylcycloheane (ae or ea) molecule is not superimposable on its mirroe image but the molecule and its mirroe image aree readily interconvertible by flipping one chair conformation into the other. Hence these are called conformational enantiomers. At room temperature these are too rapidly interconvertible to measure their optical activity. It shouls be noted that cis-1,2-dimethylcyclohexone ne constitutes a nonresolvable racemic modification; it is not the meso compound.



www.elcamino.cc.ca.us

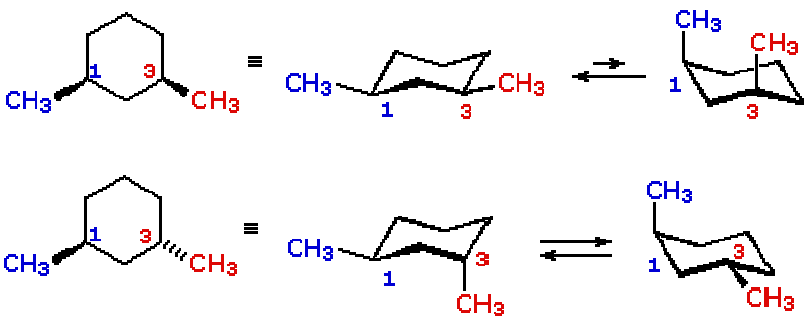
The trans-1,2-dimethylcycloheane (ee) molecule and its mirror are not superimposable hence constitute an enantiomeric pair. These are not interconvertible by flipping chair conformation. The two isomers are known as configurational isomers or configurational enantiomers. Each isomer is otically active and their mixture is resolvable.

In summary, 1,2-dimethylcyclohene exists as a pair of (configurational) diastereomers, the cis and the trans isomers. The cis isomer exists as a pair of conformational enantiomers, where as the conformational diastereomers (aa and ee).

1,3- and 1,4- dimethylcycloheanes: the above discussion about 1,2-dimethylcycloheanecan easily be extended to the 1,3- and 1,4-disubstituted cyclohexanes. In general the hair conformation with the maximum number if equatorial substituents will be the preffered conformation provided that the other forces such as dipole interaction, hydrogen bonding etc. are adsent.

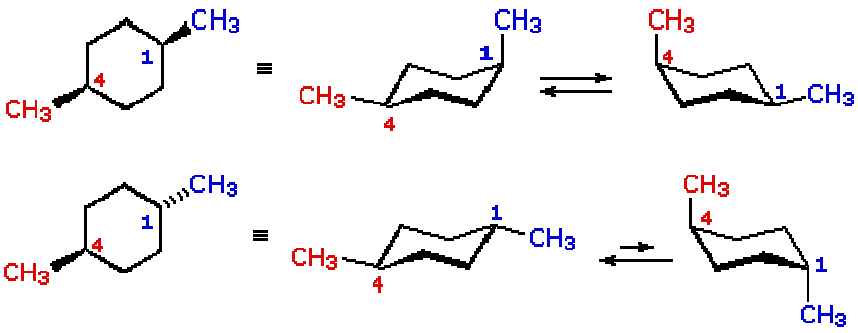
In the cae of 1,3-dimethylcyclohexane (with isentical substituents), two cis and one trans chair conformations are possible as shown below for 1,3-dimethylcycloheane.

In the case of 1,3-dimethylcycloheane the cis isomer (ee) is more stable than the trans isomer (ae).



1,3-dimethylcyclohexanehas two chiral centers, and can have no more than four stereoisomers (2^2=4). Actually, there are only three. The cis-1,3-dimethylcyclohexane has a plane of symmetry and exists as a pair of enantiomers.

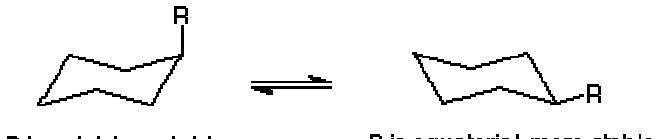
In the case of 1,4-dimethylcyclohexane (with identical substituents), one cis and two trans conformations are possible as shown below

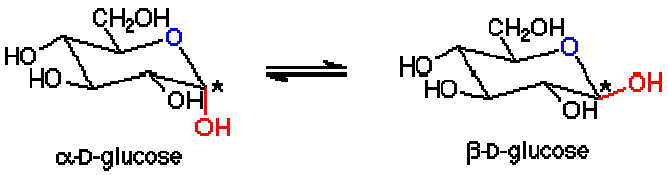


1,4-dimethylcyclohexane does not have any chiral center. It exists as cis-trans diastereomers. Neither cis nor trans form is chiral, because both have a plane of symmetry.

19.6 Conformations of Sugars

Reeves (1950) has shown that α-D-(+)-glucopyranose and β-D-(+)- glucopyranose both have the chair conformation.





In the α-D-(+)-glucopyranose the glycosidic hydroxyl is axial and in the β-anomer it is equational. As we know, it is a general rule that the conformation which has the greatest number of large groups in equatorial position is the most stable

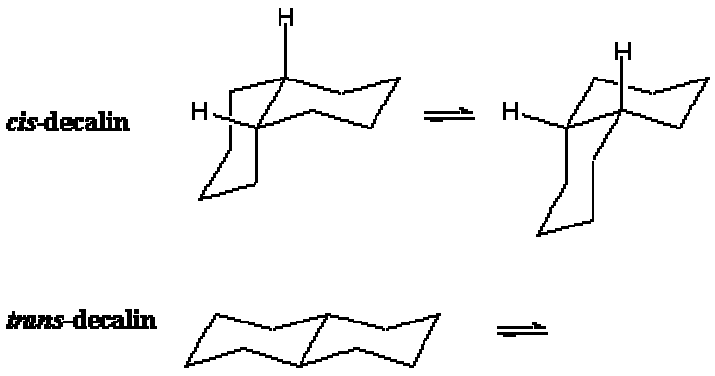
conformation. Thus, the β-anomer is more stable than the α-anomer, and so it predominates in the equilibrium mixture.

19.7 Conformations of Fused rings : DECALINS

Decalin (bicyclo[4,4,0]decane) exists in two diastereoisomeric forms cis and trans decalins, depending on the way in which the two cyclohexane rings are fused together. In both the diastereoisomers of decalin, the two cyclohexane rings are joined together in the chair conformation. Since the decalin is analogous to a 1,2-disubstituted cyclohexane, in the cis isomer the two cyclohexane rings are fused together in ea form (i.e. the equatorial bond of one ring is fused with the axial bond of the other). While in the trans isomer the two rings are fused in ee form (i.e. each ring is fused with other ring by equatorial bonds) as shown below. fig. here

The trans decalin is more stable than the cis by 2.7 kcal/mole. Thus, cis decalin can be smoothly pyrolysed to the trans isomer irreversibly. In cis decalin the ring fusion involves ae bonds, hence it is flexible and exists in two forms which are interconvertible as a result of conformational flipping similar to that of the chair conformation of monocyclic cyclohexane as shown below:

Since, trans decalin involves two equatorial bonds for the ring fusion, it is a rigid molecule and cannot undergo conformational flipping, i.e. it cannot be converted into aa conformation which also does not exist in decalin type of fused ring compounds.



no conformational flipping.

Any substituent attached to the cis decalin system is free to adopt the equatorial orientation. Cis is chiral in both the conformations which are nonsuperimposable mirror images of each other. Because of rapid interconversions of the two cis conformations. Cis decalin exists as a nonresolable enantiomeric pair. On the other hand, trans decalin has a center of symmetry and is therefore, optically inactive.

In the case of substituted decalins, substituents located at the fusion points of the two rings (angular positions) are axial with respect to one ring, while equatorial with respect to the other in cis decalins. On the other hand, in the case of trans decalins the angular substituents are axial with respect to both the rings as shown below.

It should be noted that rotation about carbon carbon bonds cannot bring about interconversations od cis and trans decalins. Among substituted decalins, the 9-methyldecalin system is most important because of its presence in many natural products, e.g. cholesterol (a steroid). When an angular methyl group is introduced the cis form becomes slightly more stable than the trans form. This is because in the trans form the methyl group has 1,3-diaxial interaction (causing strain) with four axial hydrogens (on C2, C4, C5 and C7), while with only two axial hydrogens (on C2 and C4) in the case of cis isomer.

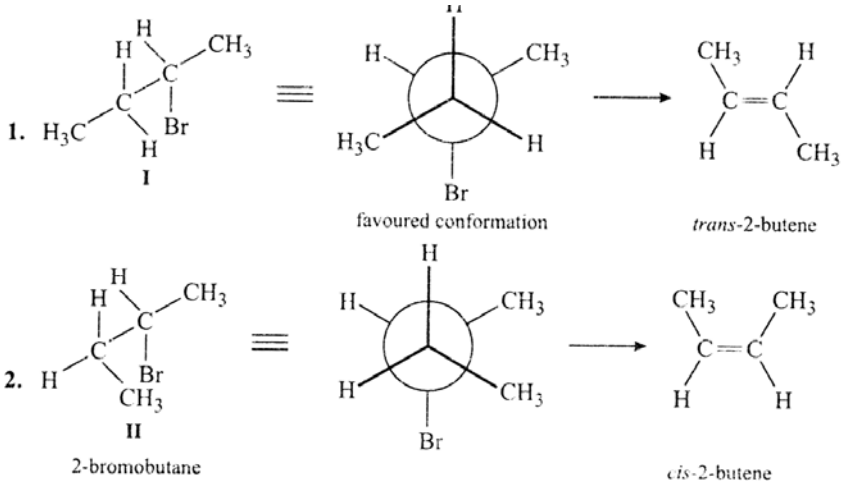
19.8 Effect of Conformation on Reactivity

There is profound effect of conformation on chemical reactivity because the stereoelectronic and steric factors are among the essential conditions for reactions. Let us discuss the effect of conformation reactivity with examples.

19.8.1 Acyclic Compounds

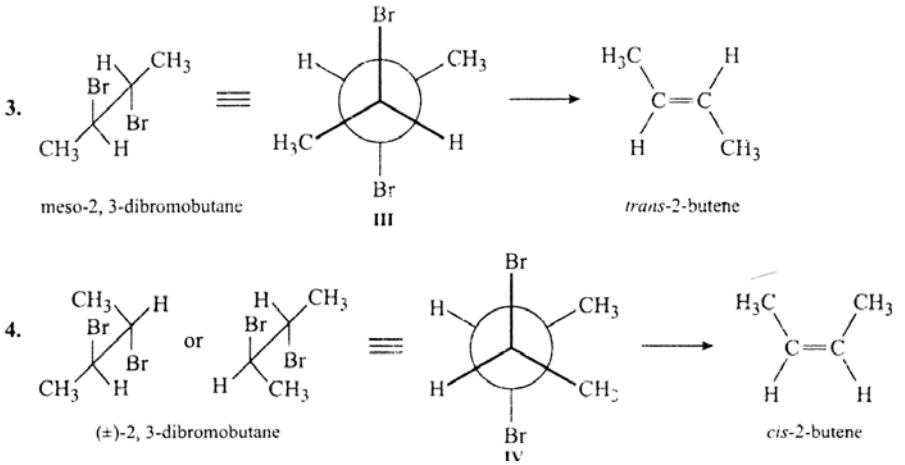
E2 reactions: E2 reactions are stereospecific and most of these are anti elimination. In anti eliminarion the five atoms involved (including the base) must be in the same plane and the eliminating groups must be trans to each other; the conformation is called anti-periplanar. This is the steroelectronic requirement of anti elimination.

For example, on E2 elimination 2-bromobutane can give either cis- or trans-2-butene. The steroelectronic requirement of the reaction must involve only those conformations of 2-bromobutane in which the eliminating groups attain an anti-periplanar arrangement. Figure now.



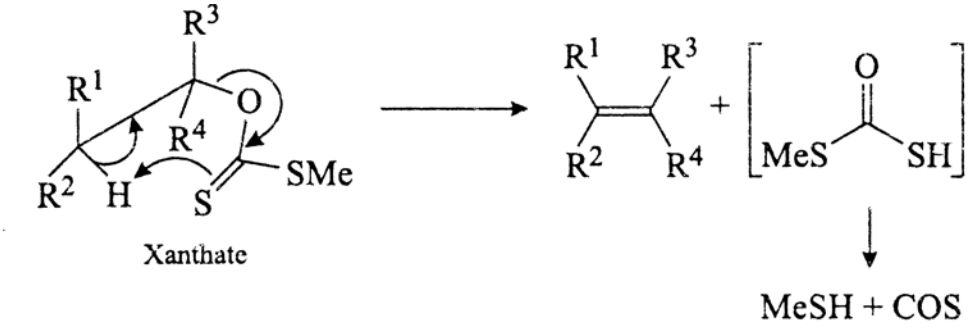
The conformations I and II satisfy this condition. Thus, I gives trans alkene, whereas II its cis isomer.It has been found that the reaction gives mainly the trans alkene; this proves that the elimination involving the conformation I proceeds more readily than through II. This is because in the transition state of the cis alkene the two bulky methyl groups are gauche to each other and exert repulsive force (van der Waals strain) which makes the transition state less stable than that in the case of trans alkene in which the two bulky methyl groups are staggered (anti). It should be noted that the reaction 1 is favoured because both the conformation I of the starting compound and the trans alkene formed are thermodynamically more stable as compared to their respective alternatives depicted in the reaction 2.

Similarly, the effect of conformation on reactivity may be demonstrated by taking the example of debrormination of 2,3-dibromobutane either with Ie or with a metal such as Zn. Elimination (E2) can occur only through a conformation of the starting compound which places the two eliminating groups (bromine atoms) in an anti-periplanar arrangement, regardless of the fact if or not this is the most stable conformation. The meso-2, 3-dibromobutane can eliminate bromine gainfully only from the conformation III to give trans-2-butene (reaction 3), whereas in reaction 4 (±)-2,3-dibromobutane IV reacts to give cis-2-butene. The reaction the (±) isomer involves a less stable transition state (the two methyl groups are gauche) compared to the meso isomer (the two methyl groups are anti), thus the elimination with iodide ions is slower by a factor of about two for the (±) than for the meso isomer.



In the above examples, the predominance of the trans isomer is explained by the Curtin Hammett principle according to which the relative proportion of the products depends only on the relative energy of the transition state of various processes but not on the relative population of the ground state conformation.

Pyrolytic eliminations: Contrary to E2 reactions, the two eliminating groups in pyrolytic eliminations lie cis to each other. For example, pyrolysis of xanthates, acetates and amine oxides are syn elimination.

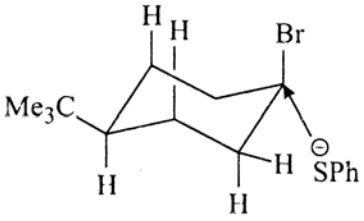


If the eliminating groups are lost from the same face of the developing double bond, the reaction is termed syn elimination; if from the opposite faces, it is termed anti elimination.

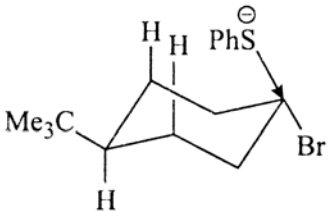
19.8.2 Cyclic Compounds

The effect of conformation on chemical reactivity has been studied mostly in the case of cyclohexanes because this ring system occurs most widely in natural products such as steroids. terpenoids, etc. Environments of axial and equatorial groups are different, hence the reactivity of a given group will depend on the conformation, i.e., whether the group is axial or equatorial. Generally, but not always, the equatorial substituents are more reactive than the corresponding axial substituent.

(a) Substitution reactions: SN^2 reactions take place more readily with axial substituent than with equatorial. For example, the SN^2 reaction of the thiophenoxide ion with 4-t-butylcyclohexyl bromide (V) having an axial Br takes place about 60 times faster as compared to the equatorial isomer VI because the attack of the thiophenoxide ion on the equatorial isomer (VI) is hindered by the β-axial hydrogens.

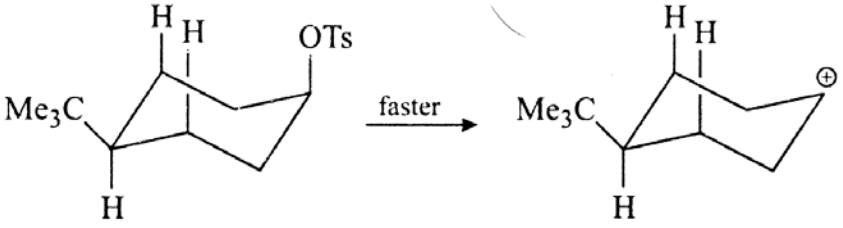


V



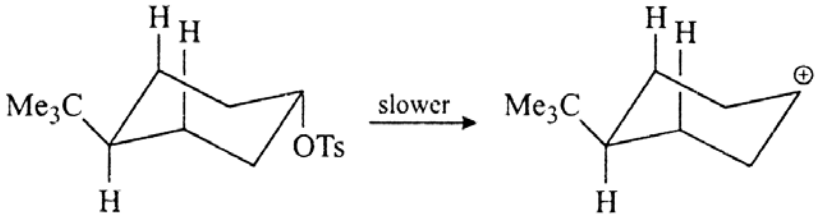
VI

SN^1 reactions proceed through the formation of carbocation which relieves the steric strain of axial isomer due to 1,3-diaxial interactions. Thus, the SN^1 reaction is sterically assisted for an asual substituent, such type of steric acceleration will not occur with the corresponding equatorial substituent. For example, the acetolysis of cis-4-t-butylcyclohexyl tosylate (VII), with an axial tosyl group. is about 3.4 times faster than that of the trans isomer (VIII).



cis

VII

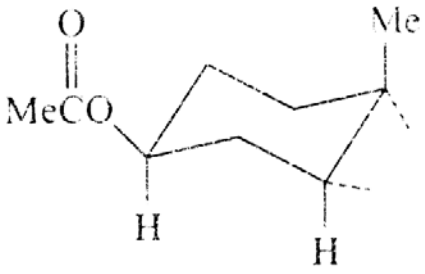


trans

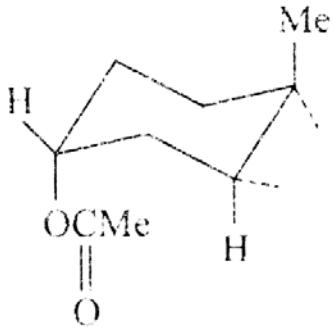
VIII

Esterification and hydrolysis: Equatorial and axial conformational isomers usually react at different rates and due to 1,3-diaxial interaction (van der Waals strain) in the axial isomer, esterification and hydrolysis occur more readily cholest anyl with the equatorial conformation. For example, cholestany acetate (having acetate group in

the equatorial position) saponifies more readily than the epicholestanyl acetate (having acetate group in the axial position).

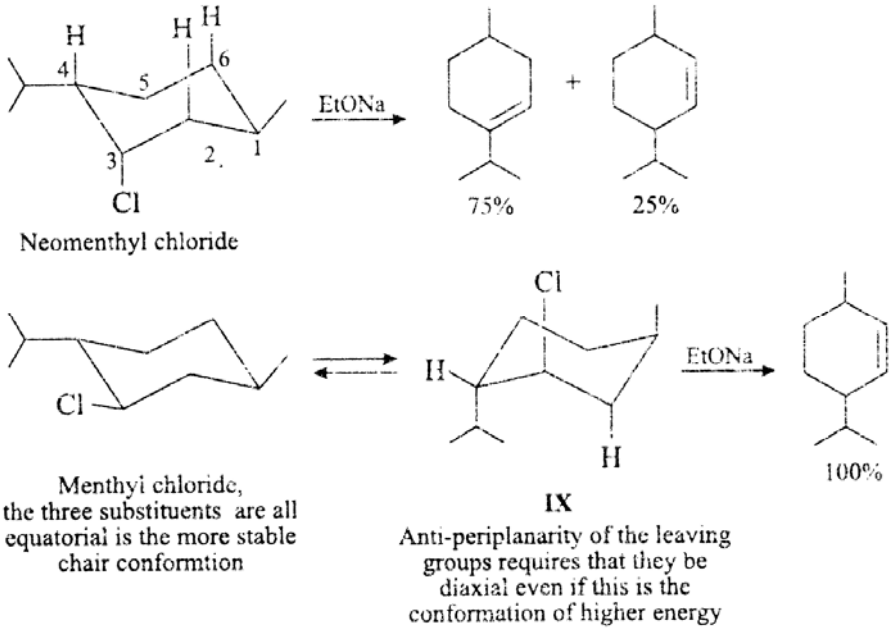


Cholestanyl acetate
(equatorial ester)
Saponifies more
readily

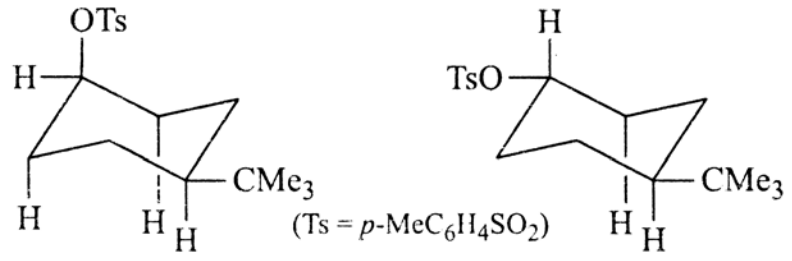


Epicholestanyl acetate
(axial ester)
Saponifies less
readily

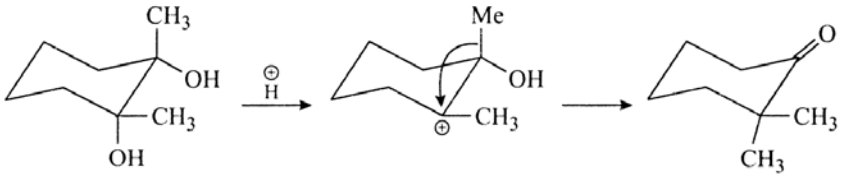
(c) Elimination reactions: As we have already noted that the stereoelectronic requirement of an E2 reaction is that the eliminating groups should be antiperiplanar. In cyclohexane ring this relationship exists when substituents on the two adjacent carbons are in axial positions. An example of an elimination reaction which is forced to occur through an unfavourable conformation is the dehydrohalogenation of menthyl chloride by the action of sodium ethoxide in ethanol. In neomenthyl chloride the eliminating groups chlorine and hydrogens at both C_2 and C_4 are axial. Thus, it readily undergoes elimination to give products. On the other hand, in the preferred conformation of menthyl chloride the chlorine is equatorial. Thus, the reaction must occur through ring flip to the unfavourable chair conformaton IX. Consequently, menthyl chloride reacts slowly as compared to neomenthyl chloride by a factor of 189 at 125°C.



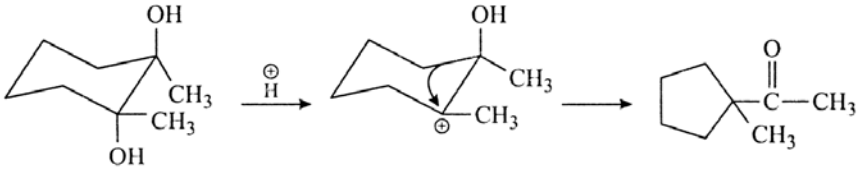
Similarly, the cis isomer of 4-t-butylcyclohexyl tosylate undergoes elimination in the presence of sodium ethoxide in ethanol 100 times faster than that of its trans isomer. This is because in the cis isomer the tosylate (OTs) group is axial and hydrogens on the adjacent carbons are anti to OTs group, while the trans isomer has an equatorial OTs group which is not anti to the hydrogen on eitherof the adjacent carbons. It should be remembered that the other chair conformation of the trans isomer . having OTs and r-tert groups in axial positions would be more favourable for the elimination but owing to the large space requirement by the r-tert group, the concentration of this form is very low.



(d) Molecular rearrangements: There are numerous examples of molecular rearrangements where the conformation governs the product formation. As an example, let us discuss the pinacol-pinacolone rearrangement of I ,2-dimethyl-1 ,2-cyclohexanediol. The cis isomer of this diol on treatment with acid undergoes a methyl shift to give 2,2-dimethylcyclohexanone, whereas the corresponding trans isomer undergoes ring contraction to give a cyclopentane derivative.

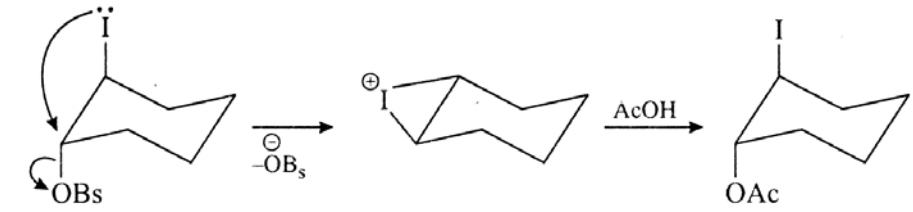


cis isomer

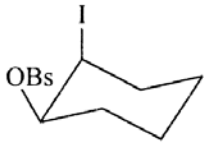


trans isomer

(e) Neighbouring group participation : In neighbouring group participation, the group partipating as a neighbouring group must be in a position to attack from the just opposite side to the leaving group. A very good example of neighbourinl group participation is the acetolysis of trans -2-iodo cycloexyl brosylate which undergoes 2.7 x 10 times faster acetolysis than the cis isomer in which the iodo group cannot attack from the backside.



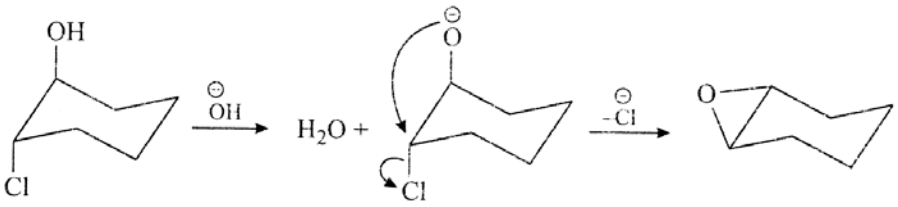
trans isomer
undergoes very fast acetolysis



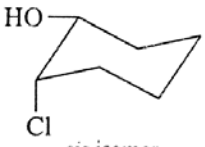
(B_s = *p*—$BrC_6H_4SO_2$—)

cis isomer
undergoes very slow acetolysis

Similarly, the trans-2-chlorocyclohexanol undergoes epoxide formation more than 100 times faster than the cis isomer. This is because the axial alkoxide ion (from the trans isomer) can attack from the backside to the axial chlorine, whereas the equatorial alkoxide ion (from the cis isomer) is not well disposed for backside attack displacing equatorial chlorine.

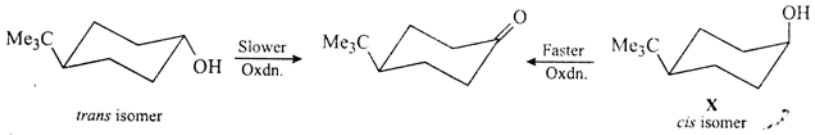


trans isomer
undergoes very fast epoxide formation



cis isomer
undergoes very slow epoxide formation

(f) Oxidation: Reactions having no stereoelectronic requirement also display rate difference between reactions of axial and equatorial isomers. For example, oxidation of both cis and trans-4- t-butylcyclohexanols with chromic acid gives the same ketone. In the preferred conformation, the cis isomer X has an axial hydroxyl group which is removed in the oxidation to allow relief from der Waals strain (l,3-diaxial interactions with hydrogens), thus the reaction is three times faster than that for the trans isomer (steric acceleration).



trans isomer

X
cis isomer

19.9 Summary

After reading this unit learners become familiar with conformation of different molecule, conformational analysis of also learners learned in this unit conformation their, then learners learn conformations of Acyclic Systems, Cycloalkanes, Sugars, Fused rings : DECALINS and Effect of Conformation on Reactivity

19.10 Review Questions/ Comprehensive Questions

1. What is conformation of molecules and its analysis?
2. Discuss conformation of Acyclic Systems.
3. Describe conformation of cyclohexane.
4. Explain the conformation of Sugars and Fused rings.
5. Discuss effect of conformation on reactivity.

19.11 References and Suggested Readings

1. Stereochemistry of Organic Compounds, D.Nasipuri,New Age International.
2. Stereochemistry of Organic Compounds, P.S.Kalsi,New Age International
3. Advance Organic Chemistry, Jerry March, John Wiley.
4. Advanced Organic chemistry, F.A.Carey and Sundberg, Plenum
5. A Text book of organic Chemistry, MK Jain, and Subhash C. Sharma, Shoban Lal & Co. Edcuational Publisher (Sixteenth Edition)

Unit–20: Introduction to electromagnetic radiation– UV: Electronic transitions, Chromophores, Auxochromes, Bathochromic and Hypsohromic Shifts, Solvent effects, Wood ward– Fieser Rules for dienes, enones and aromatic compounds Application of U.V., Instrumentation of recording of spectra

Structure of Unit

20.1 Objectives

At the end of the unit learner will be able to–

- Understand the most commonly used techniques in structure determination.

- Identification of unknown molecules with the help of spectra.
- Determine the effect of conjugation on a UV/Vis absorption spectrum.
- Determine the effect of solvent on a UV/Vis absorption spectrum.
- Develop problem solving skills generally useful in chemical analysis.

20.2 Introduction

It was believed that light travels in a straight line. But this concept could not explain some important phenomena like Interference, Refraction and Diffraction etc. To explain these phenomena, light is supposed to travel in waves. Visible light is a form of energy. It can be explained by two complimentary theories, the corpuscular theory and the wave theory. All the properties of light can be explained by considering both the theories. According to the wave theory, light travels in the form of waves. It was believed that radiant energy is emitted by fluctuation of electric charge and magnetic field. Like light, there are various forms of electromagnetic radiations such as Ultra violet, X rays , Radio waves etc.

Some of the important characteristics of electromagnetic radiation are:

(i) These are produced by the oscillation of electric charge and magnetic field residing on the atom. The electric and magnetic components are mutually perpendicular to each other and are coplanar.

(ii) These are characterized by their wavelengths or frequencies or wavelength.

(iii) The energy carried by an electromagnetic radiation is directly proportional to its frequency. The emission or absorption of radiation is quantized and each quantum of radiation is called a *photon*.

(iv) All types of radiations travel with the same velocity and no medium is required for their propagation. They can even travel through vacuum.

(v) When visible light is passed through a prism, it is split up into seven colours which correspond to definite wavelengths. This phenomenon is called *dispersion*. Thus, a group of electromagnetic radiations can be split up into various components for analysis.

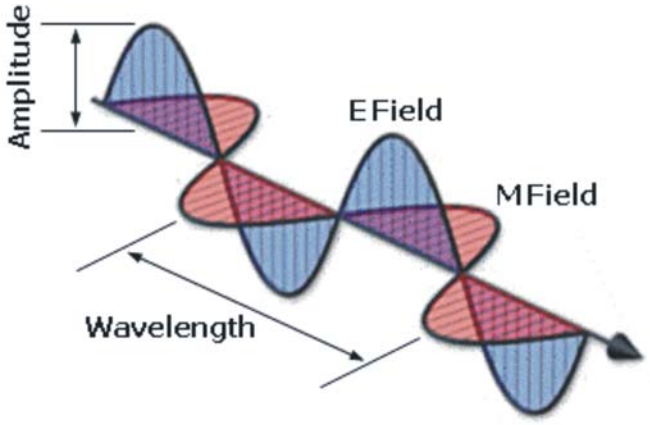
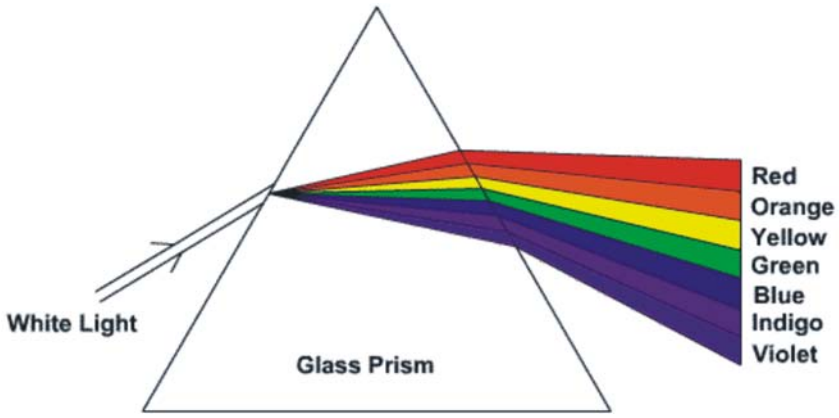


Fig. 20.2 : Dispersion.

The study of spectroscopy deals with emission as well as absorption spectra. An emission spectrum is produced by the emission of radiant energy by an excited atom. This excitation of atoms can be brought about thermally or electrically. When electric discharged is passed through the vapours of the substance, energy is absorbed and electrons in the ground state are promoted to meta stable states. When electrons from the meta stable state jump to the lower energy state, then some energy of definite frequency is released as radiation. If this radiation emitted is analyzed with the help of a spectroscopy, an emission spectrum is observed.



If electromagnetic radiations are passed through the substances under analysis for some time, then radiations of certain wavelengths are absorbed by the substance. The wavelengths which are absorbed characterized some particular functional groups present in the compound or the compound itself. This dark pattern of lines which correspond to the wavelength absorbed is called absorption spectrum. After absorption, the transmitted light is analyzed by the spectrometer relative to the incident light of the given frequency. In absorption spectrum, the absorbed energy may heat up the sample or is re-emitted.

20.3 Ultra Violet Spectroscopy

The alternate title for this technique is *Electronic Spectroscopy* since it involves the promotion of electrons (* electrons) from the ground state to the higher energy state. It is very useful to measure the number of conjugated double bonds and also aromatic conjugation within the various molecules. It also distinguishes between conjugated and non-conjugated systems; Unsaturated carbonyl compounds from -analogues; homoannular and heteroannular conjugated dienes etc. For visible and ultra-violet spectrum, electronic excitations occur in the range 200-800 and involves the promotion of electrons to the higher energy molecular orbital.

Since the energy levels of a molecule are quantised, the energy required to bring about the excitation is a fixed quantity. Thus, the electromagnetic radiation with only a particular value of frequency will be able to cause excitation. Clearly, if the substance is exposed to radiation of some different value of frequency, energy will not be absorbed and thus, light or radiation will not suffer any loss in intensity. If radiation of a desired or correct frequency is passed or made to fall on the sample of the substance, energy will be absorbed and electrons will be promoted to the higher energy states. Thus, light radiation on leaving the sample after absorption will be either less intense or its intensity may be completely lost.

Substances absorbing in the visible range will appear coloured to the human eye.The wavelength of particular radiation absorbed can also be expressed in terms of frequency or energy in kcal mole^{-1}.

$1\square = 10^{-4}$ cm

1 = 1 nm** = 10^{-7} cm = 10Å

Let us calculate the energy associated with radiations having wavelength 280 mm.

We know that $\lambda = 280\,\text{m}\mu = 280\times10^{-7}\,\text{cm}$

$E = hv$

($h = 6.62 \times 10^{-27}$ ergs sec.)

Avogadro's number $N = 6.023 \times 10^{23}$

4.18×10^{7} ergs = 1 calorie

$$E = \frac{6.62\times10^{-27}\times3\times10^{10}\times6.023\times10^{23}}{280\times10^{-7}\times4.18\times10^{7}\times10^{3}}\ \text{kcal mole}^{-1}$$

100 kcal mole^{-1}

It is not advisable to keep the compounds in ultra-violet radiations except for taking the spectrum.

A record of the amount of light absorbed by the sample as a function of the wavelength of light in μ or nm units is called absorption spectrum which generally consists of absorption bands.

The far ultra-violet region (below 200 m) is not much studied due to absorption by oxygen and nitrogen. which are usually obscured by at mosphiric absorption. Moreover, studies in these regions require vacuum instruments.

The Absorption Laws

There are two laws which govern the absorption of light by the molecules. These are–

(i) Lambert's law and(ii) Beer's law

---

* Non-bonding electrons.

** Nm means nanometers.

(i) Lambert's Law: It states that ''*When a beam of monochromatic radiation passes through a homogeneous absorbing medium, the rate of decrease of intensity of radiation with thickness of absorbing medium is proportional to the intensity of the incident radiation*''.

Mathematically, the law is expressed as–

$$-\frac{dI}{dx} =$$

where I = intensity of radiation after passing through a thickness *x*, of the medium.

dI = infinitesimally small decrease in the intensity of radiation on passing through infinitesimally small thickness, dx of the medium.

$-\frac{dI}{dx} =$ rate of decrease of intensity of radiation with thickness of the absorbing medium.

k = proportionality constant or absorption coefficient. Its value depends upon the nature of the absorbing medium.

Let I_0 the intensity of radiation before entering the absorbing medium ($x = 0$).

Then *I,* the intensity of radiation after passing through any thickness, say *x* of the medium can be calculated as:

$$\int_{I_0}^{I} \frac{dI}{I} = -\int_{x=0}^{x=x} k\,dx$$

$$\ln \frac{I}{I_0} = -kx \quad \text{or} \quad \frac{I}{I_0} = e^{-kx}$$

The intensity of the radiation absorbed, I_{abs} is given by

$$I_{abs} = I_0 - I = I_0 (e - e^{-kx})$$

The above Lambert's law equation can also be written by changing the natural logarithm to the base 10.

$$I = I_0\, 10^{-ax}$$

where a = extinction coefficient of the absorbing medium

$$\left(a = \frac{k}{2.303} \right)$$

Note: For ultraviolet spectrum, the region from 200 to 380 (called quartz region) is considered. The molecular absorption in the *UV–VIS* region depends mainly on the electronic structure of the molecule. Depending upon the presence of a common group, the ultraviolet spectrum of a complex compound and that of a simple compound may be almost identical.

(ii) Beer's Law :

This law states that: *When a beam of monochromatic radiation is passed through a solution of an absorbing substance, the rate of decrease of intensity of radiation with thickness of the absorbing solution is proportional to the intensity of incident radiation as well as the concentration of the solution.*

Mathematically, this law is stated as

$$-\frac{dI}{dx} = k' Ic$$

Where c = conc. of the solution in moles litre^{-1}.

k' = molar absorption coefficient and its value depends upon the nature of the absorbing substance.

Suppose I_0 be the intensity of the radiation before entering the absorbing solution. (when $x = 0$), then the intensity of radiation, I after passing through the thickness x, of the medium can be calculated:

$$\int_{I_0}^{I} \frac{dI}{I} = -\int_{x=0}^{x=x} k'cdx$$

or $$I = I_0 e^{-a'cx}$$

The above equation can also be written by changing the nature of logarithm to the base 10.

$$I = I_0 . 10^{-a'cx}$$

Here $\frac{k'}{2.303} = a'$ where a' = molar extinction coefficient of the absorbing solution.

Beer's law can also be stated as: *When a monochromatic light is passed through a solution of an absorbing substance, is absorption remains constant when the conc (c) and the thickness of the absorption layer (x) are changed in the inverse ratio*.

Alternative Expression: On combining the two laws, the *Beer-Lambert Law* can be formulated as below:

$$\log \frac{I_0}{I} = \in .c.l = A$$

Where I_0 = Intensity of incident light

I = Intensity of transmitted light

c = Concentration of solution in moles litre^{-1}

l = Path length of the sample (usually 1 cm)

= Molar extinction coefficient (or molar absorptivity)

A = Absorbance

Limitations of Beer Lambert Law: This law is not obeyed

(i) When different forms of the absorbing molecules are in equilibrium as in keto-enol tautomers.

(ii) When fluorescent compounds are present.

(iii) When solute and solvent form complexes through some sort of association.

20.4 Electronic Transition

When the molecule absorbs ultraviolet or visible light, its electrons get promoted from the ground state to the higher energy state. In the ground state, the spins of the electrons in each molecular orbital are essentially paired. In the higher energy state, if the spins of the electrons are paired, then it is called an excited singlet state. On the other hand, if the spins of the electrons in the excited state are parallel, it is called an excited triplet state. The triplet state is always lower in energy than the corresponding excited singlet state. Therefore, triplet state is more stable as compared to the excited singlet state In the triplet excited state, electrons are farther apart in space and thus, electron-electron repulsion is minimised. Normally the absorption of ultraviolet or visible light results in singlet ground state to excited singlet state transition, i.e., excitation proceeds with the retention of spins. An excited singlet state is converted to excited triplet state with the emission of energy as light. The transition from singlet ground state to excited triplet state is symmetry forbidden. The higher energy states are designated as high energy molecular orbitals and also called antibonding orbitals. The highly probable transition due to absorption of quantised energy involves the promotion of one electron from the highest occupied molecular orbital to the lowest available unfilled molecular orbital. In most of the cases, several transitions occur resulting in the formation of several bands.

Types of Electronic Transitions

According to the molecular orbital theory, when a molecule is excited by the absorption of energy (UV or visible light), its electrons are promoted from a bonding to an antibonding orbital.

(ii) The antibonding orbital which is associated with the excitation of σ electron is called σ^* antibonding orbital. So σ to σ^* transition takes place when σ (sigma) electron is promoted to antibonding (σ) orbital. It is represented as $\sigma \rightarrow \sigma^*$ transition.

(ii) When a non-bonding electron ** (*n*) gets promoted to an antibonding sigma orbital (σ^*), then it represents $n \rightarrow \sigma^*$ transition.

(iii) Similarly $\pi \rightarrow \pi^*$ transition represents the promotion of π electrons to an anbibonding π orbital. *i.e.*, π^* orbital, (See Fig. : 20.3)

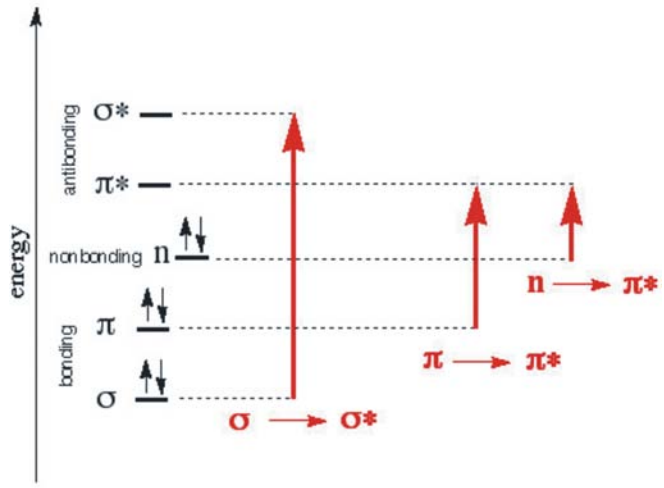
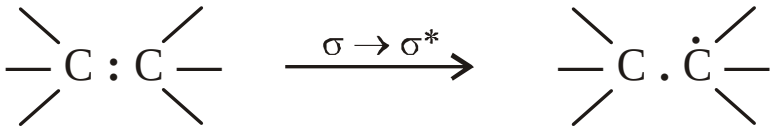


Fig.20.3: Electronic Energy levels and electronic transitions..

Similarly, when an *n*-electron (non-bonding) is promoted to antibonding p orbital, it represents $n \rightarrow \pi^*$ transition. The energy required for various transitions obey the following order:

$$\sigma \rightarrow \sigma^* > n \rightarrow \sigma^* > \pi - \pi^* > n \rightarrow \pi^*$$

(a) **$\sigma \rightarrow \sigma^*$ transitions:** It is a high energy process since a σ bond is in general very strong. The organic compounds in which all the valence shell electrons are involved in the formation of sigma bonds do not show absorption in the normal ultra-violet region. *i.e*., 180–400 mμ. For saturated hydrocarbons, like methane, propane etc. absorption occurs near 150 mμ (high energy). Consider $\sigma \rightarrow \sigma^*$ transition in a saturated hydrocarbon:



Such a transition requires radiation of very short wavelength (high energy). The usual spectroscopic technique cannot be used below 200 mμ, since oxygen (present in air) begins to absorb strongly. To study such high energy transitions (below 200 mμ). the entire path length must be vacuated*. Thus, the region below 200 mμ is commonly called vacuum **ultraviolet region.** The excitation of sigma bond electron to □□ (antibonding) level occurs with net retention of electronic spin. It is called excited singlet state which may, in turn, gets converted to excited triplet state. This region is less informative.

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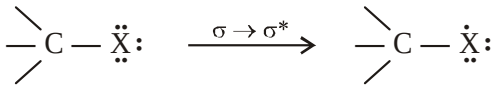
* Called sigma asterisk

(b) $n \rightarrow \sigma^*$ transition: This type of transition takes place in saturated compounds containing one hetero atom with unshared pair of electrons *(n* electrons). Some compounds undergoing this type of transitions are saturated halides, alcohols, ethers, aldehydes. ketones, amines etc. Such transitions require comparatively less energy than that required for $\sigma \rightarrow \sigma^*$ transitions. Water absorbs at 167 mμ, methyl alcohol at 174 mμ and methyl chloride absorbs at 169 mμ.

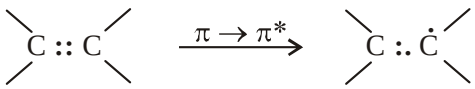
In saturated alkyl halides, the energy required for such a transition decreases with the increase in the size of the halogen atom (or decrease in the electronegativity of the atom).



Let us compare *n* $n \rightarrow \sigma^*$ * transition in methyl chloride and methyl iodide. Due to the greater electronegativity of chlorine atom, the *n* electrons on chlorine atom are comparatively difficult to excite**. The absorption maximum for methyl chloride is 172–175mμ whereas that for methyl iodide is 258 mμ as *n* electrons on iodine atom are loosely bound. Since this transition is more probable in case of methyl iodide, its molar extinction coefficient*** is also higher compared to methyl chloride.

Similarly, amines absorb at higher wavelengths as compared to alcohols and hence the extinction coefficients for amines will be larger. $n \rightarrow \sigma^*$transitions are very sensitive to hydrogen bonding. Alcohols as well as amines form hydrogen bonding with the solvent molecules. Such association occurs due to the presence of non-bonding electrons on the hetero atom and thus, transition requires greater energy. Hydrogen bonding shifts the ultra-violet absorptions to shorter wavelengths.

(c) $\pi \rightarrow \pi^*$* transitions: This type of transition occurs in the unsaturated centres of the molecule; *i.e*., in compounds containing double or triple bonds and also in aromatics. The excitation of ρ electron requires smaller energy and hence, transition of this type occurs at longer wavelength. A π^* electron of a double bond is excited to □π^* orbital. For example, alkenes, alkynes, carbonyl compounds, cyanides. azo compounds etc. show it $\pi \rightarrow \pi^*$ transition. Consider an alkene:



This transition requires still lesser energy as compared to $n \rightarrow \sigma^*$ transition and therefore absorption occurs at longer wavelengths. Absorption usually occurs within the region of ordinary ultra-violet spectrophotometer. In unconjugated alkenes, absorption bands appear around (170–190 mμ. In carbonyl compounds the band due to $\pi \rightarrow \pi^*$ transition appears around 180 mμ and is most intense. *i.e.*, the value of extinction coefficient is high. The introduction of alkyl group to olefinic linkage produces a bathochromic shift*** of the order of 3 to 5 mμ per alkyl group. The shift depends upon the type of the alkyl group and the stereochemistry about the double bond.

(d) $n \rightarrow \pi^*$ In this type of transition, an electron of unshared electron pair on hetero atom gets excited to π^* antibonding orbital. This type of transition requires least amount of energy out of all the transitions discussed above and hence occurs at longer wavelengths.

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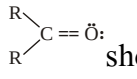
* Air must be excluded from the instrument so as to avoid absorption due to oxygen.

** Greater the probability of a particular transition, greater the value of its molar extinction coefficient, E_{max}.

*** Shift towards longer wavelength.

Saturated ketones  show both the types of transitions, *i.e.* low energy $n \rightarrow \pi^*$ and high energy $\pi \rightarrow \pi^*$ occurring around 290 $m\mu$ and 180 $m\mu$ respectively. Absorption occurring at lower wavelength is usually intense. In simple cases, it is quite easy to tell whether the transition is $n \rightarrow \pi^*$ or $\pi \rightarrow \pi^*$, since the extinction coefficient for the former is quite low as compared to that of the latter. The exact electronic structure of the molecules in the excited state (by the absorption of UV or visible light) is not known but the electronic transition involves the redistribution of electrons within the molecule. In carbonyl compounds; a high energy $n \rightarrow \sigma^*$ transition also occurs and is quite intense. Thus, in saturated carbonyl compounds, two types of transitions take place which can be classified as–

(a) High energy transitions

(i) $n \rightarrow \sigma^*$ (intense)

(ii) $\pi \rightarrow \pi^*$ (intense)

(b) Low energy transition

$n \rightarrow \pi^*$ $n \rightarrow \pi^*$ (weak)

In carbonyl compounds, the shift in the absorption depends upon the polarity of the solvent.

20.5 Chromophore

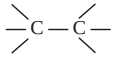
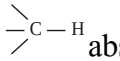
All those compounds which absorb light of wavelength between 400–800 appear coloured to the human eye. Exact colour depends upon the wavelength of light absorbed by the compound. Originally, a *chromophore* was considered any system which is responsible for imparting colour to the compound. Nitro–compounds are generally yellow in colour. Clearly, nitro group is the chromophore which imparts yellow colour. Similarly, aryl conjugated azo group is a chromophore for providing colur to azo dyes. Now, the term chromophore is used in a broader way.

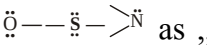
It is defined as any isolated covalently bonded group that shows a characteristic absorption in the ultraviolet or the visible region.

The absorption occurs irrespective of the fact whether colour is produced or not. Some of the important chromophores are ethylenic, acetylenic, carbonyls, acids, esters, nitrite group etc. A carbonyl group is an important chromophore, although, the absorption of light by an isolated group does not produce any colour in the ultraviolet spectroscopy. There are two types of chromophores :

(a) Chromophores in which the group contains *n* electrons and they undergo $n \rightarrow \pi^*$ transitions. Such chromophores are ethylenes, acetylenes etc.

(b) Chromophores which contain both π electrons and *n* (non–bonding) electrons. Such chromophores undergo two types of transitions i.e., $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ .Examples of this type are carbonyls, nitrites, azo compounds, nitro compounds etc.

Note : In compounds of the type ethane  and methane  absorption occurs around 150 mμ (vacuum ultraviolet region) as result of $\sigma \rightarrow \sigma^*$ transition.

For compounds containing such atoms  as ,, absorption occurs around 190 $m\mu$ as a result of $n \rightarrow \sigma^*$ transition.

There are no set rules for the identification of a chromophore. The change in position as well as the intensity of absorption depends upon a large number of factors. Following points may be helpful:

(i) Spectrum consisting of a band near 300$m\mu$ may contain two or three conjugated units.

(ii) Absorption bands near 270–350 $m\mu$ with very low intensity, ϵ_{max} 10–100 are due to $n \rightarrow \pi^*$ transitions of the carbonyl group.

(iii) Simple conjugated chromophores such as dienes or $-^{\alpha,\beta}$ unsaturated ketones have high ϵ_{max} values, *i.e.*, from 10,000 to 20,000.

(iv) The absorption with ϵ_{max} value between 1000 to 10,000 shows an aromatic system.

Table: 20.1

Chromphore	Transition	Absorption max (mμ)	ϵ_{max}	Solvent
$-\overset{|}{C}=\overset{|}{C}-$	$\pi - \pi^*$	–175	–1500	Vapour
$-C=C-$	$\pi - \pi^*$	(i) –175	–10000	Hexane
$>C=O$	$n \rightarrow \sigma^*$ $\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	160 180 285*	18000 10000 15	Hexane
R—NO_2	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	–200 –274	5000 15	Methanol
$-\overset{|}{\underset{|}{C}}=O$ OH	$n \rightarrow \pi^*$	204	60	Methanol
— N = N —	$n \rightarrow \pi^*$	338	–5	Ethanol
— $CONH_2$	$n \rightarrow \pi^*$ $n \rightarrow \pi^*$	178 220	9500 63	Exane Hexane

When aromatic nucleus is substituted with groups which can extend the chromophore, the absorption occurs at still higher values of extinction coefficients.

Note: The presence of a compound or a functional group can be confirmed by other spectroscopic techniques.

All compounds with the same functional group will absorb at the same wavelength with nearly the same extinction coefficient if the disturbing factors such as conjugation, substituents etc are absent. Some of the chromophores with their respective absorption maximum and extinction coefficientts are given in Table (20.1).

20.6 Auxochrome

An auxochrome can be defined as *any group–which does not itself act as a chromophore but whose presence brings about a shift of the absorption band towards the red end of the spectrum* (longer wavelength). The absorption at longer wavelength is due to the combination of a chromophore and an auxochrome to give rise to another chromophore. An auxochromic group is called colour enhancing

group. Auxochromic groups do not show characteristic absorption above 200 mm. Some common auxochromic groups are —OH, —OR, —NH_2, —NR_2, —SH etc. The effect of the auxochrome is due to its ability to extend the conjugation of a chromophore by the sharing of non–bonding electrons. Thus, a new chromophore results which has a different value of the absorption maximum as well as the extinction coefficient. For example, benzene shows an absorption maximum at 255$[\varepsilon_{max}$ 203]whereas aniline absorbs at 280$[\varepsilon_{max}$ 1430]. Hence, amino (—NH_2) group is an auxochrome.

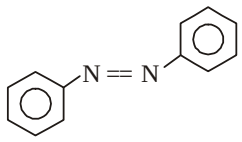
Consider the following:

λ_{max} = 280 nm
ε_{max}= 1430

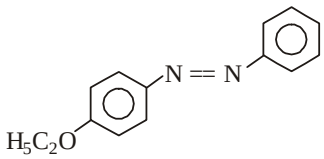
λ_{max} = 254 nm
ε_{max}= 160

In aniline, $-\ddot{N}H_2$ as a chromophore. But in anilinium ion, there is no lone pair on nitrogen atom, and does not cause only such effect.

Consider trans–Azobenzene and trans–*p*–ethoxyazobenzene.



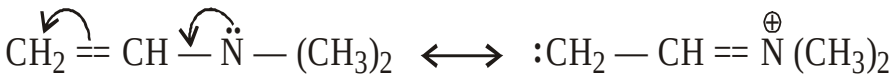
Trans-Azobenzene
λ_{max} = 320 nm
ε_{max}= 21000



Trans-p-Ethexyazobenzene
λ_{max} = 385 nm
ε_{max}= 42000

The presence of —OC_2H_5 group (an auxochrome) increases the value of λ_{max}as well as ε_{max}.

Mechanism: All auxochromic groups contain non–bonding electrons. Due to this, there is extension of conjugation of the chromophore by sharing the non-bonding electrons.



20.7 Bathochromic Effect and Hypsochromic Effect (Absorption and Intensity Shifts)

(a) Bathochromic effect: It is an effect by virtue of which the absorption maximum is shifted towards longer wavelength due to the presence of an auxochrome or by the change of solvent. (See fig. 20.4). Such an absorption shift towards longer

wavelength is called Red shift or *bathochromic shift*. The $n \rightarrow \pi^*$ transition for carbonyl compounds experiences bathochromic shift when the polarity of the solvent is decreased.

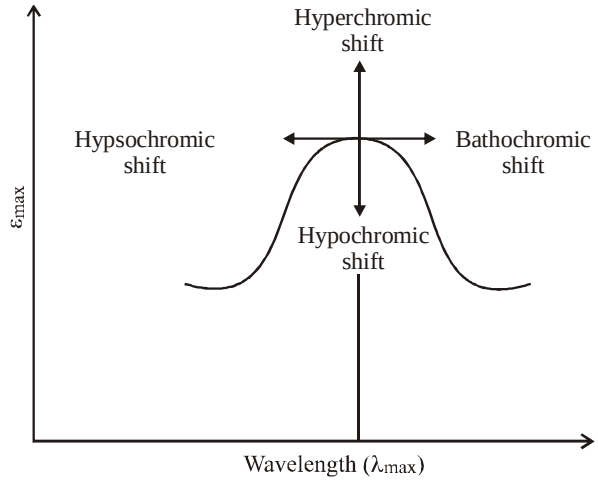
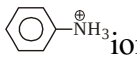


Fig. 20.4: Absorption and intensity shifts.

(b) Hypsochromic shift or effect: It is an effect by virtue of which the absorption maximum is shifted towards shorter wavelength. The absorption shifted towards shorter wavelength is called **Blue shift** or *hypso chormi c shift*.

It may be caused by the removal of conjugation and also by changing the polarity of the solvent. In the case of aniline, absorption maximum occurs at 280 μ because the pair of electrons on nitrogen atom is in conjugation with the bond system of the benzene ring. In its acidic solutions. a blue shift is caused and absorption occurs at shorter wavelength (~203 μ).

In benzene,  ion formed in acidic solution, the electron pair is no longer present and hence conjugation is removed.

(c) Hyperchromic effect: It is an effect due to which the intensity of absorption maximum increases *i.e.*, ϵ_{max} increases. For example. the B–band for pyridine at 257 ϵ_{max} μ ϵ_{max} 2750 is shifted to 262 μ ϵ_{max} 3560 for 2–methyl pyridine (*i.e.*, the value of increases). The introduction of an auxochrome usually increases intensity of absorption.

(d) Hypochromic effect: It is defined as an effect due to which the intensity of absorption maximum decreases, *i.e.*, extinction coefficient, ϵ_{max} decreases. The introduction of group which distorts the geometry of the molecule causes hypochromic effect. For example, biphenyl absorbs at 250 μ, ϵ_{max} 19000 whereas 2–methyl biphenyl absorbs at 237 μ, ϵ_{max} 10250 (decreases). It is due to the distortion caused by the methyl group in 2–methyl biphenyl.

20.8 Solvent Effects

A most suitable solvent is one which does not itself absorb in the region under investigation. A dilute solution of the sample is always prepared for the spectral analysis. Most commonly used solvent is 95% Ethanol. Ethanol is a best solvent as it is cheap and is transparent down to 210 μ. Commercial ethanol should not be used as it contains benzene which absorbs strongly in the ultraviolet region. Some other solvents which are transparent above 210 are n–hexane, methyl alcohol, cyclohexane, acetonitrile, diethyl ether etc. Some solvents with their upper wavelength limit of absorption are given in Table (20.2).

Table 20.2: Solvents used in UV–spectroscopy

Solvent	Upper wavelength limit (m μ)
Ethanol	210
Hexane	210
Methanol	210
Cyclohexane	210
Diethyl ether	210
Water	205
Benzene	280
Chloroform	245
THF (Tetrahydrofuran)	220
Carbon tetrachloride	265

Hexane and other hydrocarbons can be used as these are less polar and have least interactions with the molecule under investigation. For ultra-violet spectroscopy, ethanol, water and cyclohexane serve the purpose best.

The position and the intensity of absorption maximum is shifted for a particular chromophore by changing the polarity of the solvent. By increasing the polarity of the solvent, compounds like dienes and conjugated hydrocarbons do not experience any appreciable shift. Thus, in general, the absorption maximum for the non–polar compounds is the same in alcohol (polar) as well as in hexane (non–polar). The absorption maximum for the polar compounds is usually shifted with the change in polarity of the solvents. $^{\alpha,\beta}$ –unsaturated carbonyl compounds show two different shifts.

(i) $n \rightarrow \pi^*$ **transition (less intense):** In such a case, the absorption band moves to shorter wave–length by increasing the polarity of the solvent. In $n \rightarrow \pi^*$ transition, the ground state is more polar as compared to the excited state. The hydrogen bonding with solvent molecules takes place to lesser extent with the carbonyl group in the excited state. For example, absorption maximum of acetone is at 279 m μ in hexane as comparred to 264m μ in water (A).

(ii) $\pi \rightarrow \pi^*$ **transition (intense):** For such a case, the absorption band moves to longer wavelength by increasing the polarity of the solvent. The dipole interactions with the solvent molecules lower the energy of the excited state more than that of the ground state. Thus, the value of absorption maximum in ethanol will be greater than that observed in hexane.

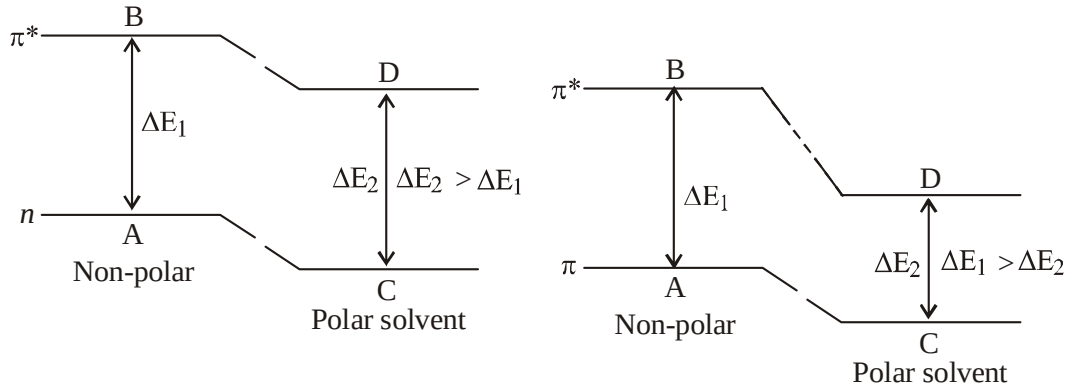


Fig. 20.5: Absorption shift with change in polarity of the solvent.

In short, π^* orbitals are more stabilised by hydrogen bonding with polar solvents like water and alcohol. It is due to greater polarity of π^* orbitalcompared to p orbital. Thus, small energy will be required for such a transition and absorption shows a red shift.

$n \rightarrow \pi^*$ transitions are also very sensitive to hydrogen bonding. Alcohols as well as amines form hydrogen bonding with the solvent molecules. Such associations occur due to the presence of nonbonding electrons on the hetero atom and thus, transition requires greater energy. In general, we can say that–

(a) If the group (carbonyl) is more polar in the ground state than in the excited state, then increasing polarity of the solvent stabilises the non–bonding electron in the ground state due to hydrogen bonding. Thus, absorption is shifted to lower wavelength.

(b) If the group is more polar in the exicted state, then absorption is shifted to longer wavelength with increase in polarity of the solvent which helps in stabilising the non–bonding electrons in the exicted state.

It has been found that increase in polarity of the solvent generally $n \rightarrow \pi^*$ shifts and $n \rightarrow \sigma^*$ bands to shorter wavelength and $\pi \rightarrow \pi^*$ bands to longer wavelengths.

Following points may also be noted in connection with the effect of solvent polarity on the various types of bands–

(i) K–band : The K-band absorption due to conjugated 'enes' and 'enones' are affected differently by changing the polarity of the solvent. Usually, K–bands due to conjugated dienes are not effected by changing the polarity of the solvent while these bands due to 'enones' show a red shift by increasing the polarity of the solvent.

(ii) R–band: The absorption shifts to shorter wavelength (blue shift) with the increase in polarity of the solvent.

(iii) B–band: The position as well as the intensity of the B-band is not shifted by increasing the polarity of the solvent. But in heterocyclic aromatic compounds, a marked hyperchromic shift (increase in $\in_{max}$) is observed by increasing the polarity of the solvent.

Conjugated Dienes

The wavelength of absorption is shifted to higher values (Bathochromic shift), if two or more chromophoric groups are present in conjugation in a molecule. For example, ethylene (one double bond) absorbs at 170 m μ ($\pi \rightarrow \pi^*$ transition) while butadiene (two double bonds in conjugation) absorbs at 217 m μ. The bathochromic shift is more pronounced if the double bonds are in conjugation as compared to the isolated double bonds in which there is a little interaction between them. The absorption maximum is usually shifted 15–45 m μ towards higher wavelength in conjugated system (compared to unconjugated) as the electron density is spread over at least four atomic centres. The value of extinction coefficient also increases. In conjugated dienes, transition results in the formation of a band, called K–band.

Table 20.3: $\pi \rightarrow \pi^*$ transition (K–band)

Compound	λ_{max} max (mμ)	$\in_{max}$
1,3-Butadiene	217	21,000
2,3 dimethy butadiene	226	21,400
1,3,5, Hexatriene	254	21,400

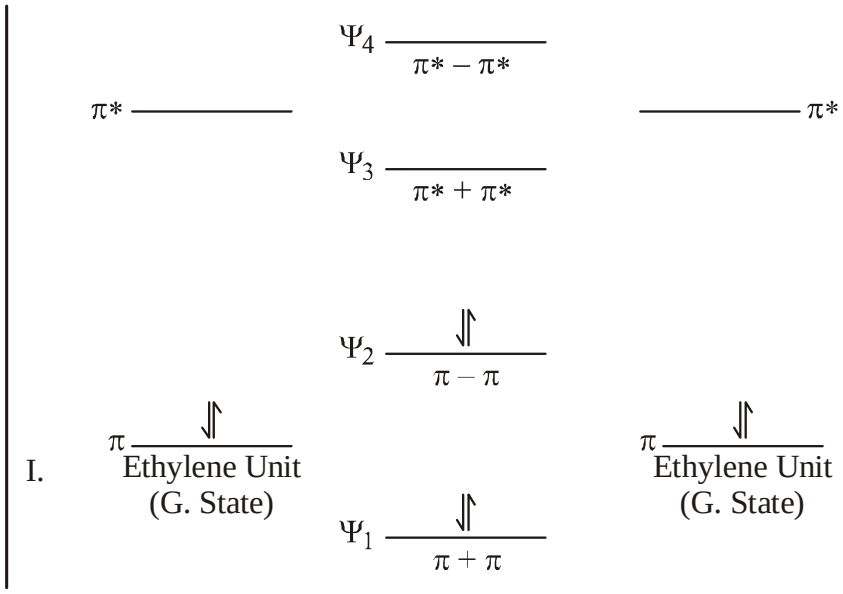


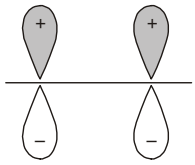
Figure 20.6: Electronic excitation in conjugated dienes

When ethylene molecule gets excited, it gives CH_2–CH_2 diradical. The electron cloud is spread on two carbon atoms and the absorption maximum occurs at 170 m. Consider the absorption maximum of 1,3-butadiene (CH_2= CH — CH = CH_2). It consists of two ethylene units. The various excitations are shown in Fig. 20.6.

The two π bonding orbitals, one from each ethylene unit interact or mix up to give rise to two new bonding orbitals.

(i) $\pi + \pi = \pi_1$ or ψ_1– having smaller energy.

(ii) $\pi - \pi = \pi_2$ or ψ_2– having smaller energy.



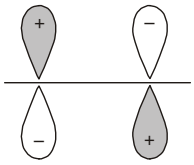


Figure 20.7: π– bonding orbitals. **Fig. 20.8: π–* antibonding orbital**

The energy of ψ_1 is less than any one of the two combining atomic orbitals.

Also two π^* orbitals (antibonding) are formed from two ethylene units which are

(i) $\pi^* + \pi^* = \pi^*_1 = \psi_3$ having smaller energy.

(ii) $\pi^* - \pi^* = \pi^*_2 = \psi_4$ having smaller energy.

The energies of ψ_3 and ψ_4 are compared with any one of the two (ρ^*) antibonding orbitals.

Thus ψ_1 can be represented as shown in the Fig.20.9.

In this case, all the four singly filled atomic orbitals have the same spin of electrons.

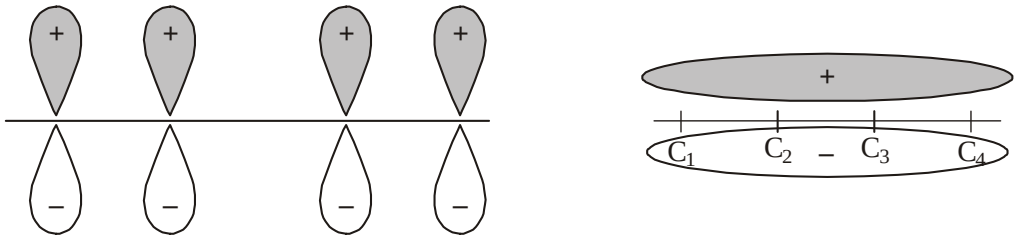


Fig. 20.9: Low energy atomic orbital (ψ_1)

Thus mixing is complete and there is no nodal plane.*

$\pi - \pi = \pi_2 = \psi_2$ can be represented as shown in Fig. 20.10.

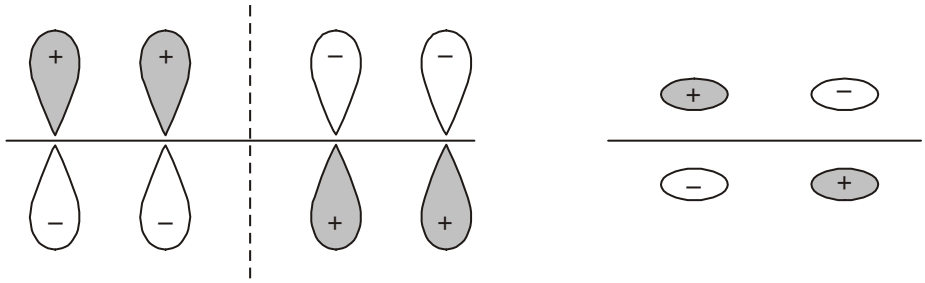


Fig. 20.10: High energy bonding orbitals(ψ_2).

In this case, we see one nodal plane.*

Clearly there are double bonds between C_1, C_2 and C_3, C_4 and there is a single bond between C_2 and C_3.

$\pi^* + \pi^* = \pi_3^* = \psi_3$ can be represented as shown in Fig. 20.11.

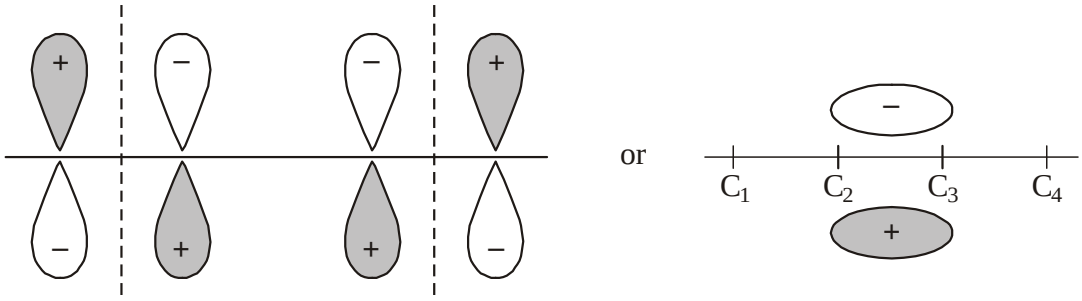


Fig. 20.11: Low energy antibonding orbitals (ψ_3)

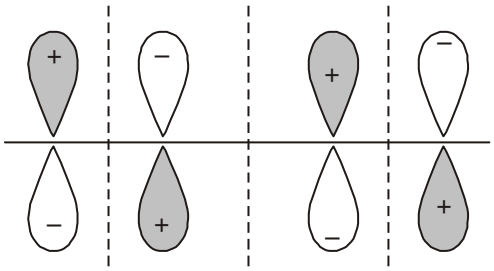


Fig. 20.12: High energy antibodning orbital (ψ_4)

In this case, there are two nodal planes and one double bond betrween C_2 and $\pi^* - \pi^* = \pi_4^* = \psi_4$ can be represented as shown in 20.12. This structure corresponds to high energy state since it involves three nodal planes.

Thus, in butadiene, four orbitals are involved. On absorption of energy, electron jumps from π_2 to π_3^*.Since the energy difference between π_2 to π_3^* is less, absorption occurs at higher wavelength. This type of $\pi \rightarrow \pi^*$ transition is called transition. **The net result is that when two double bonds are in conjugation, the energy level of higher occupied molecular orbital (HOMO) is raised and that of the lowest unoccupied molecular (antibonding) orbital(LUMO) is lowered.**

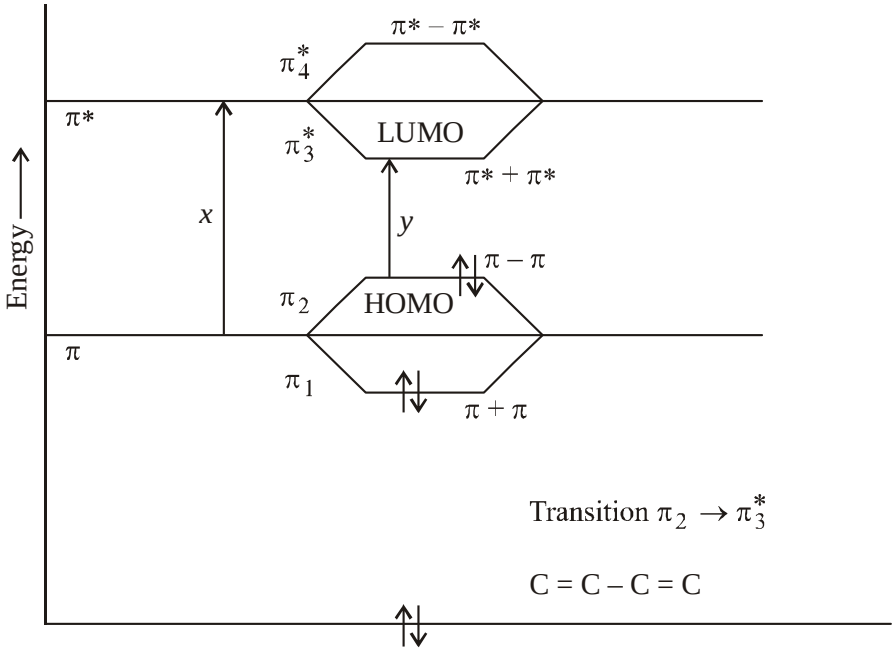


Fig.: 20.13

Now this absorption corresponds to the transition γ (low energy or higher wavelength). Similarly, when dissimilar chromophores are in conjugation, absorption occurs at longer wavelength as compared to the isolated chromophores. In general longer the conjugated system, smaller will be the energy needed to cause

$\pi \rightarrow \pi^*$ transition and therefore, absorption occurs at still longer wavelength. In a long conjugated system like carotene, absorption occurs in the visible region (higher wavelength region).

The values of absorption maximum (λ_{max} and $\in_{max}$) are more for conjugated diene as compared to those for an unconjugated alkene. A bathochromic as well as hyperchromic effect are observed when the spectrum of conjugated triene is compared to that of conjugated diene.

It is important to note that greater the number of conjugated double bonds, greater is the bathochromic shift. With continuous increase in conjugation, the absorption may even shift to the visible region. As the conjugation increases, the energy gap between HOMO and LUMO decreases, (See Fig. 20.14). In case of β–carotene which contain eleven double bonds, the absorption bands appear at (i) λ_{max} 478 nm $\in_{max}$ (139000 $\in_{max}$) and (ii) λ_{max} 452 nm (122000 $\in_{max}$).

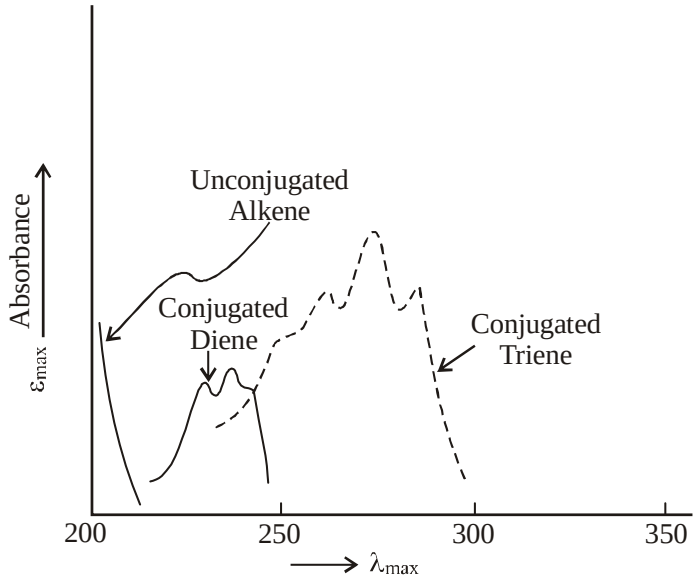


Fig. 20.14: Absorption in conjugated and unconjugated systems.

It is defined as an imaginary plane drawn perpendicular to the plane of propagation of the wave where the probability of finding the electron is zero.

20.9 Woodward-fisher Rules for Calculating Absorption Maximum in Diene

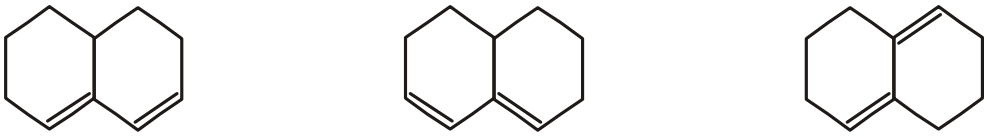
Longer the conjugated system, greater is the wave–length of absorption maximum. The intensity or absorption [$\in_{max}$] also increases with the increase in the length of the chromophore (see Fig. 20.14). The conjugated polyene system appears coloured to the naked eye if there are more than five double bonds in conjugation and absorption

occurs around or above 400 m μ (visible region). The presence of alkyl group on the double bond also causes bathochromic shift. Various types of double bonds in conjugation are described below:

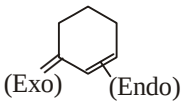
(a) Alicyclic dienes or dienes contained in an open chain system, i.e., where basic unit is butadiene system.

(b) Homo-annular conjugated double bonds are the conjugated double bonds present in the same ring. It is also called **Homodiene**. Some examples of this type are:

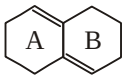
(c) Hetero-annular conjugated double bonds are the conjugated double bonds which are not present in the same ring. Some examples of this type are:



(d) Exocyclid and Endocylic conjugated double bonds : Exocyclic double bond is a double bond, part of the conjugated system, formed by any carbon atom of any ring but present outside the ring. Endocyclic double bond is present inside the ring. Such double bonds are shown in the following examples:



(Exocylic double bond to ring A)



(Contain two exocyclic, double bonds)

Woodward formulated certain empirical rules for calculating the λ_{max}* in case of dienes. These rules were later modified by Fieser in 1948. According to these rules, each type of diene has a certain fixed basic value and the value of absorption maximum (λ_{max}) depends upon :

(i) The number of alkyl substituents or ring residues on the double bond.

(ii) The number of double bonds which extend conjugation and

(iii) The presence of polar group such as –Cl, –Br,–OR,–SR etc.

Ring residue is a C–C bond, not a part of the conjugated system but attached to any one of the carbon atoms of the conjugated polyene system.

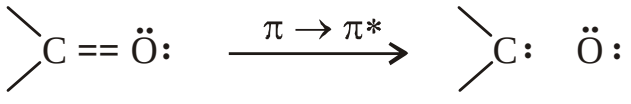
The various rules for calculating the absorption maximum in case of dienes and trienes are summarised in the Table (20.4).

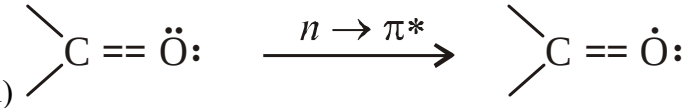
Table 20.4: Conjugated dienes and Trienes.

Solvent–Ethanol Transition involved $-\pi \rightarrow \pi^*$	
Parent value for Butadiene system or a cyclic conjugated diene	217 mμ
Acyclic Triene	245 mμ
Homoannular conjugated diene	253 mμ
Heteroannular conjugated diene	215 mμ
Increment for each substituent	
Alkyl substituent or ring residue	5 mμ
Exocyclie double bond	5 mμ
Double bond extending conjugation	30 mμ
Auxochrome	
— OR	+ 6 mμ
— SR	+ 30 mμ
— Cl* — Br*	+ 5 mμ
— NR_2	+ 60 mμ
$OCOCH_3$	0 mμ

Ultra–violet Absorption in α, β– unsaturated Carbonyl Compounds

For a carbonyl group two types of transitions occur.

(i) 

(ii) 

The first transition involves the promotion of one of the p electrons to an antibonding π^* orbital ($\pi \rightarrow \pi^*$). It is very intense and corresponds to shorter wavelength. The second transition ($n \rightarrow \pi^*$) involves the promotion of one of the non-bonding paired electron to orbital. It is less intense and corresponds to longer wave-length. It is called R-band.

In α, β- unsaturated carbonyl compounds, the double bond and the carbonyl group are in conjugation. The spectra for such compounds are simple summation of ethylene and carbonyl chromophores. A bathochromic shift is observed if two chromosphoric groups are conjugated as electron cloud is spread over at least four carbon atoms. There is a $\pi \rightarrow \pi^*$ transition due to ethylene unit which is in conjugation with carbonyl group.

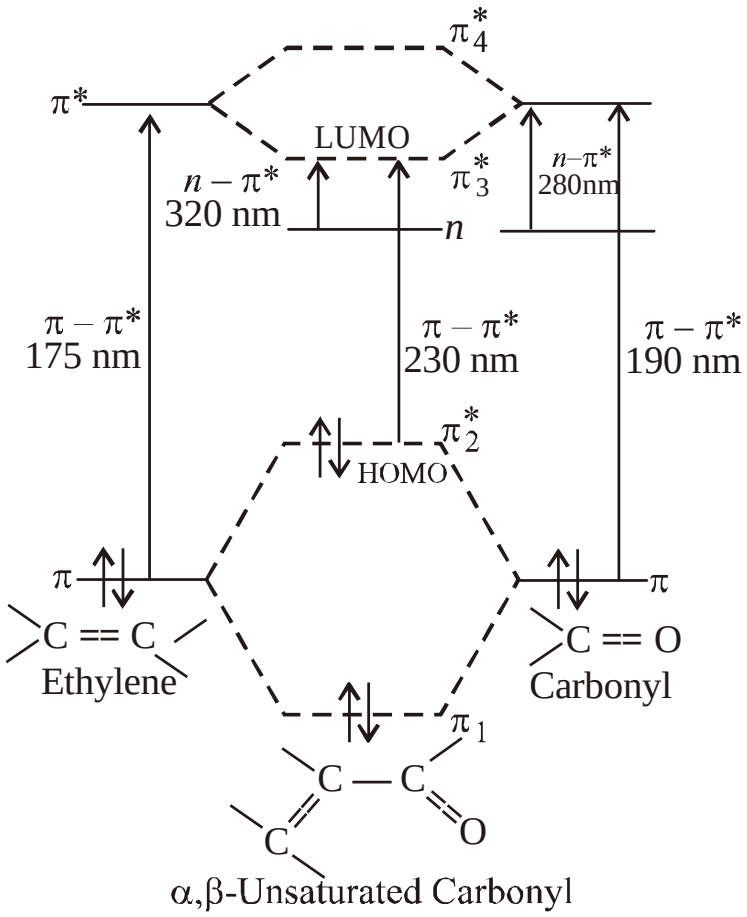


Fig. 20.15: U.V. transitions in α,β- unsaturated carbonyl compounds.

In **α,β-** unsaturated carbonyl compounds where ethylene and carbonyl groups are conjugated, both $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions show bathochromic shifts. The various transitions involved as shown above in Fig. 20.15. From the energy level diagram, it is clear that π_2 (HOMO) energy π level is higher than either of the levels of C == C. The π_3^* (LUMO) energy level is lower than that of π^* level of C == C and C == O chromophones. Since the energy difference between (HOMO) and (LUMO) is less, the $\pi \rightarrow \pi_3^*$ transition shows bathochromic effect. Similary, $n \rightarrow \pi^*$ transition (R–bond) also shows bathochromic shift.

$n \rightarrow \pi^*$ **transition in aldehydes and ketones:** Aldehydes and ketons show a weak forbidden band in the range 275 to 300 mμ due to the excitation of an oxygen lone electron to π^* orbital. Aldehydes and highly substituted a ketones absorb at upper end of the range. Polar substituents on □□□□-carbon atom in axial or equitorial position raise or lower the extremes of this range respectively. When the carbonyl group is substituted by an auxochrome as in an ester, amide etc. the π^* orbital is raised while *n* level of lone pair is hardly altered. Due to this, the $n \rightarrow \pi^*$ transition in these compounds is shifted to lower wave-length range (200–215 mμ). Clearly, a

weak band at 275 to 300 mμ $(\varepsilon_{max} 10-100)$ is a positive identification of aldehydic or ketonic carbonyl group.

α, β- unsaturated carbonyl compounds show slightly stronger $n \rightarrow \pi^*$ band or series of bands in the 300 – 350 mμ range. The positions as well as the intensity of $n \rightarrow \pi^*$ band are influenced by the transannular* interactions and also by the solvent.

Axially substituted isomers absorb at longer wavelength than equitorially substitued isomers. α,β -unsaturated acids, esters show bathochromic shift but absorb at comparateively shorter wavelengths. α,β -unsaturated amides have been shown to absorb at lower values than the corresponding acids. The absorption occurs usually in the inaccessible region. It is important to note that the positions of $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transition in carbonyl compounds vary with the nature of the solvent used.

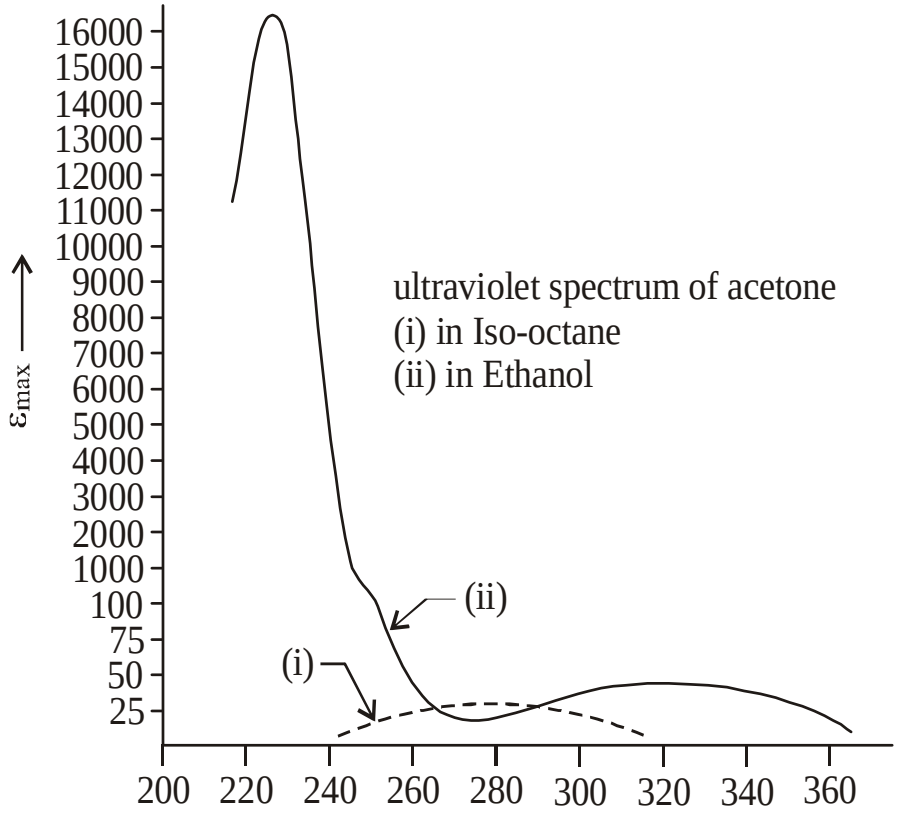


Fig. 20.16: U.V. spectrum of acetone in (i) isooctane (ii) ethanol.

By increasing the polarity of the solvent, $\pi \rightarrow \pi^*$ transition experiences a red shift while $n \rightarrow \pi^*$ transition undergoes a blue shift. The changing polarity of the solvent brings about a change in the energy difference between the levels involved in the transitions. The shift is due to the change in the stability of the ground or the excited electronic states. The absorption due to $n \rightarrow \pi^*$ transition experiences a blue shift as the degree of hydrogen bonding between the carbonyl group and the solvent increases by increasing the polarity of the solvent. In other words, the energy of n

electrons is strongly lowered by hydrogen bonding and thus, greater energy is required to promoting n electrons of π^* level.

A comparison in the ultra-violet spectra of un-conjugated carbonyl compounds (see fig. 20.17) reveals that the value of absorption maximum for carbonyl group experiences a bathochromic as well as hyperchromic effects in conjugated carbonyl compound as compared to an un-conjugated carbonyl compound.

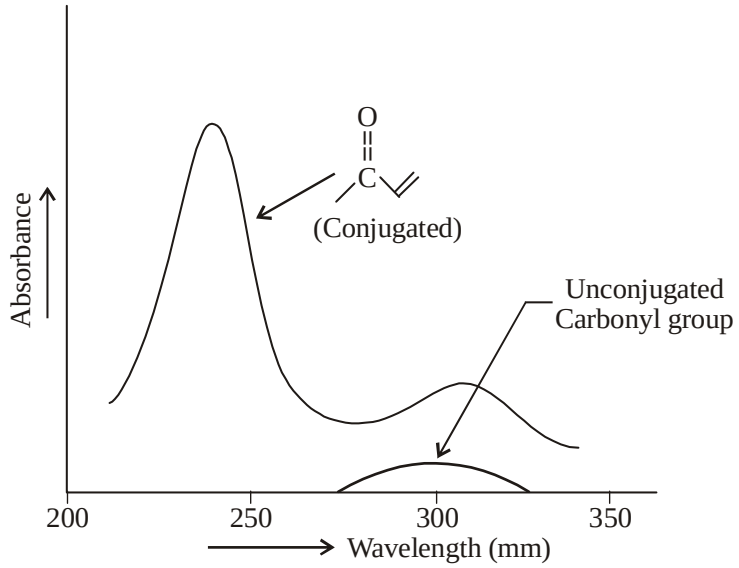


Fig. 20.17: U.V. absorption spectra for conjugated and unconjugated carbonyl compounds.

Woodward–fieser Rules for Calculating Absorption Maximum in α, β unsaturated Carbonyl Compounds

Woodward and Fieser framed certain empirical rules for estimating the absorption maximum for α, β –unsaturated carbonyl compounds. The rules were later modified by Scott as follows:

(a) The basic value of α, β –unsaturated ketone is taken as 215 m*u*. The α,β–unsaturated ketone may be a cyclic or six membered.

For a compound, = CH — COX, basic value is 215 mu, if X is an alkyl group.

If X == H, basic value becomes 207 m*u*. The basic value is 193 m*u* if X is OH or OR.

(b) If the double bond and the carbonyl group are contained in a five membered ring (cyclopentenone), then for such an □□□–unsaturated ketone, the basic value becomes 202 m□. The $\square_{max}$ for such compounds are generally above 10,000.

The structural increments for estimating $\square_{max}$ for a given $\square\square\square$–unsaturated Carbonyl compound are as follows:

(i)	For each exocyclic double bond	+ 5 mμ
(ii)	For each double bond endocyclic in five or seven membered ring except cyclo–pent–2 enone	+ 5 mμ
(iii)	For each alkyl substituent or ring residue at the	
	α –position	+ 10 mμ
	β–position	+ 12 mμ
	γ–or d- or higher position	+ 18 mμ
(iv)	For each double bond extending conjugation	+ 30 mμ
(v)	For a homoannular conjugated diene.	+ 39 mμ
(vi)	Increments for various auxochromes in the various α– ,β– ,γ– etc.positions are given in the following Table (20.5)	

Table 20.5: Chromophore increments in Carbonyl Compounds.

Chromophore	Increment in nm (or mμ) for position w.r.t. the carbonyl group			
	α–	β–	γ–	δ– or higher
—OH	+ 35	+30	—	+50
—OAc	+6	+6	+6	+6
—Cl	+15	+12	—	—
—Br	+25	+35	—	—
—OR	+35	+30	17	31
—SR	—	+85	—	—
—NR_2	—	+95	—	—

Table 20.5: Chromophore increments in Carbonyl Compounds.

Making use of the above rules, the absorption maximum for the various $\square$,$\square$–unsaturated compounds can be estimated.

Benzene and Its Derivatives

The B–band at 254 mμ in ultraviolet spectrum of benzene shows a great deal of fine structure in the vapour phase. The fineness of the structure diminishes if we scan it in hexane solution and is almost completely destroyed in ethanol solution (See Fig. 20.18).

In hexane solution, benzene shows absorption at 184 mμ., ε_{max} 60,000; 204 mμ, ε_{max} 7400 and 254 mμ, ε_{max} 204. The band at 254 mμ is the result of forbidden transitions in highly symmetrical benzene molecule. Benzene shows a series of low intensity bands between 230 and 270 mμ.

It has been noted that absorption maximum for poly–nuclear aromatic hydrocarbons moves to longer wavelength. Comparing the ultra–violet spectrum of benzene with naphthalene, we see that the value of absorption maximum as well as extinction coefficient are more for naphthalene as compared to those of benzene. Naphthalene absorbs at 480 mμ, ε_{maxmax} 11000 while anthracene absorbs at still higher value. Pentacene absorbs at 580 mμ, ε_{maxmax} 12600 and appears blue.

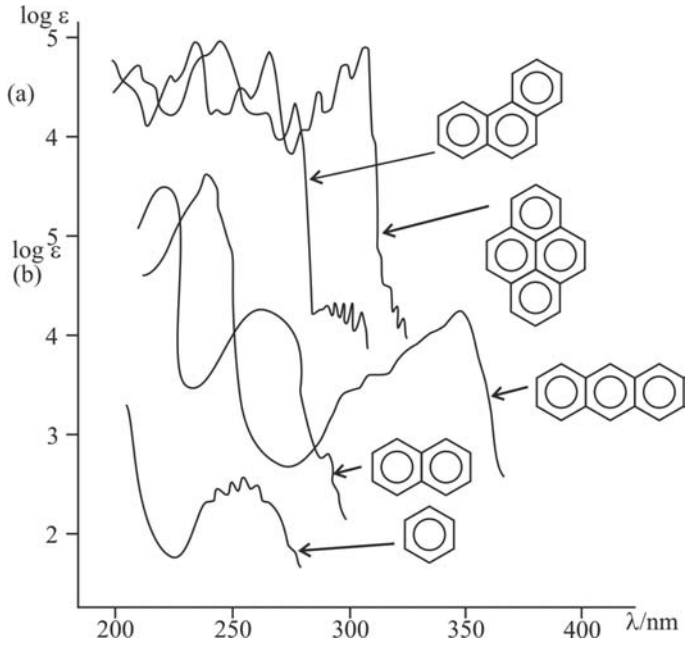
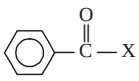


Figure 20.18: Electronic absorption spectra of typical polynuclear aromatic hydrocarbons

Rules for Calculating Absorption Maximum for Derivatives of Acyl Benzenes

Like Woodward Fieser rules, Scott devised a set of rules for calculating the absorption maximum for the derivatives of acylbenzenes. These rules help in estimatinmg the position of absorption maximum in ethanol in a number of monosubstituted aromatic ketones, aldehydes, acids and esters.

For a compound of the type 

(i) the basic value is 246 mμ. if X is an alkyl group or alicyclic residue.

(ii) if X is hydrdogen atom, the basic value becomes 250 mμ. and

(iii) the basic value is 230 mμ. if X is OH or OR. The structural increments in mμ. for further substitution on the aromatic ring in the ortho, meta and para positions are given in the Table 20.6.

Table 20.6: Auxochrome acting as a substituent

Auxochrome	Increment in mμ according to the position of the substituent		
	o–	*m*–	*p*–
Alkyl	+ 3	+ 3	+ 10
OH, OR	+ 7	+ 7	+ 25
Cl	0	0	+ 10
Br	+ 2	+ 2	+ 15
NH_2	+ 13	+ 13	+ 58
NHAc	+ 20	+ 20	+ 45
NR_2	+ 20	+ 20	+ 85
O^-	+ 11	+ 20	+ 75

Note: It is important to note that the effect of the para substituent is more pronounced for the bathochromic shift.

In disbustituted benzenes,

(a) When electronically complementary groupssuch as —NH_2 and —NO_2 are substituted para to each other, there is a pronounced bathochromic shift in the main absorption and compared to the effect of either substituent considered separately. For example, *p*–nitroaniline absorbs at 375 mμ ε_{max} 16000. It is due to the extension of the chromophore from the electron donating group to the electron withdrawing group through the benzene ring.

(b) When the two groups in the *para* positions are not complimentary or are *ortho* or *meta* to each other, then the absorption spectrum is close to that of the separate non–interacting chromophores. For example, *m*–dinitrobenzene absorbs at 200 mμ ε_{max} 13000.

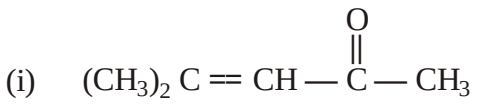
20.10 Applications of Ultra-violet Spectroscopy

Ultra–violet spectroscopy has been mainly applied for the detection of functional groups (chromophore), the extent of conjugation, detection of polynuclear compounds by comparison etc. Some important applications of ultraviolet spectroscopy are as follows:

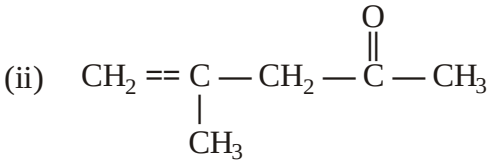
(a) Detection of functional groups. The technique is applied to detect the presence or absence of the chromophore. The absence of a band at a particular wavelength may be regarded as an evidence for the absence of a particular group in the compound. A little information can be drawn from the UV spectrum if the molecule is very complicated. If the spectrum is transparent above 200 m□, it shows the absence of (i) conjugation (ii) a carbonyl group (aldehydes and ketones) (iii) benzene or aromatic compounds and also (iv) bromo or iodo atoms. An isolated double bond or some other atoms or groups may be present. It means that no definite conclusions can be drawn if the molecule absorbs below 200 mμ.

(b) Extent of conjugation. The extent of conjugation in polyenes R—$(CH=CH)_n$—R can be estimated. Addition in unsaturation with the increase in the number of double bonds (increase in the value of *n*) shifts the absorption to longer wavelength. It is found that the absorption occurs in the visible region, *i.e*., at about 420 mμ, if *n* = 8 in the above polyene. Such an alkene appears coloured to the human eye.

(c) Distinction in conjugated and non-conjugated compounds. It also distinguishes between a conjugated and a non–conjugated compound. The following isomers can be readily distinguished since one is conjugated and the other is not.



(i) $(CH_3)_2 C == CH - \overset{\overset{O}{\|}}{C} - CH_3$



(ii) $CH_2 == \underset{\underset{CH_3}{|}}{C} - CH_2 - \overset{\overset{O}{\|}}{C} - CH_3$

The forbidden $n \rightarrow \pi^*$ band for the carbonyl group in the compound (*i*) will appear at longer wave–length compared to that for the compound (*ii*).

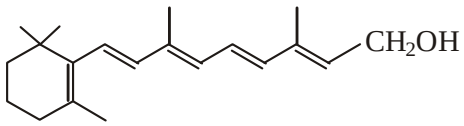
The alkyl substitution in an alkene causes a bathochromic shift. The technique is not much useful for the identification of individual alkenes.

(d) Identification of an unknown compound. An unknown compound can be identified by comparing its spectrum with the known spectra. If the two spectra coincide, the two compounds must be identical. If the two spectra do not coincide, then the expected structure is different from the known compound.

(e) Examination of Polynuclear hydrocarbons. Benzene and Polynuclear hydrocarbons have characteristic spectra in the ultra–violet and visiblez–region. Thus, the identification of the polynuclear hydrocarbons can be made by comparison with the spectra of known polynuclear compounds. The presence of substituents on the ring, generally,shifts the absorption maximum to longer wavelength.

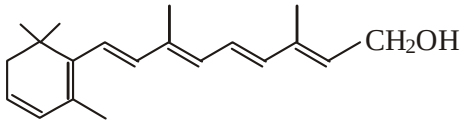
(f) Elucidation of the structure of vitamins A and K. It is useful for the elucidation of the structures of vitamins K_1 and K_2 and also those of A_1 and A_2. The ultraviolet spectra of vitamins K_1 and K_2 are due to the presence of the same chromophore, *i.e.*, 2,3 dimethyl maphtha–quinone. The absorption maxima of this compound are 243, 249, 260, 269 and 330 m□.

The elucidation of the structures of vitamins A_1 and A_2 are possible by this technique. Vitamin A_1 absorbs at 325 mμ and absorption maxima for Vitamin A_2 appear at 287 and 351 mμ. The absorption maxima appear at longer wavelength for vitamin A_2 due to the presence of additional ethylenic bond.



λ_{max} = 325 mμ

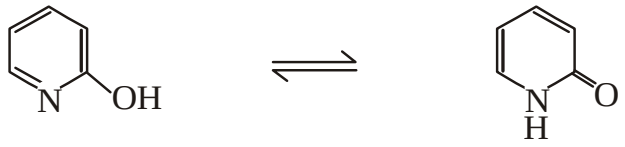
Vitamin A_1



λ_{max} = 287 mμ and 351 mμ

Vitamin A_2

(g) Preference over two Tautomeric forms. If a molecule exists in two tautomeric forms, preference of one over the other can be detected by ultra-violet spectroscopy. Consider 2–hydroxy pyridine which exists in equilibrium with its tautomeric form, pyridone–2.

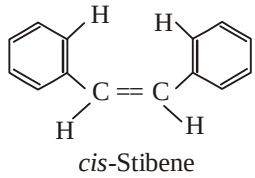


2 Hydroxy Pyridine Pyridone-2

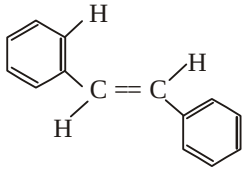
The spectra of these two compounds were found to favour pyridone–2 which is an □, □–unsaturated ketone and clearly, the equilibrium is shifted towards the right, *i.e*., Pyridone–2.

(h) Identification of a compound in different solvents. Sometimes, the structure of the compound changes with the change in the solvent. Chloral hydrate shows an absorption maximum at 290 m□ in hexane while the absorption disappears in the aqueous solution. Clearly, the compound contains a carbonyl group in hexane solution and its structure is $CCl_2.CHO.H_2O$ whereas in aqueous solution it is present as $CCl_3.CH(OH)_2$.

(i) Determination of configurations of geometrical isomers.



cis-Stibene λ_{max} = 283 mμ



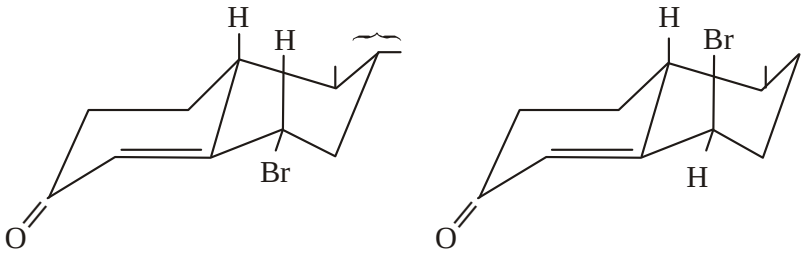
λ_{max} = 295.5 mμ

trans-Stibene

The results of absorption show that *cis*–alkenes absorb at different wavelengths as compared to their corresponding *trans* isomers. The distinction becomes possible

when one of the isomers is forced to be non–coplanar by steric hindrance. Thus, *cis* forms suffer distortion and absorption occurs at lower wavelength.

(j) Disteriguation between Equitorial and Axial Conformations. This technique also distinguishes between equitorial and axial conformations. Consider the following conformations.



The ($n \rightarrow \pi^*$) which appears at longer wavelength at α,β–unsaturated ketones is influenced by the presence of polar group in the g-position. It has been noted that the effect of an axial substituent to displace the R–band to longer wavelength is greater compared to that observed in its equitorial isomer.

(k) Determination of strength of hydrogen bond. Solvents like water, C_2H_5OH etc. form hydrogen bonds with the *n*–electrons of carbonyl oxygen. Due to this, the energy of *n*–electrons in the ground state is lowered depending upon the strength of hydrogen bonds. Thus, $n \rightarrow \pi^*$ transition of carbonyl compounds is shifted towards shorter wavelength. Hence, by measuring the $_{max}$ of a carbonyl compound in a non–polar and polar protic solvent, the strength of hydrogen bond can be determined. Consider $n \rightarrow \pi^*$ transition of acetone in hexane (at 279 nm) and that in water at 264.5 nm. The blue shift by 14.5 nm corresponds to an energy of 5 kcal mol^{-1}. Clearly, the strength of hydrogen bond between water and acetone is 5 kcal mol^{-1}. It is in fair agreement with the known strength of hydrogen bonds.

Measurement of Absorption Intensity

It may be noted that the intensity of absorption is directly proportional to the transition probability. An allowed transition will have ε_{max}value greater than 10000 while those having low transition probability will have its value less than 10000.

Selection Rules : The various electronic transitions which are governed by certain restrictions are called selection rules. These are:

(i) The transitions which involve a change in the spin quantum number of an electron during the transition do not occur. Thus, singlet–triplet transitions are forbidden.

(ii) The transitions between orbitals of different symmetry do not occur. For example, $n \rightarrow \pi^*$ transition is symmetry forbidden.

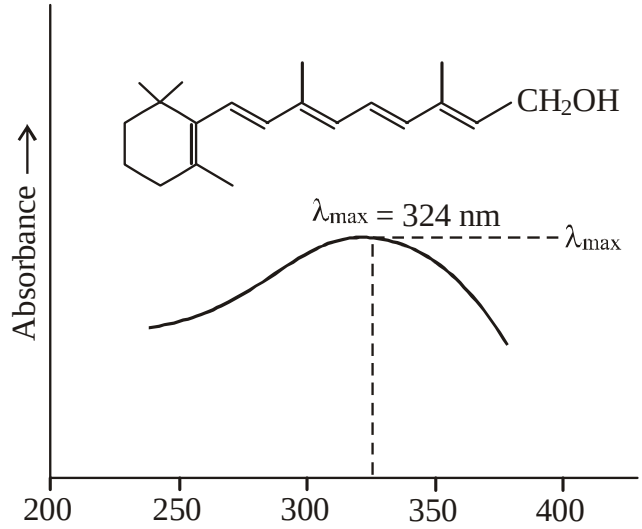


Figure 20.19 : ultra violet spectrum of vitamin A.

The wavelength of light corresponding to maximum absorption is written as e_{max} .It can be directly read from the horizontal axis as shown in Fig. 20.19 The Figure shows the ultraviolet spectrum of vitamin *A* with vertical line showing absorbance *A* which is equal to log I_0/I.

For vitamin A, the absorption maximum $(\lambda_{max})$is observed at 324 nm.

20.11 Instrumentation of Recording of Spectra

A spectrophotometer is a device which detects the percentage transmittance of light radiation when light of certain intensity and frequency range is passed through the sample. Thus, the instrument compares the intensity of the transmitted light with that of the incident light.

The modern ultra–violet-visible spectrometers consist of light source, monochromator, detector, amplifier and the recording devices. The most suitable sources of light are: **Tungsten Filament lamp and hydrogen-deuterium discharge lamp** which cover the whole of the UV–visible region. Tungsten filament lamp is particularly rich in red radiations *i.e.*, radiations with wavelength 375 mμ, while the deuterium discharge lamp covers the region below it. The intensity of the deuterium discharge source falls above 360 mμ, The single source is found satisfactory over the entire UV–VIS region. Ordinary spectrometers cover a range 220–800 mμ,. This spectroscopic technique is not useful below 200 mμ,. (inaccessible region) since oxygen absorbs strongly at 200 mμ,. and below. The region below 200 mμ,. is

called vacuum ultra–violet region. The low wavelength region can be extended upto 150 mμ, by flushing the instrument with nitrogen which absorbs below 150 mμ,. The various wavelengths of a light source are separated with a prism and then selected by slits such that the rotation of the prism causes a series of continuously increasing wavelengths to pass through the slits for recording purposes. The selected beam is monochromatic which is then divided into two beams of equal intensity. Dispersion grating can also be employed to obtain monochromatic beam of light from polychromatic radiation (UV–V/S radiation). As the dispersion of a single beam or grating is very small, it is not possible to isolate or collimate very narrow band widths. Thus, light from the first dispersion is passed through a slit and then sent to the second dispersion. After the second dispersion, light passes through the exit slit. The main advantage of the second dispersion is that the band width of the emergent light increases and the light passing through the exit slit is almost monochromatic. Also most of the stray light is suppressed.

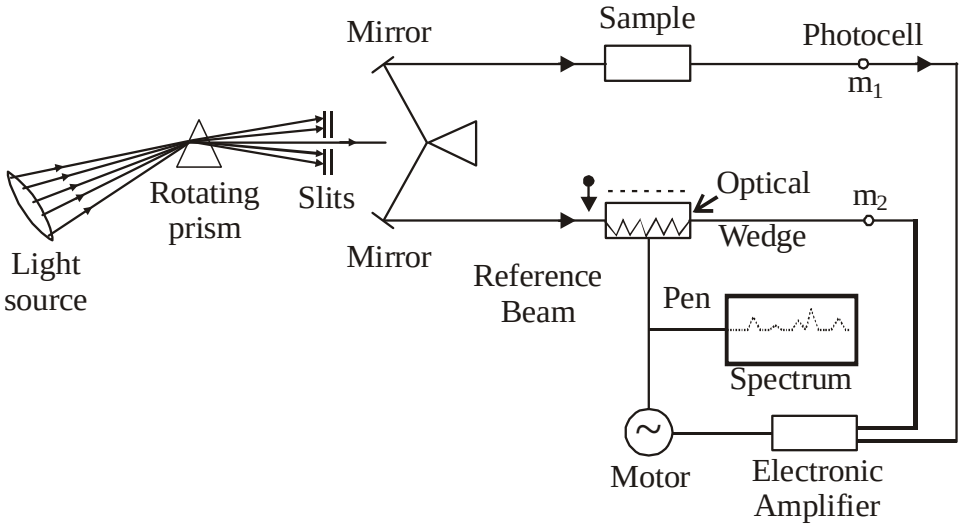


Fig. 20.20: Ultra-violet spectrophotometer.

One of the beam of selected monochromatic light (See Fig. 20.20) is passed through the sample solution and the other beam of equal intensity is passed through the reference solvent. The solvent as well as the solution of the sample may be contained in cells[1] made of a material which is transparent throughout the region under study. Glass cannot be used since it absorbs strongly in the ultra-violet region. Silica cells can be used. These must be properly stored and their optical surfaces should never be handled. Quartz cells also serve the purpose best. Glass can be used satisfactorily in the visible region. This type of spectrometer is called double beam spectrophotometer. Each absorbance measurement on the solution is accompanied by a simultaneous measurement on the pure solvent.

Usually, samples are scanned in dilute solutions. One mg of the compound under investigation (Molecular weight 100–200) is accurately weighed and dissolved in a suitable solvent to make the solution upto 100 ml volume. A little of this solution is taken in a silica cell. The thickness of the solution in the cell should be 1 cm. When the constitution of the absorbing material is unknown, the absorptivity may be sometimes expressed as $E^{1\%}_{1cm}$ Pure solvent is also taken in an exactly similar cell (Reference cell). These cells are then exposed to the monochromatic beams of equal intensity in the spectrometer. After the beams pass through the sample cell as well as the reference cell, the intensities of the respective transmitted beams are then compared over the whole wavelength range of the instrument. The spectrometer electronically subtracts the absorption of the solvent in the reference beam from the absorption of the solution. Hence, the effects due to the absorption of light by the solvent are minimised. In this way, the absorbance or the transmittance characteristic of the compound alone can be measured. The signal for the intensity of absorbance versus corresponding wavelength is automatically recorded on the graph. The spectrum is usually plotted as absorbance A ($\log_{10} I_o/I$) against wavelength $\log_{10} I_o/I$) (abcissa). The plot is often represented as ε_{max} (Extinction coefficient) against wavelength.

When the sample absorbs light, its intensity is lowered. Thus, the photoelectric cells P_1 and P_2 will receive an intense beam from the reference cell and a weak beam from the sample cell. This results in the generation of pulsating or alternating currents which flow from the photoelectric cells to the electronic amplifier. The amplifier is coupled to a small servomotor. which in turn, is coupled to a pen recorder. Thus, it records the absorption bands automatically. Actually, the amplifier is coupled to a small servomotor which drives an optical wedge into the reference beam until the photoelectric cell receives light of equal intensities from the sample as well as the reference beams.

20.12 Summary

In UV–vis spectroscopy UV radiation are used. Ultraviolet-visible (UV-vis) radiation has the property of being able to promote an electron to a higher energy level.The electron is promoted from the HOMO (highest occupied molecular orbital) to the LUMO (lowest unoccupied molecular orbital).This electronic transition occurs at a particular wavelength in the UV–vis region of the electromagnetic spectrum. At that wavelength, radiation is absorbed by the sample and this is detected by the spectrometer.The Beer–Lambert law is used to relate absorption of UV–vis radiation

to the concentration of the substance, the path length of the cell and the molar absorption coefficient. The molar absorption coefficient is a constant for every substance and is a measure of the amount of radiation absorbed per unit concentration of a substance.In this chapter various terms such as chromophore , Auxochrome, Bathochromic and Hypsochromic shift are discussed.It also discusses representation of UV spectrum.In the last effect of solvent on absorption band is discussed. Wood ward fisher rule are given for calculating the absorbance maximum in dienes , enones and aromatic compounds.

20.13 Review Questions

1. Explain the following terms :

(i) Chromophore

(ii) Auxochrome

(iii) Bathochromic schift

(iv) Hypsochromic schift

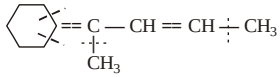
2. Discuss the effect of polar solvent on

(i) $\pi \rightarrow \pi^*$ (ii) $n \rightarrow \pi^*$

3. Explain woodward –Fieser's rule for conjugated dienes taking suitable examples.

4. Detail the chemistry of electronic spectroscopy . Give the various types of transitions in volved in this technique with one example in each case.

Example 1. Calculate the absorption maximum in the UV spectrum of



Solution: It is butadiene system. There are two alkyl substituents and two ring residues on the double bonds. Moreover, there is an exo-cyclic double bond.

The value of absorption maximum is calculated as follows:

Basic value	=	217 mm
2–alkyl substituents (2×5)	=	10 mm
2–Ring residues (2×5)	=	10 mm
1–Exocyclic double bond	=	5 mm

Calculated value = 242

The observed value is also found to be 242 mμ

20.14 Referrence Book

1. Morrison Boyd– Organic Reactions Mechanisms.
2. O.P. Agarwal– Reaction Mechanism.
3. Jerry March, Organic Chemistry.
4. Jagdamba Singh and LDS Yadav– Advanced Organic Chemistry.

Unit - 21 Vibrational Spectroscopy

Structure of Unit:

21.1 Objectives

At the end of the unit learner will be able to

- Understand about vibrational spectroscopy.
- Come to know with the details of IR spectroscopy.
- Different vibrational modes, frequencies.
- Know about important group frequencies and factors affecting them
- Be familiar about IR instrumentation and know how IR spectra of the samples are recoreded using IR spectrometer.

21.2 Introduction

The chapter deal with vibrational spectroscopy specially related to infrared spectroscopy, All molecules are constantly vibrating, and can absorb energy from an incoming photon to increase their vibrations. The two types of vibrational spectroscopy are Infrared spectroscopy and Raman spectroscopy. The main emphasis is given on Infrared spectroscopy. Infrared Spectroscopy is the analysis of infrared light interacting with a molecule. This can be analyzed in three ways by measuring absorption, emission and reflection. The main use of this technique is in organic and inorganic chemistry. It is used by chemists to determine functional groups in molecules. The chapter also highlights the factor affecting group frequencies, IR instrumentation and so on.

21.3 Vibrational Spectroscopy

All molecules are constantly vibrating, and can absorb energy from an incoming photon to increase their vibrations. The two types of vibrational spectroscopy are Infrared spectroscopy and Raman spectroscopy. Vibrational spectroscopy is the science of measuring exactly which wavelengths of light are absorbed by a molecule. This technique could be used identify an unknown molecule by comparing its absorption to that of other molecules. Or vibrational spectroscopy could be used to gain further understanding of the physical properties of a known molecule.

Introduction

Molecular vibration can be modeled by balls attached by springs. Displacing an atom from its most stable position requires energy proportional to the displacement. IR spectroscopy can be used to characterize a molecule is the energy of its vibrations falls in the infrared range. Alternatively, higher energy light can be absorbed, the re-emitted at a different wavelength and/or in a different direction; this leads to Raman spectroscopy. So a molecule can absorb radiation to change bond lengths or positions with respect to the other atoms in the molecule.[3]

From the number, frequency, and intensity of these absorptions or emissions we can gain insight into the composition of the sample being measured. The number of different absorptions is indicative of the number of different atoms and shape of the molecule. The frequency or wavelength absorbed is indicative of the energy of the bonds and vibrations. And the intensity of the absorptions is related to the concentration of the analyte.[1]

Vibrational Modes

The different possible vibrations are called vibrational modes. Vibrational modes are determined by all the different ways the atoms in the molecule can move with respect to eachother, called the vibrational degrees of freedom. Vibrational degrees of freedom differ from the total degrees of freedom in that translation (movement through space) and rotation do not contribute to the vibrational degrees of freedom.[4]

To find the number of vibrational modes one must first know the point group of the molecule. From there, the point group's character table will list all of the possible symmetry operations for the molecule. Each symmetry operation will leave some atoms in the molecule in place and/or move other atoms in the molecule. Count up the number of atoms that do not move for each symmetry operation, and multiply that number by the symmetry operation's contribution. This gives the total representation of atomic motion. From there, the vibrational modes can be found by reducing the total representation, according to the equation:

$$n=1/h*\Sigma X_R*X_I*N$$

where n is the number of modes with that symmetry, h is the total number of symmetry operations, X_I is the number of irreducible representations (the value calculated above), X_R is the number of reducible representations (the entry in the character table), and N is the number of identical symmetry operations. Finally, subtracting the rotational modes and translational modes from the reduced representation gives the number of vibrational modes.

Infrared Spectroscopy

A vibrational mode will be observed in an infrared spectrum if it leads to a change in the molecular dipole moment. Compared to Raman spectroscopy, the infrared photon is completely absorbed and its energy is transfered to the vibration of the molecule, not re-emitted. Different bonds have different energies associated with them, and require different amounts of energy to stretch or bend. In general, the stronger the bond, the more energy required to deform it. So very weak bonds will only be deformed by low energy radiation, and strong bonds will only be deformed by high energy radiation. This leads to characteristic frequencies where only certain vibrations are absorbed. For example, C-H bonds are typically the only bonds observed in the range from 2960-2850 cm^{-1}. So if an absorption is present at that frequency, it can be assumed that it is due to a C-H bond.

Infrared Spectroscopy is the analysis of infrared light interacting with a molecule. This can be analyzed in three ways by measuring absorption, emission and reflection. The main use of this technique is in organic and inorganic chemistry. It is used by

chemists to determine functional groups in molecules. IR Spectroscopy measures the vibrations of atoms, and based on this it is possible to determine the functional groups. Generally, stronger bonds and light atoms will vibrate at a high stretching frequency (wavenumber). The use of infrared spectroscopy began in the 1950's by Wilbur Kaye. He had designed a machine that tested the near-infrared spectrum and provided the theory to describe the results. Karl Norris started using IR Spectroscopy in the analytical world in the 1960's and as a result IR Spectroscopy became an accepted technique. There have been many advances in the field of IR Spec, the most notable was the application of Fourier Transformations to this technique thus creating an IR method that had higher resolution and a decrease in noise. The year this method became accepted in the field was in the late 1960's.

Theory

Infrared light imposed on a molecule will not create electronic transitions but it does contain enough energy to interact with a molecule causing vibrational and rotational changes. For example, the molecule can absorb the energy contained in the incident light and the result is a faster rotation or a more pronounced vibration. The possible rotations are around the axis of symmetry for a given molecule or either of the two perpendicular axis'. Vibrations can be in the form of a bend or a stretch for each bond. Illustrated below are possible vibrational motions for a three atom molecule (all are in the plane unless explicitly stated):

The set of equations below accounts for only one absorption but experimental studies found that there were multiple peaks for each individual molecule. Quantum Mechanics describes the different absorption maxima as J^{th} level vibrational states that account for these other frequencies observed. There are 3N-5 vibrational states for linear molecules and 3N-6 vibrational states for non-linear molecules where N is the number of atoms.

$F=-ky$

$$dE=-Fdy$$

$$\int_0^E dE = \int_0^y kydy$$

This equation describes the potential energy of the vibration

$$E=1/2ky^2$$

Because

$$F=ma$$

$$md^2y/dt^2 = -ky$$

This equation describes the periodic vibrational motion

$$y = A\cos(2\pi\nu_\mu t)$$

Where

μ= the reduced mass

$$d^2y/dt^2 = -4\pi^2\nu^2\mu A\cos(2\pi\nu_\mu t)$$

Therefore,

$$\nu\mu = 1/2\pi\sqrt{\frac{k}{\mu}}$$

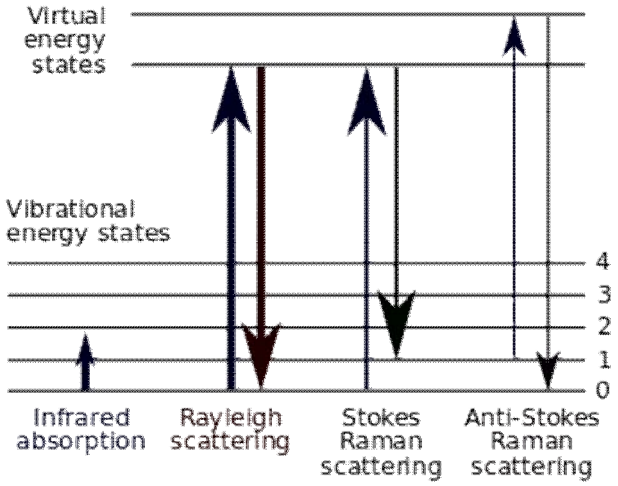
This is for the natural frequency of oscillation.

Instrumentation

The components of an IR machine are the IR source, beam splitter, monochromator, a transducer, an analog to digital converter and a digital machine to quantify the readout. The IR light exits the source and becomes split into to beams, one to be directed to the sample the other to a reference. The intensity of the beam is measured by the intensity emitted divided by the intensity observed, also known as the Transmittance. All frequencies are measured in wavenumber, cm^{-1}. To make a sample with a liquid, the liquid is placed between two pure salt sheets of NaCl and for a solid it is pressure pressed with KBr to incorporate both into one sheet. The reason for using salt to suspend the molecule is because the salt structures form a lattice that is strongly ionically bonded and will not absorb IR light because it lacks the vibrational capability. The Background scan or reference tends to be air.Below 1500 cm^{-1} the spectra have very high sensitivity and this region is known as the fingerprint region where C-C bond stretching and bending motions overlap, making it difficult to predict functional groups.[5] For more specific bond stretch frequencies

Raman Spectroscopy

A vibrational mode will be observed in Raman spectroscopy if it leads to a change in the polarizability of the electron cloud of a molecule.



If a photon has energy that is significantly higher than the energy of the vibrational states, it may either be deflected without any change in energy, or it may interact with the molecule and either take energy from it or give energy to it.

When the photon is absorbed and re-emitted in a different direction, it is called Rayleigh scattering, and this is strongly dependent on the wavelength of the incoming light. When there is a change in the energy of the photon, it is called Stokes scattering or anti-Stokes scattering, depending on whether energy is absorbed or lost by the molecule. This change in the behavior of the incoming photons can be measured, and will provide information about the concentration and chemical properties of the analyte.

21.4 Vibrational Transitions

When a molecule excited from ground state vibrational state to higher or vice versa molecule absorbs or emittes energies thus transition from one vibrational level to another is called vibrational transitions. It occures due to molecular vibrations.

One of the oldest forms of spectroscopy uses the infrared region of the electromagnetic spectrum. In order to understand IR spectroscopy, we must first consider the motion of atoms in molecules.

Atoms in a molecule do not maintain fixed positions with respect to each other, but actually vibrate back and forth about an average value of interatomic distance with a certain frequency. Think of a child on a swing. The frequency of the back and forth motion can be found by counting the number of swings in a minute. If the child is pushed on the swing when the frequency of pushing matches the frequency of the swinging the child swings higher (greater amplitude) but the frequency remains the same. Organic molecules absorb infrared radiation when the frequency of IR

radiation is synchronized with a natural vibration frequency of the molecule. When IR radiation is absorbed, the molecule begins to vibrate with a greater amplitude (but with the same frequency), and thus the molecule has gained energy.

A molecule can have the following types of motions: (1) translation of the entire molecule, which can be regarded as translation of the center of mass, (2) rotation of the molecule as a framework around its center of mass, (3) vibrations of the individual atoms within the framework, which occur in such a way that the center of mass does not change position and the framework does not rotate. The number of degrees of freedom of a particle equals the number of coordinates required to specify its position in space. A molecule has as many degrees of freedom as the total degrees of freedom of its individual atoms. Each atom has three degrees of freedom corresponding to the Cartesian coordinates (x,y,z) necessary to describe its position relative to other atoms in the molecule. For a molecule composed of n atoms there are 3n degrees of freedom associated with the momentum coordinates. For nonlinear molecules, three degrees of freedom describe rotation and three describe translation; the remaining 3n-6 degrees of freedom are vibrational degrees of freedom or fundamental vibrations. Linear molecules have 3n-5 vibrational degrees of freedom, for only two degrees of freedom are required to describe rotation. Fundamental vibrations involve no change in the center of mass of the molecule.

The ability of a compound to absorb IR energy depends on a net change in the dipole moment occurring when the molecule vibrates. Whether or not such a change occurs depends on the distribution of electrical charges in the molecule. The carbon monoxide molecule can be thought of as a carbon atom joined to an oxygen atom by means of a compressible bond. The carbon has six electrons surrounding its nucleus and oxygen has eight. During a vibration a change in the charge distribution occurs, this appears to the incident IR radiation as an oscillating charge. It is this oscillating charge that the light interacts with. When the frequency of the radiation matches the frequency of the oscillating charge the IR radiation is absorbed. Consequently, carbon monoxide shows an absorption band in the IR region at the frequency corresponding to the vibrational frequency of the nuclei. There is no net change in the dipole moment during the vibration of homonuclear molecules such as O_2, N_2, and H2, and these molecules do not absorb IR radiation. The ability of a molecule to absorb radiation during a particular vibration depends on its electrical geometry.

The water molecule consists of three atoms and is nonlinear; therefore, it should produce three fundamental vibrations. The three fundamental vibrations of the water molecule can be depicted as symmetrical stretching, asymmetrical stretching, and scissoring. The carbon dioxide molecule also consists of three atoms but is linear,

therefore, it has four fundamental vibrations: symmetrical stretching, asymmetrical stretching, scissoring in the x-y plane, and scissoring perpendicular to the x-y plane. The symmetrical stretching vibration in carbon dioxide is inactive in the infrared since it produces no change in the dipole moment of the molecule. The bending vibrations are equivalent, and are the resolved components of bending motion oriented at any angle to the internuclear axis; they have the same frequency and are said to be doubly degenerate. Some sets of vibrations are degenerate, they are identical in frequency but in perpendicular directions and these multiple vibrations only result in one infrared absorption band being seen in the spectrum. In addition, bands of low intensity may occur as overtones. As a result, the infrared spectrum of an organic compound is usually rather complex. Computer software like Mac Spartan or PC Spartan can be used to show the learners a model of the vibrations possible for a number of molecules.

The vibrational motion is quantized. At room temperature most of the molecules in a given sample will be in the lowest vibrational state. Absorption of light of the appropriate energy allows the molecule to become excited to a higher vibrational level. In general, such absorption of an infrared light quantum can occur only if the dipole moment of the molecule is different in the two vibrational levels. The variation of the dipole moment with the change in interatomic distance during the vibration corresponds to an oscillating electric field that can interact with the oscillating electric field associated with electromagnetic radiation. The requirement that absorption of a vibrational quantum be accompanied by a change in dipole moment is known as a selection rule. Such a vibrational transition is said to be infrared-active. Vibrational transitions that do not result in a change of dipole moment of the molecule during vibration are not observed directly and are referred to as infrared-inactive transitions. The greater the change in dipole moment the stronger the infrared absorption. This explains why the groups whose components differ considerably in electronegativity show stronger absorption bands.

There are two types of molecular vibrations: stretching and deformations. A stretching vibration is a rhythmical movement along the bond axis such that the interatomic distance is increasing or decreasing. A deformation may consist of a change in bond angle between bonds with a common atom (much like a pair of scissors opening and closing) or the movement of a group of atoms with respect to the remainder of the molecule without movement of the atoms in the group with respect to one another. For example, twisting, rocking, and torsional vibrations involve a change in bond angles with reference to a set of coordinates arbitrarily set up within the molecule.

Each of these vibrational modes has a natural frequency of motion. This natural frequency is determined by the mass of the atoms bonded and for stretching of a single bond the strength of the bond. The larger masses have a lower frequency and the stronger bonds have a higher frequency.

Molecular vibration

A **molecular vibration** occurs when atoms in a molecule are in periodic motion while the molecule as a whole has constant translational and rotational motion. The frequency of the periodic motion is known as a vibration frequency, and the typical frequencies of molecular vibrations range from less than 10^{12} to approximately 10^{14} Hz.

In general, a molecule with N atoms has $3N - 6$ normal modes of vibration, but a *linear* molecule has $3N - 5$ such modes, as rotation about its molecular axis cannot be observed. A diatomic molecule has one normal mode of vibration. The normal modes of vibration of polyatomic molecules are independent of each other but each normal mode will involve simultaneous vibrations of different parts of the molecule such as different chemical bonds.

A molecular vibration is excited when the molecule absorbs a quantum of energy, E, corresponding to the vibration's frequency, ν, according to the relation $E = h\nu$ (where h is Planck's constant). A fundamental vibration is excited when one such quantum of energy is absorbed by the molecule in its ground state. When two quanta are absorbed the first overtone is excited, and so on to higher overtones.

Vibrational excitation can occur in conjunction with electronic excitation (vibronic transition), giving vibrational fine structure to electronic transitions, particularly with molecules in the gas state.

Simultaneous excitation of a vibration and rotations gives rise to vibration-rotation spectra.

Vibrational coordinates

The coordinate of a normal vibration is a combination of changes in the positions of atoms in the molecule. When the vibration is excited the coordinate changes sinusoidally with a frequency ν, the frequency of the vibration.

Internal coordinates

Internal coordinates are of the following types-

- Stretching: a change in the length of a bond, such as C-H or C-C
- Bending: a change in the angle between two bonds, such as the HCH angle in a methylene group
- Rocking: a change in angle between a group of atoms, such as a methylene group and the rest of the molecule.
- Wagging: a change in angle between the plane of a group of atoms, such as a methylene group and a plane through the rest of the molecule,
- Twisting: a change in the angle between the planes of two groups of atoms, such as a change in the angle between the two methylene groups.
- Out-of-plane: a change in the angle between any one of the C-H bonds and the plane defined by the remaining atoms of the ethylene molecule. Another example is in BF_3 when the boron atom moves in and out of the plane of the three fluorine atoms.

In a rocking, wagging or twisting coordinate the bond lengths within the groups involved do not change. The angles do. Rocking is distinguished from wagging by the fact that the atoms in the group stay in the same plane.

In ethene there are 12 internal coordinates: 4 C-H stretching, 1 C-C stretching, 2 H-C-H bending, 2 CH_2 rocking, 2 CH_2 wagging, 1 twisting. Note that the H-C-C angles cannot be used as internal coordinates as the angles at each carbon atom cannot all increase at the same time.

Vibrations of a Methylene group (-CH_2-) in a molecule-

The atoms in a CH_2 group, commonly found in organic compounds, can vibrate in six different ways: **symmetric and asymmetric, stretching**, **scissoring**, **rocking**, **wagging** and **twisting**.

21.5 Important group frequencies, Factors affecting them

Group Frequencies

Detailed information about the infrared absorptions observed for various bonded atoms and groups is usually presented in tabular form. The following table provides a collection of such data for the most common functional groups. Following the color scheme of the chart, stretching absorptions are listed in the blue-shaded section and bending absorptions in the green shaded part. Since most organic compounds have C-H bonds, a useful rule is that absorption in the 2850 to 3000 cm^{-1} is due to sp^3 C-H

stretching; whereas, absorption above 3000 cm^{-1} is from sp^2 C-H stretching or sp C-H stretching if it is near 3300 cm^{-1}.

Typical Infrared Absorption Frequencies						
	Stretching Vibrations			**Bending Vibrations**		
Functional Class	**Range, cm^{-1}**	**Intensity**	**Assignment**	**Range (cm^{-1})**	**Intensity**	**Assignment**
Alkanes	2850-3000	str	CH_3, CH_2 & CH 2 or 3 bands	1350-1470 1370-1390 720-725	med med wk	CH_2 & CH_3 deformation CH_3 deformation CH_2 rocking
Alkenes	3020-3100 1630-1680 1900-2000	med var str	=C-H & $=CH_2$ (usually sharp) C=C (symmetry reduces intensity) C=C asymmetric stretch	880-995 780-850 675-730	str med med	=C-H & $=CH_2$ (out-of-plane bending) cis-RCH=CHR
Alkynes	3300 2100-2250	str var	C-H (usually sharp) C≡C (symmetry reduces intensity)	600-700	str	C-H deformation
Arenes	3030 1600 &	var med-wk	C-H (may be several	690-900	str-med	C-H bending &

	1500		bands) C=C (in ring) (2 bands) (3 if conjugated)			ring puckering
Alcohols & Phenols	3580-3650 3200-3550 970-1250	var str str	O-H (free), usually sharp O-H (H-bonded), usually broad C-O	1330-1430 650-770	med var-wk	O-H bending (in-plane) O-H bend (out-of-plane)
Amines	3400-3500 (dil. soln.) 3300-3400 (dil. soln.) 1000-1250	wk wk med	N-H (1°-amines), 2 bands N-H (2°-amines) C-N	1550-1650 660-900	med-str var	NH_2 scisso ring (1°-amines) NH_2 & N-H wagging (shifts on H-bonding)
Aldehydes & Ketones	2690-2840(2 bands) 1720-1740 1710-1720 1690 1675 1745 1780	med str str str str str str	C-H (aldehyde C-H) C=O (saturated aldehyde) C=O (saturated ketone) aryl ketone α, β-unsaturation cyclopentanone cyclobutanone	1350-1360 1400-1450 1100	str str med	α-CH_3 bending α-CH_2 bending C-C-C bending

Carboxylic Acids & Derivatives	2500-3300 (acids) overlap C-H 1705-1720 (acids) 1210-1320 (acids) 1785-1815 (acyl halides) 1750 & 1820 (anhydrides) 1040-1100 1735-1750 (esters) 1000-1300 1630-1695(amides)	str str med-str str str str str str str	O-H (very broad) C=O (H-bonded) O-C (sometimes 2-peaks) C=O C=O (2-bands) O-C C=O O-C (2-bands) C=O (amide I band)	1395-1440 1590-1650 1500-1560	med med med	C-O-H bending N-H (1¡-amide) II band N-H (2¡-amide) II band
Nitriles **Isocyanates,Isothiocyanates, Diimides, Azides & Ketenes**	2240-2260 2100-2270	med med	C≡N (sharp) -N=C=O, -N=C=S -N=C=N-, -N_3, C=C=O			

Factor affecting IR group frequencies: following factors affects the group frequencies-

- Reduced mass
- Vibrational coupling
- Fermiresonance
- Hydrogen bonding
- Electronic, resonance and inductive effect
- Bond angle
- Nature of solvent
- Interaction between solute and solvent
- Temperature
- Concentration of analyte

21.6 Applications of I.R. Instrumentation and recording of spectra

Applications and uses of I.R. Instrumentation

Infrared spectroscopy is widely used in both organic and inorganic chemistry, in research and industry. It is used in quality control, dynamic measurement, and monitoring applications such as the long-term unattended measurement of CO_2 concentrations in greenhouses and growth chambers by infrared gas analyzers.

It is also used in forensic analysis in both criminal and civil cases, for example in identifying polymer degradation. It can be used in detecting how much alcohol is in the blood of a suspected drunk driver.

A useful way of analysing solid samples without the need for cutting samples uses ATR or attenuated total reflectance spectroscopy. Using this approach, samples are pressed against the face of a single crystal. The infrared radiation passes through the crystal and only interacts with the sample at the interface between the two materials.

With increasing technology in computer filtering and manipulation of the results, samples in solution can now be measured accurately.

Some instruments will also automatically tell us what substance is being measured from a store of thousands of reference spectra held in storage.

IR spectroscopy is also useful in measuring the degree of polymerization in polymer manufacture. Changes in the character or quantity of a particular bond are

assessed by measuring at a specific frequency over time. Modern research instruments can take infrared measurements across the range of interest as frequently as 32 times a second. This can be done whilst simultaneous measurements are made using other techniques. This makes the observations of chemical reactions and processes quicker.

IR spectroscopy has also been successfully utilized in the field of semiconductor microelectronics: for example, infrared spectroscopy can be applied to semiconductors like silicon,gallium arsenide, gallium nitride, zinc selenide, amorphous silicon, silicon nitride, etc.

Recording of spectra

The infrared spectrum of a sample is recorded by passing a beam of infrared light through the sample. When the frequency of the IR is the same as the vibrational frequency of a bond, absorption occurs. Examination of the transmitted light reveals how much energy was absorbed at each frequency (or wavelength). This can be achieved by scanning the wavelength range using a monochromator. Now a days, the whole wavelength range is measured at once using a Fourier transform instrument and then a transmittance or absorbance spectrum is generated using a dedicated procedure. Analysis of the position, shape and intensity of peaks in this spectrum reveals details about the molecular structure of the sample.

This technique works almost exclusively on samples with covalent bonds. Simple spectra are obtained from samples with few IR active bonds and high levels of purity. More complex molecular structures lead to more absorption bands and more complex spectra.

Sample preparation

Gaseous samples require a sample cell with a long pathlength to compensate for the diluteness. The pathlength of the sample cell depends on the concentration of the compound of interest. A simple glass tube with length of 5 to 10 cm equipped with infrared windows at the both ends of the tube can be used for concentrations down to several hundred ppm. Sample gas concentrations well below ppm can be measured with a White's cell in which the infrared light is guided with mirrors to travel through the gas. White's cells are available with optical pathlength starting from 0.5 m up to hundred meters.

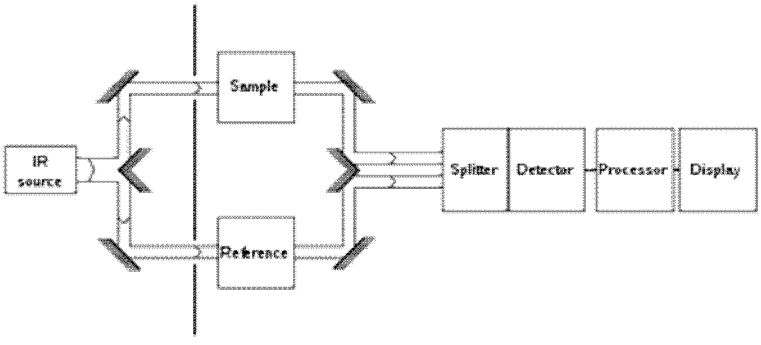
Liquid samples can be sandwiched between two plates of a salt (commonly sodium chloride, or common salt, although a number of other salts such as potassium bromide or calcium fluoride are also used). The plates are transparent to the infrared light and do not introduce any lines onto the spectra.

Solid samples can be prepared in a variety of ways. One common method is to crush the sample with an oily mulling agent (usually Nujol is used) in a marble or agate mortar, with a pestle. A thin film of the mull is smeared onto salt plates and measured. The second method is to grind a quantity of the sample with a specially purified salt (usually potassium bromide is used) finely (to remove scattering effects from large crystals). This powder mixture is then pressed in a mechanical press to form a translucent pellet through which the beam of the spectrometer can pass. A third technique is the "cast film" technique, which is used mainly for polymeric materials. The sample is first dissolved in a suitable, non hygroscopic solvent. A drop of this solution is deposited on surface of KBr or NaCl cell. The solution is then evaporated to dryness and the film formed on the cell is analysed directly. Care is important to ensure that the film is not too thick otherwise light cannot pass through. This technique is suitable for qualitative analysis. The final method is to use microtomy to cut a thin (20–100 μm) film from a solid sample. This is one of the most important ways of analysing failed plastic products for example because the integrity of the solid is preserved.

In photoacoustic spectroscopy the need for sample treatment is minimal. The sample, liquid or solid, is placed into the sample cup which is inserted into the photoacoustic cell which is then sealed for the measurement. The sample may be one solid piece, powder or basically in any form for the measurement. For example, a piece of rock can be inserted into the sample cup and the spectrum measured from it.

It is important to note that spectra obtained from different sample preparation methods will look slightly different from each other due to differences in the samples' physical states.

Comparing to a reference



Schematics of a two-beam absorption spectrometer.

To take the infrared spectrum of a sample, it is necessary to measure both the sample and a "reference" . This is because each measurement is affected by not only the

light-absorption properties of the sample, but also the properties of the instrument (for example, what light source is used, what infrared detector is used, etc.). The reference measurement makes it possible to eliminate the instrument influence. Mathematically, the sample transmission spectrum is divided by the reference transmission spectrum.

The appropriate "reference" depends on the measurement and its goal. The simplest reference measurement is to simply remove the sample (replacing it by air). However, sometimes a different reference is more useful. For example, if the sample is a dilute solute dissolved in water in a beaker, then a good reference measurement might be to measure pure water in the same beaker. Then the reference measurement would cancel out not only all the instrumental properties (like what light source is used), but also the light-absorbing and light-reflecting properties of the water and beaker, and the final result would just show the properties of the solute (at least approximately).

A common way to compare to a reference is sequentially: first measure the reference, then replace the reference by the sample and measure the sample. This technique is not perfectly reliable; if the infrared lamp is a bit brighter during the reference measurement, then a bit dimmer during the sample measurement, the measurement will be distorted. More elaborate methods, such as a "two-beam" setup, can correct for these types of effects to give very accurate results.

21.7 Summary

All molecules are constantly vibrating, and can absorb energy from an incoming photon to increase their vibrations. The two types of vibrational spectroscopy are infrared spectroscopy and Raman spectroscopy. The main emphasis is given on infrared spectroscopy. Infrared Spectroscopy is the analysis of infrared light interacting with a molecule. This can be analyzed in three ways by measuring absorption, emission and reflection. The main use of this technique is in organic and inorganic chemistry. It is used by chemists to determine functional groups in molecules. Important group frequencies are listed in the chapter, Vibrational coupling, Fermiresonance, Hydrogen bonding, Bond angle, Temperature etc are some factor which affects the group frequencies. Now a days double beam FTIR is used to analyze samples.

21.8 Review Question

1. What is vibrational spectroscopy?

2. Explain vibration ltransitions.
3. What is degree of freedom.
4. Write some important applications of IR spectroscopy.
5. How can we record a spectra in IR spectroscope?

21.9 Reference and Suggested readings

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Unit - 22 Nuclear Magnetic Resonance

Structure of Unit:

22.1 Objectives

At the end of the unit learner will be able to

- Familiar with nuclear magnetic resonance spectrometry.
- Learn the complex splitting pattern of various compound.
- Understand about NMR shift reagent and Deuterium labelling.
- Increase knowledge about integration, coupling constant nad chemical shift.

22.2 Introduction

Chapter deals with increasing the knowledge of learner for nuclear magnetic resonance and its integration, coupling constant and chemical shift. Chapter also explain brief about NMR shift reagent and Deuterium labelling in which a matter of recent research. Along with these chapter also highlights how to find the complex splitting pattern of various compound.

22.3 Definition

Nuclear magnetic resonance

Nuclear magnetic resonance (NMR) is a physical phenomenon in which nuclei in a magnetic field absorb and re-emit electromagnetic radiation. This energy is at a specific resonance frequency which depends on the strength of the magnetic field and the magnetic properties of the isotope of the atoms; in practical applications, the frequency is similar to VHF and UHF television broadcasts (60–1000 MHz). NMR allows the observation of specific quantum mechanical magnetic properties of the atomic nucleus. Many scientific techniques exploit NMR phenomena to study molecular physics, crystals, and non-crystalline materials through NMR spectroscopy. NMR is also routinely used in advanced medical imaging techniques, such as in magnetic resonance imaging (MRI).

All isotopes that contain an odd number of protons and/or of neutrons have an intrinsic magnetic moment and angular momentum, in other words a nonzero spin, while all nuclides with even numbers of both have a total spin of zero. The most commonly studied nuclei are 1H and 13C, although nuclei from isotopes of many other elements (e.g. 2H, 6Li, 10B, 11B, 14N, 15N, 17O, 19F, 23Na, 29Si, 31P, 35Cl, 113Cd, 129Xe, 195Pt) have been studied by high-field NMR spectroscopy as well.

A key feature of NMR is that the resonance frequency of a particular substance is directly proportional to the strength of the applied magnetic field. It is this feature that is exploited in imaging techniques; if a sample is placed in a non-uniform magnetic field then the resonance frequencies of the sample's nuclei depend on where in the field they are located. Since the resolution of the imaging technique depends on the magnitude of magnetic field gradient, many efforts are made to develop increased field strength, often using superconductors. The effectiveness of NMR can also be improved using hyperpolarization, and/or using two-dimensional, three-dimensional and higher-dimensional multi-frequency techniques.

The principle of NMR usually involves two sequential steps:

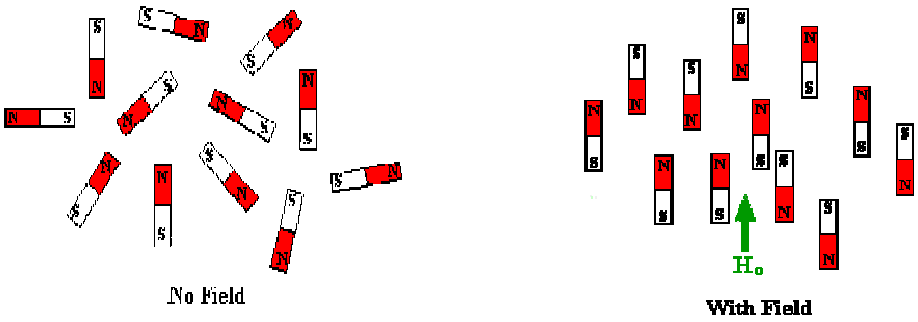
- The alignment (polarization) of the magnetic nuclear spins in an applied, constant magnetic field H0.

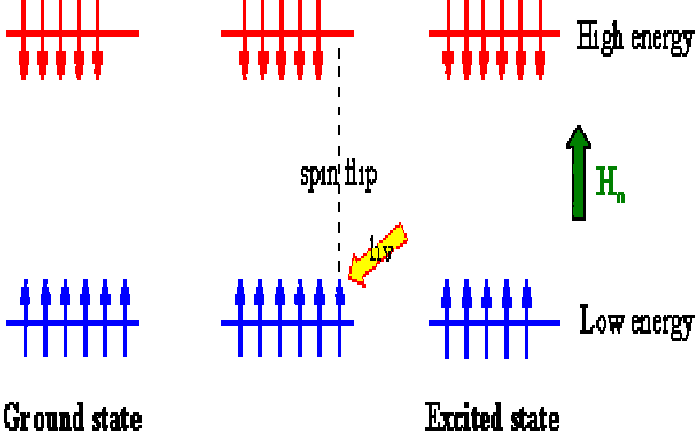
- The perturbation of this alignment of the nuclear spins by employing an electro-magnetic, usually radio frequency (RF) pulse. The required perturbing frequency is dependent upon the static magnetic field (H0) and the nuclei of observation.

  The two fields are usually chosen to be perpendicular to each other as this maximizes the NMR signal strength. The resulting response by the total magnetization (M) of the nuclear spins is the phenomenon that is exploited in NMR spectroscopy and magnetic resonance imaging. Both use intense applied magnetic fields (H0) in order to achieve dispersion and very high stability to deliver spectral resolution, the details of which are described by chemical shifts, the Zeeman effect, and Knight shifts (in metals).NMR phenomena are also utilized in low-field NMR, NMR spectroscopy and MRI in the Earth's magnetic field (referred to as Earth's field NMR), and in several types of magnetometers.

  Nuclei with an odd mass or odd atomic number have "nuclear spin" (in a similar fashion to the spin ofs electrons). This includes 1H and 13C (but not 12C). The spins of nuclei are sufficiently different that NMR experiments can be sensitive for only one particular isotope of one particular element. Since a nucleus is a charged particle in motion, it will develop a magnetic field. 1H and 13C have nuclear spins of 1/2 and so they behave in a similar fashion to a simple, tiny bar magnet.

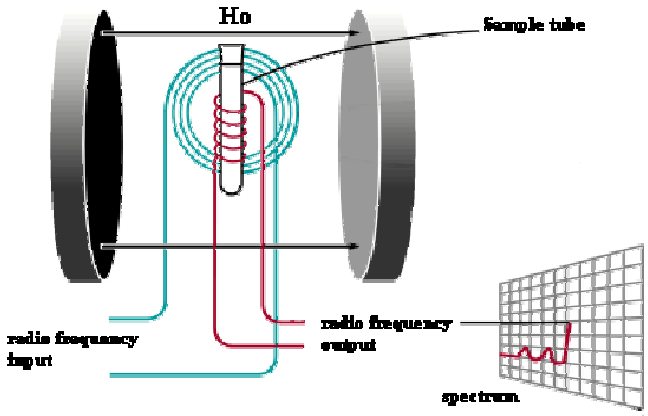
  In the absence of a magnetic field, these are randomly oriented but when a field is applied they line up parallel to the applied field, either spin aligned or spin opposed. The more highly populated state is the lower energy spin aligned situation. Two schematic representations of these arrangements are shown below:





In NMR, EM radiation is used to "flip" the alignment of nuclear spins from the low energy spin aligned state to the higher energy spin opposed state. The energy required for this transition depends on the strength of the applied magnetic field (see below) but it is small and corresponds to the radio frequency range of the EM spectrum.

As this diagram shows, the energy required for the spin-flip depends on the magnetic field strength at the nucleus. With no applied field, there is no energy difference between the spin states, but as the field increases so does the separation of energies of the spin states and therefore so does the frequency required to cause the spin-flip, referred to as resonance.



The basic arrangement of an NMR spectrometer is shown to the left. The sample is positioned in the magnetic field and excited via pulsations in the radio frequency input circuit. The realigned magnetic fields induce a radio signal in the output circuit which is used to generate the output signal. Fourier analysis of the complex output produces the actual spectrum.The pulse is repeated as many times as necessary to allow the signals to be identified from the background noise

22.4 Integration in NMR

The intensity of the signal is proportional to the number of hydrogens that make the signal. Sometimes, NMR machines display signal intensity as an automatic display above the regular spectrum. (The exact number of hydrogens giving rise to each signal is sometimes also explicitly written above each peak, making our job a lot easier.) The intensity of the signal allows us to conclude that the more hydrogens there are in the same chemical environment, the more intense the signal will be.

Introduction

We can get the following information from a ^{1}H Nuclear Magnetic Resonance (NMR) structure:

1. **The number of signals** gives the number of non-equivalent hydrogens
2. **Chemical shifts** show differences in the hydrogens' chemical environments
3. **Splitting** presents the number of neighboring hydrogens (N+1 rule)
4. **Integration** gives the relative number of hydrogens present at each signal

The integrated intensity of a signal in a ^{1}H NMR spectrum (does not apply to ^{13}C NMR) gives a ratio for the number of hydrogens that give rise to the signal, thereby helping calculate the total number of hydrogens present in a sample.NMR machines can be used to measure than signal intensity, a plot of which is sometimes automatically displayed above the regular spectrum. To show these integrations, a recorder pen marks a vertical line with a length that is proportional to the integrated area under a signal (sometimes referred to as a peak)-- a value that is proportional to the number of hydrogens that are accountable for the signal. The pen then moves horizontally until another signal is reached, at which point, another vertical marking is made. We can manually measure the lengths by which the horizontal line is displaced at each peak to attain a ratio of hydrogens from the various signals. We can use this technique to figure out the hydrogen ratio when the number of hydrogens responsible for each signal is not written directly above the peak.

Now that we've seen how the signal intensity is directly proportionate to the number of hydrogens that give rise to that signal, it makes sense to conclude that the more

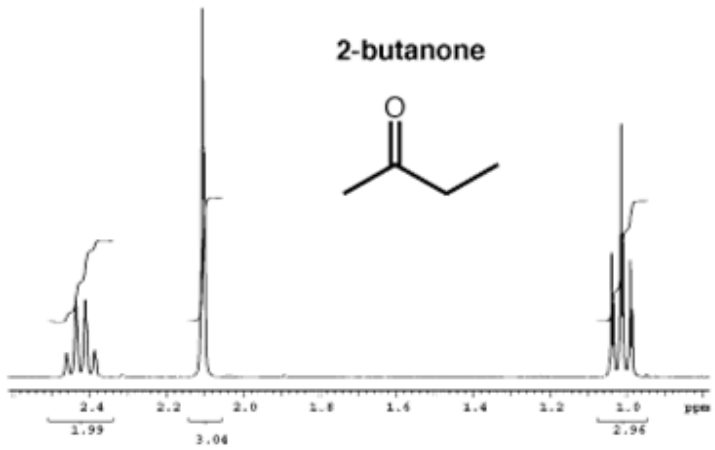
hydrogens of one kind there are in a molecule (equivalent hydrogens, so in the same chemical environment), the more intense the corresponding NMR signal will be.

Integration of ^{1}H NMR spectra

The area under each pattern is obtained from integration of the signal (or better the function that defines the signal) and is proportional to the number of hydrogen nuclei whose resonance is giving rise to the pattern. The integration is sometimes shown as a step function on top of the peak with the height of the step function proportional to the area. The integration of the patterns at δ1.1, 2.4, and 3.7 ppm for methyl propanoate is approximately 3:2:3. Note, the error in integration can be as high as 10% and depends upon instrument optimization. The integration of an ^{1}H NMR spectrum gives a measure of the proton count adjusted for the molecular symmetry. Methyl propanoate has no relevant molecular symmetry and so, the integration gives the actual proton count: 3+2+3=8 protons. In contrast diethyl ether (Et-OEt) has a plane of symmetry which makes the two ethyl groups equivalent, and so, only two signal are observed, a triplet and a quartet, with integration 3:2.

The areas represented by the integration step function is usually integrated by the instrument and displayed as numerical values under the δscale. For instance, the normalized integration values for 2-butanone are shown in Figure. Note that these values are not exact integers and need to be rounded to the nearest integer to obtain the proper value.

Integration values for the ^{1}H NMR spectrum of 2-butanone.



22.5 Chemical shift

In nuclear magnetic resonance (NMR) spectroscopy, the **chemical shift** is the resonant frequency of a nucleus relative to a standard. Often the position and number

of chemical shifts are diagnostic of the structure of a molecule Chemical shifts are also used to describe signals in other forms of spectroscopy such as photoemission spectroscopy.

Some atomic nuclei possess a magnetic moment (nuclear spin), which gives rise to different energy levels and resonance frequencies in a magnetic field. The total magnetic field experienced by a nucleus includes local magnetic fields induced by currents of electrons in the molecular orbitals (note that electrons have a magnetic moment themselves). The electron distribution of the same type of nucleus (e.g. ^{1}H, ^{13}C, ^{15}N) usually varies according to the local geometry (binding partners, bond lengths, angles between bonds, ...), and with it the local magnetic field at each nucleus. This is reflected in the spin energy levels (and resonance frequencies). The variations of nuclear magnetic resonance frequencies of the same kind of nucleus,due to variations in the electron distribution, is called the chemical shift. The size of the chemical shift is given with respect to a reference frequency or reference sample usually a molecule with a barely distorted electron distribution.

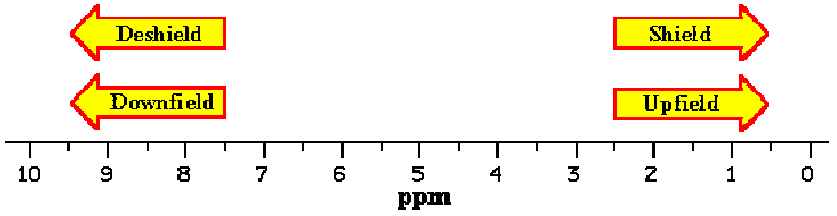
22.4 Chemical shift

Chemical Shift

- An NMR spectrum is a plot of the radio frequency applied against absorption.
- A signal in the spectrum is referred to as a resonance.
- The frequency of a signal is known as its chemical shift.

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

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



It is often convenient to describe the relative positions of the resonances in an NMR spectrum. For example, a peak at a chemical shift, d, of 10 ppm is said to be **downfield** or **deshielded** with respect to a peak at 5 ppm, or if you prefer, the peak at 5 ppm is **upfield** or **shielded** with respect to the peak at 10 ppm.

Typically for a field strength of 4.7T the resonance frequency of a proton will occur around 200MHz and for a carbon, around 50.4MHz. The reference compound is the same for both, tetramethysilane ($Si(CH_3)_4$).

Shielding in H-NMR

The magnetic field experienced by a proton is influenced by various structural factors.

Since the magnetic field strength dictates the energy separation of the spin states and hence the radio frequency of the resonance, the structural factors mean that different types of proton will occur at different chemical shifts. This is what makes NMR so useful for structure determination, otherwise all protons would have the same chemical shift.

Operating frequency

The operating (or Larmor) frequency ω_0 of a magnet is calculated from the Larmor equation

$$\omega_0 = \gamma B_0$$

where B_0 is the actual strength of the magnet in units like teslas or gauss, and γ is the gyromagnetic ratio of the nucleus being tested which is in turn calculated from its magnetic momeZt μ and spin number I with the nuclear magneton μ_N and the Planck constant h:

$$\gamma = \frac{\mu\,\mu_N}{hI}$$

Thus, the proton operating frequency for a 1 T magnet is calculated as:

$$\omega_0 = \gamma B_0 = \frac{2.79 \times 5.05 \times 10^{-27}\,\mathrm{J/T}}{6.62 \times 10^{-34}\,\mathrm{Js} \times (1/2)} \times 1\,\mathrm{T} = 42.5\,\mathrm{MHz}$$

Chemical shift referencing

Chemical shift δ is usually expressed in parts per million (ppm) by frequency, because it is calculated from:

$$\delta = \frac{\text{difference between a resonance frequency and that of a reference substance}}{\text{operating frequency of the spectrometer}}$$

Since the numerator is usually in hertz, and the denominator in megahertz, delta is expressed in ppm.

The detected frequencies (in Hz) for ^{1}H, ^{13}C, and ^{29}Si nuclei are usually referenced against TMS (tetramethylsilane) or DSS, which is assigned the chemical shift of zero. Other standard materials are used for setting the chemical shift for other nuclei.

Thus, an NMR signal that absorbs at 300 Hz higher than does TMS at an applied frequency of 300 MHz has a chemical shift of:

$$\frac{300\,\mathrm{Hz}}{300 \times 10^{6}\,\mathrm{Hz}} = 1 \times 10^{-6} = 1\,\mathrm{ppm}$$

Although the frequency depends on the applied field, the chemical shift is independent of it. On the other hand the resolution of NMR will increase with applied magnetic field resulting in ever increasing chemical shift changes.

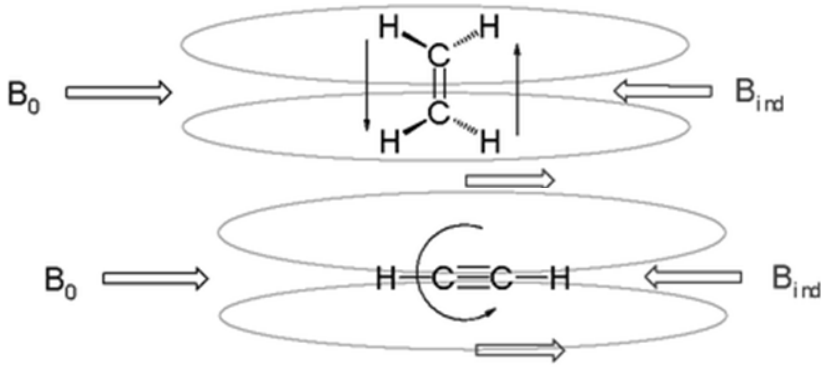
22.6 Factors causing chemical shifts

Important factors influencing chemical shift are electron density, electronegativity of neighboring groups and anisotropic induced magnetic field effects.

Electron density shields a nucleus from the external field. For example in proton NMR the electron-poor tropylium ion has its protons downfield at 9.17 ppm, those of the electron-rich cyclooctatetraenyl anion move upfield to 6.75 ppm and its dianion even more upfield to 5.56 ppm.

A nucleus in the vicinity of an electronegative atom experiences reduced electron density and the nucleus is therefore deshielded. In proton NMR of methyl halides (CH_3X) the chemical shift of the methyl protons increase in the order I < Br < Cl < F from 2.16 ppm to 4.26 ppm reflecting this trend. In carbon NMR the chemical shift of the carbon nuclei increase in the same order from around –10 ppm to 70 ppm. Also when the electronegative atom is removed further away the effect diminishes until it can be observed no longer.

Anisotropic induced magnetic field effects are the result of a local induced magnetic field experienced by a nucleus resulting from circulating electrons that can either be paramagnetic when it is parallel to the applied field or diamagnetic when it is opposed to it. It is observed in alkenes where the double bond is oriented perpendicular to the external field with pi electrons likewise circulating at right angles. The induced magnetic field lines are parallel to the external field at the location of the alkene protons which therefore shift downfield to a 4.5 ppm to 7.5 ppm range. The three-dimensional space where a nucleus experiences diamagnetic



shift is called the shielding zone with a cone-like shape aligned with the external field.The protons in aromatic compounds are shifted downfield even further with a signal for benzene at 7.73 ppm as a consequence of a diamagnetic ring current.

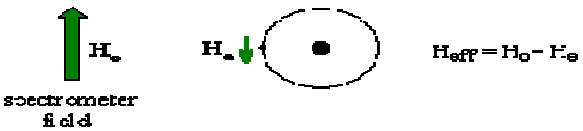
Alkyne protons by contrast resonate at high field in a 2–3 ppm range. For alkynes the most effective orientation is the external field in parallel with electrons circulation around the triple bond. In this way the acetylenic protons are located in the cone-shaped shielding zone hence the upfield shift.

The various factors include:

- inductive effects by electronegative groups
- magnetic anisotropy
- hydrogen bonding

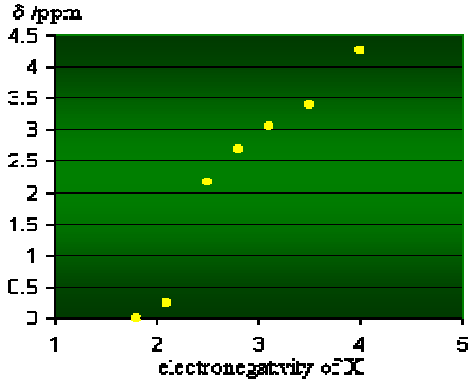
Electronegativity

The electrons around the proton create a magnetic field that **opposes** the applied field. Since this **reduces** the field experienced at the nucleus, the electrons are said to ***shield*** the proton. It can be useful to think of this in terms of vectors....



Since the field experienced by the proton defines the energy difference between the two spin states, the frequency and hence the chemical shift, □ /ppm, will change depending on the electron density around the proton. Electronegative groups attached

to the C-H system decrease the electron density around the protons, and there is less shielding (*i.e.*deshielding) so the chemical shift increases. This is reflected by the plot shown in the graph to the left which is based on the data shown below.



Compound, CH3X	CH_3F	CH_3OH	CH_3Cl	CH_3Br	CH_3I	CH_4	$(CH_3)_4Si$
X	F	O	Cl	Br	I	H	Si
Electronegativity of X	4.0	3.5	3.1	2.8	2.5	2.1	1.8
Chemical shift, /□ ppm	4.26	3.4	3.05	2.68	2.16	0.23	0

Magnetic Anisotropy

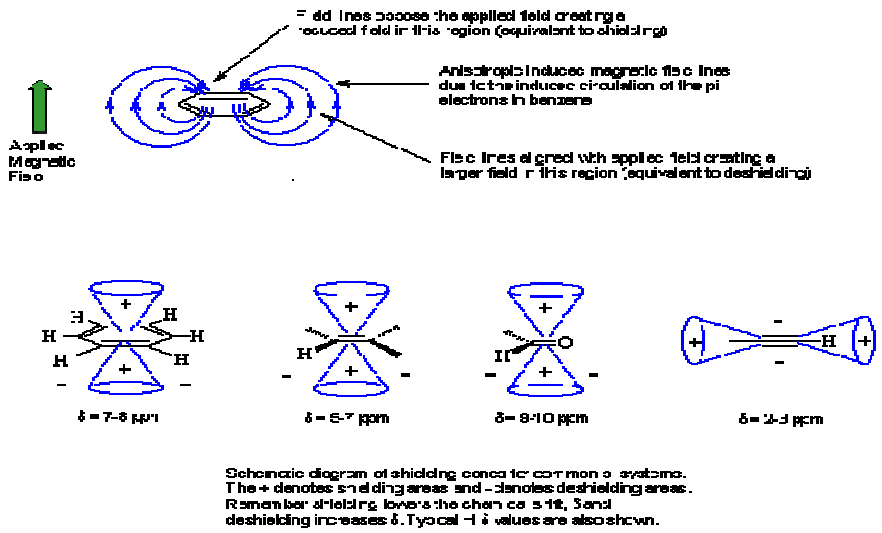
The word "anisotropic" means "non-uniform". Magnetic anisotropy means that there is a "non-uniform magnetic field". Electrons in p systems (*e.g.* aromatics, alkenes, alkynes, carbonyls *etc*.) interact with the applied field which induces a magnetic field that causes the anisotropy. As a result, the nearby protons will experience 3 fields: the applied field, the shielding field of the valence electrons and the field due to the system. Depending on the position of the proton in this third field, it can be either shielded (smaller) or deshielded (larger), which implies that the energy required for, and the frequency of the absorption will change.

These effects are cumulative, so the presence of more electronegative groups produce more deshielding and therefore, larger chemical shifts.

Compound CH_4 CH_3Cl CH_2Cl_2 $CHCl_3$

Sppm 0.23 3.05 5.30 7.27

These inductive effects at not just felt by the immediately adjacent protons as the disruption of electron density has an influence further down the chain. However, the effect does fade rapidly as you move away from the electronegative group. As an example, look at the chemical shifts for part of a primary bromide	**H signal** $-CH_2-$ CH_2- CH_2Br □**/ ppm** 1.25 1.69 3.30



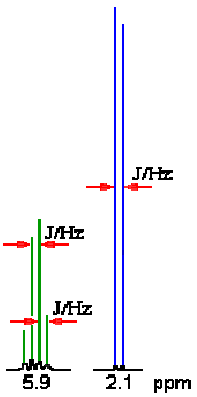
Schematic diagram of shielding cones for common systems. The + denotes shielding areas and - denotes deshielding areas. Remember shielding lowers the chemical shift, δ, and deshielding increases δ. Typical H δ values are also shown.

Hydrogen Bonding

Protons that are involved in hydrogen bonding (this usually means **-OH** or **-NH**) are typically observed over a large range of chemical shift values. The more hydrogen bonding there is, the more the proton is deshielded and the higher its chemical shift will be. However, since the amount of hydrogen bonding is susceptible to factors such as solvation, acidity, concentration and temperature, it can often be difficult to predict.

Experimentally, **-OH** and **-NH** protons can be identified by carrying out a simple **D_2O** (deuterium oxide, also known as heavy water) exchange experiment.

- Run the regular H-NMR experiment
- Add a few drops of D_2O
- Re-run H-NMR experiment
- Compare the two spectra a look for peaks that have "disappeared"



n = 0				1			singlet
n = 1			1		1		doublet
n = 2		1		2		1	triplet
n = 3	1		3		3	1	quartet
n = 4	1	4		6	4	1	quintet
n = 5	1	5	10		10	5	1 sextet

22.7 Coupling Constant

The coupling constant, J (usually in frequency units, Hz) is a measure of the interaction between a pair of protons. In a vicinal system of the general type, $\mathbf{H_a}$-C-C-$\mathbf{H_b}$then the coupling of $\mathbf{H_a}$ with $\mathbf{H_b}$, J_{ab}, must be equal to the coupling of $\mathbf{H_b}$ with $\mathbf{H_a}$, J_{ba}, therefore $J_{ab} = J_{ba}$. The implications are that the spacing between the lines in the coupling patterns are the same as can be seen in the coupling patterns from the H-NMR spectra of 1,1-dichloroethane.

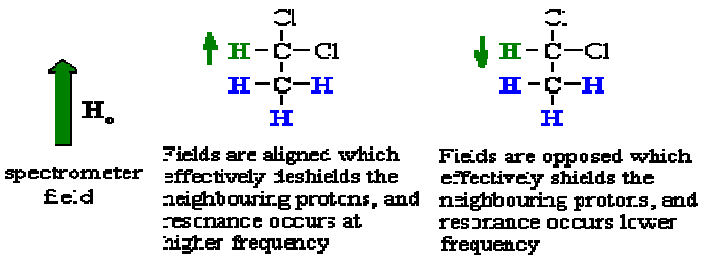
Pascal's Triangle

The relative intensitites of the lines in a coupling pattern is given by a binomial expansion or more conviently by Pascal's triangle.
To derive Pascal's triangle, start at the apex, and generate each lower row by creating each number by adding the two numbers above and to either side in the row above together. The first six rows are shown to the right.
So for H-NMR a proton with zero neighbours, n = 0, appears as a single line, a proton with one neighbors, n =1 as two lines of equal intensity, a proton with two neighbours, n = 2, as three lines of intensities 1 : 2 : 1, etc.

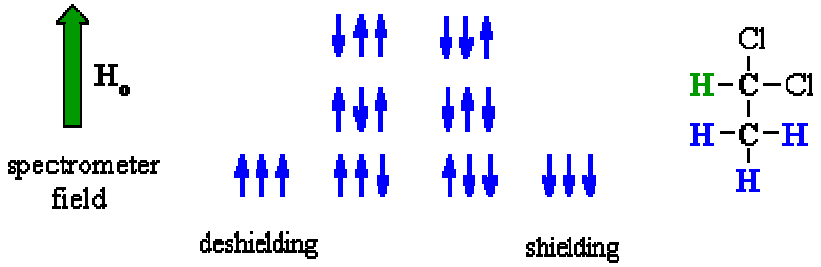
Complex Coupling Patterns

In reality, coupling patterns are often more complex than the simple n+1 rule since the neighbouring protons are often not equivlalent to each other (*i.e.* there are different types of neighbours) and therefore couple differently. In these cases, the "n+1" rule has to be refined so that each type of neighbour causes n+1 lines. For example for a proton with two types of neighbor, number of lines, $L = (n_1 + 1)(n_2 + 1)$.

Coupling arises because the magnetic field of vicinal (adjacent) protons influences the field that the proton experiences. To understand the implications of this we should first consider the effect the -**CH** group has on the adjacent -$\mathbf{CH_3}$.



Now consider the effect of the -**CH$_3$** group has on the adjacent -**CH** .



The methane -**CH** can adopt two alignments with respect to the applied field. As a result, the signal for the adjacent methyl -**CH$_3$** is split in two lines, of equal intensity, a **doublet**.

The methyl -**CH$_3$** protons give rise to 8 possible combinations with respect to the applied field. However, some combinations are equivalent and there are four magnetically different effects. As a result, the signal for the adjacent methane -**CH** is split into four lines, of intensity ratio 1:3:3:1, a **quartet**.

- The proximity of "n" equivalent H on neighbouring carbon atoms, causes the signals to be split into "n+1" lines.
- This is known as the multiplicity or splitting or coupling pattern of each signal.
- Equivalent protons (or those with the same chemical shift) do not couple to each other.
- If the neighbours are not all equivalent, more complex patterns arise.
- To a first approximation, protons on adjacent sp^3 C tend to behave as if they are equivalent.

Now we can do a more complete analysis, including the application of the "n+1" rule to 1,1-dichloroethane:

- □ = 5.9 ppm, quartet, integration = 1H, deshielded
- agrees with the -**CHCl$_2$** unit next to a -**CH$_3$** unit (n = 3, so n + 1 = 4 lines)
- □ = 2.1 ppm, doublet, integration = 3H
- agrees with -**CH$_3$** unit, next to a **-CH-** (n = 1, so n + 1 = 2 lines)

An example of an H NMR is shown below.

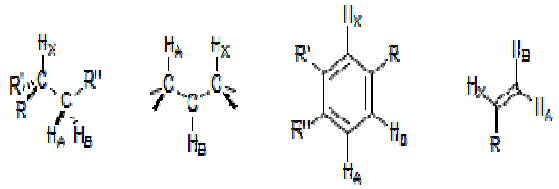
Based on the outline given above the four sets of information we get are:

5 basic types of H present in the ratio of 5 : 2 : 2 : 2 : 3. These are seen as a 5H "singlet" (ArH), two 2H triplets, a 2H quartet and a 3H triplet. Each triplet tells us that there are 2H in the adjacent position, and a quartet tells us that there are 3H adjacent. (Think of it as the lines you see, L = n + 1, where n = number of equivalent adjacent H)
This tells us we that the peaks at 4.4 and 2.8 ppm must be connected as a CH_2CH_2 unit.
The peaks at 2.1 and 0.9 ppm as a CH_2CH_3 unit. Using the chemical shift charts, the H can be assigned to the peaks as below:

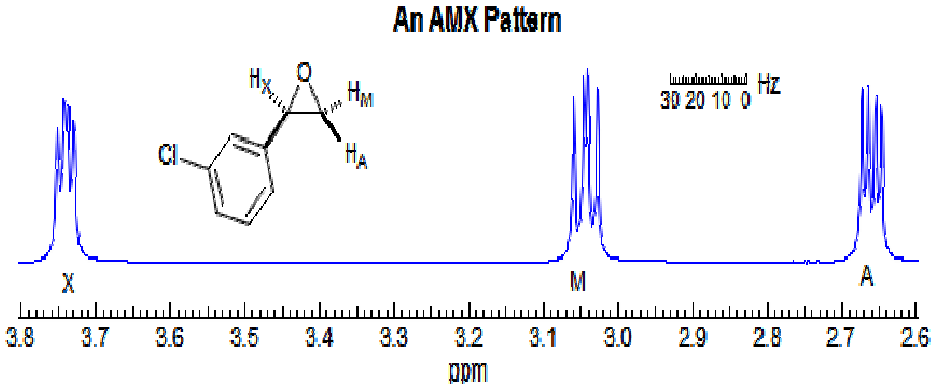
7.2ppm (5H) = Ar**H** ;
4.4ppm (2H) = C$\mathbf{H}_2$O;
2.8ppm (2H) = Ar-C$\mathbf{H}_2$;
2.1ppm (2H) = O=CC$\mathbf{H}_2$$CH_3$ and
0.9ppm (3H) = CH_2C$\mathbf{H}_3$

22.8 Complex Splitting Pattern

AMX, ABX and ABC patterns, and various related spin systems which are very common in organic molecules. some of the structural types which give ABX patterns are given below:

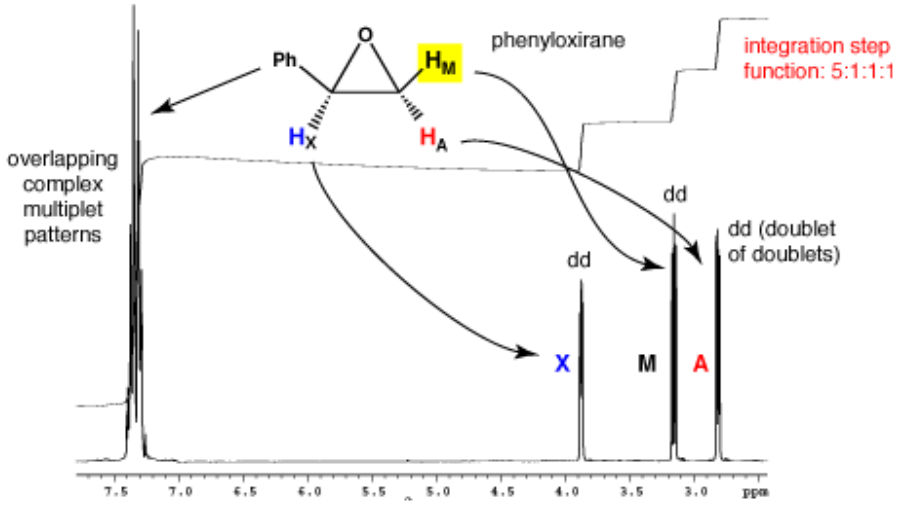


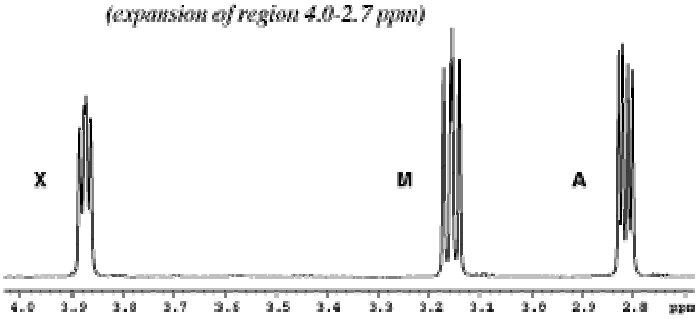
AMX Patterns. Three nuclei coupled to each other and separated by a large chemical shifts compared to the coupling between them can be analyzed in first order fashion: the **A**, **M** and **X** signals are each a doublet of doublets, and the couplings can be extracted by inspection.



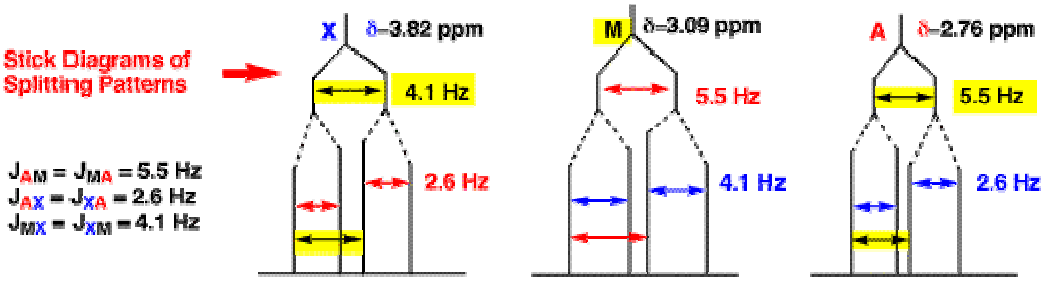
^{1}H NMR patterns are more complex than predicted by the N+1 coupling rule when coupling of one proton or set of equivalent protons occurs to two different sets of protons with different size coupling constants or when coupling occurs between protons with similar but not identical chemical shifts. The former situation can still be analyzed in terms of overlapping N+1 patterns using stick diagrams. This is shown for the spectrum of phenyloxirane which has three oxirane protons of different chemical shift all coupled to each other. The protons are labeled $\mathbf{H_A}$, $\mathbf{H_M}$, and $\mathbf{H_X}$ to reflect that they are not close to each other in chemical shift. Each resonance appears as a doublet of doublets, and the overall pattern of three doublets of doublets is called an **AMX** pattern.

^{1}H NMR spectrum of phenyloxirane showing the AMX pattern of three doublets of doublets.



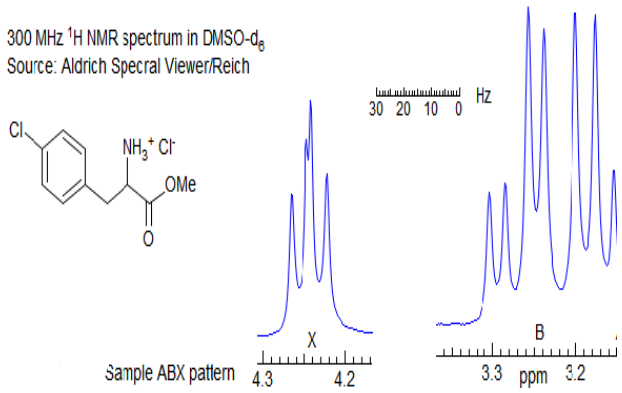


The situation of protons with close chemical shifts coupled to each other is more complex. If only two protons are coupled to each other, the pattern still appears as two doublets but the intensities are no longer 1:1 and the chemical shifts are not the centers of the doublets; the separation between the lines of each doublet is still the coupling constant J.

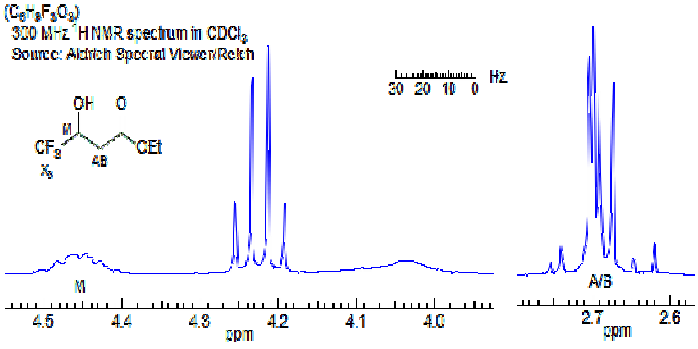


ABX Patterns. When two of the protons of an AMX pattern approach each other to form an ABX pattern, the characteristic changes in intensities of a strongly coupled system (leaning) are seen, and, as the size of *J* approaches the value of ν_{AB} more

complicated changes arise, so that the pattern can no longer be analyzed correctly by first order methods. A typical ABX spectrum is shown below:



For this spectrum ν_{AB} is less than twice J, and a first order (AMX-type) interpretation starts to become imprecise, although, in this particular case, it is unlikely to lead to a substantial misinterpretation. On the other hand, for the spectrum below (which is actually an $ABMX_3$, where X = ^{19}F), the second order effects are so large than a first order interpretation may lead to grossly inaccurate couplings, both in magnitude and sign, and a possible misassignment of the structure.



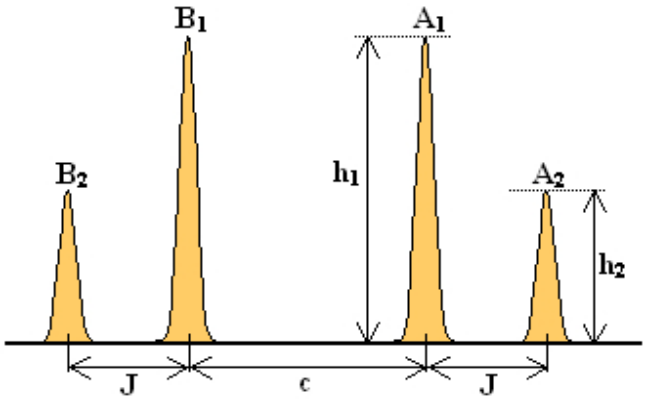
A borderline ABX pattern (actually an $ABMX_3$ pattern, since the M proton is coupled to the three fluorines. First order analysis of this one is problematic.

For these reasons, we will examine ABX patterns in some detail. In the progression from first-order NMR patterns to incomprehensible jungles of peaks, they represent the last stopping point where a complete analysis (by hand or hand calculator) is still possible, and where insights into the problems that arise in the analysis of more complex systems can be achieved. Specifically, ABX patterns are the simplest systems which show the phenomenon sometimes referred to as "virtual coupling" and they are the simplest systems in which both the magnitude and the sign of J coupling constants is significant. Furthermore, as illustrated above, there are several

pathological forms of ABX patterns which are sufficiently non intuitive that the unwary spectroscopist can mis-assign coupling constants and even structures.

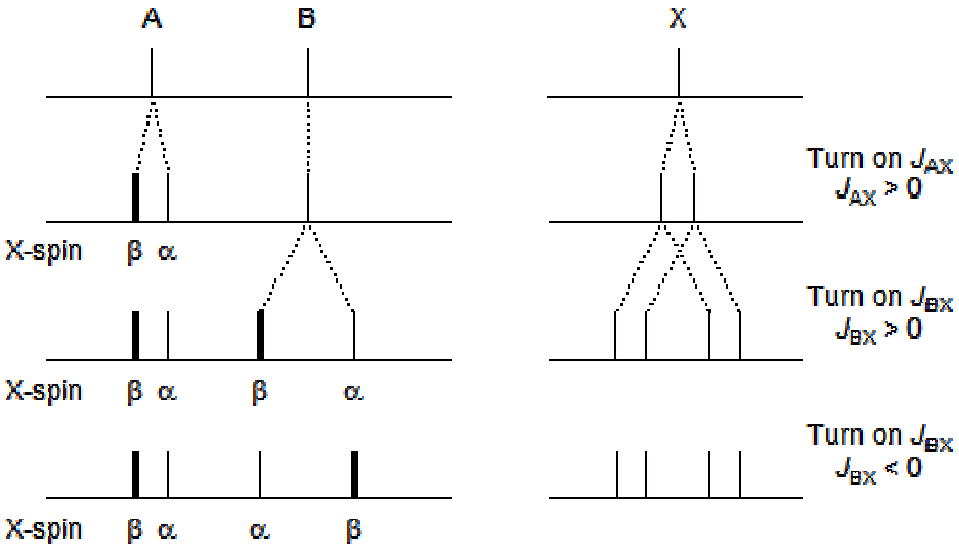
Transition frequencies and intensities in an iso(AB) spin system

The spectrum of an iso(AB) spin system is well known and described in almost every basic-level NMR textbook. It consists of four transitions which can be usually experimentally resolved as four distinct spectral peaks. The parameters of the spin system include two chemical shifts s(A) and s(B), and the scalar coupling constant J(AB). Without any lack of generality, we can assume s(A) $\leq$ s(B) and reference the spectrum so that [s(A)+s(B)]/2 = 0. This leaves just two parameters, the coupling



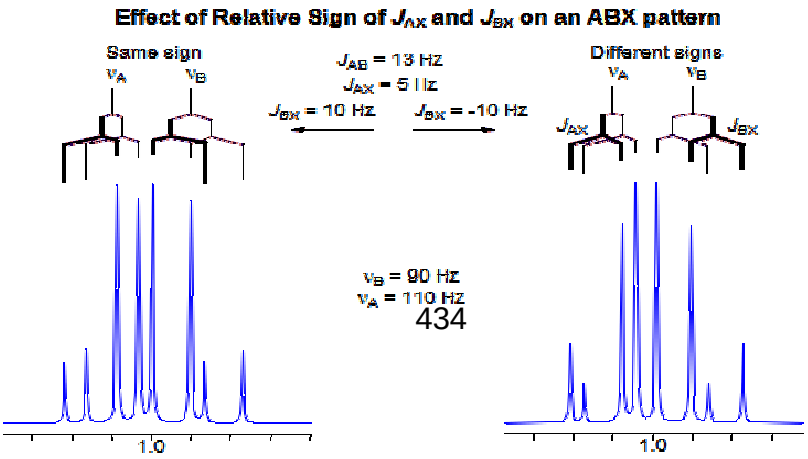
constant J and the difference of the chemical shifts Δ = s(B)-s(A), which determine the positions and intensities of the spectral peaks. Expressing *both* parameters in frequency units [Hz], the four peak positions and intensities are:

Development of an ABX Pattern. Consider the stick diagram below which represents an ABX pattern in which we sequentially turn on first the A-X and then the B-X coupling:

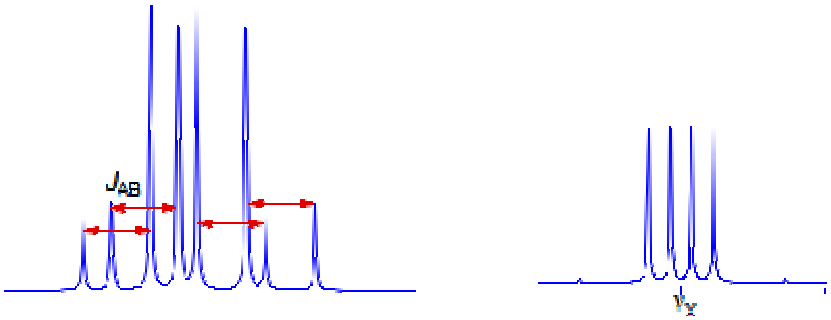


One of the two lines in the A-pattern arises from those molecules with the spin of the X-nucleus aligned against the field (β) and the other from those which have the X-spin aligned with the field (α). Similarly for the B-pattern. Note, however, that the line assignments of the pattern with both J_{AX} and J_{BX} nonzero will be different depending on the relative sign of J_{AX} and J_{BX}, as illustrated in the Figure. Up to this point the line positions are identical.

The key to understanding ABX patterns is to realize that the A and B nuclei with X = α and those with X = β are actually on different molecules, and cannot interact with each other. Thus, when we finally turn on J_{AB}, it will be the X = α line of A and the X = α line of B that will couple to form an AB-quartet. Similarly, the two X = β lines will form a second AB-quartet. Since the line intensities and line positions of an AB quartet depend on the "chemical shift" between the nuclei, it is clear that the different relative signs of J_{AX} and J_{BX} will result in different spectra. The ABX pattern is thus the simplest spin system for which the discerning spectroscopist can identify the relative signs of coupling constants by analysis of the pattern. The figure below shows the final AB part of the ABX pattern for the two cases.



Recognizing an ABX Pattern. A typical ABX spectrum consists of an unsymmetrical 8-line pattern integrating to two protons which has 4 doublets with the same separation J_{AB} (each doublet shows strong "leaning"). This is the AB part. The X part is a symmetric 6-line pattern, integrating to one proton, with four lines dominant (often looking like a dd). The 5th and 6th lines are usually small, and not often seen. J_{AB} and ν_X are directly measureable, the other parameters (J_{AX}, J_{BX}, ν_A, ν_B) must be calculated.



The AB part consists of two superimposed ab quartets (8 lines) which have normal intensities and line separations, both of which have identical J_{AB} values, but can have very different ν_{ab} values. *We will use "a" and "b" for the AB-subquartets of the AB part of an ABX pattern* Occasionally one of the ab[1] quartets has $\nu_{ab} = 0$, and appears as a singlet. Such systems appear as a five line pattern, with one ab quartet and a singlet . There are also several other deceptive forms with one or more lines superimposed.

The X part usually consists of an *apparent* doublet of doublets, although *apparent* triplets are not uncommon. There are two other lines which are often too weak to be detected (total of 6 lines). They become large when $J_{AB} > \nu_{AB}$.

22.9 SPIN DECOUPLING

It is often advantageous to remove or reverse the splitting caused by spin - spin coupling. This is called spin decoupling. Spin decoupling can be used for several reasons:

- to simplify spectra

- to assist in identification of coupling between nuclei

-to improve signal-to-noise

• How do we decouple spins from one another?

• Remembering the fact that coupling occurs because the transitions of one spin (α to β or β to α) ensue when the other (coupled) spin is in either the α or β state

- thus, to observe the coupling of one spin to another, the lifetime of the coupled spin in a given state must be long enough for the transitions of the other to occur

-this lifetime (τ1) must be greater than 1/J(J is the scalar coupling constant)

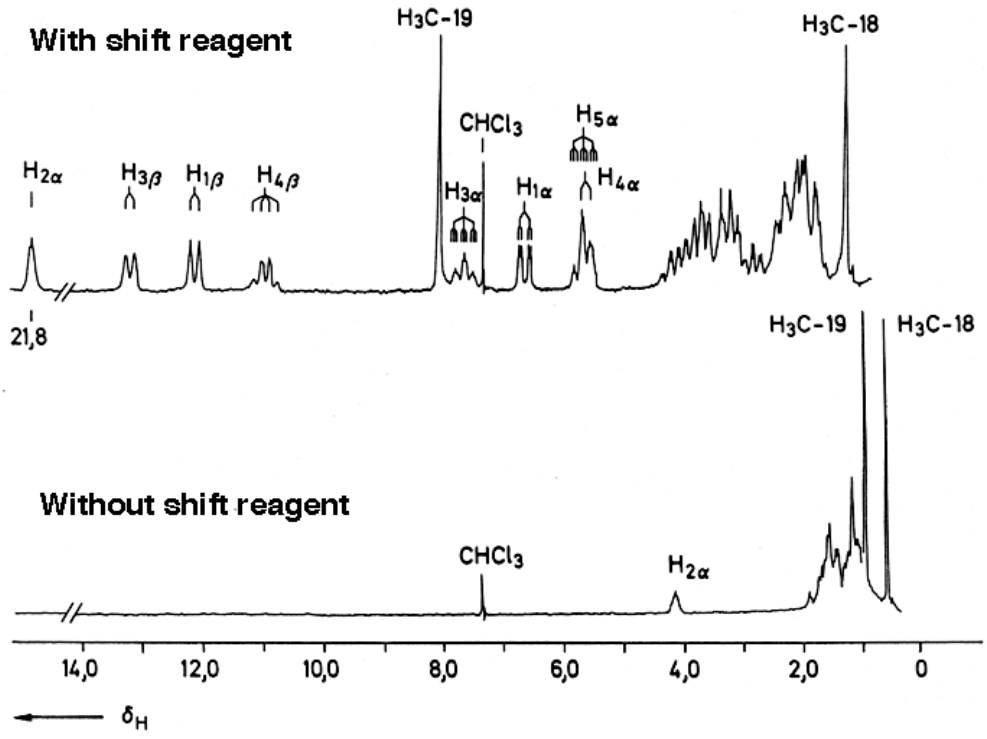
$$\tau 1 > 1/J$$

-if this lifetime is significantly shortened, the coupling (splitting of the signal) will not be observed.

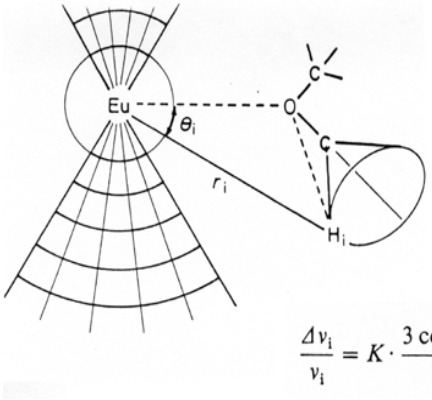
Decoupling are of two main types: selective and broad-band.

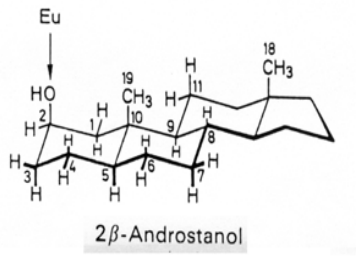
22.10 NMR shift reagents

Certain lanthanide compounds form complexes with molecules featuring -O- or -N< groups. Due to the magnetic moments of the paramagnetic lanthanide ions, this coordination leads to additional chemical shifts that decay with increasing distance to the metal ion.



The induced chemical shift depends on the distance between the paramagnetic atom (e.g. Eu) and the observed nucleus, but also on the angle between the two. The quantitative relation ship is the McConnell equation:





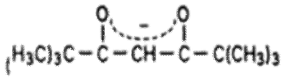
$$\frac{\Delta\nu_i}{\nu_i} = K \cdot \frac{3\cos^2\Theta_i - 1}{r_i^3}$$

The use of Lanthanide shift reagents is very useful to disentangle complex multiplet patterns and to distinguish between protons based on their proximity to the functional group coordinated to the lanthanide (-OH in our example of 2-b-Androstanol).

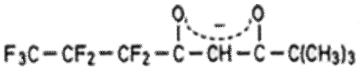
The angle dependency can produce shifts in either direction.

Of particular interest are chiral NMR shift reagents like $Eu(facam)_3$. Their complexation with a substrate leads to diastereomeric complexes which have different chemical shifts.

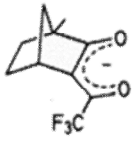
$Eu(dpm)_3$
dpm: 2,2,6,6-Tetramethyl-3,5-heptanedione



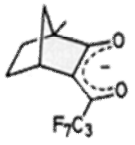
$Eu(fod)_3$ und $Eu(fod)_3$-d_{27}
fod: 6,6,7,7,8,8,8,-Heptafluoro-2,2-dimethyl-3,5-octanedione



$Eu(facam)_3$
facam: 3-Trifluoracetyl-D-camphor



$Eu(hfbc)_3$
hfbc: 3-Heptafluorobutyryl-D-camphor



22.11 Deuterium labelling

Isotopic labelling (or isotopic labelling) is a technique used to track the passage of an isotope, or an atom with a variation, through a reaction, metabolic pathway, or cell. The reactant is 'labeled' by replacing specific atoms by their isotope. The reactant is then allowed to undergo the reaction. The position of the isotopes in the products is measured to determine the sequence the isotopic atom followed in the reaction or the cell's metabolic pathway.

In isotopic labeling, there are multiple ways to detect the presence of labeling isotopes; through their mass, vibrational mode, or radioactive decay. Mass spectrometry detects the difference in an isotope's mass, while infrared spectroscopy detects the difference in the isotope's vibrational modes. Nuclear magnetic resonance detects atoms with different gyromagnetic ratios. The radioactive decay can be detected through an ionization chamber or autoradiographs of gels.

An example of the use of isotopic labeling is the study of phenol (C_6H_5OH) in water by replacing common hydrogen (protium) with deuterium (**deuterium labeling**). Upon adding phenol to deuterated water (water containing D_2O in addition to the usual H_2O), the substitution of deuterium for the hydrogen is observed in phenol's hydroxyl group (resulting in C_6H_5OD), indicating that phenol readily undergoes hydrogen-exchange reactions with water. Only the hydroxyl group was affected, indicating that the other 5 hydrogen atoms did not participate in these exchange reactions.

22.12 Summary

Chapter deals with increasing the knowledge of learner for nuclear magnetic resonance and its integration, coupling constant and chemical shift. Chapter also explain brief about NMR shift reagent and Deuterium labelling with is a matter of recent research. Along with these the chapter also highlights how to find the complex splitting pattern of various compound.

22.13 Questions / Comprehensive Questions

1. Suggest a reason why the acidic protons in a carboxylic acid appear so far downfield (about 12 ppm)?
2. Why are the signals of the compound not obscured by those of the shift reagent?
3. Why do we have to use expensive materials like lanthanides (Europium, Praseodymium, Terbium), why can't we use paramagnetic transition metal ions?

4. What would the multiplicity and the relative intensitites be for the secondary H in propane ?

22.14 Reference and suggested reading

1. A Complete Introduction to Modern NMR Spectroscopy: Roger S. Macomber.
2. Spectroscopy of Organic Compounds: P S Kalsi

   New Age International, 2004 - Chemistry, Organic - 652 pages

Unit - 23 : Mass Spectrometry

Structure of Unit:

23.1 Objectives

At the end of the unit learner will be able to

- Familiar with mass spectrometry.
- Learn the relative formula mass (relative molecular mass) of an organic compound.
- Understand about rearrangements and fragmentation modes..
- Increase knowledge about fragmentation patterns of different compounds.

23.2 Introduction

Chapter deals with increasing the knowledge of learner for mass spectrometry and its molecular ions, base peaks, different ions and fragmentation patterns. Chapter also explain brief about different rearrangements with is a matter of recent research. Alongwith these the chapter also highlights how to find the relative formula mass (relative molecular mass) of an organic compound from its mass spectrum. It also explains how high resolution mass spectra can be used to find the molecular formula for a compound.

23.3 Definition

Mass spectrometry

Mass spectrometry (MS) is an analytical technique that produces spectra (singular spectrum) of the masses of the atoms or molecules comprising a sample of material. The spectra are used to determine the elemental or isotopic signature of a sample, the masses of particles and of molecules, and to elucidate the chemical structures of molecules, such as peptides and other chemical compounds. Mass spectrometry works by ionizing chemical compounds to generate charged molecules or molecule fragments and measuring their mass-to-charge ratios.

In a typical MS procedure, a sample, which may be solid, liquid, or gas, is ionized, for example by bombarding it with electrons. This may cause some of the sample's molecules to break into charged fragments. These ions are then separated according to their mass-to-charge ratio, typically by accelerating them and subjecting them to an electric or magnetic field: ions of the same mass-to-charge ratio will undergo the same amount of deflection. The ions are detected by a mechanism capable of detecting charged particles, such as an electron multiplier.Results are displayed as spectra of the relative abundance of detected ions as a function of the mass-to-charge ratio. The atoms or molecules in the sample can be identified by correlating known masses to the

identified masses or through a characteristic fragmentation pattern.

23.4 Mass spectra – the molecular ion (M+) peak

When the vaporised organic sample passes into the ionisation chamber of a mass spectrometer, it is bombarded by a stream of electrons. These electrons have a high enough energy to knock an electron off an organic molecule to form a positive ion. This ion is called the molecular ion.

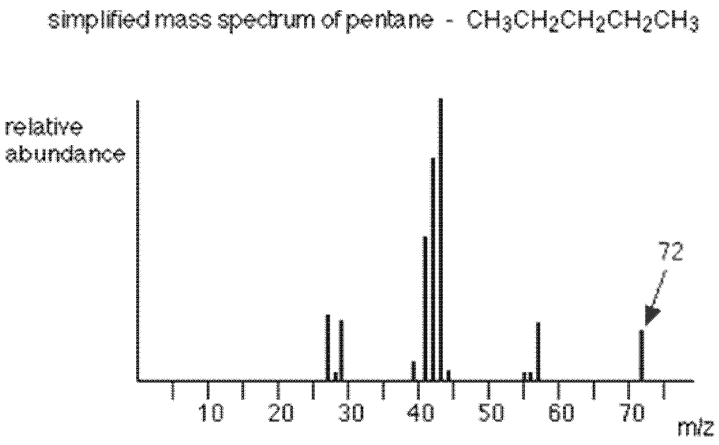
The molecular ion is often given the symbol $\mathbf{M}^+$ or $\mathbf{M}^{\bullet+}$ - the dot in this second version represents the fact that somewhere in the ion there will be a single unpaired electron. That's one half of what was originally a pair of electrons - the other half is the electron which was removed in the ionisation process.

The molecular ions tend to be unstable and some of them break into smaller fragments. These fragments produce the familiar stick diagram.

Determination of relative formulas with the help of molecular ion.

In the mass spectrum, the heaviest ion (the one with the greatest m/z value) is likely to be the molecular ion. A few compounds have mass spectra which don't contain a molecular ion peak, because all the molecular ions break into fragments. That isn't a problem you are likely to meet at A'level.

For example, in the mass spectrum of pentane, the heaviest ion has an m/z value of 72.

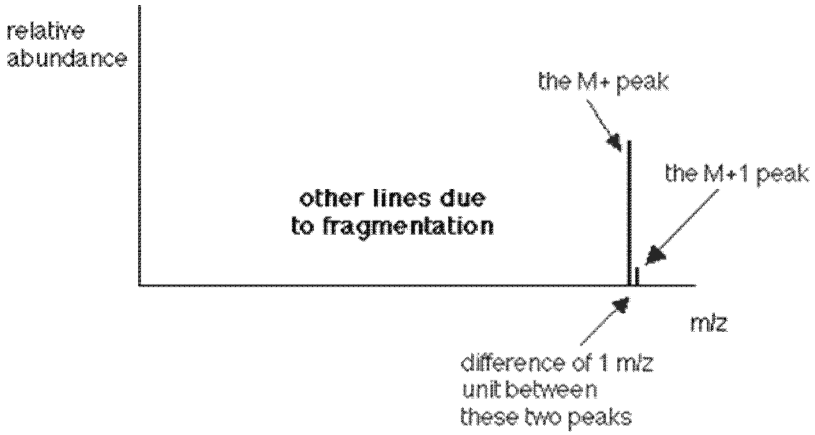


Because the largest m/z value is 72, that represents the largest ion going through the mass

spectrometer - and you can reasonably assume that this is the molecular ion. The relative formula mass of the compound is therefore 72.

Finding the relative formula mass (relative molecular mass) from a mass spectrum is therefore trivial. Look for the peak with the highest value for m/z, and that value is the relative formula mass of the compound.

There are, however, complications which arise because of the possibility of different isotopes (either of carbon or of chlorine or bromine) in the molecular ion.



23.5 Base peaks

Electron ionization mass spectra have several distinct sets of peaks: the molecular ion, isotope peaks, fragmentation peaks, and metastable peaks.

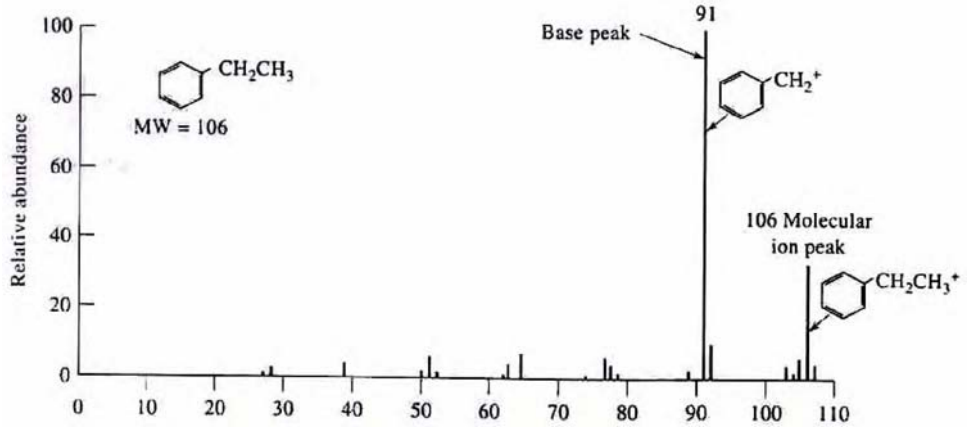
In the mass spectra the molecular ion peak is often most intense, but can be weak or missing. The molecular ion is a radical cation (M+.) as a result of removing one electron from the molecule. Identification of the molecular ion can be difficult. Examining organic compounds, the relative intensity of the molecular ion peak diminishes with branching and with increasing mass in a homologous series. In the spectrum for toluene for example, the molecular ion peak is located at 92 m/z corresponding to its molecular mass. Molecular ion peaks are also often preceded by a M-1 or M-2 peak resulting from loss of a hydrogen radical or dihydrogen.

The peak with the highest intensity is called the base peak which is not necessarily the molecular ion.

More peaks may be visible with m/z ratios larger than the molecular ion peak due to isotope distributions, called isotope peaks. The value of 92 in the toluene example corresponds to the monoisotopic mass of a molecule of toluene entirely composed of the most abundant isotopes (1H and 12C). The so-called M+1 peak corresponds to a fraction of the molecules with one higher isotope incorporated (2H or 13C) and the M+2 peak has two higher isotopes. The natural abundance of the higher isotopes is low for frequently encountered elements such as hydrogen, carbon and nitrogen and the intensity of isotope peaks subsequently low. In halogens on the other hand, higher isotopes have a large abundance which results in a specific mass signature in the mass spectrum of halogen containing compounds.

Peaks with mass less than the molecular ion are the result of fragmentation of the molecule. Many reaction pathways exist for fragmentation, but only newly formed cations will show up in the mass spectrum, not radical fragments or neutral fragments.

Metastable peaks are broad peaks with low intensity at non-integer mass values. These peaks result from ions with lifetimes shorter than the time needed to traverse the distance between ionization chamber and the detector.



23.6 Metastable Ions

Some fragment ions, undergo secondary fragmentations in the analyzer tube of the mass spectrometer; the resulting "signals" or peaks represent neither the m/e of the first ion nor that of the second ion; instead, "metastable ion" peaks are observed.

For a reaction

$$F1^+ \rightarrow F2^+$$

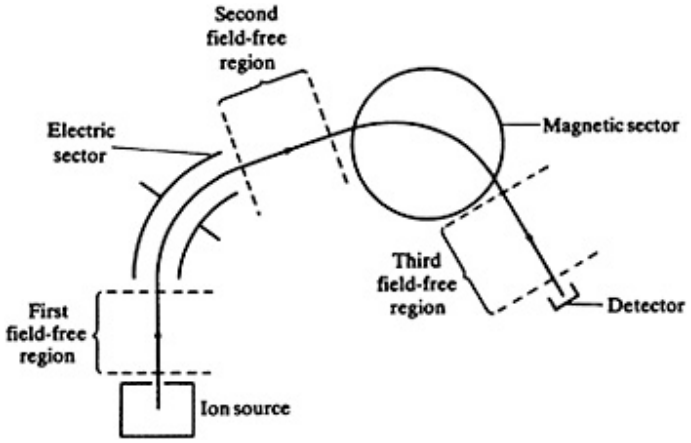
$$(m/e)_1 \qquad (m/e)_2$$

a “metastable ion” peak, m*, is observed.

$m^* = m_2^2/m_1$

metastable ion peaks require a special type of spectrometer; they give valuable information about fragmentation patterns of molecular ions.

Example



23.7 Electrospray ionization

Electrospray ionization (ESI) is a technique used in mass spectrometry to produce ions. It is especially useful in producing ions from macromolecules because it overcomes the propensity of these molecules to fragment when ionized. Additionally and arguably more importantly, ESI is advantageous over other atmospheric pressure ionization processes (e.g. MALDI) since it may produce multiple charged ions, effectively extending the mass range of the analyser to accommodate the KDa-MDa orders of magnitude observed in proteins and their associated polypeptide fragments.

Mass spectrometry using ESI is called electrospray ionization mass spectrometry (ESI-MS) or, less commonly, electrospray mass spectrometry (ES-MS). ESI is a so-called 'soft ionization' technique, since there is very little fragmentation. This can be advantageous in the sense that the molecular ion (or more accurately a pseudo molecular ion) is always observed, however very little structural information can be gained from the simple mass spectrum obtained. This disadvantage can be overcome by coupling ESI with tandem mass spectrometry (ESI-MS/MS). Another important advantage of ESI is that solution-phase information can be retained into the gas-phase.

The electrospray ionization technique was first reported by Masamichi Yamashita and John Fenn in 1984. The development of electrospray ionization for the analysis of biological macromolecules was rewarded with the attribution of the Nobel Prize in Chemistry to John Bennett Fenn in 2002. One of the original instruments used by Dr. Fenn is on display at the Chemical Heritage Foundation in Philadelphia, Pennsylvania.

Electrospray ionization (ESI) is an ionization technique for small amounts of large and/or labile molecules such as peptides, proteins, organometallics, and polymers. The ESI source operates at atmospheric pressure. A sample solution is sprayed from a small tube into a strong electric field in the presence of a flow of warm nitrogen to assist desolvation. The droplets formed evaporate in a region maintained at a vacuum of several torr causing the charge to increase on the droplets. The multiply charged ions then enter the analyzer. The most obvious feature of an ESI spectrum is that the ions carry multiple charges, which reduces their mass-to-charge ratio compared to a singly charged species. This allows mass spectra to be obtained for large molecules. For example, apo-myoglobin with a molecular weight of 16,951.5 Da produces a series of ions with charge states from +8 to +27 with mass peaks from about 600 to 2000 Da.

We typically use 50/50 H_2O/ACN as the mobile flow phase in ESI and samples are injected using a Rheodyne valve with a 10 microliter loop. Samples can also be introduced through direct infusion using a syringe pump. In addition, complex mixtures can be analyzed by coupling ESI MS with liquid chromatography (LC-MS).

Both positive and negative-ion spectra can be obtained. For positive-ion mode, 0.1% formic acid or acetic acid is usually added into the analyte solution to enhance protonation and increase sensitivity. For negative-ion mode, 0.3% NH_4OH is usually added into the analyte solution to help deprotonation and increase sensitivity. For proteins, we typically use a concentration of 100 pmol/microliter in 50/50 H_2O/ACN with 0.1% formic acid. Compounds such as porphyrins and other organometallic compounds are typically run in $CHCl_3$ at a concentration of about 100 pmol/microliter.

Buffers such as phosphate, tris, and hepes cannot be used. Even trace levels of these interfere with the ESI process. Only volatile buffers such as ammonium acetate can be used. Excess Na^+, K^+, and detergents are very bad for ESI and frequently result in no data. Detergents (PEG's and PPG's) are especially bad because they work very well by ESI and suppress ionization of analytes. It is best not to add acid to the

sample before submitting for ESI. We will dilute the sample to the proper concentration just before running the sample.

Sample amounts needed for ESI

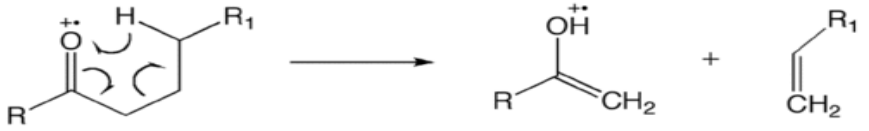
	Dry Sample (preferred)	**In Solution**
Proteins/Peptides	1µg	1µg/100µL
Polymers	1 mg	1mg/250µL
Dendrimers	1 mg	1mg/250µL
Organometallics	1 mg	1mg/250µL
Organics	1 mg	1mg/250µL

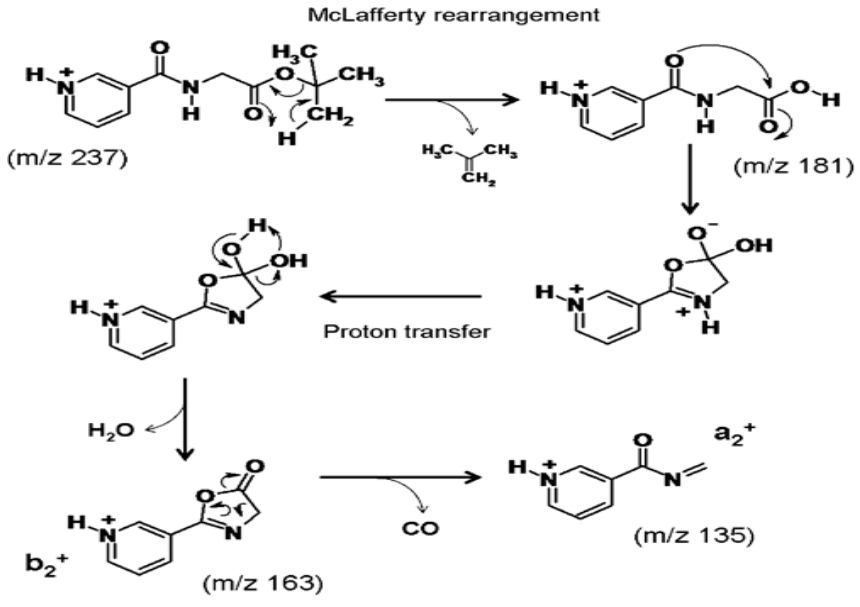
23.8 McLafferty rearrangement

The McLafferty rearrangement is a reaction observed in mass spectrometry. It is sometimes found that a molecule containing a keto-group undergoes β-cleavage, with the gain of the γ-hydrogen atom. This rearrangement may take place by a radical or ionic mechanism.

The reaction

A description of the reaction was first published by the American chemist Fred McLafferty in 1959**.**





23.9 Fragmentation modes

It is a phenomenon used in mass spectrometry to find the structural formula of a molecule through mass spectrum analysis, process called structural elucidation.

It can occur in the ion source (in-source fragmentation) where it is generally not a desired effect. Ion source conformation is an important criterium in the level of fragmentation observed.

IUPAC definition

Breakdown of a material to particles regardless of the mechanism and the size of fragments.

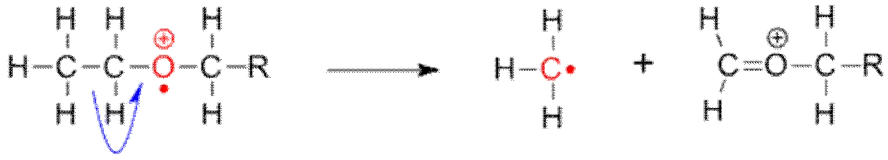
Desired fragmentation is made in the collision zone (post-source fragmentation) of a tandem mass spectrometer. It is a part of gas phase ion chemistry and there are different types of mass fragmentation:

- collision-induced dissociation (CID),
- electron-capture dissociation(ECD),
- electron-transfer dissociation (ETD),
- negative electron-transfer dissociation (NETD),
- electron-detachment dissociation (EDD),
- photodissociation, particularly infrared multiphoton dissociation(IRMPD) and blackbody infrared radiative dissociation (BIRD),
- surface-induced dissociation (SID),
- Higher-energy C-trap dissociation (HCD),
- charge remote fragmentation

The fragmentation pattern of the spectra beside the determination of the molar weight of an unknown compound also suitable to give structural information, especially in combination with the calculation of the degree of unsaturation from the molecular formula (when available). Neutral fragments frequently lost are carbon monoxide, ethylene, water, ammonia, and hydrogen sulfide.

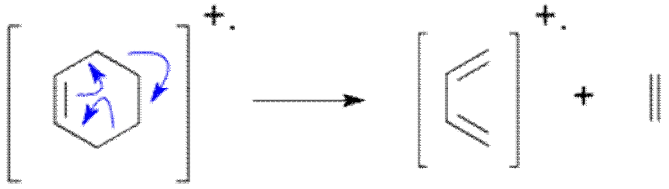
fragmentations arise from:

- homolysis processes. An example is the cleavage of carbon-carbon bonds next to a heteroatom



In this depiction single-electron movements are indicated by a single-headed arrow.

- Rearrangement reactions, for example a retro Diels-Alder reaction extruding neutral ethylene:



or the McLafferty rearrangement. As it is not always obvious where a lone electron resides in a radical cation a square bracket notation is often used.

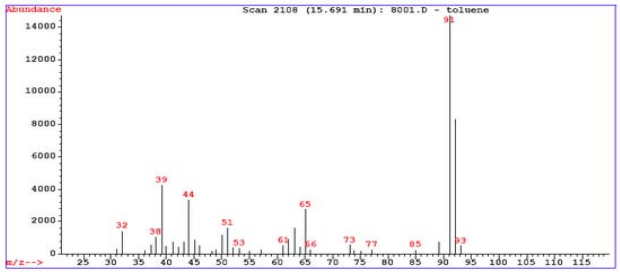
- Ion-neutal complex formation. This pathway involves bond homolysis or bond heterolysis, in which the fragments do not have enough kinetic energy to separate and, instead, reaction with one another like an ion-molecule reaction.

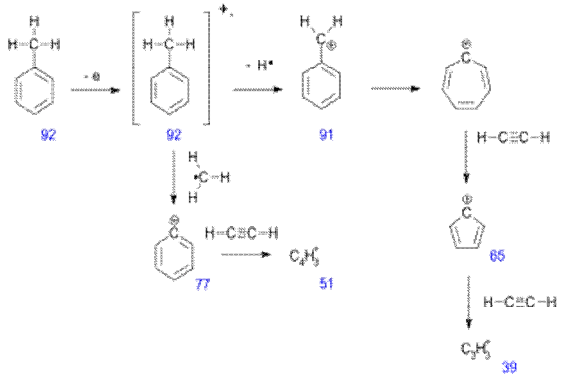
Some general rules:

- A useful aid is the nitrogen rule: if the m/z ratio is an even number, the compound contains no nitrogen or an even number of nitrogens.
- Cleavage occurs at alkyl substituted carbons reflecting the order generally observed in carbocations.
- Double bonds and arene fragments tend to resist fragmentation.
- Allylic cations are stable and resist fragmentation.
- the even-electron rule stipulates that even-electron species (cations but not radical ions) will not fragment into two odd-electron species but rather to another cation and a neutral molecule.

Toluene example

The mass spectrum for toluene has around 30 signals. Several peaks can be rationalized in this fragmentation pattern.





Schemes of fragmentation

The certain structures favour fragmentation the α-cleavage and the McLafferty rearrangement are two examples for the often observed fragmentations.

Other schemes includes Heterocyclic ring fission (HRF) or Retro Diels-Alder (RDA).

Alpha cleavage

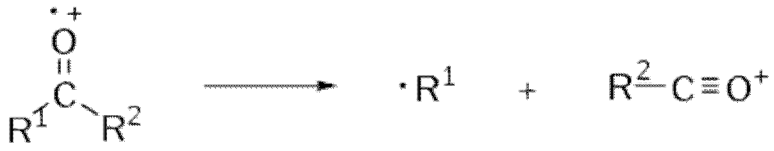
Alpha cleavage, (α-cleavage**)** in organic chemistry, refers to the act of breaking the carbon-carbon bond, adjacent to the carbon bearing a specified functional group.

Mass spectrometry

Generally this topic is discussed when covering tandem mass spectrometry fragmentation and occurs generally by the same mechanisms.

As example of a mechanism of alpha cleavage, an electron is knocked off an atom (usually by electron collision) to form a radical cation. Electron removal generally happens in the following order: 1) lone pair electrons, 2) pi bond electrons, 3) sigma bond electrons.

One of the lone pair electrons moves down to form a pi bond with an electron from an adjacent (alpha) bond. The other electron from the bond moves to an adjacent atom (not one adjacent to the lone pair atom) creating a radical. This creates a double bond adjacent to the lone pair atom (oxygen is a good example) and breaks/cleaves the bond from which the two electrons were removed.



Example of alpha cleavage

23.10 Determination of The Molecular Formula

Isotope peaks within a spectra can help in structure elucidation. Compounds containing halogens (especially chlorine and bromine) can produce very distinct isotope peaks. The mass spectrum of methylbromide has two prominent peaks of equal intensity at m/z 94 (M) and 96 (M+2) and then two more at 79 and 81 belonging to the bromine fragment.

Even when compounds only contain elements with less intense isotope peaks (carbon or oxygen), the distribution of these peaks can be used to assign the spectrum to the correct compound. For example, two compounds with identical mass of 150 Da, $C_8H_{12}N_3^+$ and $C_9H_{10}O_2^+$, will have two different M+2 intensities which makes it possible to distinguish between them.

Natural abundance of some elements

The next table gives the isotope distributions for some elements. Some elements like phosphorus and fluorine only exist as a single isotope, with a natural abundance of 100%.

Natural abundance of some elements

Isotope	**% nat. abundance**	**atomic mass**
^{1}H	99.985	1.007825
^{2}H	0.015	2.0140
^{12}C	98.89	12 (definition)
^{13}C	1.11	13.00335
^{14}N	99.64	14.00307
^{15}N	0.36	15.00011

^{16}O	99.76	15.99491
^{17}O	0.04	
^{18}O	0.2	17.99916
^{28}Si	92.23	27.97693
^{29}Si	4.67	28.97649
^{30}Si	3.10	29.97376
^{32}S	95.0	31.97207
^{33}S	0.76	32.97146
^{34}S	4.22	33.96786
^{37}Cl	24.23	
^{35}Cl	75.77	34.96885
^{79}Br	50.69	78.9183
^{81}Br	49.31	80.9163

1. **Molecular Ion**. Using mass spectrometry to determine the molecular ion allows us to identify possible molecular formulas. In the 70 eV EI spectrum, the highest m/z ion appears to be *m/z* 154. In the 13 eV EI spectrum, less fragmentation is observed because the ionization energy is much lower. The *m/z* 154 ion is significantly enhanced in this spectrum. This is is consistent with this being the molecular ion. And finally from the Chemical Ionization spectrum, the *m/z* 155 peak is consistent as an M+H adduct ion. The higher mass ions observed at *m/z* 171 and 205 could also be adducts of the molecular ion, so there may be some question about the identity of the molecuar ion. From the MS data it appears that the compound has a molecular weight of 154. Possible combinations of elements may be determined using computer programs or using tables.
2. **Isotope abundance** At this point it would be useful to reduce the number of possible formulas. One way to do this is by looking at the intensity of the

isotope peaks in the mass spectrum. The intensity of the M+1 peak in an electron ionization experiment may be used to determine the abundance of ^{13}C in the compound. From this, it is possible to determine the number of carbon atoms in the molecule. In the 70 eV EI spectrum the intensities are:

154 3.904606416

155 0.580805704

3. So the intensity of the M+1 peak is 14.9%
4. In the 13 eV EI mass spectrum the intensities are:

   154 78.30699837

   155 11.48840397

5. So the intensity of the M+1 peak is 14.7%
6. Since the natural abundance of ^{13}C is 1.1%. To a first approximation the intensity of the M+1 peak is 1.1% per C in the molecule. This would give 13.3 C's in the molecule. Rounded to 13. With C_{13} the abundance would be 14.3%. With C_{14} it would be 15.4%. This is consitant with the compound containing 13 C's. However, this is obviously not consistent with a molecular ion at *m/z* 154. This piece of information is not consistant.
7. **MS Fragments** Major fragments observed in the mass spectrum include:
   a. 139 - Loss of CH_3
   b. 136 - Loss of H_2O
   c. 121 - Loss of CH_3 and H_2O
   d. 111 - Loss of C_3H_7
   e. 98 - Loss of 56
   f. 84 - Loss of 70

   We'll come back to these to verify the final structure.
8. **Exact Mass**. Using a high resolution mass spectrometer, the exact mass of the molecular ion is found to be 154.1331 *m/z*. The programs MolForm, Elemental, and the calculator all return the same formula for *m/z* 154.1331 +/- 0.005: $C_{10}H_{18}O$ (154.135765).

9. **Combustion Analysis.** This verifies the high resolution mass spectrometry results. You should be able to verify our results by calculating the percent elemental composition.
    a. C = 78%
    b. H = 12%
10. **C-13 NMR**. The C-13 spectrum shows peak at 202.7 which is a strong indication of a carbonyl group (probably aldehyde) so there is a minimum of 1 oxygen atom.
11. **FTIR**. The FTIR spectrum shows a strong peak at 1722 cm^{-1}. This is consistent with an aldehyde.
12. **$C_{10}H_{18}O$**. All this information is consistent with the molecular formula $C_{10}H_{18}O$

Using a mass spectrum to find a molecular formula

So far we've been looking at m/z values in a mass spectrum as whole numbers, but it's possible to get far more accurate results using a high resolution mass spectrometer. You can use that more accurate information about the mass of the molecular ion to work out the molecular formula of the compound.

Accurate isotopic masses

For normal calculation purposes, you tend to use rounded-off relative isotopic masses. For example, you are familiar with the numbers:

^{1}H 1

^{12}C 12

^{14}N 14

^{16}O 16

To 4 decimal places, however, these are the relative isotopic masses:

^{1}H 1.0078

^{12}C 12.0000

^{14}N 14.0031

^{16}O 15.9949

The carbon value is 12.0000, of course, because all the other masses are measured on the carbon-12 scale which is based on the carbon-12 isotope having a mass of exactly 12.

Using these accurate values to find a molecular formula

Two simple organic compounds have a relative formula mass of 44 - propane, C_3H_8, and ethanal, CH_3CHO. Using a high resolution mass spectrometer, you could easily decide which of these you had.

On a high resolution mass spectrometer, the molecular ion peaks for the two compounds give the following m/z values:

C_3H_8 44.0624

CH_3CHO 44.0261

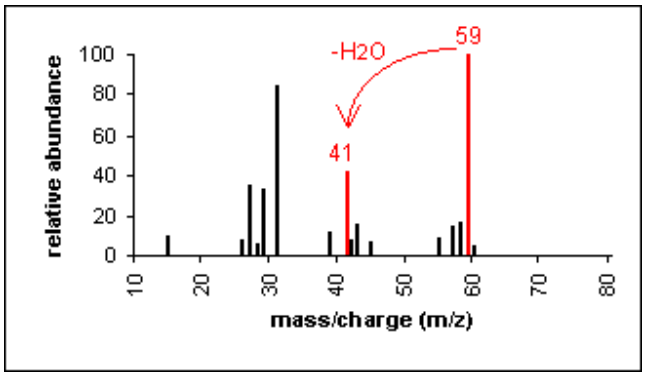
23.11 Mass Spectromelty: Fragmentation Patterns

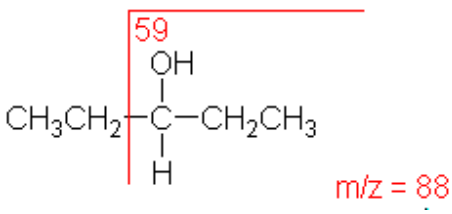
Following are examples of compounds listed by functional group, which demonstrate patterns which can be seen in mass spectra of compounds ionized by electron impact ionization. These examples do not provide information about the fragmentation mechanisms that cause these patterns.

Alcohol

An alcohol's molecular ion is small or non-existent. Cleavage of the C-C bond next to the oxygen usually occurs. A loss of H_2O may occur as in the spectra below.

3-Pentanol ($C_5H_{12}O$) with MW = 88.15

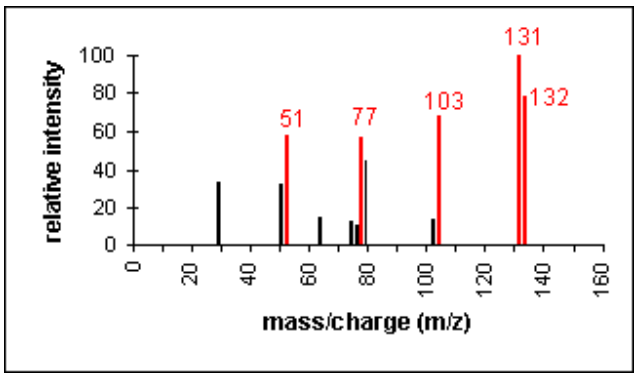


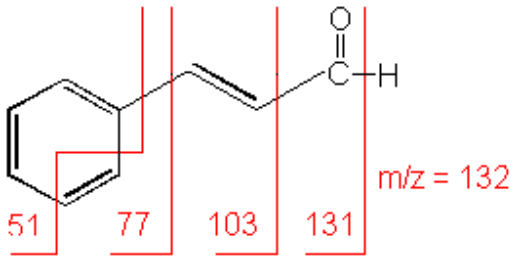


Aldehyde

Cleavage of bonds next to the carboxyl group results in the loss of hydrogen (molecular ion less 1) or the loss of CHO (molecular ion less 29).

3-Phenyl-2-propenal (C_9H_8O) with MW = 132.16

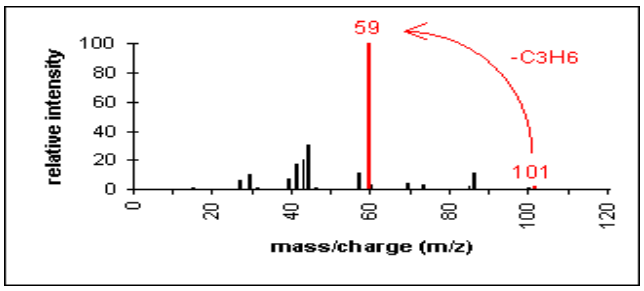


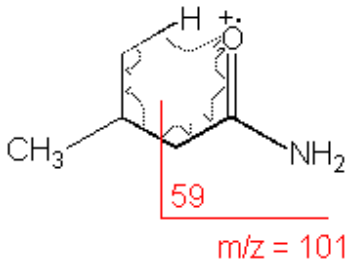


Amide

Primary amides show a base peak due to the McLafferty rearrangement.

3-Methylbutyramide ($C_5H_{11}NO$) with MW = 101.15

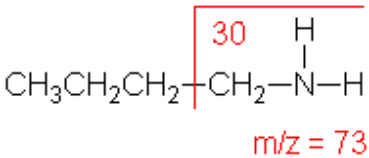


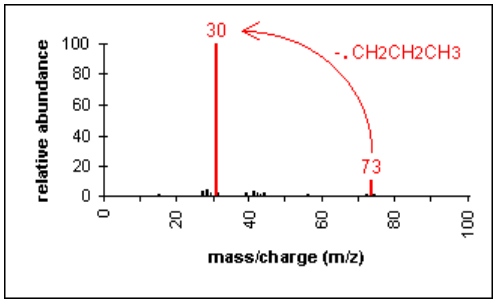


Amine

Molecular ion peak is an odd number. Alpha-cleavage dominates aliphatic amines.

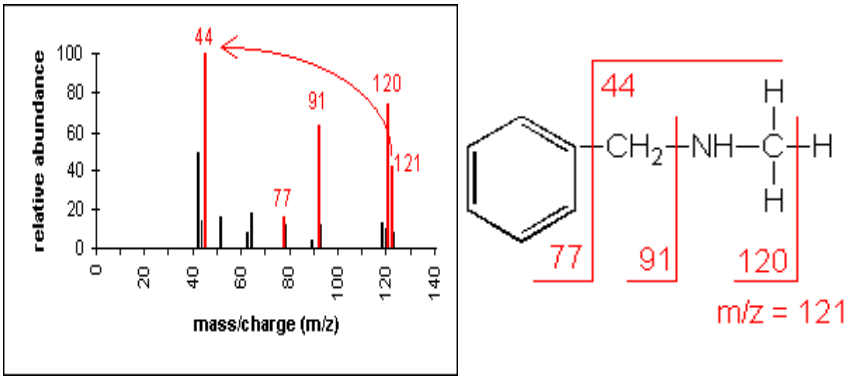
n-Butylamine (C4H11N) with MW = 73.13





Another example is a secondary amine shown below. Again, the molecular ion peak is an odd number. The base peak is from the C-C cleavage adjacent to the C-N bond.

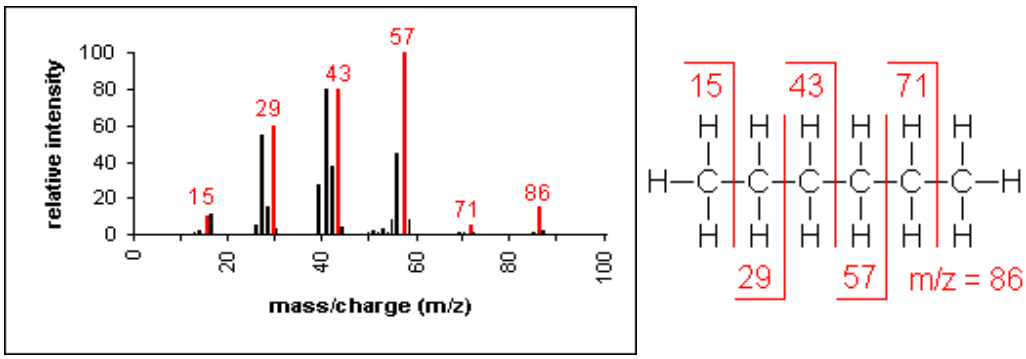
n-Methylbenzylamine ($C_8H_{11}N$) with MW = 121.18



Alkane

Molecular ion peaks are present, possibly with low intensity. The fragmentation pattern contains clusters of peaks 14 mass units apart (which represent loss of $(CH_2)nCH_3$).

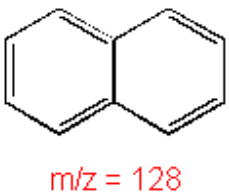
Hexane (C_6H_{14}) with MW = 86.18

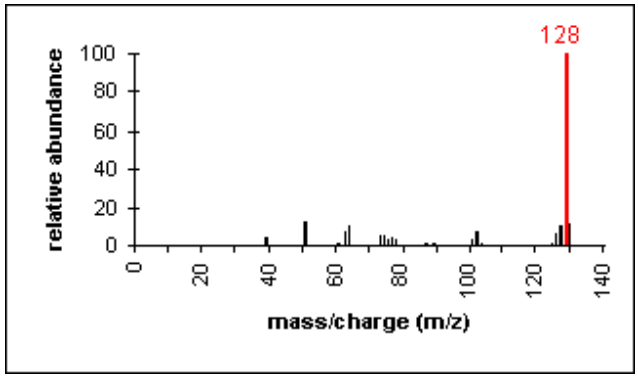


Aromatic

Molecular ion peaks are strong due to the stable structure.

Naphthalene ($C_{10}H_8$) with MW = 128.17

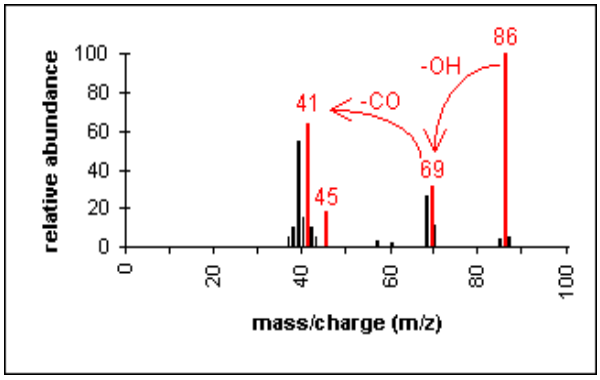


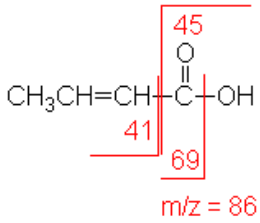


Carboxylic Acid

In short chain acids, peaks due to the loss of OH (molecular ion less 17) and COOH (molecular ion less 45) are prominent due to cleavage of bonds next to C=O.

2-Butenoic acid ($C_4H_6O_2$) with MW = 86.09

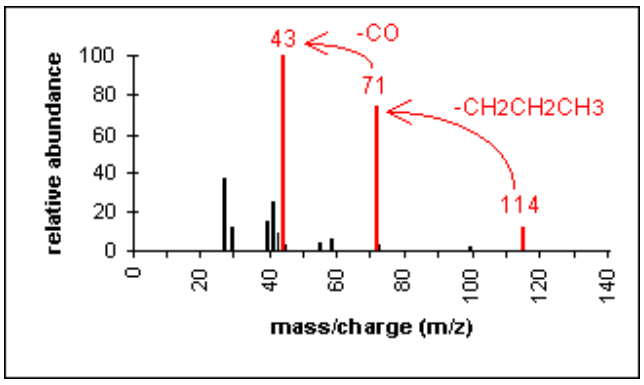


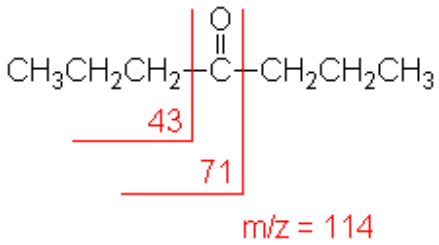


Ketone

Major fragmentation peaks result from cleavage of the C-C bonds adjacent to the carbonyl.

4-Heptanone ($C_7H_{14}O$) with MW = 114.19

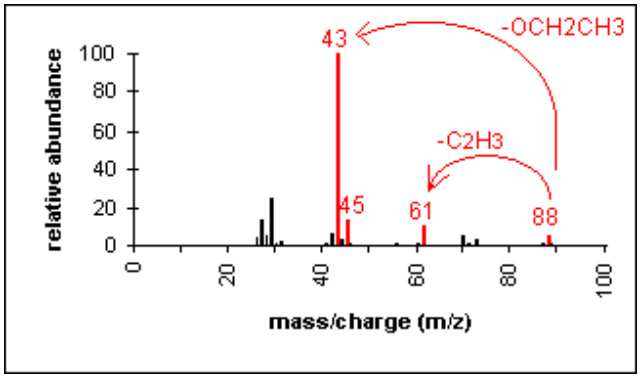


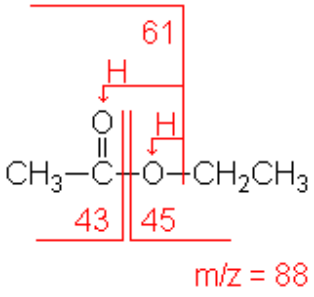


Ester

Fragments appear due to bond cleavage next to C=O (alkoxy group loss, -OR) and hydrogen rearrangements.

Ethyl acetate ($C_4H_8O_2$) with MW = 88.11

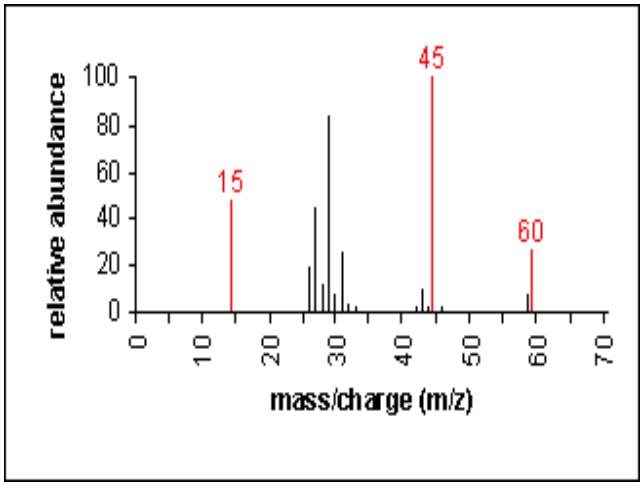


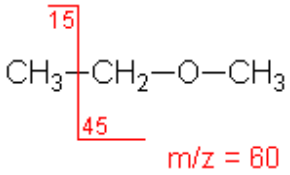


Ether

Fragmentation tends to occur alpha to the oxygen atom (C-C bond next to the oxygen).

Ethyl methyl ether (C_3H_8O) with MW = 60.10

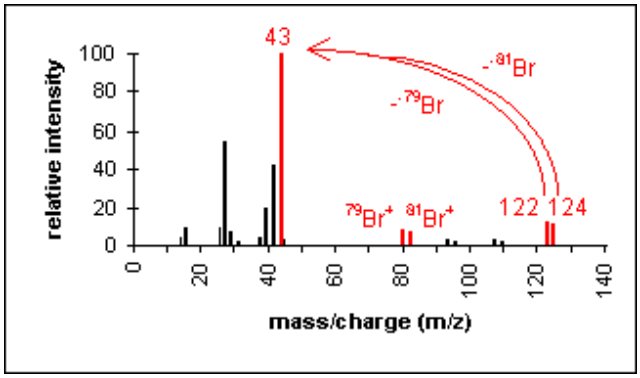


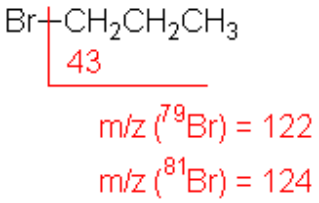


Halide

The presence of chlorine or bromine atoms is usually recognizable from isotopic peaks.

1-Bromopropane (C_3H_7Br) with MW = 123.00





23.12 Summary:

Chapter deals with increasing the knowledge of learner for mass spectrometry and its molecular ions, base peaks, different ions and fragmentation patterns. Chapter also explain brief about different rearrangements which is a matter of recent research. Alongwith these chapter also highlights how to find the relative formula mass (relative molecular mass) of an organic compound from its mass spectrum. It also explains how high resolution mass spectra can be used to find the molecular formula for a compound.

23.13 Questions / Comprehensive Questions:

1. Explain mass spectrometry in detail.
2. What is McLafferty rearrangement.
3. Explain fragmentation modes for the determination of molecular formula.
4. Write a short note on molecular ion and base peak.
5. Explain the fragmentation patterns of aldehyde, aliphatic acid and alcohol.

23.14 Reference and suggested reading

1. Elementary organic spectroscopy: Y.R.Sharma
2. Mass Spec Desk Reference, 2nd Ed. by O. David Sparkman
3. Global view publishing, june,2006, 168 page, ISBN-10-0966081390

Unit - 24 : Organic photochemistry

Structure of Unit:

24.1 Objectives

At the end of the unit learner will be able to

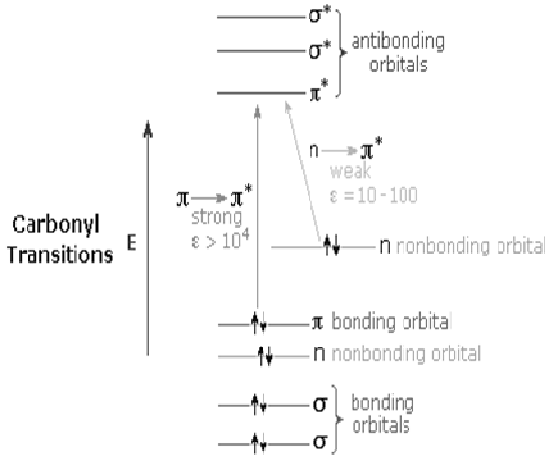
- The concept of Photochemistry.
- Learn the principle of photochemistry with ISC.
- Understand about mechanism of different rearrangements and reactions.
- Increase knowledge about photoisomerisation and its property.

24.2 Introduction

The Chapter deals with the increasing knowledge of learner for photochemistry and its mechanism, reactions, applications and structure. Chapter also explain brief about different rearrangements and reactions with is a matter of recent research. Alongwith these it also highlights the different types of reaction and photoisomerisation and its property used in photochemistry.

24.3 Definition

Photochemistry, a sub-discipline of chemistry is the study of chemical reaction that proceed with the absorption of light by atoms or molecules. Everyday examples include photosynthesis, the degradation of plastics and the formation of vitamin D with sunlight.



Alkenes undergo many important reactions that proceed via a photon-induced π to π* transition. The first electronic excited state of an alkene lack the π-bond, so that rotation about the C-C bond is rapid and the molecule engages in reactions not observed thermally. These reactions include cis-trans isomerization, cycloaddition to other (ground state) alkene to give cyclobutane derivatives. The cis-trans isomerization of a (poly)alkene is involved in retinal, a component of the machinery of vision. The dimerization of alkenes is relevant to the photodamage of DNA, where thymine dimers are observed upon illuminating DNA to UV radiation. Such dimers interfere with transcription..

The light is absorbed by chlorine molecule, the low energy of this transition being indicted by the yellowish color of the gas. The photon induces homolysis of the Cl-Cl bond, and the resulting chlorine radical converts toluene to the benzyl radical:

$Cl_2 + h\nu \rightarrow 2\ Cl\cdot$

$C_6H_5CH_3 + Cl\cdot \rightarrow C_6H_5CH_2\cdot + HCl$

$C_6H_5CH_2\cdot + Cl\cdot \rightarrow C_6H_5CH_2Cl$

Mercaptans can be produced by photochemical addition of hydrogen sulfide (H_2S) to alpha olefins.

24.4 Principles of photochemistry

Light is a type of electromagnetic radiation, which is a source of energy. The Grotthuss – Draper law states that light must be absorbed by a chemical substance in order for a photochemical reaction to take place. For each photon of light absorbed by a chemical system, no more than one molecule is activated for a photochemical reaction, as defined by the quantum yield.

Chemical reactions occur only when a molecule is provided the necessary "activation energy". A simple example can be the combustion of gasoline (a hydrocarbon) into carbon dioxide and water. In this reaction, the activation energy is provided in the form of heat or a spark. In case of photochemical reactions light provides the activation energy. Simplistically, light is one mechanism for providing the activation energy required for many reactions. If laser light is employed, it is possible to selectively excite a molecule so as to produce a desired electronic and vibrational state. Equally, the emission from a particular state may be selectively monitored, providing a measure of the population of that state. If the chemical system is at low pressure, this enables scientists to observe the energy distribution of the products of a chemical reaction before the differences in energy have been smeared out and averaged by repeated collisions.

The absorption of a photon of light by a reactant molecule may also permit a reaction to occur not just by bringing the molecule to the necessary activation energy, but also by changing the symmetry of the molecule's electronic configuration, enabling an otherwise inaccessible reaction path, as described by the Woodward–Hoffmann selection rules. A 2+2 cycloaddition reaction is one example of a pericyclic reaction that can be analyzed using these rules or by the related frontier molecular orbital theory.

Photochemical reactions involve electronic reorganization initiated by electromagnetic radiation. The reactions are several orders of magnitude faster than thermal reactions; reactions as fast as 10^{-9} seconds and associated processes as fast as 10^{-15} seconds are often observed.

Spectral regions

Photochemists typically work in only a few sections of the electromagnetic spectrum. Some of the most widely used sections, and their wavelengths, are the following:

- Ultraviolet: 100–400 nm
- Visible Light: 400–700 nm
- Near infrared: 700–2500 nm

24.5 Singlet state

A pair of spin-1/2 particles can be combined to form one of three states of total spin 1 called the triplet, or a state of spin 0 which is called the singlet. In theoretical physics, a singlet usually refers to a one-dimensional representation (e.g. a particle with vanishing spin). It may also refer to two or more particles prepared in a correlated state, such that the total angular momentum of the state is zero. Singlets and other such representations frequently occur in atomic physics and nuclear physics, where one tries to determine the total spin from a collection of particles.

A single electron has spin 1/2, and upon rotation its state transforms as a doublet, that is, as the fundamental representation of the Lie group SU(2). We can measure the spin of this electron's state by applying an operator $\vec{S}^2$ to the state, and we will always obtain $\hbar^2 (1/2)(1/2+1) = (3/4)\hbar^2$ (or spin 1/2) since the spin-up and spin-down states are both eigen states of this operator with the same eigenvalue.

Likewise, if we have a system of two electrons, we can measure the total spin by applying $\left(\vec{S}_1 + \vec{S}_2\right)^2$, where $\vec{S}_1$ acts on electron 1 and $\vec{S}_2$ acts on electron 2. However, we can now have two possible spins, which is to say, two possible eigenvalues of the total spin operator, corresponding to spin-0 or spin-1. Each eigenvalue belongs to a set of eigenstates. The "spin-0" set is called the singlet, containing one state (see below), and the "spin-1" set is called the triplet, containing three possible eigenstates.

In more mathematical language, we say the product of two doublet representations can be decomposed into the sum of the adjoint representation (the triplet) and the trivial representation, the singlet.

The singlet state formed from a pair of electrons has many peculiar properties, and plays a fundamental role in the EPR paradox and quantum entanglement. In Dirac notation this EPR state is usually represented as:

$$\frac{1}{\sqrt{2}}(|\uparrow\downarrow\rangle - |\downarrow\uparrow\rangle)$$

Triplet state

A spin triplet is a set of three quantum states of a system,each with total spin S = 1(in units of).The system could consist of a single elementary massive spin 1 particle such as a W or Z boson, or be some multiparticle state with total spin angular momentum of one.

In physics, spin is the angular momentum intrinsic to a body, as opposed to orbital angular momentum, which is the motion of its center of mass about an external point. In quantum mechanics, spin is particularly important for systems at atomic length scales, such as individual atoms, protons, or electrons. Such particles and the spins of quantum mechanical systems ("particle spin") possess several unusual or non-classical features, and for such systems, spin angular momentum cannot be associated with rotation but instead refers only to the presence of angular momentum.

Almost all molecules encountered in daily life exist in a singlet state, but molecular oxygen is an exception. At room temperature, O_2 exists in a triplet state, which would require the forbidden transition into a singlet state before a chemical reaction could commence, which makes it kinetically nonreactive despite being thermodynamically a strong oxidant. Photochemical or thermal activation can bring it into singlet state, which is strongly oxidizing also kinetically.

In a system with two spin-1/2 particles - for example the proton and electron in the ground state of hydrogen, measured on a given axis, each particle can be either spin up or spin down so the system has four basis states in all

$$\uparrow\uparrow, \uparrow\downarrow, \downarrow\uparrow, \downarrow\downarrow$$

using the single particle spins to label the basis states, where the first and second arrow in each combination indicate the spin direction of the first and second particle respectively.

More rigorously

$$|s_1, m_1\rangle|s_2, m_2\rangle = |s_1, m_1\rangle \otimes |s_2, m_2\rangle$$

and since for spin-1/2 particles, the basis states span a 2-dimensional space, the $|1/2, m_1\rangle|1/2, m_2\rangle$ basis states span a 4-dimensional space.

Now the total spin and its projection onto the previously defined axis can be computed using the rules for adding angular momentum in quantum mechanics using the Clebsch–Gordan coefficients. In general

$$|s,m\rangle = \sum_{m_1+m_2=m} C^{s_1 s_2 s}_{m_1 m_2 m} |s_1 m_1\rangle |s_2 m_2\rangle$$

substituting in the four basis states

$$|1/2,+1/2\rangle\ |1/2,+1/2\rangle\ (\uparrow\uparrow)$$
$$|1/2,+1/2\rangle\ |1/2,-1/2\rangle\ (\uparrow\downarrow)$$
$$|1/2,-1/2\rangle\ |1/2,+1/2\rangle\ (\downarrow\uparrow)$$
$$|1/2,-1/2\rangle\ |1/2,-1/2\rangle\ (\downarrow\downarrow)$$

returns the possible values for total spin given along with their representation in the $|1/2,\ m_1\rangle|1/2,\ m_2\rangle$ basis. There are three states with total spin angular momentum 1

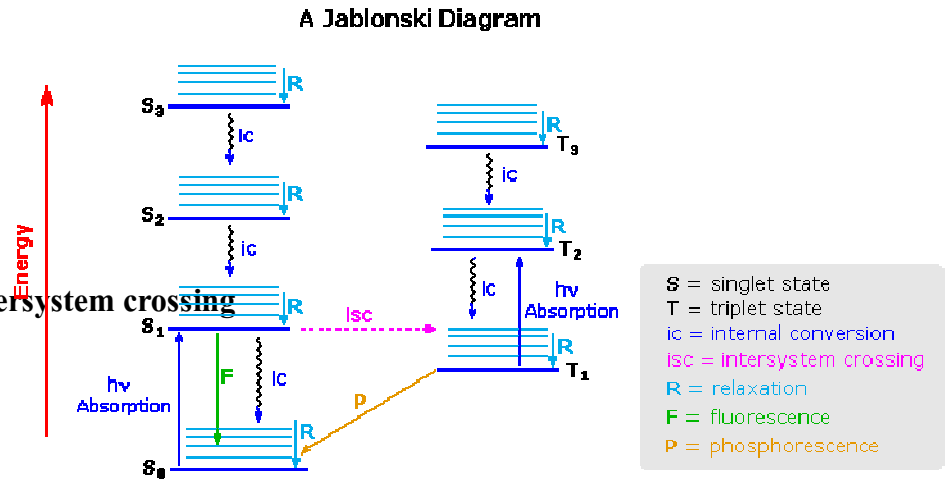
$$\left.\begin{array}{ll} |1,1\rangle & = \uparrow\uparrow \\ |1,0\rangle & = (\uparrow\downarrow + \downarrow\uparrow)/\sqrt{2} \\ |1,-1\rangle & = \downarrow\downarrow \end{array}\right\} \quad s = 1 \quad \text{(triplet)}$$

and a fourth with total spin angular momentum 0.

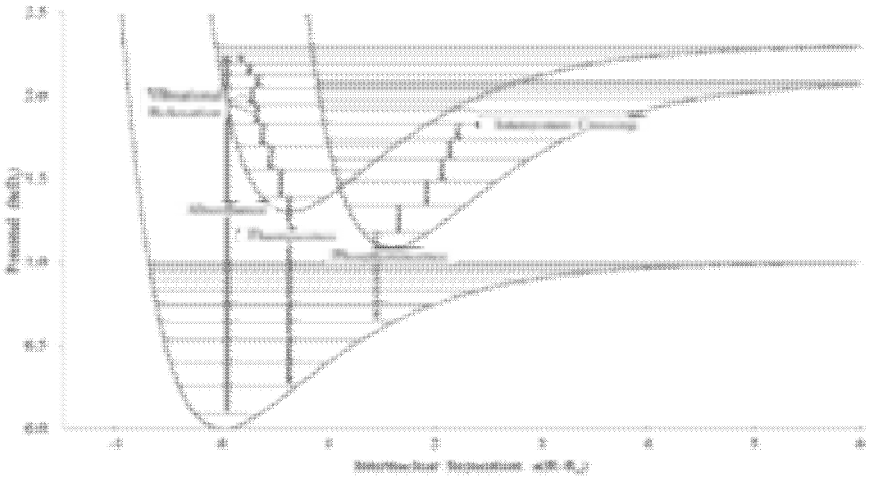
$$|0,0\rangle = (\uparrow\downarrow - \downarrow\uparrow)/\sqrt{2}\ \Big\} \quad s = 0 \quad \text{(singlet)}$$

The result is that a combination of two spin-1/2 particles can carry a total spin of 1 or 0, depending on whether they occupy a triplet or singlet state.

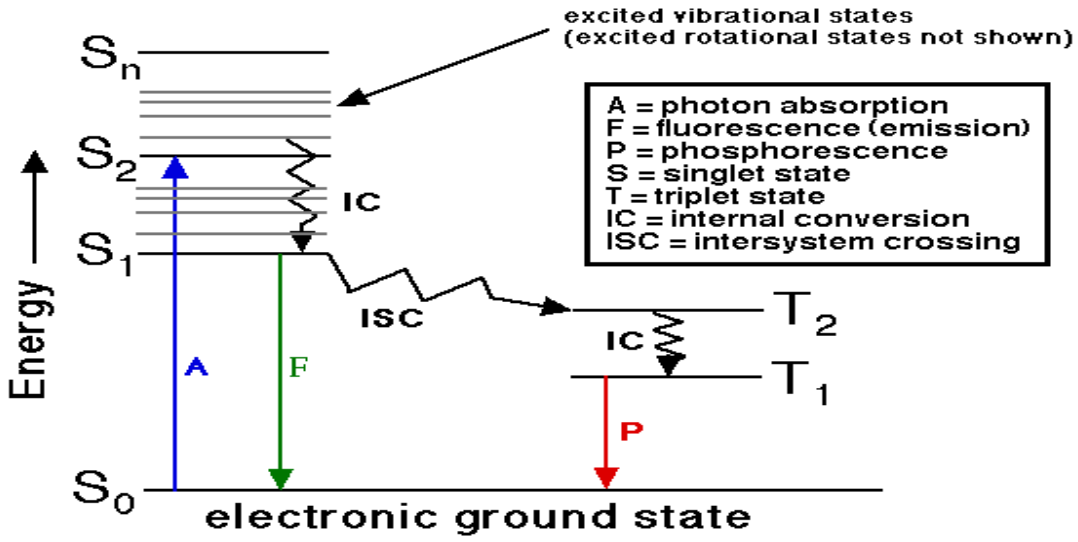
Intersystem crossing



Intersystem crossing is a radiationless process involving a transition between two electronic states with different spin multiplicity.

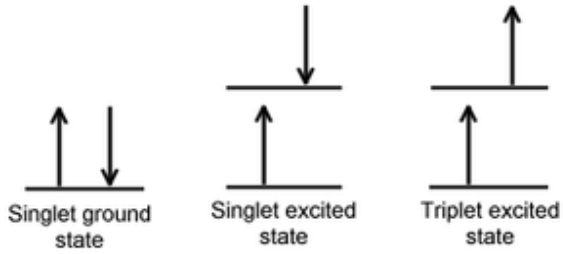


Excited electrons can undergo intersystem crossing to a degenerate state with a different spin multiplicity.



Singlet and triplet states

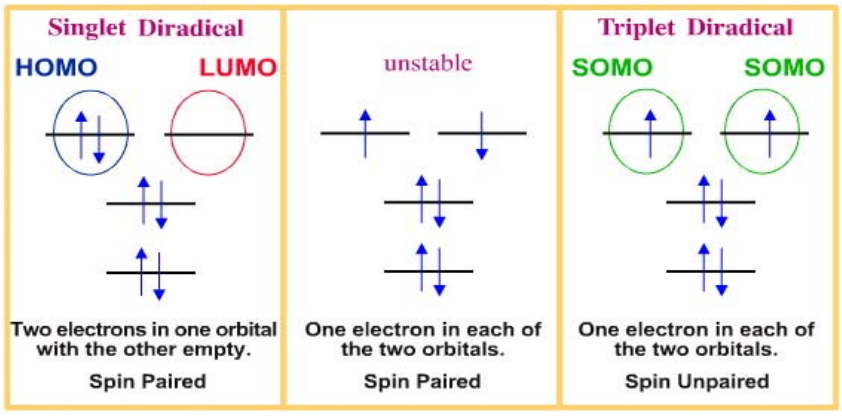
When an electron in a molecule with a singlet ground state is excited (*via* absorption of radiation) to a higher energy level, either an excited singlet state or an excited triplet state will form. A singlet state is a molecular electronic state such that all electron spins are paired. That is, the spin of the excited electron is still paired with the ground state electron (a pair of electrons in the same energy level must have opposite spins, per the Pauli exclusion principle). In a triplet state the excited electron is no longer paired with the ground state electron; that is, they are parallel (same spin). Since excitation to a triplet state involves an additional "forbidden" spin transition, it is less probable that a triplet state will form when the molecule absorbs radiation.



Singlet and triplet energy levels.

When a singlet state nonradiatively passes to a triplet state, or conversely a triplet transitions to a singlet, that process is known as intersystem crossing. In essence, the spin of the excited electron is reversed. The probability of this process occurring is more favorable when the vibrational levels of the two excited states overlap, since little or no energy must be gained or lost in the transition. As the spin/orbital interactions in such molecules are substantial and a change in spin is thus more favourable, intersystem crossing is most common in heavy-atom molecules (e.g. those containing iodine or bromine). This process is called "spin-orbit coupling". Simply-stated, it involves coupling of the electron spin with the orbital angular momentum of non-circular orbits. In addition, the presence of paramagnetic species in solution enhances intersystem crossing.

The radiative decay from an excited triplet state back to a singlet state is known as phosphorescence. Since a transition in spin multiplicity is observed, phosphorescence is another manifestation of intersystem crossing. The time scale of intersystem crossing is on the order of 10^{-8} to 10^{-3} s, one of the slowest forms of relaxation.



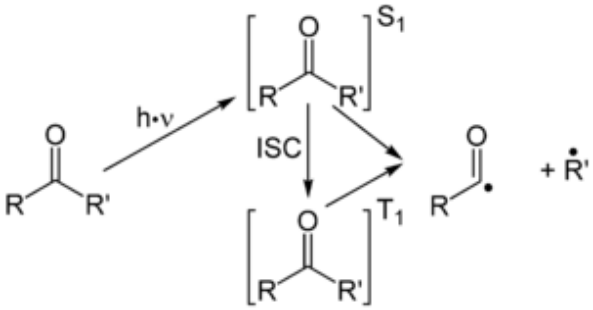
24.6 Norrish reaction

The Norrish reaction in organic chemistry describes the photochemical reactions taking place with ketones and aldehydes.This type of reaction is subdivided in

Norrish type I reactions and **Norrish type II reactions**. The reaction is named after Ronald George Wreyford Norrish.

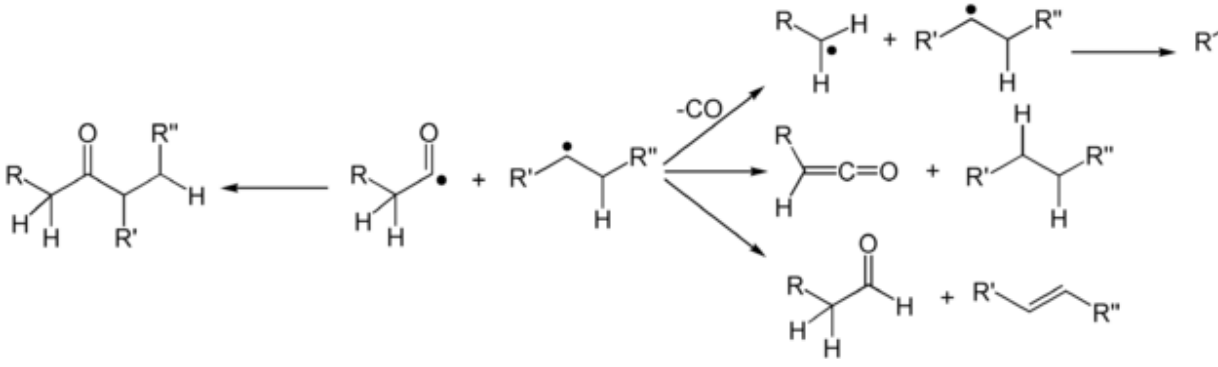
Norrish I

The Norrish type I reaction is the photochemical cleavage or homolysis of aldehydes and ketones into two free radical intermediates. The carbonyl group accepts a photon and is excited to a photochemical singlet state. Through intersystem crossing the triplet state can be obtained. On cleavage of the α-carbon carbon bond from either state, two radical fragments are obtained.



Several secondary reaction modes are open to these fragments depending on the exact molecular structure.

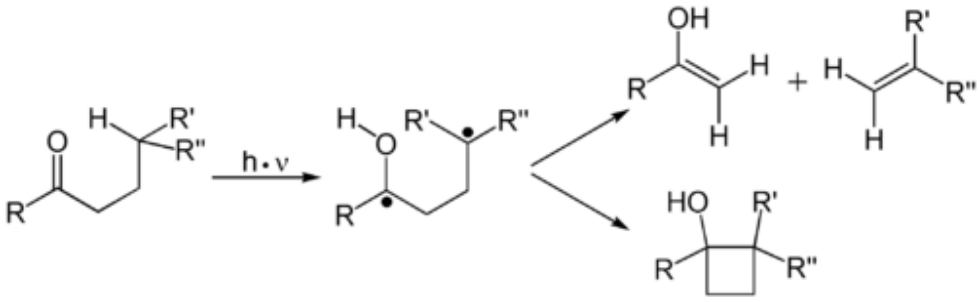
- The fragments can simply recombine to the original carbonyl compound (path A).
- By extrusion of carbon monoxide in path B, two organic residues can recombine with formation of a new carbon carbon bond
- When the carbon fragment has an α-proton available it gets abstracted forming a ketene and a saturated hydrocarbon in path C
- When the alkyl fragment contains a β-proton it gets abstracted with formation of an and aldehydes an alkene.



The synthetic utility of this reaction type is limited. It often is a side reaction for instance in the Paternò–Büchi reaction. One organic synthesis based on this reaction is that of bicyclohexylidene.

Norrish II

A **Norrish type II reaction** is the photochemical intramolecular abstraction of a γ-hydrogen (which is a hydrogen atom three carbon positions removed from the carbonyl group) by the excited carbonyl compound to produce a 1,4-biradical as a primary photoproduct (IUPAC definition).



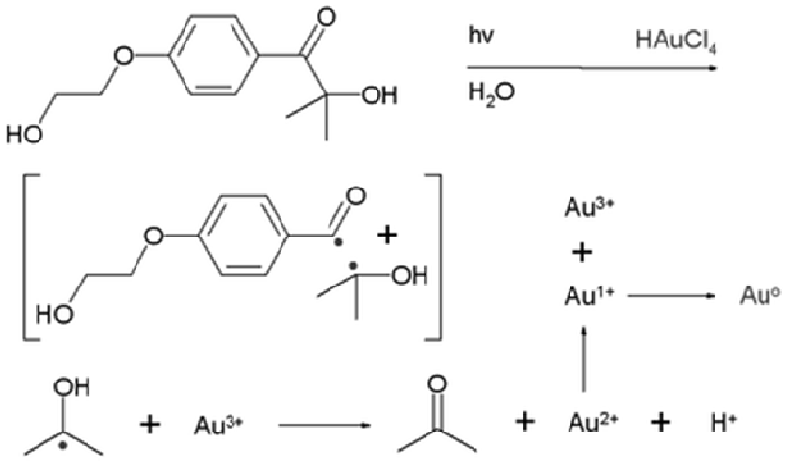
Secondary reaction are either intramolecular recombination of the two radicals to a cyclobutane compound (path A) or fragmentation to an enol and an alkene

The reaction was first reported in 1937 by Ronald George Wreyford Norrish.

Scope

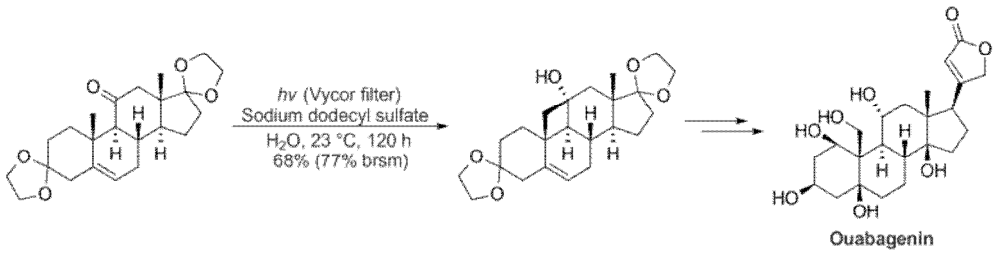
The Norrish reaction has been studied in relation to environmental chemistry with respect to the photolysis of the aldehyde heptanal, a prominent compound in Earth's atmosphere. Photolysis of heptanal in conditions resembling atmospheric conditions results in the formation of 1-pentene and acetaldehyde in 62% chemical yield together with cyclic alcohols (cyclobutanols andcyclopentanols) both from a Norrish type II channel and around 10% yield of hexanal from a Norrish type I channel (the initially formed n-hexyl radical attacked by oxygen).

In one study the photolysis of an Acyloin derivative in water in presence of hydrogen tetrachloroaurate ($HAuCl_4$) generated nanogold particles with 10 nanometer diameter. The species believed to responsible for reducing Au^{3+} to Au^0 is the Norrish generated ketyl radical.

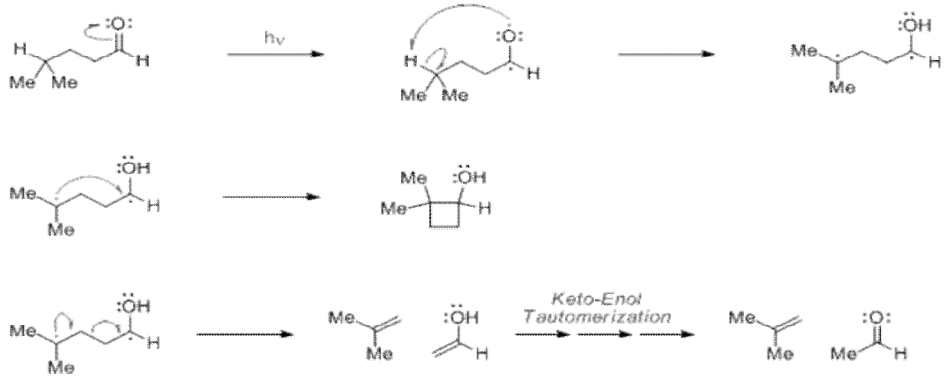


No fewer than three Norrish-type reactions feature in the classic 1982 total synthesis of dodecahedrane.

An example of a synthetically useful Norrish type II reaction can be found early in the total synthesis of the biologically active cardenolide ouabagenin by Baran and coworkers. The optimized conditions minimize side reactions, such as the competing Norrish type I pathway, and furnish the desired intermediate in good yield on a multi-gram scale.



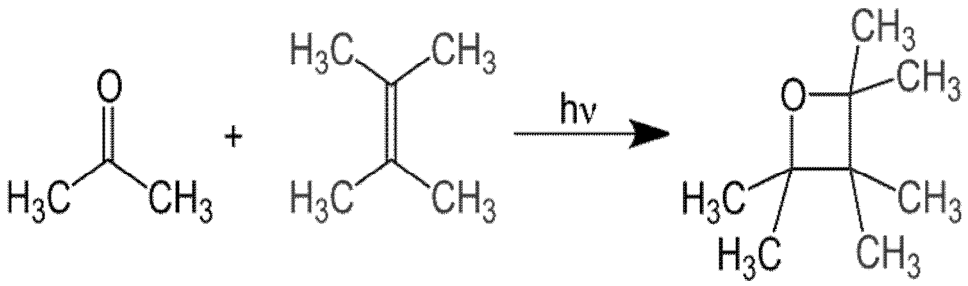
Mechanism of the Norrish Reaction (Type II)



24.7 Paterno-Büchi Reaction

The **Paternò–Büchi reaction**, named after Emanuele Paternò and George Büchi who established its basic utility and form, is a photochemical reaction that forms four-membered oxetane rings from a carbonyl and an alkene.

The Paternò–Büchi reaction has been used recently in attempt to synthesize many natural organic products. In these experiments, the chemists are chiefly concerned with the regio- and diastereoselectivity of the products.



The photochemical [2+2] cycloaddition of a carbonyl with an olefin to give an oxetane.

Mechanism of the Paterno-Buechi Reaction

The possible transitions (C=O) are shown below:

Once the carbonyl ground state has been photoexcited, either a singlet or triplet state may be formed:

n,π*-transition

Either type of transition (n,π* and π,π*) and electronic state (singlet, triplet) may participate in the first stage of this reaction, which is rationalized by invoking diradical intermediates:

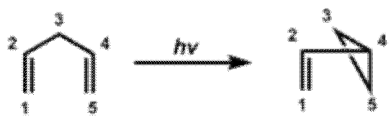
Breaking of the new σ-bonds requires more energy, and the reverse reaction is not possible using same light frequency.

Example:

Paternò-Büchi Reactions of Silyl Enol Ethers and Enamides.

24.8 Di-pi-methane rearrangement

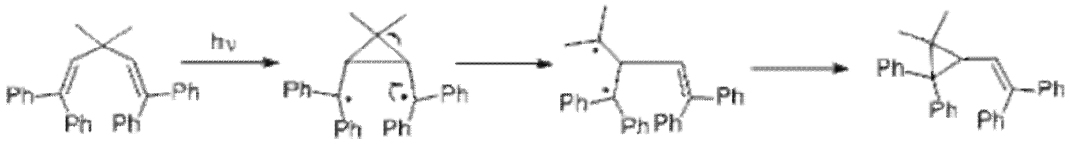
The di-pi-methane rearrangement is a photochemical reaction of a molecular entity that contains two π-systems separated by a saturated carbon atom (a 1,4-diene or an allyl-substituted aromatic ring), to form an ene- (or aryl-) substituted cyclopropane. The rearrangement reaction formally amounts to a 1,2 shift of one ene group (in the diene) or the aryl group (in the allyl-aromatic analog) and bond formation between the lateral carbons of the non-migrating moiety.



Discovery & mechanism

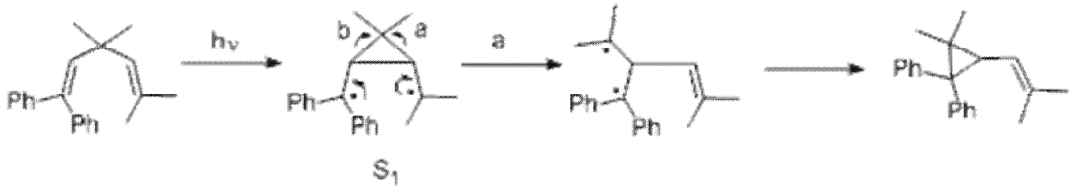
This rearrangement was originally encountered in the photolysis of barrelene to give semibullvalene Once the mechanism was recognized as general by Zimmerman in 1967, it was clear that the structural requirement was having two pi groups attached to an sp3-hybridized carbon, and then a variety of further examples was obtained. One was the photolysis of the Mariano Compound, 3,3-methyl-1,1,5,5-tetraphenyl-1,4-pentadiene. Another was the reaction of the Pratt diene

Equation 1. The mechanism of the Mariano diene rearranging



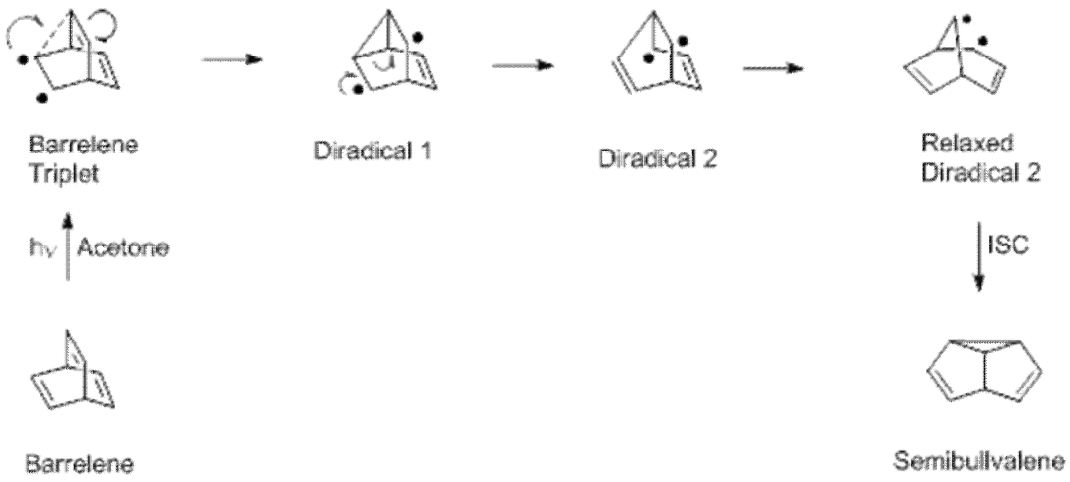
In contrast, in the case of the Pratt diene rearranging, there are two possible regiochemistries - a and b. Process a is preferred since it leaves benzhydryl odd-electron stabilization intact.

Equation 2. The mechanism of the Pratt diene rearranging; note the regioselectivity

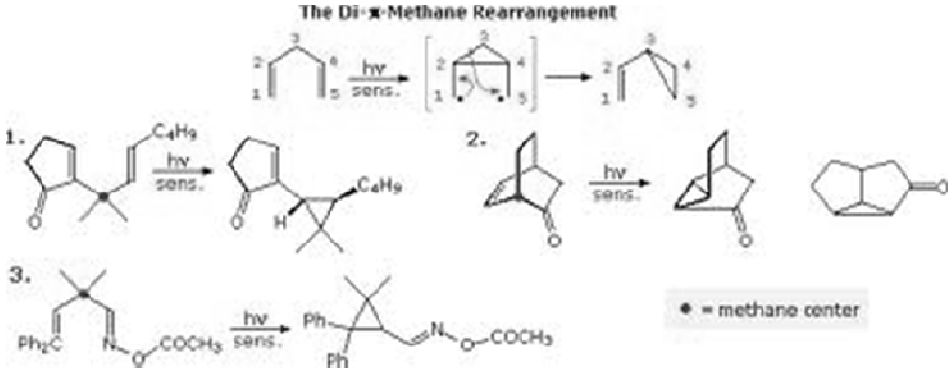


The barrelene rearrangement is now presented. It is a bit more complex than the Mariano and Pratt examples since there are two sp3-hybridized (i.e. methane) carbons. Each such bridgehead carbon has three (ethylenic) pi bonds while two are needed for the di-pi-methane rearrangement. Another difference is that the barrelene reaction requires the triplet excited state while the Mariano and Pratt acyclic dienes used the excited singlet. Thus acetone is used in the barrelene reaction; acetone captures the light and then delivers triplet excitation to the barrelene reactant. In the final step of the rearrangement there is a spin-flip, termed intersystem-crossing (ISC) to provide paired electrons and a new sigma bond.

Equation 3. The mechanism of the Barrelene to Semibullvalene transformation



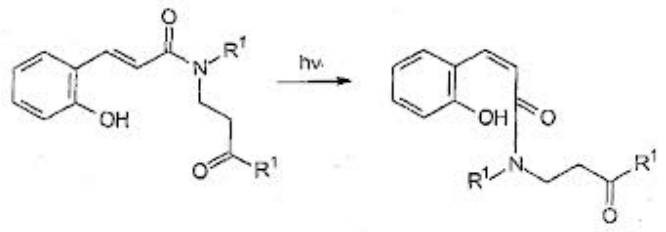
The dependence of the success of the Di-pi-Methane rearrangement on singlet versus triplet multiplicity arises primarily from the Free-Rotor Effect The triplet acyclic 1,4-dienes are free to undergo cis-trans interconversion of the diene double bonds (i.e. free-rotation) thus inhibiting the Di-pi-Methane process. The cis-trans isomerization proceeds by weakening of a pi-bond and then twisting. The singlet excited states don't rotate and then are free to undergo the Di-pi-Methane mechanism. For cyclic dienes, as in the barrelene example, the ring structure prevents cis-trans isomerization and the Di-pi-Methane can then occur.



24.9 photoisomerization

In photoisomerization no chemical bonds are broken, but the molecule changes shape. For example, absorption of optical radiation by a stilbene molecule converts the central double bond from *trans* to *cis*. As in photodissociation, this is caused by the electron distribution in the excited state being quite different from that in the ground state hence, the structure of the initially created excited singlet (by absorption of light) is most stable at 90°, or halfway between the *cis* and *trans* forms. The molecule attempts to adopt this conformation by rotating about the double bond until

the shape of its nuclei matches the distribution of its electrons. Internal conversion occurs most efficiently from this point where the S_0 and S_1 energies are close. Thus, within one or a few molecular vibrations (30–100 fs), the molecule returns to the S_0 state with excess vibrational energy. However, the 90° twist of the double bond is the least-stable conformation for the electron distribution of the S_0 state, so the molecule again rotates about the double bond. Rotation can either continue in the same direction, forming the new isomer, or go back, forming the original isomer. In reality the motions of the molecule are more complicated than described here, involving simultaneous rotation about multiple bonds. However, this simple description contains the essence of the process.



Photochemical process leading to an isomerization of the substrate, either by bond rotation, skeletal rearrangement or atom- or group- transfer.

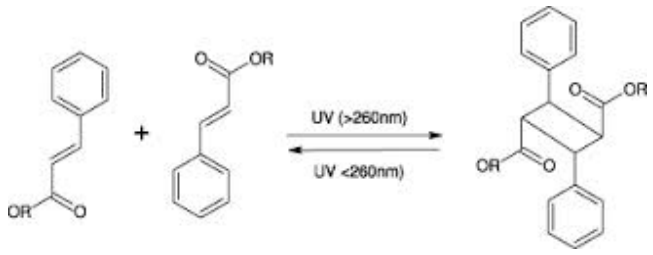
Notes:

1. Typical examples are *cis-trans* photosomerization of alkenes, polyenes and phototautomerization.
2. Photochemical pathways have the advantage over thermal and catalytic methods of giving isomer mixtures (photostationary states) rich in thermodynamically unstable isomers.
3. Photoisomerization is the primary photochemical reaction of the chromophore in several biological photoreceptors such as retinal proteins (e.g., rhodopsin), phytochromes, and the photoactive yellow protein.

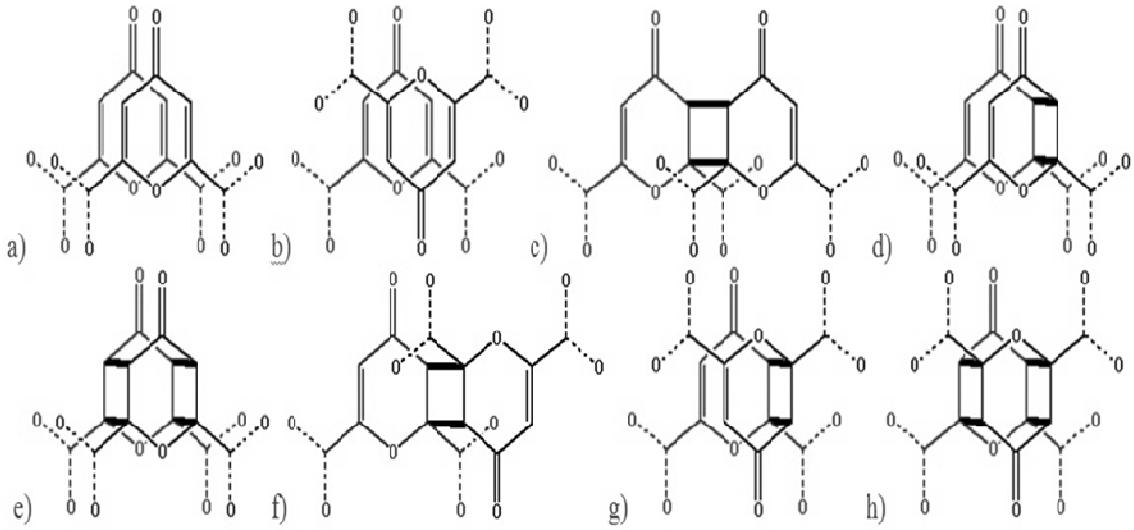
24.10 Photodimerization and photocyclization

Photodimerization is an important reaction in organic synthesis that allows the formation of new C-C bonds between two molecules. [2+2] photodimerization is a specific type, a cycloaddition reaction involving the carbon-carbon double bonds of two neighboring molecules if they, the C=C bonds, are aligned nearly parallel and within 4.2 Å. This simple reaction allows access to dimer products that might otherwise be difficult to synthesize as a single molecule. Typically, photodimerization is performed in the presence of ultraviolet light, and the method is

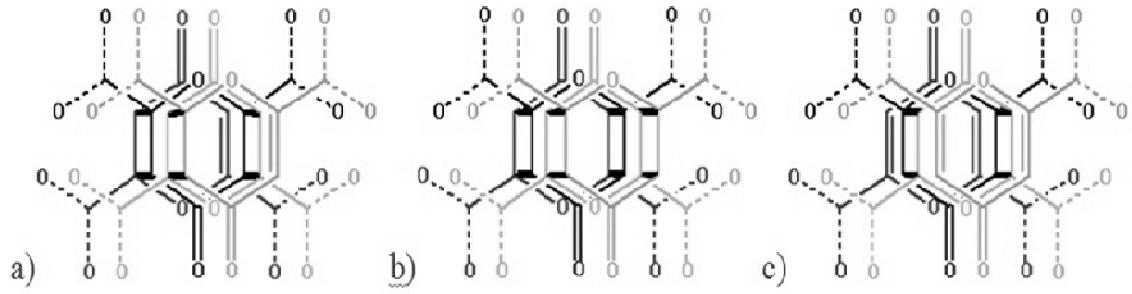
dominated by either the fluid environment in liquid phase or guest interactions (i.e., van der Waals and electrostatic forces) in confined cavities.



Recently, solid state co-crystallization (e.g., hydrogen-bond (HB)-templated complexes) has been utilized to position the two target molecules in commensurate orientation(s) for refined products. Nonetheless, directing the assembly of purely functional organic molecules into predetermined positions remains a challenge. Thus, their pre-alignment into the requisite distance for [2 + 2] photodimerization is less evident by direct crystallization.

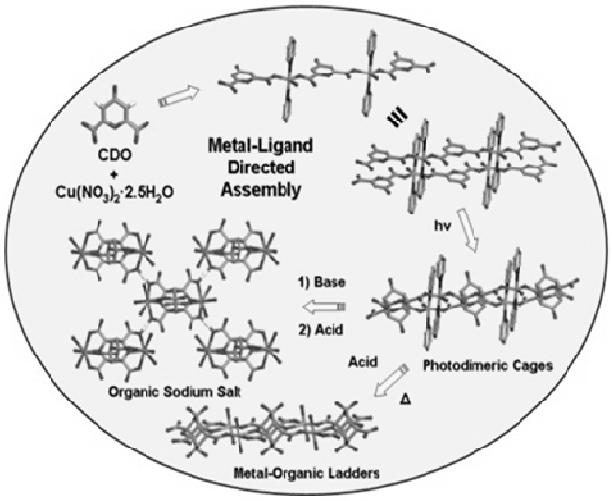


Photodimerization often leads to mixtures of products, especially when using complex olefins: CDO molecules can align a) head-to-head (parallel) or b) head-to-tail (antiparallel), which, depending on the proximity of the alkenes, can lead to a variety of photodimerization products: c) head-to-head anti, d) head-to-head syn, e) head-to-head cage, f) head-to-tail anti, g) head-to-tail syn, and h) head-to-tail cage photodimers. Blue = foreground, red = background, black = new bonds as a result of photodimerization.



The CDO ligands can also align antiparallel in sets of four (alternating head-to-tail-to-head-to-tail), which allows for multiple photodimerization pathways: a) the cyclobutane rings can form at alternating sides to give a ladderane-like molecule of syn photodimers, or dual cycloadditions can take place between b) the exterior or c) the interior CDO pairs to give one or two isolated cage photodimers, respectively. In order, from background to foreground are red, blue, green, and orange; black = new bonds as a result of photodimerization.

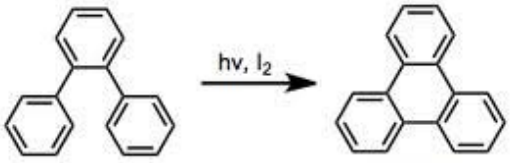
A more recent solution involves metal-ligand directed assembly of target molecules (e.g., formation of targeted metal-organic assemblies (MOAs)). To date, [2 + 2] photodimerization reactions via metal-ligand directed assembly are scarce, but our group, among others, has demonstrated its effectiveness in this pursuit, especially through single-crystal-to-single-crystal (SCSC) transformation. In addition, previous methods predominantly have been limited to only simple linear olefins (i.e., single or chain-type olefins functionalized for metal binding), whereas we have demonstrated the ability of our metal-ligand directed assembly method to target higher dimensional olefins and dimers (e.g., tetraasterane-like photodimeric cage molecules), which are of interest for biomedical applications (most-notably anti-HIV and anti-cancer activities).



Chelidonic acid can be used as a ligand in MOAs. Metal-ligand directed assembly leads to proper positioning of the CDO for photodimerization, resulting in photodimeric cage molecules that can be isolated and used for other applications or to synthesize new and interesting MOFs.

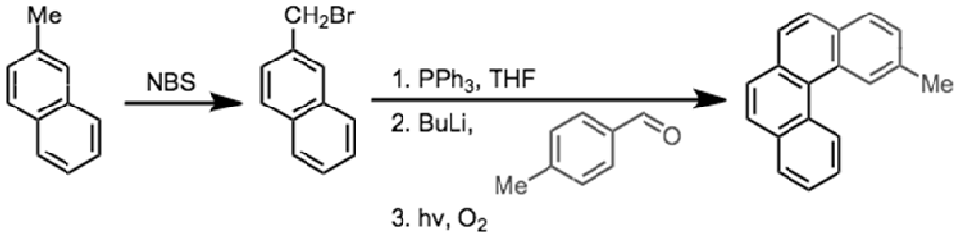
Photocyclization

Any intramolecular photochemical process leading to a ring system by formation of one new single bond, either by a concerted process (e.g., electrocyclization) or by multi-step processes such as the Norrish–Yang reaction.



Ex.1

Ex.



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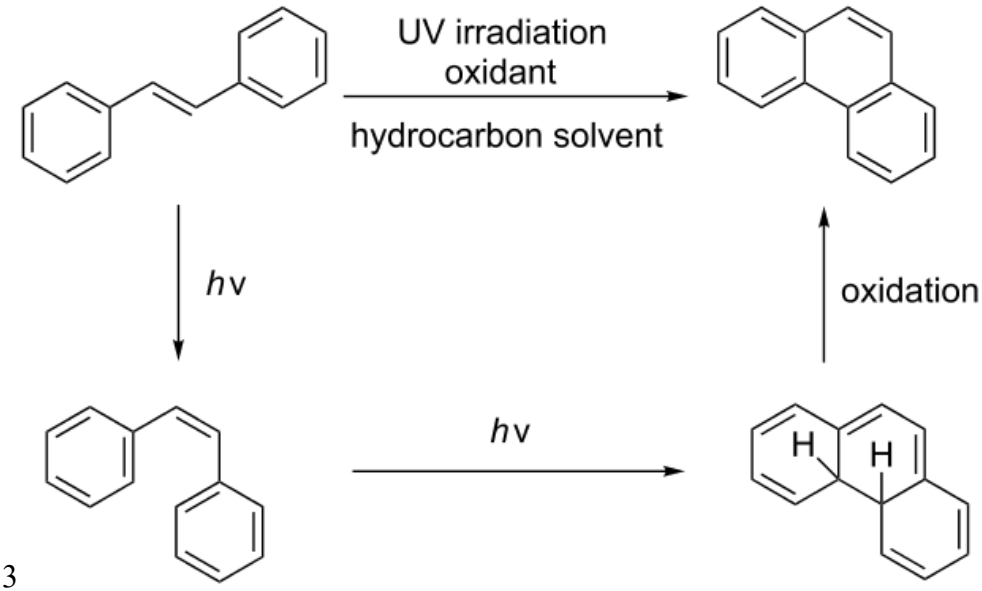
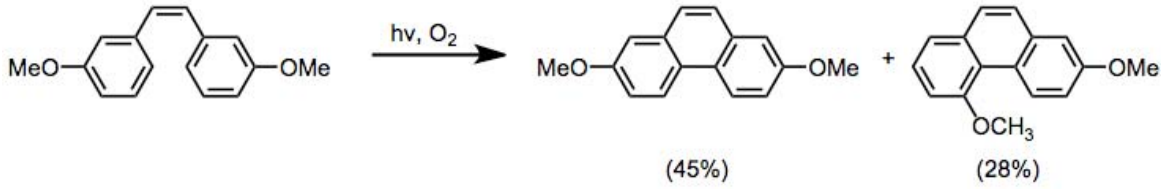
Ex.



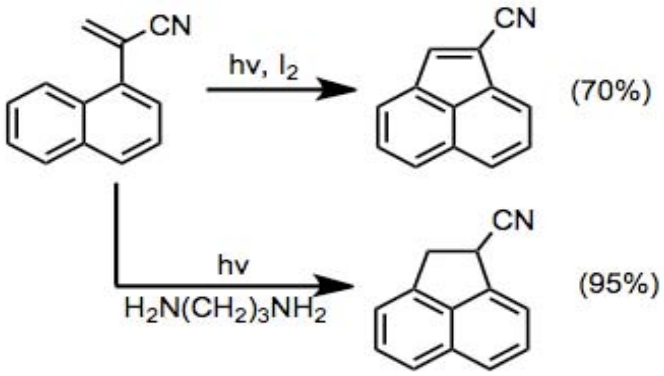
3

Photocyclization can be carried out with ortho-, meta-, and para-substituted stilbene substrates. ortho-Substituted substrates generally give 1-substituted phenanthrenes, unless the substituent is a good leaving group, in which case elimination to form

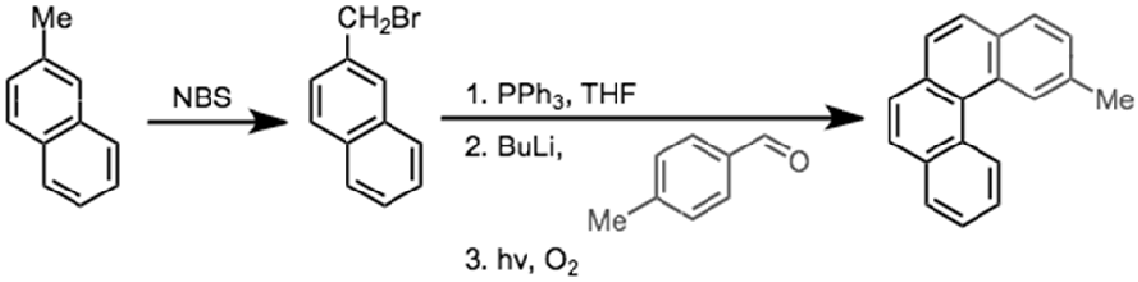
unsubstituted phenanthrene occurs. meta- Substituted substrates give mixtures of 2- and 4-substituted products.



Photocyclization can also form five-membered rings. In the vinyl naphthalene series, both oxidative and non-oxidative processes are possible; although the latter requires a proton-transfer catalyst.



Photocyclization can be used as the final step of a sequence to generate a fused aromatic ring at a benzylic position. After benzylic bromization with *N*-bromosuccinimide, transformation to the phosphonium salt, and a Wittig reaction with anaromatic aldehyde, photocyclization fuses the aromatic rings. Iteration of this sequence results in helicenes.



24.11 Summary

Chapter deals with increasing the knowledge of learner for photochemistry and its mechanism, reactions, applications and structure. It also explain brief about different

rearrangements and reactions with is a matter of recent research. Along with these it is also highlights the different types of reaction and photoisomerisation and its property used in photochemistry.

24.12 Questions:

1. Define organic photochemistry with giving suitable example.
2. Write a short note on Photodimerization and photocyclization.
3. Describe Di-pi-methane rearrangement in detail.
4. Explain the mechanism of the Paterno-Buechi Reaction
5. Write Norris type I and II reaction.

24.13 Reference and suggested reading:

1. Fundamentals of Photochemistry: K.K.Rohatgi Mukherjee
2. Introduction of Organic Chemistry: C.D.Coyle
3. F. Vogt, K. Jödicke, J. Schröder, T. Bach, *Synthesis*, 2009, 4268-4273