ORGANIC CHEMISTRY

(DCHE23)

(MSC - CHEMISTRY)

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UNIT - I

1.1.Ultra Violet and Visible Spectroscopy

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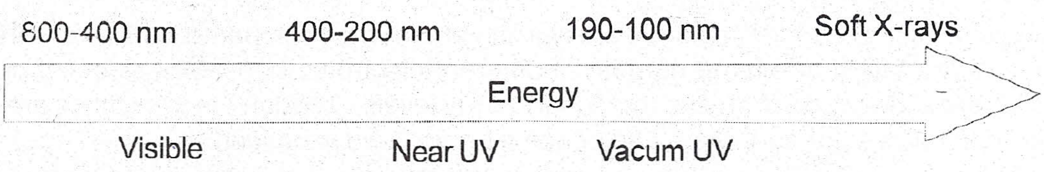
1.1. Ultra Violet and Visible Spectroscopy

1.1.1. Basic Principles :

Ultra violet and visible spectroscopy is primarily used to measure the multiple bonds or aromatic conjugation with in the molecules. The UV region starts from 200 - 400 nm and the visible region from 400 – 800 mm



When the electromagnetic radiation in UV and visible region passes through a compound with multiple bonds, a portion of the radiation is normally absorbed by the compound. The absorption depends on the wave length of the radiation and on the structure of the compound. The electrons in orbitals of lower energy are excited into orbitals of high energy by the absorption of radiation. Since the electrons are excreted in UV radiations, UV spectroscopy is also called as electronic spectroscopy. UV spectrum records the wave length of an absorption maximum (λ max) and the strength of the absorption. The extent of absorption is given as absorbance A, or transmittance T or ∈ (molar extinction coefficient also known as molar absorptivity, a measure of extent of absorption) or log ∈. The molar absorptivity as defined by the Beer Lambert's law gives the relation ship between ∈ and absorption

$$\log\frac{I_O}{I} = \in Cl \text{ or } \in = A/Cl \qquad A = \in C$$

Where I_O is the intensity of the incident radiation, I is the intensity of the transmitted radiation

A = Absorbance of the solution (optical density OD)

e = Concentration of the solution gram moles/lit (density OD) letter

l = Path length of the sample (in cm)

∈ = Molar absorptivity (extinction coefficient)

If the concentration (c) of the solute is now defined as grams perlitre then the equation becomes.

A = a c l

Where 'a' is the absorptivity and thus related to the molar absorptivity

∈ = a M

Where M is the molecular weight of the solute.

The maximum point of absorption band is indicated as λ max, which means that the position where maximum absorption. ∈ max, the molar extinction coefficient is the intensity of the band at the maximum.

1.1.2. Spectro photometer and spectrum recording

UV radiation can be generated from hydrogen / deuterium tube, while visible light can be obtained from tungsten filament. When the light (Polychromatic) is passed through the prism it is diffracted to monochromatic lights which are selectively passed through a mirror, split into two parallel beams – one passing through this solution containing the sample in appropriate solvent and other through the reference sample. The intensity of the transmitted beams of reference and sample are compared over the whole range of wavelength and is detected through photoelectric tubes generating alternating currents, which are then recorded.

Absorption bands of an UV spectrum are typically broad when compared to IR and NMR spectrum. This is due to the fact that a large number of different electronic transitions to occur between the several different allowed vibration and rotational energy levels. Though the transitions are quantized, the energy differences are very close and hence a broad band is noticed.

It is observed that only certain functional groups present in the molecule is responsible for the absorption of the light in the UV region or in the visible region and such groups are known as chromophores. Chromophore is an isolated functional group capable of absorbing visible and or UV radiation. Some of the typical chromophores are $C=C, C=N, N=N, C=O$, etc. There are certain other groups which are not directly responsible for the absorption but are capable of influencing the position and extent of absorption and the groups are known as auxochromes. An auxochrome is a functional group which does not absorb radiation longer than 200 nm but when attached to a given chromophore causes a shift in this absorption to a longer and shorter wave length and also increases the degree of absorption $-NH_2, -NHR, -OH, -OR$ etc are good auxochromes. A shift to longer wavelength absorption from original absorption is known as bathochromic shift or red shift while the shift to a shorter wavelength is known as hypsochromic shift or blue shift. An increase in intensity of absorption is called as hyperchromic effect while a decrease in the same is known as hypochromic effect.

1.1.3. Process of electronic excitation :

The bond formation between two atoms involve the over lap of two atomic orbitals each containing one electron leading to new molecular orbitals. One of them with lower in energy is bonding molecular orbital and the higher energy one is known as antibonding orbital. The bonding molecular orbital is filled with two paired electrons and this antibonding is supposed to be vacant. Some molecules have non-bonding orbitals with valence electrons. On absorption of energy by a molecule in the ultraviolet region, changes are produced in the electronic energy of the molecule due to transitions of valence electrons in the molecule. These transitions consist of the excitation of an electron from an occupied molecular orbital to next higher energy antibonding orbital. The antibonding orbital is indicated by an asterisk. The promotion of an electron from a π bonding orbital to an antibonding $\pi *$ orbital is designated as $\pi \rightarrow \pi *$ similarly $\eta \rightarrow \pi *$, $\pi - \sigma *$

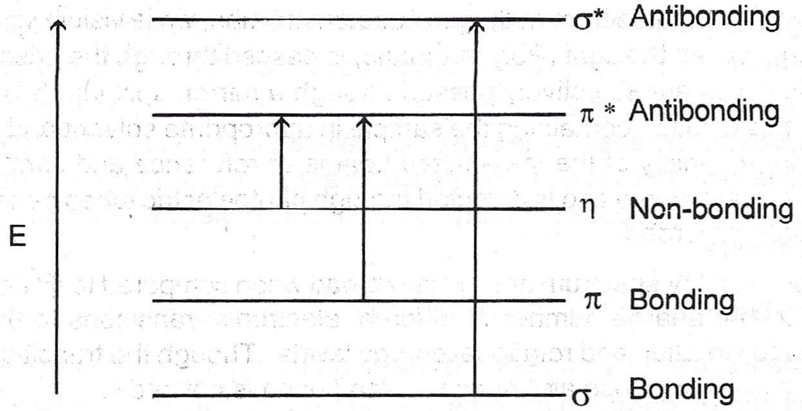


Figure - 1 : Energy levels of bonding, nonbonding and antibonding orbitals

1.1.4. Electronic transitions :

The relative energies of the more important orbitals is shown as above.

$\sigma-\sigma*$ Transition : The transition of an electron from a bonding sigma orbital to the higher energy antibonding sigma orbitals is designated as $\sigma-\sigma*$ and it is found in alkanes. Sigma bonds are in general strong, therefore it is a high energy process (Figure – 2) and these transition require very short wavelengths and high energy UV light such transition occurs in vacuum UV region i.e. below 200 nm

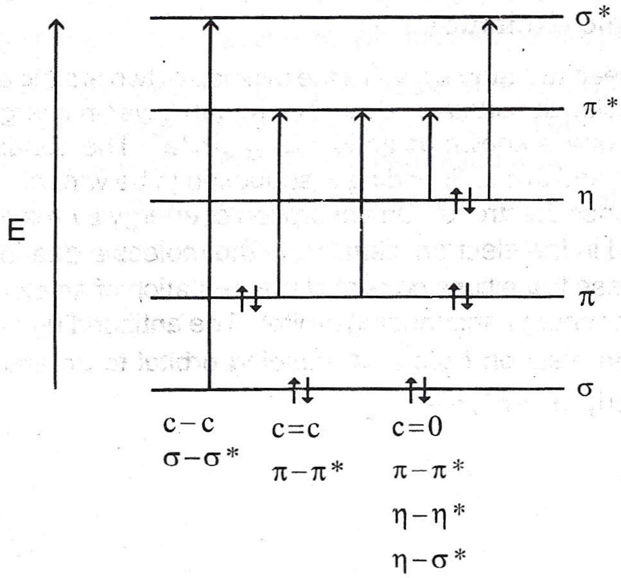


Figure - 2 : Various transition involved in UV spectroscopy

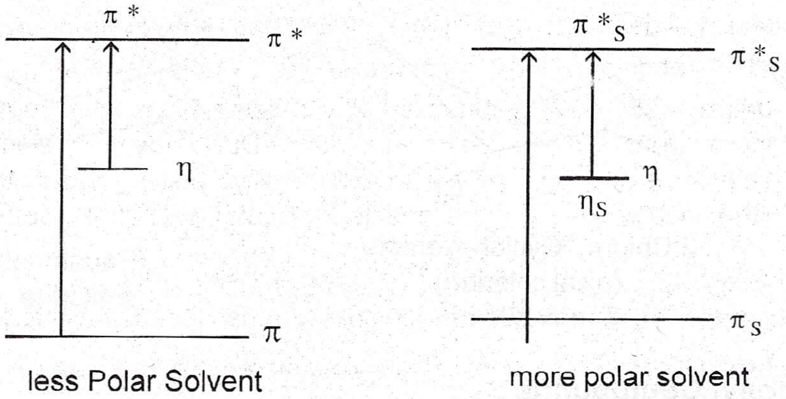
1.1.4.1. $\eta-\sigma^*$ **Transition :** It involves saturated compounds with one hetero atom with unshared pair of electrons, eg. Saturated halides, alcohols, ethers, aldehydes, ketones, amines etc. They require less energy than $\sigma-\sigma^*$ transitions. Water absorb at 167 ; methyl alcohol at 174; methyl chloride at 169 and methyl iodide at 258 nm. In saturated alkyl halides, the energy required for the transition decreases with the increase in the size of the halogen atom. Due to the more electronegativity of chlorine than to iodine the n electrons of chlorine atoms are comparatively difficult to excite. Therefore the transition is more easy in the case of methyl iodide and its molecules extinction coefficient is also higher than methyl chloride.

1.1.4.2. $\pi-\pi^*$ **Transition :** This type is found in the compounds with unsaturated centers like simple alkenes, aromatics, carbonyl compounds, etc. This transition requires less energy than $\eta-\sigma^*$ transition, this lowest energy transition absorbs around 170-190 nm in unconjugated alkenes. In the saturated ketoses the most intense bond occurs around 150 nm due to $\pi-\pi^*$ transition.

1.1.4.3. $\eta-\pi^*$ **Transition :** In this the electron of unshared electron pair on an hetero atom is excited to π^* antibonding orbital. It involves least amount of energy than all the transitions and so it gives rise to an absorption band at longer wave lengths. The $\eta-\pi^*$ transition in saturated aliphatic ketones is around 280 nm is the lowest energy transition. On the other hand the $\eta-\pi^*$ transition is a forbidden transition because the non - bonding orbital is orthogonal to π^* orbital with a poor overlap integral. Hence it leads to a very weak absorption, $\in$ value is less than 1000.

1.1.5. Effect of solvent on electronic transitions :

The solvents have absorption and they must be transparent with in the wavelength range being examined. The position and intensity of absorption b and may shift with the change in this polarity solvent in which it is being recorded. (Figure 3) The transitions of polar bonds like C=O, C=N are affected by solvent polarity. As this solvent polarity increases $\pi-\pi^*$ bands undergo red shifts (longer wavelength) while $\eta-\pi^*$ bands moves to lower wavelength region. A hypsochromic shift is observed in polar solvents if the ground state is relatively more polar than its structure in the excited state. In the other way if the excited state is more polar than the ground state, a bathochromic shift is observed. The polar solvents stabilize the π, π^* and n orbitals by salvation. The stabilization of n orbital is particularly pronounced with this by dragon. Bonding solvents and π^* is mole stabilized than π. This is because of this fact that π^* orbital is more polar.



Solvent effect

$\pi \text{ to } \pi^* > \pi_S > \pi^*_S$

$\eta \text{ to } \pi^* < \eta_S \text{ to } \pi_S$

Figure - 3 : Absorption on shift with change in polarity of the solvent

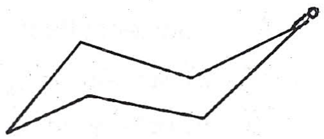
The energy of transitions for $\pi - \pi^*$ becomes less with solvation effecting red shift, while the energy of transition for $\eta - \pi^*$ becomes greater with solvation leading to blue shift when the solvent is changed from ethanol to other. The shift for a given solvent is as follows

Water = + 8 nm
Methanol = 0 nm
Chloroform = -1 nm
Dioxane = -5 nm
Diethylether = -7 nm
Hexane = -11 nm
Cyclohexane = -11 nm

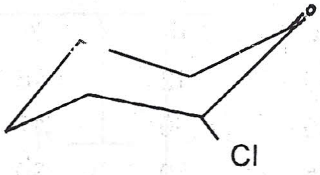
1.1.6. Ultraviolet band for carbonyl compounds :

Carbonyl compounds show characteristic absorptions due to the (non - bonding) lone pair of electrons on the oxygen atom. These non - bonding electrons are loosely held and excite to an antibonding orbital by lower energy UV radiation. Saturated aldehydes, and ketones show three absorption bands, two of them are observed in the far UV region. $\pi - \pi^*$ transition absorbs strongly near 150 nm and $\eta - \sigma^*$ transition absorbs at 190 nm. Third $\eta - \pi^*$ band appears in the near UV region 270-300 nm. This $\eta - \pi^*$ band is weak and symmetry forbidden band.

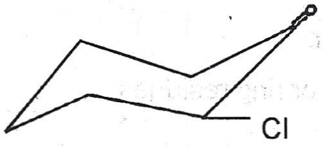
The introduction of polar substituents eg. a halogen on to the α-carbon; in the case of aliphatic ketone has no effect of the $\eta - \pi^*$ transition. In the case of cyclic ketones, the presence of similar substituents raise by 10-30 nm when it is axial and lower by 4-10 nm when it is equatorial, the λ max of the parent compound.



Cyclohexanane
X max 282 nm



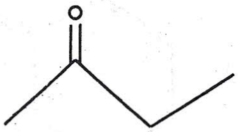
2 Chloro - Cyclohexanane
(axial chlorine)
X max 293 nm



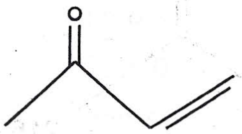
(Equatorial)
chlorine

1.1.7. Unsaturated Carbonyl Compounds :

Compounds in which a carbonyl group is conjugated with a carbon – carbon double bond have their absorption at longer wavelength due to a decrease in the difference between ground state and excited states. Thus both the $\eta-\pi^*$ and $\pi-\pi^*$ transitions are at longer wave lengths. The excited state is relatively more stabilized by conjugation than the ground state.



2 – butanone
$\eta-\pi^*\lambda$ max 277nm
$\pi-\pi^*\lambda$ max 185nm



3 – butene – 2 – one
$\eta-\pi^*\lambda$ max 324(24)
$\pi-\pi^*\lambda$ max 219(3,600)

Woodward Fieser rules : The conjugated carbonyl absorption is influenced by the structure and it was appreciated by Woodward. He compiled the rules for calculating λ max for α, β unsaturated carbonyl compounds. This helps us to study this structure of enones. With many extensions and verifications being added over the years, and summerised to calculate empirically the λ max of $\pi-\pi^*$ band of enones.

Acyclic or 6-membered α, β unsaturated Ketone (base value in ethanol) = 215 nm

5 membered α, β unsaturated ketone (base value in ethanol) = 202 nm

Acyclic or 6 membered aldehydes base value = 207 nm

Acids and esters [C=C-COOR & C=C-COOH] (Base value in ethanol) = 197 nm

α or β mono alkyl substituted acid or ester (base value in ethanol) = - 208 nm

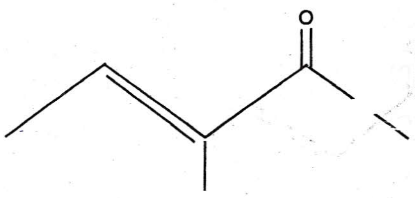
Additional conjugation = + 30 nm

If this double bond is homo annular = + 39 nm

Additional increments

Group	α	β	γ	δ
Alkyl or ring residues	10	12	18	18
Alkoxy	35	30	17	31
Hydroxy	35	30	30	50
Thioethes (-SR)	-	80	-	-
Chloro	15	12	12	12
Bromo	25	30	25	25
Acyloxy	6	6	6	6
Amino (NR2)	-	95	-	-
Exocyclic double bond		+5		

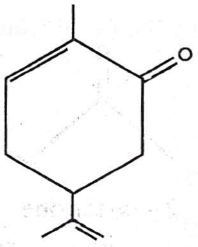
A few examples which serve to illustrate the application of these rules to a variety of α, β unsaturated carbonyl compounds.



3 - methypent 3 - enzone

215 (Base)
10 (α Subst.)
12 (β Subst.)

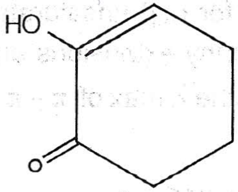
Calc. λ max 237 nm



Carvone

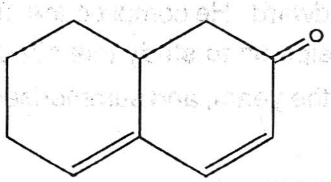
215 (Base)
10 (α Subst.)
12 (β Subst.)

Calc. λ max 237 nm



202 (base)
12 (β subst.)
35 (α subst.)

Calc. λ max 249 nm

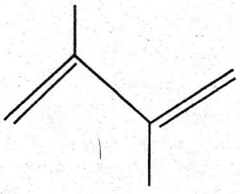


215 (base)
18 (γ Subst.)
18 (δ Subst.)
30 (extended double bond)
5 (exocylic)

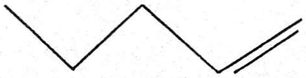
Calc. λ max 286 nm

1.1.8. Conjugated dienes

The absorption of conjugated dienes, trienes and polyenes moves progressively towards longer wavelength as the number of conjugated double bonds increases. 1,3 butadiene has the absorption maxima at 217 nm and this simple trans 1,3,5 hexatriene at 256 nm. 1,3 butadiene absorbs UV radiation of longer wave lengths than to ethylene. By adding more conjugated double bonds to a molecule, the energy required to reach the first excited decreases further. Thus more conjugated double bond in a compound longer will be this wavelength.



2,3 Dimethyl butadiene
Calc. λ max 217 + (2x5) = 227 nm
Obs. λ max = 226 nm

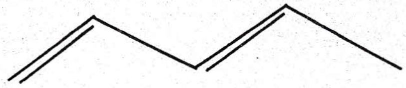


1,3 -Pentadiene
Calc. λ max 217 + 5 = 222 nm
Obs. λ max = 223 nm

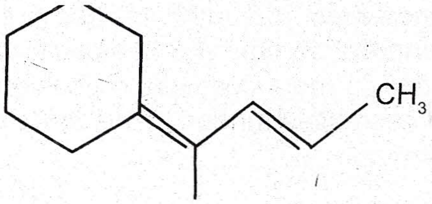
Woodward Fieser rules : In dienes and trienes, the position of the most intense band can be correlated in most instances with the substituents present. Based on the polarity of this substituents their contribution to this shift changes. The conjugated polyene system appears coloured in the visible light if there are more than five double bonds are present in conjugation. The presence of alkyl group on the double bond also causes bathochromic shift.

Conjugated diene and trienes (Solvent Ethanol)

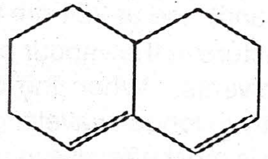
Butadiene system or cyclic conjugated diene	217 nm
Heteroannular type	214 nm
Homoannular type	253 nm
Extended double bond	30 nm
Exocyclic double bond	5 nm
Alkyl substituents or ring residues	5 nm
Auxochromes	
- OR	+ 6 nm
- SR	+ 30 nm
- NR_2	+ 60 nm
- OCO - CH_3	0 nm
- Cl, - Br (cyclic compounds)	+ 5 nm



Basic values	214
2 alkyl substituents	10 nm
Cal λ max	224 nm

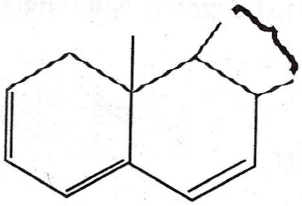


Basic values	214 nm
4 alkyl substituents	10 nm
exocyclic double bond	5
ring residues	10
Calc.λ max	239 nm



Basic values 214
3 ring residues 15
1-exocyclic double bond 5

Calc. λ max 234 nm



Basic values 253
3 rings residues 15
1-exocyclic double bond 5

Calc. λ max 273 nm

1.1.9. Conjugated Polyenes :

With the increase in the number of double bonds in conjugation the values of absorption maxima as well as intensity increase. Woodward rules work well for the conjugated systems of 4 double bonds or less. For conjugated polyenes having more than 4 double bonds the Fieser Kuhn rules are used. It is applied all trans lycopene to get the calculated absorption in case of (-CH = CH) n where n is $\geq$ 3 are given

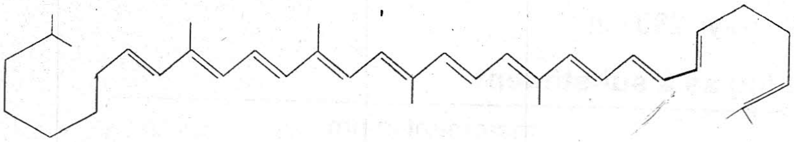
λ max (hexane) = $114 + 5M + n(48.0 - 1.7n) - 16.5\,R_{endo} - 10\,R_{exo}$ $\in_{max} = (1.74 \times 10^4)n$ where

n = no of conjugated double bonds

M = no. of alkyl or alkyl – like substituents on this conjugated system.

R_{endo} = no of rings with endocyclic double bond in conjugated system

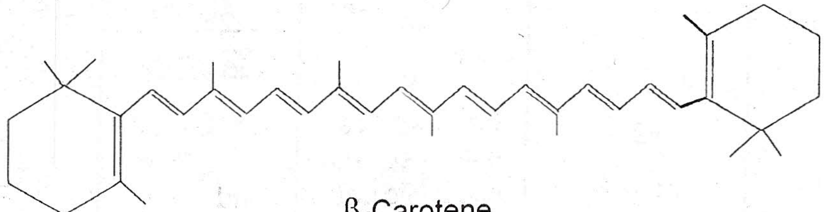
R_{exo} = no. of rings with exocyclic double bonds.



All trans lycopene

λ max (obs) 504 (170,000); 476 (186,000) nm

λ max (Calc) : 114 + 5 (8) + 11[48.0 – 1.7 (11)] –0 –0 = 476 nm.

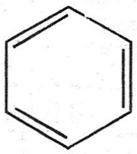


β-Carotene

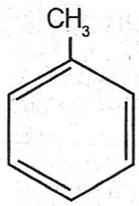
λ max (Calc.) = 453.3 nm ∈ max Calc. 19.1×10^4

λ max (obs) = 452 nm ∈ max obs $15.2. \times 10^4$

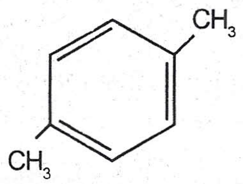
1.1.10. Ultrauviolet spectra of aromatic compounds and benzene shows three absorption bands at 184 nm (ϵ_{max} 60,000); 203.5 nm (ϵ_{max} 7,400) also called as K band) and at 254 nm (ϵ_{max} 204, often called B – band). The B – band shows a great deal of fine structure in the vapour phase. The fine structure diminishes if the spectrum is determined in polar solvents. When the benzene is substituted with simple alkyl groups the absorptions are shifted slightly to longer wavelength and the fine structure remains intact. The second alkyl group at para position is most effective in producing a red shift for polynuclear aromatic hydrocarbons moves to longer wavelength. The UV absorption as well as extinction coefficient are more for naphthalene as compared to benzene. Naphthalene absorbs at 580 nm (ϵ_{max} 12,600) and appears blue.



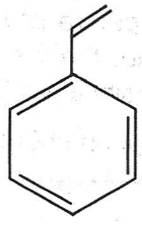
254 nm



261 nm

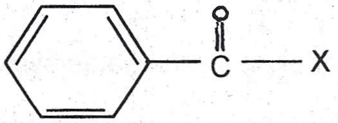


272 nm



282 nm

Rules for calculating absorption maximum for derivatives of acryl benzenes : Scott devised a set of rules to calculate the absorption maximum for the derivatives of acyl benzenes. These rules are helpful in estimating the absorption maxima for a number of mono and disubstituted aromatic aldekydes, ketones, acids and esters.



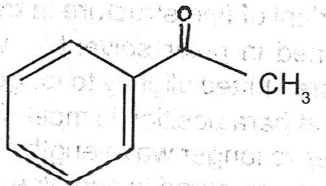
If X is an alkyl or alicyclic residence basic value is 246 nm

X is hydrogen this basic value 250 nm

X is hydroxyl or O – alkyl 230 nm

Auxochromes acting as a substituent

Auxochromic	Increment in nm		
	Position this substituent		
	Ortho	meta	para
Alkyl	+3	+3	+10
OH, OR	+7	+7	+25
Cl	0	0	+10
Br	+2	+2	+15
NH2	+13	+13	+58
NH AC	+20	+20	+45
NR_2	20	20	-85
O	11	20	75



Basic Values	246
Cl- para position	10 nm
Calcu.	256 nm
Obs. λ max	254 nm

1.1.11. UV Spectra of Heterocyclic compounds

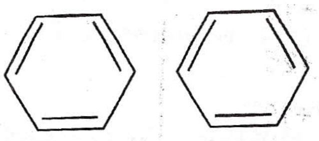
The UV spectra of five membered hetrocyclic aromatic compounds can be compared with cyclopentadiene, the cis diene analog, which shows strong diene, absorption near 200 nm and moderate intensity absorption at 238 nm.

UV absorption characteristics of five membered heterocyclic compounds.

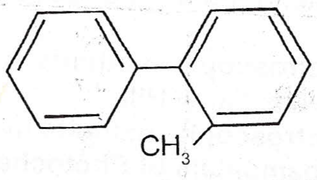
		I Band		II Band	
Parent	Substituent	X max (nm)	e max	x max nm	(e max)
Furan		200	10,000	252	1
	2-CHO	227	2,200	272	13,000
Pyrrole		183	-	209	6,730
	2-CHO	252	5,000	290	16,600
Thiophene		231	7,100		
	2-CHO	265	10,500	279	6,500
	2-Br	236	9,100	-	

1.1.12. Steric effect in biphenyls.

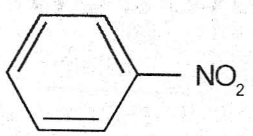
Woodward rules give reliable results only for those conjugated compounds which have no strain around the chromophore. In biphenyl if the π electron system is prevented from achieving copolarity, due to steric, crowding there is a marked shift in the absorption maximum and extinction coefficient. In the case of biphenyls and substituted biphenyls $\pi - \pi^*$ transition readily achieves copolarity, absorbs at 250 nm ∈ max 1900 but in 2 methyl biphenyl $\pi - \pi^*$ transition undergoes blue shift with diminished intensity as the two rings remain non planar.



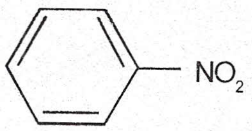
λ max 250 (∈ max 19,000)



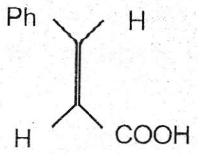
λ max 237 nm (∈ max 10,250)



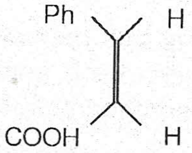
λ max 252 ($\in$ max 8,620)



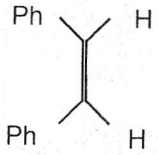
λ max 250 nm ($\in$ max 5,950)



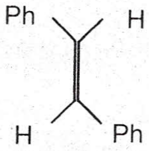
trans cinnamic acid
λ max 272 nm ($\in$ max 15,900)



cis-cinnamic acid
λ max 268 nm ($\in$ max 10,700)



cis - Stilbene
λ max 283 nm ($\in$ max 12,300)



trans - stilbene
λ max 295 nm ($\in$ max 25,000)

1.1.13 Suggested Readings

1. **Some Modern methods of Organic Synthesis, W. Carruthers, Cambridge University Press.**
2. **Advanced Organic Chemistry, Reactions Mechanisms and Structure, J. March. John Wiley**
3. **Advanced Organic Chemistry Part B, F.A. Carey and R.J. Sundberg, Plenum Press 1.**
4. **Spectrometric Identification of Organic Compounds, R. M. Silverstein, G.C. Bassler and T. C. Morrill, John Wiley.**
5. **Applications of Spectroscopy of Organic Compounds, J. R. Dyer, Prenctice Hall.**
6. **Spectroscopic methods in Organic Chemistry, D.H. Williams, I. Fleming, Tata Mc. Graw Hill**
7. **Spectroscopic methods in Organic Chemistry – Kemp**
8. **Fundamentals of Photochemistry, K.K. Rohtagi – Mukherji, Wiley – Eastern**
9. **Text Book of Organic Chemistry Vol I & II – I. L. Finar.**

1.2. INFRARED SPECTROSCOPY

Structure :

1.2. INFRARED SPECTROSCOPY

1.2.1. Introduction :

The absorption of infrared radiation by an organic compound causes the various bands in a molecule to stretch and bend. Some of the frequencies are absorbed and some other are transmitted without being absorbed. If we plot the percentage transmittance or percentage absorbance against wave number or frequency, infrared spectrum is obtained. The most important region for organic chemist is 4000 – 650 cm^{-1}or 2.5 – 15 μ. The absorption of 1R radiation can be expressed in terms of wave length or wave numbers. Generally IR spectra of organic compounds are plotted as percentage transmittance against wave number. The relation ship between wave length and wave number is as follows.

$$\text{Wavenumber} = \frac{1}{\text{Wave length in centimeters}}$$

$$\text{If the wave length is } 2.5\mu = 2.5 \times 10^{-4} \text{ cm}$$

$$\text{Wavenumber}(\bar{\nu}) = \frac{1}{2.5 \times 10^{-4}} = 4000 \text{ cm}^{-1}$$

The transitions of energy involved in infrared absorption are associated with vibrational changes with in the molecule. The molecules are constantly under going vibrations at room temperature. Each bond in the molecule has its characteristic stretching and bending vibrations which are quantized and are capable of absorbing light of that frequency lying in the IR region. The stretching vibration of two atoms connected to a bond can be compared to the vibrations of two balls attached to a spring. It requires more eneregy to stretch than to bend it. Thus stretching absorption of bond appears at higher frequency than the bending absorption of the same bond. For non linear polyatomic molecules, there will be 3n-6 nodes of vibration (3n-5 if linear) which include both stretching and bending vibrations.

1.2.2. Hooke's Law. Calculation of Vibrational frequency :

The stretching frequency ν of a bond with reasonable accuracy can be calculated applying Hooke's law of simple harmonic motions. The Hooke's law is $\nu = \frac{1}{2\pi (K/\mu)^{1/2}}$

Where μ = reduced mass is equal to $\frac{m_1 m_2}{m_1 + m_2}$

ν is the frequency of absorption

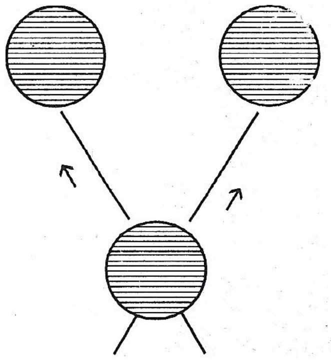
k = force constant of the bond m1 and m2 are the masses of the atoms attached to the covalent bond.

From the equation it is clear that the vibrational frequency of a bond will increase when the bond strength increases and also when this reduced mass of the system decreases. Thus greater the mass lower the frequency of absorption and carbonyl bond will have higher vibrational frequency than C-O bond and C-H will have higher frequency of absorption than C-O.

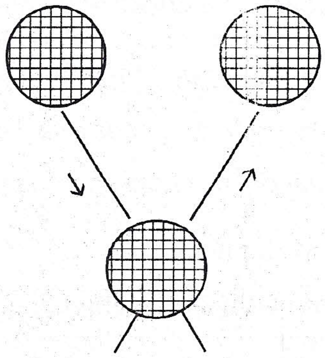
1.2.3. Molecular Vibrations :

In stretching vibration the distance between two atoms increases or decreases, however the atoms remain in the same bond axis. The vibration occur at higher frequency. In bending the distance between these atoms remain constant and position of this atoms may change.

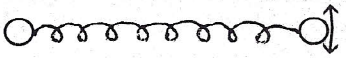
Streching Vibration



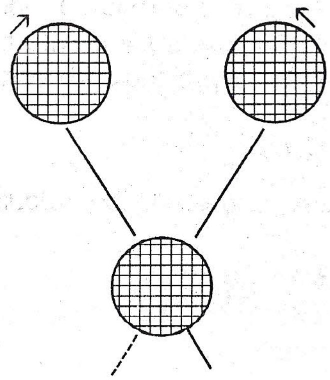
Symmetric



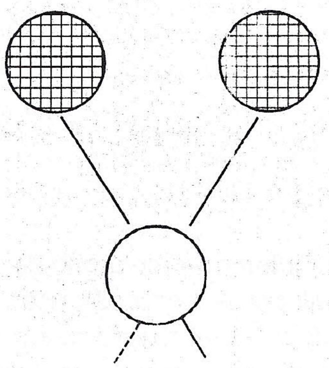
asymmetric



Bending Vibration



in plane



Out of plane

Some of the vibrations may have the same frequency - degenerate and their bands may overlap. Some vibrations may not be intense because a particular vibration should produce fluctuating dipole for it to be IR active. Otherwise it cannot interact with this fluctuating electric fields of the infrared light. So for vibration to be noticed in the spectrum it should lead to a change in the dipole moment of the molecule. Otherwise these vibrations will be IR inactive and will show less or no absorption. The absorption band intensity depends on the difference between the dipole moments of the molecule in the ground state and the vibrational excited state. Molecules with center of symmetry are IR inactive. Eg. CO_2

$O = C = O$

Overtone bands appear as weak at the integral multiplets of fundamental vibrations. A fundamental vibration at 800 cm^{-1} will give a overtone band at 1600 and 2400 cm^{-1} with decrease of intensities $\left(\frac{1}{10} \text{to} \frac{1}{100}\right)$. vibrational coupling occurs between two bands vibrating with similar frequencies if the band are close in the molecule. A fundamental vibration may couple with overtone of some other vibration and this coupling is called fermi resonance. Fermi resonance takes place when the overtone and fundamental vibration have the same symmetry property and they must be predominantly associated with a group of atoms in the same part of the molecule n-butyl vinyl ether shows Fermi resonance. The over tone of fundamental vibration at 810 cm^{-1} coincides with a band at 1640 cm^{-1}. The mixing of two bands in accordance with fermi resonance gives two bands at 1640 and 1630 cm^{-1}

1.2.4. Instrumentation :

A rod of silicon carbide or Nernst filament is heated electrically in this range of 1100-1800°C to produce IR radiations. The pulse beam is divided into two beams as reference beam and sample beam. When the beam passes through the sample, it becomes less intense due to absorption of certain frequencies. Now there is difference in this intensities of the two beams. Let I_0 be the intensity of the reference beam and I be the intensity of the beam after interaction with the sample

Absorbance : $A = \log\left(\frac{I_O}{I}\right)$

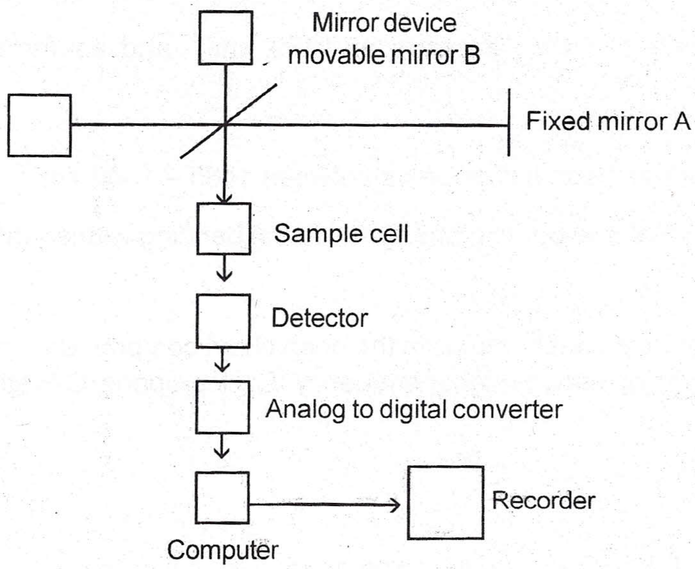
$$T = {}^{1}\!/_{I_O}$$

$$A = \text{Log}\left(\frac{1}{T}\right)$$

The detector (bolometer) changes its resistance upon heating with the radiation. The change in the temperature will cause an unbalanced signal across this circuit and the signal will be amplified and recorded. Poly styrene is used to calibrate this spectral chart.

The solid sample can be loaded by mixing with KBr in disc form. A blank disc is prepared with pure KBr and placed in the path of reference beam. KBr is transparent to the infrared region and a complete spectrum can be scanned by mixing 2% of solid sample with it. The solid samples can also be determined as a mull or a paste in nusol. Liquid samples placed as a thin film between two sodium chloride plates which are transparent to IR radiation. It is also most convenient to determine the IR spectrum in solution. Good solvents are those which have poor absorptions in IR region. Like

$CHCl_3$, CCl_4, CS_2 etc. are good solvents in IR. FT IR instrument contains a number of added advantages. A monochromator is not necessary in FT IR. Data undergo analog to digital conversion. Results of several scans are combined and hence a neat spectrum for small amount of sample can be obtained.



Schematic representation of FT IR spectrometer

1.2.5. Finger print region :

The region below 1500 cm^{-1} is rich in many absorptions which are caused by bending vibrations and the C-C, C-O and C-N stretching vibrations. The bending vibrations are more than stretching vibrations and this region is called finger print region. Some compounds contain the same functional group show similar absorption in functional group region (above 1500 cm^{-1}) but their spectra differ in finger print region. The compounds identity by IR spectra is much more characteristic than any other physical properties.

1.2.6. Applications of IR spectroscopy :

Infrared region (4000 – 650 cm^{-1}) is of prime importance for the study of an organic compound. All groups absorb characteristically with in a definite range.

1.2.6.1. Identification of an alkane residue : The compounds are made up of carbon and hydrogen only. Hydrocarbons are saturated, and unsaturated aliphatics cyclics or aromatics. Alkane residues are detected from C-H stretching and C-H bending absorptions. Most of the organic compounds possess alkane residve, C-H absorption bands in a spectrum are of little diagnostic value.

- The absorption due to C-H stretching occurs at 2840 – 3000 cm^{-1}

- $-CH_3$ group shows two distinct bands at 2962 and 2872 cm^{-1}. The former is due to asymmetric stretching and the latter is due to symmetrical stretching.
- $-CH_2$ - the asymmetrical stretching and symmetrical stretching occur at 2926 and 2853 cm^{-1} respectively
- Symmetrical bending of $-CH_3$ appears at 1375 cm^{-1} and asymmetrical bending near 1450 cm^{-1}
- $-CH_2$ group scissoring absorption appears between 1485 – 1340 cm^{-1}
- Gem diethyl exhibits in plane out of plane symmetrical bending with equal intensity at 1385 and 1370 cm^{-1}
- Cyclic alkanes absorptions are same as in the open chain compounds. However the ring strain moves the CH – stretching band to higher frequency. Cyclopropane, C-H stretching band appears at 3100 cm^{-1}

1.2.6.2. Alkenes :

- The = C – H stretching band absorbs at 3100-3040 cm^{-1}
- Non substituted = C – H (str)at 3040 – 3010 cm^{-1} and C-H bending at 700 cm^{-1} and 915 – 905 cm^{-1}.
- The C=C stretching band appears weakly at 1670 - 1640 cm^{-1}
- Conjugated C = C stretching band at 1600 - 1650 cm^{-1}
- When Fluorine is attached to olefinic carbon ν C=C increases, but when chlorine, bromine and iodine are attached it decreases.
- Due to ring strain in cyclic compounds then ν C=C is greater than unstrained cyclic and as well as open chain olefin.
- Cumulative alkene absorb around near 2000 – 3000 cm^{-1}

Alkynes :

- $\nu-C\equiv C-$ of alkynes occurs around 2260 – 2100 cm^{-1} symmetrically substituted alkynes no $\nu C\equiv C$ is observed
- Terminal alkynes give intense $\nu C\equiv C$ than non terminal ones.
- $\equiv C-H$ stretching band appears around 3350 – 3260 cm^{-1}
- $\equiv C-H$ bending appears around 650 – 610 cm^{-1}.

Aromatic Hydrocarbons

- $\nu Ar-H$ stretching band occurs is the region 3050 – 3000 cm^{-1}; $\nu C=C$ around 1650 – 1450 cm^{-1} and C-H bending vibrations at 900-700 cm^{-1}
- Monosubstituted benzene will be identified with a band at 710 – 690 cm^{-1} & 770 – 730 cm^{-1}
- Metasubstituted benzene shows two peaks at 710 – 690 and at 800 – 750 cm^{-1}
- Ortho, Para disubstituted benzene show one band each at 770-735 cm^{-1} and 840 – 800 cm^{-1} respectively.

1.2.6.3. Alcohols and phenols

$\nu O-H$ stretching band absorb at 3700-3500 cm^{-1}; $\nu O-H$ stretching intermolecular hydrogen bond region at 3400 – 3200 cm^{-1}; $\nu O-H$ stretching intramolecular hydrogen bond region at 3570 – 3450 cm^{-1}; chelate O-H stretching bond occurs in the region 3000-3520 cm^{-1}; primary alcohols $\nu C-O$ stretching bond region at 1350 – 1260 cm^{-1} another strong bond near 1050 cm^{-1} and secondary alcohols $\nu C-O$ stretching absorption at 1100 cm^{-1} in addition to another strong band at 1350 – 1260 cm^{-1}; $\nu C-O$ stretching region of tertiary alcohols can be distinguished due to appearance of strong bond at 1150 cm^{-1} and another region at 1410 – 1310 cm^{-1}; 1,2 cyclohexane diols in cis - form $\nu O-H$ stretching region at 3626 cm^{-1} in addition to another region 3600 cm^{-1}. The phenols free O-H stretching region at 3600 cm^{-1}; phehols show characteristic strong C-O stretching bond at 1200 cm^{-1} and another region at 1410 – 1300 cm^{-1}

1.2.6.4. Ethers, epoxides and peroxides

Aliphatic ethers exhibit strong bond around region at 1150 – 1085 cm^{-1} due to asymmetrical C-O-C stretching the symmetrical stretching of C-O-C is weak appearing around region at 1075 – 1020 cm^{-1}.

The aromatic ethers, the asymmetrical C-O-C stretching region at 1275 – 1200 cm^{-1}

$\nu C=C$ of vinyl ethers appear around at 1660 – 1610 cm^{-1}

1.2.6.5. Aldehydes & Ketones

The $\nu C=O$ of aliphatic ketone and cyclohexanes absorbs at 1715 cm^{-1}, while the aryl ketones exhibit at 1670 cm^{-1}. Aliphatic aldehyde $\nu C=O$ around region at 1740 – 1720 cm^{-1}. The hyper conjugative overlap of C-H in a ketone reduce its carbonyl double bond character and lower its $\nu C=O$ relative to aldehydes.

Aryl aldehydes occurs in the region at 1710 – 1685 cm^{-1} of $\nu C=O$ of $\alpha,\beta-$ unsaturated aliphatic aldehydes appears at 1705 – 1685 cm^{-1}

Aryl aldehydes with strong electronegative group is the ortho position may have its $\nu C-H$ as high at 2900 cm^{-1}

$\nu C-H$ bending region at 1390 cm^{-1} for aldehydes. Internal hydrogen bonding at $\nu C=O$ 1666 cm^{-1} (Salicylaldehyde) decreases $\nu C=O$

$\alpha_1\beta$ unsaturated ketones (saturated) $\nu C=O$ stretching region at 1685 – 1665 cm^{-1}

$\alpha_1\beta$ unsaturated (Five membered) $\nu C=O$ stretching regions at 1725 – 1710 cm^{-1}

$\alpha_1\beta$ unsaturated (Six membered) $\nu C=O$ stretching region at 1680 – 1665 cm^{-1}

Cyclohexanone $\nu C=O$ stretching region at 1725 – 1705 cm^{-1}

Cyclopentanone $\nu C=O$ stretching region at 1746 cm^{-1}

Cyclopropanone $\nu C=O$ stretching region at 1885 cm^{-1}

β Diketones usually exist is mixture of keto and enol form. The enolic form doesnot show the normal absorption of conjugated ketone. Instead, a broad bond appears in the region at 1640 – 1580 cm^{-1}, much intense than normal carbonyl absorption. This is due to intramolecular hydrogen bonding, the bonded structure being stabilized by resonance.

Quinones absorb at 1690 – 1655 cm^{-1} with conjugation it may shift to 1655 – 1635 cm^{-1}

1.2.6.6. Carboxylic acid

Carboxylic acids usually exist as dimers. Hence νOH appears in the region corresponding to hydrogen bonded OH at 3300 – 2500 cm^{-1}

$\nu C=O$ is very intense than ketones appearing around at 1760 cm^{-1} for monomeric aliphatic acid. For dimers it appears region at 1720 cm^{-1}

Internal hydrogen bonding decreases the $\nu C=O$ to a greater extent than intermolecular hydrogen bonding. Example salicylic acid absorbs at 1665 cm^{-1} while p-hydroxy benzoic acid absorbs at 1680 cm^{-1}

Aryl carboxylic acid $\nu C=O$ stretching absorbs at 1700 – 1680 cm^{-1} The carboxylate anion $\nu C=O$ stretching region at 1610 – 1550 cm^{-1}. Two bonds arising from C-O stretching and O-H bending appears near 1320 – 1210 and 1440 - 1395 cm^{-1}.

1.2.6.7. Esters, Lactones, acid halides and anhydrides.

The carbonyl stretching bond of saturated aliphatic ester appears in the region at 1750 – 1735 cm^{-1} where $\alpha_1-\beta$ unsaturated esters and benzoates have their $\nu C=O$ 1730-1715 cm^{-1} α–Halo substituents increases the $\nu C=O$ values saturated lactones have its $\nu C=O$ in the same region as in the case of esters.

$\alpha_1\beta$ unsaturated esters $\nu C=O$ stretching region at 1730 – 1715 cm^{-1}, β lactones $\nu C=O$ stretching absorbs at 1820 cm^{-1} γ-lactone $\nu C=O$ stretching region at 1780 – 1760 cm^{-1}, δ lactone $\nu C=O$ stretching absorbs at 1750 – 1735 cm^{-1}.

The $\alpha_1\beta$ unsaturated γ - lactones $\nu C=O$ stretching region at 1760 – 1740 cm^{-1}

The unconjugated acid halides absorb in the region at 1815 – 1785 cm^{-1}. While fluorides absorb at 1869 cm^{-1}; conjugated halides absorb at slightly lower frequency. The anhydrides display two stretching bonds in the carbonyl region due to asymmetric and symmetric stretching modes. Saturated anhydrides absorb near 1818 – 1750 cm^{-1}; while conjugated anhydrides absorb at 1775 – 1720 cm^{-1}. The higher frequency bond is more intense than the lower frequency bond.

The five membered $\alpha_1\beta$ unsaturated $\nu C=O$ stretching region at 1850 – 1800 cm^{-1} and another region at 1800 – 1750 cm^{-1}

1.2.6.8. Amides and Lactams : The NH stretching vibration for primary amides absorbs at 3520 – 3400 cm^{-1} as a doublet and moves to lower frequency if hydrogen bonded.

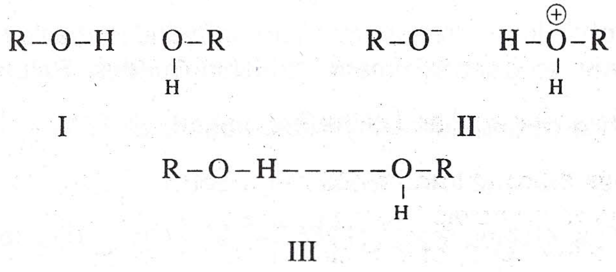
The secondary amides absorbs at 3500 – 3400 cm^{-1} for NH stretching; Tertiary amides $\nu C=O$ stretching region at 1670 – 1630 cm^{-1} while NH bending region at 1550 – 1610 cm^{-1} the β - lactams $\nu C=O$ stretching region at 1760-1730 cm^{-1} the γ - lactams $\nu C=O$ stretching region at 1700 cm^{-1} the δ - lactams $\nu C=O$ stretching region at 1680 cm^{-1}. The lactams exhibit similar features along with expected ring strain effects.

1.2.7. Effect of Hydrogen Bonding :

Hydrogen bonding brings about remarkable downward frequency shift stronger the hydrogen bonding, greater is the absorption shift towards lower wave number than the normal value. Two types of hydrogen bonds can be readily distinguished in infrared technique. Generally, intermolecular hydrogen bond gives rise to broad bands where as band arising from intramolecular hydrogen bonds are sharp and well defined. Intermolecular hydrogen bond are concentration dependent on dilution, the intensities of such bonds are independent of concentraction. The absorption frequency difference between free and associated molecule is smaller in case of intermolecular hydrogen bonding than that in intermolecular association.

Hydrogen bonding in O-H and N-H compounds deserve special attention. Mostly non-associating solvents like carbon disulphide, chlorofrom, carbontetrachloride are used because some solvents like benzene, acetene etc., influence O-H and N-H compounds to a considerable extent. The nitrogen atom is less electronegative than an oxygen atom. Hydrogen bonding in amines is weaker than that in alcohols and thus, the frequency shift in amines are less dramatic. For example, amine show N-H stretching at 3500 cm^{-1} in dilute solutions while in condensed phase spectra, absorption occurs at 3300 cm^{-1}.

In aliphatic alcohols, a sharp bond appears at 3650 cm^{-1} in dilute solutions due to free O-H group while a broad band is noticed at 3350 cm^{-1} due to hydrogen bonded O-H group. Alcohols are strongly hydrogen bonded in condensed phases these are usually associated as dimers and polymers which result in the broadening of bands at absorption frequencies. In vapour state or in inert solvents molecules exist in free state and absorbs strongly at 3650 cm^{-1}. Alcohols can be written in the following resonating structures.



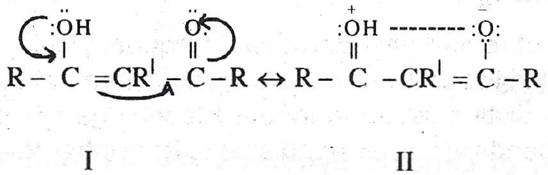
$$\underset{\text{I}}{\mathrm{R{-}O{-}H}\quad \underset{\mathrm{H}}{\mathrm{O}}{-}\mathrm{R}} \qquad \underset{\text{II}}{\mathrm{R{-}O^{-}}\quad \mathrm{H{-}}\underset{\mathrm{H}}{\overset{\oplus}{\mathrm{O}}}\mathrm{{-}R}}$$

$$\underset{\text{III}}{\mathrm{R{-}O{-}H{-}{-}{-}{-}{-}}\underset{\mathrm{H}}{\mathrm{O}}\mathrm{{-}R}}$$

Resonating structure of alcohols.

Structure III is the hydrid of structures I and II. This results in the lengthening of the original O-H group. The electrostatic force of attraction with which hydrogen atom of one molecule is attracted by the oxygen atom of another molecule makes it easier to pull hydrogen away from the oxygen atom. Thus, small energy will be required to stretch such a bond (O-H) and hence absorption occurs at lower wave number.

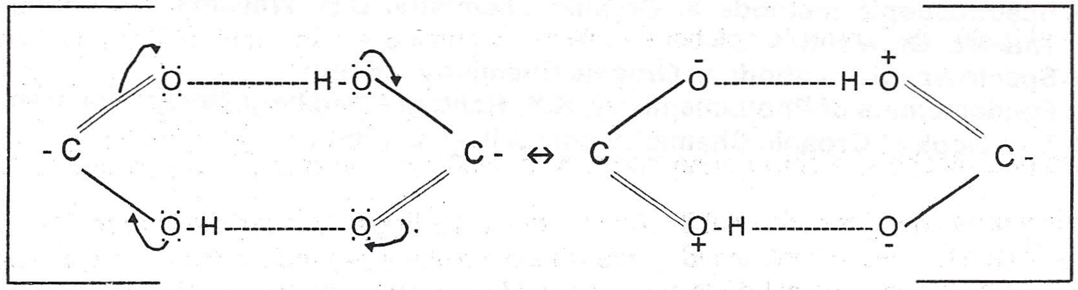
Hydrogen bonding in enols and chelates are particularly strong and absorption due to O-H stretching occurs at very low values. As these bonds are not broken easily on dilution by an inert solvent free O-H stretching may not be seen at low concentrations. It is due to the fact that the bonded structure is stabilized by resonance consider acetyl acetone.



The O-H group involved in chelation gives rise to broad absorptions between 3000-2500 cm^{-1}.

The ν_{co} absorption is the enolic form occurs at 1630 cm^{-1} and that in the keto form at 1725 cm^{-1}. From the intensities of the two peaks it is possible to determine the quantities of the enolic and the ketonic forms.

Mostly the acids exist as dimers and bridges formed as stabilized by resonance.



The formation of bridges lowers the force constant and thus $\nu C=O$ and $\nu O-H$ decrease. The larger decrease in the frequency in these dimers indicates the exceptional strengths of hydrogen bonds.

The carboxylic acid dimers very broad at 3000 – 2500 cm^{-1} due to O-H stretching. In vapour phase $\nu C=O$ absorption occurs at 1770 cm^{-1} in acetic acid and is the liquid state, absorption band appears at 1739 cm^{-1}. The benzoic acid shows a broad band at 3000 – 2500 cm^{-1} due to O-H stretching. π cloud interactions are also noted when acidic hydrogen interacts with Lewis bases such as alkenes and benzene. For examples, the frequency of O-H stretching in phenols is lowered by 40 – 100 cm^{-1}. When spectrum is taken in benzene solution as compared to that in carbon tetrachloride solution. Due to this interaction, lengthening and hence weakening of O-H bond occurs.

It is possible to distinguish between intermolecular and intramolecular hydrogen bonding by IR spectroscopy. As the dilution increases, there will be no change in the appearance and position of the hydroxyl stretching band in the case of intramolecular hydrogen bonded system but that will go on changing as the dilution progresses in the case of intermolecular hydrogen bonded system.

1.2.8. Suggested Readings

10. Some Modern methods of Organic Synthesis, W. Carruthers, Cambridge University Press.
11. Advanced Organic Chemistry, Reactions Mechanisms and Structure, J. March. John Wiley
12. Advanced Organic Chemistry Part B, F.A. Carey and R.J. Sundberg, Plenum Press 1.
13. Spectrometric Identification of Organic Compounds, R. M. Silverstein, G.C. Bassler and T. C. Morrill, John Wiley.
14. Applications of Spectroscopy of Organic Compounds, J. R. Dyer, Prenctice Hall.
15. Spectroscopic methods in Organic Chemistry, D.H. Williams, I. Fleming, Tata Mc. Graw Hill
16. Spectroscopic methods in Organic Chemistry – Kemp
17. Fundamentals of Photochemistry, K.K. Rohtagi – Mukherji, Wiley – Eastern
18. Text Book of Organic Chemistry Vol I & II – I. L. Finar.

UNIT - II

2.1. Nuclear Magnetic Resonance Spectroscopy

Structure :

2.1. Nuclear Magnetic Resonance Spectroscopy

2.1.1. General Introduction :

Nuclear magnetic resonance spectrometry is basically absorption spectrometry just like UV or IR spectroscopy under appropriate conditions in a magnetic field, a sample can absorb electromagnetic radiation in the radio frequency (rf) region. A plot of frequencies of this absorption peaks versus peak intensities constitutes an NMR spectrum. All nuclei carry a charge and in some nuclei this charge 'spins' on the nuclear axis, and this circulation of nuclear charge generates a magnetic dipole along the axis. The angular momentum of the spinning charge can be described in terms of spin numbers (I) and they have values of 0, $\frac{1}{2}$, 1, $\frac{3}{2}$, etc... The spin number (I) can be determined from the atomic mass and atomic number.

	Atomic mass	Atomic number	Example (I)
Half-integer	odd	odd or even	$^{1}_{1}H(1/2)$, $^{17}_{8}O\left(\frac{5}{2}\right)$, $^{15}_{7}N\left(\frac{1}{2}\right)$
integer	Even	odd	$^{2}_{1}H(1)$, $^{14}_{7}N(1)$, $^{10}_{5}B(3)$
Zero	Even	Even	$^{12}_{6}C(O)$, $^{16}_{8}O(O)$, $^{34}_{16}S(O)$

Several nuclei (eq $^{1}_{1}H$, $^{3}_{1}H$, $^{13}_{6}C$, $^{15}_{7}N$, $^{19}_{9}F$, $^{31}_{9}P$) have spin number I of ½ and a uniform spherical charge distribution. Nuclei with spin number I of 1 or higher have non spherical charge distribution. Such a magnetically active nucleus is placed in an external magnetic field, the nuclei, tiny bar magnets, will take up definite orientation which are quantized. The number of possible orientations will be given the equation N = 2I + 1, where I is the spin number of nucleus under consideration. Each orientation is associated with definite energy and the energy of each state can be defined. The energy difference between adjacent levels can be given by this expression $\Delta E = h\nu$

h = Planks constant

ν = Frequency of electromagnetic radiation

It is found that $\omega = \nu H_O$

ω = angular processional velocity

H_o - Applied field in gauss

ν - Gyromagnetic ratio = $\frac{2\pi\mu}{hI}$

μ = Magnetic moment of the nuclei

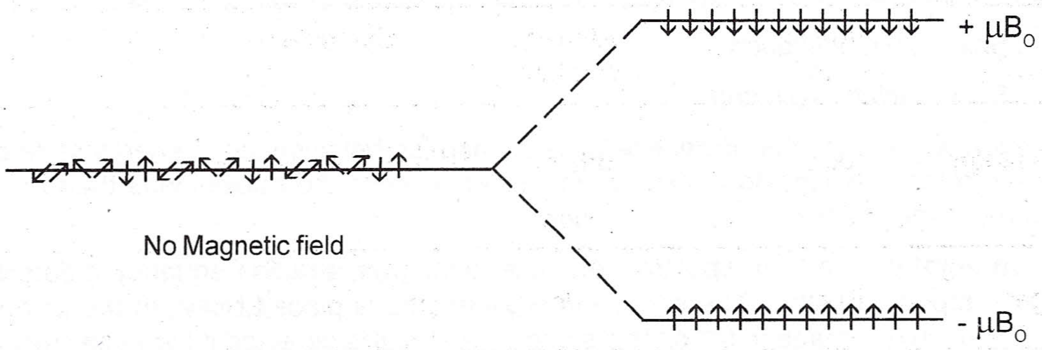
I = Spin number of the spinning magnetic

According to the fundamental NMR equation which correlates electromagnetic frequencies with the magnetic field we say $\nu H_O = 2\pi\nu$

ν = Frequency of electromagnetic radiation.

The value of the frequency ν = inserted is called precessional frequency.

For a nucleus with I = ½ this number of possible orientations in a magnetic field will be 2I + 1 $\left({}^{1}H,\ {}^{13}C,\ {}^{19}F\right)$ and taking up one of the two orientations with respect to the external field



i) Alignment with the field and

ii) Alignment against the field

When a proton is pressing this aligned orientation, it can pass into the opposed orientation by absorbing energy. From the high energy opposed orientation it comes back to the low energy aligned orientation by losing energy.

The transition from one energy state to the other is called flipping of the proton. The transition between two energy states can be brought about by the absorption of quantum of electromagnetic radiation in the radiowave region with energy hν. The energy required to bring about the transition depends upon the strength of this external field. Stronger the field greater will be the tendency of the nuclear magnet to remain lined up with it and higher frequency of radiation needed to flip the proton to the higher energy state.

We know that $\nu = \frac{\nu H_O}{2\pi}$

ν = Frequency in cycles per sec or Hz

H_o = Strength of the magnetic field in gauss

γ = Nuclear constant or Gyromagnetic ratio and is equal to 26750 for ten proton.

At 14092 gauss (1.4T) this energy required to cause flipping corresponds to electromagnetic radiation of frequency 60 million cycles per second or 60 MHz. When we irradiate this precession nuclei with a beam of electromagnetic radiation of desired frequency, then the low energy nuclei will absorb it and move to higher energy state. The precession proton will absorb energy from the radio frequency region only if the precession frequency is the same as the frequency of the radio frequency beam, then the nucleus and radio frequency beam are in resonance. Hence it is called nuclear magnetic resonance.

Relaxation Process : When the population in the two energy states becomes equal, equilibrium is established and thereafter no further absorption of energy by the nuclei. However, there is a process known as relaxation which retain the small excess population in the lower energy state through out the irradiation process.

Relaxation process involve non-radiative transitions by which a nucleus in an upper transition state return to lower spin state. There are two kinds of such relaxation process.

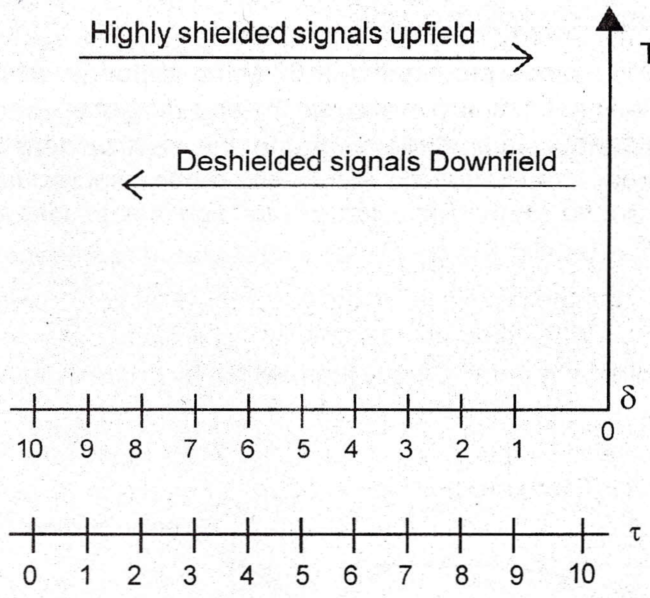
i) Spin – Spin relaxation

ii) Spin – lattice relaxation

In the former process the nuclei energy is exchanged between lower energy state and higher energy state in the surrounding nuclei. In this latter process the nuclei loose their energy to the surroundings, to the lattices.

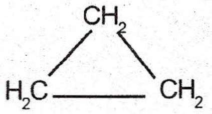
Instrumentation : In NMR spectrophotometer a magnet, a radio frequency, a detector and an amplifier are important parts. The sample in a glass tube is placed between the pole faces of a magnet. A R_f source is made to fall on this sample. A signal is detected if the nuclei resonates with the source, i.e. energy required to flip the proton is the same as that of the source. The spectrum can be obtained either by CW scan or pulse FT. Generally protons in a molecule being in different electronic environments cannot resonate at the same frequency. For practical purposes the radio frequency source is held constantly and field strength is varied. Peaks are measured by an electronic integrator that traces the height proportional to the peak area. Peak positions are measured in frequency units from a reference peak.

Chemical shift : The nucleus is shielded to a small extent by its electron cloud and whose density varies with this environment. This variation gives rise to different absorption positions usually within the range of about 750 Hz in a magnetic field corresponding to 60 MHz. The electrons under the influence of a magnetic field will circulate, and will generate their own magnetic field opposing the applied field, and hence the shielding effect. The degree of shielding depends on the density of ten circulating electrons and also on the inductive effect of other groups attached to this carbon atoms. The difference in the absorption position of a particular proton from the absorption position of a reference proton is called as chemical shift of that particular proton. Generally Tetramethylsilane is useful as reference compound.



Chemical Shift

Chemical shift for various types of protons

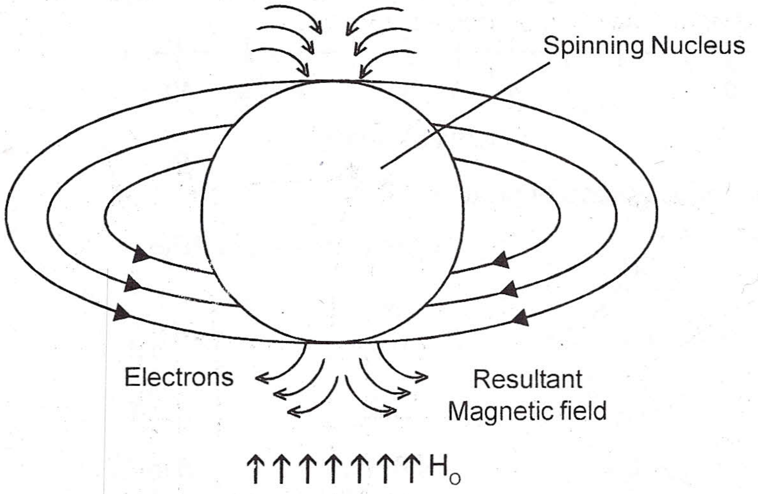
Types of protons		Chemical shift in PPM	
		δ	τ
Cyclopropane		0.2	9.8
Primary	$R-CH_3$	0.9	9.1
Vinylic	C = C-H	4.6-5.8	5.4-4.2
Acetylenic	$C\equiv C-H$	2-3.5	8-6.5
Aromatic	Ar-H	6-9.0	4-1.0
Flourides	H-C-F	4-4.5	6-5.5
Chlorides	HC-Cl	3-4	7-6
Alcohols	H-C-OH	3.4-4	6.6-6
Ethers	H-C-OR	3.3-4	6.7-6
Esters	H-C-COOR	2-2.2	8-7.8
Acids	H-C-COOH	2-2.5	8-7.5
Aldelydic	RCHO	9-10	1-0
Hydroxly	R-OH	1-5.5	9-4.5
Pheolic	Ar-OH	4-12	6 to -2
Enolic	C=C-OH	15-17	-5 to -7
Carboxylic	RCOOH	10.5-12	-0.5 to -2

2.1.2. Shielding and deshielding effects :

Hydrogen nuclei in a molecule are surrounded by the electronic charge which shields the nucleus from the influence of the applied field. Thus to overcome the shielding effect and to bring the protons it resonance, greater external field is required clearly greater the electron density around the proton, greater will be induced secondary magnetic field which opposes the applied field and thus, greater external field will cause protons absorption. The extent of shielding is represented interms of shielding parameter α. When absorption occurs, the field H felt by the proton represented as

$$H = H_O(1-\alpha) \text{---------------} (1)$$

Where H_o is the applied field strength. Clearly the field felt by proton does not corresponding to the applied field.



Diamagnetic Shielding about the Nucleus

Greater the value of α greater will be the value of applied field strength which has to be applied to get the effective field required for absorption

$$V = \frac{\nu H}{2\pi} \text{--------------------------} (2)$$

From 1 and 2

$$\nu = \frac{\nu H_O(1-\alpha)}{2\pi}$$

From this relation, it is clear that the protons with different electronic environments or with different shielding parameter can be brought into resonance in two ways.

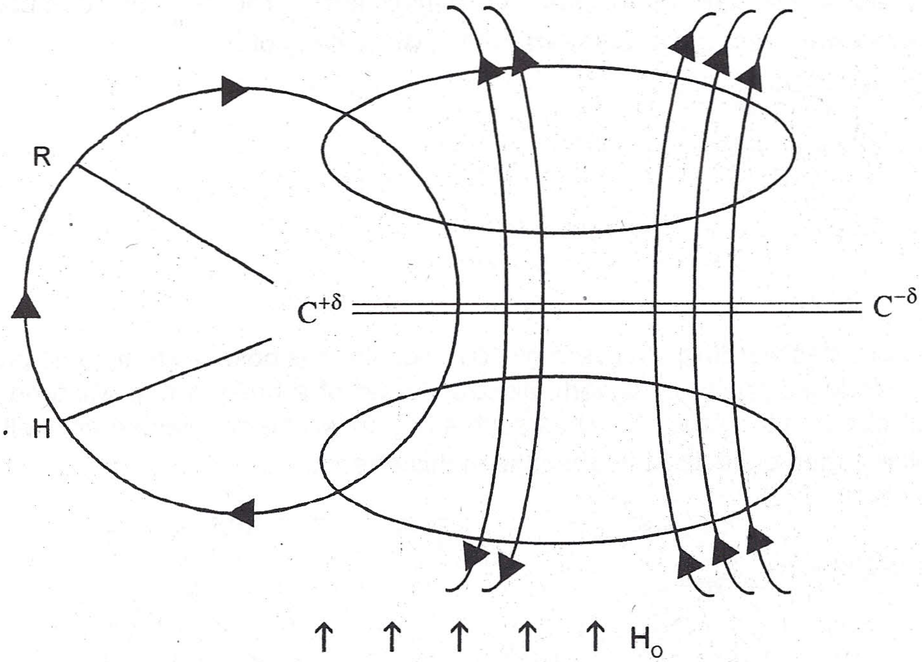
1) The strength of the external field is kept steady and the radio frequency is constantly varied.

2) The radio frequency is kept steady and the strength of the applied field is constantly varied.

The constant radio – frequency shielding shift the absorption upfield in the molecule where there is a spherical distribution of electrons around the proton. It is called positive shielding, presence of the electronegative atoms or groups cause reduction in electron density around the proton (deshielding) and thus absorption is shifted downfield (decreases) the diamagnetic and the paramagnetic effects from the neighbouring atoms and also the effects from the interatomic currents which results in the proton absorption shift.

It has been found that the absorption depends upon the manner in which the π electrons circulate under the influence of the applied field in case of ethene oriented at right angles to the direction of the applied field, the included magnetic field is diamagnetic around the carbon atoms and is paramagnetic in the region of protons. Thus protons fell more magnetic field and hence absorption occurs at low field. Similarly, aldehydic protons appear at low field.

In the case of acetylene, the proton experience a diamagnetic shielding effect. The induced magnetic field at the protons is diamagnetic but paramagnetic at the carbon atom. Thus, protons are said to be shielded and hence absorption occurs upfield.



Deshielding of aldehydic proton.

In case of olefins, acetylenes aldehydes, ketones, acids, esters, nitrides etc, if the proton is present in the positive region, it will be shielded and absorption occurs upfield. On the otherhand if the proton lies in the negative region, its absorption is downfield. In the case of benzene and other aromatic compounds strong diamagnetic currents are induced by the applied field this causes paramagnetic shielding at the aromatic protons and thus, absorption occurs downfield on the otherhand any group which is present above or below the plane of the aromatic nucleus will be shielded and absorption for such a proton occurs upfield ring current effect as is seen in benzene and other aromatic compounds is absent in saturated hydrocarbons.

Factors influencing chemical shift : Following are the factors which influence the chemical shift

a) Inductive effect
b) Vanderwaal's deshielding
c) Anisotropic effects
d) Hydrogen bonding

a) Inductive effect : A proton is said to be deshielded if it is attached with a electronegative atom or group. Greater the electronegativity of the atom, greater is the deshielding caused to the proton. If the desshielding is more for a proton, then its δ value will also be more consider the following compounds.

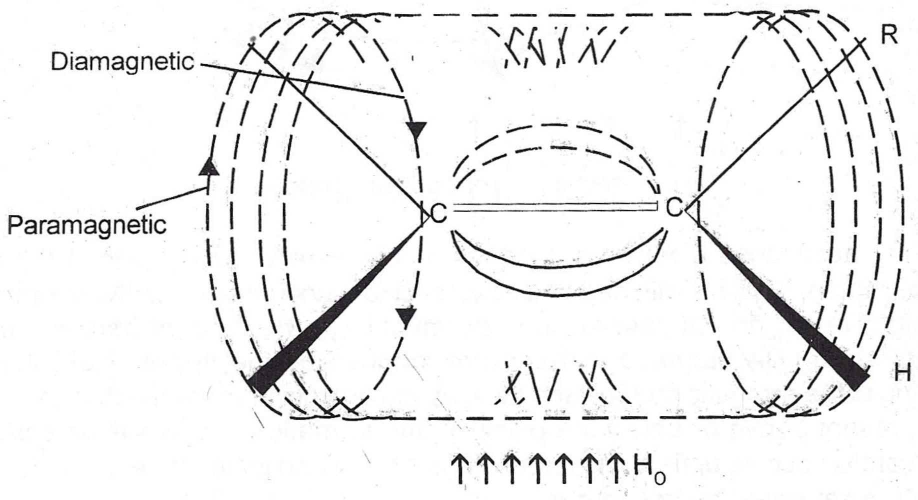
$$\text{1) } \overset{b}{CH_3}\ \overset{a}{CH_2}\ F \qquad\qquad \text{II)} \overset{b}{CH_3}-\overset{a}{CH_2}-Cl$$

Two signals are expected for each of the two compounds. Deshielding for protons 'a' is compound (I). Is more than that for similar proton in compound (II). As the distance from the electronegative atom decreases, the deshielding effect due to it diminishes. Protons b are comparatively less deshielded and hence will resonate at comparatively lower values of δ.

Tau value for CH_3 protons

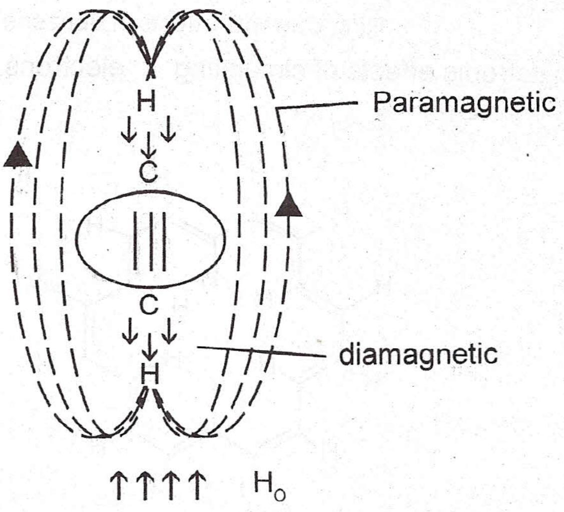
Compound	δ Value
CH_3 F	4.25
CH_3 Cl	3.1
CH_3 Br	2.64

b) Vanderwaal's deshielding : In overcrowed molecules it is possible that some proton may be occupying slighty hindered position. Clearly electron cloud of a bulky group will tend to repel the electron cloud surrounding the protons. Thus such a proton will be deshielded and will resonate at slightly higher value δ then expected the absence of this effect.



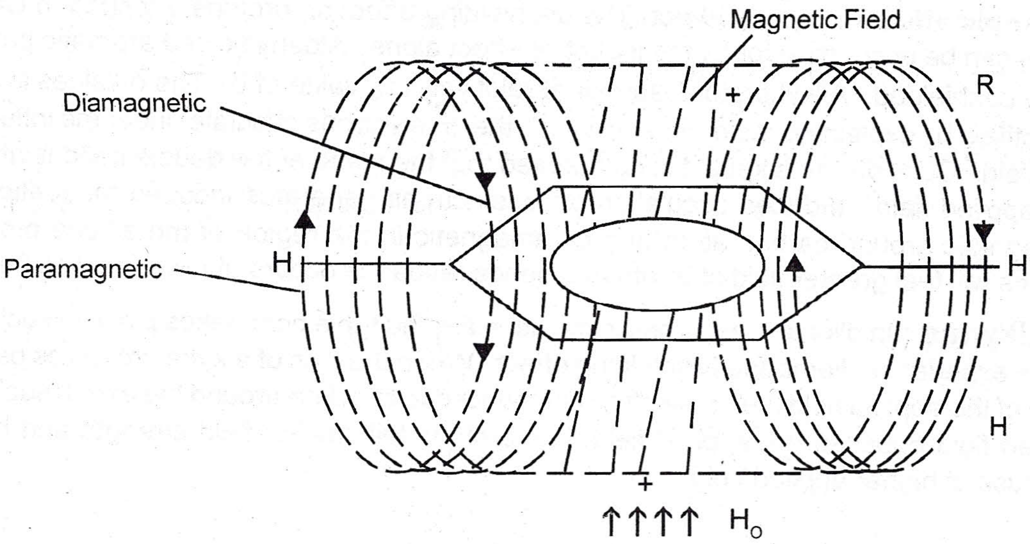
c) Anisotropic effects : (Space effect) The deshielding effect on protons attached to C=C is higher than that can be accounted for by the inductive effect alone. Aldehydic and aromatic protons are much more deshielded. Allkyl protons appear at relatively low value of δ. The δ values in each case can be justified by explaining the manner in which the π electrons circulate under the influence of the applied field. Consider an alkene it is so oriented that the plane of the double bond is at right angles to the applied field. Induced circulation of π electrons generates induced magnetic field which is diamagnetic around carbon atom and paramagnetic in the region of the alkene protons. Thus the protons will feel greater field strength and hence resoance occurs at lower applied field.

2.1.3. Alkynes : In alkynes, electronic circulation around triple bond takes place in such way that the protons experience diamagnetic shielding effect. When the axis of alkyne group lies parallel to the direction of the applied field the π electron are induced to circulate around the axis in such way that the induced field opposes the applied field thus protons fell smaller field strength and hence resonance occuss at higher applied field.



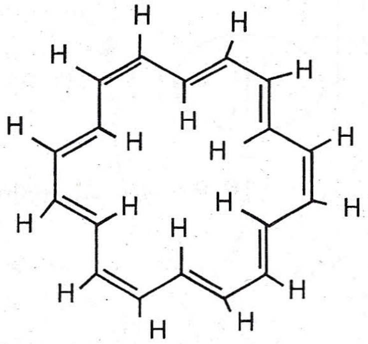
Shielding of acetylene protons

Benzene : In case of benzene, loops of π electrons are delocalised cylindrically over the aromatic ring. These loops of electrons are induced to circulate in the presence of applied field producing ring current. The induced current is diamagnetic in the center of the ring and is paramagnetic out side the ring. Thus the aromatic protons experience a magnetic field greater in magnitude than the applied field such protons are said to deshielded and hence, smaller applied field will be required to bring them to resonance. It may be noted that the protons held above and below the plane of the ring resonance at low δ value. In a molecule of toulene, the methyl protons resonate at 2.34 δ where as a methyl group attached to an acyclic alkene of the ring current in an aromatic compound as compared to the disheilding influence caused by conjugated alkene group. An excellent example of shielding and deshielding by ring currents, is given by same of the annulenes. The proton out side the ring of (18) annulenes are strongly deshielded and these inside the ring are strongly shielded.

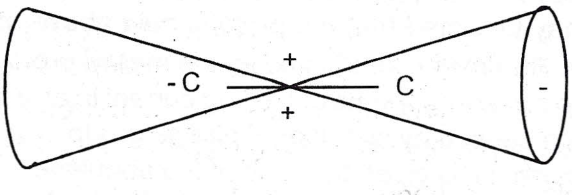


Ring Current - effects in Benzene

Compared to the anisotropic effects of circulating π electrons, the sigma electrons of C-C bond produce a small effect. The axis of C-C bond is the axis of the deshielding cone.

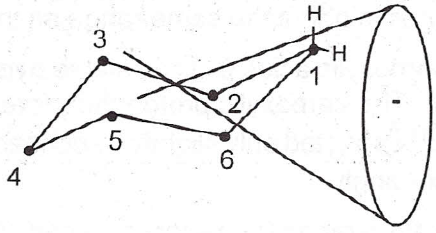


[18] Annulene



Shielding (+) and deshielding (-) zone of C-C

The above figure account for the deshielding effect of successive alkyl substituents on the proton attached to a carbon atom. Thus the protons absorb downfield in the order, RCH_3, R_2CH_2, R_3CH Also an equitorial proton in found to *absorb further downfield by 0.7-0. 1ppm than the axial proton on* the same carbon in a rigid six membered ring. The axial and equatorial protons on C_1 are oriented in the same way, with respect to C_1-C_2 and C_1-C_6 but the equatorial proton is within the deshielding conc of C_2-C_3 and C_5-C_6 bands.



Deshielding of equitorial protons of rigid six membered ring

Fig : Chemical shift range of different hydrogens.

Protons on Heteroatoms : Protons on a heteroatom differ from protons on a carbon atom in that (1) they are exchangeable, 2) they are subject to hydrogen bonding and (3) they are subject to partial or complete decoupling by electrical quadraple effects of some heteroatoms.

2.1.4. Protons on Oxygen :

2.1.4.1. Alcohols : Unless special precautions are taken the spectrum of neat ethanol usually shows the hydroxylic proton as a slightly broadened peak at δ 5.35. At the commonly used concentration of about 5-20% in a non polar solvent, such as carbon tetrachloride or deutero chloroform, the hydroxylic peak is found between δ 2 and δ 4. One extrapolation to infinite dilution or in the vapour phase, the peak is near 0.5.δ A change in solvent or temperature will also shift the hydroxylic peak.

Hydrogen bonding explains why the shift position of the hydroxylic proton depends on concentration, temperature and solvent. Hydrogen bonding decreases the electron density around the proton, and thus moves the protons absorption to lower field. The extent of intermolecular hydrogen bonding is decreased by dilution with a nonpolar solvent and with increased temperature, polar solvent introduce the additional complication of hydrogen bonding between the hydroxylic proton and the solvent. Intramolecular hydrogen bonds are less effected by their environment than intermolecular hydrogen bonds.

2.1.4.2. Phenols : The behavior of a phenolic proton resembles that of an alcoholic proton. The phenolic proton peak is usually a sharp singlet and its range, depending on concentration, solvent and temperature, is generally downfield $(\delta\sim7.5-\delta\sim4.0)$ compared with the alcoholic proton the concentration dependance of the OH peak. A carbonyl group in the ortho position shifts the phenolic proton absorption downfield to the range about $(\delta\ 12.0-\delta\sim10.0)$ because of intramolecular hydrogen bonding. Thus o-hydoxy acetophenone shows a peak at about δ12.05 almost completely in variant with concentration. The much weaker intermolecular hydrogen bonding in o-chlorophenol explains its shift range, which is broad compared with that of O-hydroxy acetophenone but narrow compared with that of phenol.

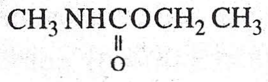
2.1.4.3. Enols : Enols are usually stabilised by intramolecular hydrogen bonding, which varies from very strong in aliphatic β –diketones to weak in cyclic α - diketone. The enolic proton is downfield relative to alcohol protons and, in the case of the enolic form of some β diketones, may be found as far downfield as δ 16.6. The enolic proton peak is frequently broad at room temperature because of slow exchange. Furthermore, the keto-enol conversion is slow enough so that absorption peaks of both forms can be observed, and the equilibriuml maintained. When strong intramolecular bonding is not involved, the enolic proton absorbs in about the same range as the phenolic proton.

2.1.4.4. Carboxylic acids : Carboxylic acids exist as stable hydrogen – bonded dimers in non-polar solvents even at high dilution. The carboxylic proton therefore absorbs in a characteristically narrow range $\delta \sim$ 13.2. $\delta \sim$ 10.0 and is affected only slightly by concentration. Polar solvents partially disrupt the dimer shift the peak accordingly.

The peak width at room temperature range from sharp to broad, depending on the exchange rate of the particular acid. The carboxylic proton exchanges quite rapidly with protons of water and alcohols to give a single peak whose position depends on concentration. Sulfhydryl or enolic protons do not exchange rapidly with carboxylic protons and individual peaks are observed.

2.1.4.5. Protons on Nitrogen : The ^{14}N nucleons has a spin number'1 of 1 and in accordance with the formula 2I+1, should cause a proton attached to it and a proton on an adjacent carbon atom to show three equally intense peak. These are two factors, however, that complicate the picture the rate of exchange of the proton on the nitrogen atom and the electrical quadruple moment of the ^{14}N nucleons.

The proton on a nitrogen atom may undergo rapid, intermediate or slow exchanges. If the exchanges is rapid the NH proton decoupled from the N atom and from the protons on adjacent carbon atoms. The NH peak is therefore a sharp singlet, and the adjacent CH protons are not split by NH. Such is the case of most aliphatic amines. If the NH exchange rate is low, the NH peak is still broad because the electrical quadrapole moment of the nitrogen nucleus induces a moderately efficient spin relaxation and thus, an intermediate life time for the spin states of the nitrogen nucleus. The proton thus sees three spin states of the nitrogen nucleus which are changing at a moderate and the proton responds by giving a broad peak. In this case, coupling of the NH proton to the adjacent protons is observed. Such is the case for pyrroles, induces, secondary and primary amides, and carbamates.

The H-N-C-H coupling takes place through the C-H, C-N and N-H bonds, but compiling between nitrogen and protons on adjacent carbon atoms is negligible. The proton – proton coupling is observed in the signal due to hydrogen on carbon. The N-H proton signal is severely broadened by the quadrupolar interaction. Ethyl N-methyl carbamate  $CH_3NH\underset{\underset{O}{\|}}{C}OCH_2CH_3$ the NH proton shows a broad absorption centered about $\delta 5.16$ and $N-CH_3$ absorption at $\delta 2.78$ is split into a doublet $(J \sim 5H_2)$ by the NH proton. The ethoxy protons are represented by the triplet at δ 1.23 and the quartet at δ 4.14. The small peak at δ 2.67 is an impurity. Aliphatic and cyclic amine NH protons absorb from ~δ 3.0 – 0.5 aromatic amines absorb from ~δ 5.0 – 3.0

2.1.4.6. Protons on Sulfur : Sulfhydryl protons usually exchange at a low rate so that at room temperature they are coupled to protons on adjacent carbon atoms or do they exchange rapidly with hydroxyl, carboxylic, or enolic protons on the same or on other molecules. However, exchanges is rapid enough that shaking for a few minutes with deuterium oxide replaces sulfhydryl protons with deuterium. The absorption range for aliphatic sulfhydryl protons or δ 1.6 – δ 1.2 for aromatic sulfhydryl protons δ 3.6. – δ 2.8 concentration, solvent and temperature affect the position within these ranges.

2.1.5. Protons on or near Halogens :

Chlorine, bromine, and iodine nuclei are completely decomposed from protons directly attached or an adjacent carbon atoms, because of strong electrical quadruple moments.

The ^{19}F atom has a spin number of ½ and compels straggly with protons the rules for coupling of protons with flourine are the same as for proton - proton coupling. The proton fluorine coupling constants are some what larger, and long - range effects are frequently found. The ^{19}F nucleus can be observed at 56.4 MH_2. Its spin is split by proton and flourine spins, and the multiplicity rules are the same as these observed in proton spectra.

2.1.6. Chemical Exchange :

In a molecule, if a proton shuttles between two magnetic environments at a rate which is much faster in comparison with the nmr transition time then the resonance observed for that proton will be simply that of the average effective field in the two environments thus only are resonance will be observed, although the proton will shuttle in the different magnetic environments. We know that the –OH proton in water has different chemical shift as compared to that of the –OH proton in acetic acid in water at an average position according to the following formula.

$$N_a\delta_a + N_b\delta_b$$

Where

N_a = Mole fraction of the proton a.

N_B = Mole fraction of the proton b

δ_a = Chemical shift of unexchanged proton a

δ_b = Chemical shift of unexchanged proton b

This clearly shows that the rate at which the –OH proton exchanges between water and acetic acid is much faster than the nuclear transition time.

The phemamer of chemical exchange can be explained by considering the nmr spectrum of anhydrous ethanol and also the spectrum of ethanol containing small quantities of water.

In the case of pure anhyrides ethanol $\overset{a}{CH_3} - \overset{b}{CH_2} - \overset{c}{OH}$ three signals are observed.

1) a triplet for CH_3 protons at 8.827 due to coupling with CH_2 protons

2) a multiplet consisting of light lines for - CH_2 - protons at 6.38 ~ the - CH_2 - protons are under the influence of two kinds of proton in different chemical environments. Thus, the multiplet consist (n+1) (n^1+1) = (3+1) (1+1) = 8 lines

3) a triplet for –OH proton at 4.72. The OH proton appears as a triplet because of coupling to - CH_2 - protons

Now if we scan the spectrum of ethyl alcohol containing water, the OH signals appcass as a singlet and its couping with adjacent - CH_2 - does not take place.

The alcohol containing some amount of water, a singlet is observed for the hydroxyl proton. The position of the singlet peak for the OH proton is slightly shifted depending upon the water content in alcohol and hence, it helps in the quantitative analysis of ethanol - water, acetic acid - water mixtures.

The spin decoupling can usually be observed at 1) high temperature and 2) by using highly polar polar solvents for the polar samples.

The spectrum of methanol (CH_3OH) at very low temperature (-40^0) shows a quartet for hydroxyl proton and a doublet for methyl protons. This shows that the chemical exchange is very slow at -40^0c as compared to the nmr transition time. But, if the temperature is raised to $+31^0c$, multiplets CH_3 and –OH protons collapse to the sharp singlets. Thus shows that the rate of chemical exchange become faster then the nmr transition time.

2.1.7. Suggested Readings

10. **Some Modern methods of Organic Synthesis, W. Carruthers, Cambridge University Press.**
11. **Advanced Organic Chemistry, Reactions Mechanisms and Structure, J. March. John Wiley**
12. **Advanced Organic Chemistry Part B, F.A. Carey and R.J. Sundberg, Plenum Press 1.**
13. **Spectrometric Identification of Organic Compounds, R. M. Silverstein, G.C. Bassler and T. C. Morrill, John Wiley.**
14. **Applications of Spectroscopy of Organic Compounds, J. R. Dyer, Prenctice Hall.**
15. **Spectroscopic methods in Organic Chemistry, D.H. Williams, I. Fleming, Tata Mc. Graw Hill**
16. **Spectroscopic methods in Organic Chemistry – Kemp**
17. **Fundamentals of Photochemistry, K.K. Rohtagi – Mukherji, Wiley – Eastern**
18. **Text Book of Organic Chemistry Vol I & II – I. L. Finar.**

2.2. MASS SPECTROMETRY

Structure :

2.2. MASS SPECTROMETRY

2.2.1. Introduction :

Mass spectrometry is one of the most versatile technique used to characterize organic compounds. It is also useful method for determining the molecular mass of the compound and its elemental composition. In this technique, the molecules are bombarded with a beam of energetic electrons. The molecules are ionized and broken up into many fragments, some of which are positive ions. Each kind of ion has a particular ratio of mass to charge (i.e.) m/e ratio. In mass spectrum a signal is obtained for each value of m/e that is represented. The intensity of each signal represents the relative abundance of the ion producing the signal. The largest peak in the spectrum is called the base peak and its intensity is taken as 100. The intensities of other peaks are represented relative to the base peak.

Mass spectra is used in the following two general ways :

i) To prove the identity of two compounds

ii) To establish the structure of a new compound

2.2.2. Instrumentation : Mass spectrometers of both low and high resolution are available. A typical 180^0 single focusing low resolution mass spectrometer shows the following components.

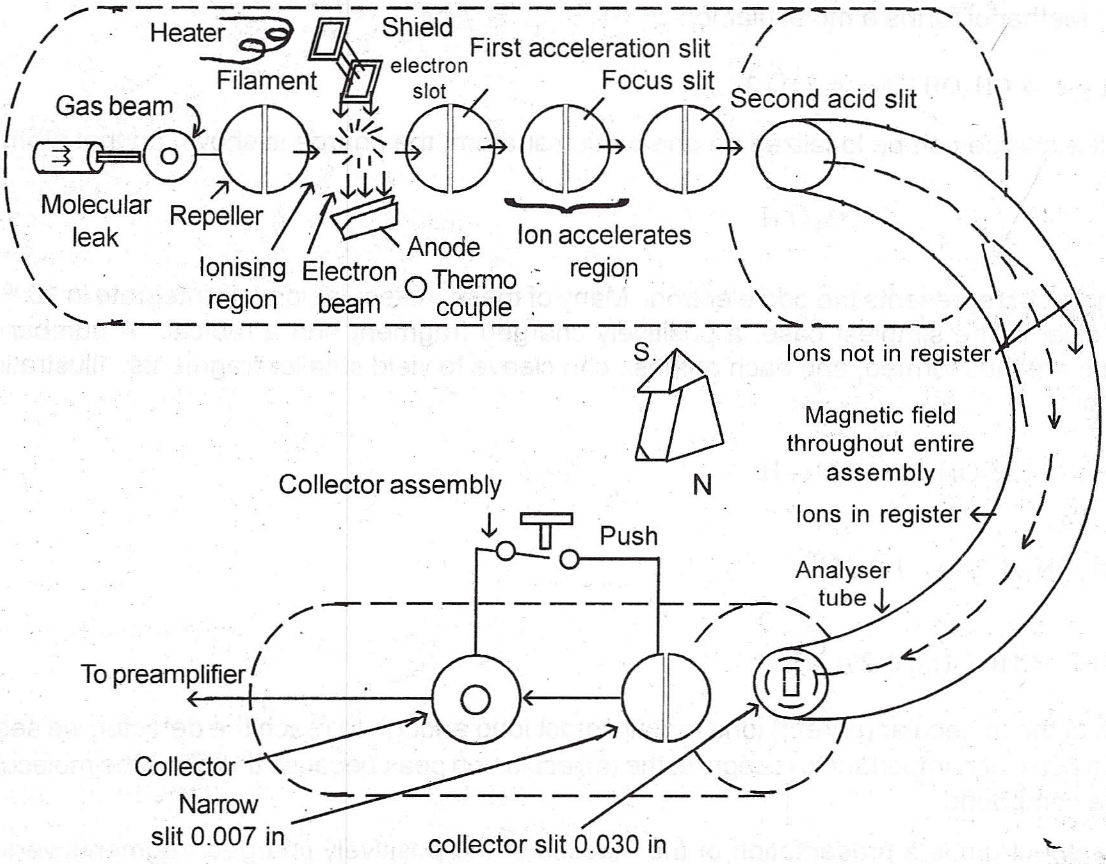
1. Sample Handling System : This consists of a device for introducing the sample, a micromanometer for determining the amount of sample introduced, a device (molecular leak) for metering the sample to the ionization chamber and a pumping system. Sample sizes for liquids and solids range from several milligrams to less than a microgram, depending on the method of introduction and the detector. For routine work, vapour pressure of 10^{-1} to 10^{-3} torr is desired.

2. Ionization and Accelerating chambers : The gas stream from the molecular leak enters the ionization chamber in which it is bombarded at right angles by an electron beam emitted from a hot filament. Positive ions produced by interaction with the electron beam are forced though the first acceleration slit by a small electrostatic field between the repellers and the first acceleration slit. A strong electrostatic force between the first and second accelerating slits accelerates the ions to their final velocities. To obtain a spectrum, either the magnetic field applied to the analyzer tube or the accelerating voltage between the first and second ion slits is varied. Thus the ions are focussed at the collecter slit as a function of mass.

3. Analyzer Tube and Magnet : The analyzer tube is an evacuated, curved, metal tube through which the ion beam passes from ion source to the collector. The magnetic pole pieces are mounted perpendicular to the plane of the diagram. The main requirement is a uniform and stable magnetic field.

4. Ion Collector and Amplifier : A typical ion collector consists of one or more collimating slits and a faraday cylinder; the ion beam impinges axially into the collector, and the signal is amplified by an electron multiplier.

5. Recorder : A widely used recorder uses five separate galvanometers that record simultaneously. Peak heights are proportional to the number of ions of each mass.

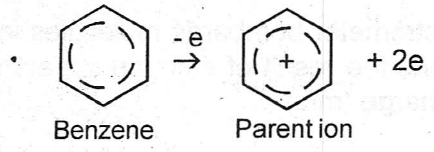


Schematic diagram of 180° single focussing Mass spectrometer

2.2.3. ION Production :

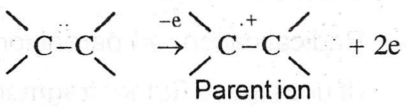
Mass spectra are routinely obtained at an electron beam energy of 70 e.v. The simplest event that occurs is the removal of a single electron from the molecule in the gas phase by an electron of the electron beam to form a molecular ion, which is a radical cation (M^{+}). The highest occupied orbital of aromatic system and non bonding electron orbitals on Oxygen and Nitrogen atoms readily lose one electron. An electron from double bond or triple bond is usually lost. In alkanes the ionization of C-C sigma bond is easier than that of C-H bonds.

$$M_{(g)} \xrightarrow{+e} M^{+}_{(g)} + 2e$$



$$R-\overset{..}{\underset{..}{O}}-H \xrightarrow{-e} R-\overset{.+}{\underset{..}{O}}-H+2e$$

Parent ion



For ex : Methanol forms a molecular ion

$$CH_3OH + e \rightarrow CH_3OH^{+\cdot}\ (m/e\ 32) + 2e$$

When the charge can be localized on one particular atom, the charge is shown on that atom.

$$CH_3\overset{\cdot +}{\underset{\cdot\cdot}{O}}H$$

The single dot represents the odd electron. Many of these molecular ions disintegrate in 10^{-10} to 10^{-3} Sec to give, in the simplest case, a positively charged fragment and a radical. A number of fragment ions are thus formed, and each of these can cleave to yield smaller fragments. Illustrating with methanol.

$$CH_3OH^{+}_{\cdot} \rightarrow CH_2OH^{+}\ (m/e\ 31) + H\cdot$$

$$CH_3OH^{+}_{\cdot} \rightarrow CH_3^{+}\ (m/e\ 15) + .OH$$

$$CH_2OH^{+} \rightarrow CHO^{+}\ (m/e\ 29) + H_2$$

If some of the molecular (parent) ions remain intact long enough to reach the detector, we see a molecular ion peak. It is important to recognize the molecular ion peak because this gives the molecular weight of the compound.

A mass spectrum is a presentation of the masses of the positively charged fragments versus their relative concentrations. The most intense peak in the spectrum, called the base peak is assigned a value of 100% and the intensities of the other peaks, including the molecular ion peak, are reported as percentages of the base peak. Sometimes the molecular peak may be the base peak.

2.2.4. Types of Ionization :

There are four types of Ionization methods.

1. Electron Impact mode
2. Chemical ionization method
3. Field disorption
4. Fast atom bombardment

1. Electron Impact Mode : In this method a mass spectrometer bombards molecules in the vapour phase with a high – energy electron beam and records the result of electron impact as a spectrum of positive ions separated on the bases of mass / charge (m/z)

$$M \xrightarrow{\text{70 ev beam}} M^{+\cdot} + 2e^{-}$$

Molecular ion (or)

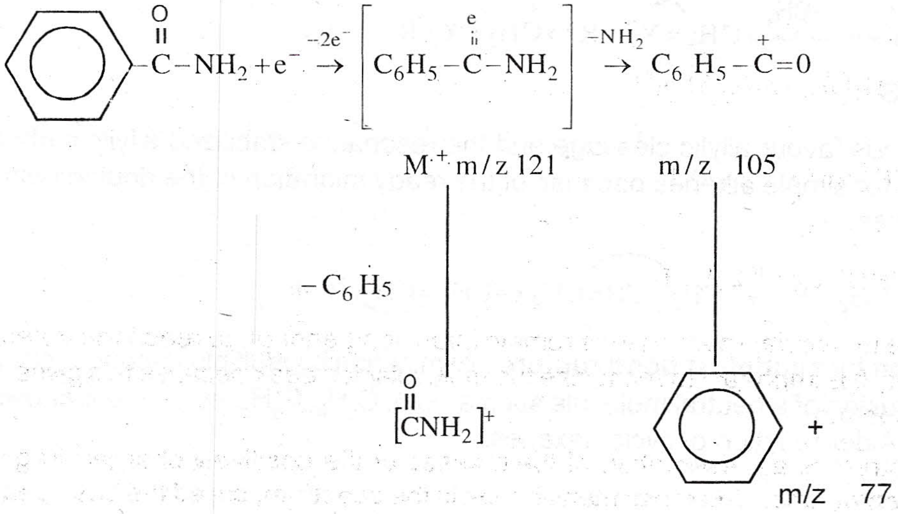
Radical cation (or) parent ion.

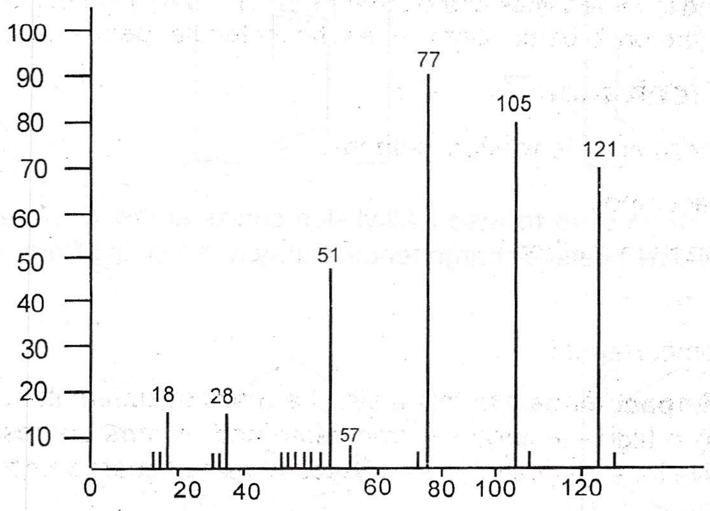
(It undergoes further fragmentation)

Sufficiently stable molecular ion cannot be formed by this method. This is because of large amount of excess energy imparted to the molecular ion by 70ev bombardment.

Base peak : A mass spectrum is a presentation of the masses of the positively charged fragments versus their relative concentrations. The largest peak in the spectrum, called the base peak. It's intensity is taken as 100% and the intensities of other peaks, including the molecular ion peak, are reported as percentages of the base peak. The molecular ion peak may sometimes be the base peak. In the below example molecular ion peak is m/z '121', and base peak is m/z 77.

Eg :





2.2.5. Fragmentation of Organic Compounds :

I σ **Bond rupture in alkane group :** This can really only be represented by assuming that, at the instant of ionization, sufficient excitation energy is concentrated on the rupturing bond to ionize it.

Cleavage is favoured at alkyl substituted carbon atoms, the more substituted, the more likely is cleavage. This is a consequence of the increased stability of a tertiary carbocation over a secondary, which in turn is more stable than a primary. Generally, the largest substituent at a branch is eliminated most readily as a radical, because a long – chain radical can achieve some stability by delocalization of the lone electron.

II **σ Bond rupture near functional groups :** This is facilitated by the easier ionization of non bonding orbitals of hetero atom than the σ bonding orbitals. The C-C bond next to a hetero atom are frequently cleaved, leaving the charge on the fragment containing the hetero atom whose non bonding electrons provide resonance stabilization.

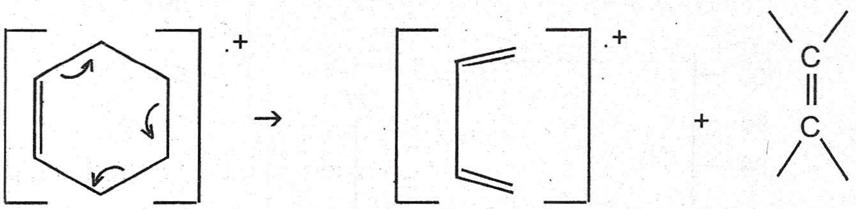
$$CH_3-CH_2-\overset{\cdot +}{Y}-R \xrightarrow{-CH_3} \overset{\cdot}{C}H_2=Y^+-R \leftrightarrow \overset{+}{C}H_2-\ddot{Y}-R$$

Y=O, NH, or S.

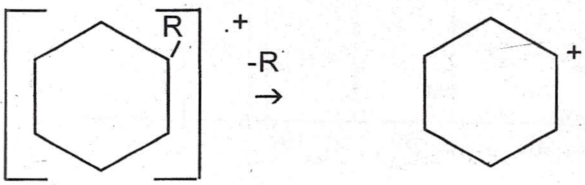
III Double bonds favour allylic cleavage and the resonance stabilized allylic carbocation. This rule does not hold for simple alkenes because of the ready migration of the double bond, but it does hold for cycloalkenes.

$$\overset{+}{C}H_2\,{}^{\cdot}\!:CH-CH_2-R \xrightarrow{-R^{\cdot}} {}^+CH_2-CH=CH_2 \leftrightarrow CH_2=CH-{}^+CH_2$$

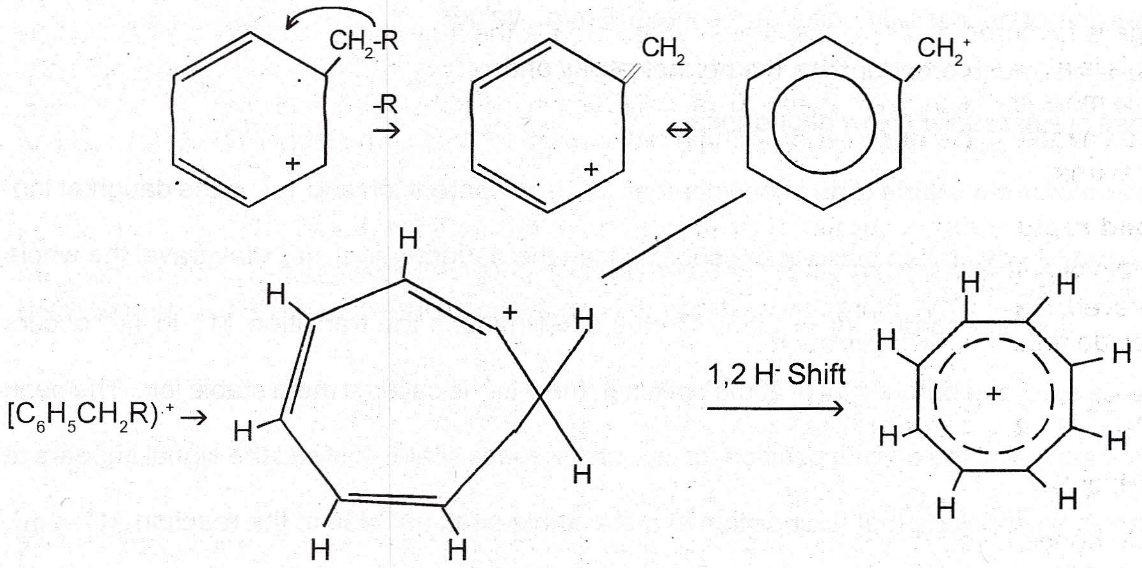
IV Elimination by multiple σ bond rupture : Elimination by multiple σ-bond rupture may occur, leading to the extrusion of a neutral molecule such as CO, C_2H_4, C_2H_2, etc,. A well known example is the Retro -Diels - Alder reaction of cyclo hexenes.



V) Saturated rings tend to lose : Alkyl side chains at the 'α' bond. This is merely a special case of branching. The positive charge tends to stay with the ring fragment.



VI) In alkyl – substituted aromatic compounds, cleavage is very probable at the bond β to the ring giving the resonance - stabilized benzyl ion or, more likely, the tropylium ion.



VI) Even Electron Rule : This is based on thermodynamic principles. It states that an even electron species will not normally fragment to two odd electron species i.e., an ion will not fragment to a radical and a radical ion since the total energy of this product mixture will be too high.

$$\underset{\text{even}}{A^{+}} \nrightarrow \underset{\text{odd}}{B^{+\cdot}} + \underset{\text{odd}}{C^{\cdot}}$$

In Preference, an ion will degrade to another ion and a neutral molecule.

$$\underset{\text{even}}{A^{+}} \longrightarrow \underset{\text{even}}{B^{+}} + \underset{\text{even}}{C}$$

Radical ions, being odd – electron species, can extrude a neutral molecule, leaving a radical ion as co product.

$$\underset{\text{Odd}}{A^{+}} \longrightarrow \underset{\text{Odd}}{B^{+}} + \underset{\text{even}}{C}$$

Radical ions can also degrade to a radical and an ion

$$\underset{\text{Odd}}{A^{+}} \longrightarrow \underset{\text{even}}{B^{+}} + \underset{\text{odd}}{C^{\cdot}} \quad (\text{or } B^{\cdot} + C^{+})$$

VII) Some times cleavage is often associated with rearrangement.

Eg. Mc Lafferty rearrangement in carbonyl compounds

2.2.6. Meta Stable Peak : Meta stable peaks can be easily determined in a mass spectrum. Some important characteristics of these peaks are :

i) They do not necessarily occur at the integral m/e. values

ii) These are much broader than the normal peaks and

iii) These are of relatively low abundance.

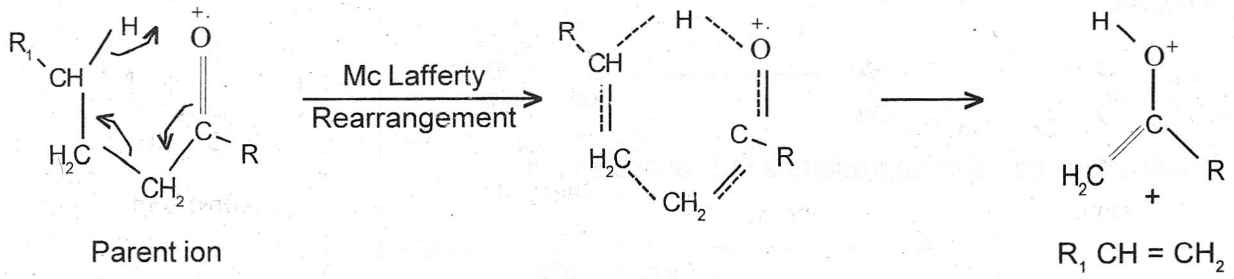
Formation of meta stable ions : consider that M_1^{+} is the parent ion and m_1^{+} is the daughter ion. If the reaction $M_1^{+} \rightarrow m_1^{+}$ takes place in the source, then the daughter ion, m_1^{+} may travel the whole analyzer region and is recorded as m_1^{+} ion. On the other hand, if the transition M_1^{+} to m_1^{+} occurs after the source exist and before arrival at the collector, then m_1^{+} is called a meta stable ion. The peak for m_1^{+} will not appear at the normal position for m_1^{+} on the mass scale. Instead the signal appears at m_1^2/M_1. Hence we conclude that the position of meta stable peak (m*)due to the reaction $M_1^{+} \rightarrow m_1^{+}$ is such that

$$m^* = m_1^2/M_1$$

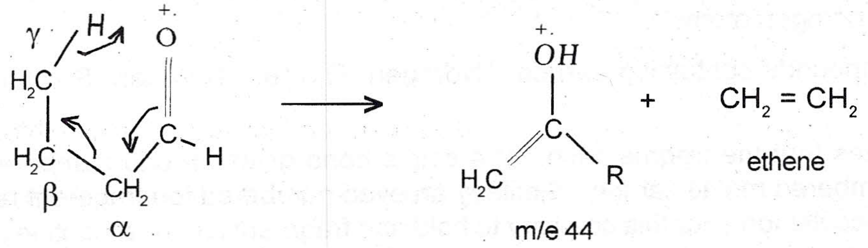
It is important to remember that for a reaction $M_1^{+} \rightarrow m_1^{+}, m^*$ (meta stable peak) has a distance blow m, on the mass scale. The distance is approximately similar to the distance that m, lies below M_1.

2.2.7. Mc Lafferty Rearrangement :

It involves the migration of γ-hydrogen atom followed by the cleavage of a β – bond. The rearrangement leads to the elimination of neutral molecules from aldehydes, ketones, amines, unsaturated compounds, substituted aromatic compounds etc. The rearrangement proceeds through a sterically hindered six membered transition state ex : Ketone.



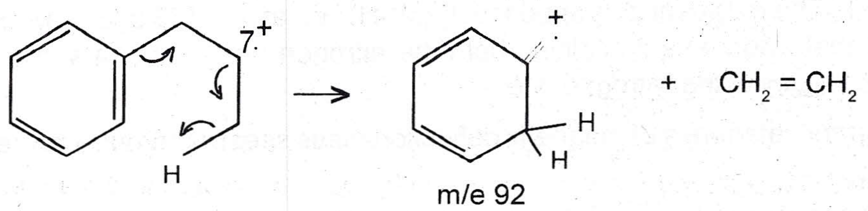
Ex : Butanal



Molecular ion

Thus the molecular formula of the unknown compound can be determined from the various fragment ions and also the parent ion of mass spectrum.

n-Propyl benzene shows a Mc Lafferty rearrangement ion peak in large abundance at m/e 92.

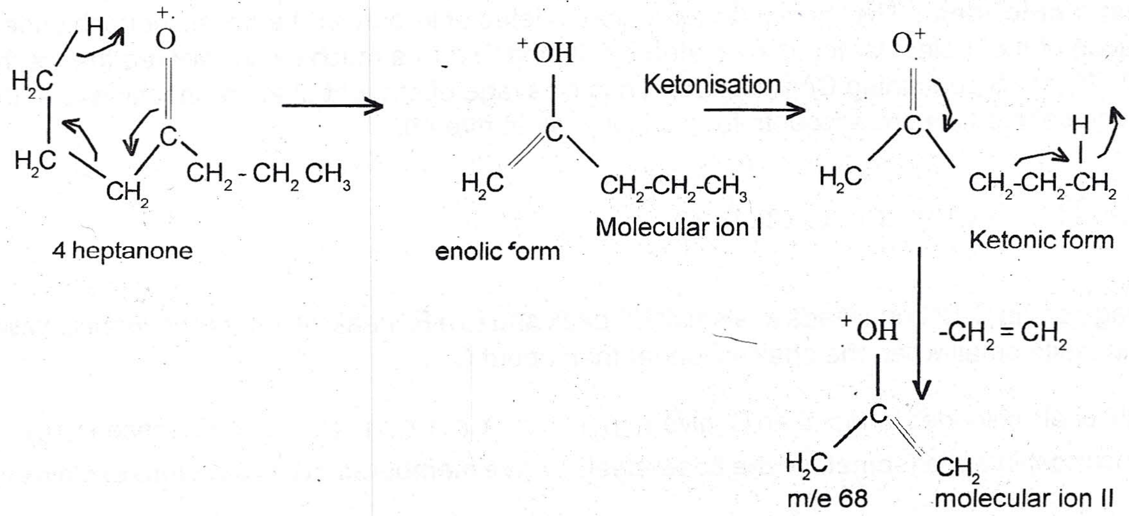


A double Mc Lafferty rearrangement is also reported in certain ketones. The second hydrogen atom originates exclusively from the γ-position. The mechanism involves.

i) Ketonisation of the intermediate enol ion by the hydrogen transfer

ii) Hydrogen transfer to enolic oxygen.

Ex : 4 - Heptanone



2.2.8. The Nitrogen Rule : It states that 'a molecule of even numbered molecular mass must contain no nitrogen atom or an even number of nitrogen atoms. An odd numbered molecular mass requires an odd number of nitrogen atoms'.

This rules for all compounds containing carbon, Hydrogen, Oxygen, Nitrogen, Sulphur and halogens.

An important rule states that the fragmentation at a single bond gives an odd numbered ion fragment from an even numbered molecular ion. Similarly an even numbered ion fragment results from an odd numbered molecular ion. For this corollary to hold, the fragment ion must contain all the nitrogen atoms of molecular ion.

Let us consider Nitro benzene ($C_6H_5No_2$). The signal for molecular ion appears at m/e 123, i.e. at odd numbered molecular mass since the compound contains only one nitrogen atom. Two important ion fragments which are formed in the small spectrum of this compound are i) NO_2^+ at m/e 4b and ii) NO^+ at m/e 30. Both these appear at even mass number.

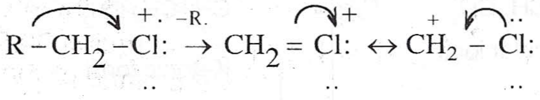
Consider 2, 4 dinitro phenol containing even number (2) of the nitrogen atoms. Its molecular ion signal appears at m/e 184. The fragment ions appear at I) (M^+-H) i.e., at m/e 183 and ii) (M^+-H-CO) at m/e 155. Thus we see that fragments containing both the nitrogen atoms appears at odd mass number. This proves the validity of the Nitrogen rule.

There are two important categories of magnetic deflection mass spectrometers. Low resolution & High resolution.

Low resolution instruments can be defined arbitrarily as instruments that separate unit masses upto m/e 2000. [R- 2000 / 2000 - 1999) = 2000]

As instrument is generally considered high resolution if it can separate two ions differing in mass by at least one part in ten thousand to fifteen thousand (R = 10,000 – 15,000). An instrument with 10,000 resolution can separate an ion of mass 500.00 from one of mass 499.95 (R = 500 / 0.05 = 10,000). This important class of mass spectrometers can measure the mass of an ion with sufficient accuracy to determine its atomic composition.

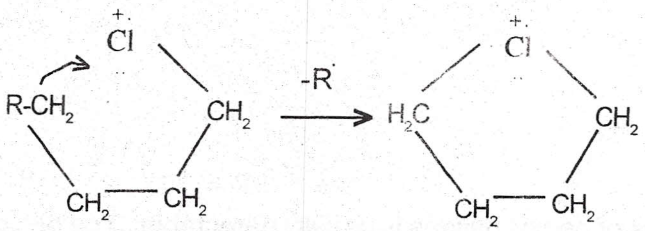
Aliphatic chlorides : The molecular ion peak is detectable only in the lower monochlorides. Fragmentation of the molecular ion is mediated by Cl atom but to a much lesser degree than is the case in –O, -N, or –S containing Compounds. Thus cleavage of straight chain monochloride at the C-C bond adjacent to Cl atom accounts for a small peak at m/e 49.



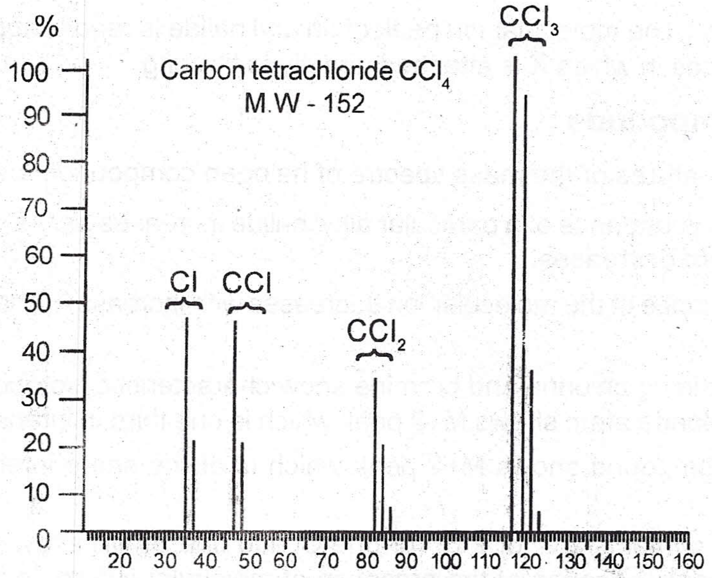
$$R-CH_2-\underset{..}{Cl}:\ \xrightarrow{+\cdot\ -R\cdot}\ CH_2=\overset{+}{\underset{..}{Cl}}:\ \leftrightarrow\ \overset{+}{CH_2}-\overset{..}{\underset{..}{Cl}}:$$

Cleavage of the C-Cl bond leads to a small Cl^+ peak and to a R^+ peak which is prominent in lower chlorides but quite small when the chain is longer than about C_5.

Straight chain chlorides longer than C_6 give $C_3H_6Cl^+, C_4H_8Cl^+, C_5H_{10}Cl^+$ ions. Of these $C_4H_8Cl^+$ ion forms the most intense (sometime the base) peak. A five membered cyclic structure explains its stability.



Loss of HCl Occurs, possibly by 1,3 elimination to give a peak (Weak or moderate) at M-36



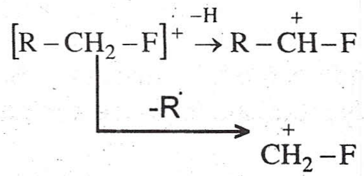
Aliphatic Bromides : The remarks under aliphatic chlorides apply to corresponding Bromides.

Aliphatic Iodides : They give the strongest molecular ion peak of aliphatic halides. Since I_2 is mono isotopic, there is no distinctive isotope peak.

Iodides cleave much as do chlorides & bromides but $C_4H_8I^+$ ion is not as evident as the corresponding chlorides and bromide ions.

Aliphatic Fluorides : They give the weakest molecular ion peaks of the aliphatic h[illegible]. Fluorine is monoisotopic and its detection in polyfluoro compounds depends on suspicious small isotopic peaks relative to molecular ion, on the intervals between peaks and on characteristic peaks.

Of these the most characteristic is m/e 69 due to ion CF_3^+ which is the base peak in all perfluoro carbons. Prominent peaks are noted at m/e 119, 169, 219...... these are increments of CF_2. The stable ions $C_3F_5^+$ & $C_4F_7^+$ give large peaks at m/e 131 and 181. In mono fluorides cleavage of the $\alpha\beta$ C-C bond is less important than in other monohalides but cleavage of a C-H bond on the $\alpha-C$ is more important. This reversal is a consequence of high E N of F atom and is rationalized by placing +ve charge on α carbon. The secondary carbonium ion thus depicted by a loss of a H atom is more stable than the I° carbonium ion resulting from loss of an alkyl radical.



$$[R-CH_2-F]^{+\cdot} \xrightarrow{-H} R-\overset{+}{C}H-F$$

$$[R-CH_2-F]^{+\cdot} \xrightarrow{-R^{\cdot}} \overset{+}{C}H_2-F$$

Benzyl Halides : The molecular ion peak of benzyl halides is usually detectable. The benzyl (or tropylium) ion from loss of the halide is favoured even over β bond cleavage of an alkyl substituent. A substituted phenyl ion is prominent when the ring is polysubstituted

Aromatic Halides : The molecular ion peak of an aryl halide is readily apparent. The M-X peak is large for all compounds in which X is attached directly to the ring.

2.2.9. Halogen Compounds :

Some important features of the mass spectra of halogen compounds are :

a) The molecular ion abundance of a particular alkyl halide increases as the electronegativity of the halogen substituent decreases.

b) The relative abundance of the molecular ion decreases with increase in chain length and increase in branching.

c) Compounds containing chlorine and bromine show characteristic isotope peaks. A compound containing one chlorine atom shows M+2 peak which is one third in intensity of parent ion peak.

d) A mono bromo compound shows M+2 peak which is of the same intensity compared to the parent peak.

e) A compound that contains 2 Cl or 2 Br or one Cl and one Br will show a distinct M+4 peak in addition to M+2 peak, because of the presence of molecular ion containing 2 atoms of heavy isotopes.

f) In the parent ion, charge resides on the halogen atom.

g) Important fragmentation mode is α – cleavage with charge retention by halogen containing fragment. Another mode leads to loss of halide radical.

$$R\overset{\curvearrowright}{-CH_2}-\overset{+\cdot}{X} \rightarrow CH_2=\overset{+}{X}+R$$

$$R-CH_2-\overset{+\cdot}{X} \rightarrow R\overset{+}{C}H_2+\overset{\cdot}{X}\text{(Preferable mode)}$$

Molecular Ion : A molecular ion is produced when a neutral molecule loses an electron. This 'e' is lost from the highest molecular orbitals of organic compounds. A molecular ion should not be represented by a localized structure unless there is a specific evidence.

Molecular Ion Peak : The ion cluster appearing at highest 'm/z' value represents the molecular ion with its attendent 'M+1'. peaks etc. Molecular ion peak may be weak or it may not appear at all. The intensity of the molecular ion peak depends on the stability of molecular ion. The most stable molecular ions are produced from purely aromatic systems. If substituents that have favourable modes of cleavage are present the molecular ion peak will be less intense and the fragment peaks relatively more intense. In general, the following group of compounds will be in the order of decreasing ability, give prominent molecular ion peaks.

Aromatic compounds > conjugated alkenes > cyclic compounds > organic sulfides > Short, normal alkanes > mercaptans Recognizable molecular ions are usually produced for these compound in order of decreasing ability.

Ketones > amines > esters > ethers > carboxylic acids ~ aldehydes ~ amides ~ halides.

The presence of an M-15 peak (loss of CH_3) or an M-18 peak (loss of H_2O or an M-31 peak (loss of OCH_3 from methyl esters) and so on, it is taken as confirmation of a molecular ion peak. An M-1 peak is common, and occasionally an M-2 peak (loss of H_2 by either fragmentation or thermolysis), or even a rare M-3 peak is reasonable.

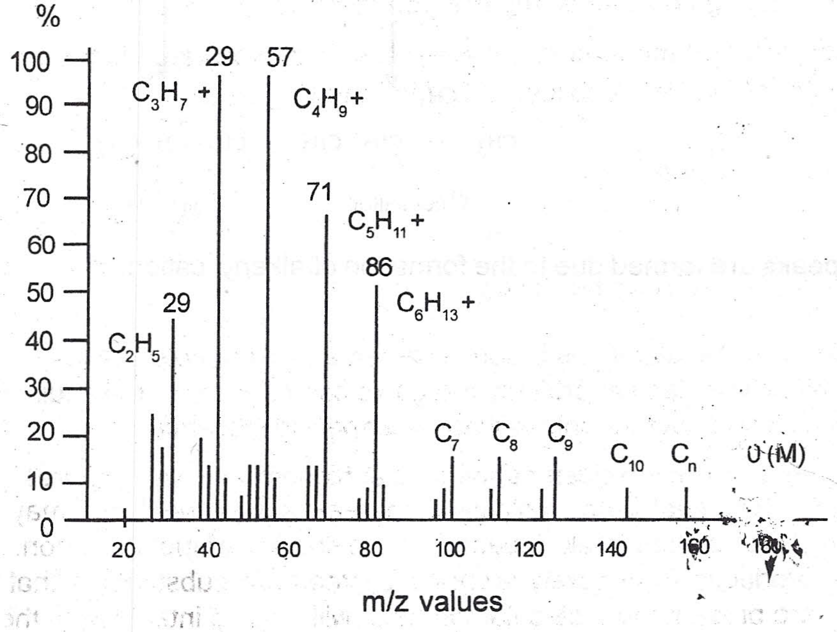
Loss of 16(O), 17(OH), or 18 (H_2O) are likely only if an oxygen atom is in the molecule.

The intensity of a molecular ion peak is comparitively greatest for straight chain compounds than branched compounds. The intensity of molecular ion peak decreases with increasing molecular weight in a homologous series except fatty acids.

2.2.10. Alkanes : The molecular ion will normally be seen in the mass spectra of the lower n-alkanes. But its intensity falls off with increased size and branching of the chain.

Eg : Dodecane

The fragmentation pattern is characterized by Clusters of peaks, and corresponding peaks of each cluster are 14 (CH_2) mass units apart. The largest peak in each cluster represents a C_nH_{2n+1} fragment and this occurs at m/z = 14 n+1, this is accompanied by C_nH_{2n} and C_nH_{2n-1} fragments. The most abundant peaks are produced by $C_3H_7^+$ and $C_4H_9^+$



Branched Chain Alkanes : Some important features of the mass spectra of branched chain alkanes are :

Bond cleavage takes place preferably at the site of branching due to such cleavage, a more stable secondary or tertiary carbonium ion results.

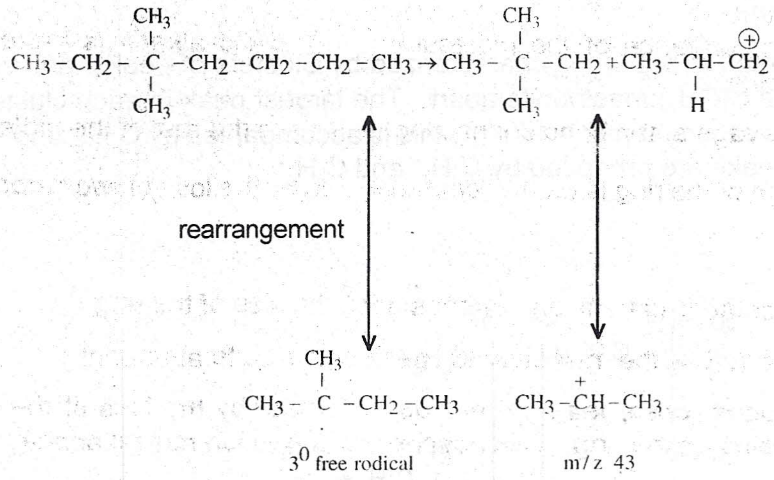
Generally, largest substituent at a branch is eliminated readily as a radical. The radical achieves stability by delocalisation of lone electron

Molecular ion is not formed

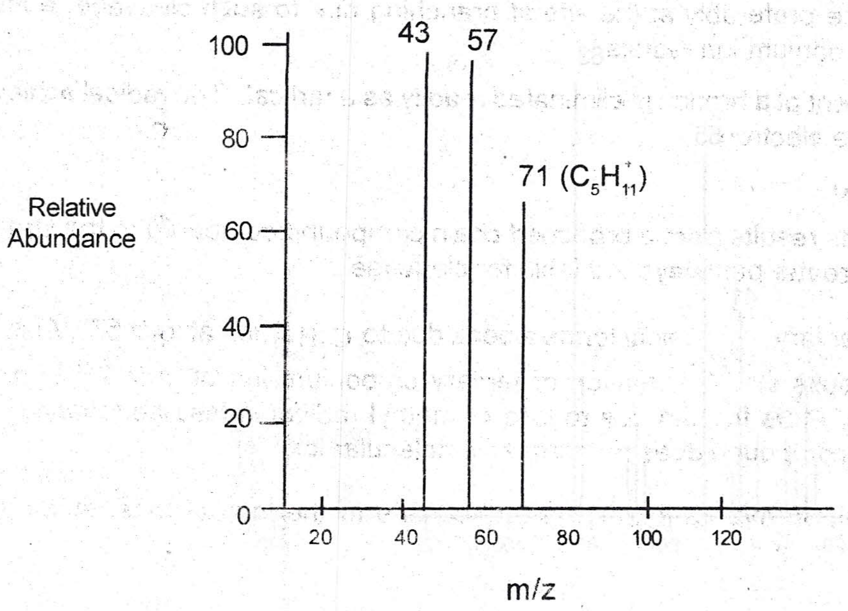
Great number of fragments results from a branched chain compound compared to the straight chain compound. It is due to greater pathways available for cleavage :

As expected, the loss of tertiary [illegible] dical forms a peak due to $C_4H_9^+$ ion at 'm/z 57'. Also the loss of n-butyl free radical results in [illegible] mation of tertiary carbonium ion at 'm/z 71' in much abundance. The peak at 'm/z 71' is formed due to loss of methyl radical in less abundance. As expected, the branched chain compound does not form any molecular ion.

The much abundant peak at 'm/z 43' $\left(C_3H_7^+\right)$ is formed due to the loss of most stable free radical.



Also small peaks are formed due to the formation of alkenyl cation.



Cyclo Alkanes :

The relative abundance of the molecular ion of cyclo alkane is more as compared to the corresponding alkane.

It favours cleavage at the bond connecting the ring to the rest of the molecule.

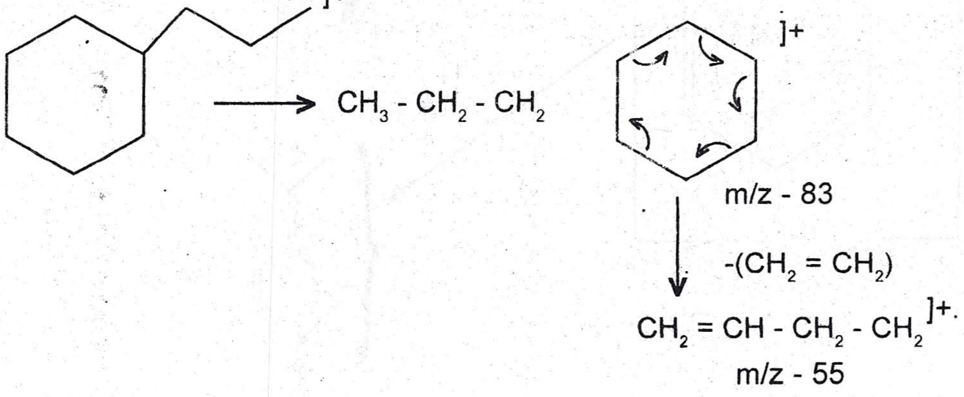
Fragmentation of the ring is usually characterized by the loss of two carbon atoms as C_2H_4(28) and $C_2H_5^+$(29)

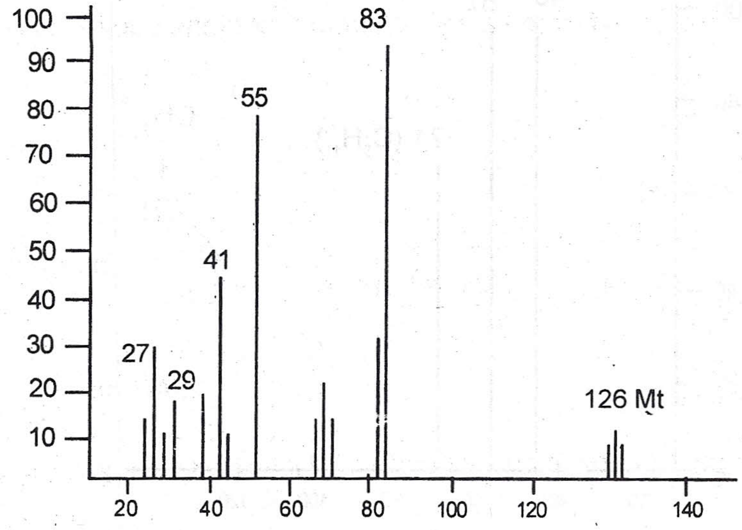
The stability of the fragment ion depends upon the size of the ring.

a) The peak m/e 128, is the molecular ion peak and is quite abundant.

b) The largest peak (base peak) at 'm/z 83' is formed by the loss of the side chain. The lone electron remains on the ring. This positively charged ion radical appears at m/z 83

c) The ion radical shows Retro - Diel's - Alder reaction and fragment ion is formed at 'm/z 55'. The abundance of this ion is very large.





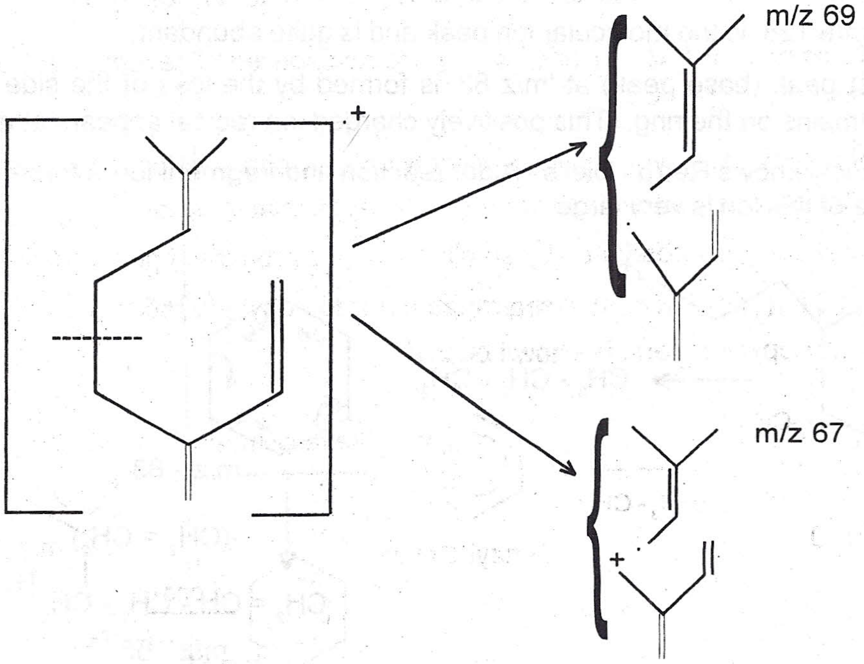
2.2.11. Alkenes :

a) The molecular ion peak in the spectra of unsaturated compound is more intense than the corresponding saturated analogues. The reason is the better resonance stabilization of the charge on the cation formed by the removal of one of $\pi -$ electrons. Mono olefins contain $C_nH_{2n-1}^+$ ions in their mass spectra.

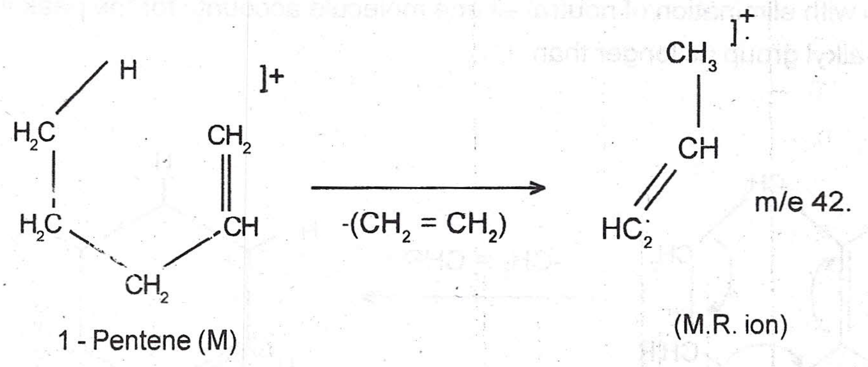
The relative abundance of the molecular ion peak decreases with increasing molecular mass.

A cyclic olefin also shows group of peaks which are 14 mass units apart.

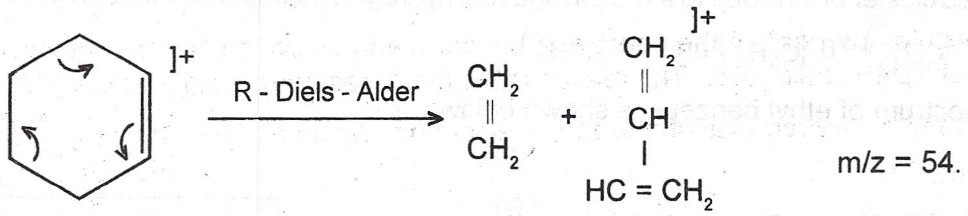
The general mode of fragmentation induced by a double bond is the allylic cleavage.



The C_nH_{2n} ions formed by Mc Lafferty rearrangement are more intense. For example, Mc Lafferty rearrangement ion is formed at m/e 42 from 1-pentene due to loss of ethylene molecule.



Cyclic olefins usually show a distinct molecular ion peak. They undergo Retro – Diels – Alder reaction.



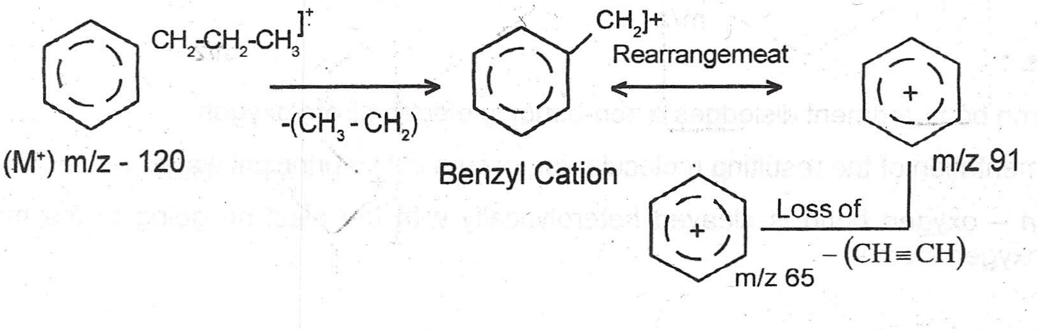
2.2.12. Alkyl Aromatic Compounds :

1. The molecular ion peak in aromatic compounds is fairly abundant as compared to the corresponding alkanes and alkenes containing the same number of carbon atoms.

2. In aromatic compounds $M^{+}+1$ and $M^{+}+2$ are also noticed. The reason is fairly large abundance of the molecular ion peak.

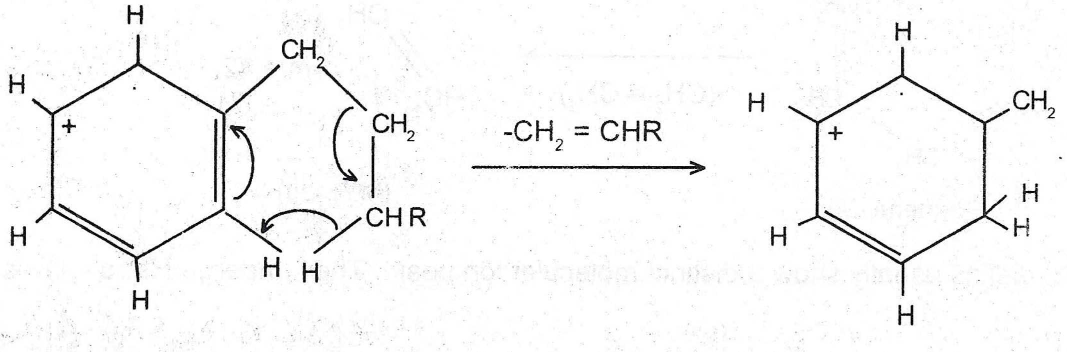
3. In case of polynuclear hydrocarbons, doubly or triply charged ions $\left(M^{2+}, M^{3+} \text{ ions}\right)$ are possibly formed. Doubly charged molecular ions (m/z) appear at integral 'm/z' values.

4. If the aromatic ring is substituted by an alkyl group, a prominent peak is formed at m/e 91. Here benzyl $\left(C_6H_5^{+} CH_2\right)$ cation formed rearrangements to tropylium cation $\left(C_7H_7^{+}\right)$. The fragmentation pattern of n-propyl benzene is shown below.



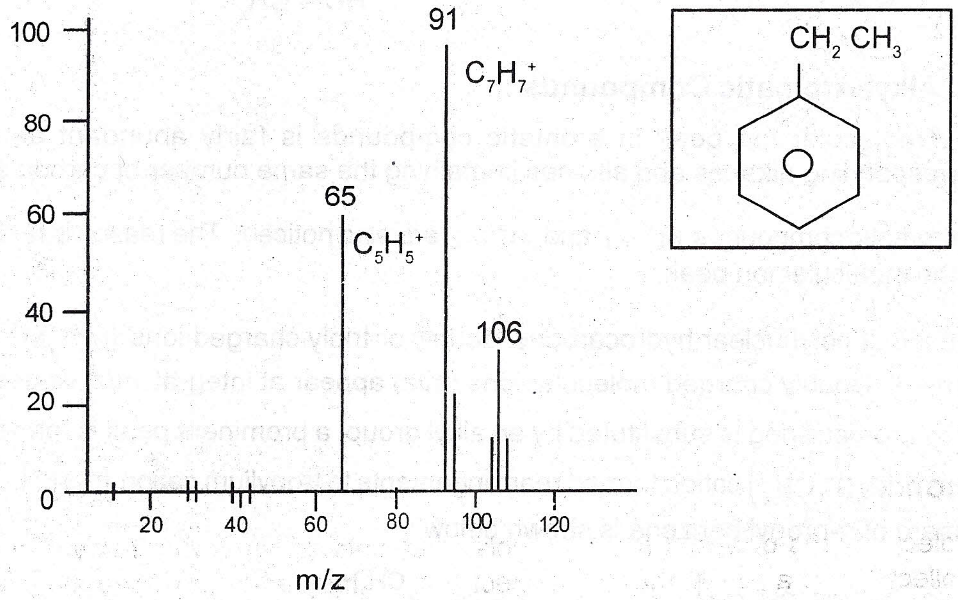
The benzyl cation formed rearranges to more stable tropylium cation which appears at 'm/e 91'. Tropylium cation in turn loses a molecule of acetylene to form $C_5H_5^+$ at m/e 65.

5. Hydrogen migration with elimination of neutral alkene molecule accounts for the peak at m/z 92 observed when the alkyl group as longer than 'C_2'.



A characteristic cluster of ions due to a α cleavage and hydrogen migration in mono alkyl benzenes appears at m/z 77 $(C_6H_6^+)$ 78 $(C_6H_6^+)$ and 79 $(C_6H_7^+)$.

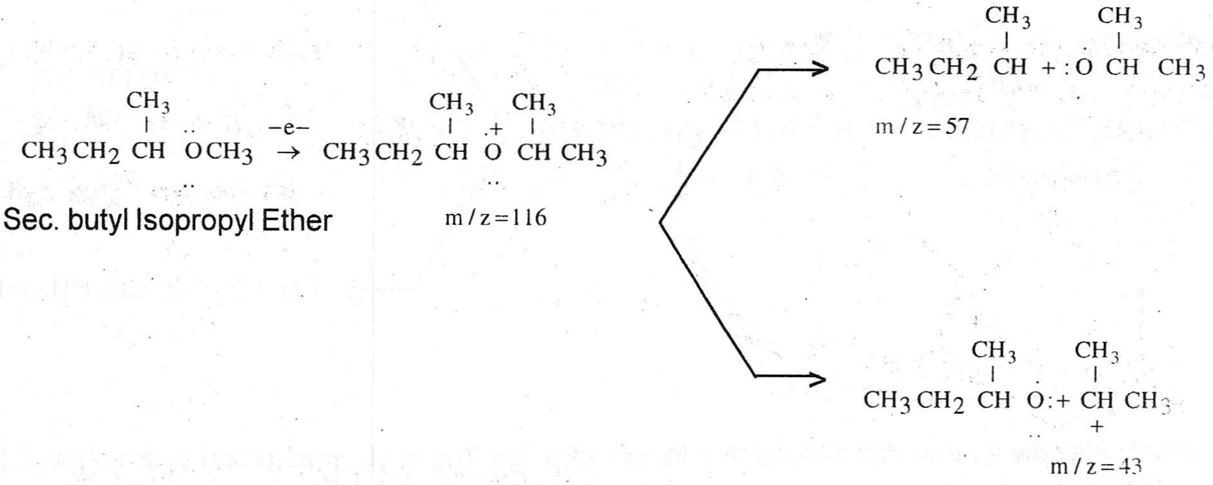
The mass spectrum of ethyl benzene is shown below



2.2.13. Ethers :

1. Electron bombardment dislodges a non-bonding electron from oxygen.
2. Fragmentation of the resulting molecular ion occurs in two principal ways.

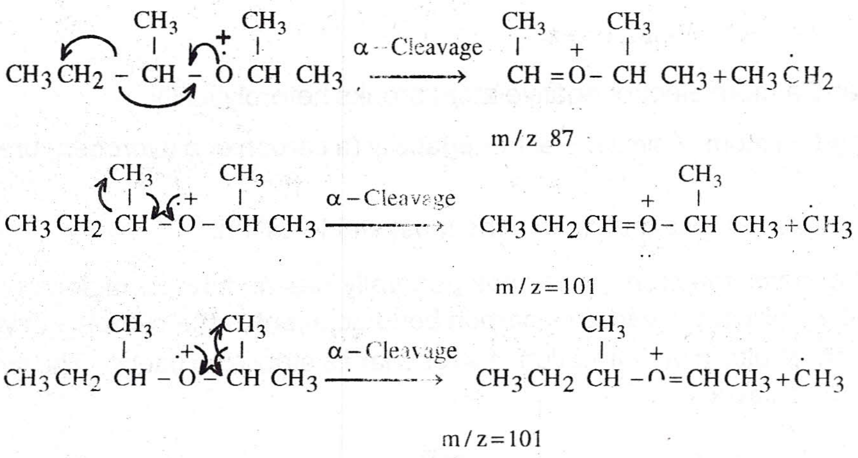
a) A carbon – oxygen bond is cleaved heterolytically with the electron going to the more electronegative oxygen atom.



Sec. butyl Isopropyl Ether

$[C_3H_7^+]$ (m/z = 43) is the molecular ion peak

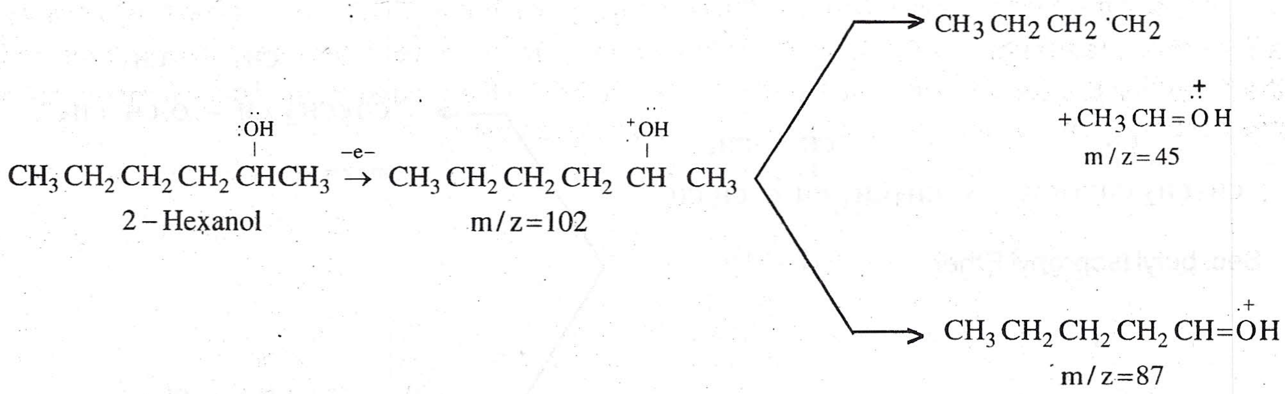
b) A carbon – carbon bond is cleaved homolytically at the α–position because it leads to a resonance - stabilized cation. The largest α - substituent is the one most readily cleaved.



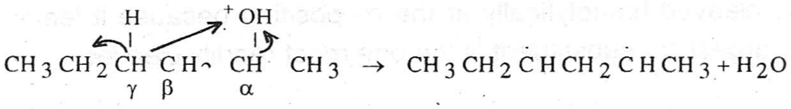
2.2.14. Alcohols :

The molecular ions obtained from alcohols fragments so readily that few of them survive to reach the collector. As a result, the mass spectra of primary and secondary alcohols show weak molecular ion peaks, and the molecular ions from 3^{o} alcohols are not detectable.

Alcohols, like alkyl halides and ethers undergo α - cleavage, with the largest α-substituent being the one most readily cleaved. Consequently, the mass spectrum of 2-hexanol shows a base peak at m/z – 45 (α-cleavage of a butyl radical) and a smaller peak at m/z = 87 (α-cleavage of a methyl radical)



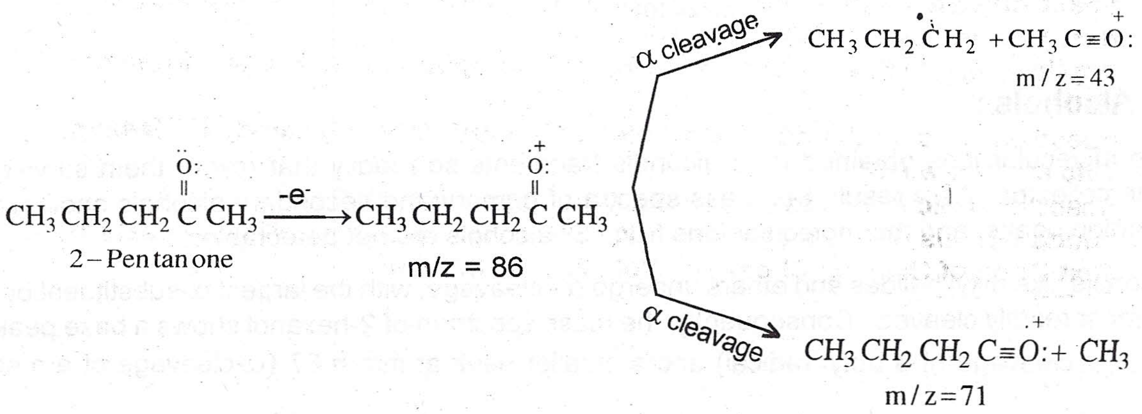
Alcohols show a peak m/z = m-18 due to loss of water that is eliminated comes from the 'OH' group of alcohol and γ – hydrogen.



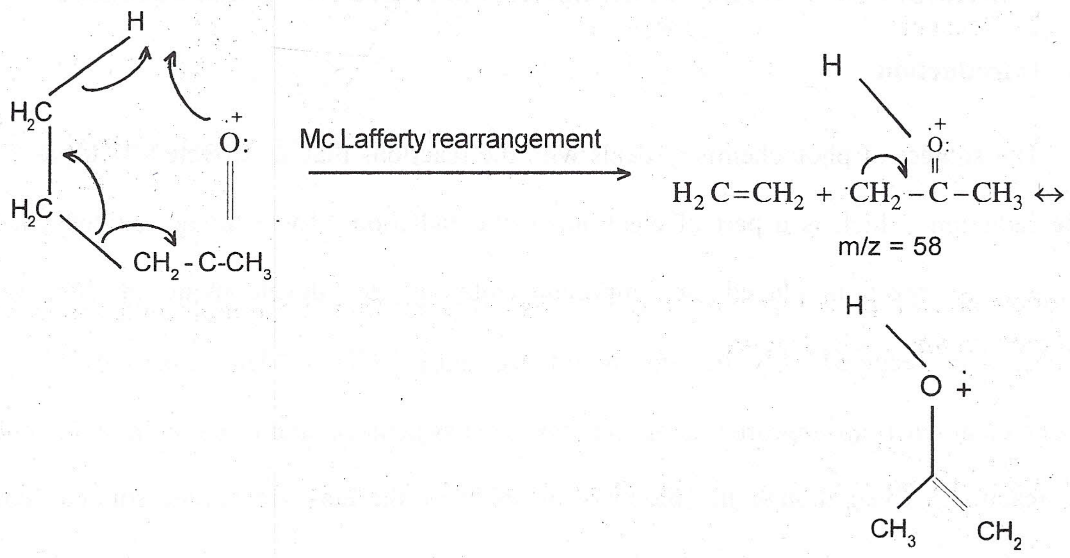
$$m / z = (102 - 18) = 84$$

1. A bond between carbon and a more electronegative atom breaks heterolytically.
2. A bond between carbon and an atom of similar electronegativity (a carbon or a hydrogen) breaks homolytically.
3. The bond most likely to break are those that lead to the most stable cation.

2.4.15. Ketones : The mass spectrum of ketones generally has an intense molecular ion peak. Ketones fragment homolytically at the carbon – carbon bond adjacent to the carbon – oxygen double bond (α-cleavage) which results in the formation of a resonance stabilized cation. The larger alkyl group is the one most easily cleaved.



If one of the alkyl groups attached to the carbonyl carbon has a γ-hydrogen, a cleavage known as a 'Mc Lafferty rearrangement' may occur. In this rearrangement the bond between the α - carbon and the β - carbon breaks homolytically and a hydrogen atom from the oxygen atom. Again, fragmentation has occurred in a way the produces a resonance stabilized cation.



2.2.16. Suggested Readings

1. **Some Modern methods of Organic Synthesis, W. Carruthers, Cambridge University Press.**
2. **Advanced Organic Chemistry, Reactions Mechanisms and Structure, J. March. John Wiley**
3. **Advanced Organic Chemistry Part B, F.A. Carey and R.J. Sundberg, Plenum Press 1.**
4. **Spectrometric Identification of Organic Compounds, R. M. Silverstein, G.C. Bassler and T. C. Morrill, John Wiley.**
5. **Applications of Spectroscopy of Organic Compounds, J. R. Dyer, Prenctice Hall.**
6. **Spectroscopic methods in Organic Chemistry, D.H. Williams, I. Fleming, Tata Mc. Graw Hill**
7. **Spectroscopic methods in Organic Chemistry – Kemp**
8. **Fundamentals of Photochemistry, K.K. Rohtagi – Mukherji, Wiley – Eastern**
9. **Text Book of Organic Chemistry Vol I & II – I. L. Finar.**

Lesson 1

PHOTOCHEMICAL REACTIONS

INTRODUCTION TO PHOTO CHEMISTRY AND PHOTO PHYSICAL PROCESSES

3.1.i) Introduction

The subject of photochemistry deals with the reactions that are affected by ultra-violet, a visible radiation, which is a part of electromagnetic radiation. Even though photosynthesis, a photochemical reaction played an important role in the development of life, organic photochemistry received only limited importance until 1940s. Many examples of organic photochemical reactions appeared before that time, but systematic studies were limited to only gas phase reaction. Even though the products of some of the early reactions, studied were not available from other methods of synthesis, solution photochemistry was neglected, largely because the reaction mixture was complex and no useful methods were developed for the isolation of products. The instruments were costly and the scientists were handicapped by the non-availability of artificial sources of visible and ultra-violet light of suitable intensity. The introduction of new spectroscopic and analytical methods reduced the difficulty in characterising the complex mixture of products of photochemical reactions and the development of organic photochemistry.

3.1.ii) Interaction of electromagnetic radiation with matter

In photochemistry a molecule absorbs radiation and promoted to highly energetic state called excited state. Therefore, it is necessary to know about radiation and excited states associated with photochemistry. The regions of electromagnetic spectrum that are important to photochemist for ultraviolet (1500-4000 A°), the near ultraviolet (2000 to 4000 A°) and the visible region (4000 to 8000 A°).

We know that the absorption of energy by molecules or atoms, which normally exist in a state of minimum electronic energy or ground state, raises them to a less stable state of higher electronic energy or excited state. The absorption process is referred to as excitation. Excited species can lose their energy by a variety of means. The most common of these are the emission of radiation and the loss of surroundings through collisions.

In a photochemical process this energy is in the form of light. Light of any wavelength has associated with it an energy value given by equation $E = h\gamma$, where γ is the frequency of the light and h is Plank's constant whose value is 6.6×10^{-27} erg. sec or 6.6×10^{-34} Joule-sec. It may be seen from the relationship $E = h\gamma$, $\gamma = C/\lambda$ and $E = hC/\lambda$ that energy is inversely proportional to wavelength i.e the larger the wavelength the lower the energy of radiation.

Since the energy levels of the molecule are quantized, the amount of energy required to raise an electron in a given molecule from one level to a higher one is a fixed quantity. Only light with exactly the frequency corresponding to this amount of energy with cause the electron to move to a higher level. If the light of another frequency is sent through a sample, it will pass out without a loss in intensity, since the molecules will not absorb it. However, if light of correct frequency is passed in the energy will be used by the molecules for electron promotion and hence the light that leaves the sample will be diminished in intensity or altogether. Therefore each substance is selective in its absorption of radiation depending on the presence of chromophores which are atoms or functional groups which usually contain p electrons or π bonds. The various wavelength ranges at which absorption takes place are determined from the absorption spectra, which are the plots of the wavelength against the amount of radiation absorbed or passing through a substance.

The total energy of the system consists of 3 components.: rotational, vibrational and electronic energies. The difference between two adjacent vibrational levels is smaller than the difference between adjacent electronic levels, and the difference between adjacent rotational levels is small still than vibrational levels i.e why a molecule at any time is in a given electronic state but also in a given vibrational and rotational state. When electron move from one electronic level to another, it moves from a given vibrational and rotational level within that electronic level to some vibrational and rotational level at the next electronic level. IR spectra involve only transitions between vibrational levels like V_0, V_1 of E_1 and rotational transitions are found in far IR. The largest of the 3 energies is electronic excitation energy and it is about 10 times that of vibrational energy. Visible and UV will cause transitions between electronic levels. The excitation energy is of high magnitude which can be comparable to bond energies of molecules, i.e. many reactions involving breakage of bonds with this energy as feasible.

3.1.iii) Quantum yield

The quantitative relationship between the number of molecules which react or are formed and the number of photons absorbed in a unit time is given by quantum yield ϕ.

$$\phi = \frac{\text{Number of molecules undergoing a particular process}}{\text{Number of quanta absorbed by the system}}$$

The number of molecules reacting or formed per unit time is measured by any convenient analytical kinetic technique, and the number of photons absorbed per unit time is measured by actinometer (a chemical or physical device capable of counting photons). Thus if for every photon absorbed a molecule undergoes a certain photochemical process, the quantum yield for the process is unity. If other processes, such as fluorescence or phosphorescence compete with the one under consideration, the quantum yield will be less than unity. Thus the quantum yield of photochemical reactions, referring specifically to the primary process, is always ≤ 1, The primary process is here defined as starting with the absorption of a photon and ending with the disappearence of the molecule or its deactivation to a non reactive state.

3.1.iv) Electronically excited states (Singlet and triplet states and forbidden transitions)

Electronically excited states are obtained by the promotion of an electron from bonding molecular orbital to antibonding molecular orbitals. Bonds are considered to be spaces of higher electron density between adjacent atoms; they are physical representations of molecular orbitals The latter are wave functions concerned with expressing the probability of finding electrons and they can be expressed interms of linear combination of atomic orbitals.

In photochemistry we deal mostly with three types of molecular orbitals characterized by their spacial properties (1) "σ" orbitals formed by the axial overlap of atomic orbitals, (2) π orbitals formed by parallel overlap of pure p orbitals and (3) n-orbitals which contain non-bonding electron pair on atoms such as oxygen and nitrogen which are localised on those atoms. These three molecular orbitals (σ, π and n) which are of lower energy are usually populated in the ground state and are called bonding orbitals. The absorption of light energy by orgnaic compounds in the visible and UV region involves promotion of electrons in the σ, π and n orbitals to higher energy states. These higher energy states are described by molecular orbitals that are vacant in the ground state are commonly called "antibonding orbitals." The antibonding orbitals associated with σ and π are σ^* and π^*. As the "n" electrons do not form bonds, there are no antibonding orbitals associated with them.

In most organic molecules all electrons in the ground state are paired, each member of a pair possessing opposite spin, as demanded by the Pauli principle,. When one of a pair of electrons is promoted to an orbital of higher energy, however, the Pauli principle no longer applies because the two electrons are no longer sharing an orbital, and the promoted electron may in principle have the same spin as its former partner or the opposite spin. When referring to the relative spins of two such electrons, one speaks of the multiplicity of the molecule. The term originally referred to the number of spectral lines in the atomic absorption and emission spectra observed in magnetic fields of appropriate strength. It is defined by $2S + 1$, where S is the total spin – the absolute value of the sum of the spin quantum numbers involved (+ ½ or -½).

In most photochemical reactions only two half-vacant orbitals are associated with a molecule in the excited state, the orbital from which the transition takes place and the antibonding orbital to which the electron is promoted, and consequently only two values for multiplicity are obtained, 1 and 3. The former in which the spin has been preserved is called the "singlet" state and the latter, in which the spins are parallel, is the "triplet" state. Most organic molecules in the ground state are singlets. Thus a molecule in which two unpaired electrons have the same spin is called a triplet, while one in which all spins are paired is a singlet. Thus atleast in principle, for every excited singlet state there is a corresponding triplet state. In most cases the triplet state has a lower energy than the corresponding singlet. Therefore a different amount of energy and hence a different wavelength is required to promote an electron from the ground state (which is almost always a singlet) to an excited singlet than to the corresponding triplet state.

It would thus seen that promotion of a given electron in a molecule, could result either in a singlet or a triplet excited state depending on the amount of energy added. However, this is often not the case because transitions between the energy levels are governed by selection rules which state that certain transitions are "forbidden." There are several types of forbidden transitions, out of which spin-forbidden transitions and symmetry-forbidden transitions are more important.

a. Spin forbidden transitions

Transitions in which the spin of an electron changes are not allowed, because a change from one spin to the opposite involves a change in angular momentum, and such a change would violate the law of conservation of angular momentum. Therefore, a singlet-triplet and triplet-singlet transitions are forbidden, whereas singlet-singlet and triplet-triplet transitions are allowed. The presence of heavy atoms, unpaired electrons or a magnetic field results in a breakdown of the selection rules, and singlet-triplet conversions then take place, even though according to the rules of spin conservation they are not "allowed."

b. Symmetry forbidden transitions

Orbitals are frequently designated by their symmetry properties. The σ orbital of H_2 is often written φ_g. The g stands for grade. A gerade orbital is one in which the sign of the orbital does not change when it is reflected through its center of symmetry. The σ* orbital is ungerade (designated φ_u). The ungerade orbital changes sign when reflected through its center of symmetry. Selection rules state that g → u and u → g transitions are allowed and that g → g and u → u transitions are forbidden.

5)

3.1.v) Types of transitions and carbonyl chromophore

When an electron in a molecule is promoted it usually goes into the lowest available vacant orbital, though promotion to higher orbitals is also possible if any are available. For most organic molecules there are consequently four types of electronic excitation (transition).

1. $\sigma - \sigma^*$: Alaknes, which have no "n" and "π" electrons can be excited only in this way.

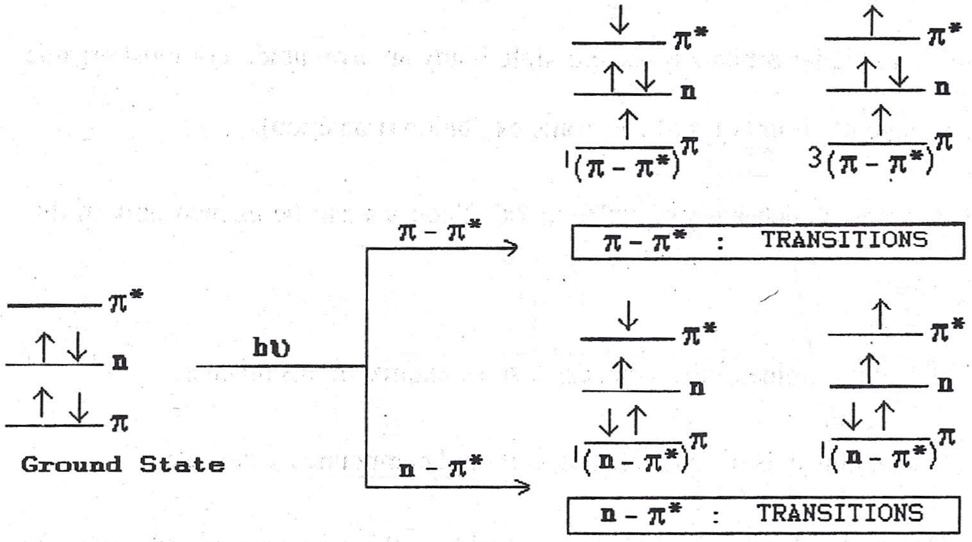
2. $n - \sigma^*$ Alcohols, amines, ethers etc. can also be excited in this manner.

3. $\pi - \pi^*$: This pathway is open to alkenes, carbonyl compounds, esters etc.

4. $n - \pi^*$: Aldehydes, ketones, esters etc. can under go this transition in addition to the above three. :

The four excitation types listed above are in the order of decreasing energy. Thus the light of highest energy is necessary for $\sigma - \sigma^*$ excitation, whereas $n - \pi^*$ transitions are caused by light of lowest energy. Of the four excitation types listed above the $\pi - \pi^*$ and and $n - \pi^*$ are more important in organic photochemnistry than the other two.

Transitions and their multiplicity in carbonyl compounds

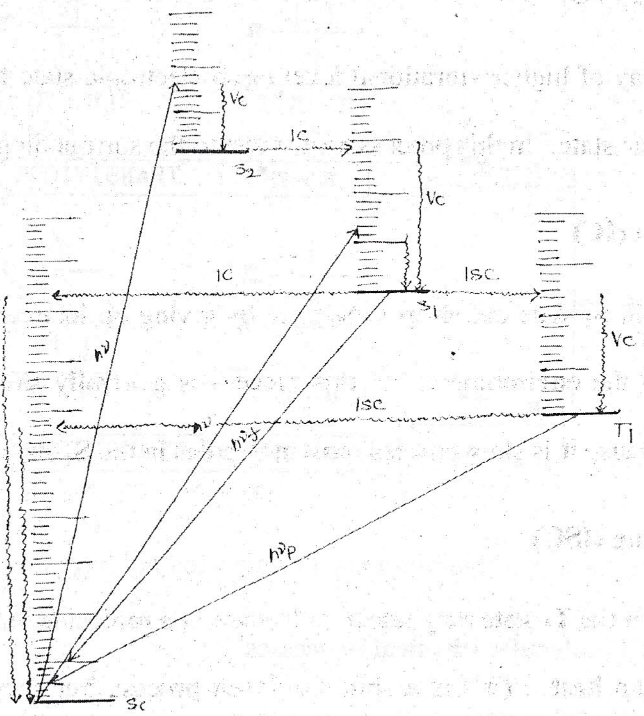


S_1 state always has $n - \pi^*$ configuration but T_1 state need not have $n - \pi^*$ configuration.

3.1.vi) The fate of excited molecule: Physical processes

(Deactivation of excited states)

When a molecule has been photochemically promoted to an excited state, it does not remain there for long time. Most promotions are from S_0 to the S_1 state. As we have seen promotions from S_0 to triplet states are forbidden, promotions to S_2 and higher excited states take place, but in liquids and solids these higher states usually drop very rapidly to S_1 state. The energy which is lost when S_2 or S_3 molecules drops to S_1 is given up in small increments to the environment by collisions with neighbouring molecules. Such a process is called energy cascade. In a similar manner, the initial excitation and decay from higher singlet states initially populate many of the vibrational levels of S_1, but these also cancade down to the lowest vibrational level of S_1. Therefore in most cases the lowest vibrational level of the S_1 state is the only important excited singlet state. This state can undergo various physical and chemical processes. The physical processes are best represented by a diagram called Jablonski diagram.



Modified Jablonski Diagram Showing transitions between excited states and ground state. Radiative processes are shown by straight lines; radiation less processes by wavy lines. IC= Internal conversion; ISC = Intersysten. crossing; VC=Vibrational cascade; $h\nu_f$ = fluorescence, $h\nu_p$ = phosphorescence.

Photo physical process is of two types – (1) unimolecular photo physical processes and (2) bimolecular photo physical processes. The bimolecular photo physical process is also called photo sensitization or triplet energy transfer. Uni molecular photo physical processes involve loss of energy by an excited states with excess energy leading to deactivation or decay of excited states. This deactivation or decay of an excited state is of two types – (1) Thermal decay which include vibrational cascade, internal conversion and inter-system crossing and (2) Radiative decay which include fluorescence and phosphorescence.

Vibrational cascade (VC)

Thermal decay of higher vibrational level of an electronic state to lowest vibrational level of the same electronic state. In this process heat is lost to the surroundings including solvent.

Internal conversion (IC)

A molecule in S_1 state can drop to S_0 state by giving up its energy in the form of heat in small increments to the environment, but this process is generally slow because the amount of energy is large. Because it is slow process most molecules in the S_1 state adopt other pathways.

Inter-system crossing (ISC)

A molecule in the T_1 state may return to S_0 state or a molecule in S_2 state may cross over to T_1 state by giving up heat. This is a spin forbidden process but occurs to different extent in different compounds. For example, carbonyl compounds have high inter-system crossing efficiency whereas olefins and conjugated dienes have minimum or zero inter-system crossing efficiency.

Fluorescence ($h\nu_f$)

Change over of higher electronic state by emission of radiation to the lower electronic state of same multiplicity is called fluorescence.

Fluorescence ($h\nu_p$)

Change over of higher electronic state by emission of radiation to the lower electronic state of different multiplicity is called phosphorescence.

3.1.vii) Transfer of excitation energy

This is a secondary means of producing electronically excited states. The method involves transfer of excitation energy from an electronically excited molecule to the ground state of another molecule, and is generally used for producing triplet states. This energy transfer is also called as photosensitization and is intended for the generation of triplet states of compounds with low inter-system crossing efficiency. In this process excess of a compound with very high inter-system crossing (ISC) efficiency (eg: benzophenone) is mixed with a compound with a very low inter-system crossing efficiency (example: butadiene) and irradiated at λ_{max} of compound with high ISC efficiency. The triplet energy transfer occurs from benzophenone to butadiene at every collision between molecules. In this process the compound with high ISC efficiency is called Donar and the compound with low ISC efficiency is called acceptor and the Donar is also called photo sensitizer.

$$\text{Benzophenone + Butadiene} \xrightarrow{h\gamma} \text{Triplet state of butadiene}$$

The important.requirements for a good sensitizer is that (1) the energy of sensitizer must be at least 3 K cal more than that of acceptor and (2) for a good sensitizer the triplet energy (E_{T1}) and singlet energy (E_{S1}) of Donar should be in between those of acceptor. Imagine a donar-acceptor system such that only the donar absorbs the incident light, and the triplet energy of the donar is at least 3 K cal/mole greater than the triplet energy of the acceptor. Light absorption by the donar produces singlet excited donar ^1D, which undergoes inter-system crossing, giving triplet excited donar ^3D. Triplet excited donar then collides with acceptor, producing triplet excited acceptor ^3A and ground state donar D.

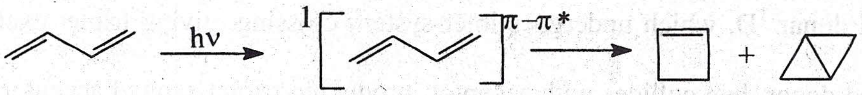
$$D + h\nu \longrightarrow {}^1D$$

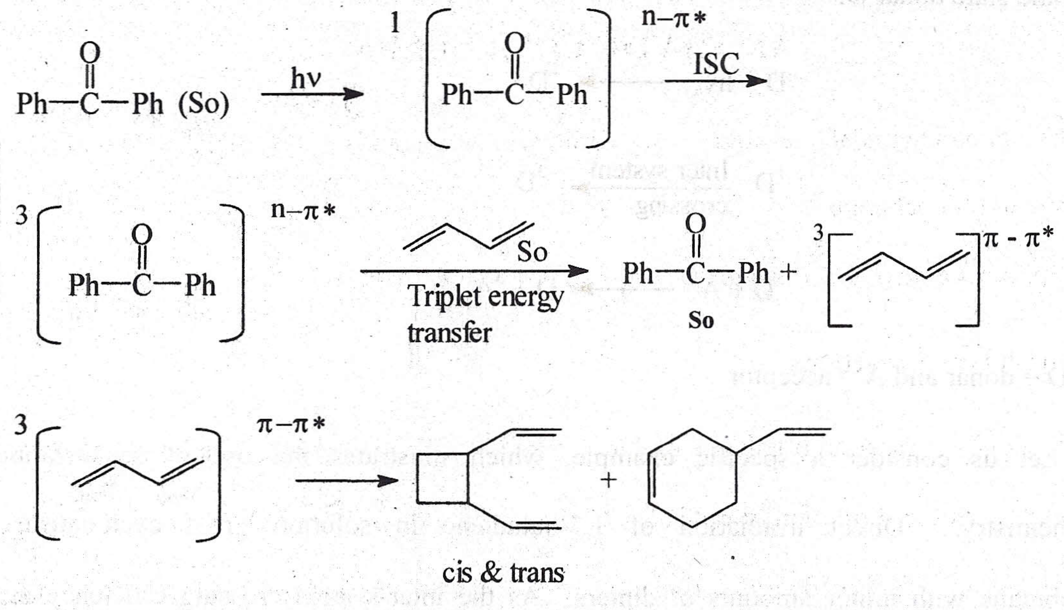
$${}^1D \xrightarrow[\text{crossing}]{\text{Inter system}} {}^3D$$

$${}^3D + A \longrightarrow D + {}^3A$$

where D = donar and A = acceptor

Let us consider a specific example, which illustrates the use of sensitization in photochemistry. Direct irradiation of 1,3-butadiene in solution gives cyclobutene and bicyclobutane with minor amounts of dimers. As the inter-system crossing efficiency in 1,3-butadiene is zero triplet derived products are not formed. Triplet excited 1,3-butadiene produced by energy transfer from triplet excited benzophenone gives only dimers.





Model Question:

1. Write a note an quantum yield.

2. What are electronically excited states? Explain their nomenclature and difference in stability and reactivity.

3. Explain the types of transitions we can expect in carbange compounds.

4. Describe different photo physical processes involved in deactivation of excited states and draw the Jablonski diagram incaparating different photo physical processes.

5. Explain the process of photo sensitization

Recommended books:

1. Importance of antibonding orbitals by jaffe and orchin.
2. Molecular reactions and photo chemistry, by charles dupey and O.L. chapman.
3. Molecular photo chemistry, by Turro

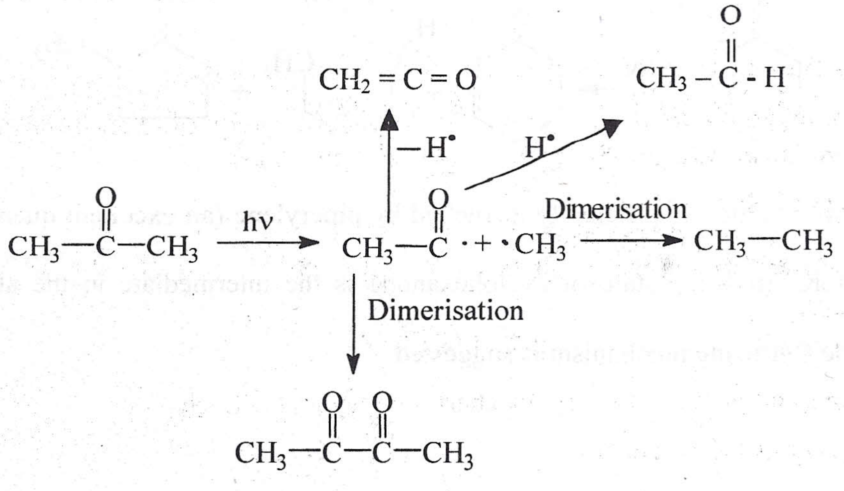
LESSON II

PHOTOCHEMISTRY OF CARBONYL COMPOUNDS, OLEFINS AND AROMATIC COMPOUNDS

The photochemical reactions of carbonyl compounds are mainly classified as intermolecular photochemical reactions and intra molecular photochemical reactions. The intra molecular photochemical reactions involve Norish type I and type II reactions.

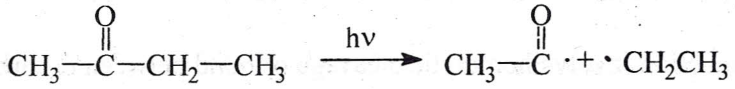
3.2.i) Norish type I reactions

Norish type I reaction involve homolytic cleavage of bond between α-carbon and carbonyl carbon resulting in the formation of radicals. These radicals undergo hydrogen transfer, hydrogen elimination, dimerisation or disproportionation leading to the formation of variety of products. Type I reactions occur more efficiently in vapour phase, but the reaction is suppressed in solution phase due to solvent case effect.

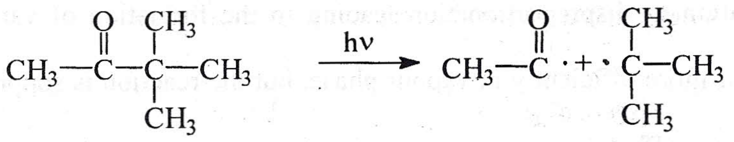


The half vacant non-bonding orbital of $n - \pi^*$ excited state overlaps the σ-bond orbital between the carbonyl carbon and the α-carbon. This overlap facilitates cleavage of the α-bond. The carbon atom of the carbonyl group undergoes rehybridization during the process of formation of acyl radical. Both singlet and triplet states having $n - \pi^*$ configuration undergo Norish type I cleavage, also called as α-cleavage.

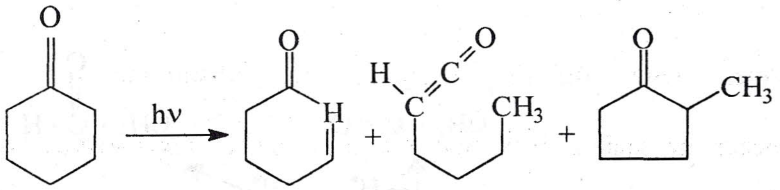
In unsymmetrical carbonyl compounds the α-bond which gives rise to more stable free radical by fission is cleaved



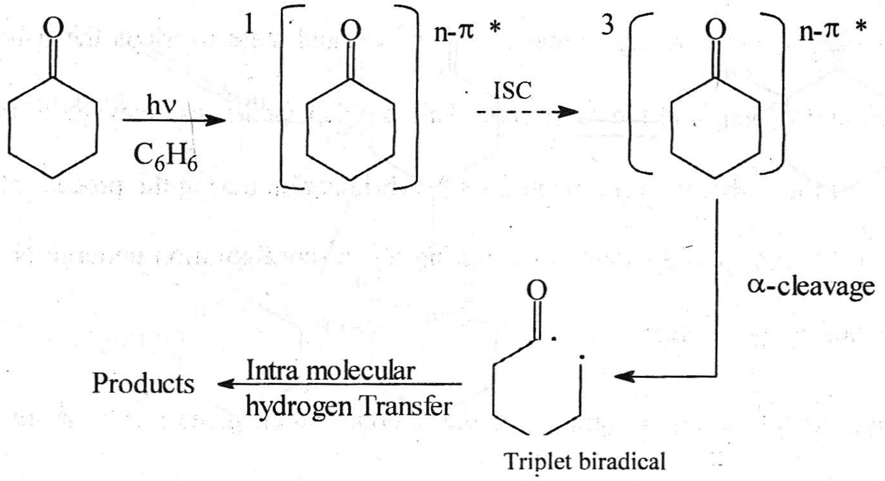
$$CH_3-\overset{O}{\overset{\|}{C}}-CH_2-CH_3 \xrightarrow{h\nu} CH_3-\overset{O}{\overset{\|}{C}}\cdot + \cdot\, CH_2CH_3$$



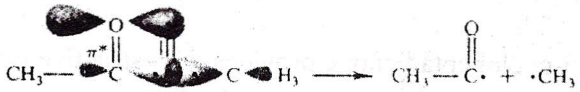
$$CH_3-\overset{O}{\overset{\|}{C}}-\underset{CH_3}{\overset{CH_3}{\overset{|}{C}}}-CH_3 \xrightarrow{h\nu} CH_3-\overset{O}{\overset{\|}{C}}\cdot + \cdot\,\underset{CH_3}{\overset{CH_3}{\overset{|}{C}}}-CH_3$$



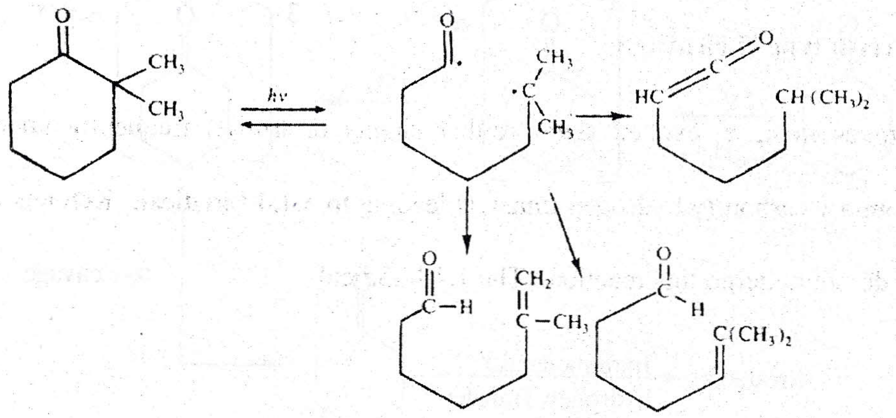
The above reaction is efficiently quenched by piperylene (an excellent quencher of triplet states). Therefore $^3(n - \pi^*)$ state of cyclohexanone is the intermediate in the above reaction. Based on this the following mechanism is suggested.



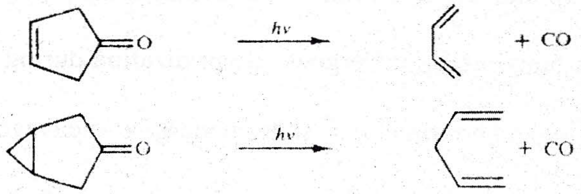
The half-vacant nonbonding orbital of the *n*, π^* excited state overlaps the σ-bond orbital between the carbonyl group and the α-carbon. This overlap facilitates cleavage of the α-bond. The carbon atom of the carbonyl group undergoes rehybridization during the process of formation of the acyl radical. Both singlet and triplet *n*,π^* states undergo α-cleavage.



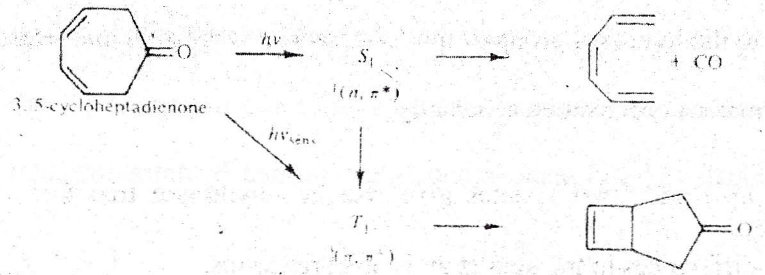
In molecules with differing degrees of substitution on the α-carbons, α-cleavage will occur in such a way that the most stable alkyl radical is formed. 2,2-Dimethylcyclohexanone, for example, cleaves to give the tertiary alkyl radical rather than the primary alkyl radical. The ultimate products are formed by intramolecular hydrogen transfer reactions.



Suitable placed double bonds or cyclopropane rings greatly facilitate α-cleavage.



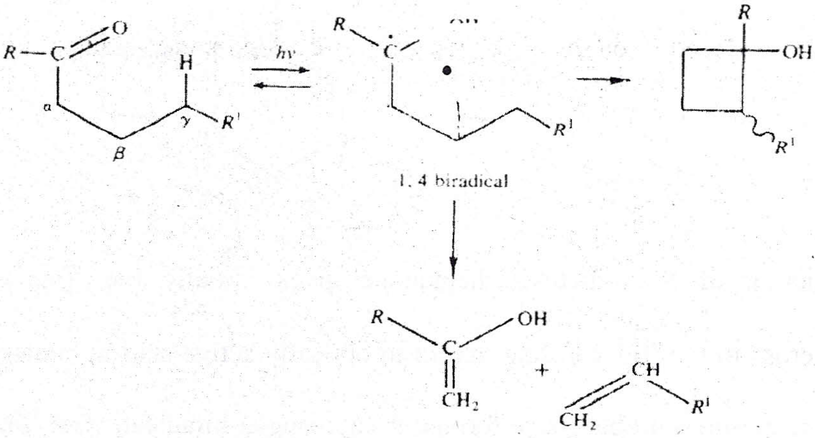
The photochemistry of 3,5-cycloheptadienone provides an instructive example. Direct irradiation gives rise to S_1, which has the $^1(n,\pi^*)$ configuration.



figuration and undergoes α-cleavage, leading ultimately to decarbonylation. The T_1 state produced by energy transfer has the $^3(\pi,\pi^*)$.configuration and leads to isomerization of the diene.

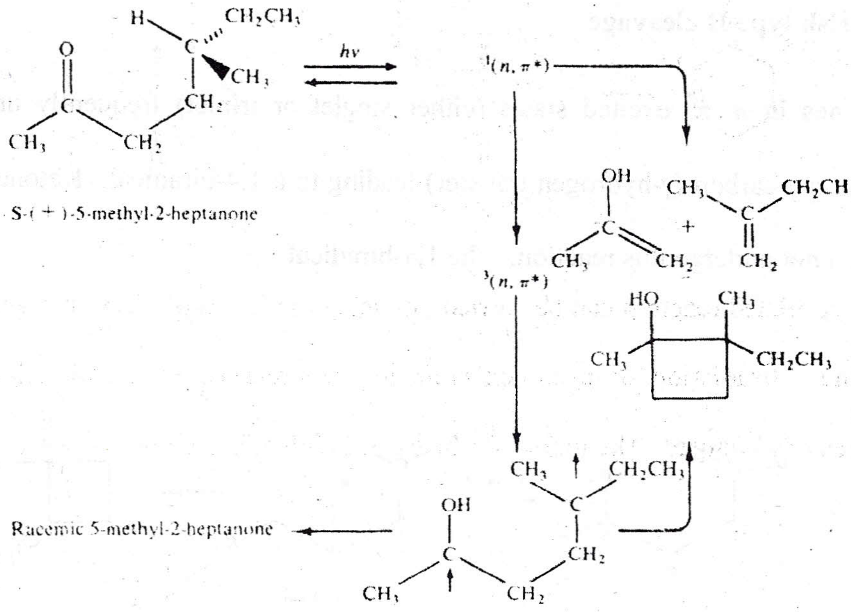
3.2.ii) Norrish type II cleavage

Ketones in n, π^* excited states (either singlet or triplet) frequently undergo hydrogen transfer from a γ-carbon (γ-hydrogen transfer) leading to a 1,4-biradical. Ketones with low-lying π,π^* states do not undergo this reaction. The 1,4-biradical



can revert to starting ketone, Cyclise to a substituted cyclobutanol, or cleave to an olefin and the enol of a ketone. The latter process is known as Norrish type II cleavage. Solvents that can hydrogen bond to the hydroxyl group of the 1,4-biradical stabilize it and retard the reverse reaction and product formation occur move efficiently.

Both $^1(n,\pi^*)$ and $^3(n,\pi^*)$ states give rise in γ-hydrogen transfer. There are, however, distinguishable differences in the singlet and triplet reactions.

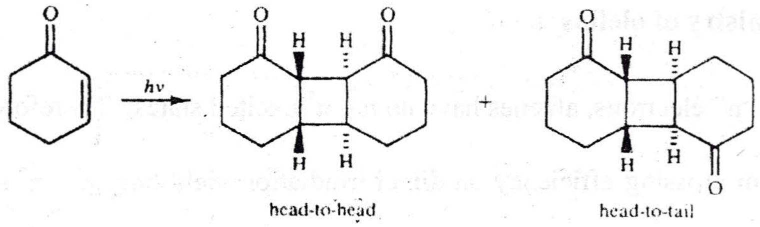


Irradiation of S-(+)-methyl-2-heptanone gives initially the $^1(n,\pi^*)$ state, which can intersystem cross to the $^3(n, \pi^*)$ state, return to optically active starting material, or react to give products. The products probably are formed from a singlet biradical. The $^3(n, \pi^*)$ state gives rise to a triplet biradical, which can decay to racemic starting material or go on to products.

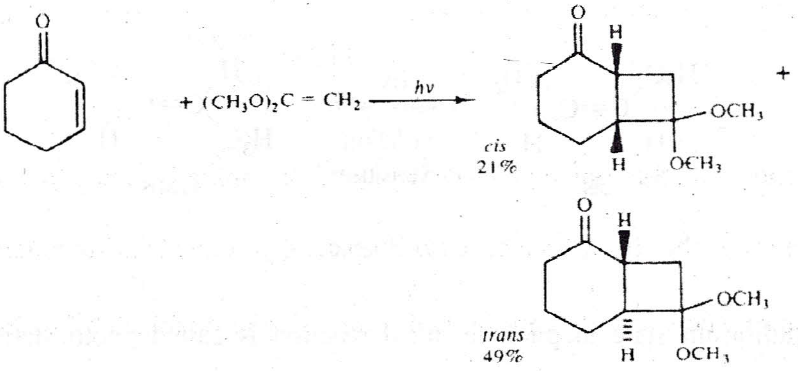
3.2.iii) Photochemistry of α,β-unsaturated ketones

The photochemistry of α,β-unsaturated ketones is rich and varied with many facets of mechanistic interest.

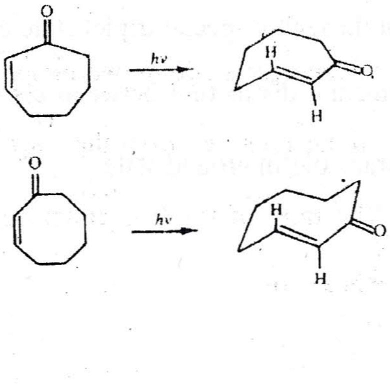
Irradiation of 2-cyclohexenone gives rise to two major photodimers. These dimers may be formed via an excimer (excited dimer) derived from the $^3(\pi,\pi^*)$ cyclohexenone and a molecule of ground state cyclohexenone. The ratio of the two dimers depends on the solvent used. Polar solvents favour formation of the head-to-



head dimer. A related reaction can be carried out using olefins in place of the second molecule of cyclohexenone. Irradiation of cyclohexenone in the presence of 1,1-dimethoxyethylene, for example, gives two adducts. The gighly strained trans adduct is the major product.



When the enone system is in a seven-or eight-membered ring, cis-trans isomerism rather than dimer formation occurs. These trans-enones are reactive and unstable, but they can be studied by spectroscopic methods, trans-2-Cyclooctenone has been isolated.



3.2.iv) Photochemistry of olefins

Having no "n" electrons, alkenes have no $n - \pi^*$ excited states. Therefore most olefins due to zero inter-system crossing efficiency on direct irradiation yield only $\pi - \pi^*$ singlet state $[^1(\pi - \pi^*)]$, whereas triplet sensitized irradiation result in the formation of $^3(\pi - \pi^*)$.

The most important reactions of triplet states are (1) cis-trans isomerisation and (2) protonation.

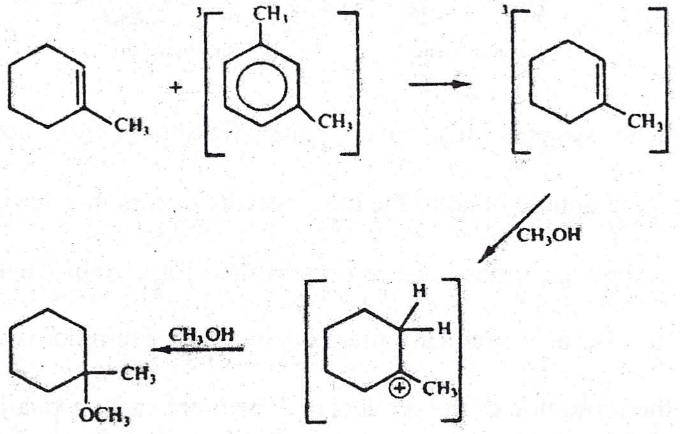
cis-trans isomerisation

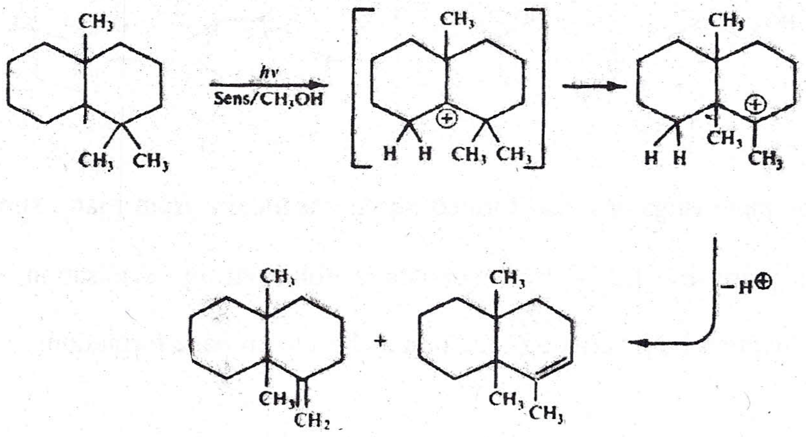
2-Butene

This equilibrium state in photochemical reaction is called photo stationary state. The system is said to be in photo stationary state, when further irradiation does not cause any change in product composition. The important observation that has been during cis-trans isomerisation is that the reaction is sensitized by sensitizers whose triplet energy is lower than that of olefin (against common rule). To account for this it is suggested that the isomerisation does not proceed through a normal triplet state, but through a special triplet state called perpendicular triplet state or twisted triplet state. In this form, the distinction between cis and trans is lost, and the twisted triplet can return to either cis or trans olefin ground state.

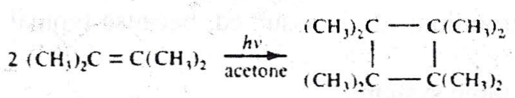
Protonation

Triplet states of cyclohexenes and cycloheptenes, which cannot undergo facile cis-trans isomerisation, protonate readily. Acids as weak as methanol are sufficient, and a sensitized irradiation of a cyclic olefin in methanol makes a useful synthetic method for producing an ether. The intermediacy of a carbonium ion is assumed, because typical carbonium ion rearrangements have been observed in suitable systems.

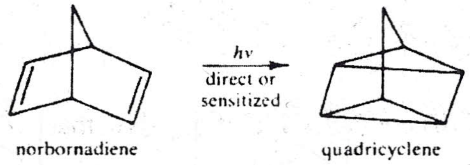




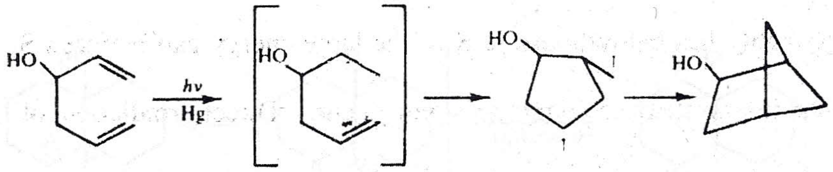
Olefins may also undergo photochemical dimerization, just as unsaturated ketones do. The dimers are formed by reaction of triplet olefin with ground state olefin. Intramolecular as well as intermolecular examples of this reaction are known. The photoisomerization of norbornadiene to quadricylene occurs on direct or sensitized irradiation.



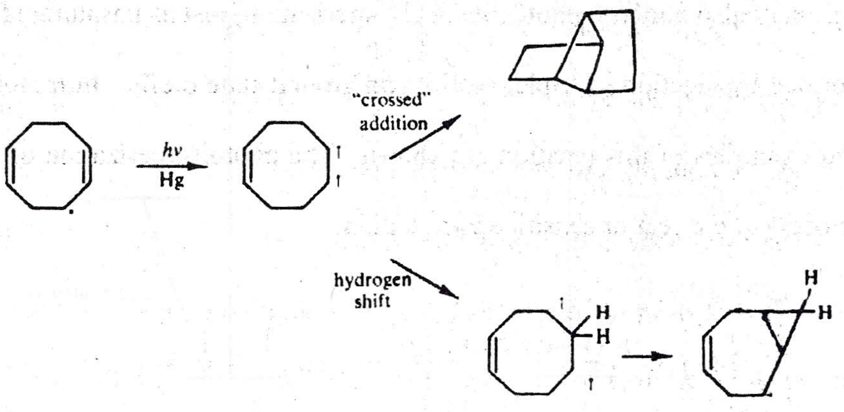
$$2\,(CH_3)_2C=C(CH_3)_2 \xrightarrow[\text{acetone}]{h\nu} \begin{array}{ccc}(CH_3)_2C & - & C(CH_3)_2\\ | & & |\\ (CH_3)_2C & - & C(CH_3)_2\end{array}$$



In 1,5-hexadiene systems that have greater flexibility than norbornadiene, mercury-sensitized addition of one double bond to the other usually occurs in a "crossed" sense, giving rise to bicyclic systems. Although it has not been established for certain whether or not the reaction occurs by way of a discrete biradical intermediate, this example is written with such an intermediate so that the formation of the product may be more easily visualized.



Cyclo propane rings are also formed photo chemically from many simple olefins. The cyclo propanes arise by 1,2 – hydrogen shifts followed by cyclisation. For ex: 1,5 – cyclooctadiene invalves both "crossed" addition and cyclo propane formation.



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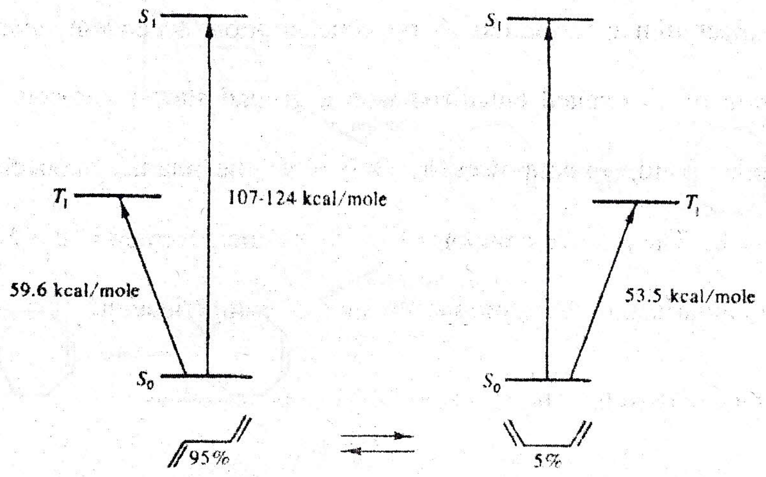
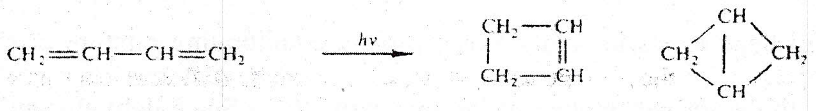
3.2.v) Conjugated olefins

The photochemistry of conjugated olefins, like that of conjugated ketones, is more complex than that of the simple analogs. For the present, we shall consider some of the simpler aspects of the photochemistry of conjugated dienes.

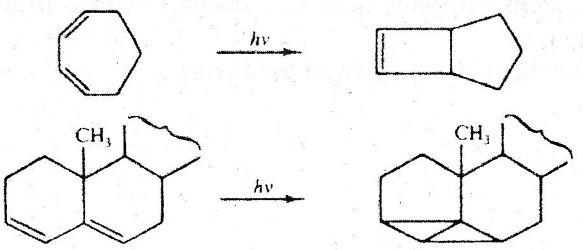
1,3-Butadiene exists in solution as a rapidly equilibrating mixture of transoid and cisoid conformers, with the former predominating by nearly 20:1. Since light absorption occurs without any change in nuclear positions, there are excited states corresponding to each isomer. In Fig. below the energetics of the system are shown. The exact energies of the S_1 states are not known, but cisoid S_1 probably lies below transoid S_1. The large energy gap between S_1 and T_1 accounts for the fact that intersystem crossing does not occur. Direct irradiation of 1,3-butadiene in solution thus gives rise to chemistry only from the S_1 state.



The products of the irradiation of 1,3-butadiene in solution are cyclobutene and bicyclobutane, in a proportion depending upon the solvent used. Neither cyclobutene nor bicyclobutane is found in the vapor phase irradiation of 1,3-butadiene.

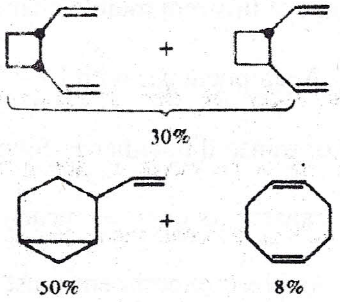


Irradiation of 1,3-dienes in which the diene conformation is determined by the structure suggests that cisoid-1,3-butadiene may be the precursor of cyclobutene and that transoid-1,3-butadiene may be the precursor of bicyclobutane.



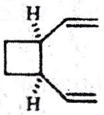
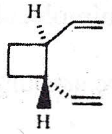
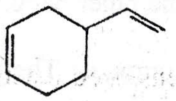
If a concentrated solution of 1,3-butadiene is irradiated, some dimer formation can be detected, although even under the best of circumstances less than 10% dimer formation has been reported. We expect dimer formation to be concentration dependent, since it involves the bimolecular reaction of an excited butadiene with a ground state butadiene. The ring closure reactions, on the other hand, are unimolecular. Only when the butadiene concentration is high can dimerization compete. The relative amounts of the four dimers formed in the direct irradiation are shown below for comparison with the products from triplet dimerization.

$$^{1}[CH_2{=}CH{-}CH{=}CH_2] + CH_2{=}CH{-}CH{=}CH_2 \longrightarrow$$



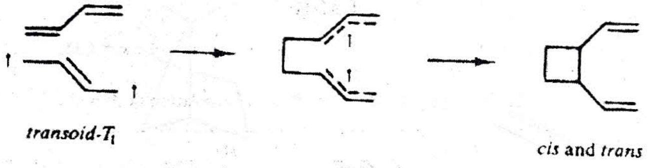
The chemistry of the T_1 state of 1,3-butadiene is quite different from that of the S_1 state. A mixture of dimers is formed in greater than 75% yield, and neither cyclobutene nor bicyclobutane can be detected in the sensitized (triplet) reaction. The dimer mixture obtained from T_1 also differs significantly from that given by S_1. The dimer composition also depends upon the energy of the sensitizer used to populate T_1. The results for the two sensitizers, acetophenone and benzil, are given in Table (below).

Table

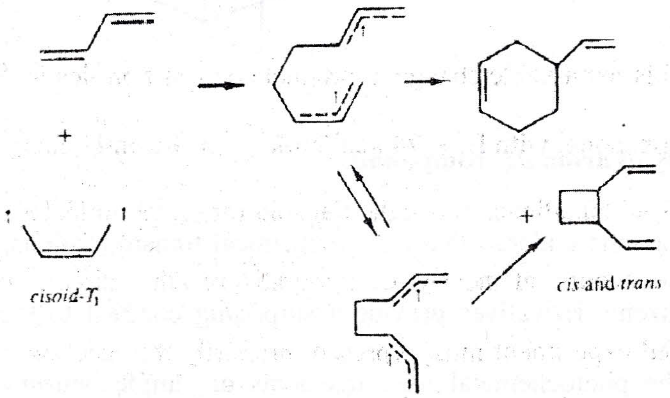
		% composition of dimers		
Sensitizer	E_T (kcal/mole)			
$C_6H_5COCH_3$	74	82	14	4
$C_6H_5COCOC_6H_5$	57	49	8	43

The origin of this remarkable change in product composition lies in the relative energies of the sensitizers. Acetophenone, with E_T = 74 kcal/mole, is sufficiently energetic to transfer energy to either cisoid or transoid butadiene. Since the transoid form predominates by a large margin, and since energy transfer occurs at nearly every collision, the dimer composition from the acetophenone-sensitized experiment must represent primarily the reaction of transoid-T_1. Benzil (E_T = 54 kcal/mole), on the other hand, is energetic enough to transfer energy to cisoid butadiene but not transoid butadiene. The 49:8:43 ratio of dimers must represent the dimer production from cisoid-T_1. If a sensitizer with a triplet energy of less than 54 kcal/mole were used, no dimer formation would be observed.

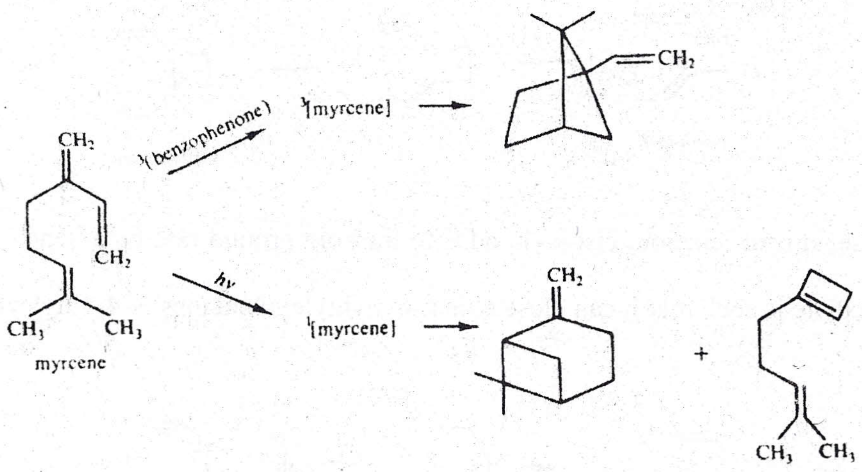
A more detailed analysis of the product ratio tends to confirm this analysis. We hypothesized that when acetophenone is the sensitizer, transoid-T_1 is the reacting species, adding to ground state butadiene. Since the latter is over 95% transoid itself, we have a transoid triplet to transoid ground state addition. The geometry of this intermediate insures that only cis and trans divinylcyclobutanes will be formed, since allyl radicals are known to retain their geometric identity.



In the benzil-sensitized reaction, cisoid-T_1 adds to transoid ground rate butadiene. The geometry of this intermediate is such that it can close either to divinylcyclbutanes or 4-vinylcyclohexene.



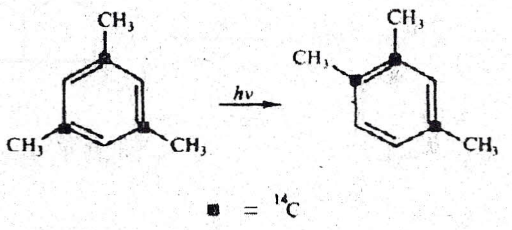
The photochemistry of the terpene, myrcene, provides an example in which monomeric products derived from the excited singlet and excited triplet states are quite different. Direct irradiation of myrcene gives a complex mixture of products, two of which are shown. The triplet state of myrcene, formed by energy transfer from triplet benzophenone, gives only the bicyclo [2,1,1] hexane derivative shown.



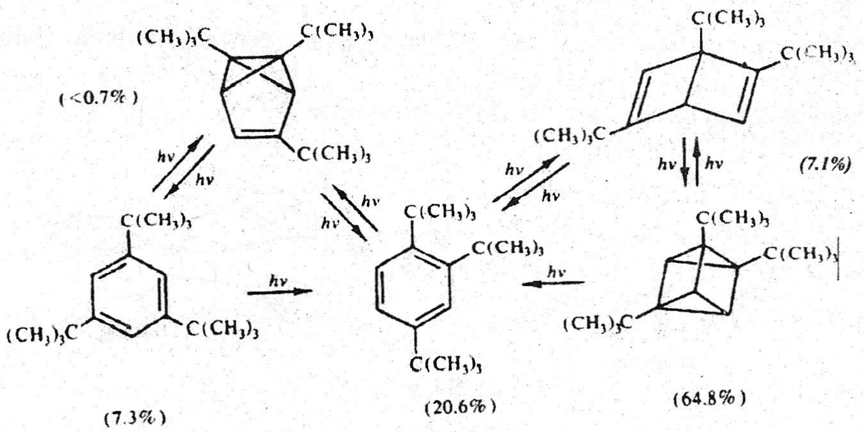
3.2.vi) Photochemistry of aromatic compounds

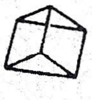
Aromatic compounds undergo many photochemical transformations. The photochemical transformations of benzene derivatives provide a surprising contrast to the thermal stability of aromatic systems. The photochemical rearrangements of simple benzene derivatives provide direct routes to several highly strained molecules. Irradiation of benzene, for example, gives benzvalene and fulvene. Furthermore, alkyl benzenes undergo photochemical isomerization to other isomeric alkyl benzenes.

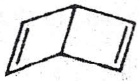
The photoisomerization of 1,3,5-trimethylbenzene to 1,2,4-trimethylbenezene has been shown by ^{14}C-labeling experiments to involve a rearrangement of the atoms in the benzene ring. Additional insight concerning the complexity of this process comes



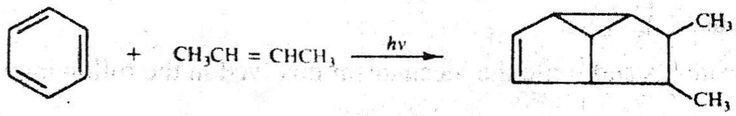
from the investigation of the photochemistry of 1,35-tri-t-butylbenzene and 1,2,4-tri-t-butylbenzene. In this system a photostationary state (a pseudo-equilibrium) is established which involves a benzvalene derivative, a prismane derivative, and a Dewar benzene derivative, as well as the two tri-t-butylbenzenes. The figures in parentheses give the composition of the photstationary state mixture.

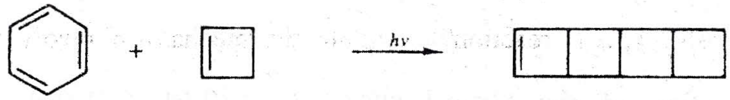


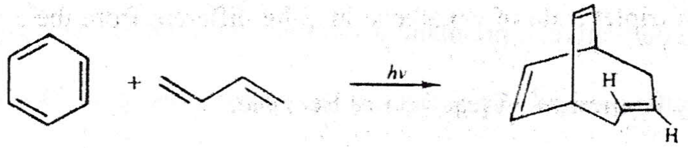

prismane


Dewar benzene

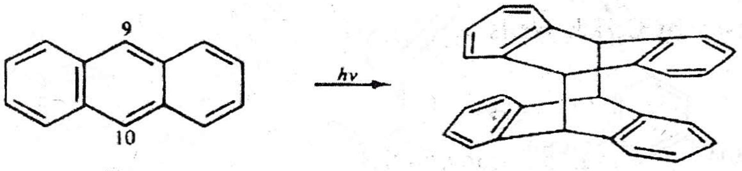
Benzene derivatives also add to olefins and dienes. The addition to simple olefins involves rearrangement as well as addition. In the addition to butadiene there







is reason to believe that the double bond in that portion of the molecule derived from butadiene is trans. Naphthalenes, anthracenes, and polyacenes in general undergo photodimerization. Anthracene may be taken as an example. Two anthracene



anthracene

molecules join at the 9,10-positions in the dimerization.

Model Questions:

1. Predict the products and write the mechanism involved in the following reaction.

(a) Cyclohexanone $\xrightarrow{h\nu}$?

(b) 2, 2-dimethyl cyclohexanone $\xrightarrow{h\nu}$?

2. What is Norish Type II reaction? Explain the mechanism involved by taking a suitable example.

3. What are the important photochemical reactions exhibited by α, β-unsaturated ketones.

4. What are the most important reactions of triplet states of olefins? Explain with examples.

5. The chemistry of triplet state of Butadiene in quite different from the singlet state of Butadiene – Explain.

6. Explain the photo isomerisation reactions of Benzene.

Recommended Books:

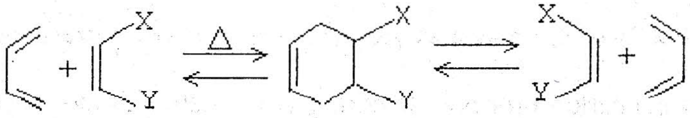
1. The Text book of organic chemistry, by cram and Hammond.
2. Molecular Reactions and Photochemistry by Dupey and Chapman.
3. Organic Photochemistry by Turro.
4. Photo Chemistry by C.H.J. Wells.

LESSON III

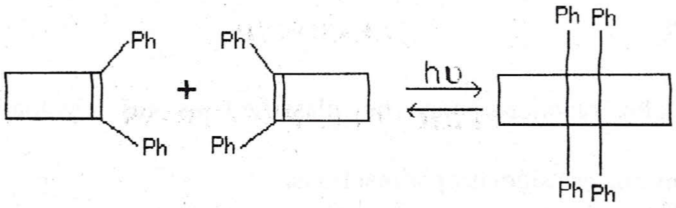
PERICYCLIC REACTIONS

3.3.i) Introduction

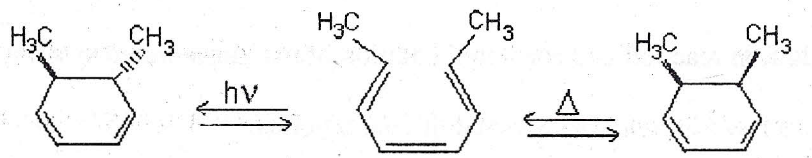
In addition to number of reactions whose mechanism is established by trapping intermediates there remained a group of reactions which are not affected by radical initiators, polar solvents and catalysts. All attempts to trap the intermediates were unsuccessful and these reactions will proceed through a cyclic transition state in a one step process i.e. these are concerted reactions called Pericyclic reactions. They are further characterised by the fact that at least one component of the reactants and the products is unsaturated and the changes in bonding take place through reorganisation of electrons (pair wise) within a closed loop of interacting orbitals (hence the name pericyclic). For example Diel's Alder reaction involving condensation of butadiene and a substituted ethene is a pericyclic reaction which is reversible.



These reactions are largely effected thermally or photochemically. The above reaction is thermally allowed reaction whereas the reaction between two monoenic systems is photochemically allowed.



Similarly these two effects give different stereo chemical results For example



trans-5, 6-dimethyl cyclohexa-1, 3-diene

trans, cis, trans- 2, 4, 6 - octatriene

cis-5,6 dimethyl cyclohexa-1, 3-diene

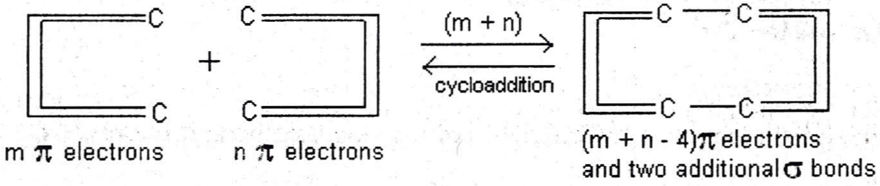
Woodward and Hoffman in 1965, 1970 gave theoretical explanations for these reactions with the help of certain rules known as Woodward and Hoffman rules based on the principle of conservation of orbital symmetry which may be briefly stated as follows: In the pericyclic reactions, a set of MO's of the reactants are transformed into a corresponding set of MO's of the products through a concerted process. If during the transformation, symmetry of the concerned orbitals is conserved i.e the orbitals remain in phase thus maintain some degree of bonding through out the process, the reaction involves a relatively low energy transition state and is called symmetry allowed reaction. On the other hand if orbital symmetry is destroyed the reaction will not occur in concerted manner and is said to be forbidden reaction. For their contribution to these reactions, Woodward and Hoffman were given noble prize.

3.3.ii) Classification

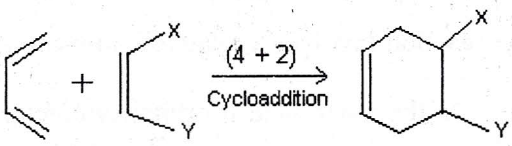
These pericyclic reactions may be classified as (a) Cycloaddition reactions, (b) Electrocyclic reactions and (c) sigmatropic reactions.

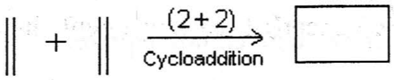
(a) Cycloaddition reactions

Cycloaddition reaction is a concerted addition of two unsaturated systems to form a ring of atoms having two fewer π bonds and two additional σ bonds.



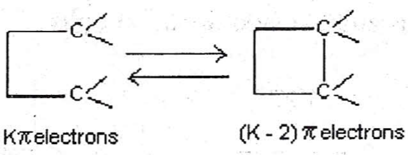
The reverse process is called cyclo reversion. Cyclo addition reactions constitute an important class of C-C bond forming reactions which are used for the synthesis of many complex molecules. For example,





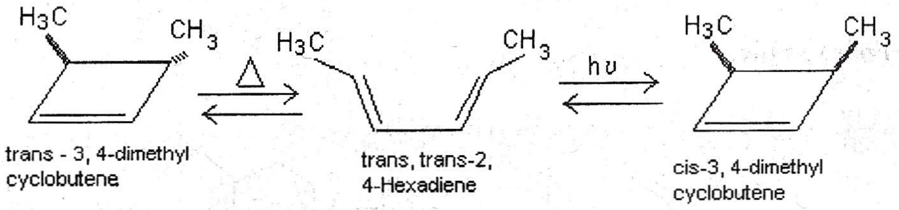
(b) Electrocyclic reactions

An electrocyclic reaction is a concerted reaction in which a σ bond is formed between the termini of a conjugated polyene. Therefore the net change being the conversion of a π bond into a σ bond or the reverse i.e ring opening involves the conversion of σ bond into π bond and ring closing involves the conversion of π bond into σ bond. Of the open chain partner contain K π electrons the cyclic partner contains (K-2)π electrons.



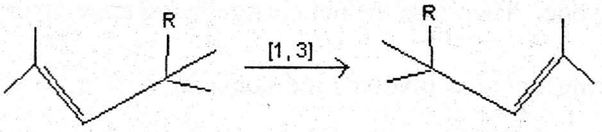
The forward reaction is called electrocyclic ring closing and the reverse reaction is called electrocyclic ring opening.

For ex:

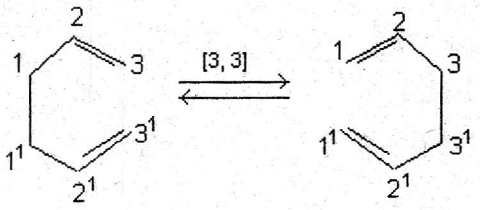


(c) Sigmatropic reactions

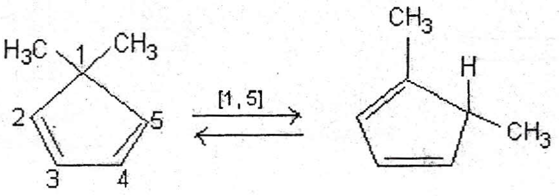
Sigmatropic reactions are concerted rearrangements in which a σ bonded atom or a group migrates from one end of the π system to the other end. These are named by putting i and j between the brackets which indicate the number of atoms each end of σ bond has moved between the forming and breaking of a bond. Therefore the allylic arrangements are 1,3-sigmatropic rearrangements.



Cope rearrangement



In this process all the single bonds in the conjugated chain or chains become double, and vice-versa. This should be remembered because confusion sometimes arises in the assignment of the order of sigmatropic shifts in cyclic system; thus the rearrangement of 5,5-dimethyl cyclopentadiene to 1,5-isomer is a 1,5-and not a 1,2-shift.

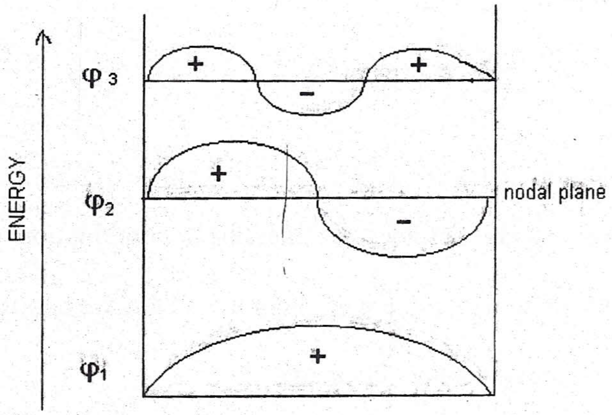


The selection rules here is that concerted shifts are allowed thermally if $(i + j) = 4n + 2$ and photochemically if $(i + j) = 4n$, provided that both groups migrate suprafacially; if one of them is involved in an antarafacial manner, the requirement is just opposite.

3.3.iii) Shapes of molecular orbitals

To explain the contribution of Woodward and Hoffmann towards pericyclic reaction, one must know about the shape and symmetry properties of molecular orbitals.

We know the individual electrons of an atom can be symbolised by wave functions, ψ and some physical analogy can be drawn between the behaviour of such a "wave-like" electron and the standing waves that can be generated in a strong fastened at both ends – the electron in a one dimensional box analogy. The one dimensional limitation arises, of course, because the electron's standing waves will be in 3 dimensional, and the strings in only one; the first 3 possible modes of vibration will thus be



7)

In the first mode φ , the amplitude of the wave increases from zero to a maximum and then decreases to zero again; in the second, φ_2 the amplitude increases to a maximum, decreases through zero to a minimum, and then back to zero again, i.e the phase of the wave changes once, while in the third mode, φ_3, the amplitude changes from zero to a maximum, through zero to a minimum through zero to a maximum again, and then finally back to zero; i.e. there are two nodes, and the phase of the wave changes twice. Displacements above the nodal plane are conveniently disignated +, and those below -. The lobes of, for example, a 2p atomic orbital, which has a nodal plane, thus differ in phase; and are conveniently designated as + and -, i.e. (Fig. ( )]. This can however, lead to confusion because of usual association of + and – with charge and phase differences, which are purely relative, will therefore be designated hereby shading and no shadings in [Fig. 2].

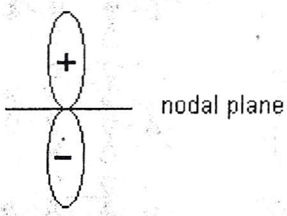


Fig.1

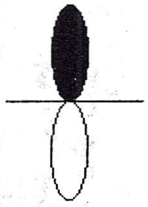
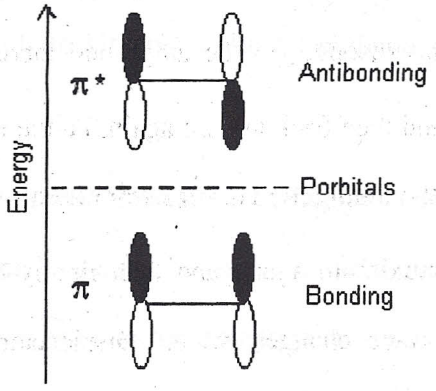
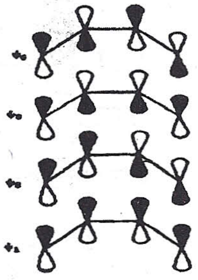


Fig.2

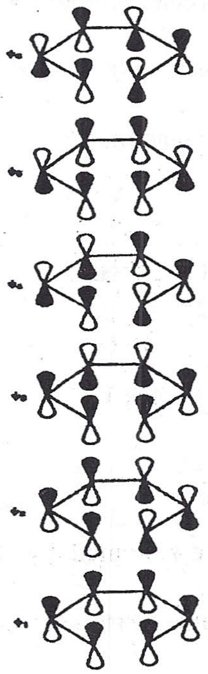
Molecular orbitals are obtained by the linear combination of atomic orbitals, and the question of phase will, of course, arise with them too. Thus we can write the two MOs (π and π^*) arising from the two p atomic orbitals in ethene.



the four molecular orbitals (φ_1, φ_2, φ_3 and φ_4) arising from the four PAO's in butadiene in the cisoid conformations and six molecular orbitals (ψ_1 to ψ_6) arising from 6 PAO's in Hexatriene.



Molecular orbitals of Butadiene

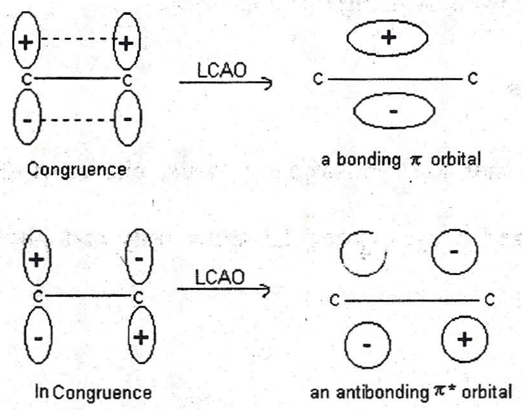


Molecular orbitals of Hexatriene

The importance of considering the phase of orbitals is that only orbitals of the same phase will overlap, and so result in bonding situation; orbitals of different phase lead to repulsive, antibonding situation.

Woodward and Hoffman recognised molecular orbital symmetry control in concerted reactions. These scientists published a series of papers which demonstrated that concerted reactions occur readily when there is congruence between the orbital symmetry characteristics of the reactants and products. Reactions lacking such congruence proceed poorly or not at all. Congruence of orbital symmetry means that the bonding character of all occupied molecular orbitals is preserved at all stages throughout the reactions.

The importance of orbital symmetry (or phase) congruence is widely recognised in simple moleculr-orbital theory for example the adjacent p atomic orbitals may interact in a bonding (congruent) or an antibonding (incongruent) fashion.



Woodward and Hoffman extended this fundamental concept to systems undergoing concerted reactions

3.3.iv) Analysis of pericyclic reactions

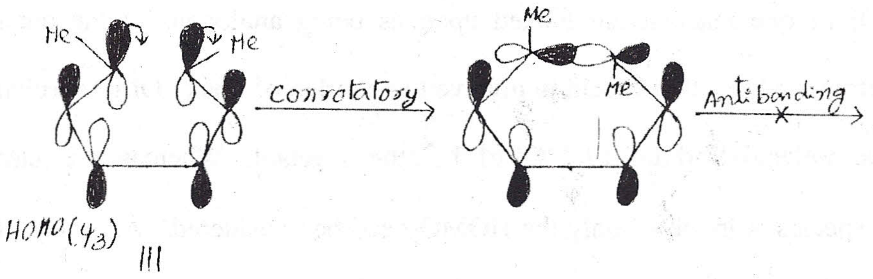
To make these predictions (put forth by Woodward and Hoffmann), it was necessary to consider the relative phases, i.e. symmetry, of all the orbitals involved during the transformation of reactants into products. It can be understood by following two methods – (1) Fontier orbital approach; and (2) correlation diagram approach. Fontier orbital approach is the simple model by which we can explain the predictions. In this method, the electrons in the highest occupied molecular orbital (HOMO) of one reactant are looked upon as being analogous to the outer (valence) electrons of an atom, and reaction is said to involve the overlap of this (HOMO) orbital with the lowest unoccupied molecular orbital (LUMO) of the other reactant. Whereas in electro cyclic reactions, only one species is involved only the HOMO need be considered. A variety of pericyclic reactions can be reviewed by using this approach.

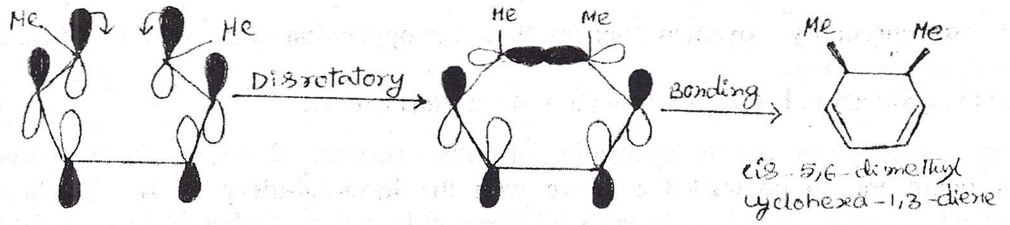
3.3.v) Electrocyclic reactions

We have already seen that the cyclisation of trans, cis, trans -2, 4,6-octatriene proceeds thermally to yield cis-5,6-dimethyl cyclo hexa-1,3-diene only and photochemically to yield the corresponding trans isomer

$$\begin{array}{c}\text{trans-5,6 dimethyl}\\ \text{cyclohexa-1,3-diene}\end{array} \overset{h\nu}{\rightleftarrows} \begin{array}{c}\text{trans, cis, trans-2,4,6}\\ \text{-octatriene}\end{array} \overset{\Delta}{\rightleftarrows} \begin{array}{c}\text{cis-5,6 dimethyl}\\ \text{cyclohexa-1,3-diene}\end{array}$$

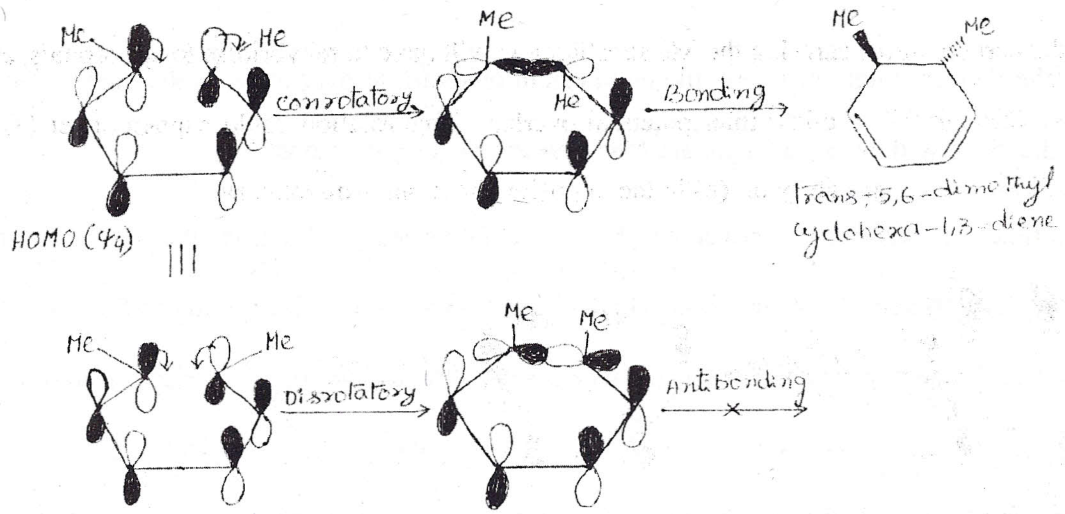
only; in either case the equilibrium lies almost completely over towards the cyclic form. The degree of stereo selectivity in fact so great that the thermal cyclisation yields < 0.1% of the trans isomer, despite the latter being thermodynamically more stable than the cis form. The six MO's of trans, cis, trans –2,4,6-octatriene arising from the six PAO's are (φ_1, φ_2, φ_3 and φ_4, φ_5, φ_6,. For thermal inter conversion to occur we have to consider the ground state electronic configuration of triene. As there are 6 p electrons to accomodate two per orbital – the HOMO will be φ_3. To form the C-C σ bond on cyclisation, the p orbitals on the terminal carbon atoms of the conjugated system (the carbon atoms carrying the Me substituents) will have to rehybridise to sp^3 orbitals, and each rotate through 90° to allow thier potential overlap. This rotation could happen either (a) in the same direction – conrotatory or (b) in the opposite directions – disrotatory.





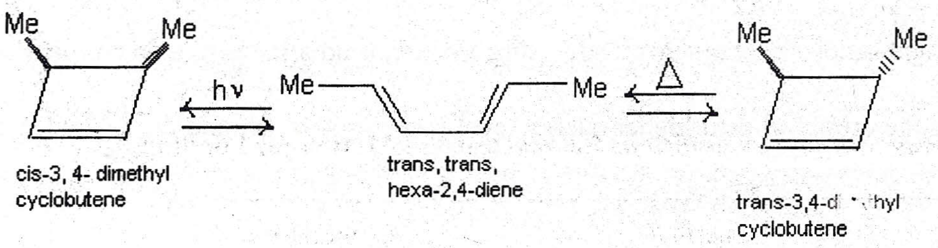
Conrotation movement results in the opposition of sp^3 orbitals of opposite phase – an antibonding situation, while disrotatory movement results in the opposition of sp^3 orbital of the same phase a bonding situation, leading to formation of the cyclohexadiene in which the two Me groups are cis.

For photochemical reaction to occur we have to consider the electronic configuration of triene in excited state. On photochemical ring-closure, irradiation results in the promotion of an electron into the orbital of next higher energy level is $\varphi_3 \xrightarrow{h\upsilon} \varphi_4$ and the ground state LUMO (φ_4) thus now becomes the HOMO:



It is now conrotatory movement that results in the opposition of sp^3 orbitals of the same phase-the bonding situation, leading to formation of the *trans* isomer.

It is interesting to contrast the above with the hexa-2,4-diene ⇆ 3,4-dimethyl cyclobutene situation. Here exactly the opposite stereo chemical inter-relationships are observed, i.e. *trans, trans hexa – 2,4-diene* is associated thermally with trans 3,4-dimethyl cyclobutene and photochemically with the *cis isomer.*



For the thermal interconversion the equilibrium tends to lie over towards the diene. The HOHO for the diene will be φ_2 as there are four p electrons to accommodate.

This time it is conrotatory movement that results in a bonding situation, and formation of trans dimethyl cyclobutene. For the photochemical inter conversion (which tends to the over in favour of the cyclobutene), irradiation of the diene result in the promotion of an electron into the orbital of next higher energy level is $\varphi_2 \longrightarrow \varphi_3$ and the ground state LUMO (φ_3) thus now becomes the HOMO.

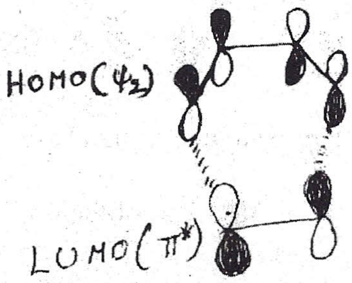
Thus disrotatory movement now results in a bonding situation, and formation of the cis dimethyl cyclobutene.

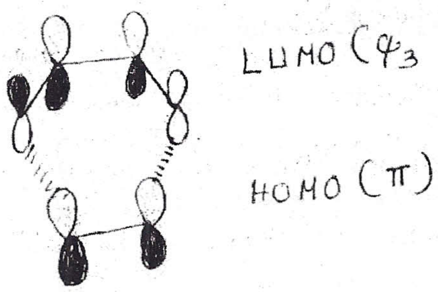
This difference in behaviour obiously stems from the way in which the relative phase, at the terminal carbons, of the HOS of the two systems are arranged, is their symmetry, the phase bring the same for the HoHO (φ_3) of the 6 π electron system, and for the LUMO (φ_3) of the 4 π electron system, the phase bing different for the HOMO (φ_2) of the 4 π electron system, and for the LUHO (φ_4) of the 6 π electron system. The same phase involves disrotatory movement for band making/band-breaking to occur, the opposite phase involves cis rotatory movement for bond making/bond-breaking to occur. Alternative the thermal/photo chemical antithesis is summarised in the generalisations.

No of π electrons	Conditions for reaction	Motion for bonding
4n	Thermal	Conrotatory
4n	Photochemical	Disrotatory
4n + 2	Thermal	Disrotatory
4n + 2	Photochemical	Conrotatory

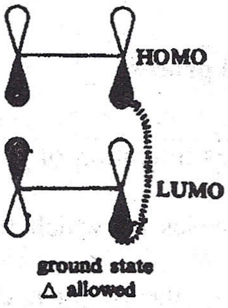
3.3.vi) CYCLO ADDITIONS

In cyclo additions two components are commonly involved and the feasibility of a particular process will be determined by the whether overlap can take place between HOMO of are compartment and the LUMO of the other. Thus for a diene plus a monoene





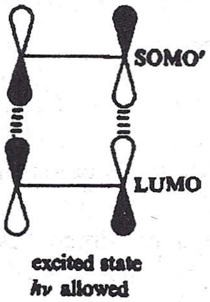
The situation is a bonding are and concerted addition will be feasible, which ever component has the HOMO, or the LUMO. The cyclo addition is said to be symmetry allowed. By the contrast, for two monene components.



This is a general situation for thermal, concerted reactions. Those involving $4 \pi e + 9 \pi e$ systems proceed readily e.g. the Die's Alder reaction, whereas those involving $2 \pi e + 2 \pi e$ systems e.g. the cyclo dimerisation of alkenes, do not. We might, however expect that photo chemical cyclo-dimerisation of alkenes would be symmetry allowed, as irradiation will promote an electron are component, into the orbital of next higher energy level is $\pi \xrightarrow{h\upsilon} \pi^*$ and its ground state LUMO (π^*) thus now becomes the HOMO

HOMO ($\xrightarrow{h\upsilon} \pi^*$)

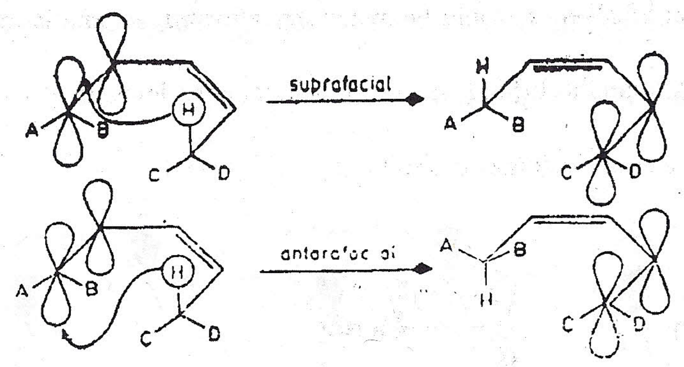
LUMO (π^*)



Many such reactions may indeed be carried out preparatively under photochemical conditions. One phtochemical $(2\pi + 2\pi)$ cyclo addition that does however proceed (via) a concerted process is the example we have already referred to.

3.3.vii) Suprfacial and Antarafacial process

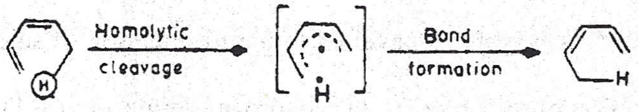
Since a sigmatropic reaction involves migration of σ bond across the π electron system there are two different stereo chemical courses by which the process may occur. When the migrating σ bond moves across the same of the conjugated system, it is called a suprafacial process where as in the antara facial process the migrating σ bond is reformed on the opposite π electron face of the conjugates system. The following [1,5] sigmatropic shift illustrates both these process and their stereo chemical consequences.



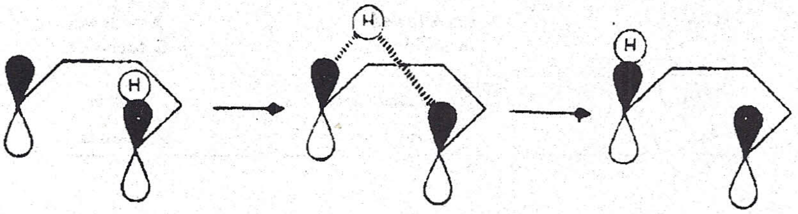
Due to steric reasons, suprfacial migrations are more common than antarafacial shifts. However, with the lengthening of the conjugates system, some times it is possible for a σ bond to migrate to the opposite p electron face.

3.3.viii) Analysis of sigmatropic rearrangement FMO method

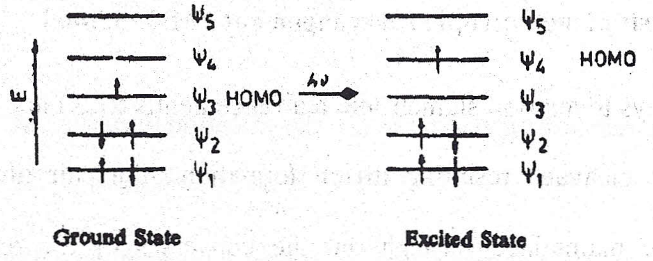
One of the ways to analyse sigmatropic rearrangementis to assume that the migrating bond undergoes homolytic cleavage resulting in teh formation of a pair of radicals. As bonding characters one to be maintained through out the converses of the rearrangement, the most important bonding interaction will be between the HOMO's of the two species produced by this cleavage. This is to be expected as it is these orbitals that contain the unpaired electrons. We shall illustrate this analysis by examining the [1,5] sigmatropic shift of hydrogen in which the homolytic cleavage results in the production of a hydrogen atom and pentadienyl radical.



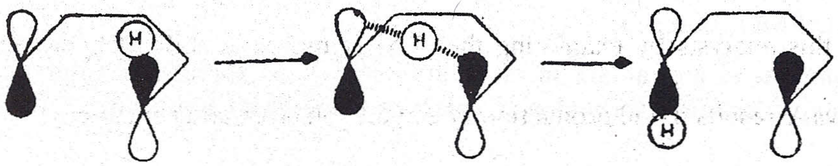
Ground state electronic configuration of pentadienyl radical is φ^2, $\varphi_2^2\varphi_3$. Since HOMO (φ_3) of this radical has similar sign as the terminal lobus (plane symmetry) [1,5] supra facial migration will be a thermally allowed process



The first excited state of the pentadieny radical has the configuration $\varphi_1^2\varphi_2^2\varphi_4$ (Fig) and the symmetry characteristics of HOMO (φ_4) are the reversed (c_2 symmetry)



[1,5] suprafacial migration is no longer possible and the sift has to be an antara facial process.



Similar analysis of such systems have led to the formulation of selection rules which state that if a sigmatropic reaction of the order [i, j] (hydrogen migration i = 1) has i + j = 4q + 2, then thermal reaction is suprafacial and photochemical process will be antara facial. However, for those cases in which i + j = 4q the rules are reversed and the thermal reactions are antarafacial while the photochemical reaction will be suprafacial. These rules are summarised in the Table.

$(i+j)$	Δ allowed hν forbidden	hν allowed Δ forbidden
$4q$	*antara*	*supra*
$4q+2$	*supra*	*antara*

Model Questions

1. What are pericyclic reactions and explain the classification of pericyclic reactions.

2. Write the shapes of 6 molecular orbitals of Hexatriene. Indicate the number of nodes and symmetry properties.

3. Predict whether the following reaction is allowed thermally or photochemically by FMO approach

trnas, trans, hexa-2,4-diene ⇆ trans – 3, 4 – dimethylcyclobutene

4. π^4S, + π^2S cycloaddition reaction in thermally allowed, but photo chemically forbidden. Explain by using FMO approach.

5. What are suprafacial and antara facial migrations. [1,5] suprafacial migration in thermally allowed and photo chemically forbidden. Explain by using FMO approach.

Recommend books:

1. Pericyclic reactions by S.M. Kukherji.
2. Conservation of Orbital symmetry by R.B. Woodward.
3. Organic Reactions and orbital symmetry by Gilchrist and Storr.
4. Pericyclics and photochemistry by Mukherji.

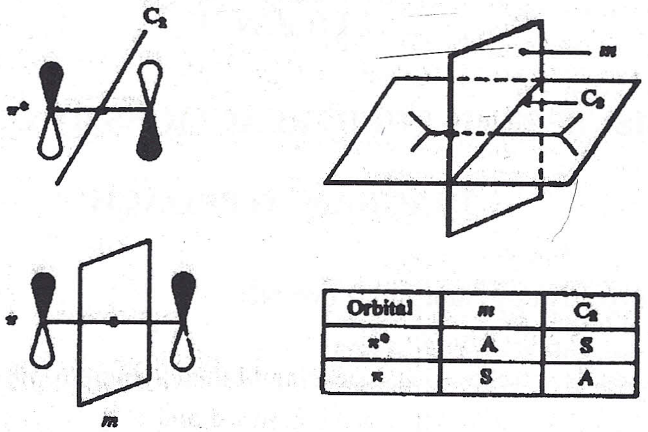
LESSON IV

ANALYSIS OF PERICYCLIC REACTIONS BY CORRELATION DIAGRAM APPROACH

3.4.i) Symmetry properties of molecular orbitals

Molecular orbitals are classified according to their symmetry properties. The symmetry of these orbitals may be due to (1) mirror plane symmetry (m) and (2) two fold axis symmetry (C_2). If the molecular orbital has a mirror plane (m), perpendicular to the plane of the atoms which bi sects the molecular orbital into two halves, each of which is a mirror image of the other, it is said to have mirror plane symmetry or m-symmetry. On the other hand, if the molecular orbital has a symmetry about a two fold axis passing at right angles in the same plane, and through the centre of the frame work of the atoms forming the molecular orbitals, it is said to have a two fold axis (C_2) of symmetry. Whether the given molecule orbital has a two fold axis of symmetry or not can be readily ascertained by rotation of the molecular orbital through 180°. If the resultant molecular orbital is exactly identical with the original one, it is said to have a two fold axis of symmetry.

Let us examine the symmetry property of π-orbitals of ethylene in ground state and also in the excited state. The ground state bonding orbital (π) is symmetric (S) with respect to mirror plane (m) and anti-symmetric (A) with respect to the two fold rotation axis C_2. On the other hand, the anti-bonding orbital π* of ethylene is anti-symmetric with respect to mirror plane symmetry and symmetric with respect to the two fold axis as shown below.



Orbital	m	C2
π*	A	S
π	S	A

A similar consideration leads to the following symmetry properties for the four π-molecular orbitals of 1,3-butadiene and six molecular π-orbitals of hexatriene.

Symmetry properties of π-molecular orbitals of 1,3-butadiene

Molecular orbital	Mirror plane symmetry (m)	Two-fold axis symmetry (C_2)
ψ_1	Symmetric	Antisymmetric
ψ_2	Antisymmetric	Symmetric
ψ_3	Symmetric	Antisymmetric
ψ_4	Antisymmetric	Symmetric

Symmetry properties of the π-molecular orbitals of hexatriene

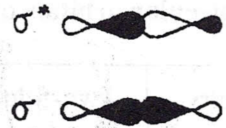
Molecular orbital	*Mirror plane symmetry* (m)	*Two-fold axis symmetry* (C_2)
ψ_1	Symmetric	Antisymmetric
ψ_2	Antisymmetric	Symmetric
ψ_3	Symmetric	Antisymmetric
ψ_4	Antisymmetric	Symmetric
ψ_5	Symmetric	Antisymmetric
ψ_6	Antisymmetric	Symmetric

Symmetry properties and nodes

In a linear conjugated π-system, the wave function φ_n has n-1 nodes. Further, it has also been noticed that whenever the value of (n-1) is zero or an even integer φ_n will be symmetric with respect to mirror plane symmetry and anti-symmetric with respect to two-fold axis symmetry. On the other hand, when n-1 is an add integer φ_n will have a two – fold symmetry but will be anti-symmetric with respect to the mirror plane symmetry.

Sigma orbital of a C-C covalent bond has a mirror plane symmetry, and since a rotation of 180° through its mid-point regenerates the same sigma orbital, it also has a C_2 symmetry. The σ^* orbital in anti-symmetric with respect to both 'm' and C_2.

7A

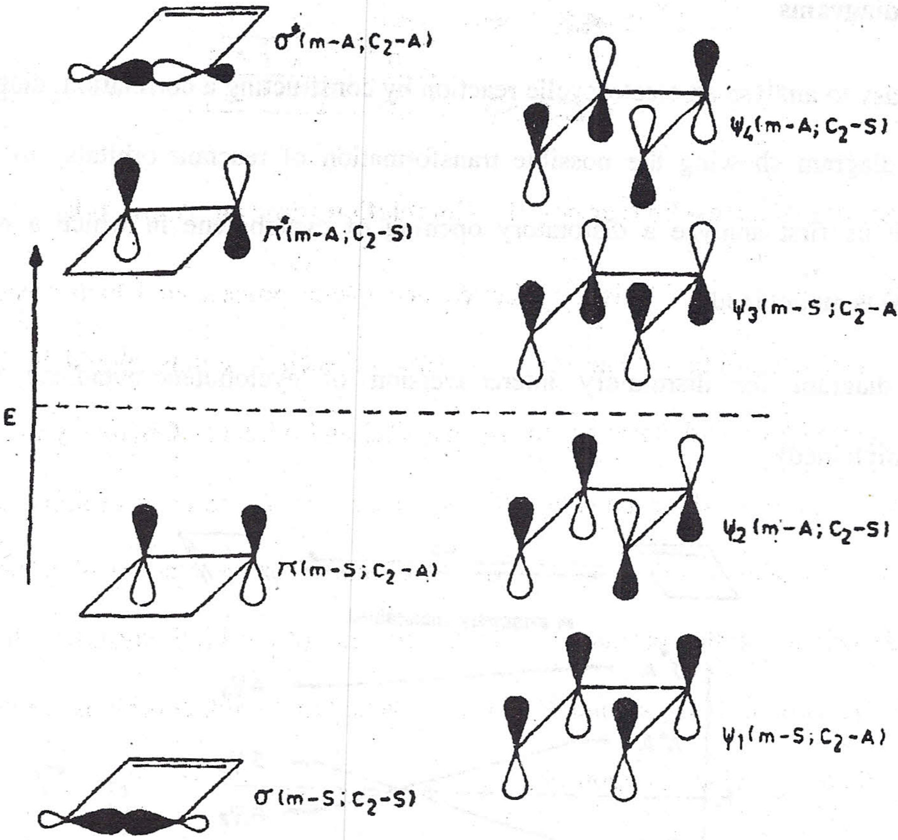


Orbital	m	C_2
σ*	A	A
σ	S	S

3.4.ii) Analysis of electro cyclic reactions by Correlation Diagram Approach

An electro cyclic reaction is a concerted and cvclic process in which reactant orbitals transform into product orbitals. The transition state of such reactions should be intermediate between the electronic ground states of starting material and product. Obviously the most stable transition state is the one which conserves the symmetry of the reactant orbitals in passing to product orbitals. In other words, a symmetric (S) orbital in the reactant must transform into a symmetric (S) orbital in the product and antisymmetric (A) orbital must transform into an antisymmetric (A) orbital. If the symmetries of the reactant and product orbitals are not the same, the reaction will not take place in a concerted manner.

Let us exemplify the above principle by analyzing cyclobutene-butadiene transformation. The ring opening (or ring closing) may be a disrotatory process in which the groups as saturated carbons rotate in opposite directions, or alternatively, it may be proceed (via) conrotation involving the rotation of the groups in the same direction. In the case of disrotatory ring opening, cyclobutene preserves a plane of symmetry (m), throughout the transformation while a two-fold (C_2) symmetry axis is maintained at all times in the conrotatory mode of ring opening.

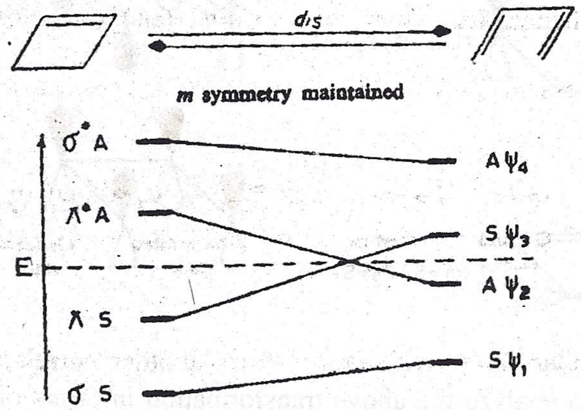


We are now set to analyze the above transformation in terms of the fundamental rule of conservation of orbital symmetry as proposed by wood ward and Hoffmann. The directly involved orbitals of the cyclobutene are σ and π and the related antibonding orbitals σ* and π*, these orbitals pass on to the four π molecular orbitals of butadiene viz ψ_1 ψ_2 ψ_3 ψ_4. All these orbitals are listed in the order of increasing energy in the above diagram along with their mirror plane and C_2 symmetry properties. In the ground state of cyclo butene and butadiene only σ π and ψ_1 ψ_2 are filled with electron pairs.

Correlation diagrams

It is easy to analyse an electrocyclic reaction by constructing a correlation diagram, which is simply a diagram showing the possible transformation of reactant orbitals to the product orbitals. Let us first analyze a disrotatory opening of cyclobutene in which a mirror plane symmetry (m) is maintained.

Correlation diagram for disrotatory interconversion of cyclobutene-butadiene system (m-symmetry maintained)



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In constructing this correlation diagram we have to simply connect by lines the various orbitals of cyclo butene and butadiene keeping in view that there is correlation between orbitals of the same symmetry, having minimum energy differences. The following two conclusions can be immediately be drawn by a close inspection of such a diagram.

(a) We expect a thermal transormation to takes place only when the ground state orbitals of the reactants correlate with the ground state orbitals of the products. Although in the above diagram, the cyclobutene ground state orbital, σ, correlates with the butadiene ground state orbital, ψ_1, the π orbital of the former does not correlate with ψ_2 of latter. Instead it correlates with ψ_3

which is an excited state and an antibonding orbital. Thermal transformation of cyclobutene ⇆ butediene system by disrotatory process is thus symmetry forbidden.

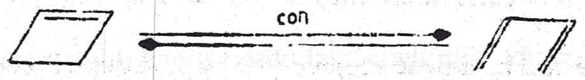
$$\sigma^2\pi^2 \xrightarrow[\times]{\Delta \quad dis} \psi_1^2\psi_3^2$$

$$\psi_1^2\psi_2^2 \xrightarrow[\times]{\Delta \quad dis} \sigma^2\pi^{*2}$$

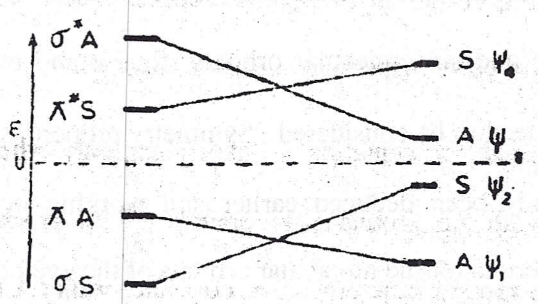
(b) Irradiation of cyclo butene produces the first excited state in which an electron is promoted from π to π* and in this case σ, π and π* orbitals of cyclobutene correlate with ψ₁ ψ₂ ψ₃ orbitals of butadiene. In other words, the first excited state of cyclobutene correlates with the first excited state of butadiene and hence disrotatory ring opening (and ring closing_) is photochemically asymmetry allowed process

$$\underset{\text{Ground state}}{\sigma^2\pi^2} \xrightarrow{h\nu} \underset{\text{First excited state}}{\sigma^2\pi\pi^*} \rightleftharpoons \underset{\text{First excited state}}{\psi_1^2\psi_2\psi_3} \xleftarrow{h\nu} \underset{\text{Ground state}}{\psi_1^2\psi_2^2}$$

Working on similar lines, we can construct another correlation diagram for the con-rotatory opening in which a C_2 symmetry is maintained through out the reaction.



C_2 symmetry maintained



Two conclusion may be drawn from the above correlation diagram.

Since there is correlation between the ground state orbitals of cyclobutene and butadiene ($\sigma^2\pi^2 \leftrightarrows \psi_1{}^2\psi_2{}^2$) a thermal conrotatory process in either direction is a symmetry allowed process

The first excited state of cyclobutene ($\sigma^2\pi\ \pi^*$) correlates with the upper excited state ($\psi_1{}^2\ \psi_2\ \psi_4$) of butadiene thus making it a high energy symmetry forbidden process. Similarly the first excited state of butadiene ($\psi_1{}^2\ \psi_2\ \psi_3$) correlates with a high energy upper excited state ($\sigma^2\pi\ \sigma^*$) of cyclobutene. In other words, a photochemical conrotatory process in either direction is symmetry forbidden.

$$\sigma^2\pi^2 \xrightarrow{h\nu} \sigma^2\pi\pi^* \not\longrightarrow \psi_1^2\,\psi_2\,\psi_4$$

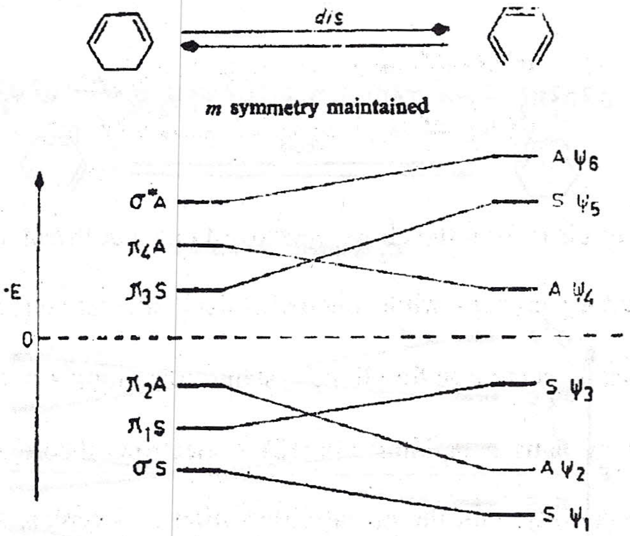
$$\psi_1^2\,\psi_2^2 \xrightarrow{h\nu} \psi_1^2\,\psi_2\,\psi_3 \not\longrightarrow \sigma^2\pi\,\sigma^*$$

Thus it becomes clear from the above considerations that thermal oopening of cyclobutene proceeds in a conrotatory process while photochemical interconversion involves a disrotatory mode. These generalisations are true for all the systems containing 4 n π electrons where n = 0, 1, 2, etc. However for systems containing (4n +2) π electrons theoretical prediction is entirely different and is in conformity with the actual observations. A typical system of this type is the interconversion of cyclohexadiene and hexatriene. In this transformation. Six molecular orbitals ($\psi_1 - \psi_6$) of heaxa triene and six molecular orbitals (four π and two σ) of cyclohexadiene are actually involved and so need to be considered. Symmetry properties of the six molecular orbitals of hexatriene have already been deduced earlier and working in similar lines, we have the following symmetry properties for the molecular orbitals of the cyclohexadiene.

Symmetric properties of molecular orbitals of cyclohexadiene

	m	C_2
σ^*	A	A
π_4	A	S
π_3	S	A
π_2	A	S
π_1	S	A
σ	S	S

The correlation diagram for disrotatory pathway is constructed in the same way as in the case of cyclobutene-butadiene transformation.



The following conclusions may be drawn from these correlation diagrams.

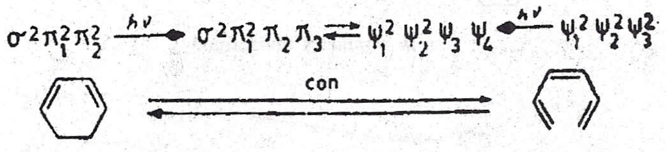
(a) In the disrotatory mode (m-symmetry) ground state bonding orbitals of cyclohexadiene correlate with the ground state bonding orbitals of hexatriene and so it is a thermally allowed process.

$$\sigma^2\pi_1^2\pi_2^2 \xrightarrow{\Delta\ .\ dis} \psi_1^2\psi_2^2\psi_3^2$$

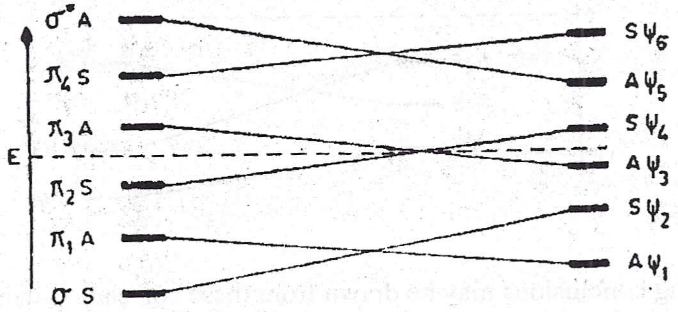
(b) But in the conrotatory mode (C_2 symmetry) ground state bonding orbitals of cyclo hexadiene do not correlate with the ground state bonding orbitals of hexatriene (fig. below) since the presence of two electrons in ψ_4 is a very high energy process, a conrotatory mode is prohibited under the thermal conditions.

$$\sigma^2\pi_1^2\pi_2^2 \xrightarrow{\Delta\ \times\ \text{con}} \psi_1^2\psi_2^2\psi_4^2$$

(c) However if we promote an electron to π_3 orbital in cyclohexadiene (obviously by irradiation) then the orbitals of the reactant with C_2 symmetry correlate with the first excited state of the product.



C_2 symmetry maintained



Therefore, photochemical interconversion is symmetry allowed in conrotatory pathway. These generalisations are true for all the systems containing (4n + 2) π electrons, when n = 0.,1,2 etc. Thus Woodward and Hoffmann rules for electrocyclic reactions may be summed up in the form of table

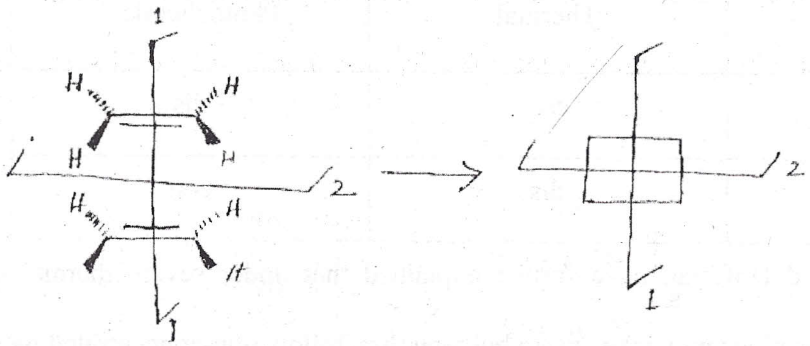
Number of π electrons	Thermal	Photochemical
4n	con	dis
4n + 2	dis	con

Woodword and Hoffman have further explained that under severe thermal conditions, symmetry forbidden reations may takes place but then they follow non-concentrated path and their energy of activation is 10-15 Kcal/mole higher than those of symmetry allowed reactions. It is because of this energy difference that most of the electrocyclic reactions follow Woodward and Hoffmann rules.

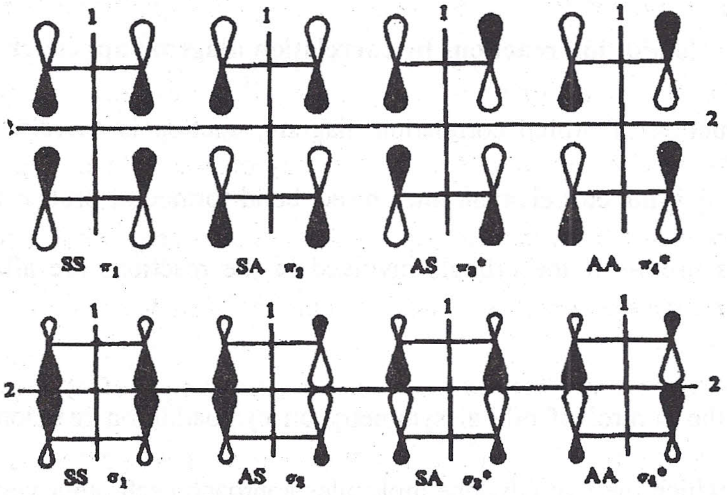
3.4.iii) Analysis of cycloaddition reactions by correlation diagram approach

In the construction of orbital correlation diagram, caution is exercised in choosing the symmetry elements. A symmetry element must bisect bond formed or broken in the process and symmetry element is useless if the orbitals involved in the reactions are all symmetric or all antisymmetric.

To illustrate the control of orbital symmetry on cycloaddition reactions, we choose the simplest example in which the two ethylene molecules approach each other vertically ($\pi^2S+ \pi^2S$) to the form of a molecule of cyclobutane. Such a system has vertical and horizontal planes of symmetry which are referred to as 1 and 2, respectively.

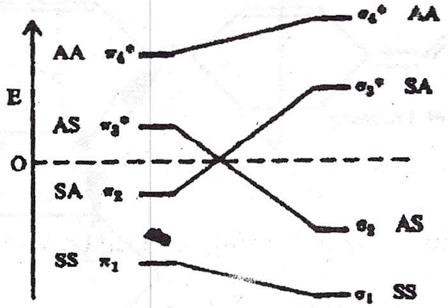


In the above transformation we are mainly concerned with the 4 π orbitals of the two ethylene molecules and the four σ orbitals of cyclo butane.



The shapes and symmetrical properties of these four π orbitals (π_1,π_2 bonding; π_3*, π_4* antibonding) and four σ orbitals (σ_1,σ_2 bonding; σ_3*, σ_4* antibonding) have been illustrated in the above fig. symmetry classifications (SS, SA, AS and AA) with respect to the plane of symmetry 1 are given first nd with respect to 2 next.

On the basis of the above information, a correlation diagram may be drawn in which the reactant and product orbitals of like symmetry having minimum energy differences are connected by lines.

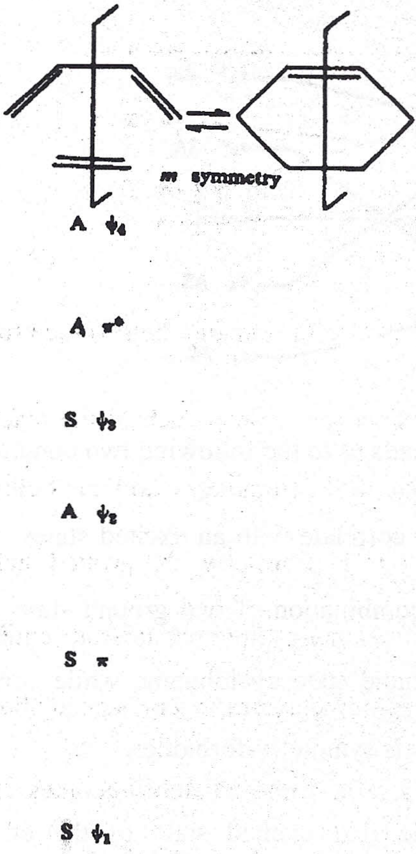


A close examination of the diagram leads us to the following two conclusions.

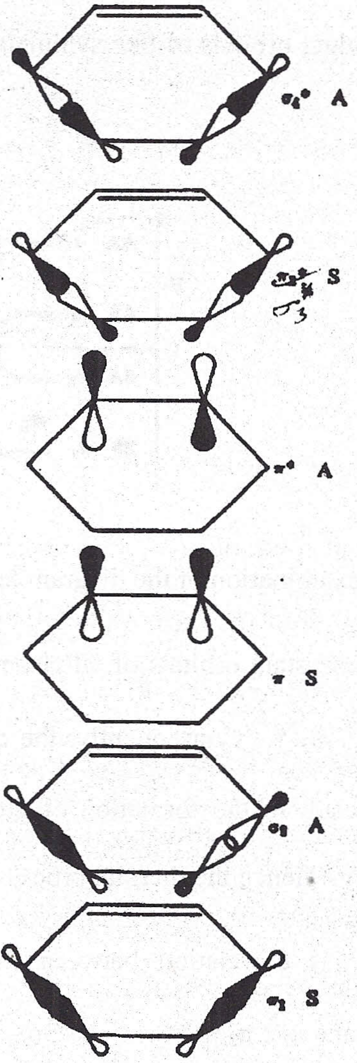
1. The ground state orbitals of ethylene correlate with an excited states of cyclobutane, π_1^2, $\pi_2^2 \leftrightarrows \sigma_1^2$, σ_3^{2*}. Consequently, the combination of two ground state ethylene molecules cannot result in the formation of ground state cyclobutane while conserving the orbital symmetry. Hence the thermal process is symmetry-forbidden.

2. As there is correlation between the first excited state of the ethylene system and cyclobutane π_1^2, $\pi_2\ \pi_3^* \leftrightarrows$ σ_1^2, $\sigma_2\ \sigma_3^*$, the photochemical process is symmetry-allowed.

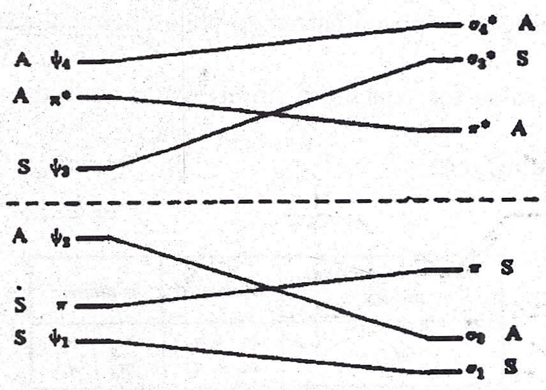
A similar correlated diagram may be constructed for the Diels Alder reaction which is π^4s + π^2s cyclo addition reaction. In this case there is only a single vertical plane of symmetry bisecting carbon frame work of two reactants and the product.



Butadiene and ethylene π-MOs with symmetry properties



Cyclohexene orbitals with symmetry properties



Correlation an dia gram for π4S + π2S cycloaddition and the reverse process.

In this transformation we have to consider six orbitals each of the reactants and products. The ground state orbitals of the reactants are ψ_1 ψ_2 (of Butadiene) and π (of ethylene) while ψ_3, π* and ψ_4 are the corresponding antibonding orbitals. Similarly, the ground state orbitals of cyclo hexene are represented by σ_1, σ_2 and π; the remaining three orbitals are antibonding. All these orbitals and symmetry properties and the correlation diagram is represented above.

From the inspection of the above diagram it immediately becomes clear that there is a smooth transformation of the reactant orbitals into the product orbitals.

$$\psi_1^2 \pi^2 \psi_2^2 \rightleftharpoons \sigma_1^2 \sigma_2^2 \pi^2$$

The Diels-Alder reaction (π^4s + π^2s cyclo addition) is, therefore, a thermally allowed process. On the other hand, photochemical transformation is not possible as the first excited state of the reactant does not correlate with the first excited state of the product. Rather it correlates with the upper excited state of the product

$$\psi_1^2 \pi^2 \psi_2 \psi_3 \not\longleftrightarrow \sigma_1^2 \sigma_2^2 \pi \pi^*$$

Hence there is symmetry-imposed barrier to photochemical reactions of ($\pi^4s + \pi^2s$) type. The generalised selection rules for concerted (m+n) cyclo addition reactions are shown below where q is an integer including zero.

Number of electrons $m+n$	Δ *allowed*	*hν allowed*
$4q$	$m_s + n_a$ $m_a + n_s$	$m_s + n_s$ $m_a + n_a$
$4q + 2$	$m_s + n_s$ $m_a + n_a$	$m_s + n_a$ $m_a + n_s$

It should be noted that sometimes formal correlation diagrams cannot be drawn as in the case of concerted (4s + 2a) and (6s + 2a) cyclo addition, even though the former is forbidden and the latter allowed under thermal conditions.

Model Questions:

1. Write the shapes and symmetry properties of 6 molecular orbitals of cyclohexene.

2. Construct a correlation diagram for disrotatory inter conversion of cyclobutene – Butadiene system and predict whether the reaction is allowed thermally or photochemically.

3. Construct a correlation diagram for conrotatory inter conversion of cyclohexadiene – Hexatriene system and predict whether the reaction is allowed thermally or photochemically.

4. By constructing a correlation diagram predict whether $\pi^2S + \pi^2S$ cyclo addition reaction is allowed thermally or photochemically.

5. Construct a correlation diagram for Diels Alder reaction and predict whether the reaction is allowed thermally or photochemically.

Recommend books

1. Conservation of orbital symmetry by R.B. Woodward.

2. Pericyclic reactions by S.M. Mukherji.

3. Pericyclics and photochemistry by Mukherji.

ALKALOIDS

4.1.1 Definition

The term alkaloid was first of all introduced by W. Meissner in 1819. Originally the name alkaloid (which means alkali like, alk = alkoli, oids = like) was given to all organic bases isolated from plants. Meissner, first of all, reserved this term for the basic introgeneous compounds isolated from plants. Konigs (1880) defined alkaloids as naturally occurring organic bases which contain a pyridine ring. The definition is capable of embracing only a limited number of compounds, so the definition was again modified by Ladenburg who suggested that alkaloids should be defined as "naturally occurring compounds of plant origin having a basic character and containing at least one nitrogen atom in a heterocyclic ring system. The alkaloids are now generally defined as physiologically active, basic compound of plant kingdom, in which at least one nitrogen atom forms part of a cyclic system.

The example of the first type of compounds are ephedrine adrenalone, noradrenaline, etc which do not have nitrogen atom in a ring system, but in the side chain. Examples of the second type of compounds of purine group such as caffeine, thiobromine and xanthine which are physiologically active nitrogenous bases. But are not regarded as alkaloids.

4.1.2 Nomenclature

A large number of alkaloids derive their names from the plant from which they are isolated viz., paparverine from papaner somenijerus, hydrastine and barberine from berberis velgoris. A few alkaloids are named from their physiological action such as morphine (Germany morphine – God of dreams) only one group of alkaloids pelleterine has been named after the alkaloid chemist P.J. Pelletier. The minor alkaloids are named by adding one prefix or suffix to the name of the principal alkaloid.

4.1.3 Occurrence

As many as more than two thousand alkaloids have been isolated and are well known. But they are found only in 10 – 15% of all the vascular plants. Alkaloids occur almost exclusively in flowering or seed bearing dicotyledons. They are nearly found in lower plants like algae, fungi etc. (the ergot alkaloids which occur in one or two families of fungi are the exception). Alkaloid content of plants varies with the season, age and its locality closely related alkaloids are generally found in the same plant nearly twenty four alkaloids have been isolated from opium poppy.

Since the alkaloids are basic in nature, they are mostly prevent as salts of acids of plants usually of tannic, malic, oxalic, citric as nearly of acetic acid and lactic acid. The structurally related alkaloids are present as salt of the same organic acid e.g. all the opium alkaloids are present as salts of meconic acid.

4.1.4 Isolation

The isolation of alkaloids from their plant sources is usually not difficult first all the presence of an alkaloid is ascertained in the experimental plant for which the plant extract is treated with various alkaloidal reagents such as tannic acid, picric acid, picrolonic acid, potassium mermeric iodide, with which the alkaloids either give a precipitate (or) turbidity.

The dried and powdered plants material is first extracted with petroleum ethers and then filtered for the removal of soluble fats. The residue is then extracted with methyl alcohol to remove cellulosic and other insoluble material and the filtrate so obtained is evaporated. The evaporated mass is dissolved in water, acidified to pH 2 and finally stream distilled to remove methyl alcohol. The dark residual solution is either allowed t stand for several days in a refrigerator or heated with molten paraffin to remove suspended impurities. The filtrate is extracted with either or chloroform to remove water soluble non basic organic material and then stem distilled when the steam volatile alkaloids are separated. The solution of the rest of the alkaloid salts is made alkaline and again extracted with either or chloroform and the ethereal layer obtained after this extraction is evaporated to give crude alkaloids.

The resulting crude alkaloid mixture is separated into individual alkaloids by means of fractional crystallization, fractional precipitation. C.C, portion C., G.O.

4.1.5 General methods for determining structure of alkaloids

The following methods are useful to elucidate the structure of alkaloids.

1. After a pure specimen has been obtained it is subjected to qualitative and quantitative analysis. From the above analysis the molecular weight and molecular formula of the alkaloids have been determined.

2. When alkaloid contains oxygen, the functional nature of this element is determined.

a. Hydroxyl group : The presence of this group may be ascertained by the action of the acetic anhydride, acetyl chloride (or) benzoyl chloride on the alkaloid.

b. Carbonyl group : The solubility of the alkaloid in aqueous Na_2CO_3 or NH_3 indicates the presence of carbonyl group.

c. Oxo group : The presence of oxo group is readily ascertained by the formation of oxime, semicarbozone and phenyl hydrazone

d. Hydrolysis of the alkaloid and an examination of the products led to information that the compound is an ester, lactone, amide, lectam or a betaine.

e. Methoxyl group : The alkaloid is heated with conc. HI at its boiling point (120°C), the methoxyl groups are converted into methyliodide, which is then absorbed by ethanolic $AgNO_3$ and the AgI is weighed.

8)

f. Methylene dioxyl group (-OCH_2-O-) : The presence of this group is indicated by the formation of formaldehyde when the alkaloid is heated with HCl (or) H_2SO_4.

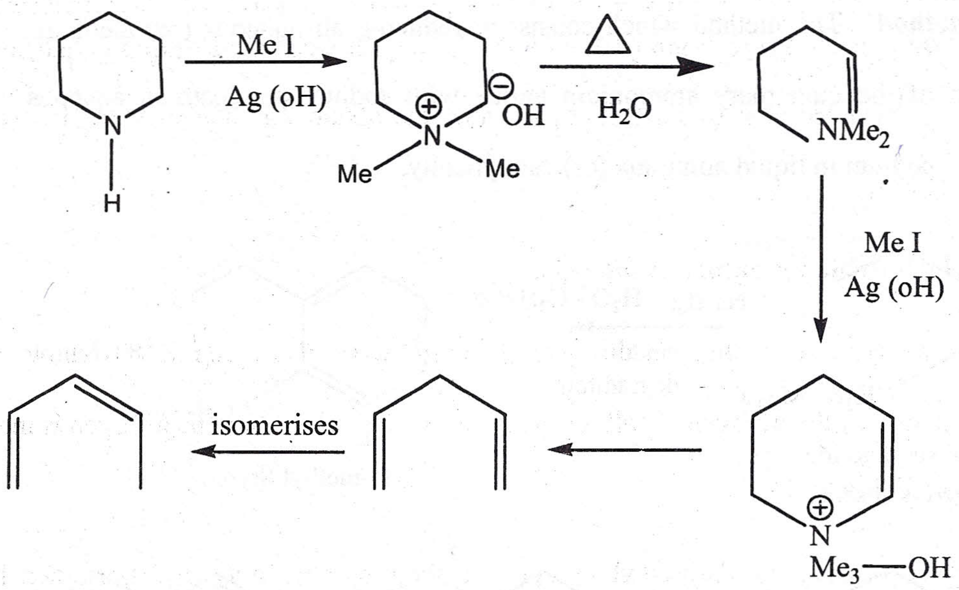
4.1.6 The Functional nature of nitrogen

a. The general reaction of the alkaloid with Ac_2O, CH_3I and HNO_2 show the nature of the nitrogen. If all the reactions are negative, then the nitrogen is most probably tertiary.

b. The presence of N-methyl groups and their number may be determined by means of the Herzig-Meyer method. When the alkaloid is heated with HI at 150 – 300°C under pressure, N-Methyl groups are converted into methyl iodide.

4.1.7 Hofmann's exhaustive Methyation method

This is very important process is alkaloid chemistry. Since by its means heterocyclic rings are opened with the elimination of nitrogen, and the nature of the carbon skeleton is thereby obtained. The general procedure is to hydrogenate the heterocyclic ring, convert this compound to the quaternary methyl ammonium hydroxide which is then heated. In this stage a molecule of water is eliminated a hydrogen atom in the β position with respect to the nitrogen atom containing with hydroxyl group and the ring is opened at the nitrogen atom on the same side as the β-hydrogen atom eliminated. The process is repeated on the product, this results in the complete removal of the nitrogen atom from the molecule leaving on unsaturated hydrocarbon isomerises to a conjugated diene.



Degradation : This is the most important step in elucidating the structure of the degraded products it will be very easy to know the structure of the original molecule. The various degradative reactions used in elucidating the structure of alkaloids.

1 Hoffman exhaustive Methylation method

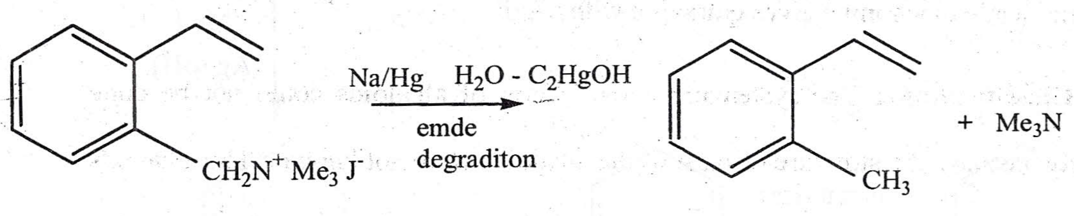
The method is based on the fact that when quaternary ammonium hydroxides are heated they decompose with the loss of water and clearage of a carbon-nitrogen linkage to give an olefin. The quaternary ammonium hydroxide is obtained by the complete methylation of the amine.

$$CH_3CH_2CH_2N\,Me_2 \xrightarrow[Ag_2O]{Me\ I} CH_3CH_2CH_2\,\overset{+}{N}Me_3\overset{-}{O}H \xrightarrow[200\ ^{o}C]{\Delta}$$

Quaternary ammonium hydroxide

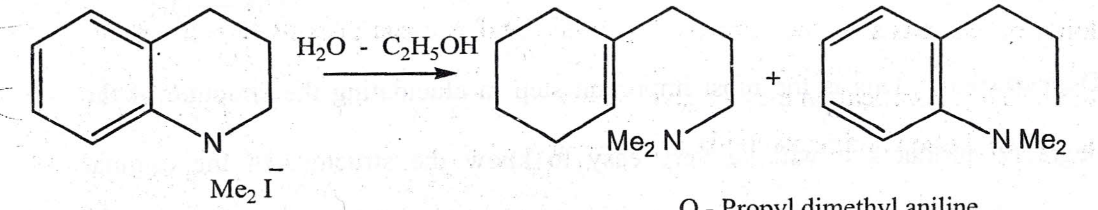
$$CH_3\,CH = CH_2 + Me_3N + H_2O$$

Emde method : The method which consist in reducing an aqueous (or) alcoholic solution of the quaternary ammonium halide with sodium amalgam in aqueous ethanol, sodium in liquid ammonia (or) catalytically.



Tetrahydro isoquinoline
β - Hydrogen is absent

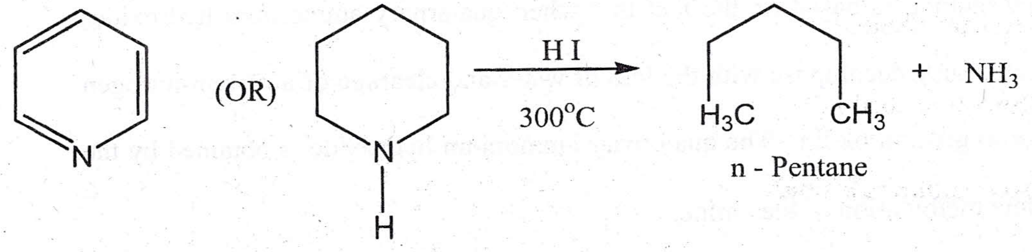
O-methyl Styrene



β - Hydrogen is Present

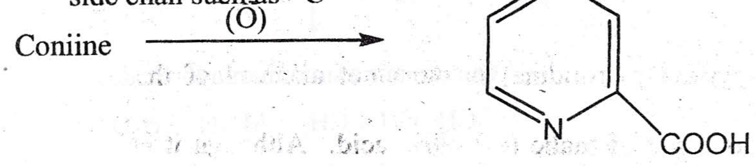
O - Propyl dimethyl aniline

Reductive degradation : The pyridine (or) piperidine nuclei in some cases may be eliminated as ammonia and n-pentane by heating with hydridic acid at 300°C



n - Pentane

Oxidation : Oxidation frequently gives valuable information about the fundamental structure of alkaloids and the position and nature of some of the factonal groups (or) side chan such as >C = C <



Picolinic Acid

Zinc dust (or) alkali distillation *Distillation of the alkaloid (or) its product over hot zinc dust sometimes degrade it to a stable aromatic derivative.* For example : Morphine gives phenanthrene on distillation with zinc dust combine gives 2-propyl pyridine, while cinchonine gives quinoline with alkali.

4.1.8 Classification : The systematic classification of alkaloids could not be done earlierly because the structure of most of the alkaloids were not known. The alkaloids were classified according to the plant genera in which they were found. E.g. Cinchona, ephdra, opium rouwoflia. It is probably most satisfactory to classify the alkaloids on the basis of the nature of main skeletal nucleus present in a group of alkaloids. The classification may be given below.

a. Phenyl ethyl amine alkaloids

b. Pyrrolidine alkaloids

c. Pyridine alkaloids

d. Pyridine pyrrolidine alkaloids

e. Tropane alkaloids

f. Quinoline alkaloids

g. Iso quinoline alkaloids

h. Phemanthrene alkaloids

i. Indole alkaloids

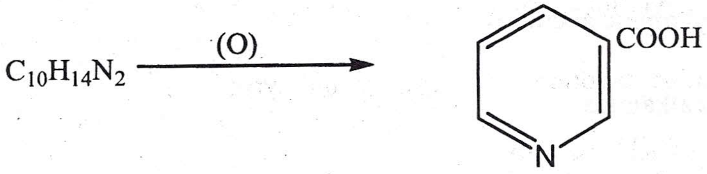
j. Tropolone alkaloids

4.1.9 Nicotine : It (1-methyl-2-β-pyridyl pyrrolidine) is the chief alkaloid of the to acco plant. Where it is present as a salt of malic (or) citric acid. Although it is distributed throughout the plant, its highest concentration is found in the leaves. in varying amounts 0.6% to 8.0%. Its name nicotine was given in the honour of Sir J. Nicot who introduced tobacco in France.

The formula was first of all, given by Pinner in 1892 but was confirmed by Pictet, its structure is based on the result of degradative methods like oxidation and on direct synthesis.

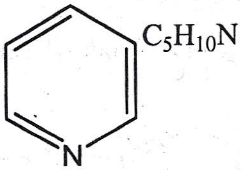
a) Molecular formula : Analysis and molecular weight determination shows its composition as $C_{10}H_{14}N_2$.

b) Oxidation : When oxidized with dichromate sulphuric acid (or) (permanganate (or) nitric acid) nicotine forms nicotinic acid



Nicotine Acid

This shows that the nicotine molecule contains a pyridine necleui substituted in the β-position.



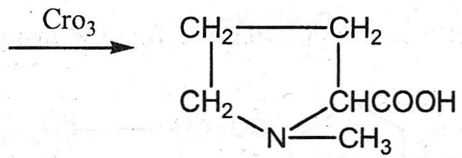
Di-tertiary base : Nicotine forms diacid salts, such as the dihydrochloride, $C_{10}H_{14}N_2$: 2HCl and it forms two isomeric monomethiodides and a dimethiodide indicating the presence of two nitrogen atoms. Hence the side chain can not be a piperidine nucleus.

Nature of the side chain : Since the side chain, $C_5H_{10}N$ has the same composition as the piperidyl group and for sometime it was assumed that nicotine was piperidyl pyridine.

Herzig and Meyer's method shows the presence of one N.CH_3 group and this must be present in side chain. Again, when a nicotine zinc chloride is distilled with lime, the products pyridine methylamine and pyrrole are obtained.

The side chain is C_4H_7.N.CH_3. Hence the side chain is very likely a pyrolidine system. The presence of N-Methyl pyrrolidine nucleus is nicotine is very clearly indicated by the conversion of nicotine into hygrinic acid

$$C_{10}H_{14}N_2 \xrightarrow{CH_3\,I} C_{10}H_{14}N_2\ \ CH_3\,I \xrightarrow[NaOH]{K_4[Fe(CN)_6]} C_{10}H_{23}NO_2CH_3$$

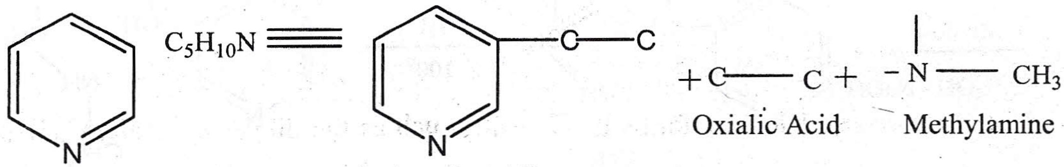


1 - Hygrinic acid

Also, on mild oxidation, nicotine is changed into nicotyrine

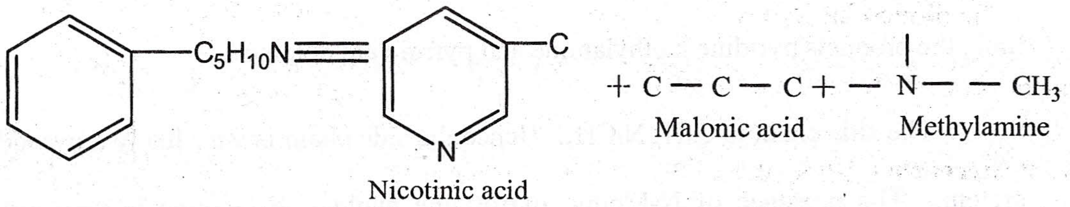
$$C_{10}H_{14}N_2 \longrightarrow \underset{\text{Nicotyrine}}{C_{10}H_{10}N_2} + 4H$$

Treatment of nicotine with bromine in presence of acid gives dibromo cotinine, $C_{10}H_{10}NO_2\ Br_2$. This on heating with a mixture of sulphous acid and sulphuric acid forms 3-acetyl pyridine, oxalic acid and methylamine.

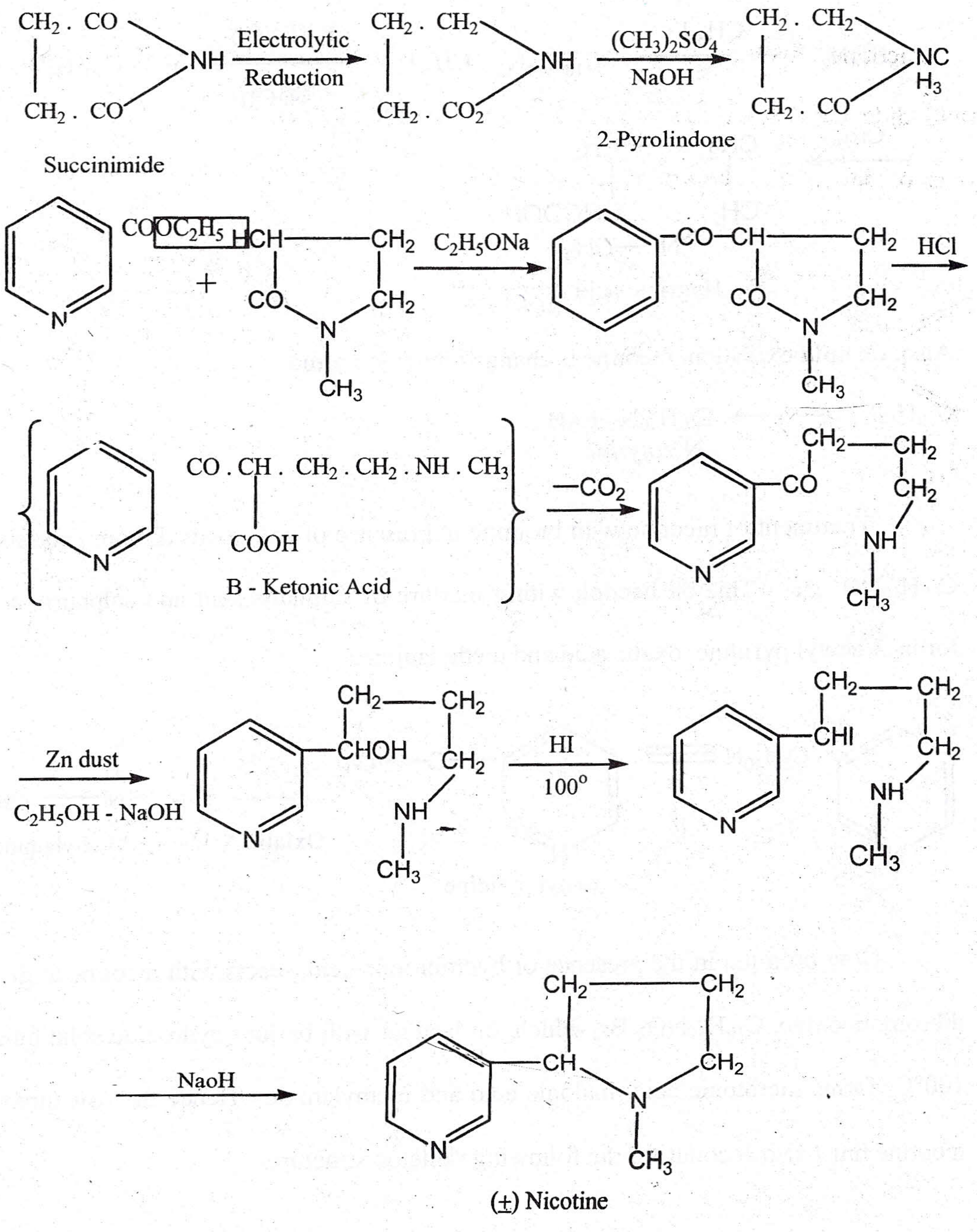


3- Acetyl pyridine

Now bromine in the presence of hydrobromic acid, reacts with nicotine to give dibromoticonine, $C_{10}H_{10}NO_2\ Br_2$ which, on heating with barium hydroxide solution at 100°C, forms nicrotonic acid, malonic acid and methylamine. Hence the structure of nicotine must also account for the following skeleton structures.



Synthesis : Spath and Bretschneider's synthesis (1928)

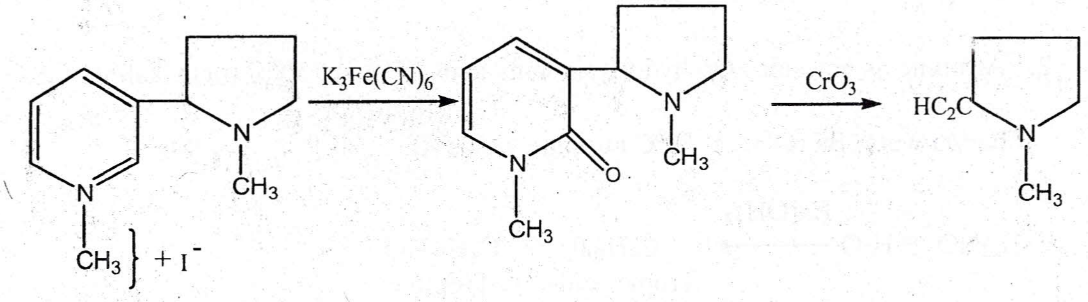


(±) Nicotine

The dl-nicotine is resolved by means (+)-tartaric acid, the synthetic (-)-nicotine is identical with the natural compound.

4.1.10 Stereochemistry : Nicotine contain pyridine ring and pyrrolidine ring. The pyrrolidine ring has L- configuration and rotating in the plain polarized line towards left side. It is Leo form. It is confirmed by Karrer by the following reaction.

Nicotine hydrodide forms nicotine isomethiodide when warmed with methyliodide and this, oxidation with potassium ferricyanide, is converted into nicotine with, an oxidation with chromium trioxide, gives L (-) hygrinic acid.



Nicotine isomethiodide

Nicotone

L(-)-hygrinic acid

4.2.1 Atropine ($G_7H_{23}NO_3$) m.p = 118°C

It occurs in deadly night shade (Atropa delladome) together with Hyoscyamine. Hyoscyamine is optically active (α) D-22°, but readily racemises to atropine is (+) hysocyamine.

When warmed with barium hydroxide solution, atropine is hydrolyzed to (±) tropic acid and trapine (an alcohol), thus is the tropine ester of tropic acid. When (-)-hysocyamine is hydrolysed with cold water, tropine and (-)-tropic acid are obtained.

1. Molecular formula : The molecular formula of atropine as deduced from the analytical data is $C_{17}H_{22}NO_3$.
2. Atropine as an ester : On hydrolysis with acids, HCl at 130°C (or) alkalines i.e, baryta water Ba $(OH)_2$ at 60°C atropine yields (I).

$$C_7H_{22}NO_3 + H_2O \xrightarrow{Ba(OH)_2} \underset{\text{Tropic acid}}{C_9H_{10}0_3} + \underset{\text{Tropine}}{C_8H_{15}NO}$$

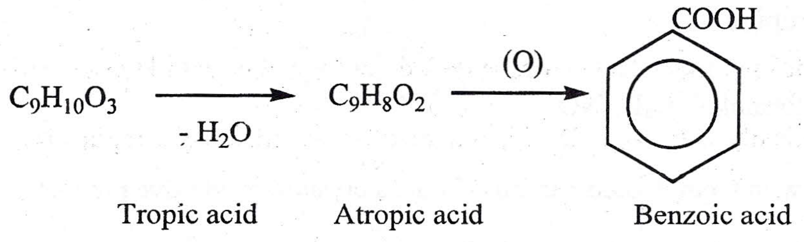
He evaporated a mixture of tropine and tropic acid in presence of hydrochloric acid and obtained atropine. Atropine can not be an amide because tropine, the product of hydrolysis is a tertiary base.

4.2.2 Structure of topic acid :

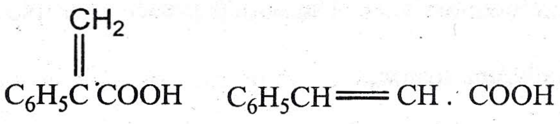
a. Its molecular formula is $C_9H_{10}0_3$.

b. It contains the carboxyl group as well as alcoholic group as determined by usual tests.

c. Tropic acid, on heating with baryta water, gives atropic acid which on vigorous oxidation with chromic acid yields benzoic acid.

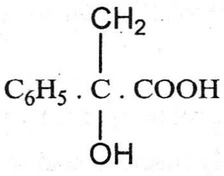


Again atropic acid, isomeric with cinnamic acid, may be represented as



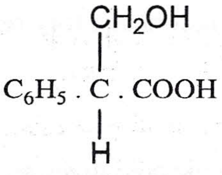
$$\underset{\text{I}}{C_6H_5\overset{\overset{CH_2}{\|}}{C}COOH} \qquad \underset{\text{II}}{C_6H_5CH{=}CH\,.\,COOH}$$

But since II is a well known compound, the cinnamic acid, I must be atropic acid. Lastly since atropic acid is formed by the dehydration of tropic acid, addition of a molecule of water to the former would therefore give tropic acid. Hence tropic acid must be either II (or) III



$$C_6H_5\,.\,\overset{\overset{CH_2}{|}}{\underset{\underset{OH}{|}}{C}}\,.\,COOH$$

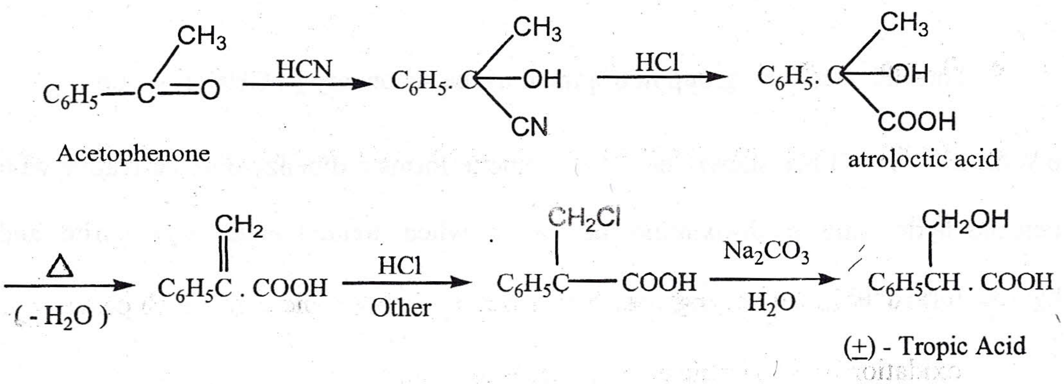
III



$$C_6H_5\,.\,\overset{\overset{CH_2OH}{|}}{\underset{\underset{H}{|}}{C}}\,.\,COOH$$

IV

Mackenzie and wood (1919) :



4.2.3 Structure of tropine

a. Its molecular formula is $C_8H_{15}NO$

b. When treated with methyl iodide, tropine forms a crystalline additive product

$$C_8H_{15}NO + CH_3I \longrightarrow C_8H_{15}NO.CH_3I$$

The nitrogen atom is, therefore, tertiary. The actual presence of N-methyl group is indicated by the results of alkaline fusion.

c. Tropine presence of dehydrating agents like sulphuric acid is glacial acetic acid, is changed into tropidine.

$$\underset{\text{Tropine}}{C_8H_{15}ON} \longrightarrow \underset{\text{Tropidine}}{C_8H_{13}N + H_2O}$$

It indicates that tropine contains a secondary (or) tertiary alcoholic hydroxyl group.

d. Tropine on gentle oxidation with cromic acid gives an optically inactive ketone, tripinone.

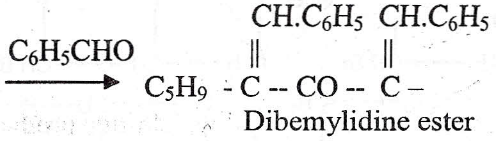
$$C_8H_{15}ON \xrightarrow{Cro_3} C_8H_{13}ON$$

Thus the alcoholic group in tropine must be secondary (> CHOH) group

e. Wilsttater (1897) has shown th[illegible]inone forms a dibenzyldine derivative with benzaldehyde, and a di-oximino derivative when treated with aryl nitrite and hydrochloric acid

$$C_5H_9N + CH_2 - CHOH - CH_2 \xrightarrow{O} C_5H_9N - CH_2 - CO - CH_2 -$$

Propinone

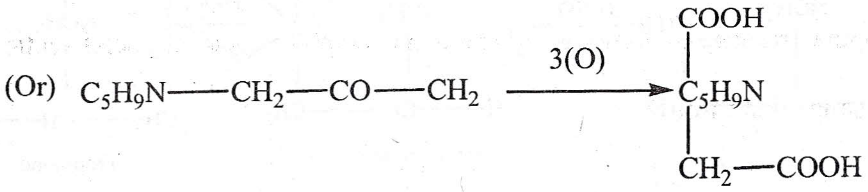


$$\xrightarrow{C_6H_5CHO} C_5H_9 - \overset{\overset{CH.C_6H_5}{\|}}{C} - CO - \overset{\overset{CH.C_6H_5}{\|}}{C} -$$

Dibemylidine ester

f.Tropinone on further oxidation gives a dicarboxylic acid, tropinic acid with the same number of carbon atoms

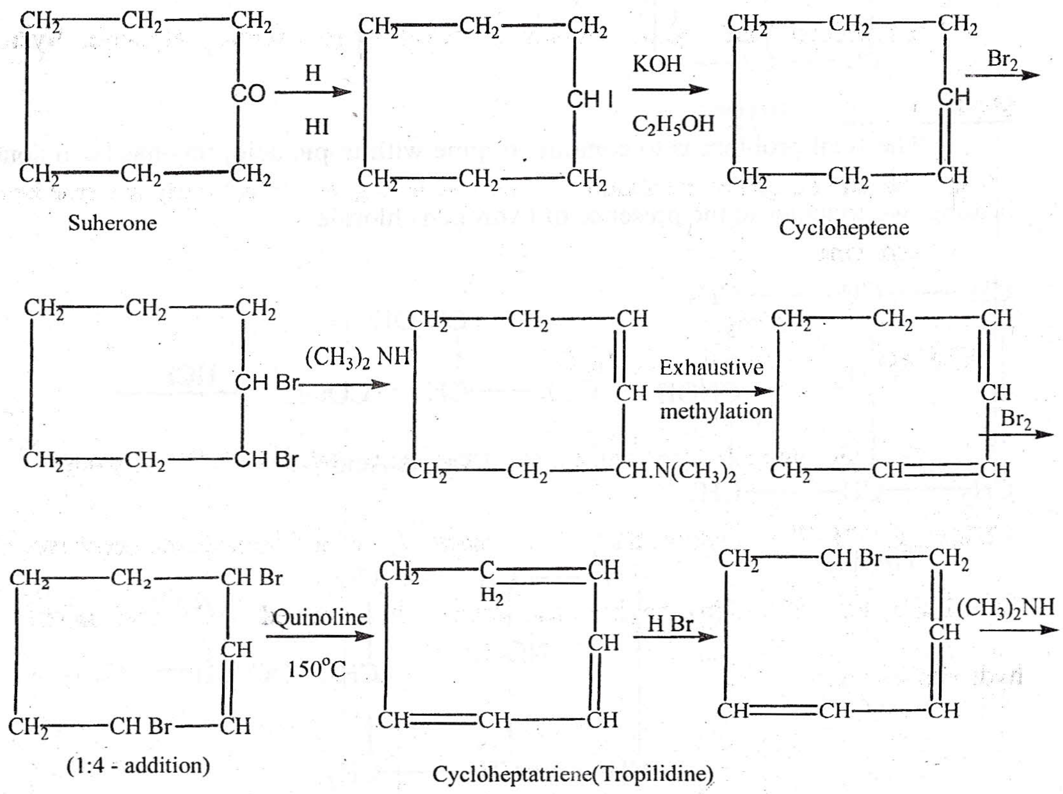
$$C_8H_{13}ON \xrightarrow{3(O)} C_8H_{13}ON$$

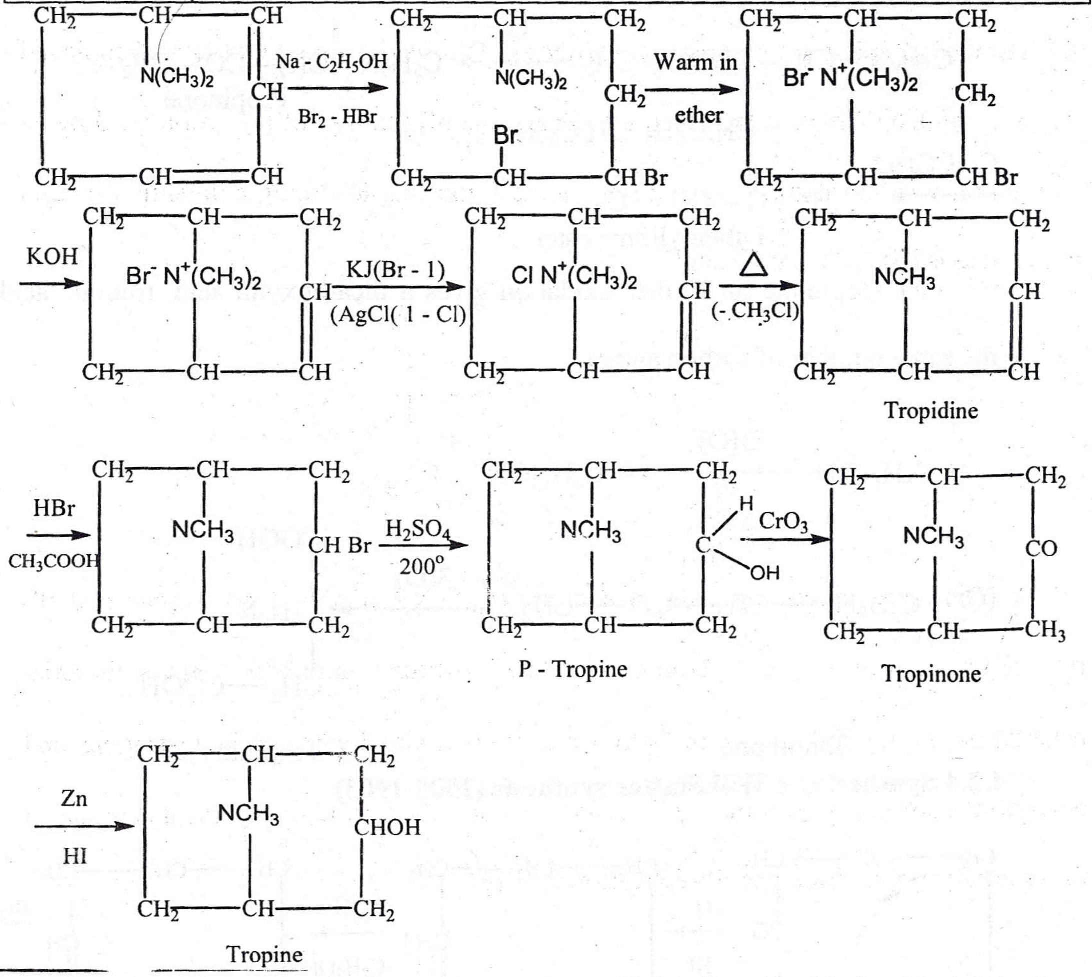


$$\text{(Or)}\ C_5H_9N - CH_2 - CO - CH_2 \xrightarrow{3(O)} \underset{\underset{CH_2 - COOH}{|}}{\overset{\overset{COOH}{|}}{C_5H_9N}}$$

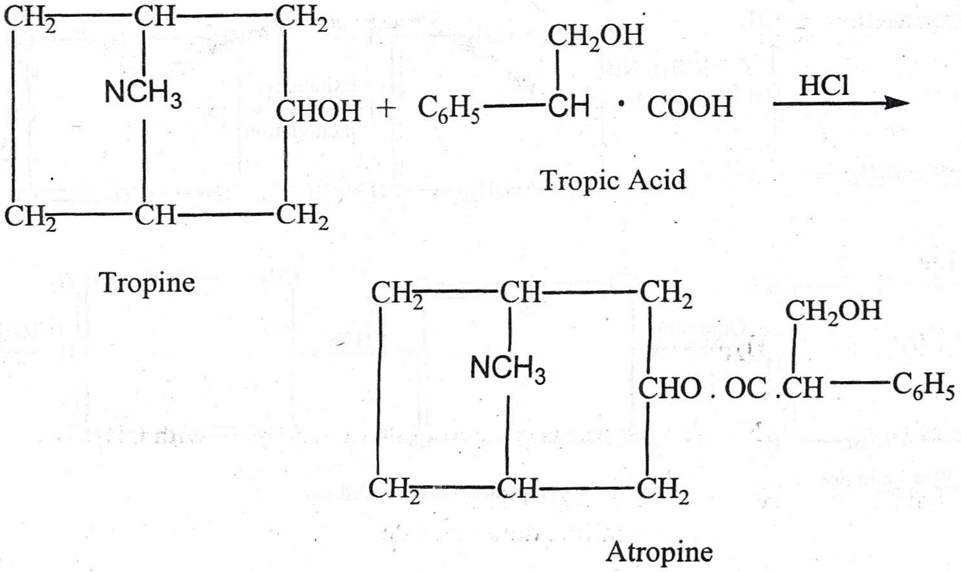
Tropinone Tropinic Acid

4.2.4 Synthesis : 1 Will Statter synthesis (1900-1903)

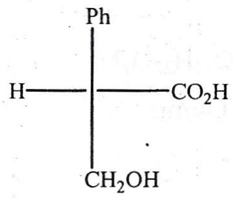




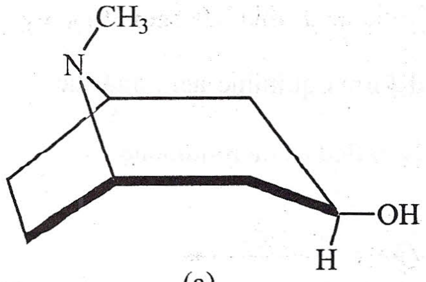
The final problem is to combine tropine with tropic acid; this has been done by heating two together in the presence of hydrogen chloride.



4.2.5 Stereo chemistry : Atropine, $C_{17}H_{23}NO_3$, consists of tropine molity and tropic aid molity. FODOR have established the absolute configuration of (-)- tropic acid by its correlation wit (-)- alanine. According to the Cann-Ingold-Prelog convention natural tropic acid is (S)- (-) – tropic acid

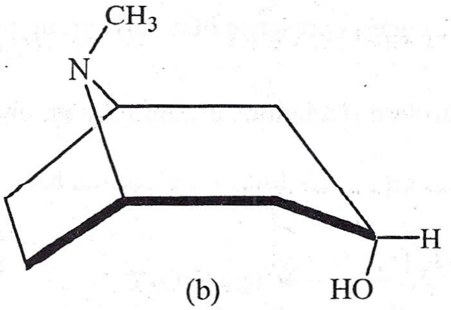


Tripinone can be reduced to a mixture of two alcohols and tropine and Ψ-tropine (psedotropine). Fodor proposed the boat confirmation in both isomers, the axial orientation of methyl group in both isomers,but axial hydroxyl in Ψ-tropine and equatorial hydroxyl in tropine. The evidence was based on rearrangements similar to those used for ephedrine and Ψ- ephedrine



(a)

Ψ - Tropine



(b)

Tropine

4.2.6 Quinine

1. Molecular formula : $C_{20}H_{24}N_2O_2$

2. Presence of two tertiary N atoms : It forms dimethoidide on treatment with CH_3I.

$$C_{20}H_{24}N_2O_2 + 2CH_3I \rightarrow C_{20}H_{24}N_2O_2.2CH_3.I$$

Crystalline dimethiodide

3. Presence of secondary alcoholic group : Since quinine forms a mono acelate and mono benzoate, one – OH group must be present and this is secondary alcoholic in nature.

$$\underset{\text{Quinine}}{C_{20}H_{20}N_2} \xrightarrow{Cro_3} \underset{\text{Quininone}}{C_{20}H_{22}O_2N_2}$$

4. Presence of a methyl group : The second oxygen atom is quinine is present as – OCH₃ group

$$- O - CH_3 \xrightarrow[HCl]{\Delta} \underset{\text{Methylchloride}}{CH_3Cl} + - OH$$

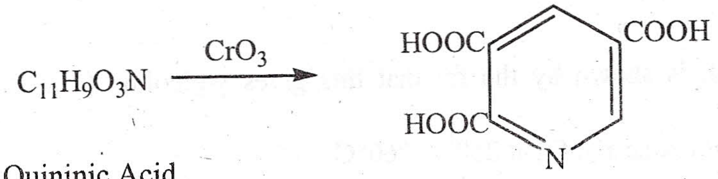
5. Presence of vinyl group (-CH =CH₂) : On controlled oxidations with KMnO₄ quinine gives a mono carboxylic acid and formic acid. The formation of formic acid suggests presence of a vinyl group in quinine.

6. Controlled oxidation of quinine with chronic acid forms quininic acid and the other component known as 'second half' commonly called as meroquinene

$$C_{20}H_{24}O_2N_2 \xrightarrow[\text{Controlled oxidation}]{Cro_3} \underset{\text{Quininic acid}}{C_{11}H_9O_3N} + \underset{\text{Meroquinene}}{C_9H_{15}NO_2}$$

7. Structure of quininic acid

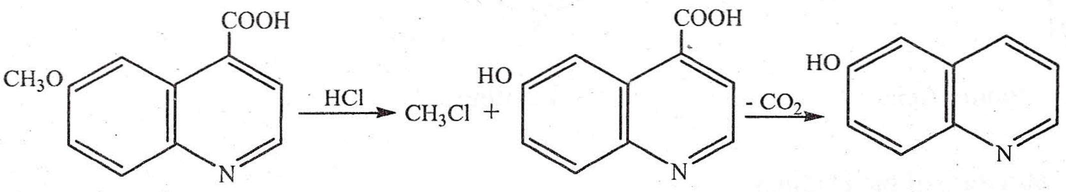
Quininic acid on oxidation with chronic acid forms pyridine – 2 : 3 : 4 tri-carboxylic acid.



Quininic Acid

Pyridine 2 : 3 : 4 - Tricarboxylic Acid

Position of – OCH_3 group : Quininic acid on heating with hydrochloric acid is demthylated and then decarboxylation of the demethylated product gives 6-hydroxy quinoline



1, Quinic Acid

6-Hydroxy Quinoline

Structure of meroquinene :

1. The molecular composition of meraquinene is $C_6H_{15}O_2N$
2. Presence of ethylenic linkage : On reduction, neroquinene takes up one molecule (H_2) of hydrogen which suggests that ethylenic double bond is present in it.

$$C_9H_{15}O_2N \xrightarrow[H_2]{\text{Cat. reduction}} C_9H_{15}O_2N$$

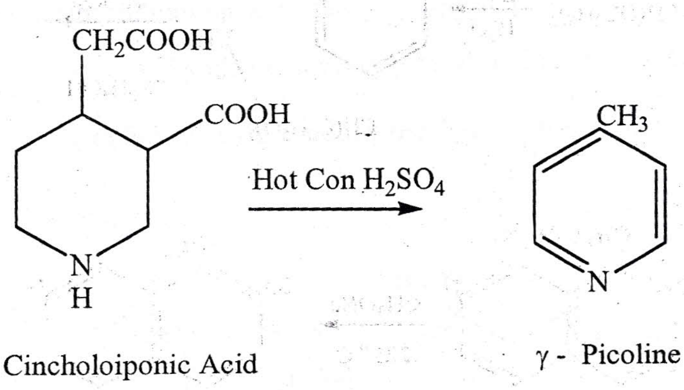
3. On oxidation with acidic $KMnO_4$, meroquinine yields a dicarboxylic acid, cinchololoiponic acid and formic acid. Cincholoiponic acid on further oxidation gives loiponic acid.

$$C_9H_5O_2N \xrightarrow[KMnO_4]{\text{Acidic}} HOOOH + C_8H_2NO_4 \xrightarrow{O} C_7H_{11}NO_4$$

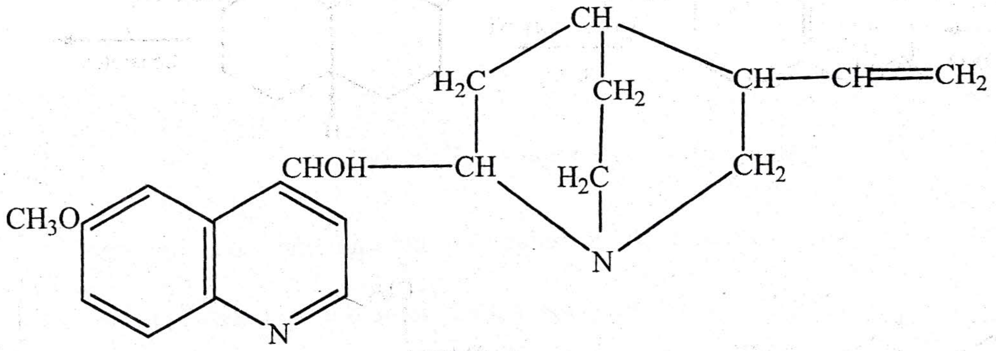
Cincholoiponic Acid

Loiponic acid

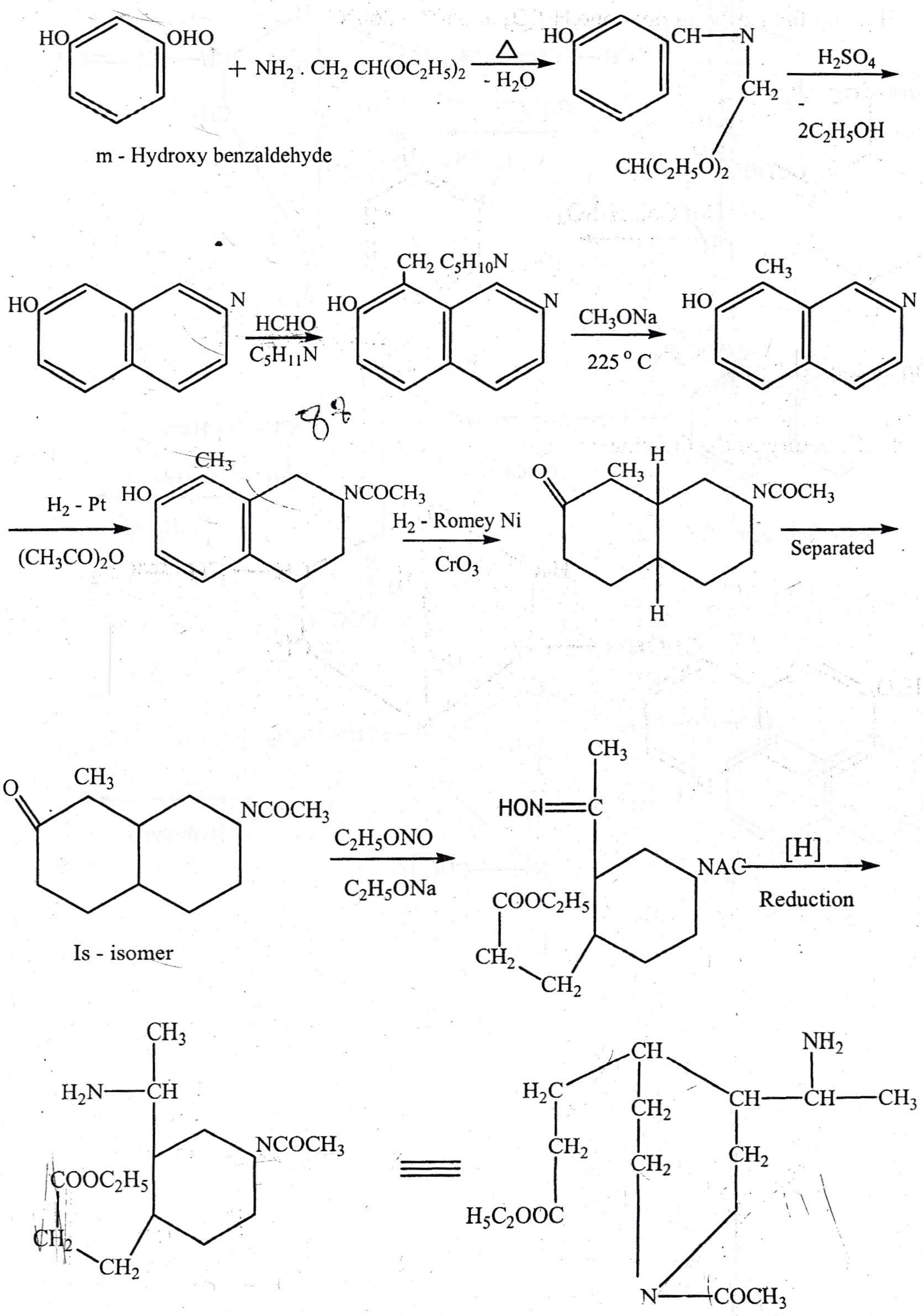
Cincholoponic acid, is shown by the fat that this gives γ-picoline (4-methyl pyridine) by the action of hot conc.H_2SO_4 at 250° – 260°C



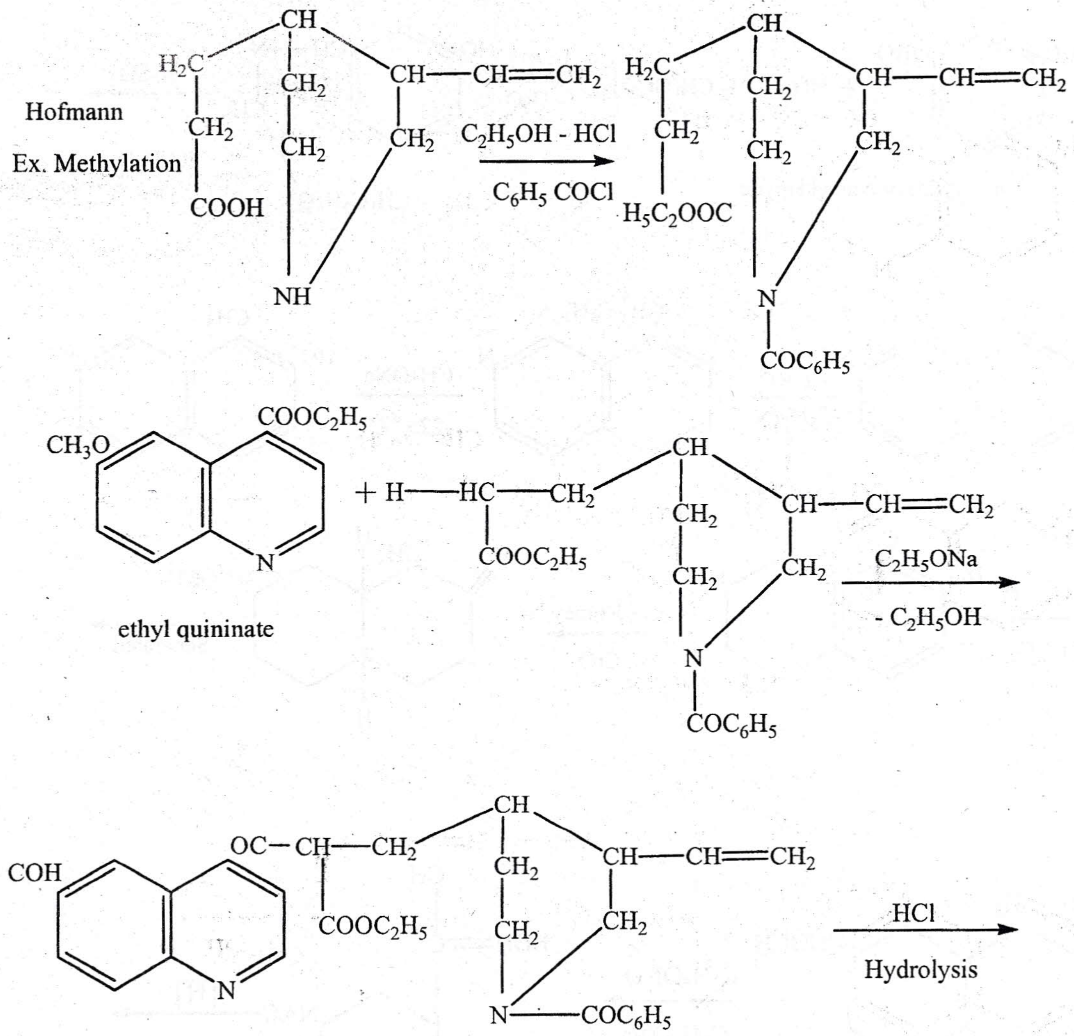
4. Structure of the Quinine



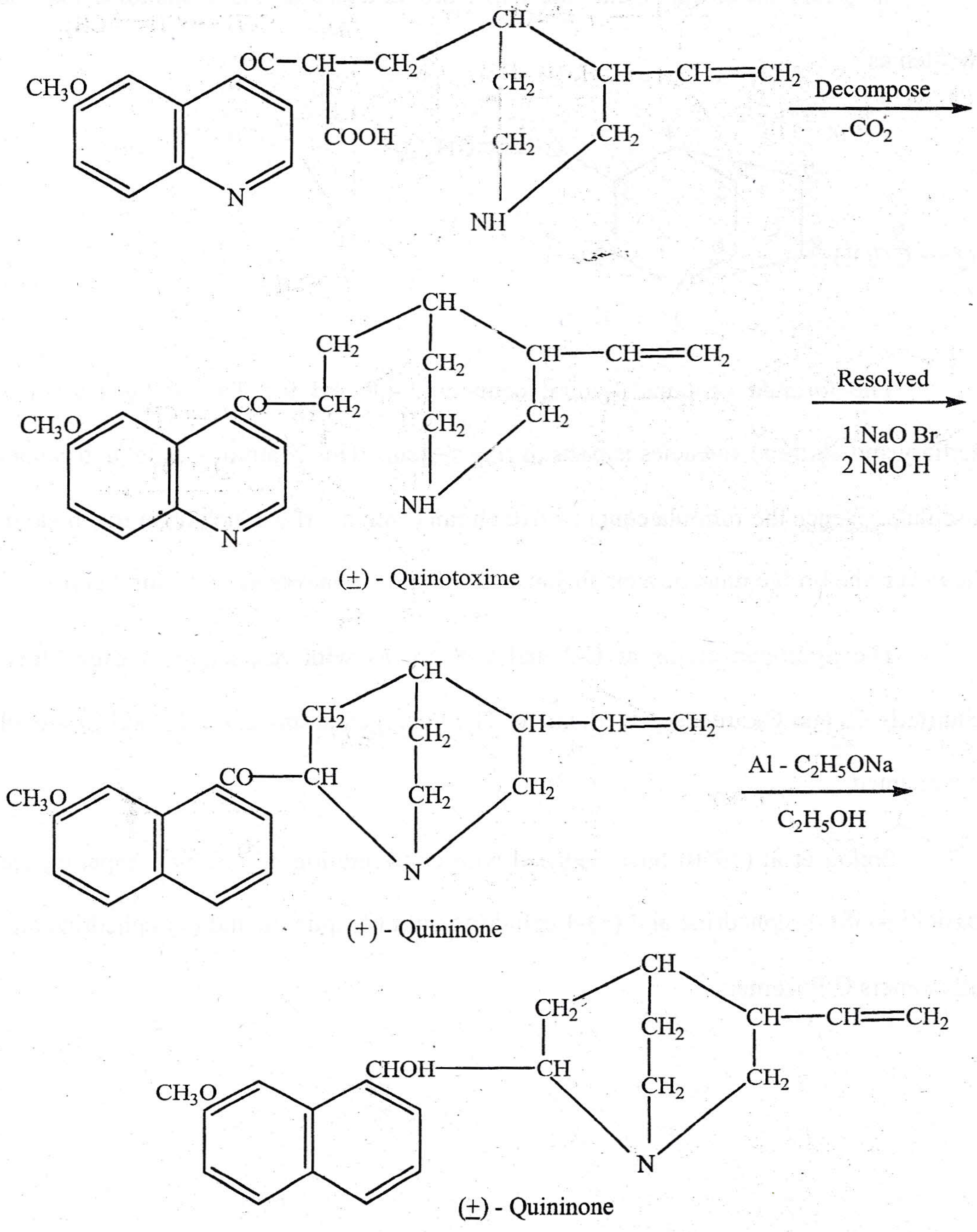
4.2.7 **Synthesis** (R.B.Woodword, W.E. Doering, 1944)



8?

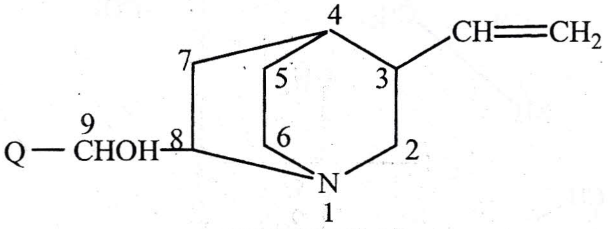


ethyl quininate


Decompose
-CO_2
Resolved
1 NaO Br
2 NaO H
(±) - Quinotoxime
Al - C_2H_5ONa
C_2H_5OH
(+) - Quininone
(±) - Quininone

4.2.8 Stereochemistry

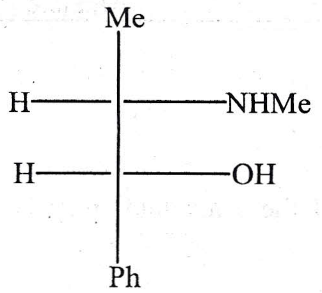
If Q-represents the 'Quinoline half', the structure of these alkaloids may be written as



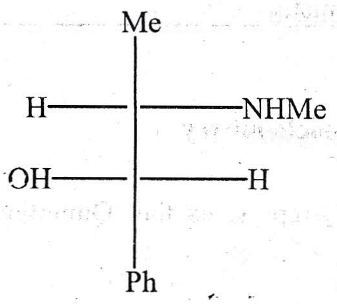
The formula contains 4-chiral contains 3,4,8 and 9. The nitrogen atom is tertiary and all three valencies is parts of ring system. This N atom is chiral and cannot oscillate. Hence the formula contains five chiran centres.. If we include nitrogen atom, however, the bridge must be a cis fusion atoms 1 and 4 behaves as one 'chiral unit'

The hydrogen atoms at C-3 and C-8 are as with respective to each other. Similarly C_4 and C_8 are also cis oriented. The hydrogen atoms at C_3, C_4 and C_8 are all cis oriented.

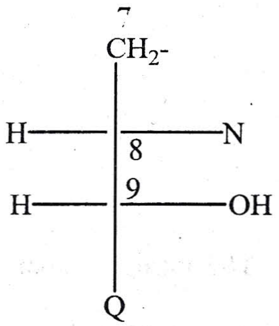
Prelog et al (1950) have deduced with configuration at C-9 by comparing the basicities of (-)- ephedrine and (+)-4 ephidrine with (2)-quinine and (+) ephedrine and all isomers C-9 isomers.



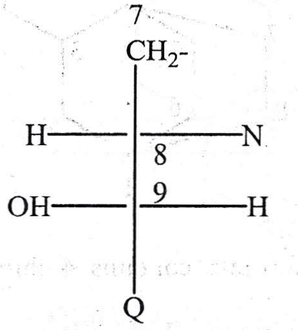
(-) - ephedrine



(+) - Ψ - ephedrine

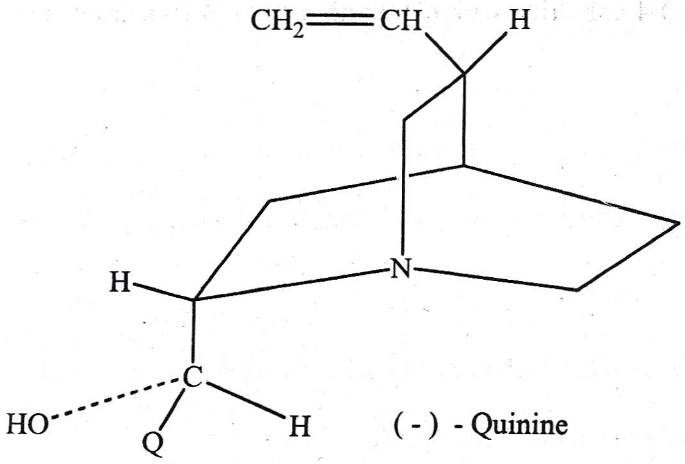


(-) - quinine



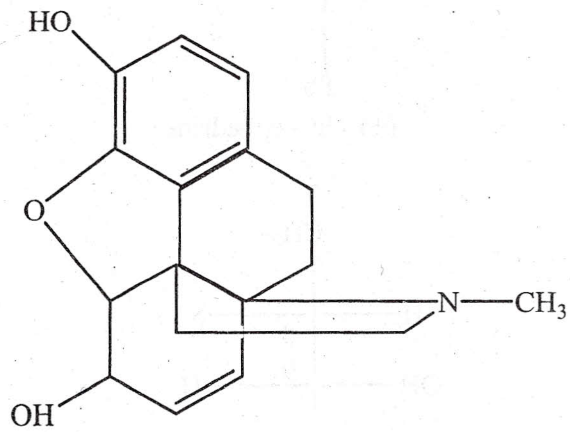
(+) - ephedrine

Inspection of the pKa values shows that Ψ-ephedrine is a stronger base the ephedrine. Similarly ephequinine is a stronger base than quinine basing on the results the authors purposed similar configuration for (+)-ephaquinine and (+)Ψ-ephedrine both of them of having three configuration on other hand erythreo configuration is purposed for (-)-quinine and (-)-ephedrine. It is therefore no possible to write absolute configuration(-)-quinine.



(-) - Quinine

4.3.1 Morphine



Molecular formula $C_{17}H_{19}O_3N$

Nature of N-atom : One molecule of methyliodide is added to morphine is from quatarnary salt. This sources that contains tertiary nitrogen atom. It is conformed by Haffmann's degradation.

Nature of oxygen : Morphine when acetylated (or) benzlated it gives diacetyl (or) dibenzyl derivation. This indicates morphine contains two – OH groups

$$C_{17}H_{17}ON(OH)2 \xrightarrow{C_{13}COCl} C_{17}H_{17}ON\ (OCOCH_3)_2$$

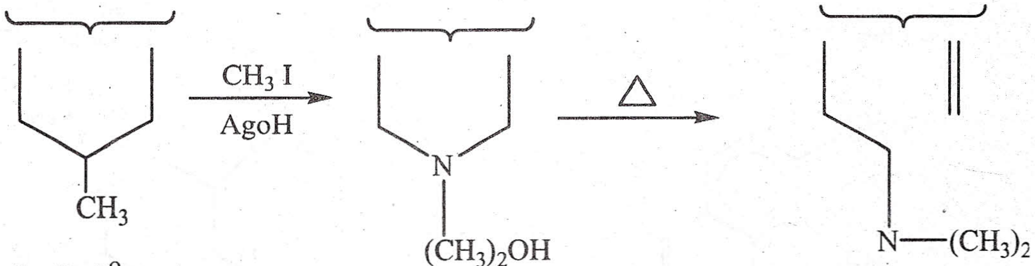
$$C_{17}H_{17}ON(OH)2 \xrightarrow{C_6H_5COCl} C_{17}H_{17}ON\ (OCOC_6H_5)$$

With $FeCl_3$ morphine gives characteristic colour, it is also solubility NaOH solution to form mono sodium salt. Which is reconverted into morphine but possessing CO_2 gas through it.

Presence of athylenic bond : When codeine reduced catalytically $C_{18}H_{23}O_3N$ suggesting the presence of an isolated ethylenic bond.

Presence of benzene nucleus : Morphine when brominated gives a mono bromo derivative along with evolution of HBr. This indicates that morphine contains benzene nucleus

If codiene contains a cyclic tertiary amine system, the product obtain would passes less number of carbon atoms and there is also loss of nitrogen. The experimental results indicates that codiene contains cyclic 3° amine system.



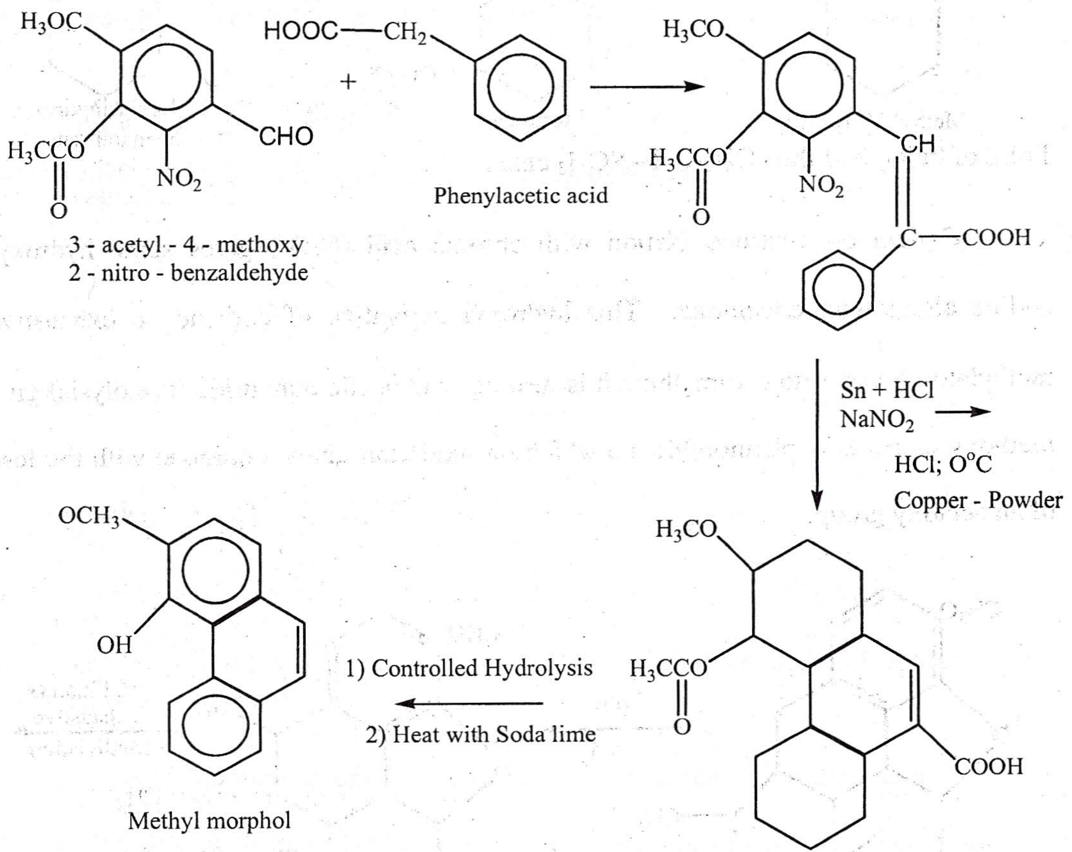
Cyclic 3° amine system

3° amine system in α – codeinmethene

When codeine is treated with CH_3I, it gives codeine methiodide this when boiled with NaOH solution it gives α-methyl morphine this on heating with AC_2O gives a mixture of methyl morphol and ethanol dimethyl amine

$$\begin{tikzcd}
\begin{array}{c}\text{Morphine}\\ C_{17}H_{19}O_3N\end{array} \arrow[r, "CH_3I"] & \begin{array}{c}\text{Codiene}\\ C_{18}H_{21}O_3N\end{array} \arrow[r, "CH_3I"] & \begin{array}{c}\text{Codeine methiodide}\\ C_{19}H_{24}O_3N^{+}I^{-}\end{array} \arrow[d, "NaOH"] \\
\begin{array}{cc}\text{Methyl morphol} + \text{ethanol dimethylamine} \\ C_{15}H_{12}O_2 \qquad (CH_3)_2CH_2CH_2OH\end{array} & & \begin{array}{c}\alpha\text{-methyl morphimethine}\\ C_{19}H_{23}O_3N\end{array} \arrow[ll, "AC_2O"']
\end{tikzcd}$$

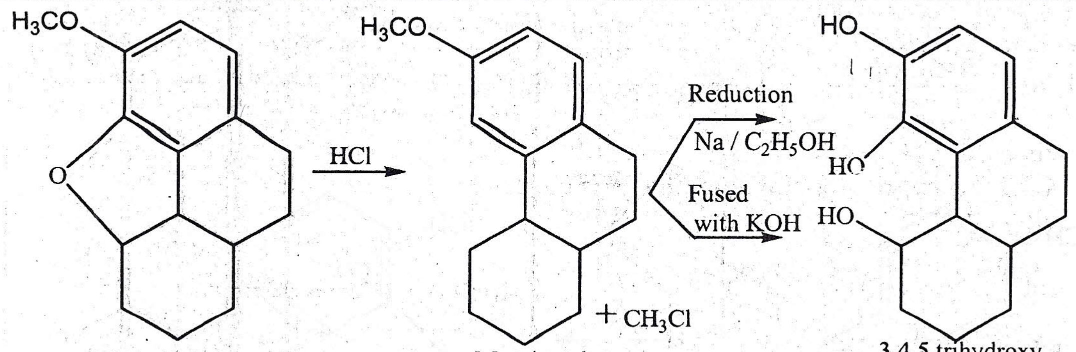
4.3.2 Structure of methyl morphol :Synthesis



4.3.3 Structure of morphenol :

a) β-methyl morphomethine when heated with water it gives a mixture trimethyl amine, ethylene and methyl morphinol

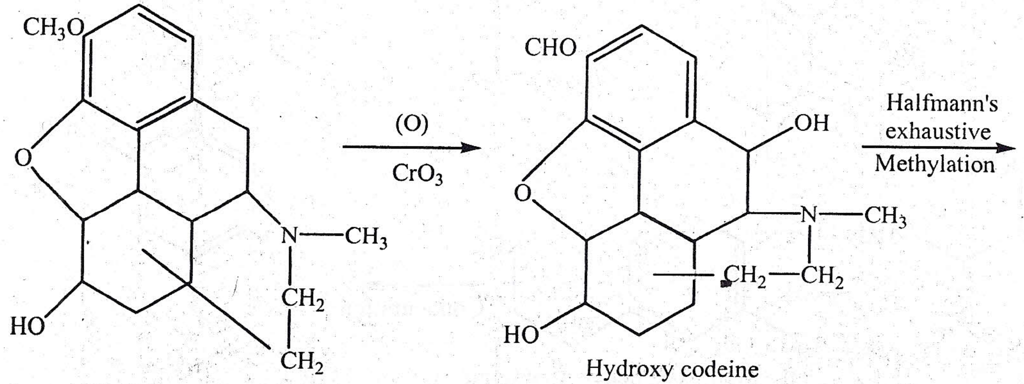
b) Methyl morphinol when heated with HCl, it undergoes d-methylation to form morphinol. It contains one phenolic hydroxyl group and inhert oxygen atom



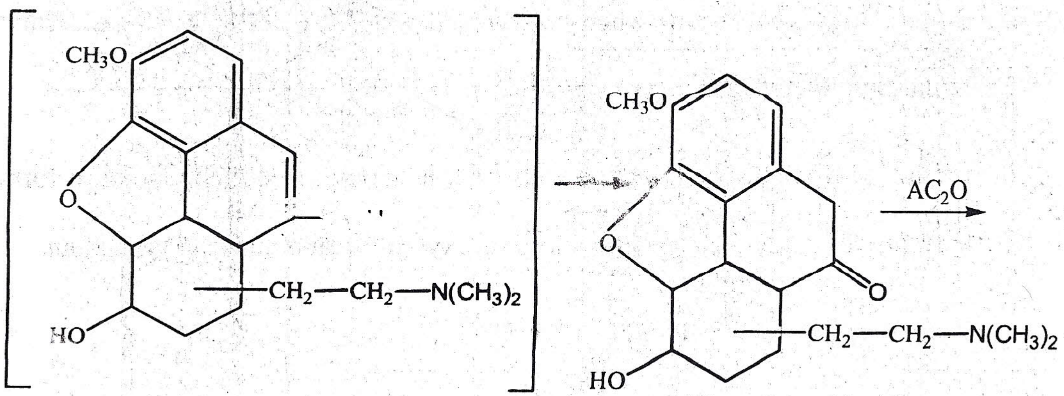
Methyl Morphenol Morphenol 3,4,5 trihydroxy phenanthrene

Point of linkage of the $-CH_2$-CH_2-NCH_3 chain

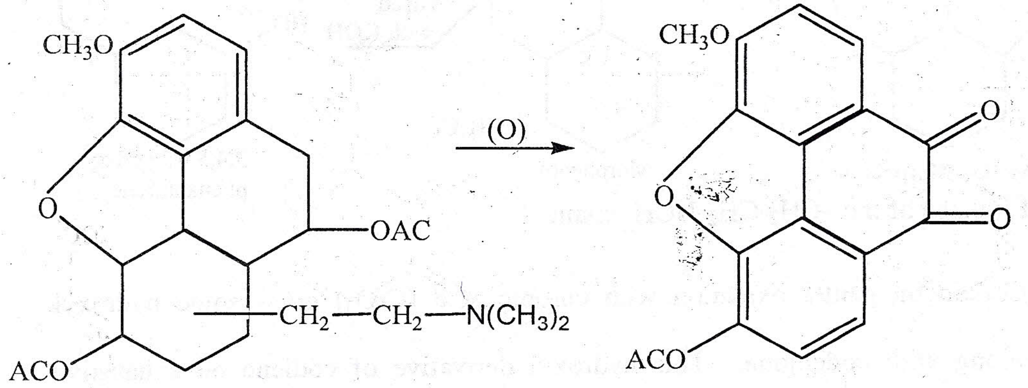
Codein on gentle oxidation with chronic acid (CrO_3) gives some hydroxyl codine along with codeinone. This hydroxyl derivative of codiene on exhaustive methylaton given keto codimethine it is heating with acetic onhydride (acetolysis) give methoxy diaacetoxy phemonthreone which on oxidation gives a quinone with the loss of an acetoxy group.



Partial structure of codeine Hydroxy codeine



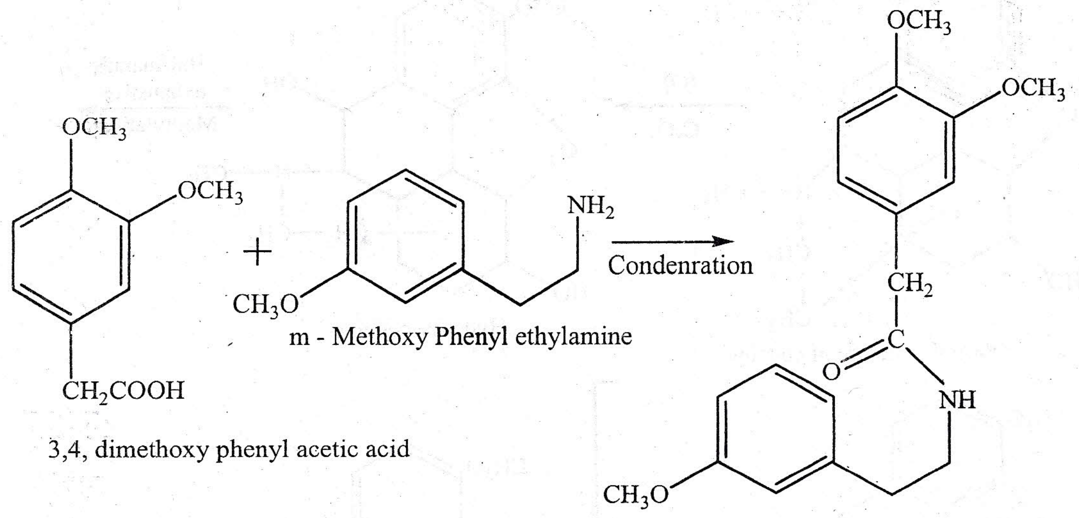
Ketocodeimethine



Methoxy diacetoxy Phenathrene

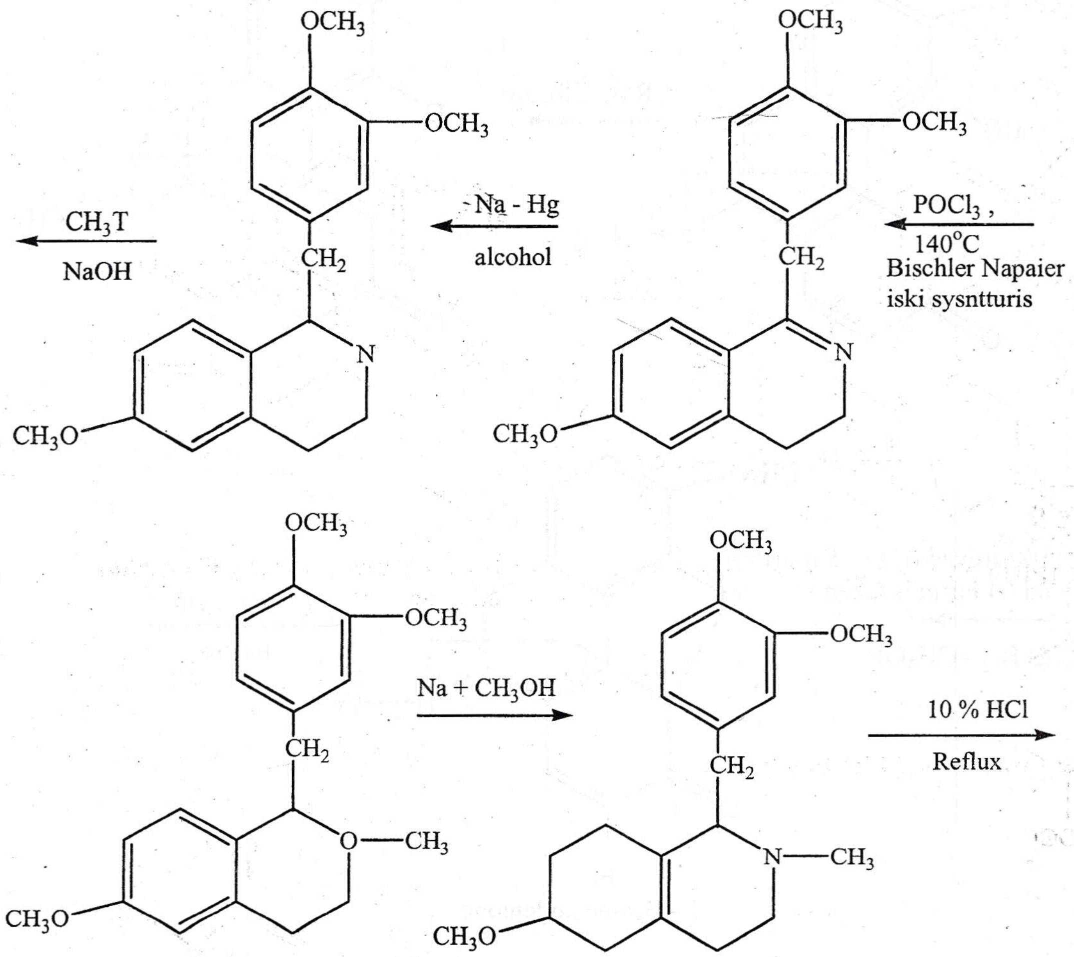
Methoxy mono acetoxy Phenanthra - quinone

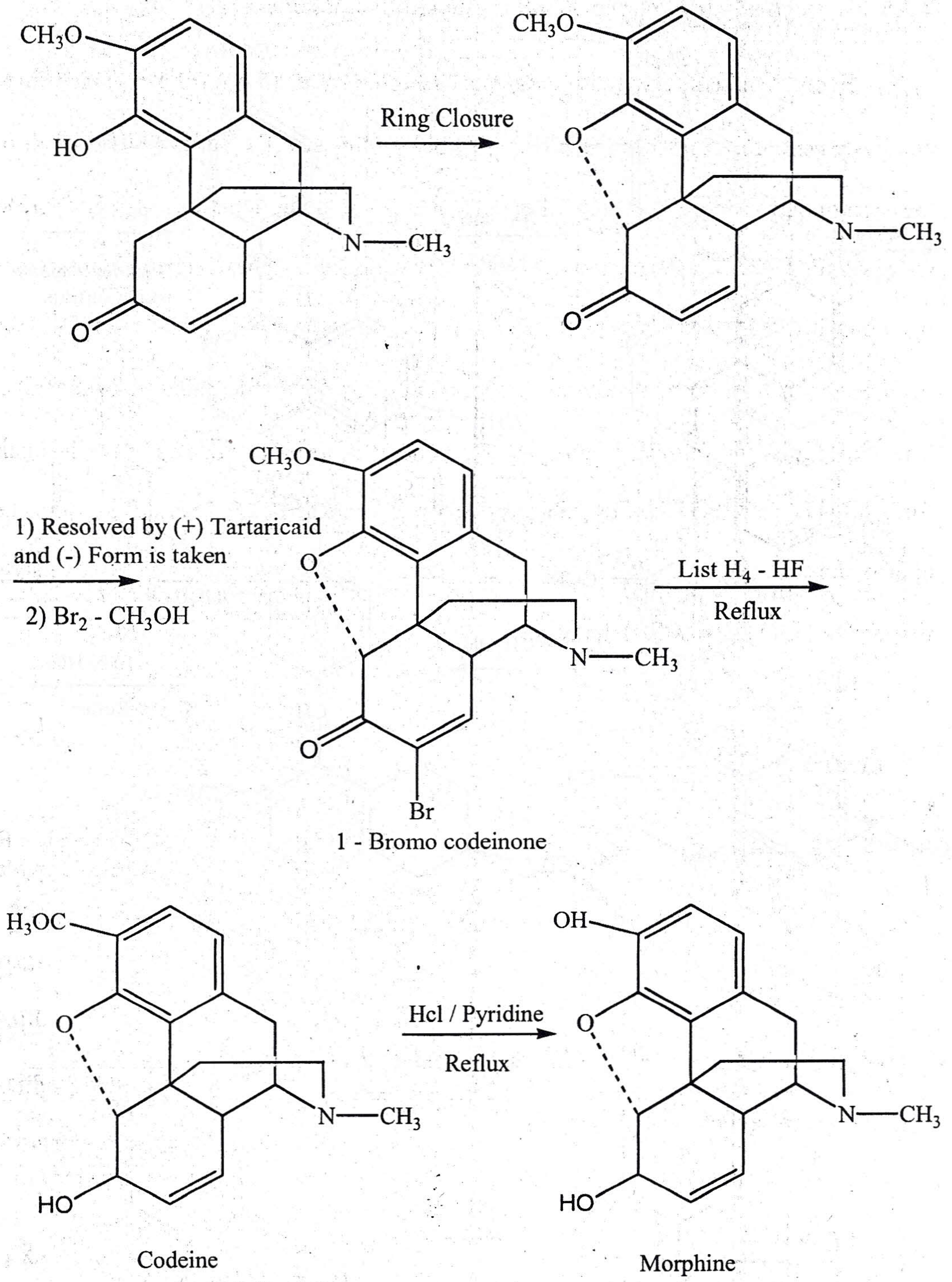
4.3.4 Synthesis of Morphine :



m - Methoxy Phenyl ethylamine

3,4, dimethoxy phenyl acetic acid


OCH$_3$
OCH$_3$
CH$_2$
N
CH$_3$O
POCl$_3$,
140°C
Bischler Napaier
iski sysntturis
Na - Hg
alcohol
CH$_3$T
NaOH
O
CH$_3$
Na + CH$_3$OH
N
CH$_3$
10 % HCl
Reflux



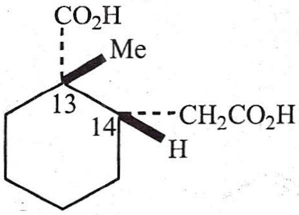
1 - Bromo codeinone

Codeine

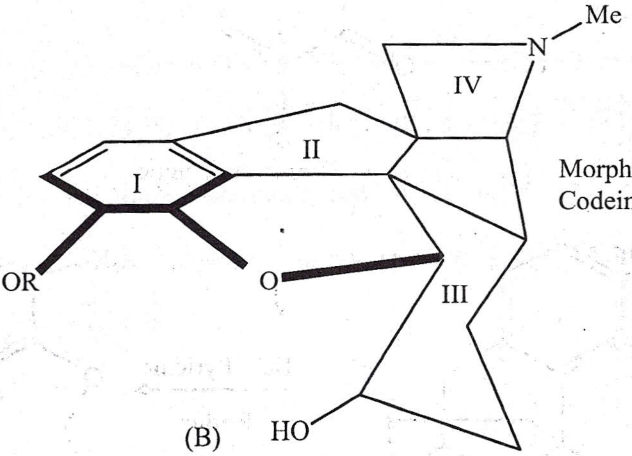
Morphine

4.3.5 Stereochemistry: Stereochemistry morphin and codeine

Each of these compounds contains five chiral centres (5,6,9, 13 & 14) the bridge end system is present across the positions 9, 13 and it is in the cis form. So, each of these compounds exsist in 8 pairs of enensiomers. The hydrogen atom at C-5, C-6 and C-14 are all cis and the bridge at C-9 and C-13 is also cis. These stereochemistry has been confirmed by x-ray analysis. The absolute stereochemistry at C-13 andC-14has been established from the dicarboxylic acid (A) obtained from degradation of thebaine. The configurational formula of morphine and codeine may be written as (B). The chair form has been used for the cyclohexanening and rings I, II and the oxide bridge lie approximately in the plane of the paper and ring III and IV are approximately perpendicular to the plane of the paper.



(A)

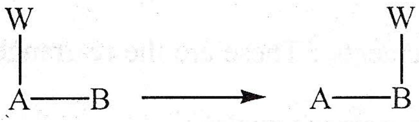


(B)

Morphine : R = H
Codeine : R = Me

4.6.1 General mechanistic considerations

In a rearrangement reactions a group moves from one atom to another in the same molecule. In most rearrangement reaction in migratory groups the migration from an atom to an adjacent one and it is called 1,2-shift. However, in some rearrangement reactions migration to longer distances can also be observed. The migratory group (W) may move with its electron pair, without its electron pair (or) with just one electron, thus, the migratory group may act as an necleophile, electrophile or a free radical. The atom 'A' is called 'migration origin' and 'B' is the migration terminus.



All above reactions have been grouped together under the name rearrangement reactions or molecular rearrangements. Thus, molecular rearrangement may be defined as follows.

"It is the electron which involves reshifting of the sequence of the atoms to form

Molecular rearrangement may be grouped under the following two headings.

1. Intramolecular molecular-rearrangement : If rearrangement occur within the same molecule, they are said to be intramolecular. In these rearragneemtns the migrating group does not get detached completely from the system in which rearrangement is taking place.

2. Intermolecular molecular rearrangement : If rearrangements involve the migration of the group between two molecules, they are said to be intermolecular. In these rearrangements, the migrating group is first detached and reattached at another site.

4.6.2 Types of molecular rearrangements : The molecular rearrangements can be conveniently classified into the following types.

1. Nucleophilic rearrangement : These are the rearrangement reactions in which the migrating group (nucleophile) gets migrated to electron deficient centre
2. Electrophilic rearrangements : these are the rearrangement reactions in which the migrating group (electrophile) gets migrated to electron-rich catre (atom).
3. Free radical rearrangements : These are the rearrangement reactions in which the migrating group moves to a free radical catre
4. Aromatic rearrangements : These are the rearrangement reactions in which the migrating moves to aromatic nucleus.

The just three types of molecular rearrangements are intro molecular while the fourth type of molecular rearrangement may be intramolecular, intermolecular or both.

4.6.3 Rearrangements to electron deficient atom or nucleophilic rearrangements : These rearrangements are much more common than electrophilic or free radical 1,2-shift rearrangements. These are the rearrangement reactions in which the migrating group moves from a carbon atom to an adjacent electron deficient atom which has only six electrons in its valency shell. The electron deficient atom arises due to the loss of some electronegative group (:Y) with its bonding electrons during the migration. The rearrangements are also known as 1,2-shifts. The electron deficient atom may be carbon, nitrogen or oxygen. The group which migrates is most often hydrogen, alkyl or aryl group. The other group containing oxygen, nitrogen or sulphur atoms may also migrate. The important types of 1,2-shifts can be represented as follows.

These rearrangements may proceed through a classical or a nonclassical (bridged) carbonium ion intermediate or both. The whole process may be depicted as follows.

In some cases, a pair of unshared electrons on the migrating group gets facilitated by the formation of the intermediate. In other cases, such as carbon or hydrogen (R = - C – or H), one pair of electrons is able to bind three atoms momentarily together. The formation of the bridged carbonium ions in 1,2-shifts is regarded as an example of neighbouring group participation, and when the rate is increased because of this effect the rearrangement is termed as anchimerically assisted.

The arrangements of this group have been further divided into three types on the basis of the nature of the atom where the migrating group gets moved. The three types are as follows :

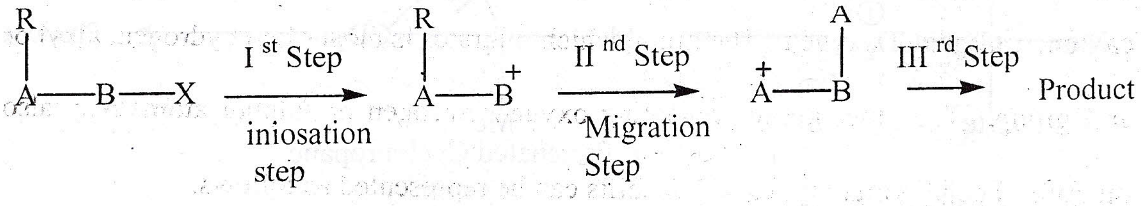
a) rearrangements to electron deficient carbon

b) rearrangements to electron deficient nitrogen and

c) rearrangements to electron deficient oxygen

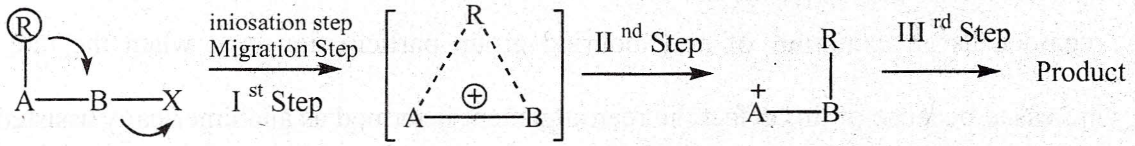
4.6.4 Nature of migration

Most nucleophilic 1,2-shifts are intramolecular. The migratory group (W) does not become free but always remains connected in some where to the substrate. Depending on the nature of the migration the reaction may ends with inversion of configuration or recemisation with respect to the migration origin (A) or migration terminus (B). the molecular rearrangement takes place in the steps. They may be



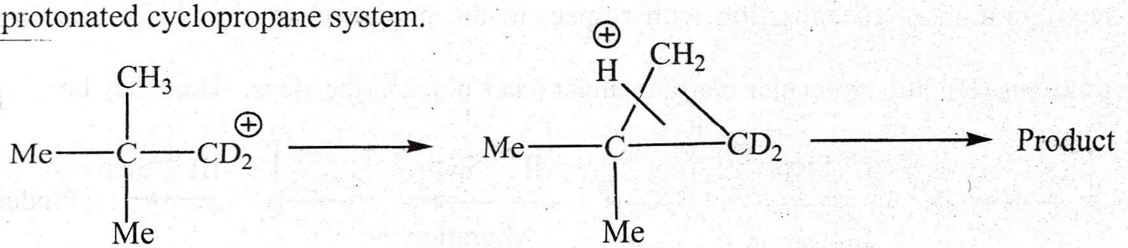
If recemisation is foundent at migration terminus (B), then it is probable the inversation step takes place before the second step and that a positively charge carbon is present at 'B'. These rearrangement reaction is an SN^1 type process with respective 'B'.

If inversion occurs at B, then the inversation step (first step) and migration step (second step) takes place by converted mechanism, the rearrangement reaction is an SN^2 type process with respective B.



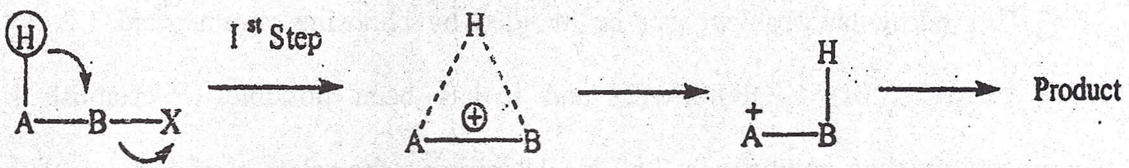
In these case participation by R assist in removal of X which is similar to neighbouring group participation reactions. In the intermolecular rearrangement reaction the bond between R and A is broken, on other hand in the intramolecular rearrangement reactions the migrating group does not get detached completely from the system in which rearrangement taking place.

The rearrangement reactions may proceed through an intermediate formation or hypothetical transition state formation (I). When R is aryl or vinyl groups, then (I) is probability on intermediate the rearrangement results with increasing rate of reaction due to achim ric assistance of migratory group when R is alkyl group, then, I is protonated cyclopropane system.

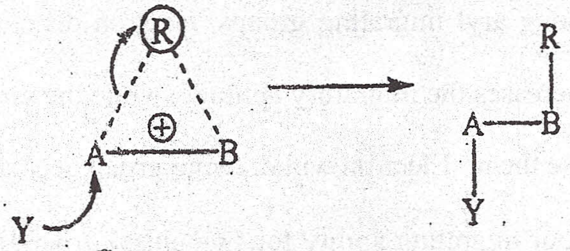


Protanated Cyclopropane System I

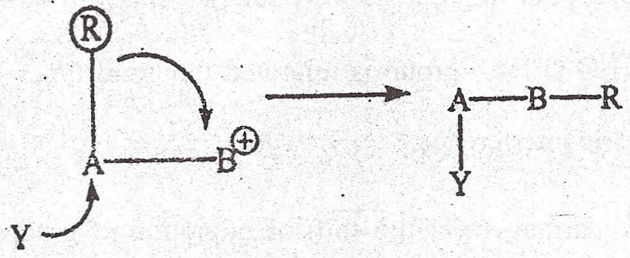
When R is hydrogen atom migrated from migration origin (A) to migration terminus (B), then I is transform state or intermediate.



The stereochemistry at migration origin (A) is less often involved there is because that in most cases it does not end up as a tetrahydral atom. On some rearrangement reactions inversion of conformation at migration origin (A) is noticed. In such cases the reaction proceeds through an SN^2 type process.



inversion at A & B



inversion at A only

4.6.5 Migratory aptitude

All groups do not migrate with equal ease in 1,2-nucleophilic rearrangements. A number of experiments have been carried out to determine the relative migratory aptitude of groups in these types of rearrangements and in general the relative ease of migration is found to be

$pH > Me_3C > MeCh_2 > Me$

This is the rearrangement of the 1,2-diol, Ph_2 C(OH) C(OH), it is the Me that is found to migrate and not C_6H_5 as might have been expected from the sequence above. However, the reaction here is controlled by preferential protonation on that OH group which will lead to the more stable carbocation (1a rather than 1b) and the migration of Me rather than Ph is there by predetermined.

This particular problem can be avoided by choosing symmetrical 1,2-diols suchas PhArC (OH) C(OH)PhAr(2) and it has been possible to establish by experiments on such compounds (i.e.) by determining the relative proportions of the two ketones 2a and 2b that are produced, the relative migratory aptitude sequence is

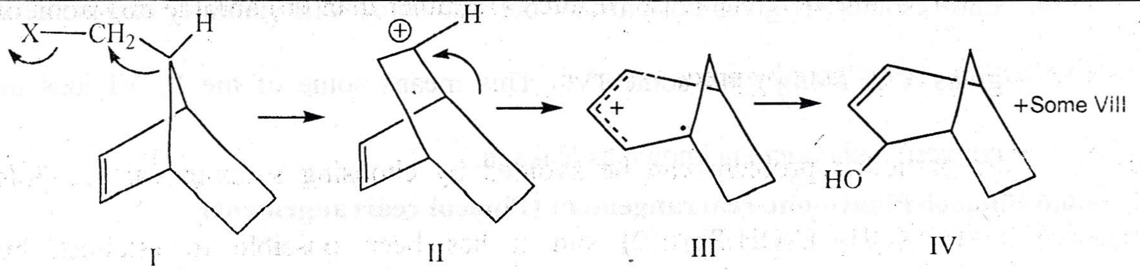
$$\underset{500}{P-MeOC_6H_4} > \underset{15.7}{P-MeC_6H_4} > \underset{1.0}{C_6H_5} > \underset{0.7}{p-ClC_6H_4} > \underset{0.3}{o-MeOC_6H_4}$$

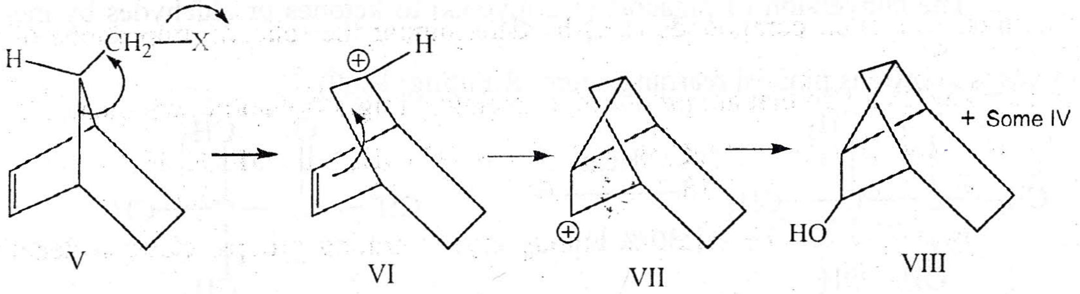
However, it can be said that among aryl migrating groups, electron denoting substituents in para and meta positions increases the migratory aptitude, while the same substituents in the ortho positions decrease them. Electron withdrawing group decrease migrating ability in all positions. The poor migrating ability for O – anisyl group has steric cause. For example; O – $CH_3O\ C_6H_4$ – group is migrated thousand times less than P-$CH_3OC_6H_4$ – group due to setric interference.

Trans migration : In Backmann's rearrangement the shift of migration of groups is always trans to the leaving – OH group. The pinacole rearrangement occurs in such a manner that the migrating group is always trans to the leaving hydroxyl group. It is an important consequence in alicyclic system.

Memory effects : Solvolesis of the endo bicyclic compound (I) gave mostly the bicyclic allylic alcohol (IV), along with a smaller amount of the tricyclic alcohol (VIII) on the other hand solvolesis of the exo isomer (V) gave mostly the tricyclic alcohol (VIII), with a smaller amounts of (IV).

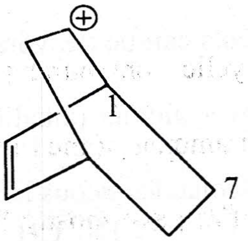
The two isomers gave entirely different ratios of the products, though the carbo cation initially formed (II, VI) seems to be the same for each rearrangement.



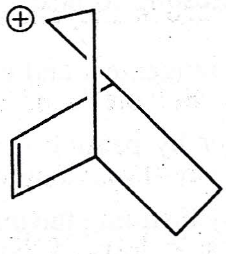


In the case of I, a second rearrangement (a shift of1,7 bond) follows, while with V it is an intramolecular addition of the positive carbon to the double bond that follows. “The formation of carbocations (II, VI), how they were formed before the go on to the second step is known as memory effect”. It is attributed to the following reasons.

1. The twisted carbocation II positive charge is nearer to the 1,7 bonds in the molecule
2. The twisted carbocation VI positive charge is nearer to the double bond of the molecule



II



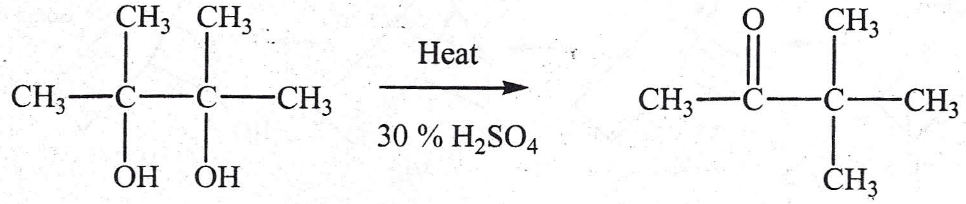
VI

3. The rearrangement involves non classical carbocations and the reactions proceeds in step wise mechanism but not concerted mechanism

4. Endo isomer (I) gives not only IV but also some VIII similarly exo isomers V gives VIII along with some IV. This means some of the II, VI ions inter convert, a phenomena known as leakage.

4.6.6 Pinacol-Pinacolone rearrangement (Pinacol rearrangement)

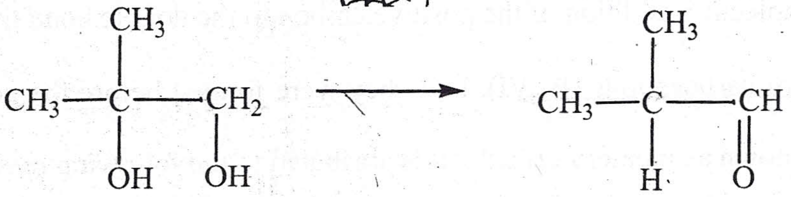
The conversion of pinacols (1,2 glycols) to ketones or aldehydes by means of acids is known as pinacol rearrangement (R.Fitting, 1860).



$$CH_3-\underset{OH}{\overset{CH_3}{C}}-\underset{OH}{\overset{CH_3}{C}}-CH_3 \xrightarrow[30\ \%\ H_2SO_4]{Heat} CH_3-\overset{O}{\overset{\|}{C}}-\underset{CH_3}{\overset{CH_3}{C}}-CH_3$$

2, 3 - Dimethyl - 2, 3 - Butanediol
(Pinacol)

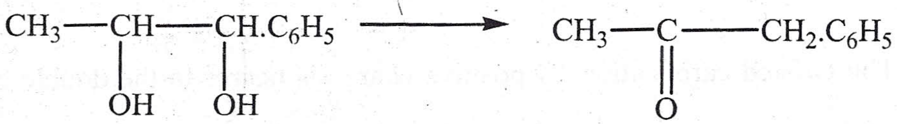
Methyl *t* - butyl ketone
(Pinacolone)



$$CH_3-\underset{OH}{\overset{CH_3}{C}}-\underset{OH}{CH_2} \longrightarrow CH_3-\underset{H}{\overset{CH_3}{C}}-\underset{O}{\underset{\|}{CH}}$$

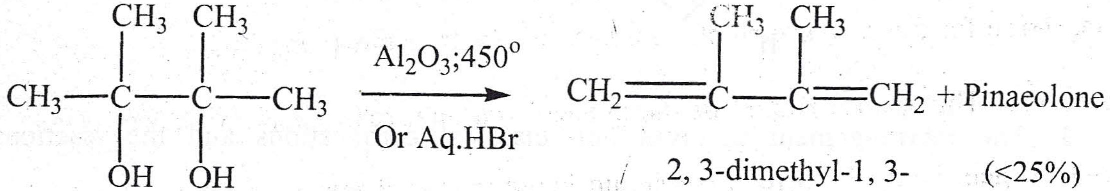
2 - Methyi propan - 1, 2 - Diol

Isobutyraldehyde



$$CH_3-\underset{OH}{CH}-\underset{OH}{CH}.C_6H_5 \longrightarrow CH_3-\underset{O}{\underset{\|}{C}}-CH_2.C_6H_5$$

It is interesting to note that diols other than 1,2 diols dehydrate normally i.e., without any rearrangement and even the pinacols can be dehydrated to normal product i.e., olefins either by passing their vapours over alumia (alkaline conditions) at high temperature or by distilling the mixture of pinacoland aqueous HBr.



$$CH_3-\underset{OH}{\overset{CH_3}{C}}-\underset{OH}{\overset{CH_3}{C}}-CH_3 \xrightarrow[Or\ Aq.HBr]{Al_2O_3;450^o} CH_2=\overset{CH_3}{C}-\overset{CH_3}{C}=CH_2 + Pinaeolone$$

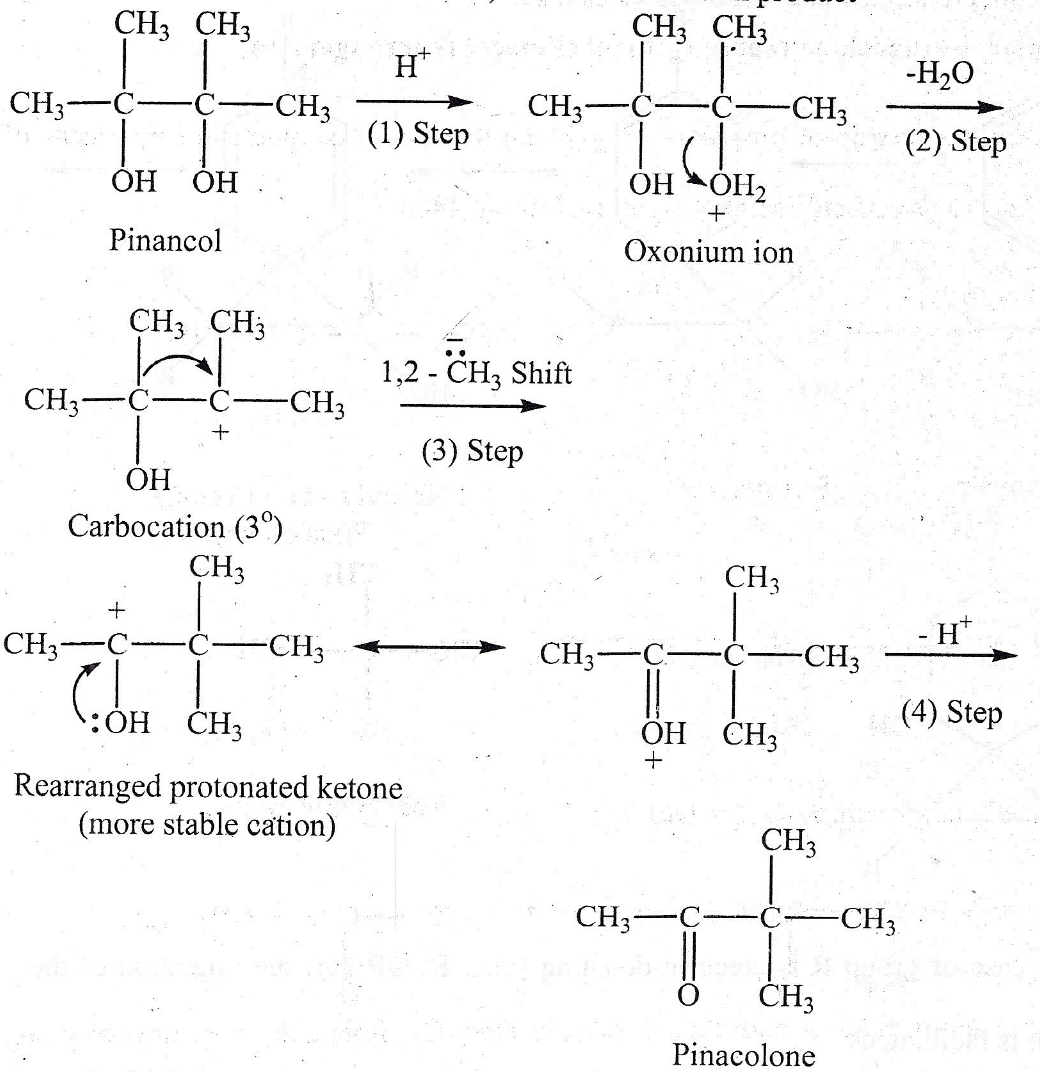
Pinacol

2, 3-dimethyl-1, 3-
butadiehe(<75%)

(<25%)

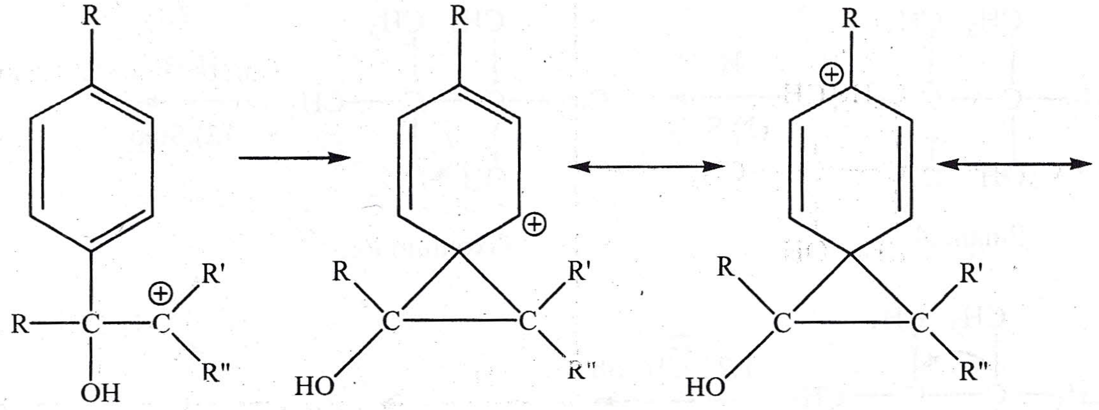
Mechanism : The reaction involves four steps

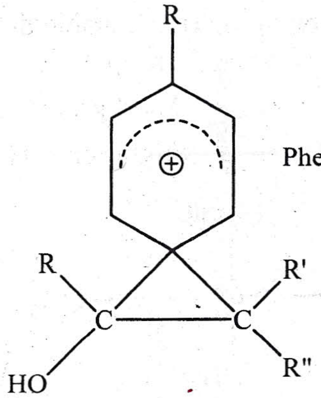
1) Protonation of an OH; 2) Loss of H_2O to form a carbocation; 3) 1,2 shift of H;R (or) Ar to form a more stable cation and 4) Loss of H^+ to form product



It is important to note that although both the initial and the rearranged carbonium ions are tertiary, the rearranged cation is a resonance-stabilized oxonium ion (a protonated carbonyl). The resonance stabilization is undoubtedly an important driving force for the rearrangement. Loss of proton from the rearranged ion produces pinacolone. The special feature of the pinacol rearrangement is the presence of the second oxygen atom which provides its unshared pair of electrons needed during the rearrangement of the cation.

When an aryl group migrates an intermediate of structure I is obtained. The resonance hybrid of I is called the phenonium ion.



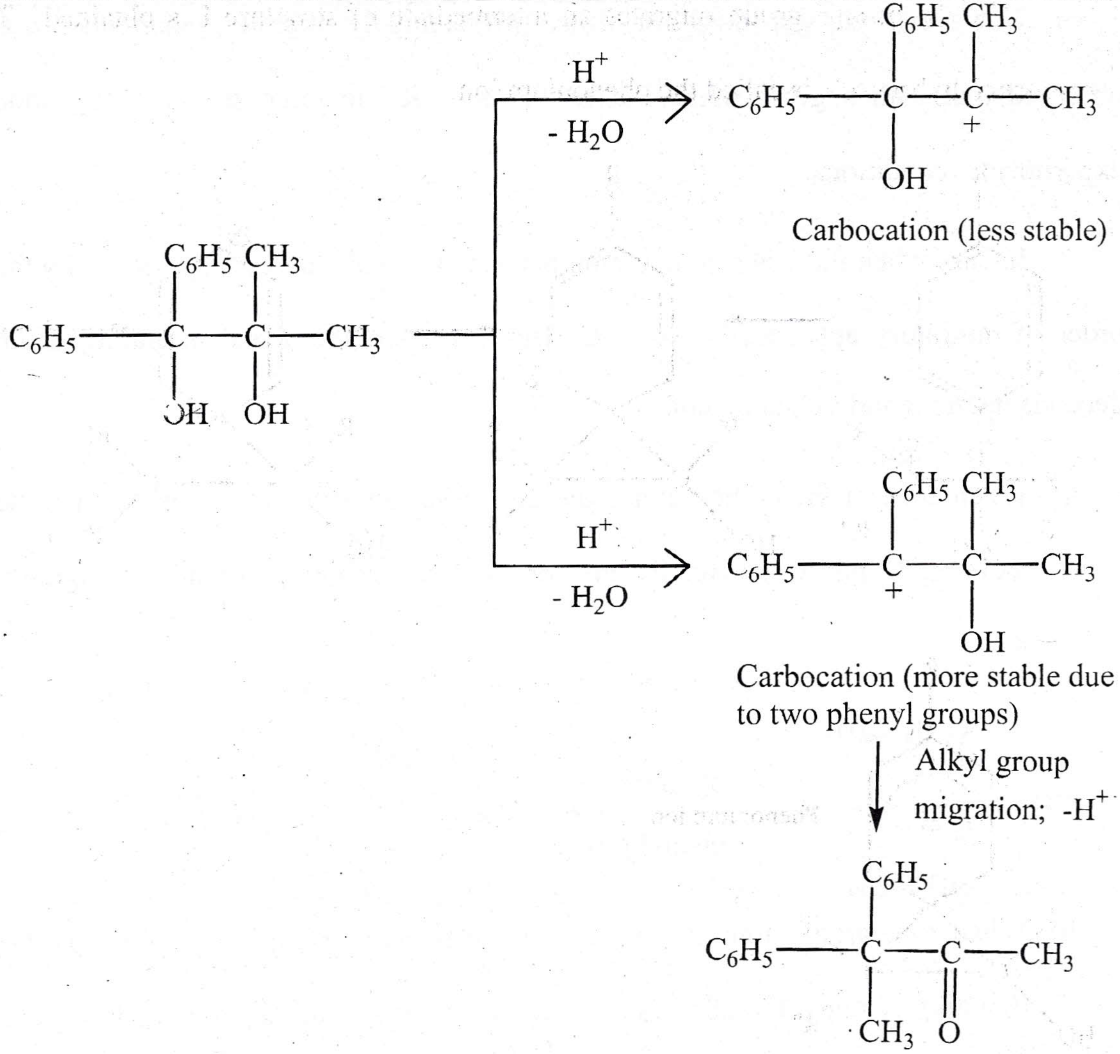


Phenonium ion

In case of group R is electron-donating (viz., R, OR etc) the migration of the aryl group is facilitated.

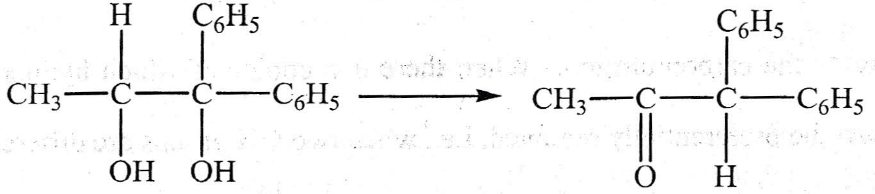
Features of pinacol rearrangement

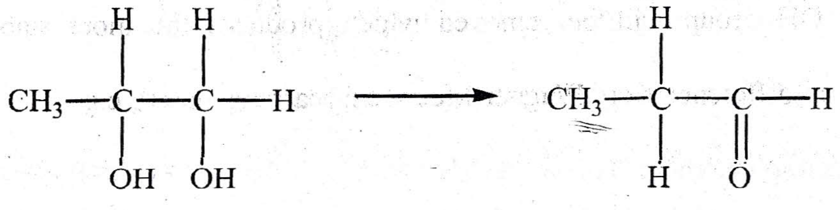
i) Stability of the carbonium ion. When there is a choice as which hydroxyl group will be preferentially removed, i.e., when two OH groups are different then that OH group will be removed which produces the more stable carbocation (difference from Wagner-Meerwein rearrangement), e.g.



3,3-Diphenyl -2-butanone

ii) Migratory aptitude of the group. The migrating group in the pinacols may be alkyl, aryl or even hydrogen atom. Hydrogen may migrate in preference to – R or –Ar, as in the following examples.

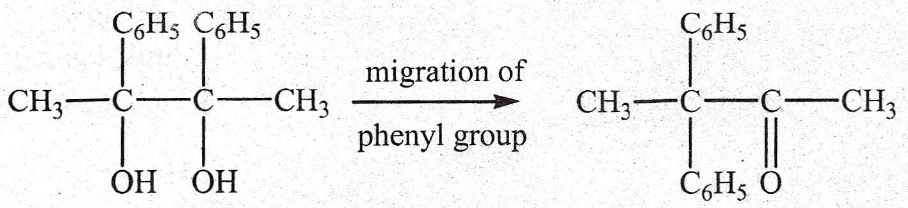




However, hydrogen does not always preferentially migrate. Sometimes it is observed that with a given pinacol either- H or – R can migrate, depending upon experimental conditions.

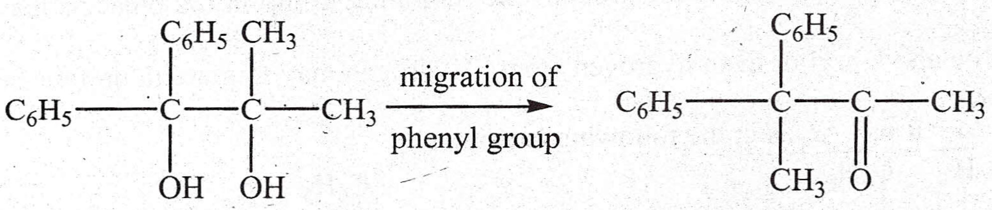
In case when there is a competition between alkyl and aryl groups generally the order of migratory aptitudes is Ar > R. But, however, the actual migrating group depends upon the individual glycol.

a) When each of the carbon atoms the glycol has an aryl and an alkyl group the more nucleophilic (potentially electron rich) aryl group preferentially migrates, e.g.

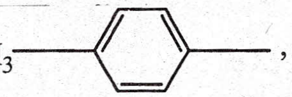


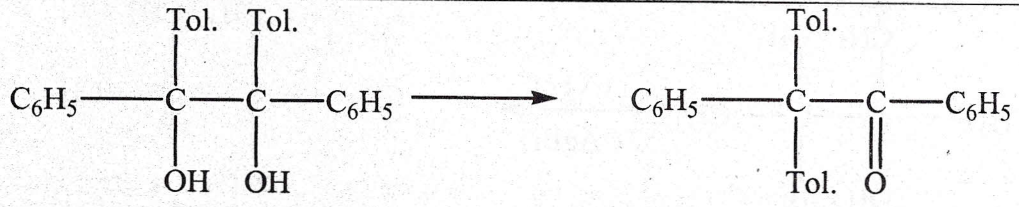
$$CH_3-\overset{C_6H_5}{\underset{OH}{C}}-\overset{C_6H_5}{\underset{OH}{C}}-CH_3 \xrightarrow[\text{phenyl group}]{\text{migration of}} CH_3-\overset{C_6H_5}{\underset{C_6H_5}{C}}-\underset{O}{\overset{\|}{C}}-CH_3$$

b) When one carbon atom of the glycol possesses two aryl groups while the other two alkyl groups, the alkyl group migrates owing to the greater stability of its carbonium ion.



$$C_6H_5-\overset{C_6H_5}{\underset{OH}{C}}-\overset{CH_3}{\underset{OH}{C}}-CH_3 \xrightarrow[\text{phenyl group}]{\text{migration of}} C_6H_5-\overset{C_6H_5}{\underset{CH_3}{C}}-\underset{O}{\overset{\|}{C}}-CH_3$$

Lastly, when the migratory competition is between two aryl groups, then the one which is a better nucleophile (more powerful electron donor towards carbon) migrates preferentially. Thus the migratory aptitude follows the order. P-anisyl > p-tolyl > phenyl > p-chlorophenyl > p-anisyl. This can be visualized by the following example (Where, Tol. ═CH_3  , ═P—tolyl)



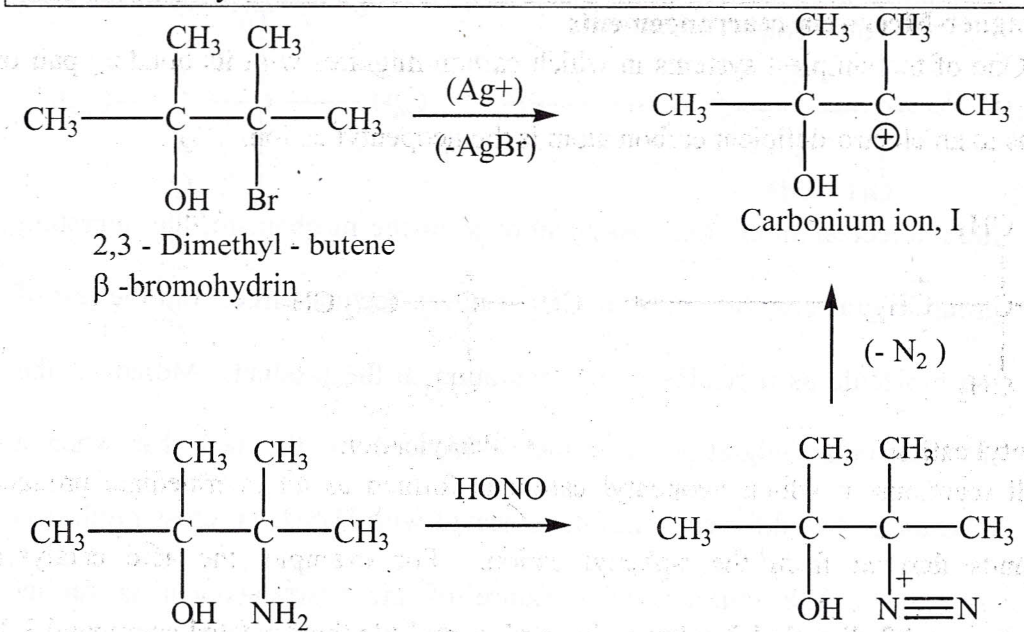
iii) Intramolecular migration : As mentioned in the mechanism, the migrating group migrates within molecule i.e., it never becomes free from the rest of the molecule as it retains its configuration in the product. Moreover, the intramolecular migration is further evidenced by the fact that when a mixture of two different pinacols is heated with H_2SO_4 no cross product is obtained. The intramolecular nature of the rearrangement is further indicated by the use of tracer technique. If rearrangement, in which there is a hydride shift, is carried out in deuteriated solvent (e.g., D_2O, MeOD, etc.) no deuterium incorporated into the new C-H (D) bond in the final rearranged product.

iv) Steric effect : The migration of the group is also effected by steric factor viz., MeO.C_6H_4-group migrates thousand times less than the p-MeO. C_6H_4-group.

v) Transmigration : The migrating group migrates to the opposite (trans) side of the leaving group (see mechanism) which has important consequences in alicylic system

Extension and application

In addition to 1,2-diols, β-halohydrins undergo rearrangement in the presence of Lewis acid, and β- amino alcohols via the diazonium ion, on treatment with nitrous acid to pinacolone.

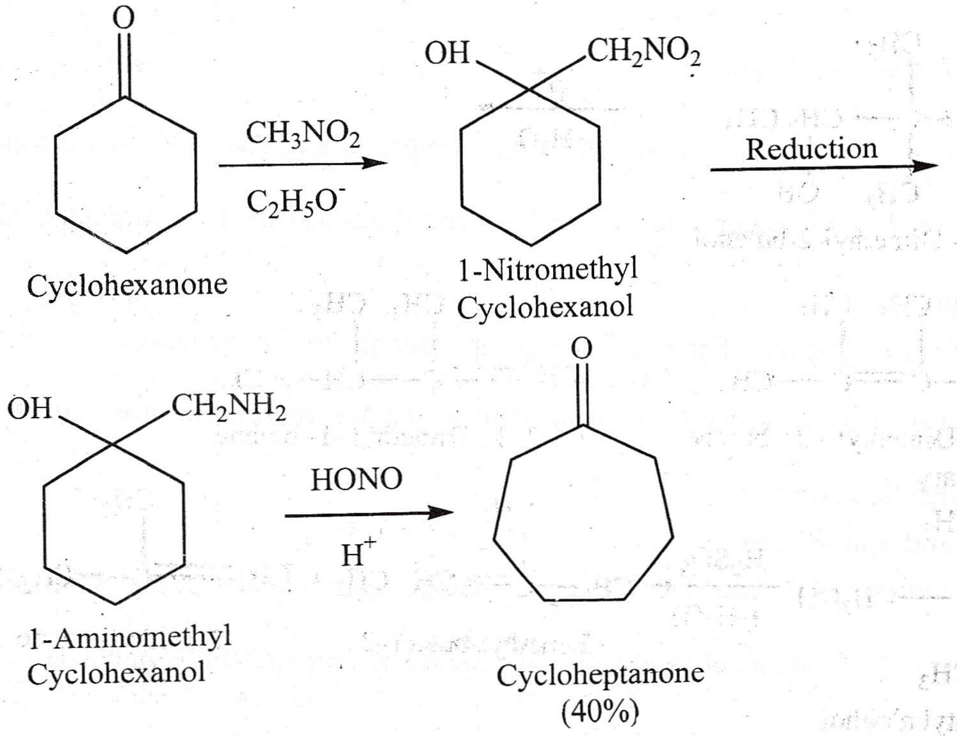


2,3 - Dimethyl - butene
β -bromohydrin

Carbonium ion, I

β -aminoalcohol

The latter extension of pinacol rearrangement has a synthetic application e.g. synthesis of cyclohepatanone from aminomethyl cyclohexanol which in turn is obtained from cyclohexanone..



Cyclohexanone

1-Nitromethyl
Cyclohexanol

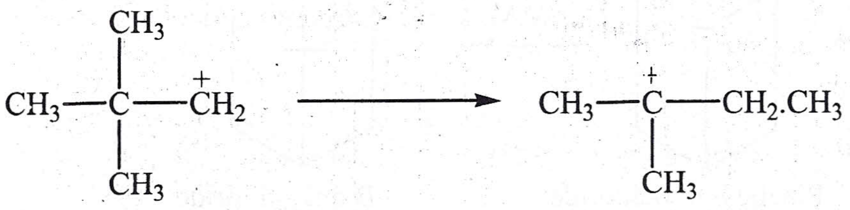
1-Aminomethyl
Cyclohexanol

Cycloheptanone
(40%)

The yield of cycloheptanone is considerably better than can be achieved from readily available compound via a ring closure reaction.

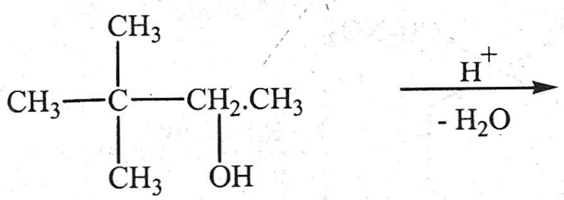
4.6.7 Wagner-Meerwein rearrangements

One of the simplest systems in which carbon migrates with its bonding pair of electrons to an electro-deficient carbon atom is the neopentyl cation.

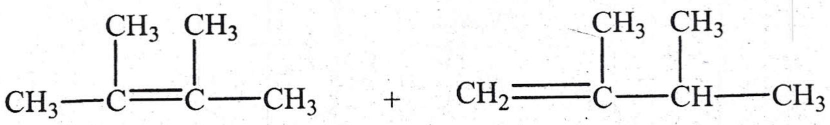


Neopentyl cation t - Pentylcation

Thus all reactions in which neopentyl cation is formed as an intermediate produce compounds derived from the t-phenyl cation. For example, the acid catalysed dehydration of 3,3-dimethyl-2-α-butanol affords very little the expected compound 3,3-dimethyl-1-butane, but yields mainly a mixture of 2,3-dimethyl-2-butene and 2,3-dimethyl-1-butene.

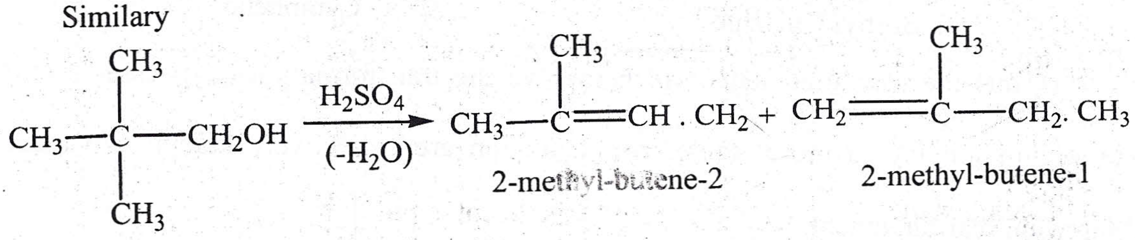


3, 3 - Dimethyl-2-butanol



2, 3 - Dimethyl - 2 - butene 2, 3 - Dimethyl -1- butene

Similary

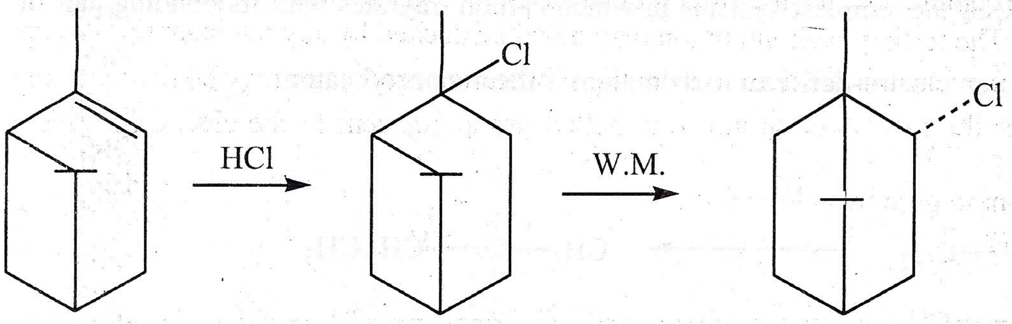


2-methyl-butene-2 2-methyl-butene-1

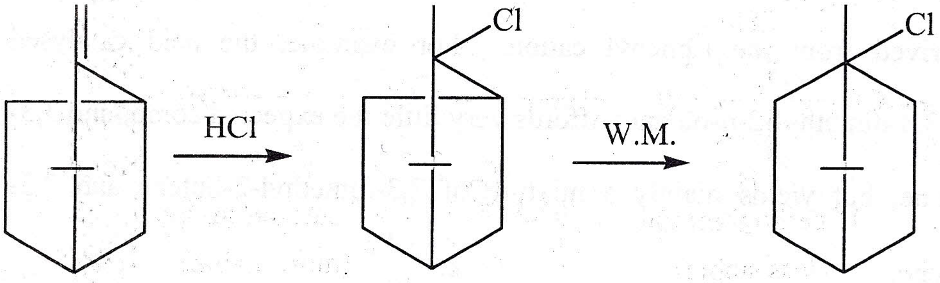
Neopentyl alcohol

The rearrangement is also exhibited by alicyclic compounds, the important examples are given below.

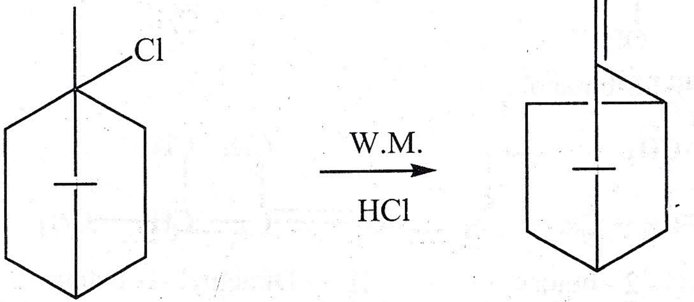
a) Pinene hydrochloride to bornyl chloride



b) Camphene hydrochloride to isobornyl chloride.

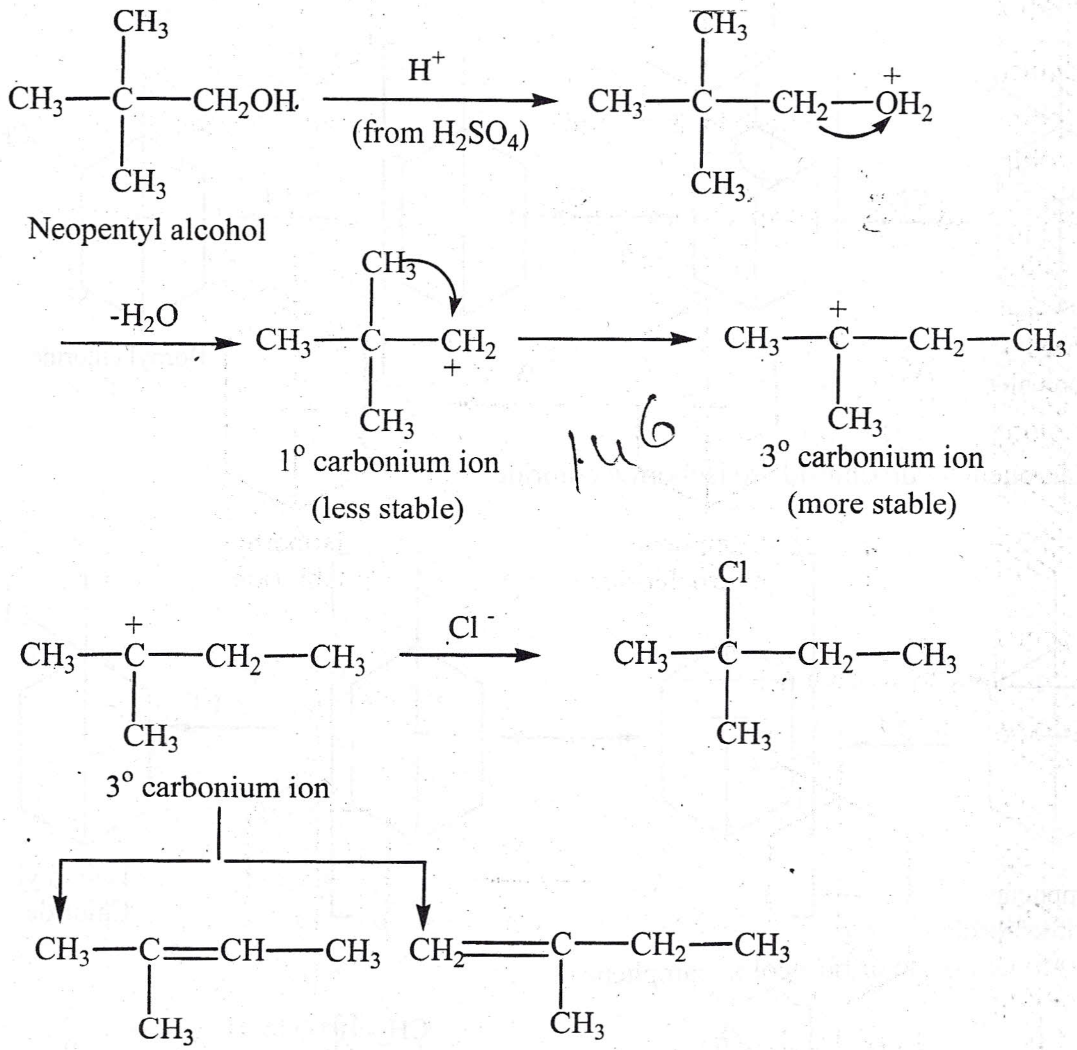


c) Bornyl chloride to camphene.



Thus the rearrangements which involve the transformation of a lesser stable carbonium ion into a more stable carbonium ion are collectively known asWagner Meerwein rearrangement.

Mechanism : The first stage of the reaction is the protonation of the hydroxyl group followed by the loss of water molecule to yield a carbonium ion. Now since the so formed primary carbonium ion is relatively unstable, it rearranges itself to a more stable tertiary carbenium ion by the migration of a methyl group with its pair of bonding electrons. The tertiary carbonium ion may now be attacked by any nucleophilic species present in the reaction medium to form the substitution product or may be deprotonated form either the methylene group or a methyl group adjacent to the electron deficient carbon atom to give two olefins.



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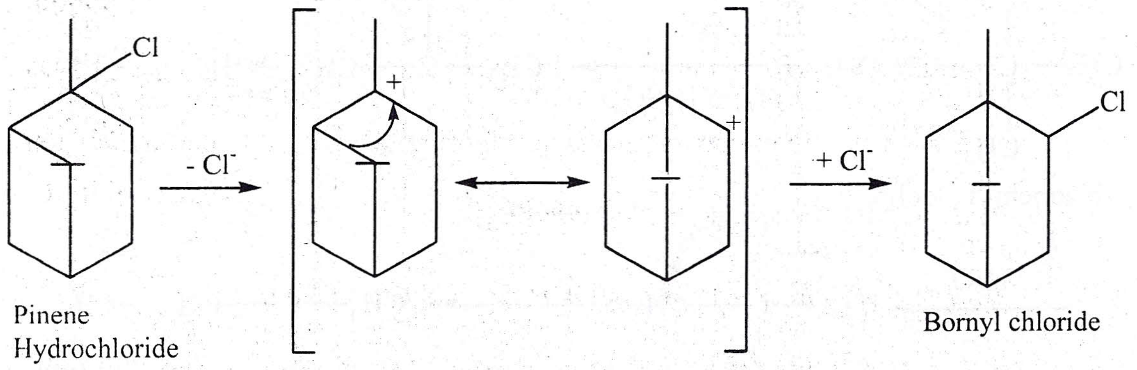
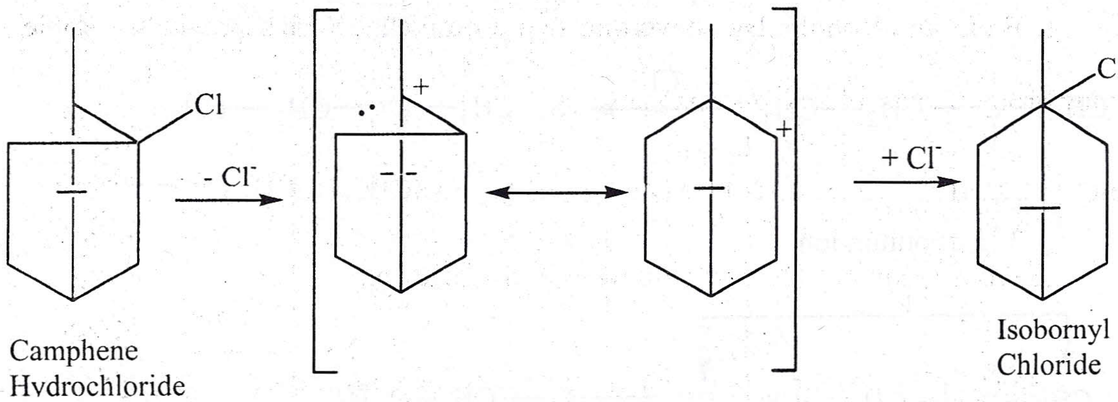
So in this case it is important to note that the driving force for the rearrangement resides in two factors viz., i) the greater stability of the resulting tertiary carbonium ion than a primary carbonium ion, and (ii) steric repulsion between the three methyl groups of the starting material which is reduced when one of the methyl groups moves to the adjacent carbon. Rearrangement is especially favourable under these circumstances, and less so when a secondary carbonium ion is formed.

Mechanism in allcyclic system (bicyclic terpenoids)

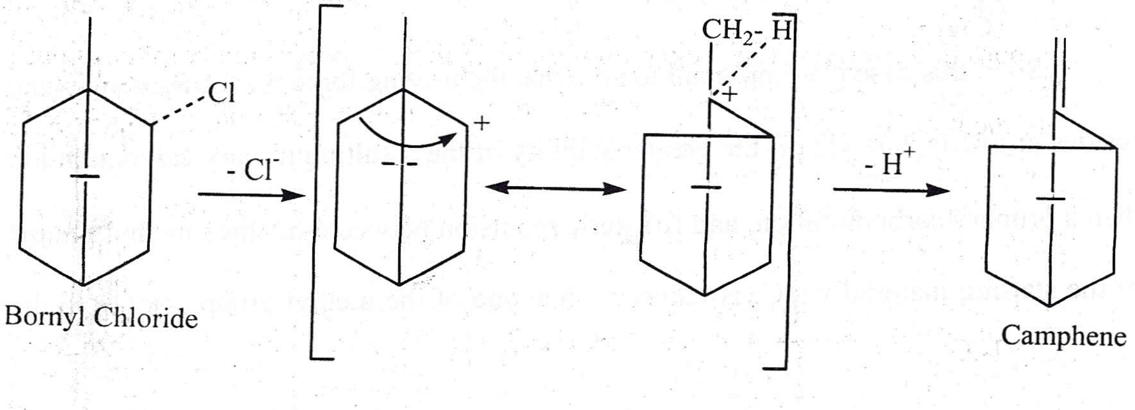
a) Pinene hydrochloride to bornyl chloride.



b) Camphene hydrochloride to isobornyl chloride.



c) Bornyl chloride or borneol to camphene.



Note that in the first example the relief of strain (i.e., the transformation of the strained four membered ring into the less strained five membered analogue) provides a powerful driving force for rearrangement.

Principle features of Wagner-Meerwein rearrangement.

1. The carbonium ion in general may be generated in a variety of ways.

   a. From a halide : By using a strongly ionizing solvent or by adding a Lewis acid such as silver ion or mercuric chloride which helps carbonium ion formation by abstracting the halide ion, e.g.

   $$Me_3C - CH_2 - Cl + Ag^+ \rightarrow Me_3C - {}^+CH_2 + AgCl$$

   b. From an alcohol : By treatment with acid to promote heterolysis, e.g.

   $$Me_3C - CH_2 - OH \overset{H^+}{\rightleftharpoons} Me_3C - {}^+CH_2 + H_2O$$

   c. From an alcohol : By converting into a derivative which provides a stable leaving group suchas toluene p-sulphonate, e.g.

   $$Me_3C - CH_2 - OSO_2.C_6H_4.CH_3\text{-}P \rightarrow Me_3C - {}^+CH_2 + O^-SO_2.C_6H_4.CH_3\text{-}P$$

   d. From an amine : By treatment with nitrous acid., e..

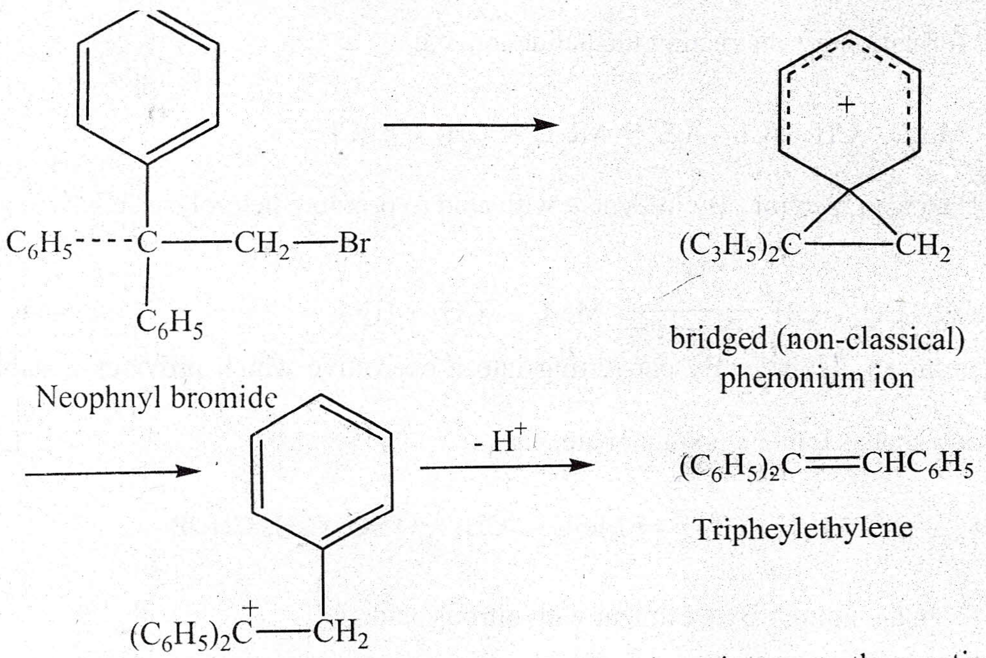
   $$Me_3C - CH_2 - NH_2 \xrightarrow{HONO} Me_3C - CH_2 + N^+ \equiv N \xrightarrow{-N_2} Me_3C - {}^+CH_2$$

2. The migratory group may be hydrogen atom, aryl or alkyl group. The two important examples of hydrogen migrations in the carbonium ion rearrangement are mentioned below.

$$Me_2\overset{H}{C} - \overset{+}{C}H_2 \longrightarrow Me_2\overset{+}{C} - CH_3$$

$$CH_3.CH_2.CH_2.NH_2 \xrightarrow[\text{(ii) - }N_2]{\text{(i) HONO}} CH_3.CH_2.\overset{+}{C}H_2 \longrightarrow CH_3.\overset{+}{C}H.CH_3$$

Among the aryl and alkyl groups,aryl groups have a far greater migratory aptitude than alkyl groups. For example, neophyl bromide undergoes solvolysis with rearrangement many thousand times faster than neopentyl bromide under the same conditions. This difference in the rate of reaction is due to the fact that the rate determining step in the reaction of neopentyl bromide involves the formation of the high energy primary carbonium ion, whereas the reaction of neophyl bromide involves the formation of a lower energy bridged carbonium ion.

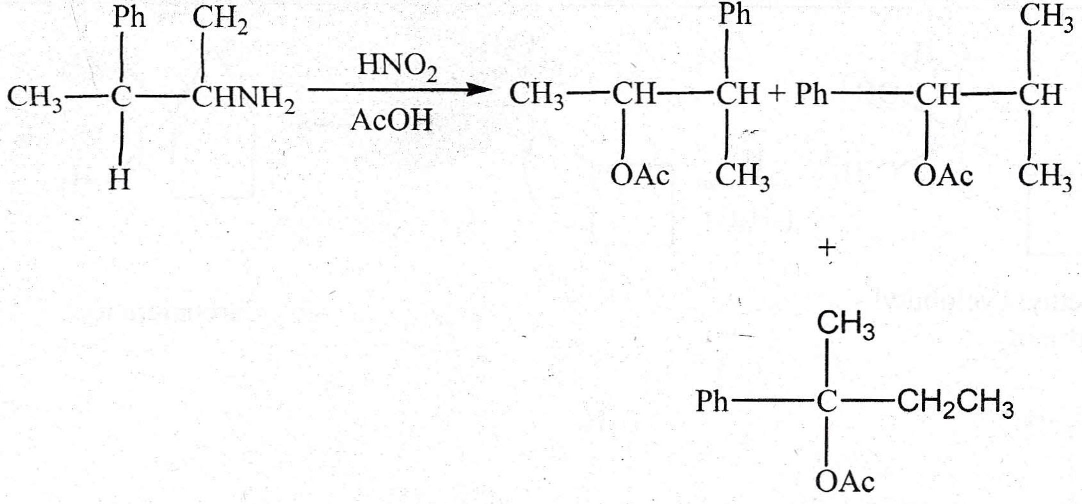


The aryl group is said to provide anchimeric assistance to the reaction.

The presence of electron releasing group in the aromatic ring (e.g. P-OCH$_3$) increases the rate of migration of the aryl group while the electron-attracting (e.g., P-Cl) lowers the rate of migration.

However, it is important to note that the enormously greater tendency for rearrangement of aryl groups than of alkyl groups or hydrogen does not apply to deaminations. For example, treatment of 3-phenyl-2-butylamine with nitrous acid in acetic acid gives comparable amounts of all the three acetates derived from the

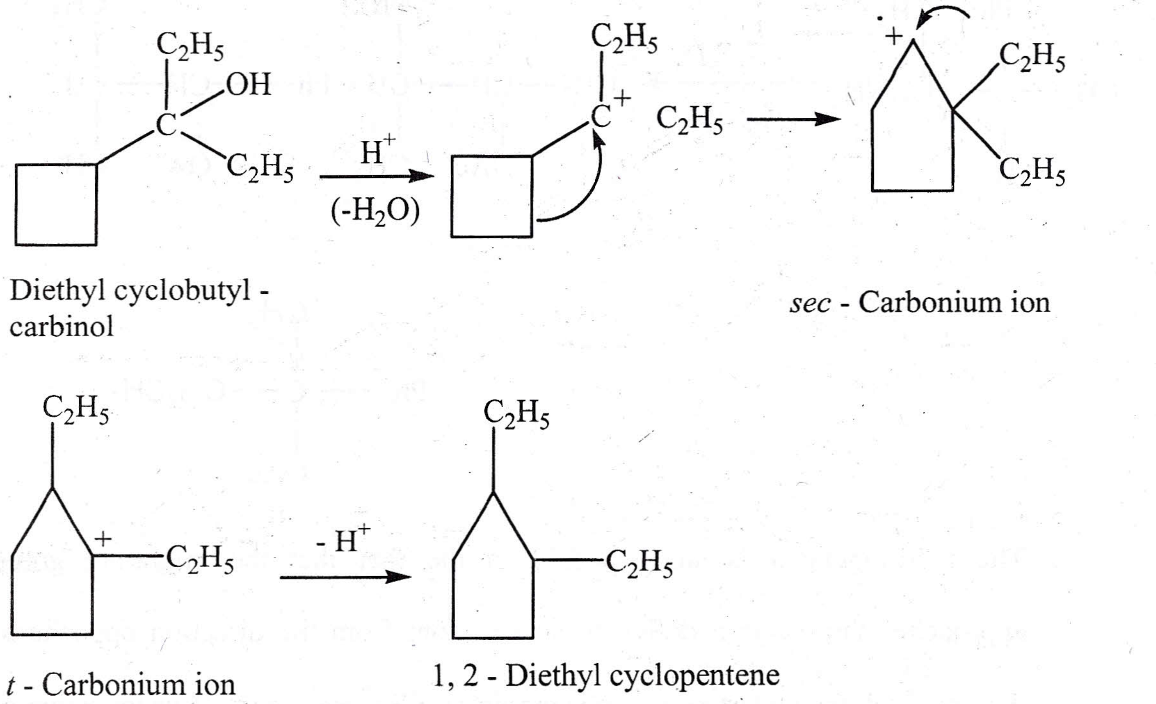
with sodium alkoxide.



3. The rearrangement is stereospecific in the fact that the migrating group approaches the electron deficient carbon atom from the direction opposite to that in which the departing group is moving (cf S_N^2 reaction). Thus inversion of configuration occurs at the electron deficient carbon. The stereospecificity of the reaction has significant consequences in alicyclic chemistry

4. In some cases two or more rearrangements may occur successively. For example, the initial carbonium ion obtained by treating diethylcyclobutylcarbinol with acid rearranges by ring expansion (relief of strain) to a secondary carbonium ion which in turn undergoes a further rearrangement to yield a tertiary carbonium ion. The latter then undergoes deprotonation and forms the olefin.

13



Diethyl cyclobutyl - carbinol

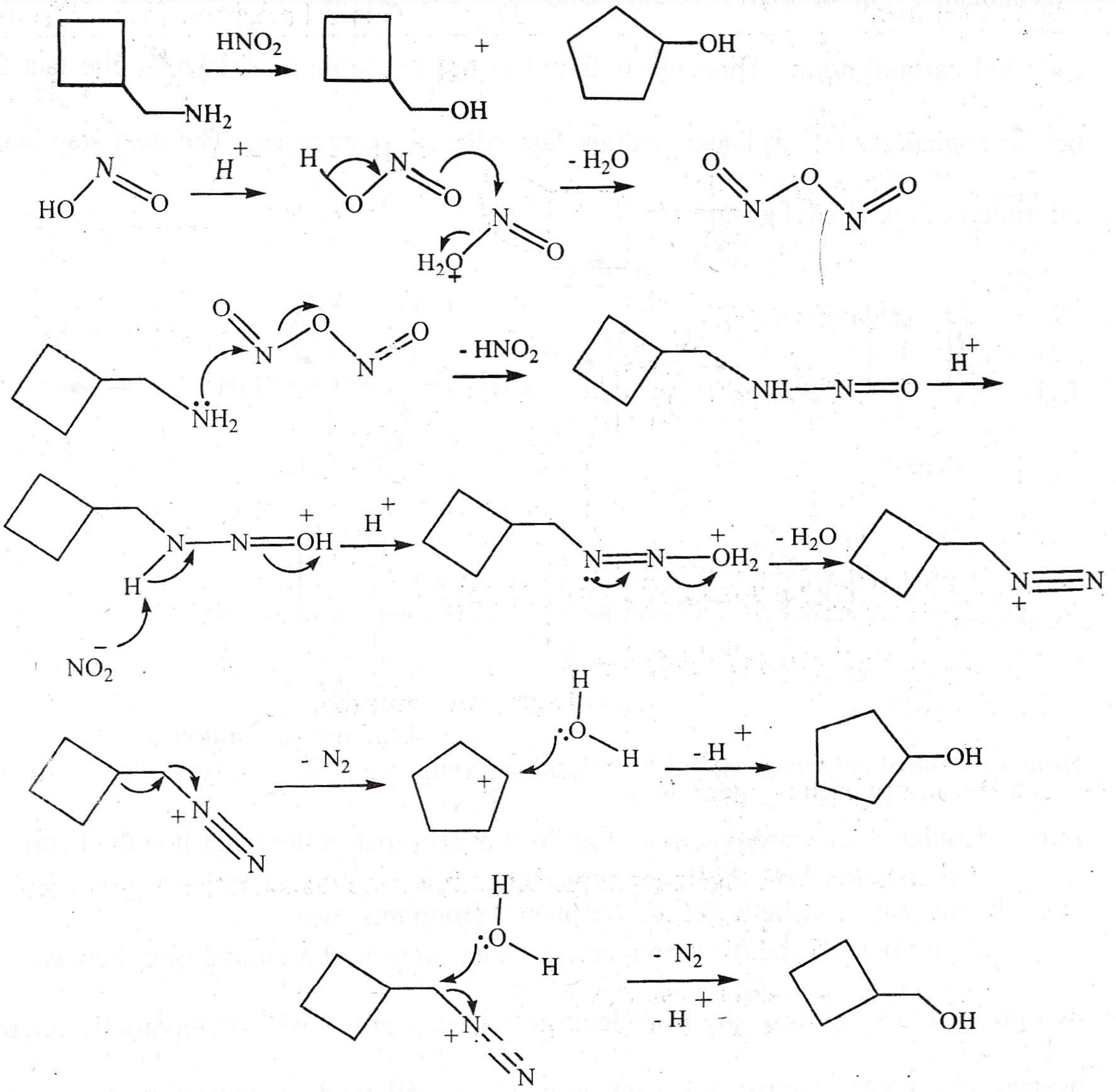
sec - Carbonium ion

t - Carbonium ion

1, 2 - Diethyl cyclopentene

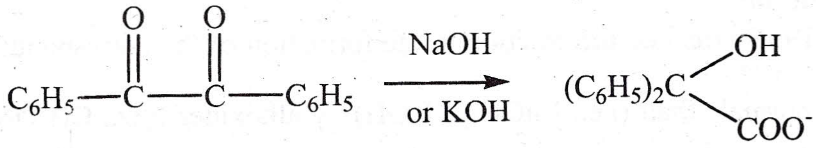
4.6.8 Demjanov rearrangement

Carbocation rearrangement of primary amines via diazotization to give alcohols.



4.6.9 Benzil-Benzilic acid rearrangement

The transformation of α-diketones (Benzil) to α-hydroxy acids by means of hydroxide ion is known as benzilic acid rearrangement. The best known example is the conversion of benzyl into benzilic anion.



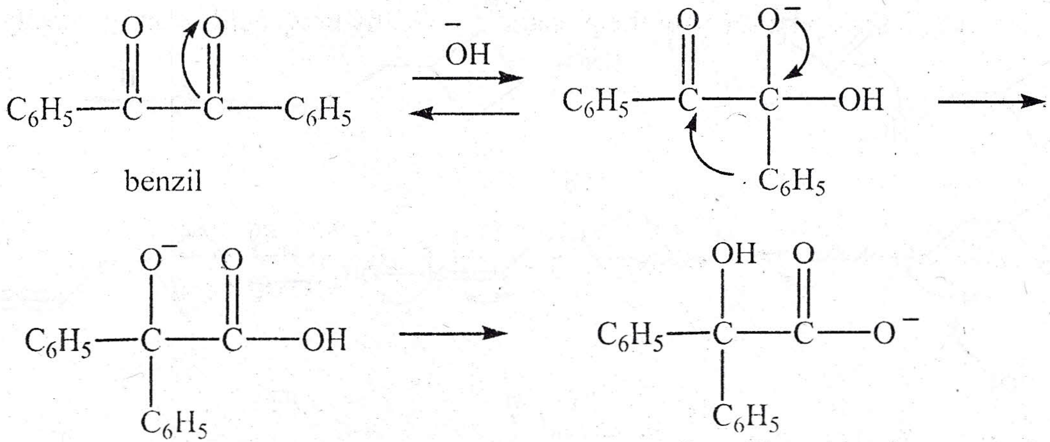
$$C_6H_5-\overset{\overset{O}{\|}}{C}-\overset{\overset{O}{\|}}{C}-C_6H_5 \xrightarrow[\text{or KOH}]{\text{NaOH}} (C_6H_5)_2C\begin{matrix}OH\\COO^-\end{matrix}$$

Benzil

Benzitic acid anion

Pfeif in 1956 observed that barium and thallous hydroxides are more effective than the

Mechanism : The first step of the reaction is the addition of hydroxide ion to the carbonyl carbon atom. This step is found to be reversible as shown by the fact the benzyl exchanges O^{18} in basic solution faster than it rearranges. The next step being migration of the phenyl group.

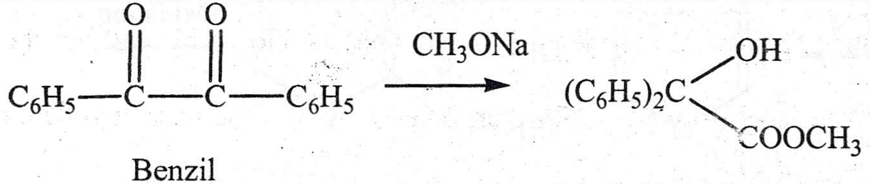


Note that the mechanism of benzilic acid rearrangement is exactly analogous to the intramolecular cannizzaro reaction of glyoxal except that in the latter it is the hydrogen atom that migrates, while in the former phenyl group migrates.

In the benzilic acid rearrangement when there is the competition between the two possible aryl groups, 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 and thus the hydroxide ion will attack carbon atom of the other carbonyl group. Since a phenyl group is involved, it is possible that during this 1,2-shift a phenonium ion is formed as an intermediate.

Extension and applications

Deoring et al. 1956 extended the reaction to the formation of the corresponding ester by replacing the normal alkali (i.e., NaOH or KOH) by alkoxides (viz., CH_3ONa, Me_3COK, etc.). thus benzyl may directly be converted into alkyl benzilate by treatment

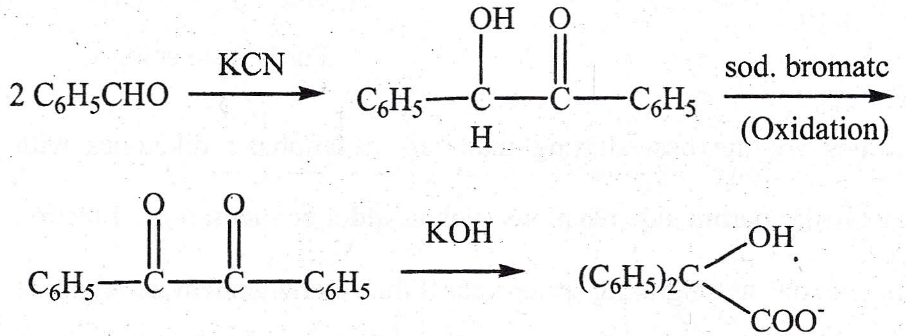


Benzil

Methyl benzilate

The reaction may be used for the preparation of α-hydroxy acids from the easily accessible starting materials, e.g.,

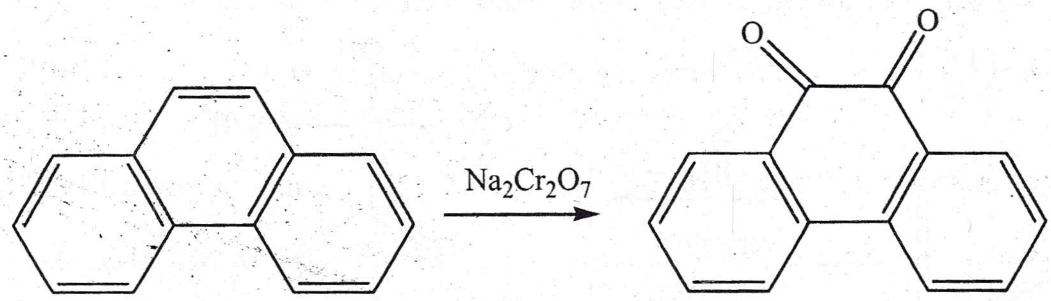
a)



Benzil

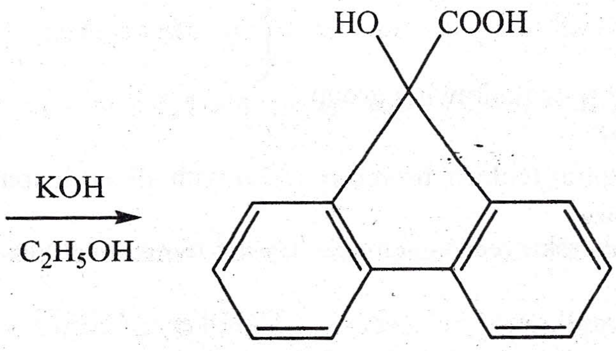
Benzitic acid anion

b)



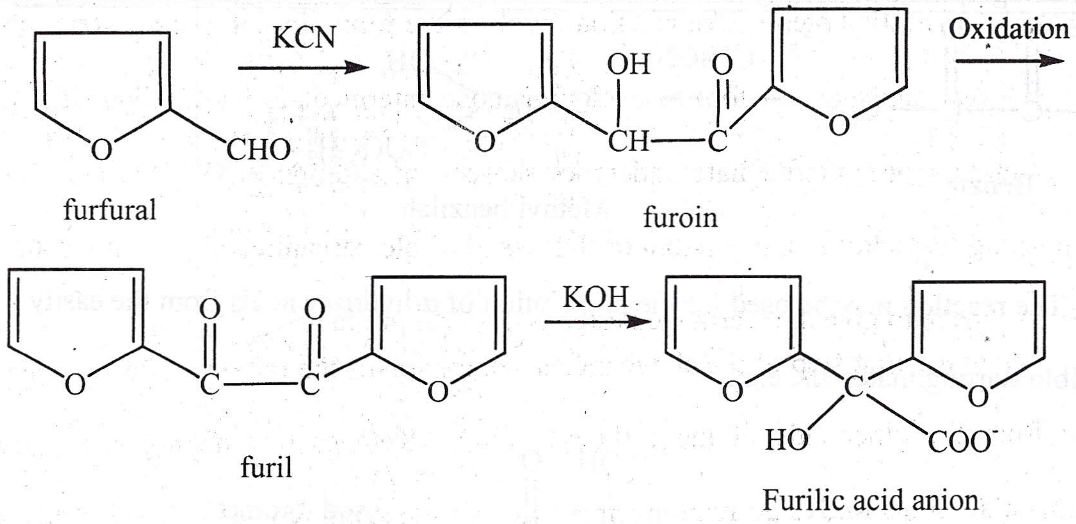
Phenanthrene

9, 10-phenathraquinone

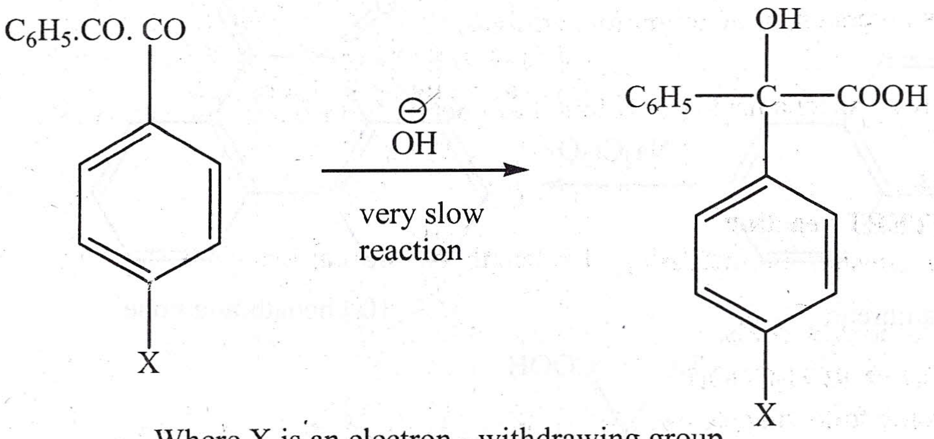


9-hydroxyfluorene-9-carboxylic acid

c)



Diaryl diketones are the best starting materials as aliphatic diketones with enolizable hydrogen usually permit side reactions such as aldol condensation. Electron withdrawing substituents on the migrating group retard the rearrangement as might be expected, since the migration is to an electron poor carbonyl carbon atom.



Where X is an electron - withdrawing group

4.6.10 Favarskii rearrangement

The reaction of α-haloketones (chloro, bromo or iodo) with alkoxide ion to give rearranged esters is called the favorskii rearrangement. Cyclic α—haloketones lead to ring contraction

In case, hydroxide ion (or) an amine is used as base in place of alkaxide ion, the final product is free acid (as salt) and amide respectively.

Mechanism : The first step of the reaction involves the formation of a carbanion with undergoes rearrangement to form a cyclopropanone intermediate I (1,3-elimination). The cyclopropanone intermediate undergoes subsequent addition of OH^- followed by ring opening to yield the more stable of the two possible carbanions followed by the proton exchange to give the rearranged ester as the final product.

Note the first step of the above mechanism involves the removal of α-hydrogen atom from the other side of the carbonyl group. Ketones that do not have such hydrogen atom also undergo rearrangement to give the same type of product. This is usually called the quasi-Favorskii rearrangement. An example is found in the preparation of demerol.

The mechanism of quasi Favorskii rearrangement does not involve the formation of cyclopropanone intermediate. The mechanism called semibenzillic mechanism involves inversion at the migration terminus.

The semibenzilic mechanism is also found to operate in the ring contraction of α-nalocylobutanones.

4.6.11 ARNDT-EISTERT reaction

The reaction consists in increasing the length of the carbon chain by one methylene group in carboxylic acids.

$$RCOOH \rightarrow RCH_2COOH$$

The reaction involves the following stems :

The acid is first converted to acid chloride which reacts with excess of diazomethane to form diazoketone. The latter on irradiation with light of heating with Ag_2O in the presence of water splits off nitrogen and rearranges to ketene (this rearrangement of diazoketone to ketene is known as Wolff rearrangement). The ketene then reacts with water to form a higher homologue of the starting acid.

$$RCOOH \xrightarrow{SOCl_2} RCOCl \xrightarrow[-CH_3Cl-N_2]{2CH_2N_2} RCOCHN_2 \xrightarrow{Ag_2O} R-CH=C=O \xrightarrow{H_2O} RCH_2COOH$$

Excess of diazomethane is used to consume the liberated hydrochloric acid

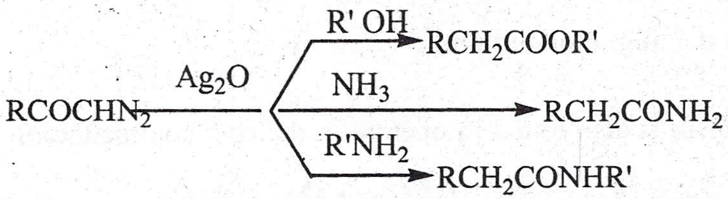
$$RCOCl + CH_2N_2 \rightarrow RCOCHN_2 + HCl$$

$$CH_2N_2 + HCl \rightarrow CH3Cl + N_2$$

In absence of excess diazomethane, diazoketone is lost in reacting with HCL to form chloromethyl ketone.

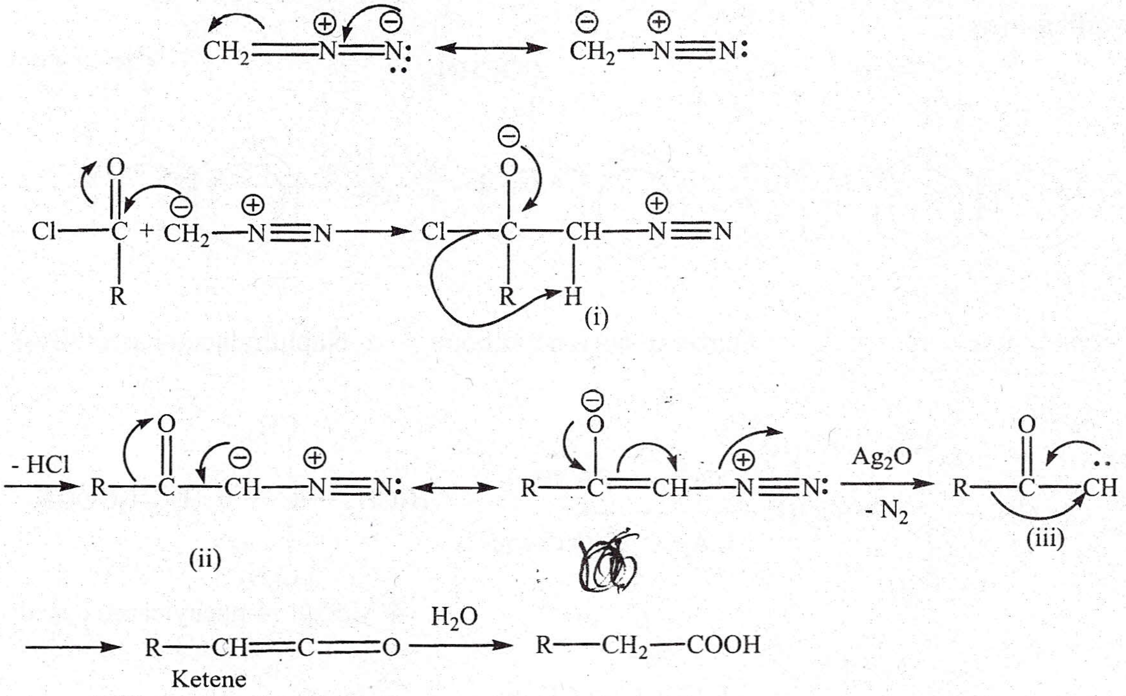
$$RCOCHN_2 + HCl \rightarrow RCOCH_2Cl + N_2$$

If alcohol, ammonia or amine is present in place of water then ester, amide or substituted amide respectively is formed



Besides Ag_2O, the reaction is catalysed by colloidal platinum, silver, copper, etc., and sometimes heat. The group R may be alkyl, aryl, heterocyclic or alicyclic and may contain reducible groups which remain unaffected. Acidic groups react with diazomethane and diazoketone.

Mechanism : **Nucleophilic attack of diazomethane on the carbonyl carbon of the acid** chloride gives an intermediate (i) which eliminates a molecule of HCl to give diazoketone (ii). Diazoketone then splits off a molecule of nitrogen to form a carbene (iii) which rearranges to ketene. The highly reactive ketene readily reacts with the nucleophile present (H_2O) to form the next higher acid.



The presence of carbine (iii) has not been detected and therefore the two steps – splitting of nitrogen and migration of R group – may be concerted.

$$R\overset{13}{C}OCHN_2 \xrightarrow[H_2O]{Ag_2O} RCH_2\overset{13}{C}OOH$$

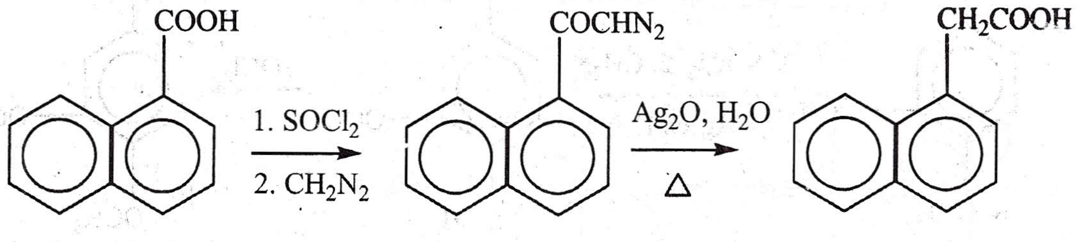
The mechanism has been supported by the fact that ketones have been isolated or trapped. Further, isotopic labeling experiment has shown that the carbonyl carbon of diazoketone is present in the resulting acid as the carboxyl carbon.

The group R migrates with retention of configuration, for an optically active acid on conversion to its higher homologue and subsequent Barbier-Weiland and degration gives the original acid with the same configuration.

Mild reaction conditions permit this synthesis without affecting complex or reducible groups in the substrate. The yield is high. It has, therefore, many synthetic applications, especially in the field of natural products.

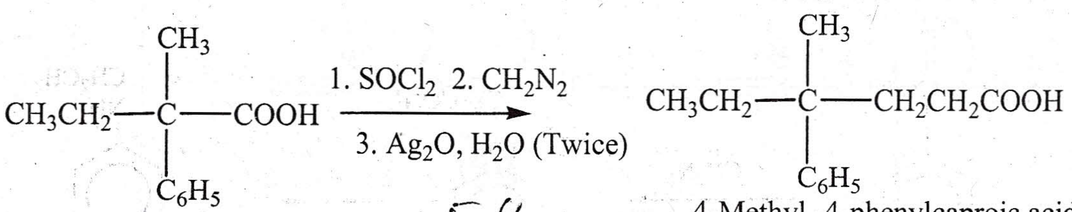
Applications

1.



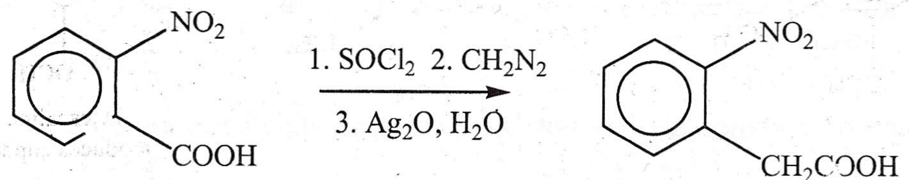
α - Naphthoic acid Diazo–α–acetonaphthone α–Naphthylacetic acid(80%)

2.



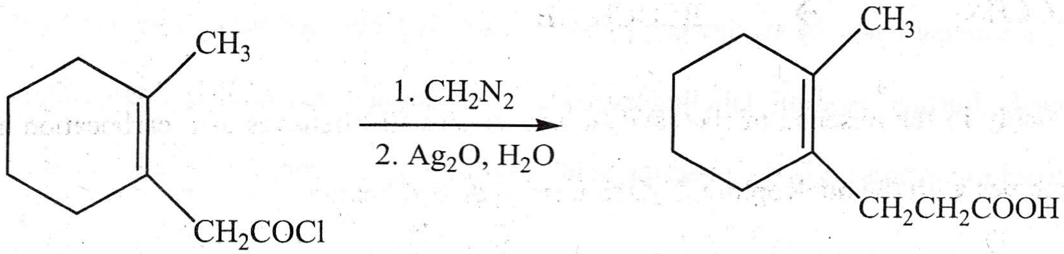
4-Methyl -4-phenylcaproic acid

3.



o-Nitrobenzoic acid 2-Nitrophenylacetic acid

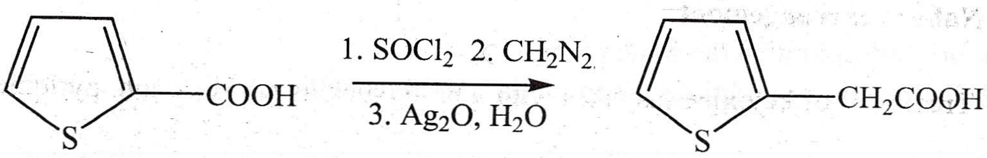
4. Double bond in the substrate remains unaffected



2 - Methyl cyclohexenyl
acetic acid chloride

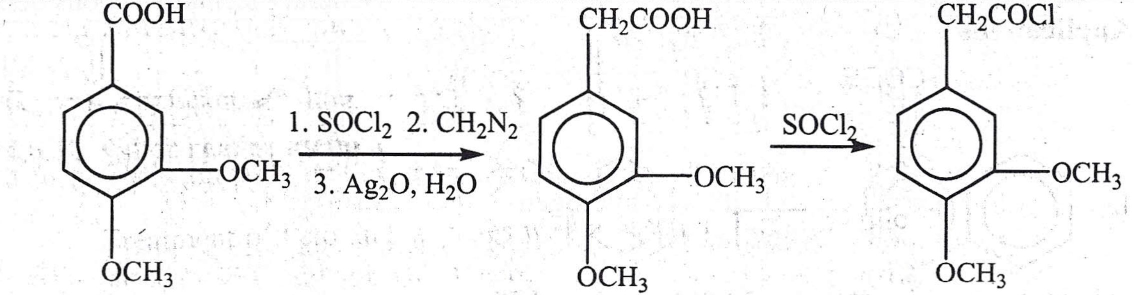
2 - Methyl cyclohexenyl
Propionic acid

5.



2 - Thienylacetic Acid

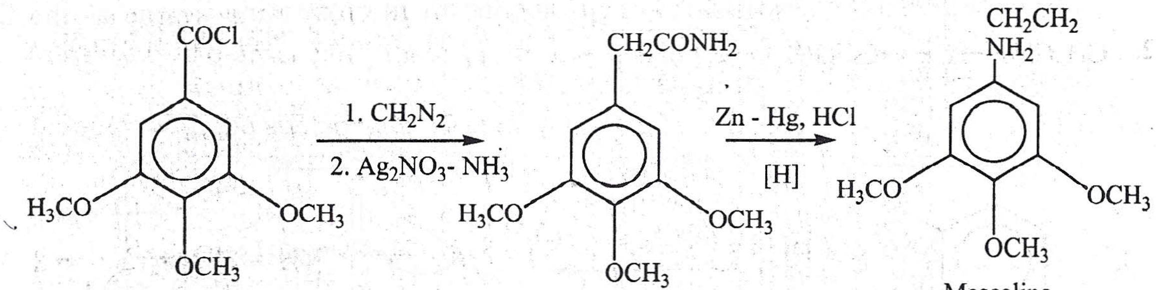
6. Synthesis of homoveratroyl chloride, an intermediate for papaverine synthesis migration of phenyl, methyl and hydrogen.



3,4-Dimethoxy benzoic acid

Homoveratroyl chloride

7. Synthesis of mescaline.

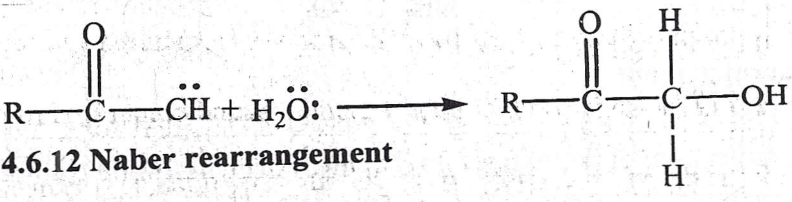


Mescaline
(produces euphoris)

8. Diazoketones on treatment with aqueous formic acid give hydroxyl ketones

$$RCOCHN_2 \xrightarrow{HCOOH + H_2O} RCOCH_2OH$$

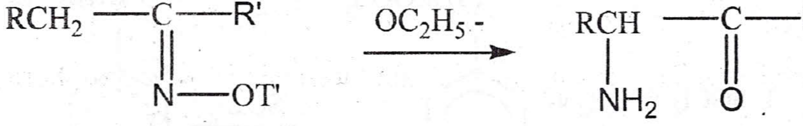
Probably in the absence of the catalyst, the species (iii) behaves as a carbocation and combines with the nucleophile, H_2O to form hydroxyl ketone



$$R-\overset{O}{\overset{\|}{C}}-\ddot{C}H + H_2\ddot{O}: \longrightarrow R-\overset{O}{\overset{\|}{C}}-\overset{H}{\underset{H}{C}}-OH$$

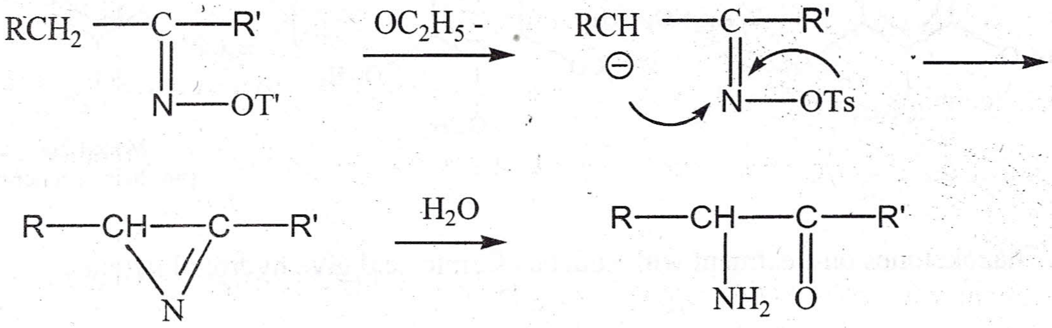
4.6.12 Naber rearrangement

Treatment of ketoxine tasylates with a base (such as ethoxide ion, pyridine etc) to form α-amino ketones is known as Neber rearrangement.



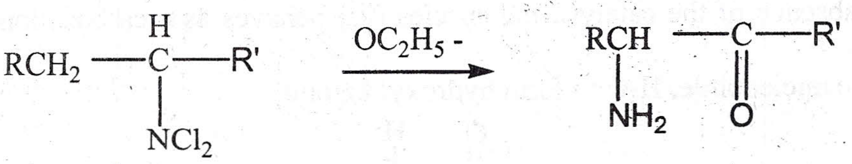
Where R = Aryl, alkyl or hydrogen
R' = Alkyl or aryl

Mechanism : The complete mechanism consists (or) three steps (1) the loss of more acidic proton to form carbonium (2) rearrangement of carbanion to form azirine intermediate and (3) Hydrolysis of the ozirine to form α-amino ketone as the final product.



Azirine intermediate

Neber rearrangement can also be applied to N, N-dichloro-amines.



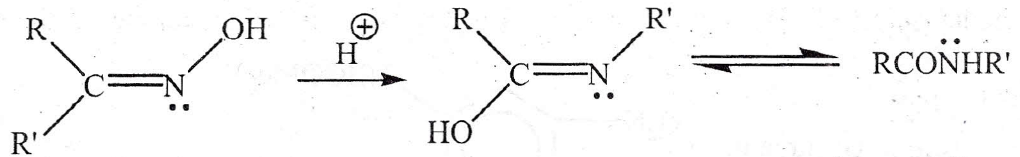
4.5.13 Beckmann rearrangement

The acid catalyzed conversion of ketoximes to N-substituted amides is known as Beckmann rearrangement. The [illegible] is catalysed by acidic reagents such as, H_2SO_4, $SOCl_2$, SO_3, P_2O_5, PCl_5, $C_6H_5SO_2Cl$, etc.

The reaction involves the migration of a group from carbon to electron-deficient nitrogen.

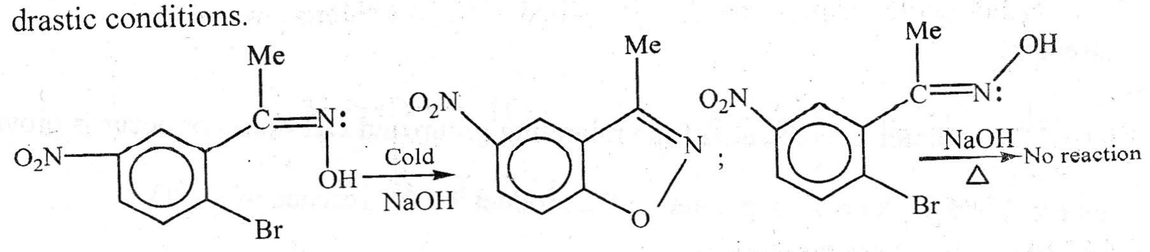
$$RR'C{=}NOH \xrightarrow{\overset{\oplus}{H}} RCONHR' \text{ or } R'CONHR$$

Some aldoximes undergo the rearrangement in the presence of polyphosphoric acid (PPA) but the reaction is not a general one. The migration of the group depends not on the migratinal aptitude but upon the orientation of the group in relation of the OH group. It is found that the migrating group is always anti (i.e., rrans) to the hydroxyl group. Thus, the reaction is stereospecific.



That it is always the antigroup which migrates has been has been confirmed by the rearrangements of the two isomeric oximes of 2-bromo-5-nitroacetophenone. The structures of the two isomeric oximes were first determined by an elegant method as given below.

On treatment with cold NaOH solution, one isomer (I) was cyclized to 3-methyl-5-nitrophenyl isooxazoine (III) while the other isomer(II) remained unaffected even under drastic conditions.

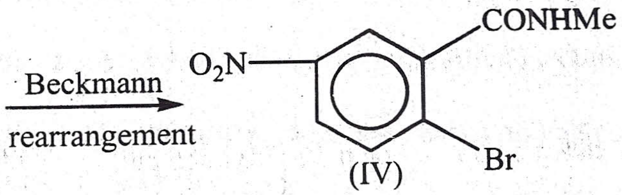


(I) (III) (II)

Obviously, the OH and Br groups in isomer (i) are close enough for reaction and cyclization. Hence, the Me and OH groups are anti i.e., trans) to each other. In isomer (ii), the OH and Br groups are far apart for reaction, i.e., the Me and Oh groups are syn Ii.e., cis) to each other. Thus, the structures of isomers(i) and (ii) are confirmed.

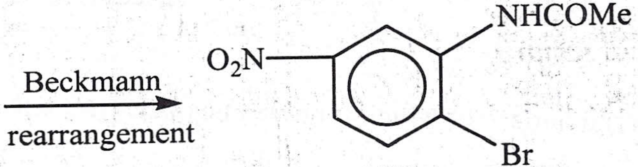
Now, on subjecting the two isomers to Beckmann rearrangement it is found that (a) isomer (i) gives N-methyl-2-bromo-5-nitrobenzamide (iv) indicating the migration of the antigroup Me to the nitrogen atom and (b) isomer(ii) gives N-(2-bromo-5-nitrophenyl)-acetamide (v) dueto the migration of the anti-aryl group to the nitrogen atom.

Isomer (I)



(IV)

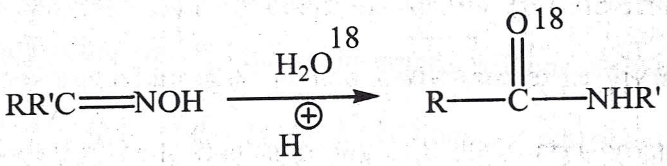
Isomer (II)



(V)

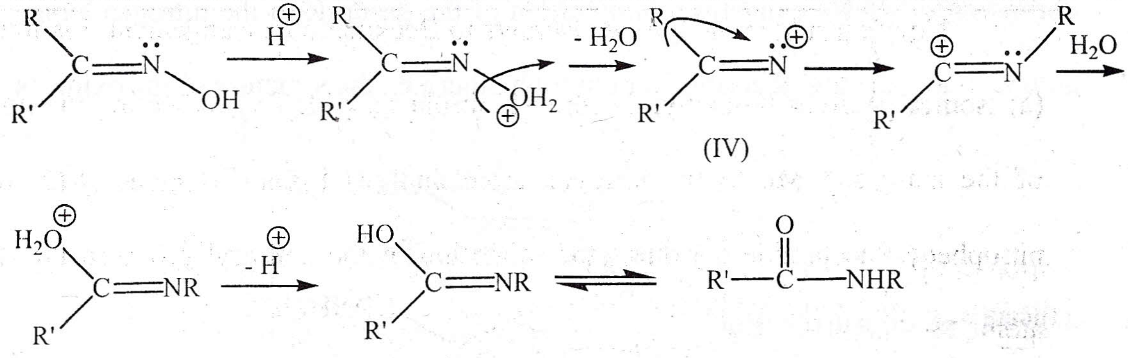
Oxime esters and ethers also undergo Beckmann rearrangement. The acidic reagents convert the OH group to a better leaving group-acids convert OH to H_2O, other reagents convert OH to an ester-leaving group, e.g., $OPCl_4$ from PCl_5, $OSO_2C_6H_5$ etc. The reaction is facilitated by heat, polar solvents or an increase in the acid strength.

The direct interchange of the migrating group and OH does not occur is proved by the fact that ^{18}O is incorporated in the product in the presence of $H_2{}^{18}O$.



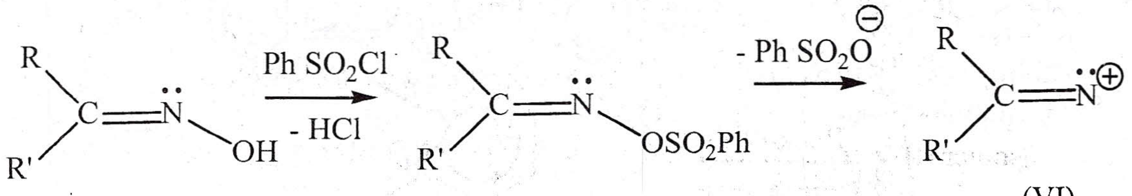
$$RR'C{=}NOH \xrightarrow[\oplus H]{H_2O^{18}} R-\overset{O^{18}}{\overset{\|}{C}}-NHR'$$

Mechanism : The mechanism of the reaction has been suggested as given below.



(IV)

With other acidic reagents, e.g., $PhSO_2Cl$. the same intermediate (VI) is obtained.



(VI)

In strong acids,the reaction proceeds with the protonation of the OH group of the oxime with subsequent loss of water to yield the species (VI) with electron-deficient nitrogen which is also obtained with other acidic reagents by the loss of ester group. The migration of R then gives a carbocation. The attack of water molecule on the carbon followed by the loss of proton given the amide.

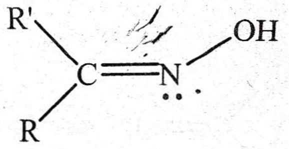
The migrating group retains its configuration and hence the migrating group does not become completely free during the migration, otherwise the reaction can not be stereospecific. Thus, the migfation and the breaking of N-O bond may be concerted or at least very rapid. This has been supported by crossover experimens.

Applications

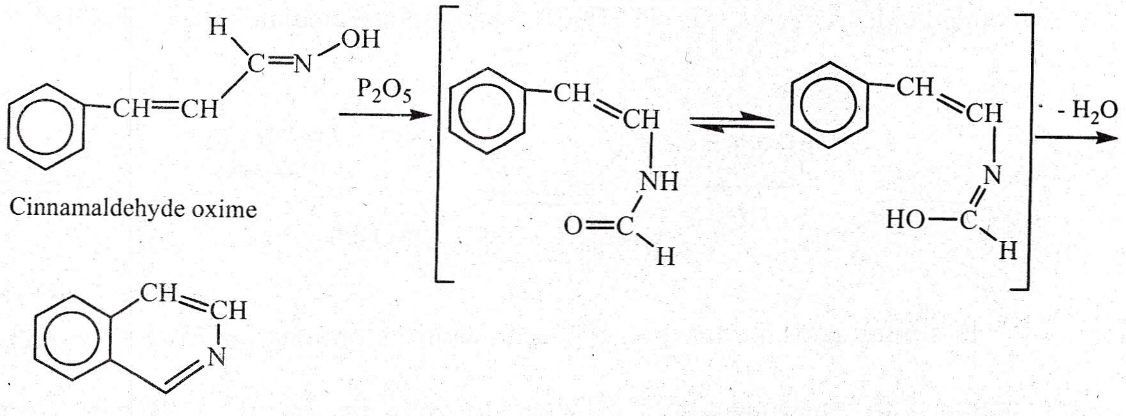
1. configuration of ketoximes can be assigned : A ketoxime gives an amide on Beckmann rearrangement. From the products of hydrolysis of the amide, the structure of the amide is known and for that matter, the configuration of the oxime is known.

$$R'RCNOH \xrightarrow{\overset{\oplus}{H}} R'CONHR \xrightarrow{H_2O} RNH_2 + R'COOH$$

Formation of RNH_2 indicates the migration of the group R to the nitrogen atom. The groups R and OH are, therefore, anti to each other i.e., the structure of the oxime is



2. synthesis of isoquinoline

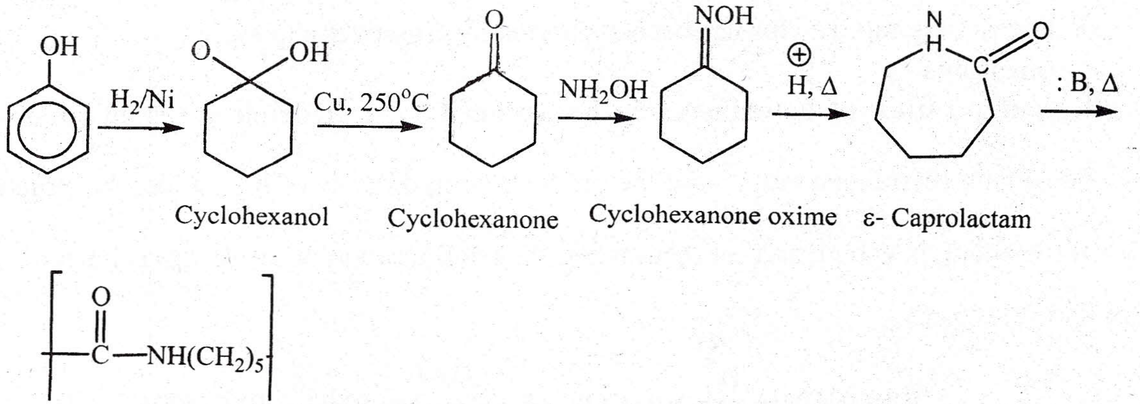


Cinnamaldehyde oxime

Isoquinoline

3. Synthesis of lactams : Alicyclic ketones of all ring sizes undergo the Beckmann rearrangement of their oximes to yield lactams.

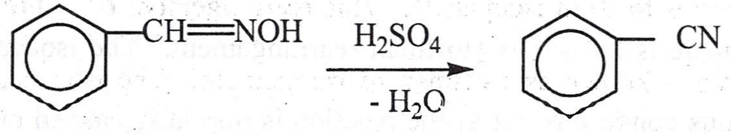
A product of considerable industrial importance is perlon (valuable textile polymer) which is prepared from ω-carprolactam. This is obtained by the Beckmann rearrangement of cyclohexanone oxime it is synthesized from phenol as below.



Cyclohexanol Cyclohexanone Cyclohexanone oxime ε- Caprolactam

Similarly, cyclopentanone oxime gives 2-piperidone under Beckmann condition.

Aldoximes under the Beckmann reaction conditions undergo dehydration to nitriles.



Benzaldoxime

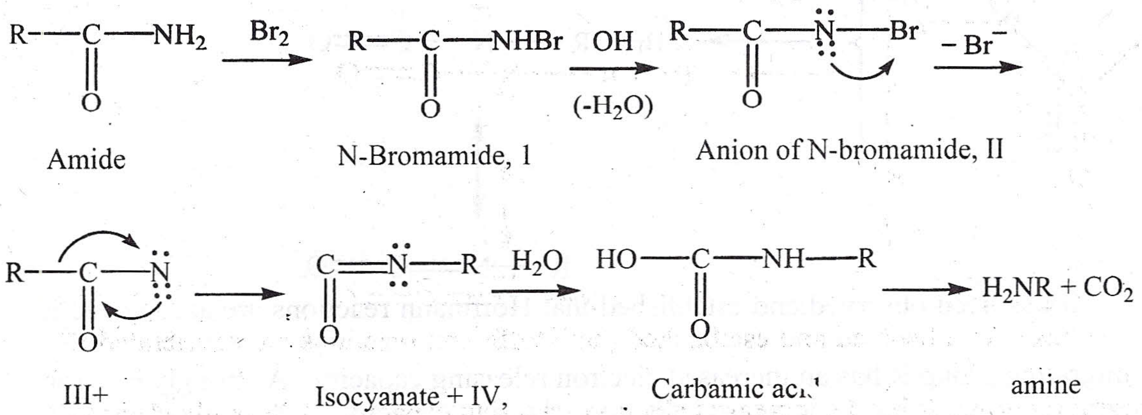
Benzonitrile
(Phenyl Cyanide)

4.6.14 Hofmann reaction, Hofmann degradation of amides or Hoffman rearrangement

The conversion of an amide to an amine with one carbon atom less by the action of alkaline hypohalite (or) bromine in alkali is known as the Hofmann reaction. The overall reaction for this conversion may be represented as below.

$RCONH_2 + Br_2 + 4\,KOH \rightarrow RNH_2 + 2KBr + K_2CO_3 + 2\,H_2O$

Mechanism : This reaction is found to follow the following path.

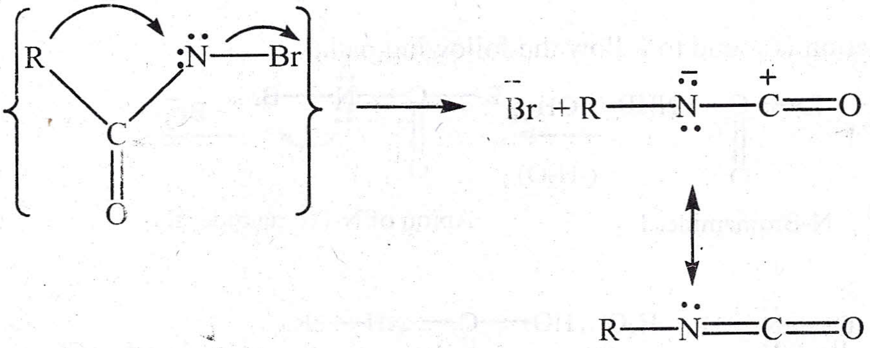


The formation of N-bromamide I, its anion II and isocyanate IV as the intermediate products and hence the above mechanism for Hofmann reaction is proved further reaction with the reagents to yield amine as the final product.

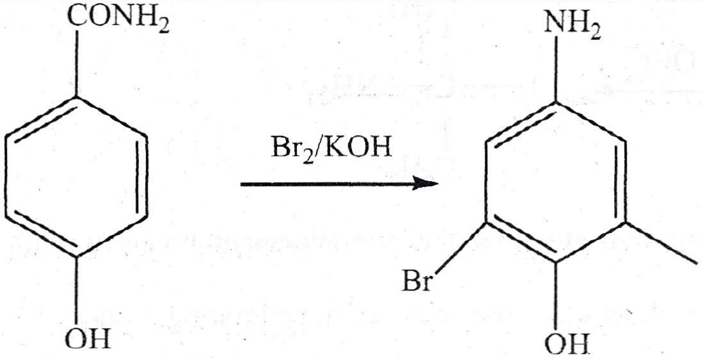
Note that the elimination of bromide ion form the anion of N-bromamide II forms a highly unstable neutral species RCON, which has only a sextet of valency 14 by their isolation under suitable conditions. These intermediate species can undergo electrons around the nitrogen atom. This species is therefore highly electron deficient on nitrogen and it gains some stability by the migration of the methyl group with its pair of bonding electrons to form isocyanate. This rearrangement of N bromamide or its anion to isocyanate is known as Hoffman rearrangement. The isocyanate may be isolated in anhydrous conditions but as the reaction is normally carried out in aqueous or alcohololic solution the isocyanate is converted into amine or urethane, respectively.

$$\underset{\text{Urethane}}{RNHCOOR^1} \xleftarrow{R^1OH} \underset{\text{Isocyanate}}{R-N=C=O} \xrightarrow{H_2O} \underset{\text{Amine}}{RNH_2 + CO_2}$$

However, Wright (1968) by using ^{14}C – and N^{15} – labelled compounds observed that the intermediate III (acyl nitrene) may not involve during the Hoffman, Curtius and Lossen rearrangements, and the compound II is directly converted into isocyanate i elimination of halide ion and migration of alkyl group take place simultaneously.



It has been observed and established that Hoffmann reactions are accelerated if the migrating group R has an increased electron releasing capacity. A strongly electron donating migrating group not only eases the departure of Br from the bromamide anion, but also enables to satisfy the electron deficiency of the residual nitrogen atom more effectively. Thus the rate of amine formation from p-hydroxy benzamide is more rapid than that for benzamide itself due to the activating effect of the phenolic – OH group.

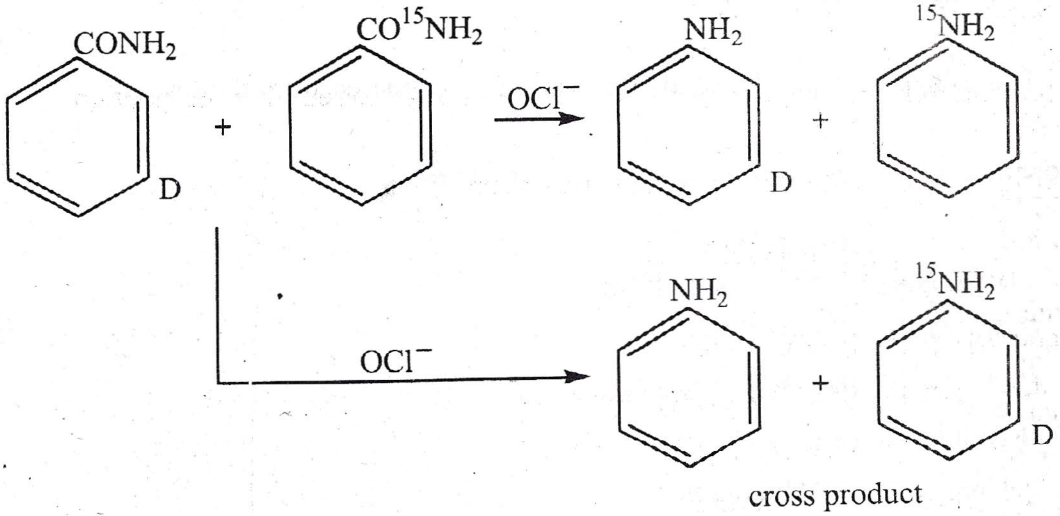


In general, the p-substituted benzamides show the following order of reactivity.

$-OCH_3 > -CH_3 > -H > -Cl > -NO_2$

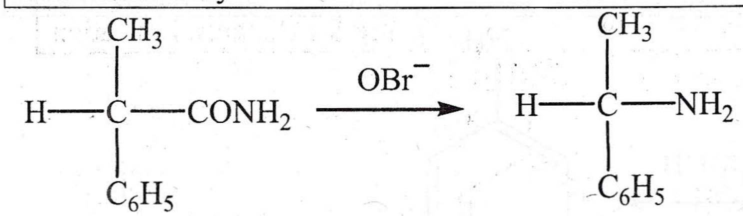
Intramolecular nature of Hoffman rearrangement : The intramolecular nature of the rearrangement can be shown by the following two experiments.

i) When a mixture of m-deuteriobenzamide and benzamide - ^{15}N are treated with alkaline chlorine, only two products (m-deuterioaniline and aniline – ^{15}N) are found to be produced; no cross products is produced which would have been formed if the phenyl group from one molecule had become attached to nitrogen of another.



cross product
(not formed)

ii) When optically active α-phenyl propionamide undergoes the Hoffman degradation, α-phenylethyl amine of the same configuration is obtained.



$$H-\overset{\overset{CH_3}{|}}{\underset{\underset{C_6H_5}{|}}{C}}-CONH_2 \xrightarrow{OBr^-} H-\overset{\overset{CH_3}{|}}{\underset{\underset{C_6H_5}{|}}{C}}-NH_2$$

This reaction also indicates that the rearrangement proceeds with complete retention of configuration about the chiral centre of the migrating group.

Applications : i) Primary aliphatic and aromatic amines : Hoffman reaction provides an efficient route for making both aliphatic and aromatic primary amines from amides containing upto seven carbon atoms, while the higher amides form cyanides which can be converted into amines by reduction.

$$RCONH_2 \xrightarrow{Br_2/KOH} RNH_2$$

Where, $R = CH_3 -$ to C_6H_{13}-

$$RCH_2CONH_2 \xrightarrow{Br_2/KOH} RCN \rightarrow RCH_2\,NH_2$$

Where, $R => C_6H_{11}$-

The following type of primary amines can be prepared from the reaction

a) Preparation of methylamine, alinine, benzylamine etc.

$$CH_3CONH_2 \xrightarrow{Br_2/KOH} CH_3\,NH_2$$

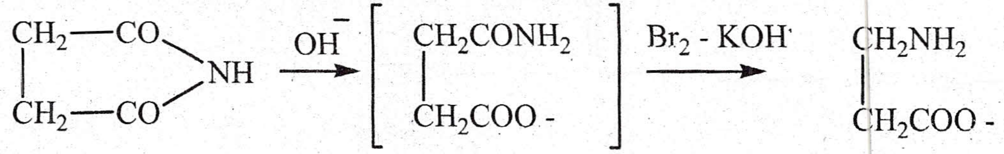
$C_6H_5CONH_2 \rightarrow C_6H_5NH_2$

$C_6H_5CH_2CONH_2 \rightarrow C_6H_5CH_2NH_2$

$H_2NCO.NH_2 \rightarrow H_2N.NH_2$

Urea Hydrazine

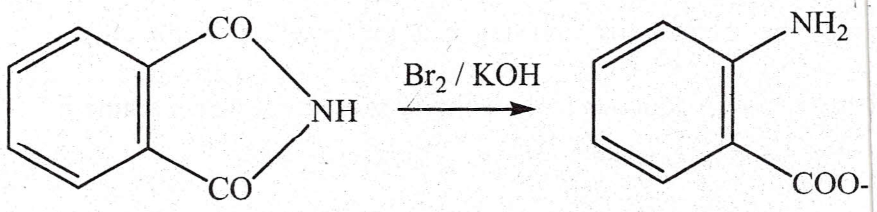
b) Preparation of amino acids : β Alanine e.g., can be obtained in about 45% yield by treating succinimide with bromine and aqueous caustic potash; reaction occurs through the half amide of succinic acid.



Succinimide

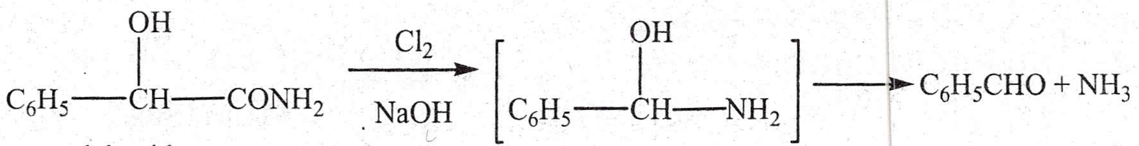
β - alanine

In a similar way anthranilic acid can be prepared from phthalimide



ii) Preparation of aldehyde : α, β-Unsaturated acids and α-hydroxy acid amides are converted into aldehydes by Hoffmann reaction according to the following steps

$$R.CH{=}CH.CONH_3 \xrightarrow{Cl_2/NaOH} R.CH{=}CHNHCOCH_3 \xrightarrow{HCl} RCHO$$



$$C_6H_5-\overset{OH}{\overset{|}{C}H}-CONH_2 \xrightarrow[NaOH]{Cl_2} \left[C_6H_5-\overset{OH}{\overset{|}{C}H}-NH_2\right] \longrightarrow C_6H_5CHO + NH_3$$

mandelamide

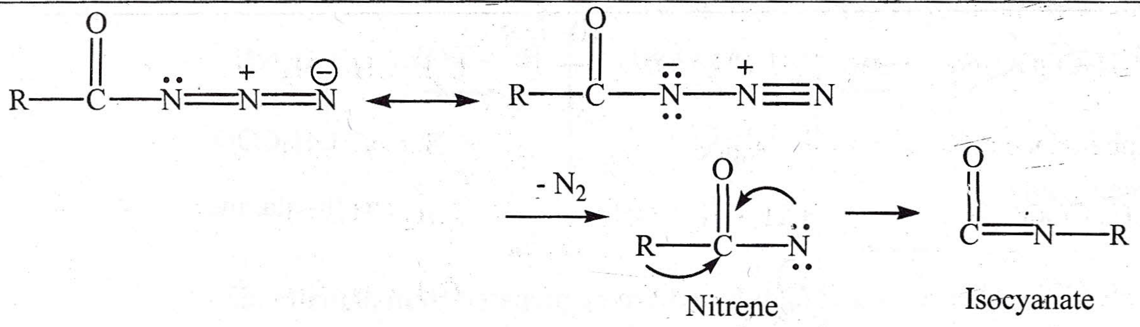
4.6.15 Curtius rearrangement

The decomposition of acids azides on heating to give isocyanates is known as Curtuis reaction, citius degradation of amid azides (or) cirtius rearrangement.

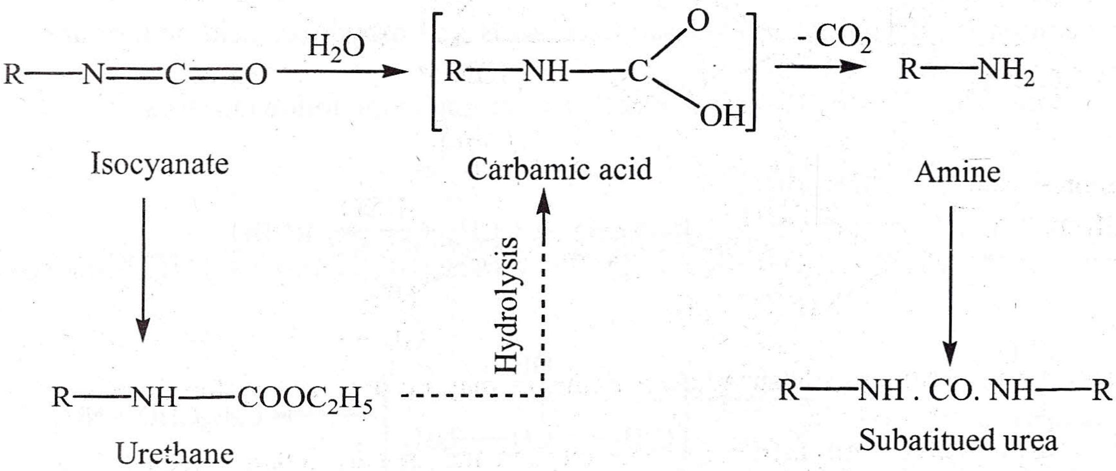
$$\underset{\text{Acid Azide}^1}{RCON_3} \xrightarrow[-N_2]{\text{Heat}} \underset{\text{Isocyanate}}{RNCO}$$

Mechanism : The mechanism of Cirtius reaction is quite similar to Hofmann reaction and can be represented as below

15



The isocyanate may be isolated by carrying out the reaction in an aprotic solvent such as chloroform, while in aqueous and alcoholic solvents it forms amine or urea and urethane respectively.

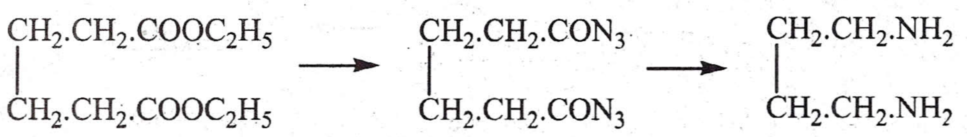


However, Wright (1968) observed that the acyl nitrene is not formed as an intermediate during the reaction

Application : i) Preparation of primary amines. Although Curtius rearrangement involves the mildest conditions for the preparation of primary amines (having carbon atom less) free from secondary and tertiary amines. If requires the preparation of the azides

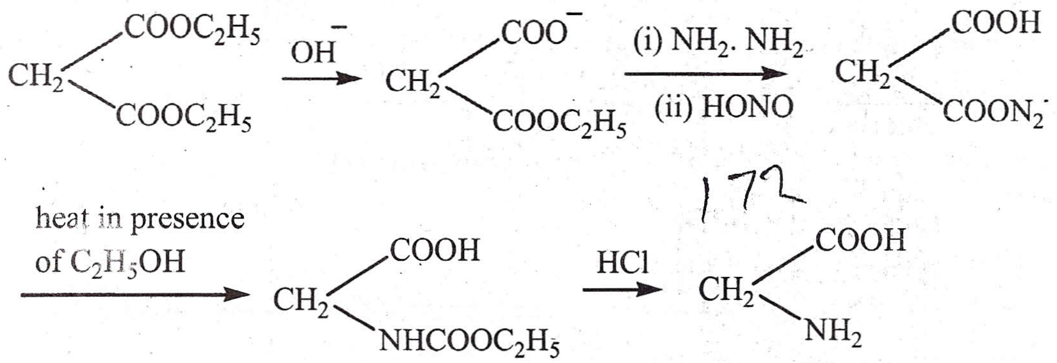
$$C_6H_5CH_2COOC_2H_5 \longrightarrow C_6H_5CH_2CON_3 \xrightarrow[\text{(ii) } H_2O]{\text{(i) Heat}} C_6H_5CH_2NH_2$$

Ethylphenylacetate Azide Benzylamine



Ethyladipate Tetreamethylenediamine (Putrescine)

ii) Preparation of α-amide acids : The curtius rearrangement has been applied in the synthesis of α-amino acids, e.g.



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Glycine

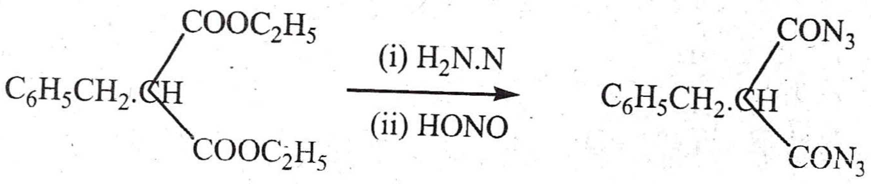
iii) Preparation of urethanes : N-substituted urethanes may be prepared by the Curtius reaction. The acid azide is refluxed in benzene solution and then an alcohol is added.

$$\underset{\text{Acid Azide}}{R.CO.N_2} \xrightarrow{-N_2} \text{or } R.NCO \xrightarrow{R.OH} \underset{\text{Urethane}}{R.NH.COOR^1}$$

iv) Preparation of aldehydes . α,β-unsaturated acids and α-hydroxy acids as in Hoffmann reaction are converted into aidehydes by the Curtius reaction, e.g.

$$CH_3.CH(OH).COOH \rightarrow CH_3.CH(OH).CON_3 \rightarrow [CH_3.CH(OH).NH_2] \rightarrow CH_3CHO + NH_3$$

Certain aldehydes may be prepared from substituted malonic ester via acid azides, i.e., by Curtius reaction.



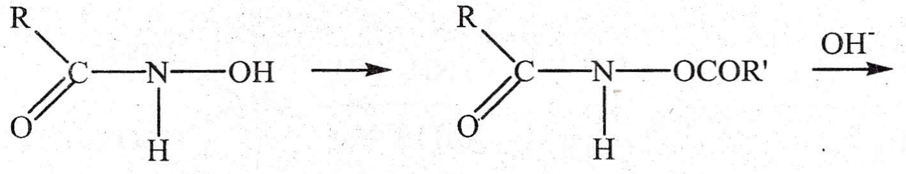
$\rightarrow C_6H_5CH_2CHO$

Diethylbenzylmalonate Phenyl acetaldehyde

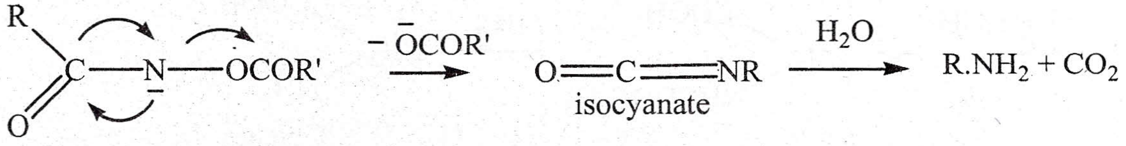
Lossen rearrangement

The conversion of hydroximic acid or its esters into primary amine is known as Lossen reaction.

Mechanism : The mechanism of the lossen rearrangement is closely related to that of Hofmann rearrangement. Except that in the former the leaving group is carboxylate anion while in the latter it is bromide anion.



hydroxamic acid ester of hydroxamic acid



Applications : As the hydroxamic acid is difficult to obtain, the reaction is of limited importance.

Schmidt reaction

Carboxylic acids react with hyddrazoic acid in the presence of concentrated sulphuric acid to give amine directly, reaction being known as Schmidt reaction.

$$RCHO + HN_3 \xrightarrow{H_2SO_4} R\text{-}NH_2 + CO_2 + N_2$$

The reaction also takes place between aldehydes or ketones and hydrozoic acid to form a mixture of cyanides and formyl derivatives of primary amines and amides respectively.

$$RCOOH + HN_3 \xrightarrow{H_2SO_4} R.CN + RNH.CHO$$

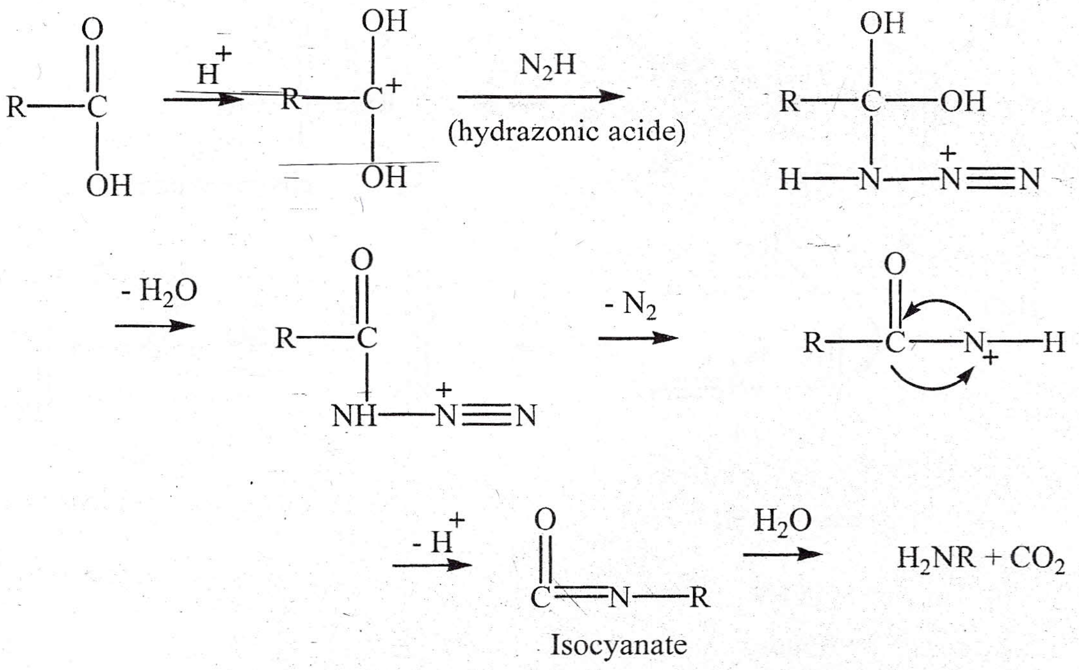
Aldehyde Cyanide Formyl derivative of amine

$$RCOR + NH_3 \xrightarrow{H_2SO_4} RCONHR + N_2$$

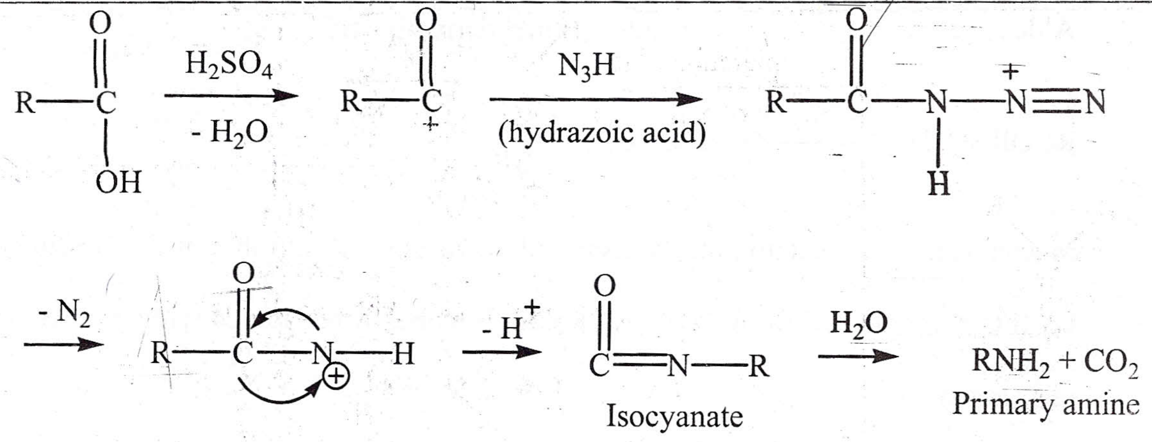
Mechanism : The reaction mechanism with acids is similar to that of the Hoffman and Curtius reactions, while with aldehydes and ketones it resembles with the Beckmann rearrangement.

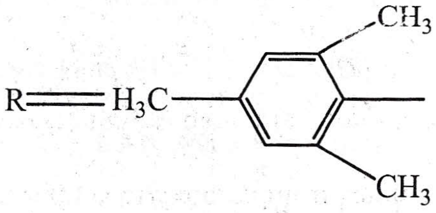
Reaction with acids : The reaction occurs through the acid azide which in presence of conc.sulphuric acid is present as its conjugate acid. The latter loses nitrogen on heating or without heating depending upon the nature of the acid used.

- The reaction with acid viz., benzoic acid, which require heating for the removal of nitrogen from acid azide proceeds as below.

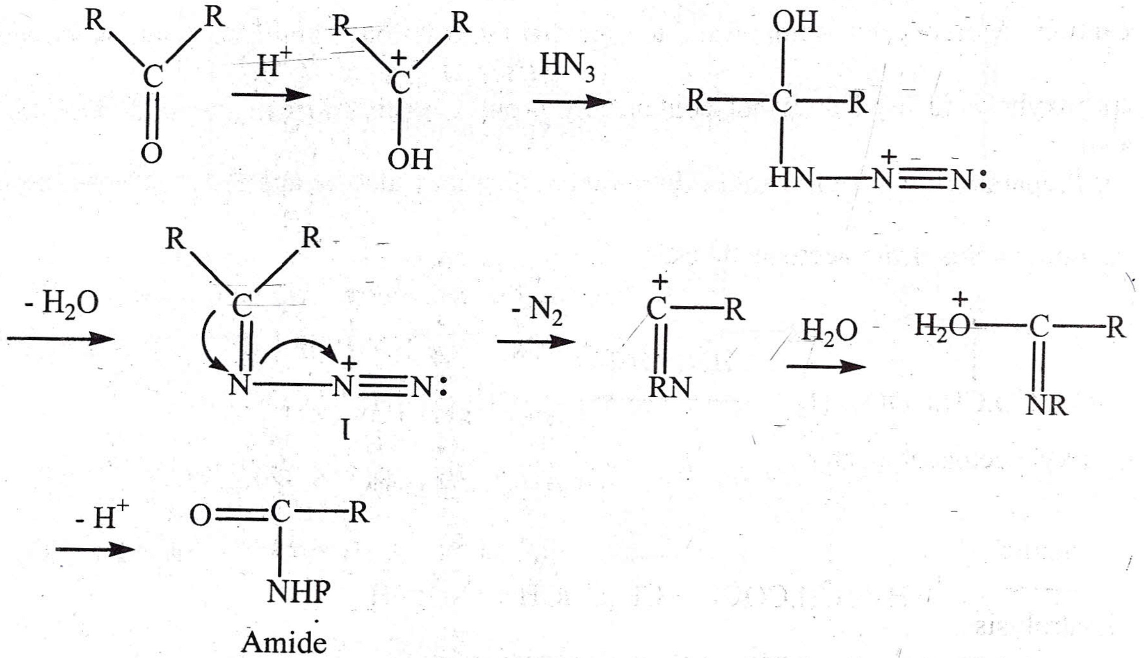


- The reaction with sterically hindered acids, viz mesitoic acid (2,4,6-trimethylbenzoic acid), which do not require heating for the removal of nitrogen proceeds as below.

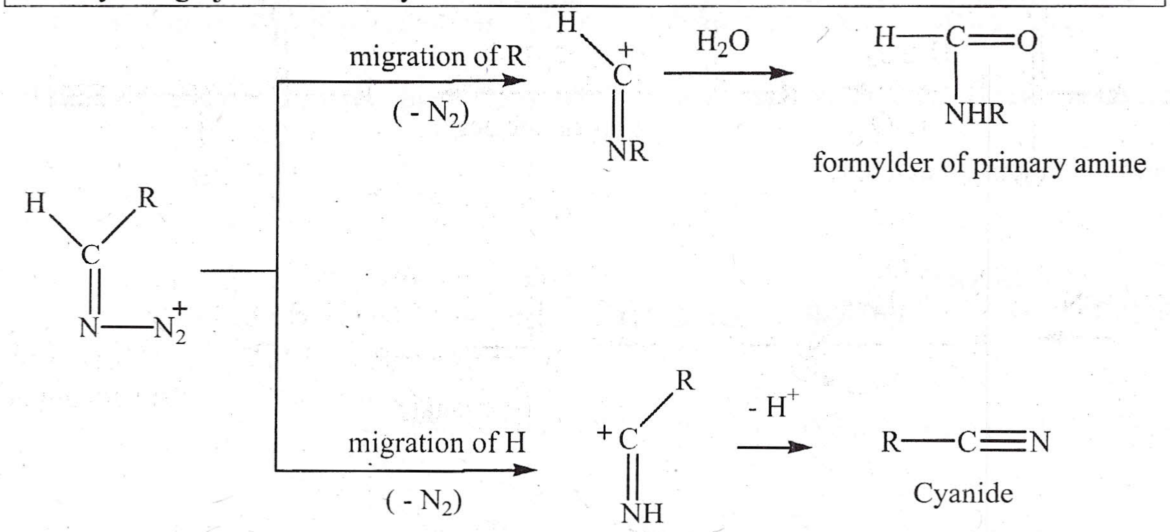




Reaction with ketones and aldehydes. The mechanism of the reaction is uncertain. Smith in 1941 proposed the following mechanism for ketones.

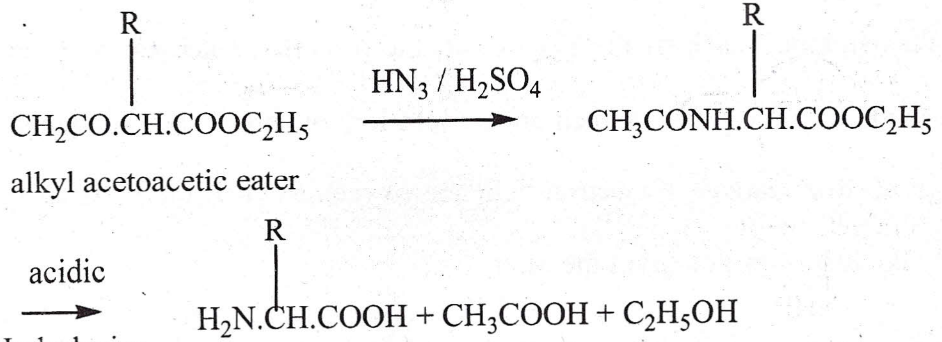


For aldehyde, the mechanism is the same, except that the ~~ion I~~ in the above case is now I_a and hence R or H can migrate to form a mixture of formyl derivative of primary amine and cyanide respectively.



Application : i) Preparation of primary amines : although Schmidt reaction is a direct method for the preparation of primary amines from carboxylic acids and gives usually better yield than the Hofmann or Curtius reaction, it is somewhat dangerous owing to the explosive and poisonous nature of the hydrazoic acid and thus must be applied with caution. Moreover, it is important to note that the reaction is applicable only when the carboxylic acid used does not contain any group sensitive to concentrated sulphuric acid.

ii) Preparation of α-amino acids, Schmidt reaction may also be applied for the synthesis α-amino acids from acetoacetic ester.



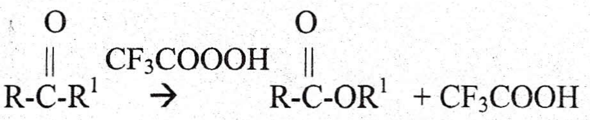
$$\underset{\text{alkyl acetoacetic eater}}{CH_2CO.\overset{\overset{R}{|}}{C}H.COOC_2H_5} \xrightarrow{HN_3 / H_2SO_4} CH_3CONH.\overset{\overset{R}{|}}{C}H.COOC_2H_5$$

$$\xrightarrow[\text{Hydrolysisc}]{\text{acidic}} H_2N.\overset{\overset{R}{|}}{C}H.COOH + CH_3COOH + C_2H_5OH$$

4.6.16 BAEYER VILLIGER REARRANGEMENT

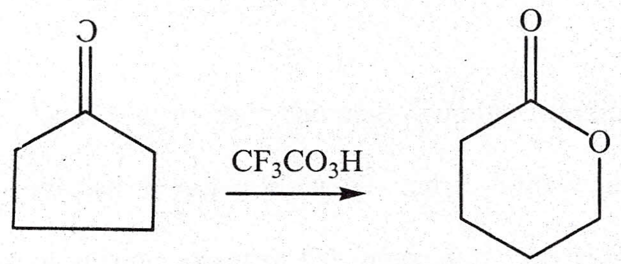
Baeyer-Villiger rearrangement is an example of the migration of a group from carbon to electron deficient oxygen.

The reaction involves the oxidation of ketones to esters by the treatment with peracids such as peraacetic acid, perbenzoic acid, pertrifluoroacetic acid, permonosulphuric acid etc.



$$\overset{\overset{O}{\|}}{R\text{-}C\text{-}R^1} \xrightarrow{CF_3COOOH} \overset{\overset{O}{\|}}{R\text{-}C\text{-}OR^1} + CF_3COOH$$

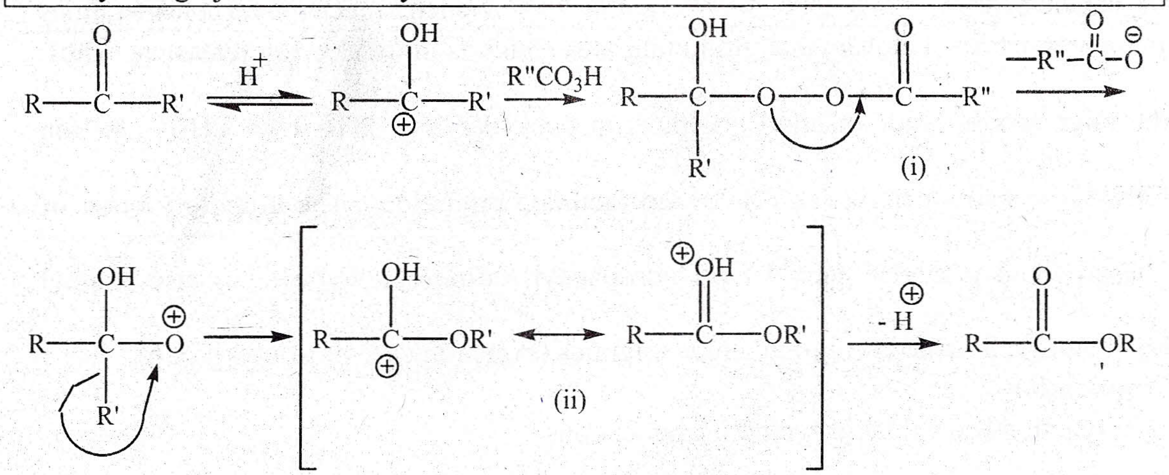
Cyclic ketones are converted to lactones with ring expansion



Cyclopentanone Lactone

The overall reaction is an insertion of oxygen atom between the carbonyl group and the adjacent carbon in ketone. Organic solvents which are inert under the conditions of reaction may be used. The choice of solvent depends upon the solubility of the reactants. Commonly used solvents are glacial acetic acid and chloroform.

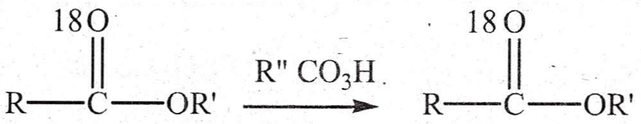
Mechanism : Nucleophilic attack of the peracid on the protonated ketone gives an intermediate peroxide (i). The peroxide then undergoesn loss of carboxylate anion and migration of a group from carbon to electron deficient oxygen to yield the protonated ester (ii). Finally the loss of proton gives the ester.



Where R' is equal to CH_3, C_6H_5,CF_3 , etc.

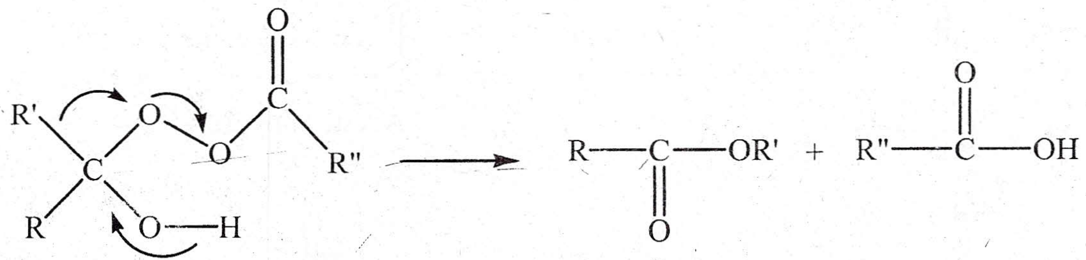
The reaction is catalysed by acids. Electron-releasing groups in the ketone and electron withdrawing groups in peracids promote the reaction rate. Pertrifluoroacetic acid is very effective because trifluoroacetate ion is a good leaving group.

The mechanism is supported by the fact that the labeled oxygen atom of the ketone is entirely present in the cathonyl oxygen of the ester.



$$R-\overset{^{18}O}{\overset{\|}{C}}-OR' \xrightarrow{R''\,CO_3H} R-\overset{^{18}O}{\overset{\|}{C}}-OR'$$

The loss of carboxylate anion and the migration of the group may be concerted. Syrkin has suggested that the peroxide (i) transforms into products by a cyclic mechanism, which shows that the last three steps may be concerted.



The migrating group retains its configuration as in other concerted reactions. For acylic compounds the migrating group, R' must be 2°, 3° or vinylic. However, migration of 1° alkyl group may be brought about by using CF_3CO_3H or BF_3-H_2O_2 as reagent.

Baeyer-Villiger oxidation can be brought about with H_2O_2 and base also in some cases.

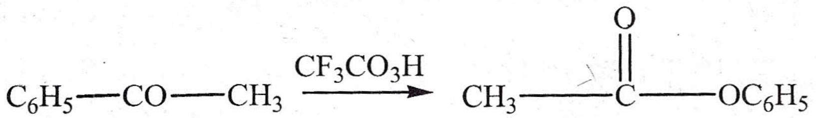
In unsymmetrical ketones, that group migrates which is more electron releasing. Thus, the migratory aptitude of alkyl groups is in the order 3° > 2° > 1° > CH_3. Electron releasing substitutents in the aryl group facilitate migration. The migratory order of aryl groups is ρ-tolyl > phenyl > p-chlorophenyl > p-nitrophenyl etc. In case of alkyl aryl ketones, it is the aryl group which migrates (except in case of t-butyl group)

Applications

The reaction has valuable synthetic applications

1. Esters : Esters which are difficult to synthesize can be prepared by this method.

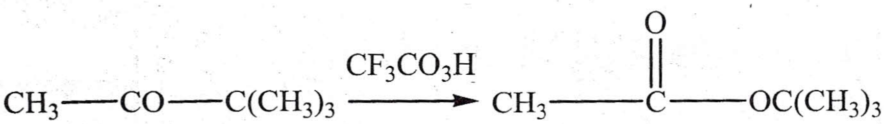
(a)



$$C_6H_5-CO-CH_3 \xrightarrow{CF_3CO_3H} CH_3-\overset{\overset{O}{\|}}{C}-OC_6H_5$$

Acetophenone Phenylaceltate

(b)

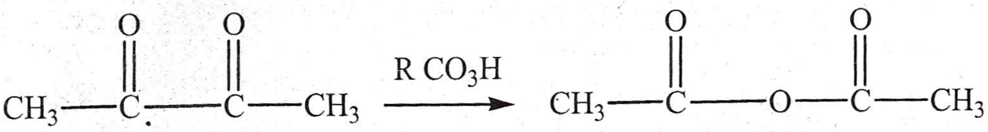


$$CH_3-CO-C(CH_3)_3 \xrightarrow{CF_3CO_3H} CH_3-\overset{\overset{O}{\|}}{C}-OC(CH_3)_3$$

Pinacolone *t* - Butylacetate

2. Anhydrides when 1,2 diketones or o-quinones are subjected to Baeyer-Villiger rearrangement, anhydrides are produced.

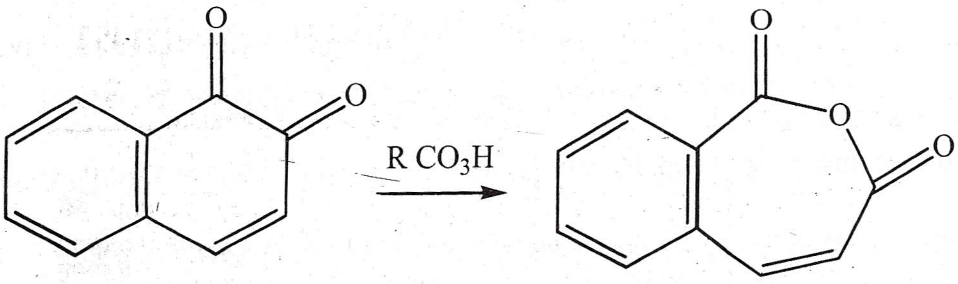
(a)



$$CH_3-\overset{\overset{O}{\|}}{C}-\overset{\overset{O}{\|}}{C}-CH_3 \xrightarrow{R\,CO_3H} CH_3-\overset{\overset{O}{\|}}{C}-O-\overset{\overset{O}{\|}}{C}-CH_3$$

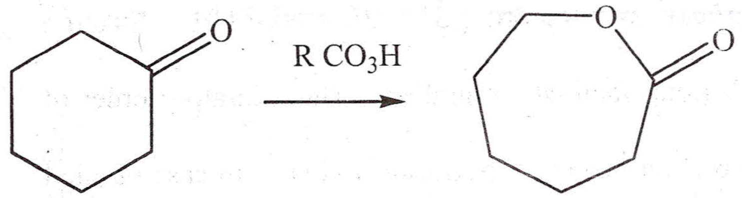
Diacetyl Acetic anhydribe

(b)



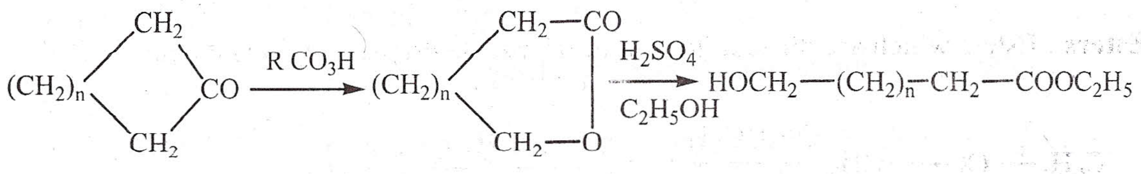
α - Naphthaquinone

3. Lactones Cyclic ketones are converted to lactones with ring expansion



Cyclohexanone ε - Caprolactone

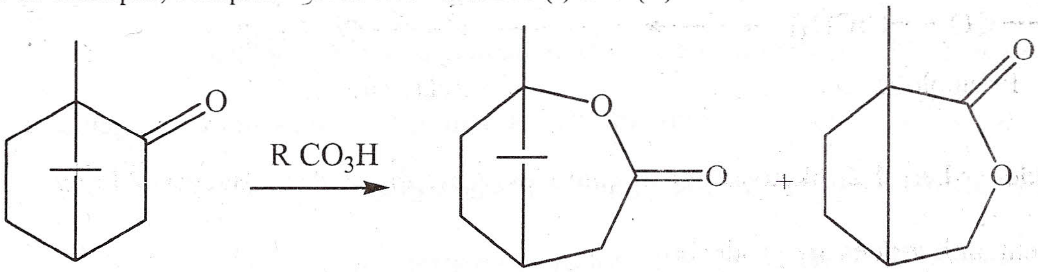
Long chain hydroxyesters can be prepared from large ring size ketones.



Lactone

With some condensed cyclic ketones, two lactones in varying proportions are formed.

For example, camphor gives two lactones (i) and (ii)

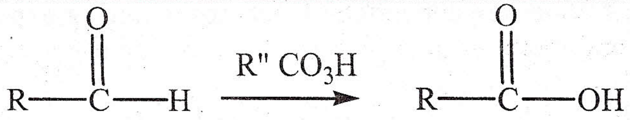


I (75%) II (25%)

Lactone (i) is the normal product formed by the migration of the tertiary bridge head carbon while lactone (ii) has been formed by the migration of the methylene group. The reason for the formation of two lactones in different proportions is steric factor.

4. Elucidation of structure. The ester obtained as a result of the rearrangementmay be hydrolysed to acid and alcohol from which structure of the substrate can be determined.

The reaction is not successful with aldehydes. Aliphatic aldehydes are oxidized to acids by the migration of the hydrogen.



$$R-\overset{\overset{\Large O}{\|}}{C}-H \xrightarrow{R''CO_3H} R-\overset{\overset{\Large O}{\|}}{C}-OH$$

4.6.17 Questions

Molecular rearrangements

1. Describe briefly general mechanistic consideration in molecular rearrangements?
2. Write short note on a) Nature of migration in molecular rearrangement; b) Migratory aptitude and c) Memory effects
3. Discuss of the following rearrangements on the basis of electronic theory.

   a) Beckmann rearrangement; b) The Pinacol-Pinacolone rearrangement and c) The Hofmann rearrangement
4. Write short note on the following rearrangements

   a) Wagner- Meerwein; b) Benzil-Benzlic acid and c) Favorskiik
5. Give modern views regarding the mechanism of the following rearrangement

   a) Demjanov; b) Armdt-Eistert and c) Beyer-Villiger
6. Describe the mechanism of the following rearrangement

   a) Neber; b) Curtius; c) Schmidt and d) Lossen
7. Give one example with mechanism for the molecular rearrangement involving electron deficient carbon?
8. Give one example with mechanism for the molecular rearrangement involving electron deficient nitrogen?
9. Give one example with [illegible]m for the molecular rearrangement involving electron deficient oxygen?
10. Give one example with mechanism for the molecular rearrangement involving electron rich atom?

Terpenoids

1. Explain general methods of structure determination of terpenoids?

2. Write short notes on the stereochemistry of the following

   a) Citral b) Geraniol c) Terpineol

3. Describe the structure determination and stereochemistry of menthol

4. Illustrate the structure determination and stereochemistry of faransol

5. Deduced the structure of geraniol and conform its structure by the synthesis

6. Deduced the structure of α-terpineol and conform its structure by the synthesis

7. Deduced the structure of citral and conform its structure by the synthesis

8. Write shot notes on a) isoprene rule b) special isoprene rule

9. Write the synthesis of the following : a) Citral b) Geraniol

10. Write the synthesis of the following : a) α-terpineol b) Menthol c) Faransol

Alkaloids

1. Explain general methods of structure determination of alkaloids

2. Write short note on stereochemistry of the following

   a) Atropine b) Quinine c) Nicotine

3. Describe the structure determination and stereochemistry of morphine

4. Illustrate the structure determination and stereochemistry of nicotine

5. Deduced the structure determination and structure of atropine by the synthesis

6. Deduced the structure determination and structure of quinine by the synthesis

7. Write the synthesis of the following

a) Nicotine b) Quinine

8. Write the synthesis of the following

a) Atropine b) Morphine