First Year

Paper I : Organic Chemistry I

Unit I

Mechanism of electron displacement in organic molecules:

Effect of structures in the dissociation constant of acids and bases -EDA complexes crown ether complexes - inclusion compounds - Quantitative treatment of the effect of structure on reactivity - the Hammett relationship - significance of reaction and substituent constants Application of the Hammett equation - Limitations and deviations.

Introduction to reactions mechanism - reactive intermediates - free radicals carbenes - nitrenes - carbanions - carbocations - Formation and stability of these species.

Aromatic electrophilic disubstitution partial rate factors.

Kinetic and non Kinetic methods of, determining organic reaction mechanism.

Unit II

Stereochemistry

Study of symmetry of molecules - as symmetric and dissymmetric molecules r concept of chirality and optical isomerism - molecules with more than one chiral centre Axial chirality in allenes, biphenyls and spiranes.

R, S - notation of the above molecules, stereospecificity and steroselectivity, asymmetric synthesis - Cram's rule - Prelog's rule.

E, Z- nomenclature of geometrical isomers

Conformational Analysis :

Conformations of cyclic systems up to six - membered rings - conformational analysis of mono - and substituted cyclohexanes - Effect of conformation of decalins perhydro phenanthrenes.

Unit III

Alkaloids

Structure, synthesis and stereochemistry of the following alkaloids. Quinine, Norphine, Lysergic acid and Tylophorine - Biosynthesis of alkaloids.

Antibiotics :

Structure and synthesis of the following: Chloramphenicol, cephalosporin - C, penicillin, streptomycin and Tetracyclin

Unit IV

Aromaticity :

Benzenoid and non - benezenoid aromatic compounds - Huckel' s rule concept of homo aromaticity and anti-aromaticity - systems with 2, 4, 6, 8 and 10 electrons. Annulenes - Fulvene. azulene and tropolones.

Heterecyclic Compounds:

Synthesis and reactions of sydromes, carbazole and imidafole - structure elucidation of flavones, quercetin, cyanin, caffeine, theobromine and theophylline.

Unit V

Aliphatic and aromatic nucleophilic substitution

S_N1 and S_N2 mechanisms - effect of substrate structure, nucleophile, leaving group and the solvent on nucleophilic substitution - symphoria - NGP due to and electrons S_N1, S_N2, S_Ni and S_Ni ; mechanisms.

Eliminations:

E_1, E_2 and E_1 CB mechanisms - effect of the substrate structure, base solvent and the leaving group on elimination - Hofmann, Saytzeff and Bredt's rules.

Aromatic nucleophilic substitution Benzyne mechanism Von Richter rearrangement.

Mechanism of addition to multiple bonds:

Stereochemical factors in the addition of the following to carbon - carbon double bonds hydrogen halogens, hydrogen halide - hydroboration - hydroxylation.

Mechanism of Mannich reaction, Claisen ester condensation, Dieckman n condensation, Stobbe condensation Darzen's reaction, Refomatsky reaction, Wittig and Grignard reactions Stork's enamine reaction - Michael addition.

References :

Unit I

1. The Modem Structural Theory of Organic Chemistry
   L.N. Fergusar - Prentice Hall.
2. Mechanism and Structure in Organic Chemistry
   E.S. Gould - Henry Holt & Co.
3. Mechanism and Theory in Organic Chemistry
   T.H. Lowry and K.S. Richardson.
4. .Organic Chemistry -
   S. Pine Me. Gaw Hill, Kogakusha Ltd.,

5. Advanced Organic Chemistry -
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6. Organic Chemistry - R.T. Morrison and Boyd, Prentice Hall
7. A Guide book to Mechanism in Organic Chemistry
   P.Sykes - Orient Longman.
8. Organic Chemistry Vol. I .I. L Finar, ELBS
9. Fundamentals of Organic Reaction Mechanism
   J.M. Harris and C.C. Warnser - John Wiley & Sons
10. Reaction Mechanism in Organic Chemistry - Bansal
11. Advanced Organic Chemistry - Part - A
    F.A. Carey and R.J. Sundberg
12. Correlation Analysis Organic Chemistry -
    J. Shorter - Clarendress . Press, Oxford

Unit II

1. Stereochemistry of Carbon Compounds -
   E.L. Eliel, Mc. Graw Hill.,
2. Introduction to Stereo chemistry -
   K. Mislow - Benjam,
3. Stereochemistry -
   V.M. Potapov - MIR publishers
4. Stereochemistry of Organic Compounds - Principles & Applications,
   D.Nasipuri - Wiley Eastern Ltd.
5. Stereochemistry - conformation and Mechanism -
   R.S. Kalsi - Wiley Eastern
6. Organic Chemistry - Vol II - ELBS

Unit - III

1. The Alkaloids - Bentley - Inter Science Publishers
2. Chemistry of Alkaloids - Pelletier
3. The Chemistry of Organic Natural products -
   O.P. Agarwal - Goel publishing House.

4. Organic Chemistry Vol II - I.L. Finar, ELBS
5. Monograph series as "The Alkaloids"
6. Medicinal Chemistry - A. Burges - Academic Press

Unit IV

1. Aromatic Character and Aromaticity - G.M. Badger - Cambridge
2. Aromaticity - S.J. Garelt - Mc. Graw Hill.
3. Advanced Organic Chemistry - J. March, Wiley.
4. Organic Chemistry Col. I & II - Finar, ELBS
5. Chemistry of Heterocyclic compounds - R.M. Acheson - Wiley Eastern
6. The Chemistry of Organic Natural Products - O.P. Agarwal - Goel Publishing House

Unit V

1. The Mechanism and Theory in Organic Chemistry T.R. Lowry and K.S. Richardson
2. Advanced Organic Chemistry - J. March, Wiley
3. Mechanisms and structure in Organic Chemistry E.S. Gould - Henry Holt & Co, New York.
4. Fundamentals of Organic Reaction Mechanisms J.M. Harris and C. Wamser - John Wiley & Sons.
5. A Guide Book to Mechnism in Organic Chemistry
6. Reaction Mechanism in Organic Chemistry - Bansal
7. Organic Chemistry - R.T. Morrison & R. N. Boyd
8. Stereochemistry of Carbon Compounds - E.L. Eliel - Mc Graw Hill
9. Organic Chemistry Vol II - I.L. Finar
10. Advanced Organic Chemistry - Part A F.A. Corey, and RJ. Sundberg - Plemum press.

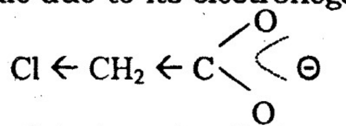
UNIT – I

INFLUENCE OF STRUCTURE ON ORGANIC ACIDS AND BASES

Among the various structural factors operating in organic molecules, polarization effects and steric effects play a major role in deciding the strength of acids and bases. The operation of these effects mainly influence the stability of their conjugate part of the acids and bases.

1) Inductive Effect

Consider a molecule of Chloro acetic acid. The Chloroacetate anion is found stabilized by the presence of a Chloroine atom which causes a permanent polarization in the molecule due to its electronegative behaviour.



This causes a drifting of electron density towards the atom (-I effect), thereby dispersing the negative charge of the carboxylate anion, throughout the molecule. The conjugate base of Chloroacetic acid is hence stabilized as revealed by the enhancement of the acidity of the molecule. As the methyl hydrogens are successively replaced by more number of such atoms with – I effect, the acidity is drastically increased.

	$(K \times 10^{-5})$
CH_3COOH	1.75
$ClCH_2CO_2H$	155
Cl_3CCO_2H	121,000
F_3CCOOH	500,000

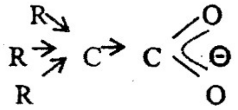
In general, groups with – I effect when attached to the acids behave in a similar manner, in the following order.

$-\oplus NR_3 > \oplus NH_3 > NO_2 > CN > F > Cl > Br > I > OR > Ar$ etc

However, acids containing groups with + I effect are found less acidic, in the order: $O^{\ominus} < COO^{\ominus} > CR_3 < CR_2 < CH_2R < CH_3$ etc In the given examples here under,

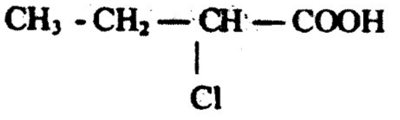
	$K \times 10^{-5}$
$H.COOH$	17.6
CH_3 COOH	1.75
$(CH_3)_2$ CH.COOH	1.51
(CH_3) C.COOH	0.89

the electron releasing alkyl groups decrease the acidity since they help accumulate the negative charge over the anion, further destabilizing the conjugate base (anion) as shown.

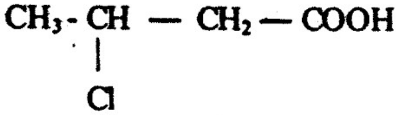


But inductive effect is a weak effect and is found to die out with distance as revealed in the acidity of the following butyric acids.

$CH_3-CH_2-CH_2-COOH \quad - 1.52 \times 10^{-5}$



$CH_3-CH_2-CH(Cl)-COOH \quad - 139 \times 10^{-5}$

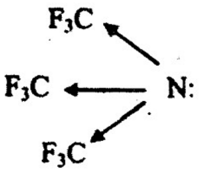


$CH_3-CH(Cl)-CH_2-COOH \quad - 8.9 \times 10^{-5}$

$Cl-CH_2-CH_2-CH_2-COOH \quad - 3 \times 10^{-5}$

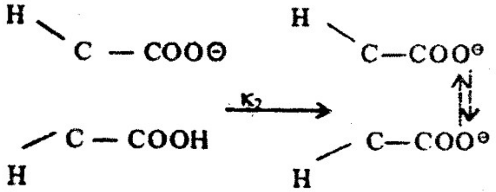
As expected, the α -Chloro butyric acid is found to be the most acidic, as the Chlorine is placed very close to the reaction centre. The acidity is progressively decreasing in β and γ-acids. The basic character of amines is also retarded when a –I group is attached to the reaction centre as in the case of tris - trifluoromethyl group. Similarly an alkyl group with + I effect considerably enhances the basic character of Ammonia

$$CH_3 \rightarrow NH_2 > NH_3$$

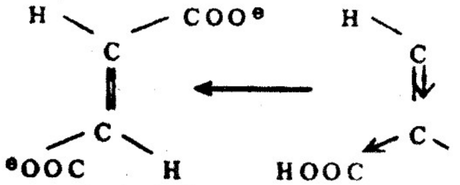


2) Field Effects

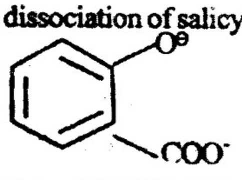
Even though inductive effects are inoperative over long distances through carbon chain, in certain molecules where the groups are cis – oriented, the effect is transmitted through space more effectively. These field effects are better conveyed through the solvent medium rather than through the bonds, as observed in the second dissociation of maleic acid.



The +I effect of each of the carboxylate anion is directly transmitted through the medium affecting the stability of the maleate dianion. The operation of field effect in the molecule is apparent from the very low value of K_2 (2.6×10^{-7}), compared to the fumerate dianion where it is much higher (300×10^{-7}). In the latter molecule, the + I effect can be transmitted only through the carbon chain.

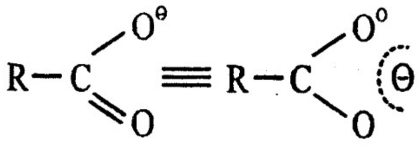


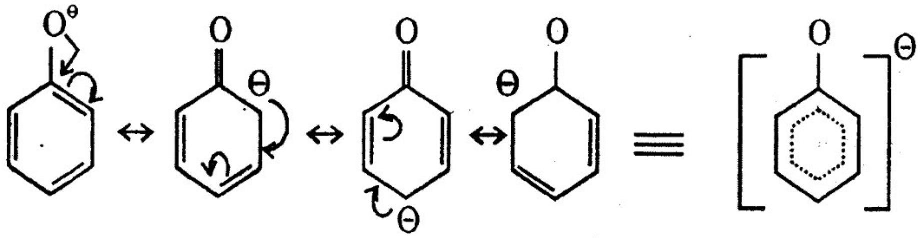
A similar effect could operate in the II dissociation of salicylic acid, reducing the K_2 considerably.



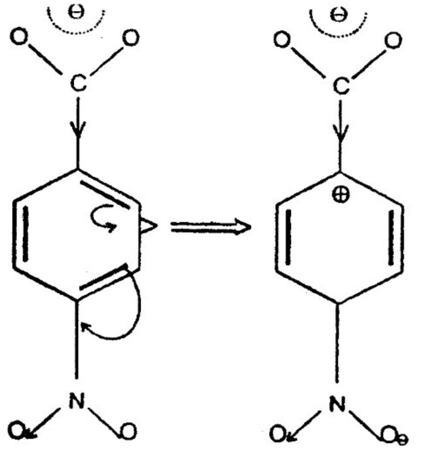
3) Mesomeric Effect

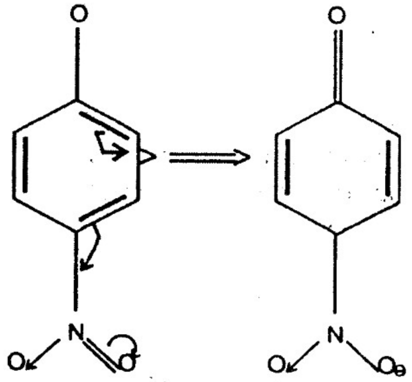
The delocalisation and dispersal of the charge of the conjugate part of the acid or base through mesomeri effect, also result in the stabilization of the ion. It is noticed in the carboxylate ion, phenolate ion etc.





For this reason, any carboxyl molecule or phenol is acidic irrespective of the other groups attached. The acidity is further enhanced when a NO_2 group attached to the molecule.





In aromatic acids and phenols, the acidity however depends upon the position of the Nitro group. The P – Nitro phenol is found to be 565 times more acidic than phenol and the most acidic among the nitro phenols.

Phenol — 1.7×10^{-10}
O–No_2 — 7.5×10^{-8}
m–No_2 — 1×10^{-8}
p–No_2 — 9.6×10^{-8}

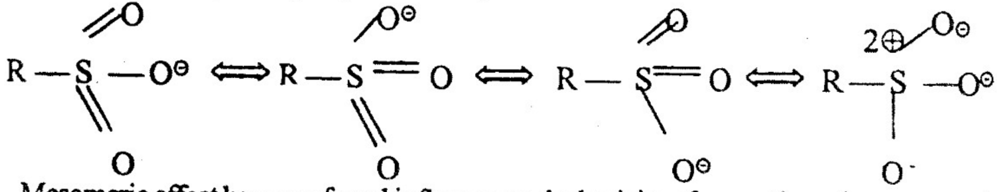
The combined –I and –M effect of the NO_2 group is found to operate in Ortho and Para derivatives whereas the mesomeric effect cannot operate in meta derivative, hence the low K value.

In benzoic acids, the acidity constants of the meta and Para derivatives do not markedly differ as in phenols, as the reaction centre and the group attached are not directly connected through resonance unlike in the case of substituted phenols.

Benozoicacid		6.3×10^{-5}
P–No$_2$	"	36×10^{-5}
m–No$_2$	"	32×10^{-5}
P–NH$_2$	"	1.4×10^{-5}
m–NH$_2$	"	1.9×10^{-5}

But the acidities of phenols and carboxylic acids is incomparable since the contributing structures of the carboxylate anion have the negative charge confined only to the electronegative oxygen but in phenols, most of the contributing structures have the negative charge over the less electronegative carbon atoms. Hence the carboxylate structures have a lesser energy compared to those of phenols, and an inherently high acidity.

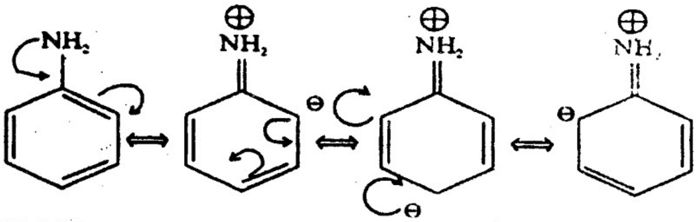
Sulphonic acids are found to be even stronger acids than carboxylic acids since the combined –I and –M effect of the sulphone group has a stronger delocalization influence



Mesomeric effect has a profound influence on the basicity of aromatic amines as revealed by their low basicity constant (Kb) compared to the aliphatic amines or ammonia.

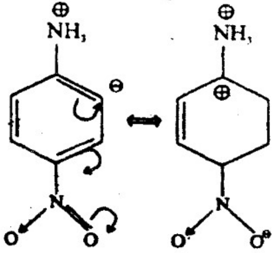
NH$_3$	1.8×10^{-5}
RNH$_2$	4×10^{-4}
ArNH$_2$	4.2×10^{-10}

The incomparably low value of Kb of aniline is due to the participation of the lone pair of electrons over nitrogen in resonance with the π electrons of the ring. As a result, the molecule is stabilized by resonance, but the conjugate acid of aniline viz. anilinium ion has no such stabilization, since the



$$C_6H_5NH_2 \text{ (Stabilised)} + H^+ \rightarrow C_6H_5N^{\oplus}H_3 \text{ (Not Stabilised)}$$

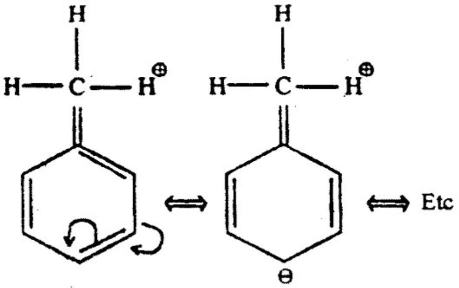
Nitrogen atom cannot take a valency of 5. However, electron releasing substituents such as CH$_3$, OCH$_3$, NH$_2$ etc. stabilize the anilinium ion and enhance the basicity, but the reverse effect is noticed with electron withdrawing substituents such as NO$_2$, Cl etc as given under,



	K_b □10^{-10}
Aniline	4.2
P - NH_2	140
P - OCH_3	20
P - CH_3	12
P - Cl	1
:OCH_3	''OCH_3
P - NO_2	0.001
(Stabilized)	

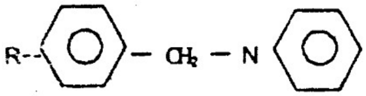
HYPER CONJUGATION

When a multiple bond is connected to a α - hydrogen atom in any molecule, there operates a special type of delocalization leading to stabilization of the molecule, affecting their chemical behaviour. In a molecule like toluene the following contributing structures are possible due to the involvement of the σ electrons of the C - H bond and the adjacent P electrons. This phenomenon has come to be known as s- P conjugation.



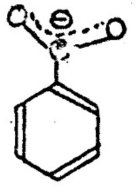
The H – atom is not moving from the original position and any of the three H – atoms could involve in this type of resonance also known as no-bond resonance. This hyperconjugative effect is apparent from the increase of resonance energy of the molecule (37.5 k.cals) compared to that of benzene (36 k.cal). This is also reflected in all the related properties of such molecules.

This concept was introduced by Baker and Nathan when they noticed the unexpected order of reactivity of P – substituted Benzyl halides with pyridine. It was expected that the reaction would be fastest if t – bu group is attached. However the reaction was fastest with methyl group at para position since it can exert hyper conjugation.

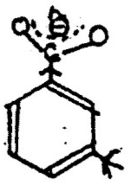


Consider the acidity of benzoic acid. Compared to the m - methyl derivative the p – methyl substituted acid is found to be less acidic

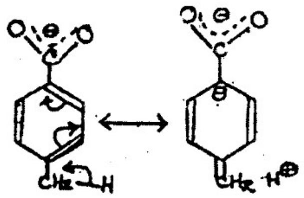
The p – toluic acid is found to be least acidic even though the + I effect of the methyl group is less pronounced in that position compared to the m – toluic acid. This could be explained based on the possible hyper conjugative effect which destabilizes the anion.



(Ka = 6.3 X 10^{-5})

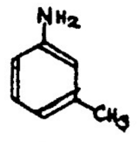


(Ka = 5.4 X 10^{-5})

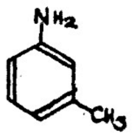


(Ka = 4.2 X 10^{-5})

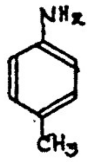
Similar effects are noticed in p – toluidine which is more basic than m – toluidine.



(K_b = 4.2×10^{-10})



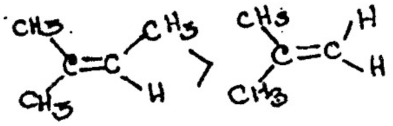
(5×10^{-10})



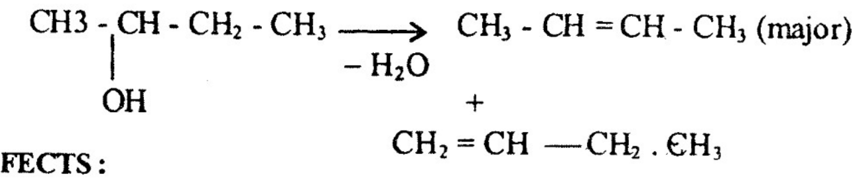
(12×10^{-10})

The operation of hyperconjugation in P – toluidine towards the NH2 group, retards the participation of the lone pair over Nitrogen in resonance with the π electrons of the benzene ring, hence increasing the basicity of the molecule.

The stability of more highly branched olefins as stated by the Sytzeff rule is based on the hyper conjugative stability in such molecules.



As the number of α - hydrogen atoms increases in olefins, the stability also increases due to the number of possible hyper conjugative contributing structures. Hence in dehydrations and dehydro halogenations (elimination reactions), the more branched olefin is formed in major quantities.

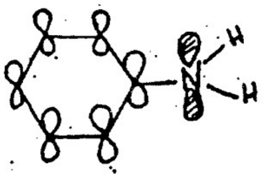


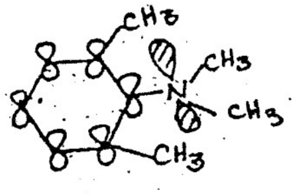
$$CH3 - \underset{\underset{OH}{|}}{CH} - CH_2 - CH_3 \xrightarrow[-H_2O]{} CH_3 - CH = CH - CH_3 \text{ (major)} + CH_2 = CH - CH_2 . CH_3$$

STERIC EFFECTS :

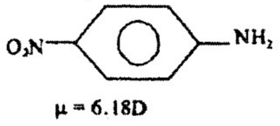
One of the pre conditions of resonance to operate in molecule says that the parts of the molecule participating in resonance must lie in the same plane and any structural modification which destroys coplanarity will cause Steric inhibition to resonance.

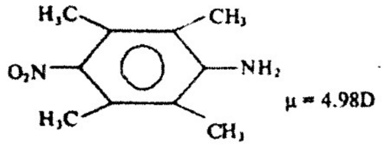
Consider 2,6 dimethyl N, N – dimethyl aniline. Due to the presence of bulky CH_3 groups at Ortho positions, the free rotation around the C – N bond is restricted and during the process, the dimethylamino group is tilted out of plane from the benzene ring.



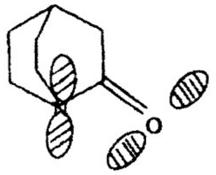


This has resulted in the enhancement of basicity of the molecule compared to the unsubtituted aniline, since the lone pair of electrons over the nitrogen atom largely remain unaffected and they cannot effectively participate in resonance. Similar effect is noticed in P – Nitro amino durine, where the nitro group as well as the amino group are flanked by bulky Ortho methyl groups. The increase in basicity is revealed also from the dipole moment values.



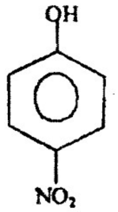


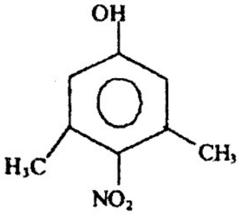
Even structural modification in molecules leading to non-coplanarity can cause inhibition to resonance and difference in acid–base behaviour. (e.a) Quinuclidone –2



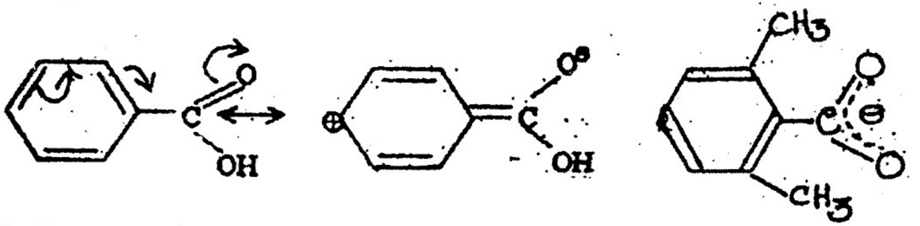
Here the lone pair of electrons over N – atom can not participate in resonance with the carbonyl group as the orbitals concerned are not in the same plane. Hence the molecule does not behave like an amide where normally resonance operates, and becomes basic due to the availability of the lone pair.

Acidity of nitro phenols is also influenced by the steric inhibition to resonance, when the nitro group is inhibited by the methyl groups from withdrawing electrons through – M effect.

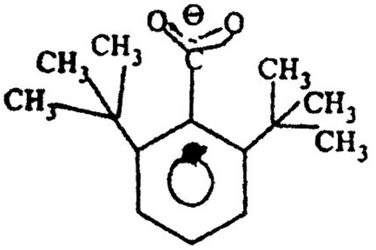




Any Ortho substituted benzoic acid is found to be more acidic, since the Ortho substituent distorts the carboxyl group from the ring, thereby preventing the operation of resonance through the carbonyl group with the ring.



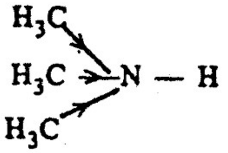
In the free benzoate anion, resonance freely operates destabilizing the carboxylate anion itself.



Less solvated

ortho	pka ArCOOH
H	4.17
Me	3.91
NO_2	2.71
Cl	2.94
dit-but	6.14

However, 2,6 ditert-butyl benzoic acid is found less acidic than benzoic acid and this phenomenon is attributed to what is called Steric inhibition to solvation. The solvation effect is found to be the predominant effect compared to the resonance effect in such large molecules whose ions are less solvated. This is also true in the case of aliphatic amines. Among the primary, secondary and tertiary amines, the latter is expected to be the most basic, as the alkyl groups are election releasing. But the large size of the molecule defies the solvation of the respective ammonium ion, hence making it least basic.



$[CH_3 - NH_3]$

(Less Solvated) **More solvated**

Hence the observed order of basicity is:

$$(CH_3)_2NH > CH_3NH_2 > (CH_3)_3N$$

EFFECT OF HYBRIDIZATION

The type of hybridization of the carbon or nitrogen atom also decides the acid-base character of a number of molecules with multiple bonds. Consider ethane, ethylene and acetylene molecules which differ in hybridization.

$H_3C - CH_3$ (pKa >45) SP^3

$H_2C = CH_2$ (pKa 37) SP^2

$HC \equiv CH$ (pKa 25) SP

The high electro negativity of the acetylide ion indicates that the carbon has the ability to keep the C – H electron towards itself, leading to the dissociation of the H as a proton.

$$HC \equiv CH \xrightarrow{\quad} HC \equiv C^{\ominus}: + H^{\oplus}$$

The behaviour of acetylene molecule is different from that of the other two molecules which differ in the nature of hybridizaiton. The highest S – character (50%) of the carbon makes it the most electronegative and the H – is rendered acidic. This is revealed from the action of a strong base like $NaNH_2$, in abstracting a proton from acetylene.

$$HC \equiv CH \xrightarrow{Na / NH_3} HC \equiv C: Na^{\oplus}$$

Sodium acetylide

Nitrogen atoms attached to carbon atoms through different degrees of hybridization also behave differently with regard to their basicity. A multiply bonded Nitrogen has a greater electro negativity due to greater S – character, hence it is less basic compared to a singly bonded Nitrogen. Accordingly, the pKa values of the corresponding conjugate acids differ as under:

$(CH_3)_3 N^{\oplus}H$

9.8

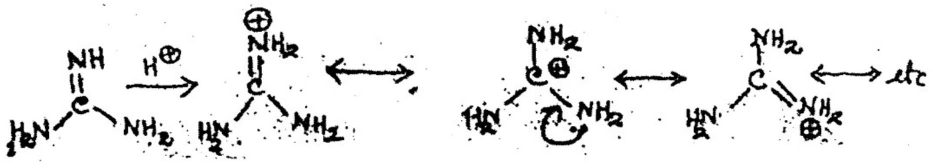
5.2

$CH_3 - C \equiv NH^{\oplus}$

< 0

The amount of S – character increases with decrease of basicity, the generalization same as realized in the case of acids.

However certain multiply bonded nitrogen atoms are found to be even more basic as observed in guanidine where the double bonded nitrogen is preferentially attacked by the proton. The guanidinium ion is stabilized by resonance, thereby making guanidine strongly basic as that of alkali metal hydroxides or quarternany ammonium hydroxides.



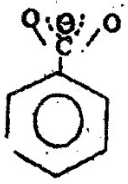
A multiply bonded oxygen is also less basic compared to a single bonded one, as reflected in vinyl ethyl eithe

$$CH_2 = CH - \ddot{O} - CH_2 - CH_3 \Leftrightarrow \overset{\ominus}{C}H_2 - CH = \overset{\oplus}{O} - CH_2 - CH_3$$

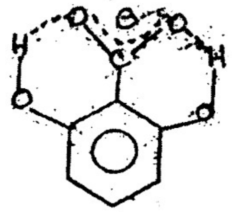
The rendered is oxygen less basic as the ether is found insoluble even in cone. H_2SO_4 and it forms no Oxonium salt, unlike diethyl either.

HYDROGEN BONDING

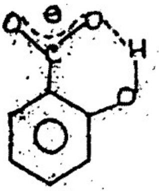
The abnormal acid-base character of a number of molecules could be explained in terms of hydrogen bonding. The Ortho dihydroxy benzoic acid is found to be more than 30 times acidic compared to benzoic acid as the benzoate anion is stabilized by chelation through hydrogen bonding.



(pKa 4.7)



(2.3)



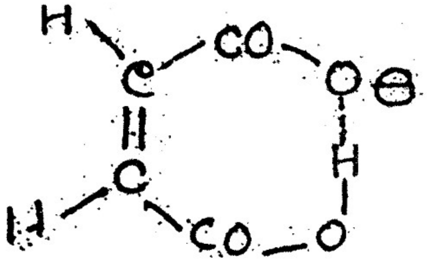
(2.98)

The second dissociation in salicylic acid (OH ionization) is abnormally low (13.8) due to the effective hydrogen bonding in the salicylate ion.

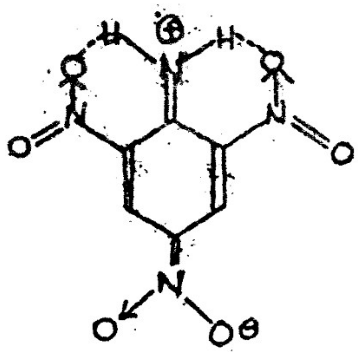
The steep decrease in the K_2 value of maleic acid is also due to the strong hydrogen bonding in the maleate anion, apart from the field effect operating in the ion.

$K_1 = 1.5 \times 10^{-2}$

$K_2 = 2.6 \times 10^{-7}$

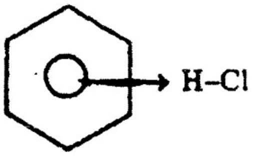


Similar observations are noticed in the basicity of 2,4,6 trinitro aniline which is 40,000 times less basic compared to the N,N -, dimethylamino derivative. Perfect chelation in the molecule due to hydrogen bonding, renders the molecule planar enough for resonance to operate, hence retarding the basicity.



EDA COMPLEXES

π electrons in an olefinic bond are mobile enough to attack strong acids, hence acting as Lewis bases. Aromatic nucleus with a ring of p electrons also act as a base interacting with suitable acids. (e.g)

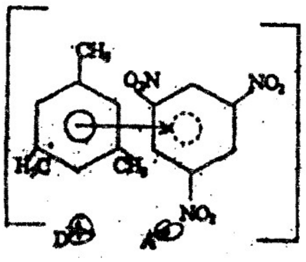


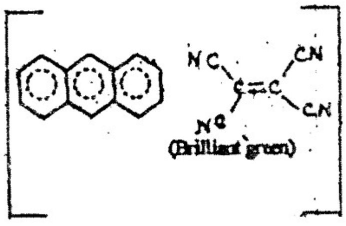
These π - complexes are otherwise known as charge transfer complexes since some of the π electron cloud is transferred across the molecule. If the olefinic system or the aromatic nucleus acts as the p electron donor (Base) and the other molecule an acceptor (acid) then the adduct formed is also known as an **Electron Donor Acceptor Complex.**

There are three types of EDA complexes. The donors are always organic molecules mostly aromatic or even aliphatic hydrocarbons. The acceptor molecules differ.

1) Complexes in with the Acceptor is also an Organic Molecule

Aromatic or aliphatic hydrocarbons with powerful electron with drawing groups act as the acceptor molecules, such as tetracyanoethylene, tetra nitro methane, picric acid, trinitrobenzene etc.. The donor molecules are normally the polynuclear hydrocarbons or benzene molecule containing electron releasing groups.





The donor molecule has a low ionization potential and the acceptor molecule has a high electron affinity. Some of the p electron density from the donor has leaked into the acceptor molecule, while the rings of the two molecules lie parallel to each other.

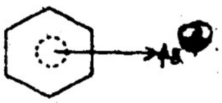
The EDA complexes are found to be intensely coloured, due tot the appearance of a new band in the visible region when an electronic transition occurs from the donor to the acceptor. The transition occurs from the highest filled M.O of the donor to the lowest empty M.O of the acceptor, when a photon is absorbed by the complex.

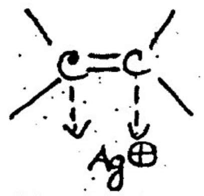
The bonding between the D and A is very weak and held together by vanderwaals forces as in [D,A], as well as of ionic nature as [D^+A^-]. Overall, the molecule is regarded as a resonance hybrid of these two forms, where the ionic contribution is limited.

$$D + A \longrightarrow [D,A] \qquad [D^+A^-]$$

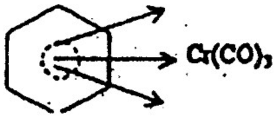
2. Complexes in which Acceptor is a Metal Ion

Silver ions form complexes with benzene, and also with simple olefins to form a 1:1 compound. Two bonds are believed to have formed, one σ - in nature, formed due to the overlap of filled π orbital of the olefin with the empty 5s orbital of the metal.





The other bond is π in nature formed by the overlap of the 4d orbital of the metal and the π * of the olefin. However, the bonds are not centred at any atom but as a whole.



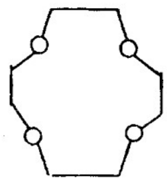
Metal carbonyls also form similar complexes with olefinic and aromatic systems.

3) Complexes in which Acceptors are Halogen

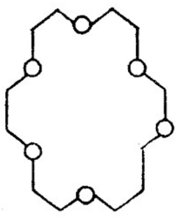
Iodine, Bromine and Chlorine molecules as well as their interhalogen compounds form complexes with amines, aromatic hydrocarbons, ketones etc. Iodine for instance develops an abnormal colour when dissolved in Benzene much different from the normal purple colour. It is due to the charge transfer complex formed by quadrupole-induced dipole interaction, Benzene acting as the quadrupole. The resulting solution has considerable dipole moment different from that at benzene or Iodine.

CROWN ETHER COMPLEXES

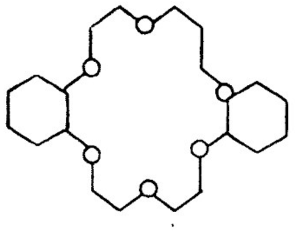
Large ring compounds with several hetero atoms such as oxygen, nitrogen or sulphur placed at symmetrical positions, are known as crown ethers. The following ethers form different varieties.



12-crown-4

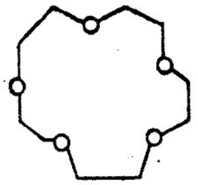


18-crown-6

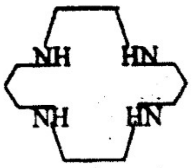


dicyclohexano 18-crown-6

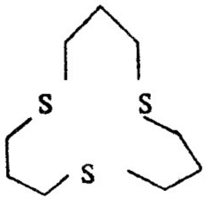
The prefixing number indicates the order of the ring and the suffix stands for the number of hetero atoms.



15-crown-5



14-crown-4



12-crown-3

Crown ethers are good complexing agents mostly with alkali metal ions and ammonium ion. The selectivity of the metal ions in forming complexes with crown ethers is mainly due to the size of the cavity of the crown ether. Thus $Li^{\oplus}$ is bound by 12 – crown ethers whereas 18 – crown binds only $K^{\oplus}$ ion but not Li. However, there is no bonding between the constituents of the crown ether complex, only weak van derwaal's forces are involved.

Crown ethers serve as cryptands to separate alkali metal ions through the formation of cryptates (complexes), as they can selectively form complexes with certain metal ions only, leaving the others in solution.

Crown ethers also find an important application in synthetic organic chemistry as phase-transfer catalysts. For instance the use of KCN as catalyst in an organic phase is not possible as it cannot dissolve in this phase. However when it is taken along with a cryptand such as dicyclohexano18-crown-6, K^+ is enclosed within the organic phase thereby transferring the catalyst in to the organic phase from the inorganic medium.

INCLUSION COMPOUNDS

The addition compound between the molecules, one host having a crystal lattice in which there is just enough space to accommodate a guest molecule, is called an inclusion compound. It is of two types, one in which the space for the guest is available in the form of long tunnels, hence known as channel complexes and the other called clathrate compounds or cage compounds as the space for the guest is enclosed

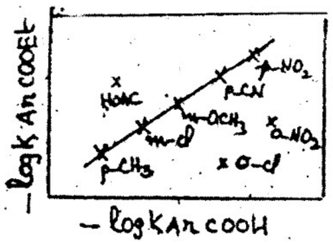
Urea has a hexagonal lattice when crystallised in the presence of straight chain molecules such as octane, 1-bromo octane etc but not with 2-bromo octane or 2-methyl octane. Since branched chain molecules and cyclic compounds cannot fit into the channels, urea makes it possible to isolate the straight chain molecules from the branched chain compounds. While inside the channels, the guest molecules have no chemical bonding with the host but only held by van derwaal's forces as in the crown ether complexes.

LINEAR FREE ENERGY RELATIONSHIP

According to transition state theory, the standard free energy of activation of a reaction is proportional to its rate constant and the standard free energy is proportional to the equilibrium constant of the reaction. When Hammett plotted the logarithm of the rate constant for hydrolycis of a series of esters to that of the ionization constant (Equilibrium constant) for the corresponding acids, a linear relationship was noticed between the two logarithmic factors as indicated by the formation of a straight line. Hence there exists a Linear Free energy Relationship (LFR)

$$\text{Ar COOEt} \xrightarrow{H_2O} \text{ArCOOH} + \text{EtOH}$$

$$\text{Ar COOH} \xrightarrow{K} \text{ArCOO}^{\ominus} + \text{H}^{\oplus}$$



However the O-substituted Aromatic molecules and the aliphatic series do not fall on the straight line as in these molecules steric effects predominate compared to the polar effects in the m and p – substituted acids & esters. As such, the Linear Free energy Relationship between the two sets of K values could be taken as a measure of the polar effect caused by the substituent on the rate of the reaction. Hence it could be written for the straight line,

(1) ——— $\text{Log } K_X = P \log K_X + C$, ($\therefore y = mx + c$ for a straight line)

where P is the slope of the straight line and the suffix x stands for any substituent.

When there is no substituent (ie) for the standard molecules,

(2) ——— $\text{Log } K_O = \rho \log K_O + C$

(1) – (2) $\longrightarrow$

$$\log \frac{K_X}{K_O} = \rho \log \frac{k_X}{k_O} \quad \text{———3}$$

The $\log \frac{K_x}{K_o}$ (or) $\log \frac{K_x}{K_o}$ terms refer to the change in free energy of that reaction while passing on from the standard molecule to the substituted one. As there exists a linear relationship between the two reaction series for the meta and para substituted molecules, one of these terms could be taken as a measure of the change in the polar effect of the substituent when substituted in the place of H – atom. Hence, log $K_x = \sigma_x$ where σ_x is called a substiutent constant, which is defined as the quantitative measure of the polar effect of the substituent on the rate of the reaction. The equation (3) becomes

$$\log \frac{K_x}{K_o} = \sigma \ X \rho$$

Since, ρ is a constant for any particular reaction, it is called reaction constant which is a measure of the susceptibility or vulnerability of the reaction to the polar effects of the substituent. Leaving aside the suffix, the equation could be written in a more general form as,

$$\log \frac{K}{K_o} = \sigma \ \rho$$

This equation called Hammett Equation is also a linear free energy relationship, as it is in the form of a linear equation.

$$\begin{array}{lcccc} \log & K & = & \sigma\rho & + & \log K_o \\ & (y) & & (xm) & & (C) \end{array}$$

Significance of σ (substituent constant)

Every substituent has a definite value for σ irrespective of the reaction. The magnitude and sign of σ are significant. A large negative value indicates the highly repelling nature of the substituent and a large positive value denotes the high electron withdrawing ability of that substituent at that position. For instance $\sigma_{mNO2} = +0.71$ and $\sigma_{pNO2} = +0.78$ reveal that the $-NO_2$ group is strongly electron withdrawing at the para position since –I and –M effects are operating whereas it is only –I effect at the meta position

Substiluent	σ_m	σ_p
NH_2	-0.16	-0.66
$N(CH_3)_2$	-0.21	-0.83
OH	+0.12	-0.35
OCH_3	+0.115	-0.27
CH_3	-0.07	-0.17
H	0 (as per definition)	0
Cl	+0.37	+0.227
Br	+0.39	+0.23
I	+0.35	+0.28
$-COCH_3$	+0.306	+0.52
CN	+0.56	+0.66
NO_2	+0.71	+0.78
$^{\oplus}N(CH_3)_4$	+0.90	+0.86

The strong electron releasing character of the amino groups is brought out by the large negative value at the para position due to the +M effect, and they activate the Ortho and Para positions for electrophilic substitution. Only a small negative value at meta position shows that the groups can not activate the meta position in an electrophilic substitution.

The generally high positive values of the halogens for meta positions indicate that the ring is deactivated at meta position, more than that at Para position where they have comparatively more negative value, hence they are O, P directing.

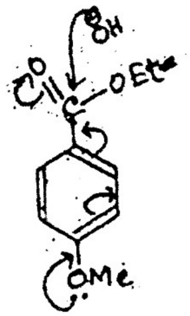
Differing signs for OH and OCH_3 groups for meta and para position indicate that the inductive and mesomeric effects are operating in opposite directions. Hence these groups have strong +M effect at para position (high negative) and activate the para position for electrophilic substitution, whereas positive value for meta position indicates electron withdrawal due to –I effect.

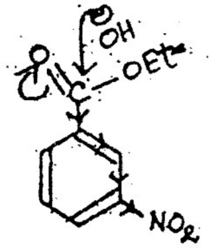
Significance of ρ (reaction constant)

Every reaction has a definite r value when the reaction occurs at a definite temperature and in a particular medium, no matter which m or p-substituent is present. For the ionization of p & m-substituted benzoic acids at 25°C in water, r = 1.00, as per the definition of σ_x, hence considered as a standard reaction. Since r is the slope of the straight line fore Hammett equation, it is possible to get it by plotting log k/k_0 vs σ_x for m & p positions.

Greater the ρ value, greater is the influence of the substituent through its polar effect on the reaction rate. Hence in the acid catalysed hydrolysis of methyl benzoate at 25°c, $\rho = -0.03$, indicating that the reaction rate is least influenced by the polarity of the substituent. On the other hand, ethyl benzoate under base catalysed conditions hydrolyses with $\rho = +2.51$, thus indicating the high influence of the polarity of the substituent on the reaction rate. A negative value for r indicates the development of positive charge near the reaction centre in the transition state and vice versa. The sign of ρ is also significant in combination with that of σ, for making useful predictions.

When σ and ρ values are positive $K > K_0$, (ie) the reaction rate is accelerated for all reactions whose ρ values are positive when substituted by electron withdrawing substituents. Accordingly, in the base catalysed hydrolysis of ethyl benzoates (ρ = +2.51), when a NO_2 group is attached at the meta position (σ = 0.71), $k/k_0 = 63.5$ and the reaction must be accelerated by 63.5 times. This prediction has been experimentally proved.



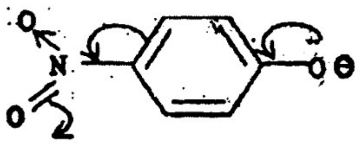


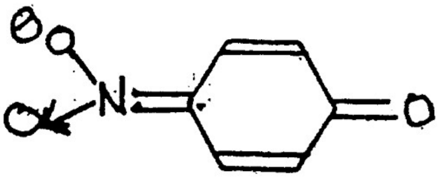
Similarly when a para OCH_3 group is introduced in the same substrate, (σ = -27 and ρ = +2.51), $k < k_0$, the reaction rate must be slowed down as the transition state is not stabilized. It has been shown experimentally that the reaction rate is retarded, as $k/k_0 = 0.21$,

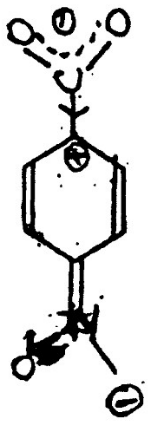
(ie) $k = 0.21\ k_0$.

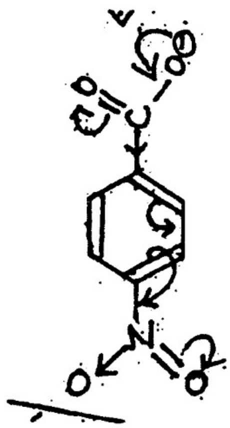
Deviations from Hammett Equation

Generally the equation holds good as long as the polar effect operating between the substituent and the reaction centre is purely inductive in nature. Deviations have been noticed when the reaction centre is directly connected by resonance with the substituent, and the phenomenon known as through conjugation









In p- Nitro phenol, the reaction centre viz, the phenolate oxygen and the Nitro substituent at para position are directly connected by resonance whereas in p-NO_2 benzoic acid, even though resonance is operating between the two ends, the resonance effect is carried to the reaction centre viz. the carboxylate oxygen only through induction mechanism and not by 'through conjugation'. Hence the σ_{PNO2} for ionization of benzoic acid cannot fit into the p-NO_2 phenol molecule and deviations are observed giving rise to non-liner plots. As per Hammett equation, $\sigma_{PNO2} = 0.78$ and $\rho = 2.1$ for the ionization of phenol, $k/k_n = 44$, but the experimental value is 680.

In molecules where 'through conjugation' operates, these substituents could be made to fall in line with Hammett equation using an alternate set of $\sigma^{\ominus}$ values for groups with –M effect and σ⊕ for +M effect, by consideration of σ_m values of such substituent when purely inductive mechanism prevails. For instance, $\sigma^{\pounds K}_{TPNO2} = +1.27$ and that of CN = +0.88. similarly $\sigma\oplus_{PN112} = -1.30$ and that of $OCH_3 = -0.78$.

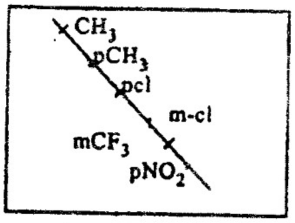
Applications of Hammett Equation

Significance of the stustituent constant and the reaction constant in predicting and calculating the rates of reaction serves as one of the important applications of Hammett equation (Refer Previous Pages)

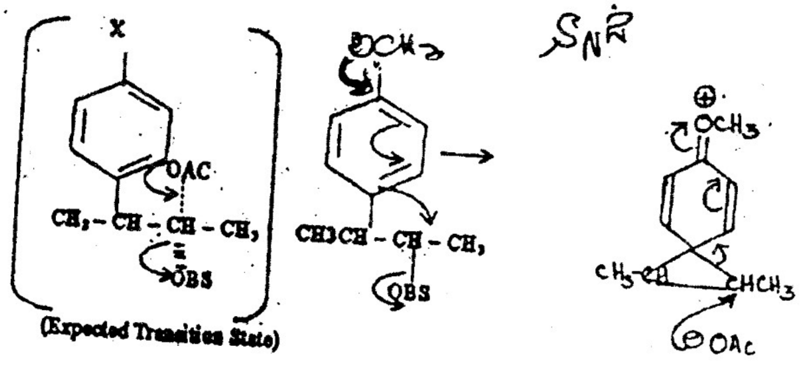
Whenever deviations are observed from the linearity of the equation, as indicated by the shape of the plot either concave or convex in shape, it is understood that the expected mechanism is not operating in the molecule. In a number of such instances, corrective mechanisms have been suggested and corroborated by experimental evidences.

1) Acetolysis of Meta or Para Substituted 2-Butyl Broslate

The given molecule is expected to undergo an SN^2 type of substitution at a fairly faster rate as the brosylate group is one of the best leaving groups. Since the ρ value is found to be negative (-1.46), this reaction must be accelerated by electron releasing substituents (σ in negative), according to Hammett equation.



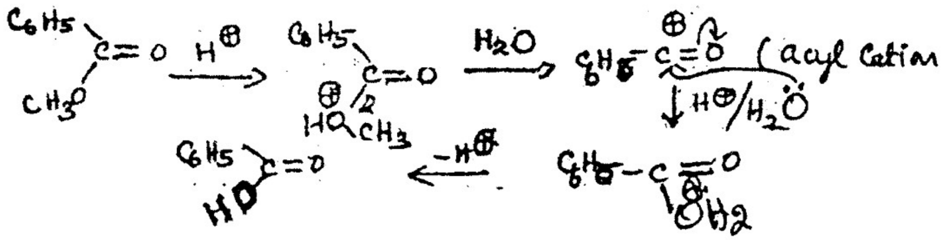
However the rate is found to increase enormously even strongly deviating from the linearity forming a concave curve when the group is strongly electron releasing. Hence an alternate reaction pathway has been suggested, which involves a neighbouring group participation mechanism, resulting in the formation of a stable cyclic phenonium ion intermediate, unlike the normal transition sate in an SN^2 mechanism.



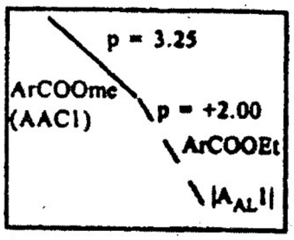
(Expected Transition State)

2) Acid Catalysed Hydrolysis of Ethyl Benzoate

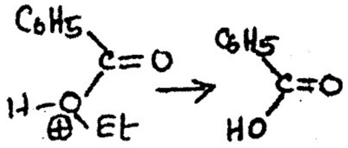
Hydrolysis of methyl benzoate with 99.9% H_2SO_4 has a e value of –3.25, which is unusually high for a normal A_{AC}^2 pathway (e = +0.03 with dil.H_2SO_4). The large negative value indicates the development of high positive charge near the reaction centre. Hence the mechanism in agreement with this concept must be as under (A_{AC}^1)



However, for ethyl benzoate, the pathway abruptly changes when the substituents are strongly electron withdrawing (σ_x is large positive),



indicating a decrease in the positive charge near the reaction centre (ρ = +2.00). This could be explained by the loss of an ethyl cation to relieve the reaction centre of the positive charge. But in the methyl ester with strongly electron withdrawing subsittudnts, the removal of a less stable methyl cation is not favoured.



$CH_3CH_2^{\oplus}$

These different mechanistic pathways in similar molecules under similar reaction conditions, would have gone unnoticed but for the Hammett equation.

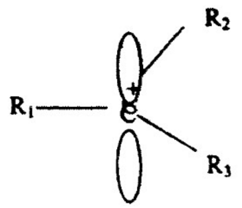
ORGANIC REACTION MECHANISM

Reaction Intermediates

The rate at which chemical reaction occurs, among other factors depends on the nature and stability of the intermediates formed during the course of the reaction. Unless the intermediate is sufficiently stabilized at the rate determining stage, rate of formation of the product is affected. The most common intermediates encountered in organic reactions are carbocations, carboanions, carbenes, nitrenes and free radicals.

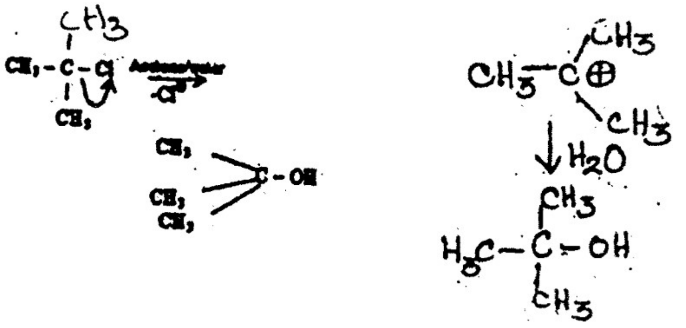
1) Carbocations (Carbonium Ions)

These positively charged carbon ions have an open sextet, hence election deficient in nature. They are planar in structure with (triangular) SP^2 hybridization, having an empty p-orbital perpendicular to the plane.

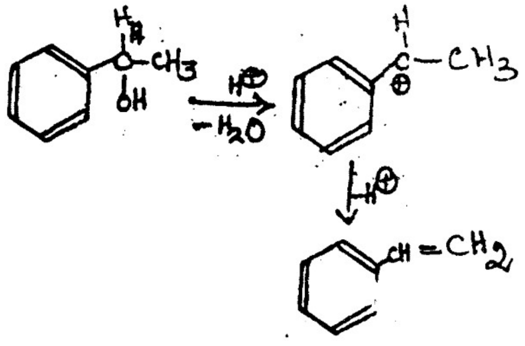


They are normally generated due to the heterolytic cleavage of a C - X bond where X is a heteroatom. Mostly SN^1 and E^1 reactions proced through the formation of carbonium ions. (refer under Nucleophilic substitution and elimination reactions)

(e.g)

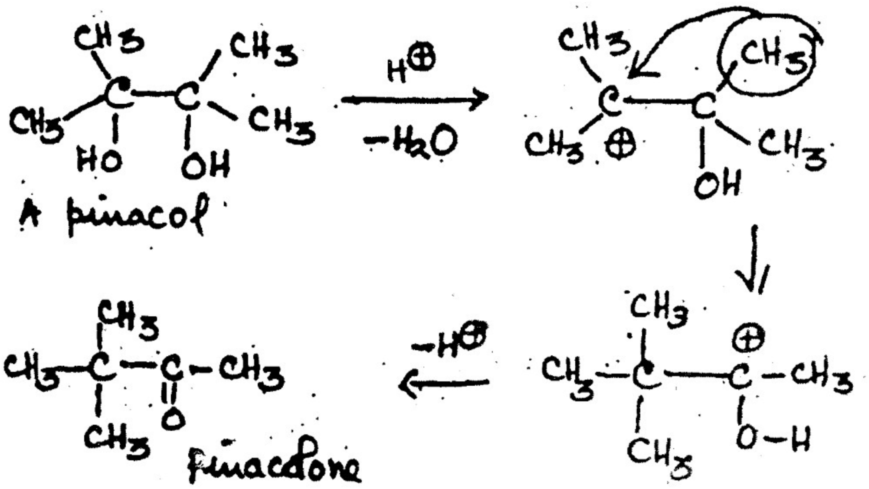


Similarly in an elimination reacti



A number of organic rearrangements proceed through the formation of carbonium ion intermediates.

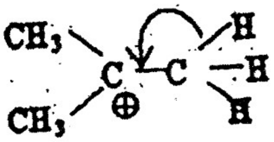
(e.g)

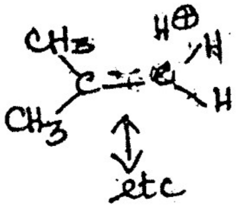


Two carbonium ion intermediates have been generated during the course of the reaction.

Stability of Carbonium Ions

Normally the stability of carbonium ions decreases in the order: tertiary > secondary > primary. This order of stability is mainly based on the hyperconjugation operating in these systems, causing stabilization due to charge delocalization.





At least nine hyper conjugative contributing structures are possible in the t-butyl carbonium ion, enhancing the stability. In the isopropyl carbonim ion only six structures are possible and in ethyl, only three such structures contribute. Accordingly their resonance energies decrease in the same order,

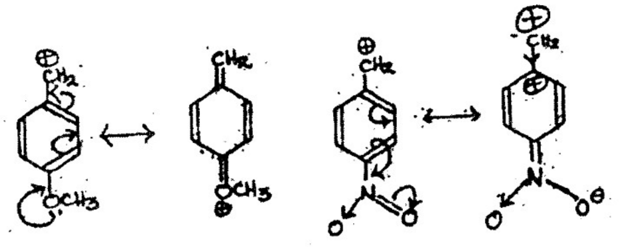
84 k.cals mol^{-1} > 60 k.cal mol^{-1} >36 k.cal mol^{-1},

for tertiary, secondary and primary structures.

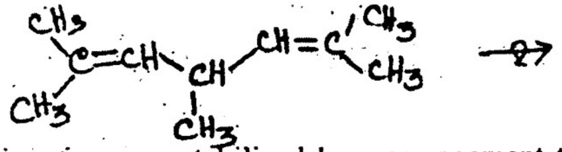
Resonance stabilization is a major factor in aromatic as well as allylic systems.

$H_2 = CH - \overset{\oplus}{CH_2} \qquad \overset{\oplus}{CH_2} - CH = CH_2$

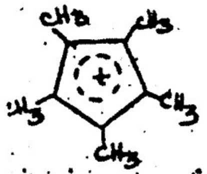
Electron releasing groups are found to stabilize and electron withdrawing groups destabilize the carbonium ions.



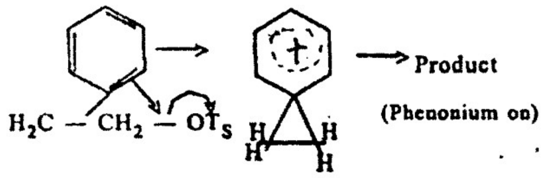
(stablized) (destabilized)



Certain open chain carbonium ions are stabilized by rearrangement to form cyclic carbonium ions.(e.g)

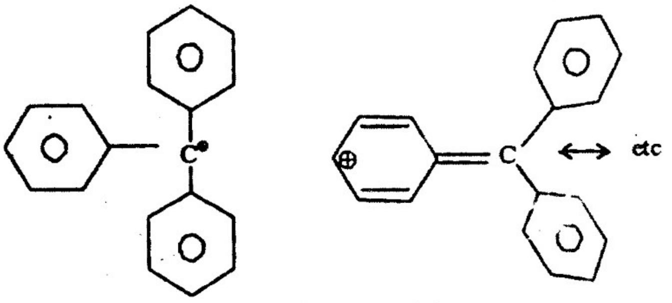


Bridged carbonium ions are found to exist in a number of nucleophilic substitution reactions when a neighbouring group participates in reactions (e.g)



Such a non-classical carbonium ion formation has accelerated a number substitution reactions.

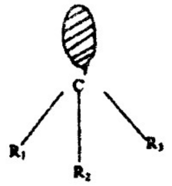
All these carbonium ions have been detected by spectroscopic techniques but not isolated, as their lifetime is less. However, one of the most stable carbocations like triphenyl methyl as its perchlorate has been isolated.



High resonance stabilization has made it possible to isolate such ions.

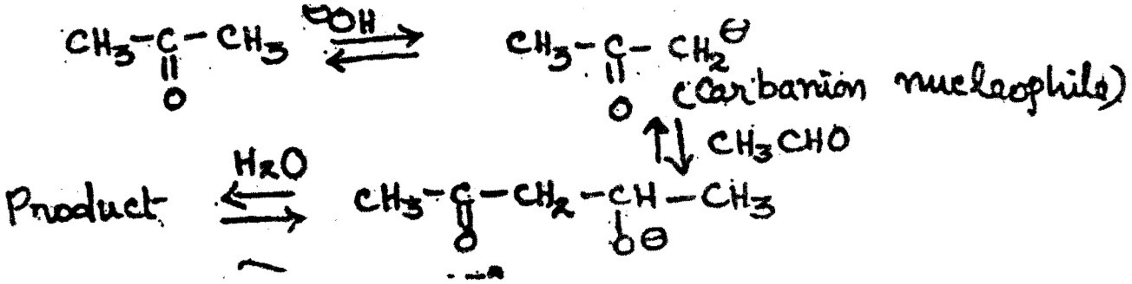
2) Carboanions (Carbanions)

A carbanion has a completed octet, with an unshared electron pair and a pyramidal configuration, the lone pair being at the apex of the pyramid. In contrast to the carbonium ion, the carbanionic carbon is SP^3 hybridized.



Carbanions are normally generated during the heterolytic cleavage of a C – H bond, and a number of condensation reactions and molecular rearrangements proceed through the formation of a carbanion intermediate, which acts as a nucleophile. In base catalysed reaction strong bases are used only to abstract a proton from the substrate molecule so as to form a carbanion.

(e.g) In an aldol type condensation, an aldehyde or ketone loses a proton to form a carbanion, which later on acts as a powerful nucleophile.

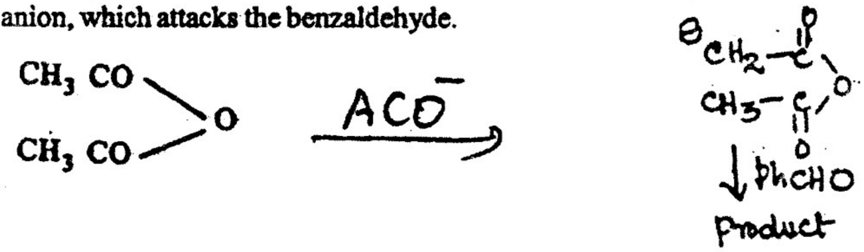


$$CH_3-\underset{\underset{O}{\|}}{C}-CH_3 \overset{^{\ominus}OH}{\rightleftharpoons} CH_3-\underset{\underset{O}{\|}}{C}-CH_2^{\ominus} \text{ (carbanion nucleophile)}$$

$$\uparrow\downarrow CH_3CHO$$

$$\text{Product} \overset{H_2O}{\rightleftharpoons} CH_3-\underset{\underset{O}{\|}}{C}-CH_2-\underset{\underset{O^{\ominus}}{|}}{CH}-CH_3$$

In the perkin's reaction, the base (Acetate ion) removes a proton from the anhydride to form a carbanion, which attacks the benzaldehyde.

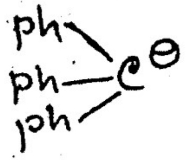


$$\begin{matrix}CH_3CO \\ CH_3CO\end{matrix}\!\!>O \xrightarrow{AC\bar{O}} \begin{matrix}{}^{\ominus}CH_2-\overset{\overset{O}{\|}}{C}\diagdown \\ \qquad\qquad O \\ CH_3-\underset{\underset{O}{\|}}{C}\diagup\end{matrix}$$

$$\downarrow PhCHO$$

$$\text{Product}$$

Similarly triphenyl methyl carbanion is produced when sodamide acts on triphenyl methane.



Stability of Carbanions

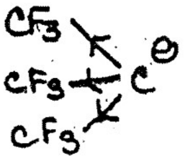
Any factor that delocalises the negative charge over the carbon will stabilize the ion. Among these factors are:

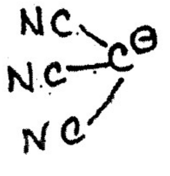
a) Electron withdrawing inductive and mesomeric effects.

b) Increase in S character ate the carbon.

c) Conjugation & aromatisation.

Methyl carbanion $(CH^{\ominus}_3)$, is stabilized enormously when strongly electron withdrawing fluorine atoms are attached,



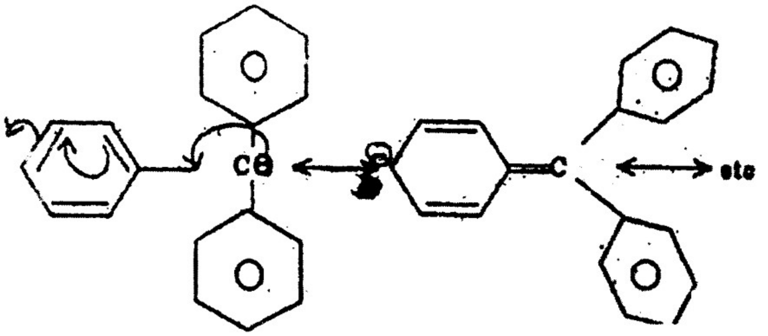


as indicated by the pK$_a$ values of the corresponding acids given in brackets. In contrast, electron releasing alkyl groups are found to destabilize the anions in the following order:

$^{\ominus}CH_3 > CH_3-CH^{\ominus}_2 > (CH_3)-C^{\ominus}H > (CH_3)_3\ C^{\ominus}$

(Most stable) (Least stable)

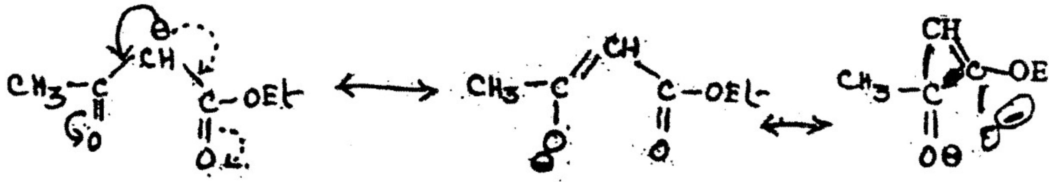
Similarly the triphenylmethyl carboanion is more stable compared to the t-butyl carbanion, due to the mesomeric effect operating in the former.



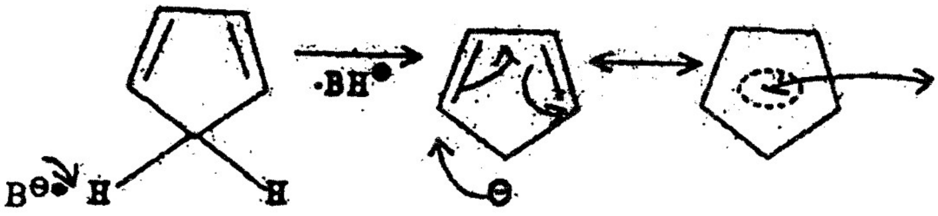
The easy formation of acetylide carbanion compared to that in ethylene and ethane, shows the hybridization effect working in these ions. The highest S-character in the acetylide carbon, not only facilitates the removal of hydrogen to form the anion but also stabilizes the carbanion by withdrawing the charge towards the nucleus. Hence the observed order:

$CH_3 - CH^{\ominus}_2 < CH_2 = C^{\ominus}H < CH \equiv C^{\ominus}$

The interaction of negative charge with the π electrons in β -ketoesters indicates the conjugative ability of the lone pair in stabilizing the carbanions, coupled with the strong electron withdrawal by the carboxyethyl group.

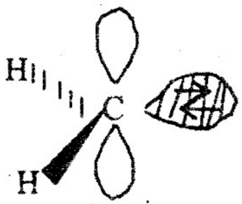


The cyclopentadienyl carbanion with an aromatic sextet is found to have an extra stability in the form of aromaticity which facilitates the abstraction of a proton by a base from the diene to form the carbanion.

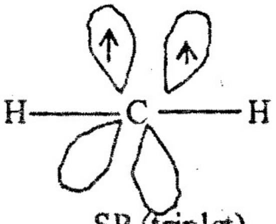


3) Carbenes

Carbenes are the derivatives of methylene ($:CH_2$) where the carbon is SP^2 hybridized in the singlet state and SP hybridized in the triplet state.

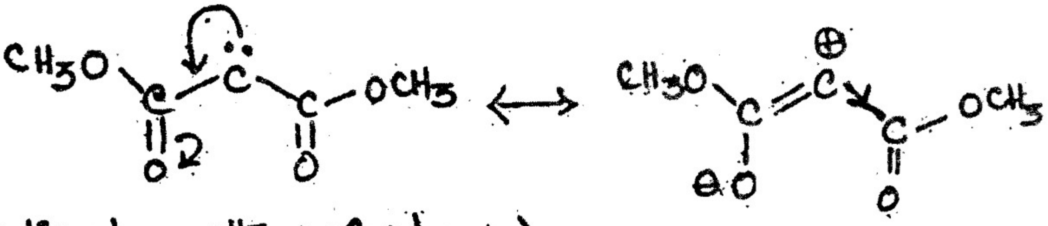


SP^2 (singlet)



SP (triplet)

These are highly electron deficient reactive species having only transient existence and they have not been isolated. However suitably substituted carbenes are found stabilized due to delocalization. They have, been generated by a host of methods, during the course of certain reactions.



(dicarbomethoxy carbene)

Diazo compounds undergo photochemical decomposition to furnish singlet carbene, when irradiated in ether (singlet). However,

$$H_2C\ N_2 \xrightarrow{h\gamma} :CH_2 + N2$$
(Singlet)

when irradiated in the presence of a photosensitizer the triplet carbene is produced which is found to be more stable.

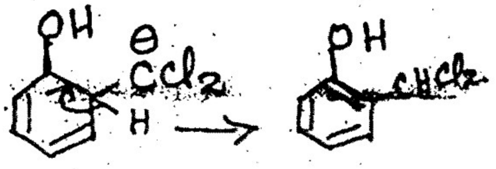
$$H_2CN_2 \xrightarrow[Ph_2CO]{h\nu} \underset{(triplet)}{:CH_2} + N_2$$

In the haloform reaction as well as in the Reimer-Tiemanr reaction, dichloro carbene is the reactive intermediate, due to thermal eliminations.

$$CHCl_3 + OH^- \longrightarrow {}^{\ominus}CCl_3 + H_2O$$

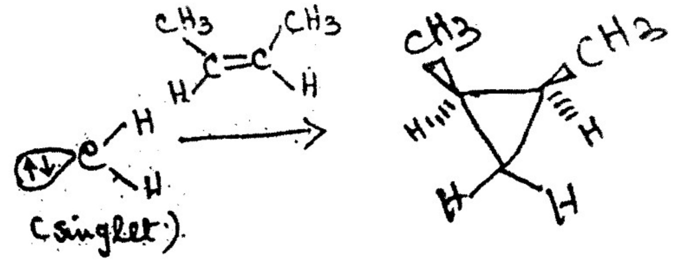
$${}^{\ominus}CCl_3 \longrightarrow :CCl_2 + Cl^-$$

In the Reimer – Tiemann reaction, dichloro carbene acts as the electrophile.

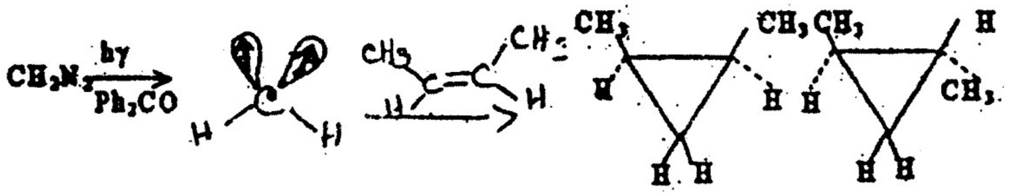


Since carbenes are highly reactive, they have never been isolated in the free state but trapped in a combined state, through addition of olefins producing a cyclopropane derivative.

Singlet carbene addition is found to be sterospecific.(e.g)



But triplet carbene addition to olefins is no longer stereo specific, since it involves spin inversion across the olefinic bond.



4) Nitrenes

There are univalent reactive nitrogen derivatives (R – N), electrically nutral isoelectronic with carbenes and exist in the singlet as well as triplet electronic states.

The simplest of nitrenes is HN similar to carbenes, they are also electron deficient species.

$$\underset{(singlet)}{R - \ddot{N}\ \uparrow\downarrow} \qquad\qquad \underset{(triplet)}{R - \ddot{N}\uparrow\uparrow\cdot}$$

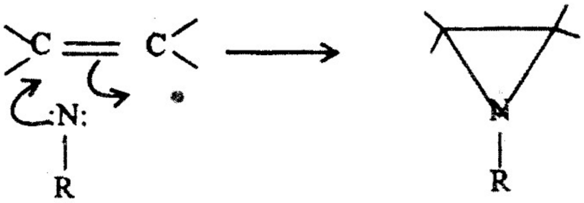
They are normally generated by the photolysis of an azide or hyarazoic acid. Alkyl isocyanates also give nitrenes on irradiation.

$$HN_3 \xrightarrow[\text{(uv)}]{h\gamma} N_2 + \ddot{\underset{\cdot\cdot}{N}}H$$

$$RN = \overset{\oplus}{N} = \overset{\ominus}{N} \xrightarrow{h\gamma} R-\ddot{N} + N_2$$

$$R-N=C=O \xrightarrow{h\gamma} R-\ddot{N} + CO$$

They are even more reactive than carbenes, and act as electrophiles



Self coupling also occurs leading to

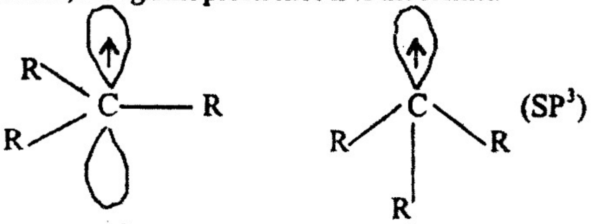
$$R\ddot{N}: + \ddot{\underset{\cdot\cdot}{N}}R \longrightarrow R-\ddot{N}=\ddot{N}-R$$

$$R_2CH-\ddot{N}: \longrightarrow R_2C=NH$$

5) Free Radicals

Fragments of molecules carrying odd electrons are known as free radicals. They are highly unstable species whose lifetime is incomparably low relative to that of any other intermediates and hence a tendency to dimerise.

The shape of the alkyl free radical is not yet conclusively established. It is considered to take a planar or a pyramidal configuration, though the preference is to the former.



(SP²) (Planar) (SP³) (Pyramidal)

Electronegative groups attached to the radical make it more pyramidal, the character increasing in the order, as the S – character of the hybridized orbital is also found to increase in the order.

$$\bullet CH_3 < \bullet CH_2F < \bullet CHF_2 < \bullet CF_3$$

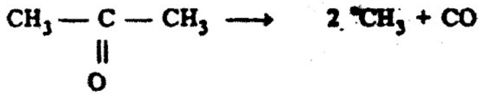
(mostly planar) (mostly pyramidal)

But the planar radical has the odd electron in a pure P – orbital. The relative ease of formation of acyclic free radicals compared to that at bridge head position indicates the greater tendency towards the planar geometry.

Generation of Free Radicals

a) Photolysis & Tnermolysis

Use of an intense UV light (200 nm) in irradiation of organic molecules (Flash photolysis) generate free radicals easily compared to any other techniquès.



$$CH_3-\underset{\underset{O}{\|}}{C}-CH_3 \longrightarrow 2\,{}^{\bullet}CH_3 + CO$$

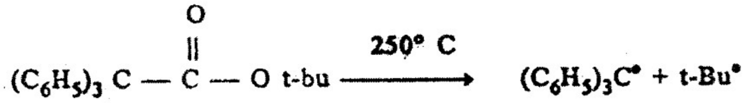
$$Cl_2 \xrightarrow{h\gamma} 2Cl^{\bullet}$$

$$RO-N=O \xrightarrow{h\gamma} RO^{\bullet} + NO$$

$$R-N=N-R \xrightarrow{h\gamma} 2R^{\bullet} + N_2$$

$$C_6H_5-C\equiv C-I \xrightarrow[\text{Benzene}]{h\gamma} C_6H_5C\equiv C^{\bullet} + I^{-}$$

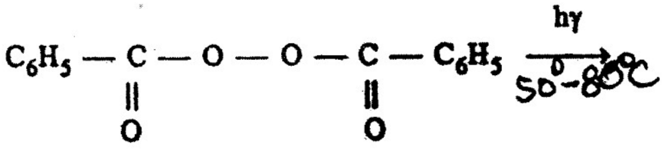
In general organic molecules with high bond dissociation energy can be dissociated homolytically at a sufficiently low temperature, under photochemical conditions if certain groups in the molecule can absorb UV radiation, (e.g) Dissociation of azo, diazo, peroxides, acetates etc require 150° to 250°c



$$(C_6H_5)_3C-\overset{\overset{O}{\|}}{C}-O\text{ t-bu} \xrightarrow{250^\circ C} (C_6H_5)_3C^{\bullet} + \text{t-Bu}^{\bullet}$$

$$\text{t}-\text{bu}-N=N-\text{t}-\text{bu} \xrightarrow{180-200^\circ C} 2\text{t.bu}^{\bullet} + N_2$$

Dissociation of peroxides into free radicals is easier compared to other free radicals, requiring lower energy (50°–80°c) hence generated under photo chemical or thermal conditions



$$C_6H_5-\underset{\underset{O}{\|}}{C}-O-O-\underset{\underset{O}{\|}}{C}-C_6H_5 \xrightarrow[50^0-80^0C]{h\gamma}$$

$$2C_6H_5 + 2CO_2$$

b) Redox Process

In Fenton's reagent, hydroxyl free radicals are generated by a redox process. In the oxidation of phenols using $K_3[Fe(CN)_6]$, the electron acceptor is the metal in the high oxidation state (Fe^{3+})

$$Fe^{2+} + HO-OH \longrightarrow Fe^{3+} + OH + OH^{\ominus}$$