

General Organic Chemistry

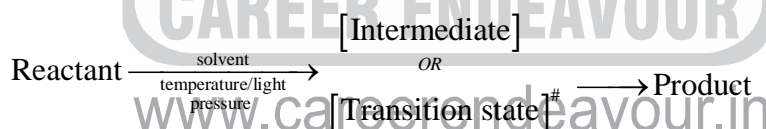
1.1 Introduction:

Organic reaction involve the breaking and making of covalent bonds. The breaking and making of covalent bonds usually occurs in several discrete steps before transformation into product. The detailed sequential description of all steps of the transformation into products is called the mechanism of a reaction.

Complete information regarding all the steps is seldom obtained. However, a good deal of data can be gathered from the following

- study of kinetics of the reactions
- isolation of intermediate, if isolable.
- study of reactions in the presence of other similar substrate.
- study of the isotopically labelled atom in the reactants.
- trapping of free radicals
- crossover experiments
- stereochemical aspects etc.

Reaction mechanism containing following tools



(i) Reactant :

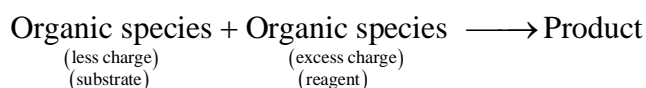
Reactant are classified into substrate and reagent

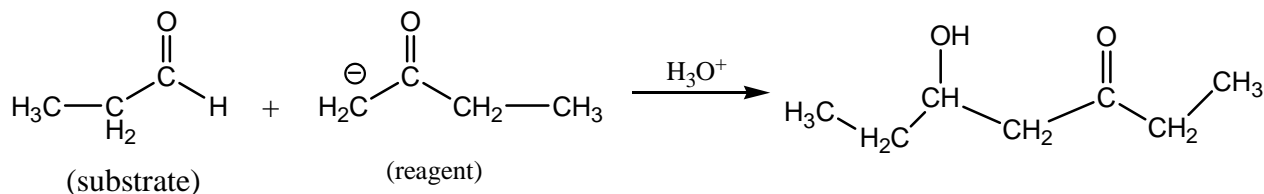
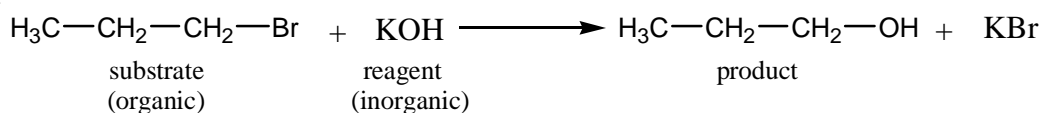
- substrate \Rightarrow species at which reagent attack.
- Reagent \Rightarrow attacking species (more reactive species)

Case-I: If reaction occurs between organic and inorganic species, organic species act as substrate and inorganic species act as reagent.

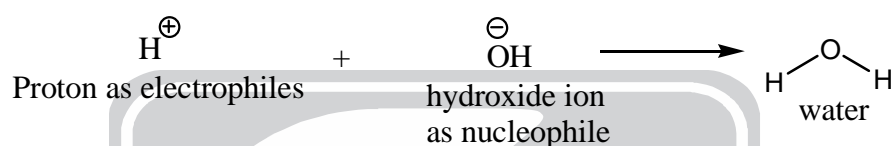


Case-II: If reaction takes place between organic species then higher charge species act as reagent, other species act as substrate.



Example:**1.2. Electrophiles :**

(Electron loving species) electrophiles are electrons-deficient species and tend to attack the substrate at a site of high electron density. They may be neutral species as exemplified by Lewis acid (such as BF_3 , AlCl_3 , ZnCl_2), carbene and carbocations.

**Classification of electrophiles:**

(a) Species having positive charge

Example : H^+ , R^+ , Cl^+ , NO^+ , NO_2^+ , $\text{C}_6\text{H}_5-\text{N}_2^+$, $\text{CH}_3-\text{C}^+=\text{O}$ etc.

(b) Neutral species having vacant p-orbitals

Example : BF_3 , BCl_3 , BBr_3 , carbene, etc.

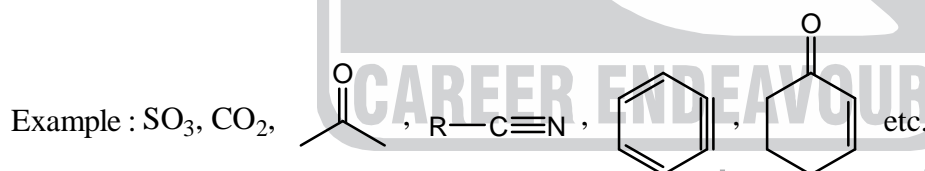
(c) Species having vacant d-orbital

Example : FeCl_3 , ZnCl_2 , FeCl_2 etc.

(d) Species having low lying σ -antibonding molecular orbital.

Example : Br_2 , Cl_2 , I_2 etc.

(e) π -bonding molecule:



(f) Element in their atomic state:

Example : O, S etc.

1.3. Nucleophiles:

(Nucleus-loving species) Nucleophiles are electron donor species. Nucleophilic reagents tend to attack the electron deficient species (electrophiles).

Classification of Nucleophiles:

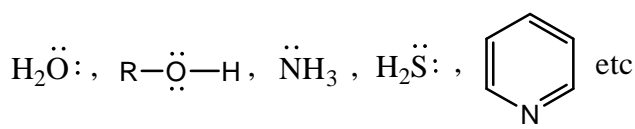
(a) Negative charge species:

OH^- , OR^- , SH^- , SR^- , R^- , Cl^- , Br^- , I^- etc

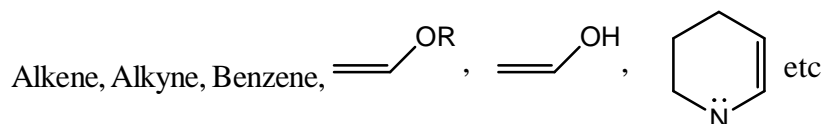
(b) Organometallic reagent:

R^-MgX , R^-Li , R_2^-CuLi , R_2^-Cd , R_2^-Zn etc

(c) Lone pair containing species:



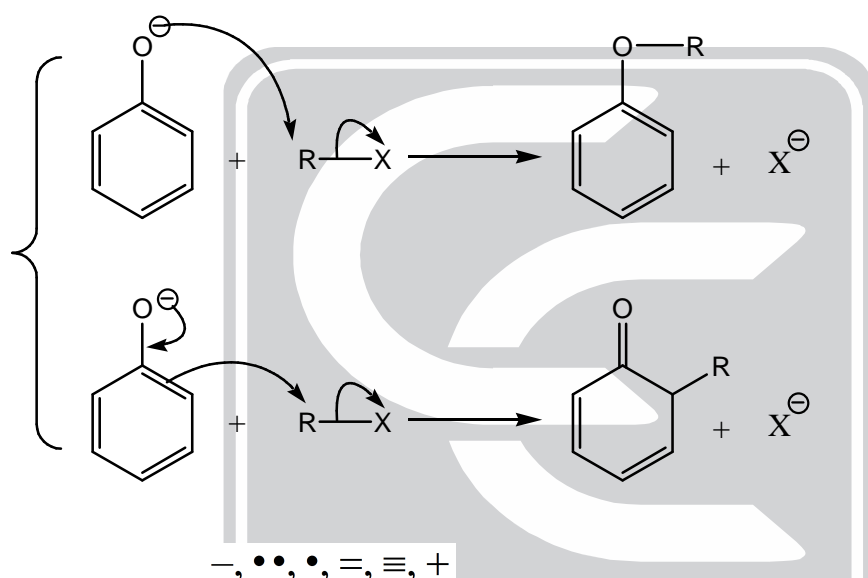
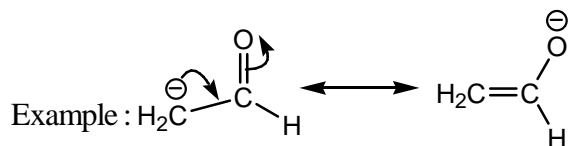
(d) π -bonded molecules:




Note: Some species behave as the electrophiles as well as nucleophiles

Example : Br_2 , Cl_2 , I_2 , etc.

Ambidentated nucleophile : Those nucleophile which possess more than one site for E^+ attack but at the same time only one side is used to form bond with electrophile. It is called ambidentated nucleophile, such type of ambidentated nucleophile are regioselective.

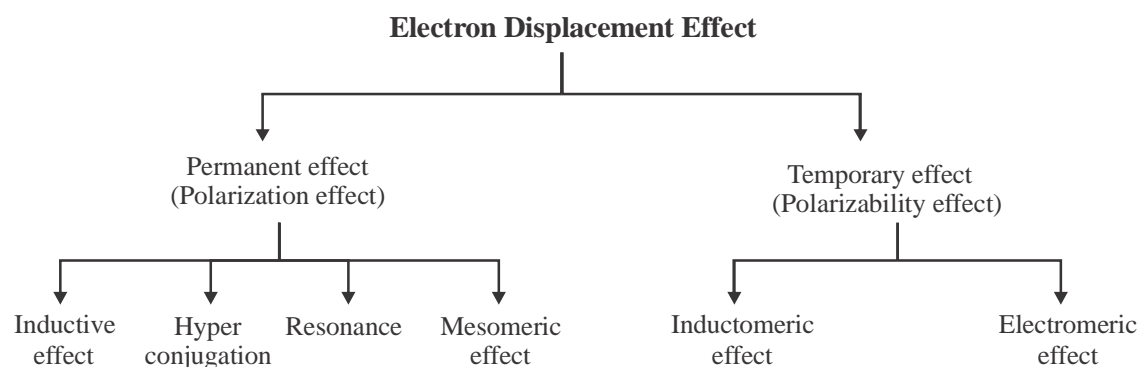


Note:  Decreasing order of nucleophilicity
[Electronegativity \propto % of s-character]

Note : Electron Displacement Effects:

Effect occurring due to displacement of electron in organic compound is called **Electron Displacement Effect** or electron delocalisation effect.

Electron displacement effect is of mainly two types.

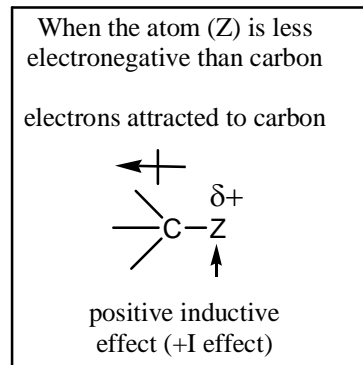
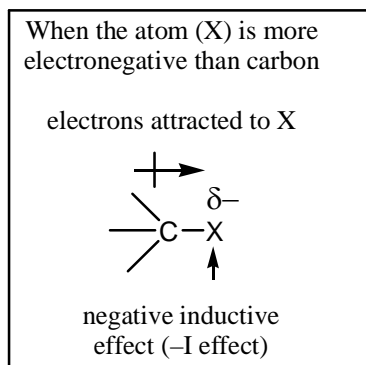


Other Effect:

(a) Steric inhibition of resonance (b) Ortho effect.

1.4. Inductive effects:

In a covalent bond between two different atoms, the electrons in the σ – bond are not shared equally. The electrons are attracted towards the most electronegative atom. An arrow drawn above the line representing the covalently bonded electrons shifts towards higher electronegative atom can show this. Electrons are pulled in the direction of the arrow.

**-I groups**

X=Br, Cl, NO₂, OH, OR, SH,
SR, NH₂, NHR, NR₂, CN, CO₂H,
CHO, COR

The more electronegative the atom(X),
the stronger the -I effect

+I groups

Z=R(alkyl or aryl),
metals (e.g. Li or Mg)

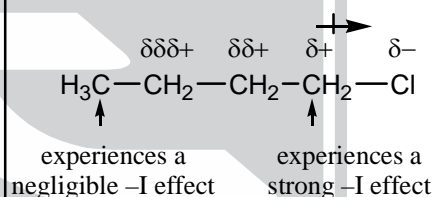
The more electropositive the atom (Z),
the stronger the +I effect.

Pauling electronegativity scale

K = 0.8	I = 2.5
C = 2.5	Br = 2.8
N = 3.0	Cl = 3.0
O = 3.5	F = 4.0

Higher the value, more
electronegative will be atom

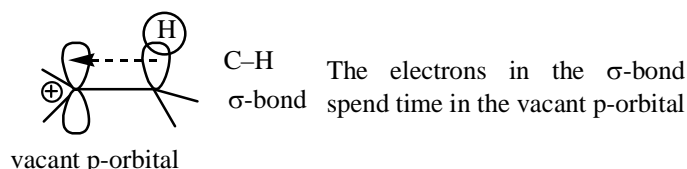
The inductive effect of the atom rapidly
diminishes as the chain length increases



The overall polarity of a molecule is determined by the individual bond polarities, formal charges and lone pair contributions, and this can be measured by the dipole moment (μ). Higher the dipole moment (measured in debyes (D)), more polar will be compound.

1.5. Hyperconjugation: www.careerendeavour.in

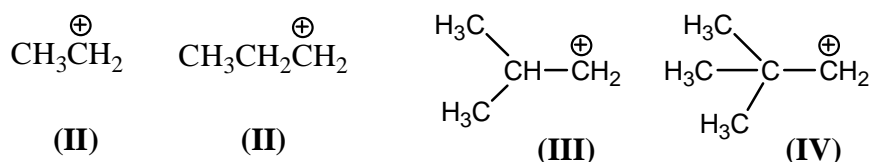
A σ – bond can stabilise a neighbouring carbocation (or positively charged carbon) by donating electrons to the vacant p-orbital. The positive charge is delocalised or ‘spread out’, and this stabilising effect is known as “no-bond resonance”.

**Points to Remember :**

Number of α hydrogen \propto number of hyperconjugating structure \propto stability

$$\propto \frac{1}{\text{Heat of hydrogenation}} \propto \text{Polarity} \propto \text{dipole moment} \propto \frac{1}{\text{bond length}}$$

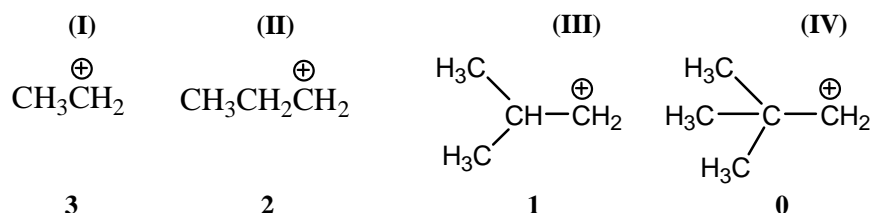
Problem : The correct order for the stability among following compound is



(a) I > II > III > IV (b) I > III > IV > II (c) IV > III > II > I (d) IV > III > I > II

Soln. Number of α hydrogen \propto stability.

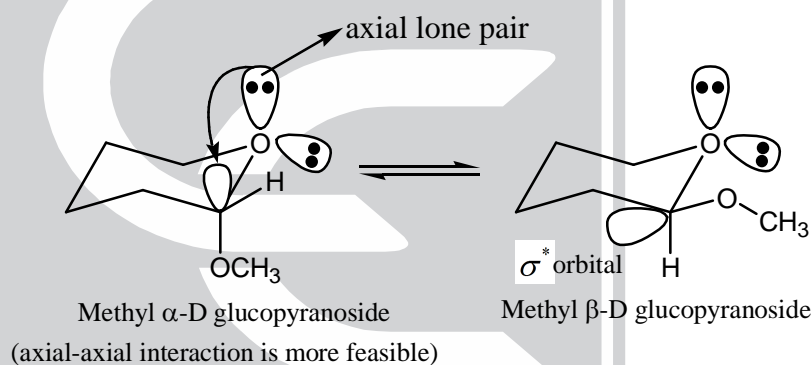
Thus,



Stability, I > II > III > IV

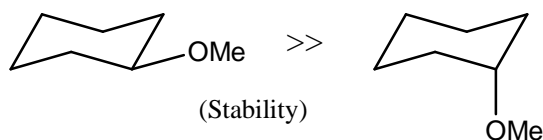
Hence, option (a) is correct.

Problem : Which is more stable methyl α -D glucopyranoside or methyl β -D glucopyranoside.



There is stabilising interaction i.e. hyperconjugation between the unshared pair on the hetero atom and σ^* orbital for the axial C–X bond in the case of α anomer, thus it is more stable as compared to its β analogue in which there is no such interaction.

Note : If oxygen is replaced by carbon, there is no such stability interaction as like as above. Thus, stability can only be decided on steric ground. Thus stability order for such species will be

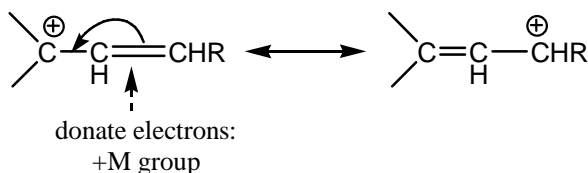


1.6. Mesomeric effects:

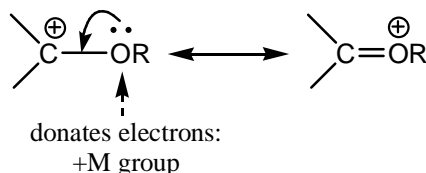
Whilst inductive effects pull electrons through the σ – bond framework, electrons can also move through the π – bond network. A π – bond can stabilise a negative charge, a positive charge, a lone pair of electrons or an adjacent bond by resonance (i.e. delocalisation or ‘spreading out’ of the electrons). Curly arrows are used to represent the movement of π or non-bonding electrons to give different resonance forms. It is only the electrons, not the nuclei, that move in the resonance forms and a double-headed arrow is used to show their relationship.

(a) Positive mesomeric effect:

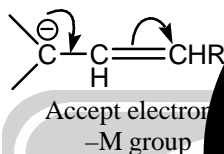
- When a π -system donate electrons, the π -system has a positive mesomeric effect (+M effect).



- When a lone pair of electrons is donated, the group donating the electrons has a positive mesomeric effect.

**(b) Negative mesomeric effect:**

- When a π -system accepts electrons, the π -system has a negative mesomeric effect (-M effect).



The actual structures of the cations or anions are resonance forms. All resonance forms must have the same overall charge and the same number of electrons.

-M groups generally contain an empty orbital or a π -bond(s):
 CHO, C(O)R, CO₂H, CO₂Me, aldehydes, ketones, acids, esters, alkenes etc.

+M groups generally contain at least a lone pair of electrons or a π -bond(s):
 $\ddot{\text{Cl}}$, $\ddot{\text{Br}}$, $\ddot{\text{O}}\text{H}$, $\ddot{\text{O}}\text{R}$, $\ddot{\text{S}}\text{H}$, $\ddot{\text{N}}\text{H}_2$, $\ddot{\text{N}}\text{HR}$, $\ddot{\text{N}}\text{R}_2$, aromatic, alkenes etc.

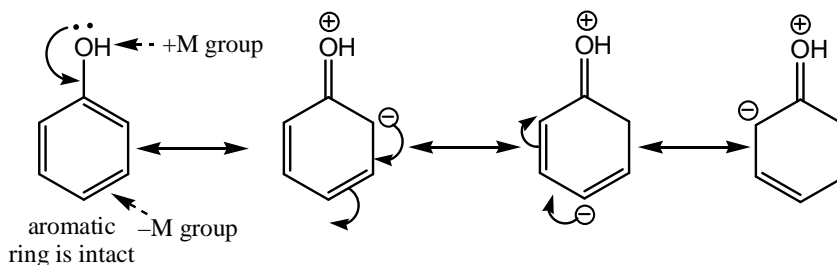
Aromatic (or aryl) groups and alkenes can be both +M or -M effect.

In neutral compounds, there will always be a +M and -M group(s):

One group donates (+M) the electrons and the other group(s) accepts the electrons(-M).



All resonance forms are not of the same energy. In phenol, for example, the resonance form which the intact aromatic benzene ring is expected to predominate.



As a rule of thumb, the more resonance structures an anion, cation or neutral π -system can have, the more stable it is.

Inductive versus mesomeric effects:

Mesomeric effects are generally stronger than inductive effects. A +M group is likely to stabilise an anion more effectively than a +I group.

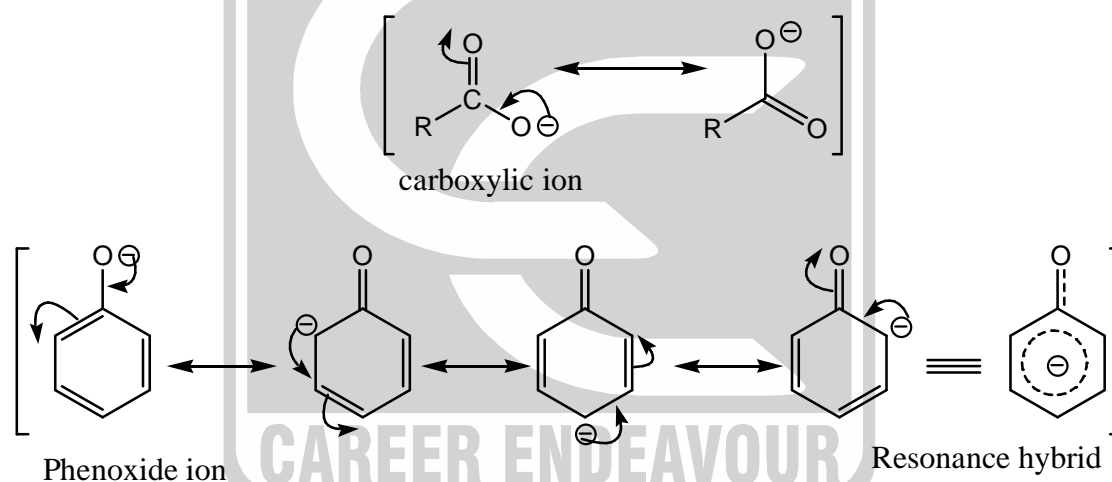
Mesomeric effects can be effective over much longer distances than inductive effects, provided that conjugation is present (i.e. alternating single and double bonds). Whereas inductive effects are determined by distance, mesomeric effects are determined by the relative positions of +M and -M groups in a molecule.

1.7. Resonance:

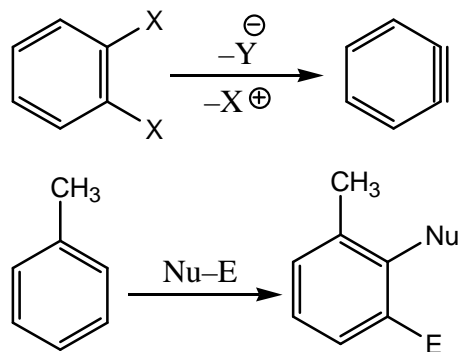
The different structure of a compound divided by different methods of pairing electrons in a fixed atomic skeleton are called resonance or canonical structure. The actual structure of the compound is then a combination of these structures and hence the compound is called a resonance hybrid. A hybrid is more stable than any one of the contributing structures. The contributing resonance structures are shown by double-headed arrows (\leftrightarrow) indicating that the real structure involves both ways of pairing electrons.

Key point about resonance:

- Resonating structure/contributing structure/canonical structure are imaginary/hypothetical, while resonance hybrid is the true structure.
- Resonance involves the delocalization of lone pair and π -electrons.
- Resonance is an intramolecular process.
- Resonance must follow the Lewis octet rule, i.e. C-atom, N-atom never pentavalent and O-atom never tetravalent.
- In the resonating structure arrangement of atoms remains the same, there should differ only w.r.t. arrangement of electrons.
- Resonance stabilisation is greatest, when there are equivalent resonating structures.



- The energy difference between resonance hybrid and most stable resonating structure is called resonance energy.
- Resonance works only at ortho and para positions with equal intensity; it never works at the meta position.
- Resonance proceeds in the system via π -electrons.
- Hyperconjugation works just like resonance.

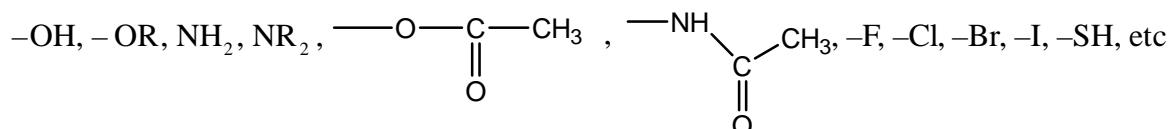
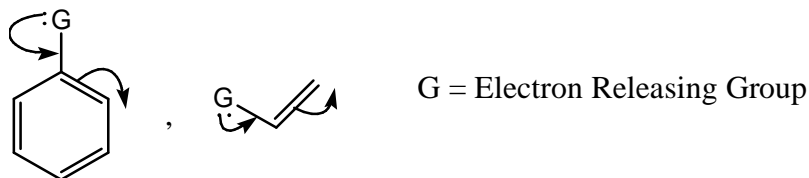
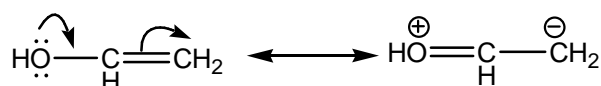


Classification of Resonance:

(A) +R effect (B) -R effect

(A) +R effect (Electron releasing effect):

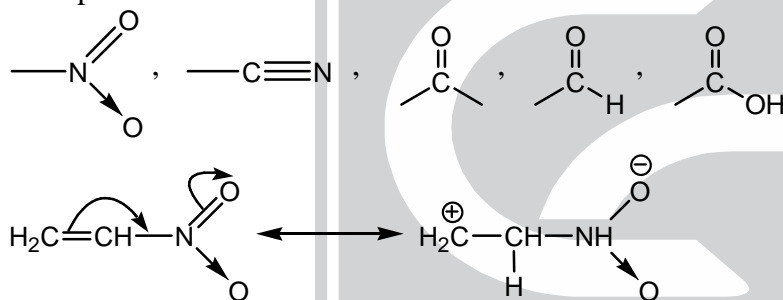
Lone pair of electron density containing compound attached with conjugation.

**(B) -R effect (Electron withdrawing effect):**

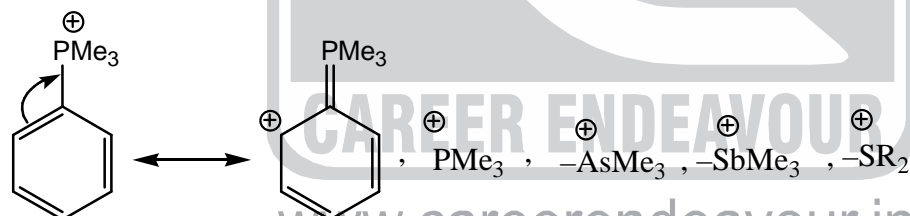
Electronegative atom attached with multiple bond containing compound

(a) Electron withdrawing resonance effect

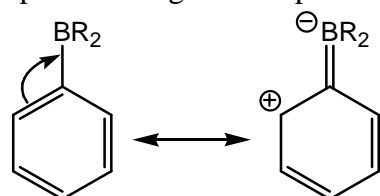
Example :



(b) Species having Vacant d-orbitals

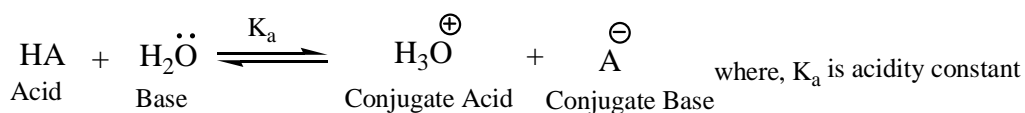


(c) Species having vacant - p - orbitals:

**1.8. Application of inductive effect, hyperconjugation and mesomeric effect:****Acidity and basicity:**

Acids: An acid is a substance that donates a proton (Bronsted-Lowry). Acidic compounds have low pK_a values and are good proton donors, as the anions (or conjugate bases), formed on the deprotonation, are relatively stable.

In water:



The more stable the conjugate base the stronger the acid

$$K_a = \frac{[\text{H}_3\text{O}^+][\text{A}^-]}{[\text{HA}]}$$

As H_2O is in excess

$$\text{p}K_a = -\log_{10} K_a$$

The higher the value of K_a , the lower the $\text{p}K_a$ value and the more acidic is HA

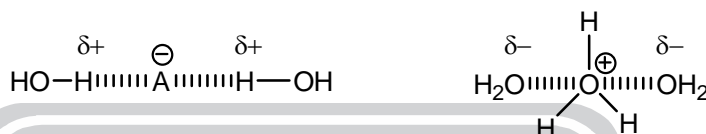
The $\text{p}K_a$ -value equals the pH of the acid when it is half dissociated. At pH above the $\text{p}K_a$ the acid exists predominantly as the conjugate base in water. At pH below the $\text{p}K_a$, it exists predominantly as HA.

pH = 0 (strongly acidic)

pH = 7 (neutral)

pH = 14 (strongly basic)

The $\text{p}K_a$ -values are influenced by the solvent. Polar solvents will stabilise cations and/or anions by solvation, in which the charge is delocalised over the solvent (e.g. by hydrogen-bonding in water).



The more electronegative the atom bearing the negative charge, the more stable the conjugate base (which is negatively charged).

$\text{p}K_a$	3		16		33		48
Most acidic	HF	>	H_2O	>	NH_3	>	CH_4
	increasing electronegativity						

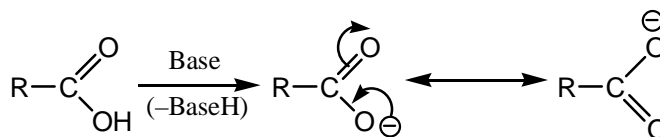
Therefore, F^- is more stable than H_3C^- .

The conjugate base can also be stabilised by $-I$ and $-M$ groups which can delocalise the negative charge. (The more spread out the negative charge, the more stable it is)

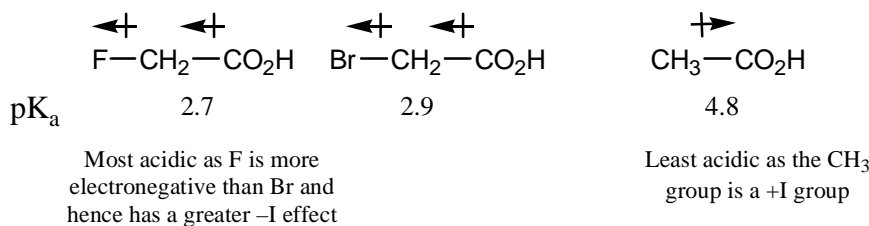
$-I$ and $-M$ groups therefore lower the $\text{p}K_a$, while
 $+I$ and $+M$ groups raise the $\text{p}K_a$

(a) Inductive effects and carboxylic acids:

The carboxylate anion is formed on deprotonation of carboxylic acids. The anion is stabilised by resonance (i.e. the charge is spread over both oxygen atoms) but can also be stabilised by the R group if this has a $-I$ effect.



The greater the $-I$ effect, the more stable the carboxylate anion and the more acidic is carboxylic acid.

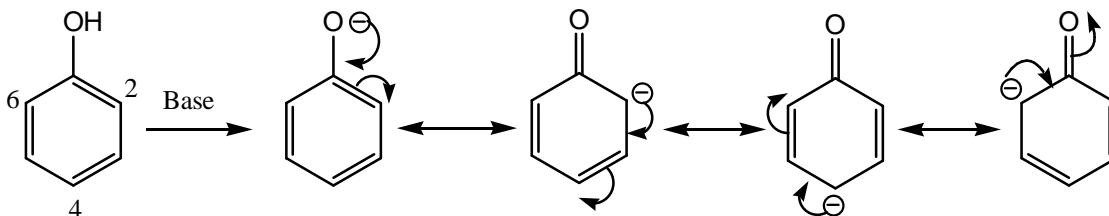


(b) Inductive and mesomeric effects and phenols:

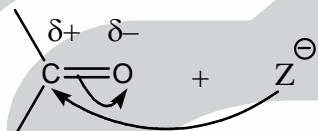
Mesomeric effects can also stabilise positive and negative charges.

The negative charge needs to be on adjacent carbon atom for a $-M$ group to stabilise it
The positive charge needs to be on adjacent carbon atom for a $+M$ group to stabilise it

On deprotonation of phenol the phenoxide anion is formed. This is stabilised by delocalisation of the negative charge at the 2-, 4- and 6-positions of the benzene ring.

**Temporary Effect :****(a) Electromeric Effect :**

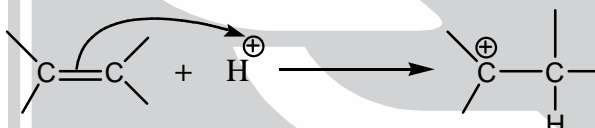
- Temporary effect.
- Takes place between two atoms joined by a multiple bond
- Occurs at requirement of attacking reagent.



Instantaneous shift of electron pair of carbonyl group towards oxygen.

It is of two types.

(1) +E effect : Transition of electron towards the attacking reagent.



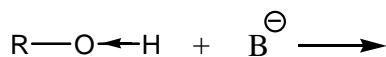
(2) -E effect :

Transition of electron away from attacking reagent.

**(b) Inductomeric Effect ;**

- Temporary effect.
- Takes place in sigma bonded system
- In presence of attacking reagent, transition of a electron cloud takes place more readily.

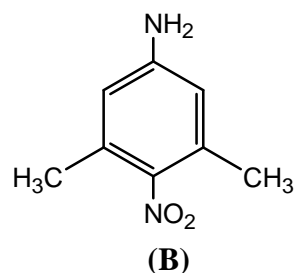
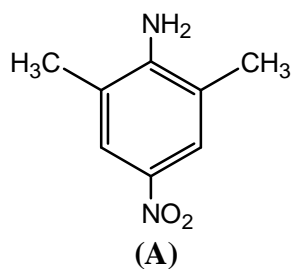
Example :



In presence of base B, movement of sigma electron takes place faster.

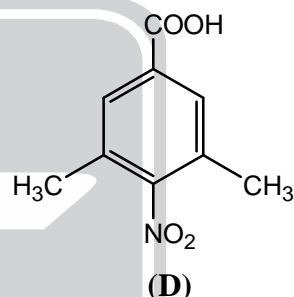
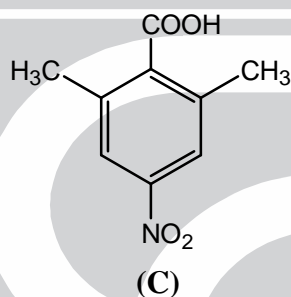
(3) Other Effect :**(a) Effect of inertia/steric inhibition of resonance:**

Resonance ability of an atom is lost if it loses planarity with the other part of the system due to steric crowding by bulky group in adjacent positions.



The above two compounds A and B have everything identical except position of the two methyl group. It is expected that A should be stronger base than B due to closeness of two electron donating methyl group to $-\text{NH}_2$. The fact is opposite to this. In compound B $-\text{NO}_2$ is surrounded by two bulky methyl group and they sterically repel the $-\text{NO}_2$ group. In order to minimize the steric repulsion by the two adjacent methyl group, the nitro group loses planarity with the benzene ring. So, now $-\text{NO}_2$ due to lack of planarity weigh ring, not able to resonate. This is known as steric inhibition of resonance. Thus in B, $-\text{NO}_2$ is not decreasing basic strength by resonance. In A $-\text{NO}_2$ lies in the plane of the ring, it is in resonance with the ring, decreases basic strength of $-\text{NH}_2$ by resonance, hence weaker base.

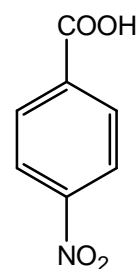
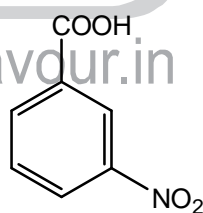
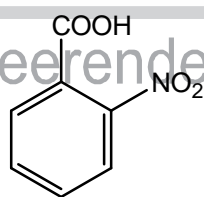
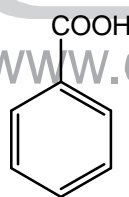
Similarly we can explain the acidic strength of C and D



C is stronger acid inspite of closeness of two electron donating methyl group to $-\text{COOH}$.

(b) Ortho effect: If any electron withdrawing group present on ortho position of the benzoic acid. It always increases acidic nature of acid because this group increases outer resonance of the ring toward acidic nature. Similarly if any group present on ortho position of aniline, it decreases basic nature. This effect is known as ortho effect.

Problem : The correct order of acidity among the following compound I-IV is



- (a) II > III > IV > I (b) IV > II > III > I (c) II > IV > III > I (d) IV > III > II > I

Soln. Because of ortho effect o-nitro benzoic acid is most acidic followed by para and meta.

Thus order will be II > IV > III > I.

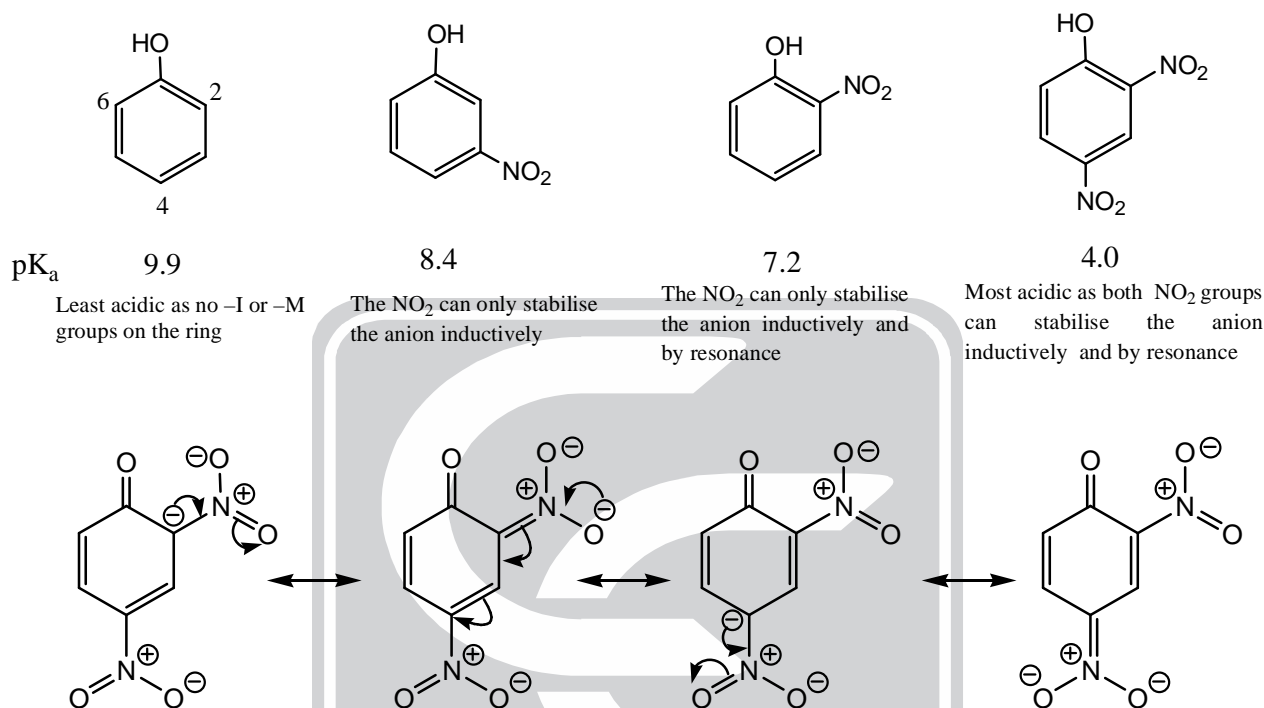
Hence, option (c) is correct.

Keynotes in Organic Chemistry:

- If $-\text{M}$ groups are introduced at 2-, 4- and/or 6-positions, the anion can be further stabilised by delocalisation through the π -system, as the negative charge can be spread onto the $-\text{M}$ group. We can use double-headed curly arrows to show this process.

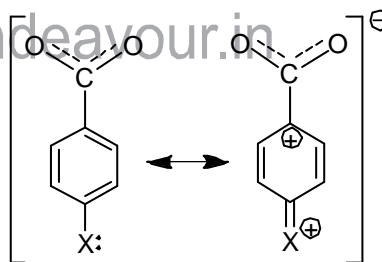
- If $-M$ groups are introduced at the 3- and/or 5-positions, the anion can not be stabilised by delocalisation, as the negative charge cannot be spread onto the $-M$ group. There is no way of using curly arrows to delocalise the charge onto the $-M$ groups.
- If $-I$ groups are introduced on the benzene ring, the effect will depend on their distance from the negative charge. The closer the $-I$ group is to the negative charge, the greater will be the stabilising effect. The order of $-I$ stabilisation is therefore 2-position > 3-position > 4-position.
- The $-M$ effects are much stronger than $-I$ effects.

Example: The NO_2 group is strongly electron-withdrawing; $-I$ and $-M$.

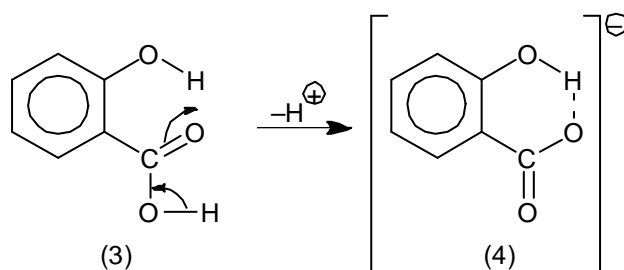


The presence of groups such as OH , OMe , or halogen an electron-withdrawing inductive effect, but an electron-donating mesomeric effect when in the o - and p - positions, may, however, cause the p -substituted acids to be weaker than the m - and, on occasion, weaker even than the unsubstituted acid itself, e.g. p -hydroxybenzoic acid:

	pK_a of $\text{XC}_6\text{H}_4\text{CO}_2\text{H}$				
H	Cl	Br	OMe	OH	
o -4.20	2.94	2.85	4.90	2.98	
m -4.20	3.83	3.81	4.09	4.08	
p -4.20	3.99	4.00	4.47	4.58	



It will be noticed that this compensating effect becomes more pronounced in going $\text{Cl} \approx \text{Br} \rightarrow \text{OH}$, i.e. in increasing order of readiness with which the atom attached to the nucleus will part with its electron pairs. The behaviour of o -substituted acids is, as seen above, often anomalous. Their strength is sometimes found to be considerably greater than expected due to direct interaction between the adjacent groups. Thus intramolecular hydrogen bonding stabilises the anion (4) from o -hydroxybenzoic (salicylic) acid (3) by delocalising its charge, an advantage not shared by its m - and p - isomers, nor by o -methoxy benzoic acid:



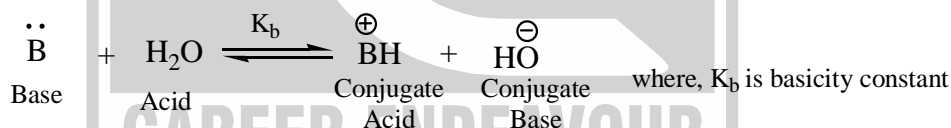
Intramolecular hydrogen bonding can, of course, operate in the undissociated acid as well as in the anion, but it is likely to be considerably more effective in the latter than in the former - with consequent relative stabilisation - because the negative charge on oxygen in the anion will lead to stronger hydrogen bonding. The effect is even more pronounced where hydrogen bonding can occur with hydroxyl groups in both *o*-position, and 2, 6-dihydroxybenzoic acid is found to have $pK_a = 1.30$.

Dicarboxylic Acids:

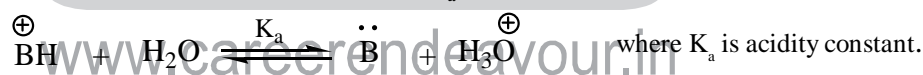
Acid	pKa Value	Acid	pKa Value
HCO ₂ H	3.77	HO ₂ CCO ₂ H	1.23
CH ₃ CO ₂ H	4.76	HO ₂ CCH ₂ CO ₂ H	2.83
CH ₃ CH ₂ CO ₂ H	4.88	HO ₂ CCH ₂ CH ₂ CO ₂ H	4.19
C ₆ H ₅ CO ₂ H	4.17	HO ₂ CC ₆ H ₄ CO ₂ H	<i>o</i> - 2.98; <i>m</i> - 3.46; <i>p</i> - 3.51

Bases: A base is a substance that accepts a proton (Bronsted-Lowry). Basic compounds have high pK_a -values and are good proton acceptors, as the cations (or conjugate acids), formed on protonation, are relatively stable.

In water:



The strength of bases are usually described by the K_a - and pK_a -values of the conjugate acid.

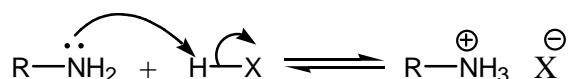


$$K_a = \frac{[\text{B}][\text{H}_3\text{O}^+]}{[{}^+\text{BH}]} \quad [\text{As } \text{H}_2\text{O} \text{ is in excess}]$$

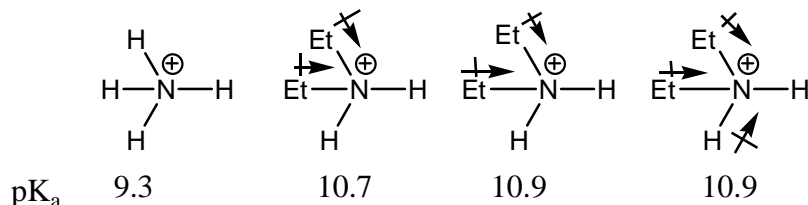
- If B is a strong base, then $\overset{\oplus}{\text{BH}}$ will be relatively stable and not easily deprotonated. $\overset{\oplus}{\text{BH}}$ will therefore have a high pK_a -value
- If B is a weak base, then $\overset{\oplus}{\text{BH}}$ will be relatively unstable and easily deprotonated. $\overset{\oplus}{\text{BH}}$ will therefore have a low pK_a -value.

The cation can be stabilised by +I and +M groups, which can delocalise the positive charge. (The more 'spread out' the positive charge, the more stable it is).

(c) **Inductive effects and aliphatic (or alkyl) amines:** On protonation of amines, ammonium salts are formed.



The greater the +I effect of the R group, the greater the electron density at nitrogen and the more basic the amine. The greater the +I effect, the more stable the ammonium cation and the more basic the amine.



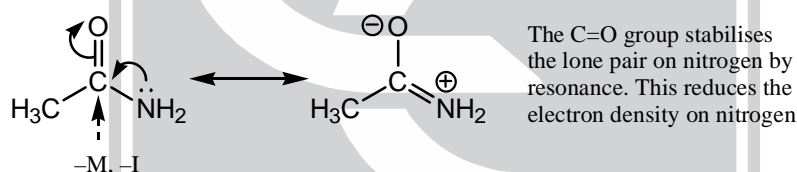
The pK_a -values should increase steadily as more +I alkyl groups are introduced on nitrogen. However, the pK_a -values are determined in water, and the more hydrogen atoms on the positively charged nitrogen, the greater the extent of hydrogen-bonding between water and the cation. This solvation leads to the stabilisation of the cations containing N–H bonds.

In organic solvents (which can not solvate the cation), the order of pK_a s is expected to be as follows:



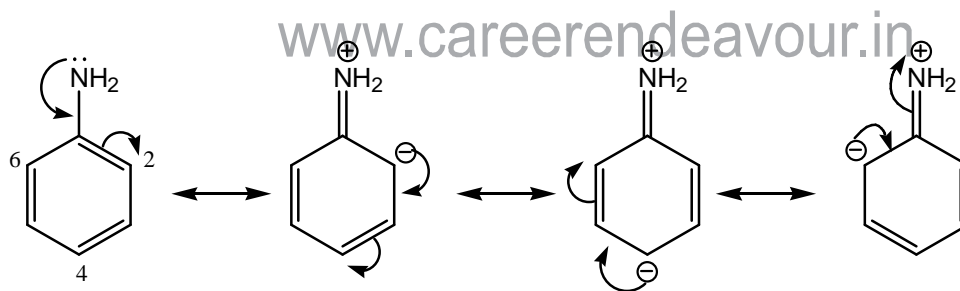
The presence of –I and/or –M groups on nitrogen reduces the basicity, and hence, for example, amides are poor bases.

Ethanamide has a pK_a of –0.5.

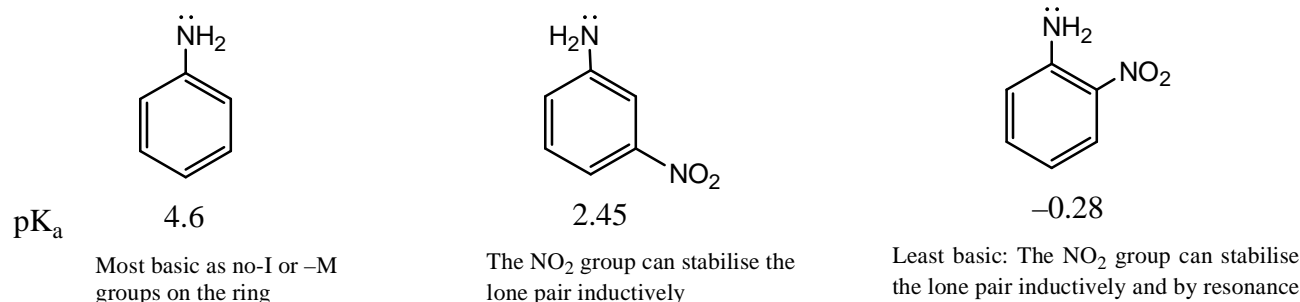


(d) **Mesomeric effects and aryl (or aromatic) amines:**

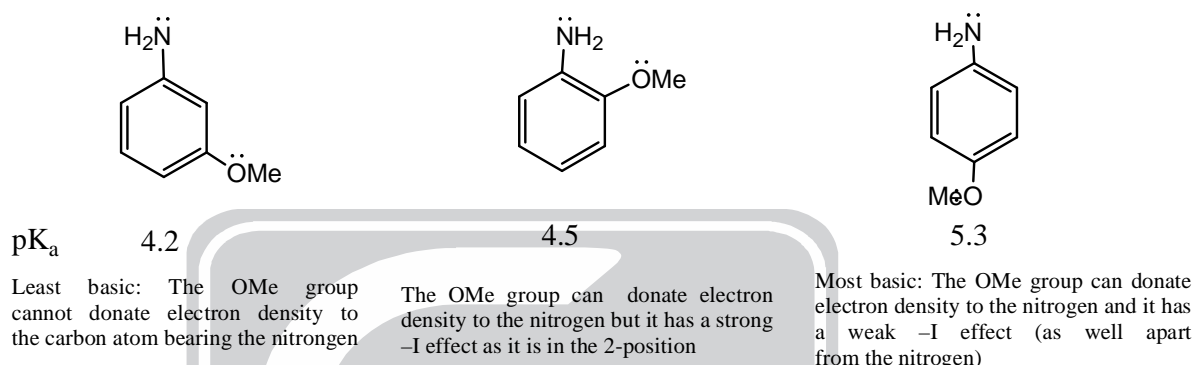
The lone pair of electrons on the nitrogen atom of aminobenzene (or aniline) can be stabilised by the delocalisation of the electrons onto the 2-, 4- and 6-positions of the benzene ring. Aromatic amines are therefore less basic than aliphatic amines.



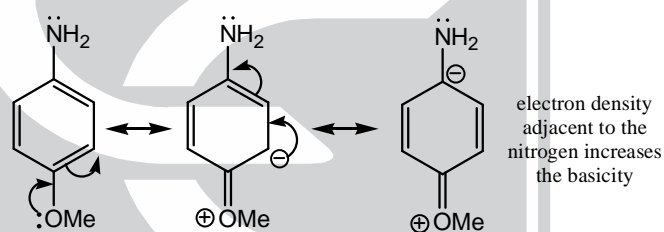
- If –M groups are introduced at the 2-, 4- and/or 6-positions (but not at the 3- or 5-position), the anion can be further stabilised by delocalisation, as the negative charge can be spread onto the –M group. This reduces the basicity of the amine.
- If –I groups are introduced on the benzene ring, the order of –I stabilisation is 2-position > 3-position > 4-position. This reduces the basicity of the amine.



- If +M group (e.g. OMe) are introduced at the 2-, 4- or 6-position of aminobenzene, then the basicity is increased. This is because the +M group donates electron density to the carbon atom bearing the amine group.

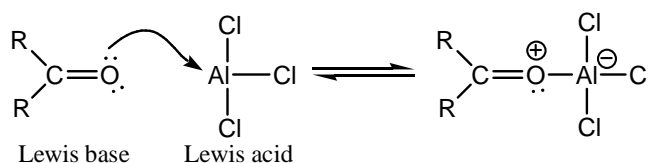


Curly arrows can be used to show the delocalisation of electrons onto the carbon atom bearing the nitrogen.



(e) Lewis acids and base:

- A Lewis acid is any substance that accepts an electron pair in forming a coordinate bond. Examples include H^+ , BF_3 , $AlCl_3$, $TiCl_4$, $ZnCl_2$ and $SnCl_4$. They have unfilled valence shells and hence can accept electron pairs.
- A Lewis base is any substance that donates an electron pair in forming a coordinate bond. Examples include H_2O , ROH , $RCHO$, R_2CO , R_3N and R_3S . They all have a lone pair(s) of electrons on the hetero atom (O, N or S)



(f) Basicity and hybridisation:

The greater the 's' character of an orbital, the lower is energy the electrons and the more tightly the electrons are held to the nucleus. The electrons in an sp -orbital are therefore less available for protonation than those in an sp^2 - or sp^3 -hybrid orbital and hence the compounds are less basic.

