

Chapter 3

INDUCTIVE EFFECT:

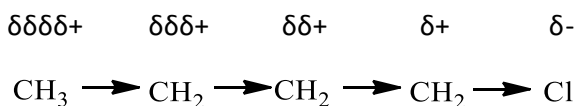
The polarization of a bond due to electron withdrawing or electron donating effect of adjacent groups or atoms is called inductive effect.

Salient features of inductive effect:

- ❖ It arises due to electronegativity difference between atoms forming a sigma bond.
- ❖ It is transmitted through the **sigma bonds (σ)**.
- ❖ The magnitude of inductive effect decrease while moving away from the groups causing it.
- ❖ It is a permanent effect.
- ❖ It influences the chemical and physical properties of compounds.

ILLUSTRATION OF INDUCTIVE EFFECT:

The C-Cl bond in the butyl chloride, $\text{CH}_3\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-Cl}$ is polarized due to electronegativity difference. The electrons are withdrawn by the chlorine atom. Thus, the first carbon atom gets partial positive charge. In turn, this carbon atom drags electron density partially from the next carbon, which also gets partial positive charge. Thus, the inductive effect is transmitted through the carbon chain.



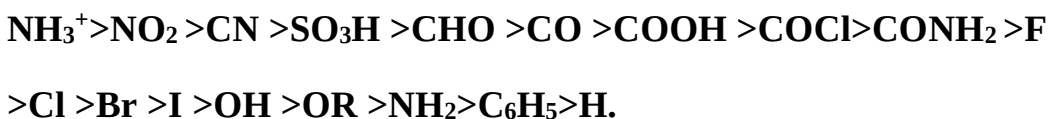
However, the inductive effect weakens away along the chain and is not significant beyond 3rd carbon atom.

TYPES OF INDUCTIVE EFFECT:

The inductive effect is divided into two types depending on their strength of electron withdrawing or electron releasing nature with respect to hydrogen.

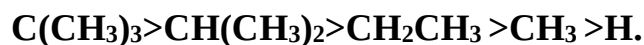
1) Negative inductive effect (-I):

The electron withdrawing nature of groups or atoms is called as negative inductive effect. It is indicated by (-I). Following are the examples of groups in the decreasing order of their (-I) effect:



2) Positive inductive effect (+I):

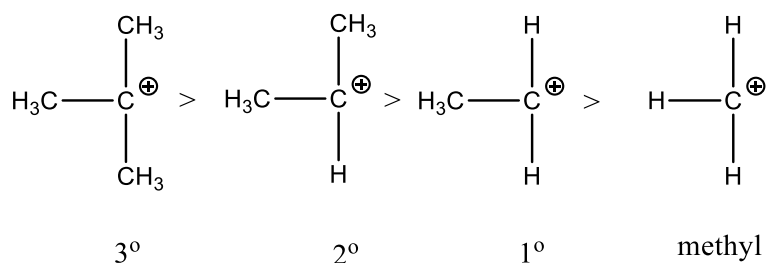
The electron withdrawing nature of groups or atoms is called as negative inductive effect. It is indicated by (-I). Following are the examples of groups in the decreasing order of their (-I) effect:



APPLICATION OF INDUCTIVE EFFECT:

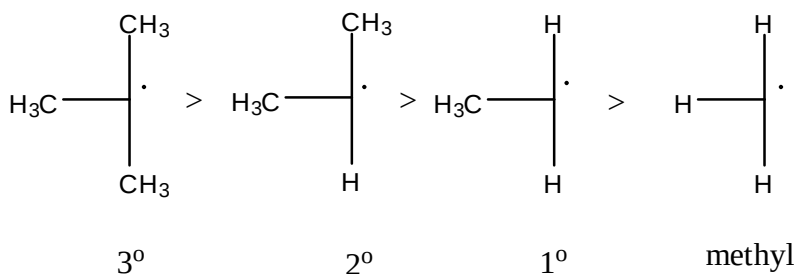
Stability of carbonium ions:

The stability of carbonium ions increases with increase in number of alkyl groups due to their +I effect. The alkyl groups release electrons to carbon, bearing positive charge and thus stabilizes the ion. The order of stability of carbonium ions is:



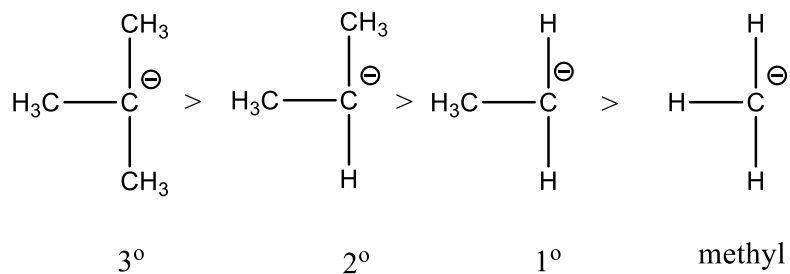
Stability of free radicals:

In the same way, the stability of free radicals increases with increase in the number of alkyl groups. Thus the stability of different free radicals is:



Stability of carbanions:

However, the stability of carbanions decreases with increase in the number of alkyl groups since the electron donating alkyl groups destabilize the carbanions by increasing the electron. Thus, the order of stability of carbanions is:



Acid strength of carboxylic acids and phenols:

Effect of I (inductive effect) on acidity:

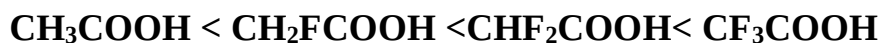
(A) However, the +I groups decrease the acidic strength.

Formic acid is stronger than acetic acid since the $-\text{CH}_3$ groups destabilizes the carboxylate ion.

(B) The electron withdrawing groups (-I) decrease the negative charge on the carboxylate ion and thus by stabilizing it. Hence the acidic strength increases when (-I) groups are present.

E.g.

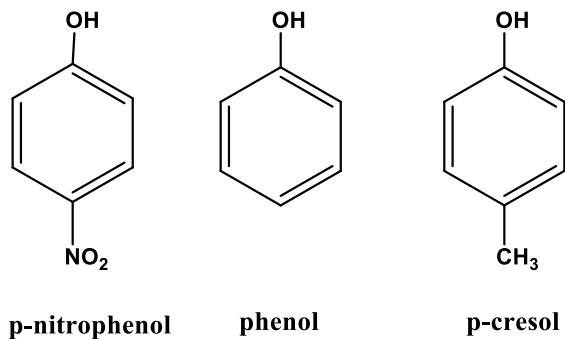
- i. The acidic strength increases with increase in the number of electron withdrawing Fluorine atoms as shown below:



- ii. On the same lines, the acidic strength of phenols increases when (-I) groups are present on the ring.

E.g. the p-nitro phenol is stronger acid than phenol since the $-\text{NO}_2$ group is a (-I) group and withdraws electron density. Whereas the para-cresol is weaker acid than phenol since the $-\text{CH}_3$ group shows positive (+I) inductive effect.

Therefore the decreasing order of acidic strength is:



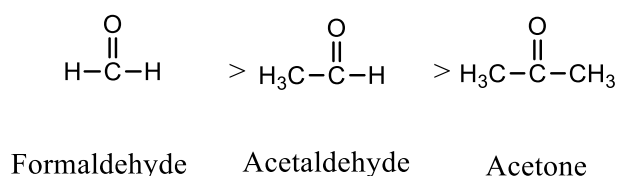
Basic strength of amines:

The electron donating groups like alkyl groups increase the basic strength of amines by increasing the electron density over N and increasing the stability of formed cation. Whereas the electron withdrawing groups like aryl, groups decrease the basic nature. Therefore, alkyl amines are stronger Lewis bases than ammonia, whereas aryl amines are weaker than ammonia. Thus, the order of basic strength of alkyl and aryl amines with respect to ammonia is: $\text{CH}_3\text{NH}_2 > \text{NH}_3 > \text{C}_6\text{H}_5\text{NH}_2$

Reactivity of carbonyl compounds:

The +I groups increase the electron density at carbonyl carbon i.e decrease the +ve charge on carbonyl carbon. Hence their reactivity towards nucleophilic decrease. Thus, formaldehyde is more reactive than acetaldehyde and acetone towards nucleophilic addition reactions.

Thus, the order of reactivity follows:



RESONANCE OR MESOMERIC IN ORGANIC CHEMISTRY:

Sometimes, it is not possible to represent the molecule or ion with only one structure. More than one structure have to be proposed. However, none of them explains all the observed properties of the molecule. The

solution is to write a weighted average of all the valid structure, which explains all the properties. This condition is usually referred to as ***resonance, mesomerism, or delocalization.***

The representation of structure of a molecule as a weighted average of two or more hypothetical structures, which only differ by the arrangement of electrons but with some positions for atoms is referred to as ***resonance.***

Salient features of resonance:

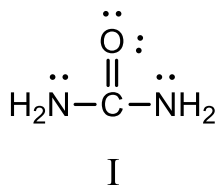
- The hypothetical structures with different arrangement of electrons but with identical positions for atoms are called resonance structures, canonical forms, or contributing structures.
- The resonance structures are only imaginary and the actual structure of the molecule is considered as the hybrid of all the valid resonance structures.

Resonance hybrid: the weighted average of contributing structures is known as resonance hybrid. It is considered as the actual structure.

- The energy of resonance hybrid is always less than the energy of any of the contributing resonance structure.
- The resonance structures are formed (only on paper!?) due to delocalization of electrons and not by changing the positions of atoms.
- The delocalization of electrons is shown using curved arrows.

Illustration:

From the following structure (I)- representing urea,

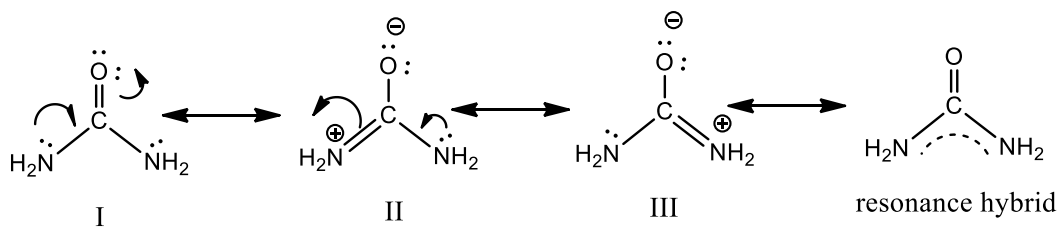


Note: the contributing structures are always shown to be linked by using double-headed arrows ($\longleftrightarrow$).

It is observed that:

- 1) Urea is a monoacidic base,
- 2) It has shorter than expected bond length for C-N bond and
- 3) It shows dipole moment.

Hence, to account for above observation, the actual structure of urea is represented as a resonance hybrid of following resonance structure.



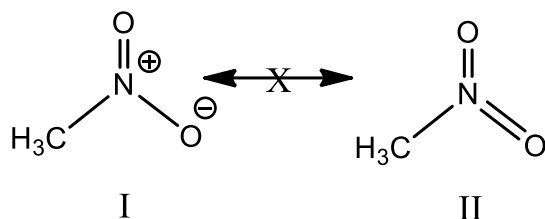
RULES THAT HELP IN WRITING VALID RESONANCE STRUCTURES

The valid resonance structures must satisfy the following rules:

- ❖ They must be valid Lewis structures obeying octet rule.

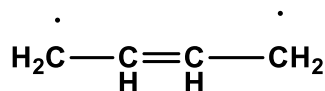
E.g carbon or nitrogen with five bonds is not allowed.

In the structure (II), the nitrogen atom violated the octet. It has 10 electrons around it.

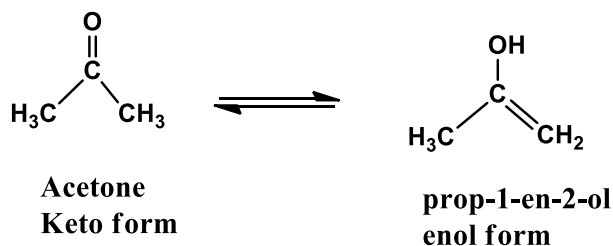


not a valid structure since the valence of nitrogen is exceeded to 5

- ❖ They should possess the same number of electrons and equal net charge.
- The number of unpaired electrons in them must be the same.
E.g. following structure for butadiene is not valid.



- The positions of atoms should be same in all the resonance structures.
E.g. the following are not the resonance structures, since the position of one hydrogen atom is not same. Indeed, they are different molecules, which are in dynamic equilibrium with each other. These are called tautomers. Also, note that these molecules are linked by two half-headed arrows and not by a single double-headed arrow.



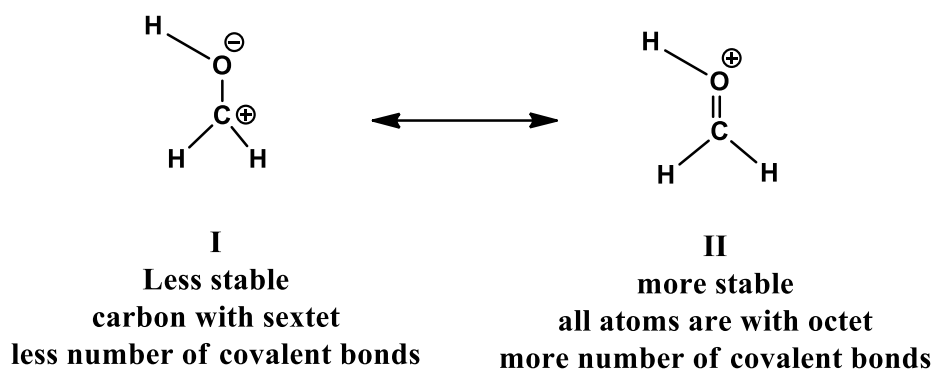
- The bond order of two connecting atoms may vary between two different resonance structures.
- The resonance structures may or may not be equivalent.
- The atoms that are part of the delocalized system must be arranged in one plane or nearly so. The reason is to get maximum overlap between the orbitals.

STABILITY OF RESONANCE STRUCTURES:

- ❖ The actual structure i.e., resonance hybrid of a molecule has lower energy than any of the contributing form and hence the resonance is a stabilizing phenomenon.
- ❖ Greater the number of contributing structures, greater is the stability of the resonance hybrid.
- ❖ Not all the structures contribute equally to the hybrid.
- ❖ Greater the stability of a resonance structure, larger is its contribution to the resonance hybrid.

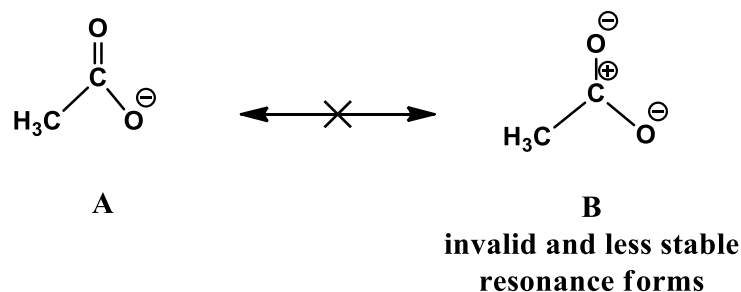
Rules to decide the major contributor to the hybrid in the decreasing order of preference are given below:

- ❖ The contributing structures that have atoms with full octets are more stable than the ones with open octets.
- ❖ The contributing structure with more covalent bonds is more stable.
e.g. among the following, the structure II is more stable since all the atoms have octet configuration and there are more covalent bonds.



- Resonance structures with fewer charges are more stable than structures of more charges.

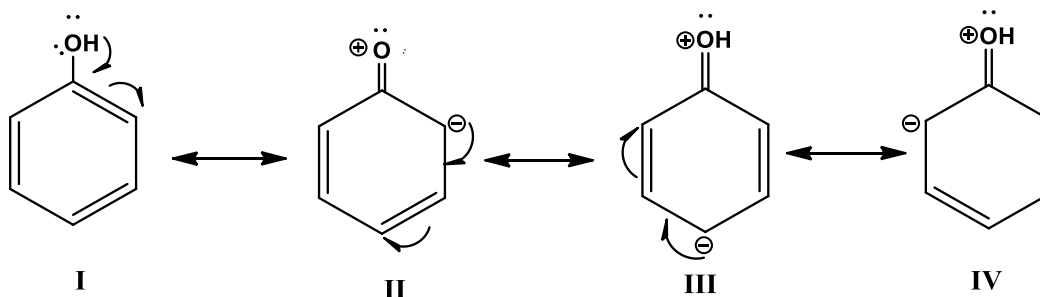
E.g. the second structure B with two negative charges is less stable than structure A.



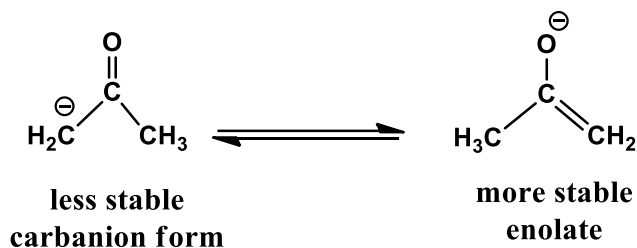
- The structure with less charge separation is more stable.

E.g.

Among the following resonance forms of phenol, the structure I is more stable since it has no charge. Whereas the structures II and IV have less charge separation and are more stable than the structure III.



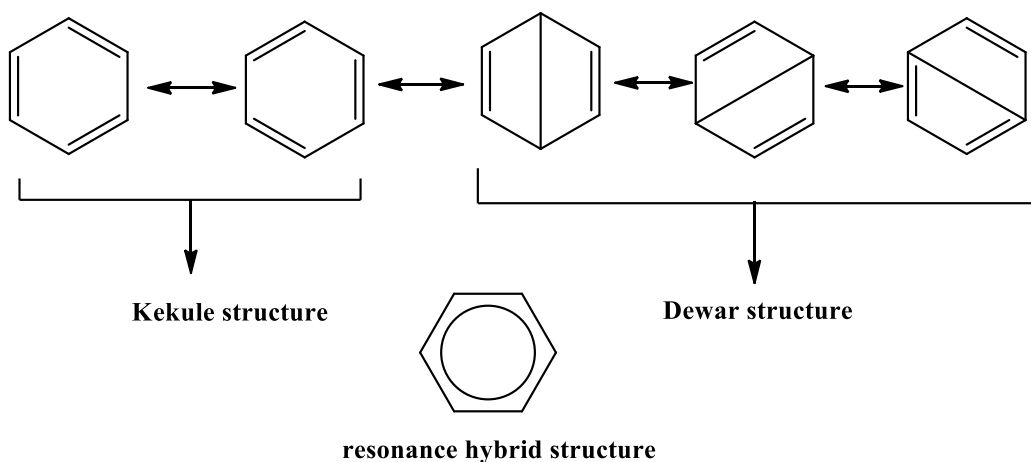
- The structure with charge dispersal or delocalization over more number of atoms is more stable.
- The structures in which the atoms bearing the conventional charges are more stable i.e., the more electronegative atom should bear negative charge while the relatively less electronegative atom should bear positive charge. e.g.



Resonance stabilization energy: The difference between the energy of resonance hybrid and that of most stable resonance structure of a molecule is known as the resonance stabilization energy of that molecule.

EXAMPLES OF RESONANCE STRUCTURES:

- 1) The following resonance structures can be written for benzene, which are hypothetically possible due to delocalization of a π - electrons. The Kekule structures have more weightage than Dewar structures.



The actual structure of benzene is thus shown to be the hybrid of these contributing structures. The bond order of every C-C bond is 1.5 and hence the every C-C bond length is reported to be same and equals to $1.39 \text{ \AA}$, which is in between the bond length values of C-C single bond ($1.54 \text{ \AA}$) and C=C double bond ($1.33 \text{ \AA}$).

Due to resonance, benzene gets extra stability and does not undergo electrophilic addition reactions. However, it shows electrophilic substitution reactions. This phenomenon is known as aromaticity.

RESONANCE EFFECT OR MESOMERIC EFFECT:

The electron withdrawing or releasing effect attributed to a substituent through delocalization of p or π electrons, which can be visualized by drawing various canonical form, is known as mesomeric effect or resonance effect. It is symbolizes by M or R.

Negative resonance or mesomeric effect (-M or -R):substituents or groups that withdraw electrons by delocalization mechanism from rest of the molecule and are donated by -M or -R. show it. The electron density on rest of the molecular entity is decreased due to this effect.

E.g. $-\text{NO}_2$, Carbonyl group ($\text{C}=\text{O}$), $-\text{C}\equiv\text{N}$, $-\text{COOH}$, $-\text{SO}_3\text{H}$ etc.

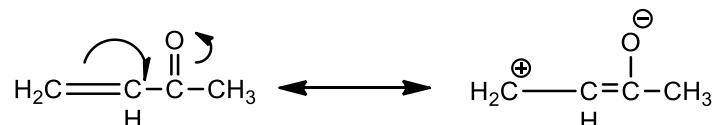
Positive resonance or mesomeric effect (+M or +R):The groups show positive mesomeric effect when they release electrons to the rest of the molecule by delocalization. These groups are donated by +M or + R due to this effect, the electron density on rest of the molecular entity is increased.

E.g. $-\text{OH}$, $-\text{OR}$, $-\text{SH}$, $-\text{SR}$, $-\text{NH}_2$, $-\text{NR}_2$ etc.

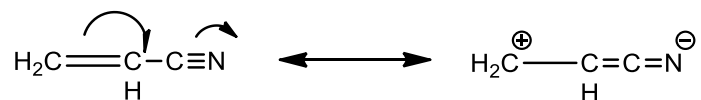
ILLUSTRATION & APPLICATIONS OF RESONANCE

EFFECT (OR) MESOMERIC EFFECT:

- 1) The negative resonance effect (+R or +M) of carbonyl group is shown below, it withdraws electrons by delocalization of π -electrons and reduces the electron density particularly on 3rd carbon.

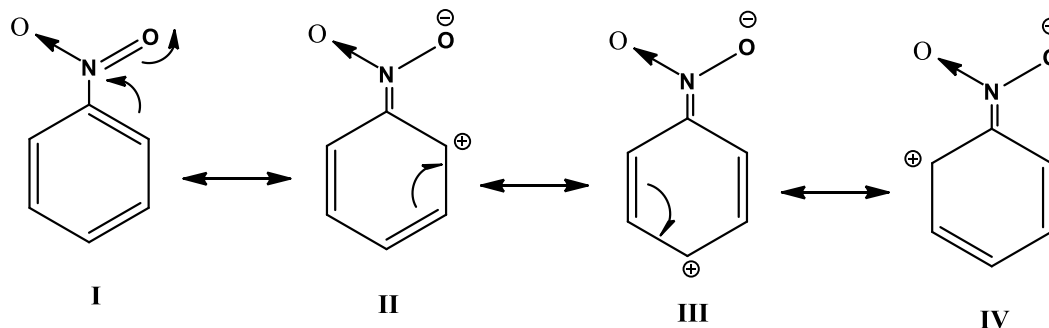


- 2) The negative mesomeric effect (-R or -M) shown by cyanide group in acrylonitrile is illustrated below, the electron density on third carbon decreases due to delocalization of π electrons towards cyanide group.



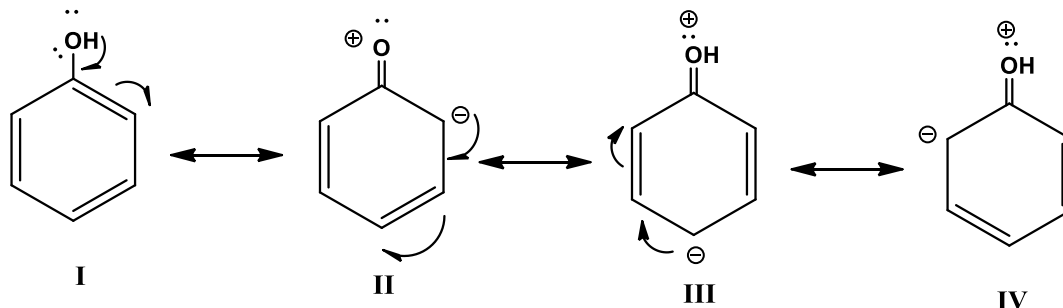
Because of negative resonance effect, the above compounds act as good **Michael acceptors**.

- 3) The nitro group, $-\text{NO}_2$, in nitrobenzene shows $-M$ effect due to delocalization of conjugated π electrons as shown below. Note that the electron density on benzene ring is decreased particularly on ortho and para positions.



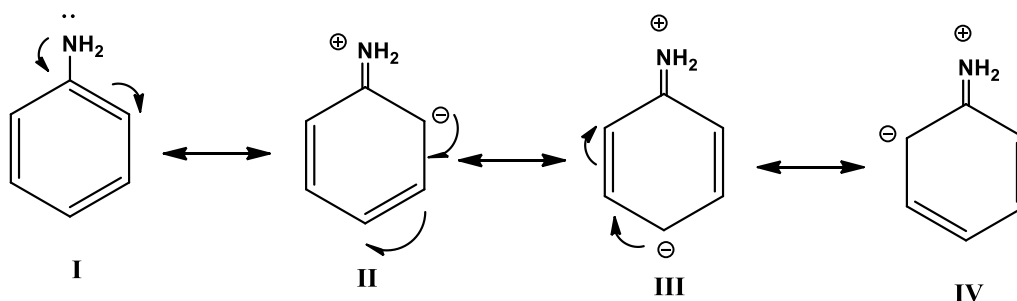
This is the reason for why nitro group deactivates the benzene ring towards electrophilic substitution reaction.

- 4) In Phenol, the -OH group shows +M effect due to delocalization of lone pair on oxygen atom towards the ring. Thus, electron density on benzene ring is increased particularly on ortho and para positions.



Hence, phenol is more reactive towards electrophilic substitution reactions. The substitution is favored more at ortho and para positions.

- 5) The -NH_2 group in aniline also exhibits +R effect, it releases electrons towards benzene ring through delocalization. As a result, the electrons density on benzene ring increases particularly at ortho and para positions, thus aniline activates the ring towards electrophilic substitution.



It is also worth mentioning that the electron density on nitrogen in aniline decreases due to delocalization, which is the reason for its less basic strength when compared to ammonia and alkyl amines.

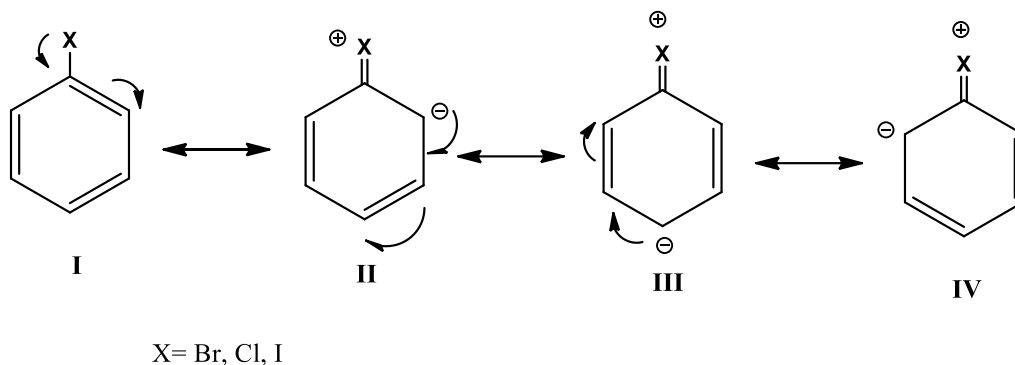
INDUCTIVE EFFECT Vs RESONANCE EFFECT

In most of the cases, resonance effect is stronger and outweighs inductive effect.

For example, the $-\text{OH}$ and $-\text{NH}_2$ groups withdraw electrons by inductive effect ($-\text{I}$). However, they also release electrons by delocalization of lone pairs ($+\text{R}$ effect). Since the resonance, effect is stronger than inductive effect the net result is electron releasing to rest of the molecule. This is clearly observed in phenol and aniline, which are more reacting than benzene towards electrophilic substitution reactions.

Whereas the inductive effect is stronger than the resonance effect in case of halogen atoms. There are electronegative and hence exhibit I effect. However at the same time they also release electrons by delocalization ($+\text{R}$ effect) of lone pair.

This is evident in case of reactivity of halobenzenes, which are less reactive than benzene towards electrophilic substitution due to $-\text{I}$ effect of halogens. However, it interesting to note that the substitution is directed at ortho and para positions rather than meta position. It can be ascribed to the fact that the electron density is increased at ortho and para positions due to $+\text{R}$ effect of halogens as shown below.



HYPERCONJUGATION (or) NO BOND RESONANCE (or)

BAKER-NATHAN EFFECT:

The delocalization of α -electron or lone pair of electrons into adjacent π -orbital or p-orbital is called hyperconjugation.

It occurs due to overlapping of α -bonding orbital or the orbital containing a lone pair with adjacent adjacent π -orbital or p-orbital.

Conditions for hyperconjugation

- There must be α -CH group or lone pair on atom adjacent to sp^3 hybrid carbon or other atoms like nitrogen, oxygen etc.

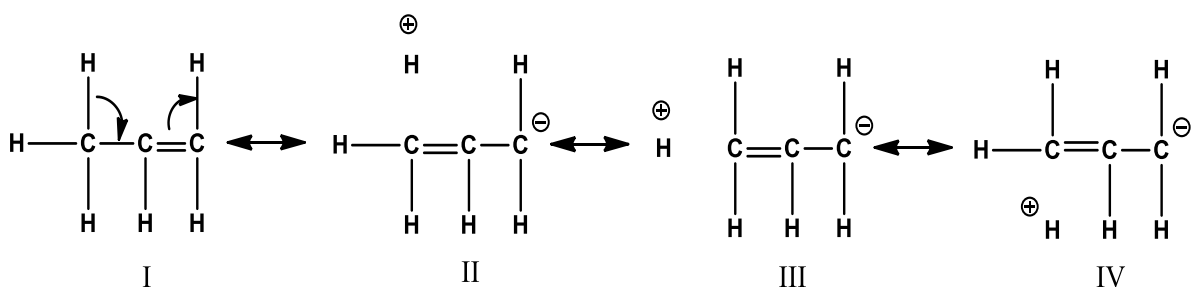
Application of hyperconjugation:

Example:

1) In propene, the α -electrons of CH bond of methyl group can be delocalization into the π -orbital of doubly bonded carbon as represented below.

In the same way, the other hydrogen on the methyl group also participate in the hyperconjugation. This is possible due to free rotation of C-C bond so that the other C-H bonds can also participate in the hyperconjugation. Thus,

the propene molecule can show following resonance structures, which confer stability to



No bond resonance shown by propene to hyperconjugations

In the contributing structures, (II), (III) & (IV) of propene, there is NO bond between α -carbon and one of the hydrogen atom. Hence, the hyperconjugation is also known as “no bond resonance”.

These equivalent contributing structures i.e., (II), (III) & (IV) are also polar in nature and hence are responsible for the dipole moment of propene (0.36 D).

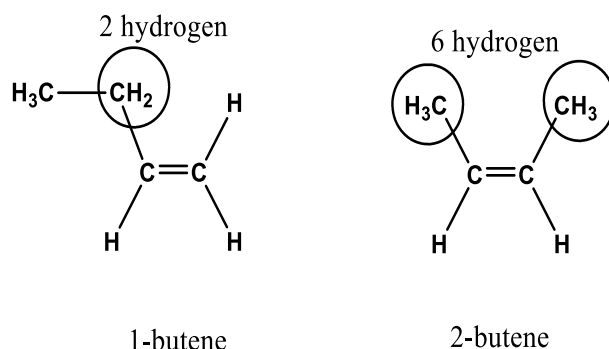
The C-C bond lengths in propene are equal to 1.48. Its value is in between 1.54 (of C-C) and 1.34 (of C=C). It is because the bond order of C-C bonds is approximately 1.5 due to hyperconjugation.

This type of hyperconjugation is also referred to as sacrificial hyperconjugation since one bond is missing.

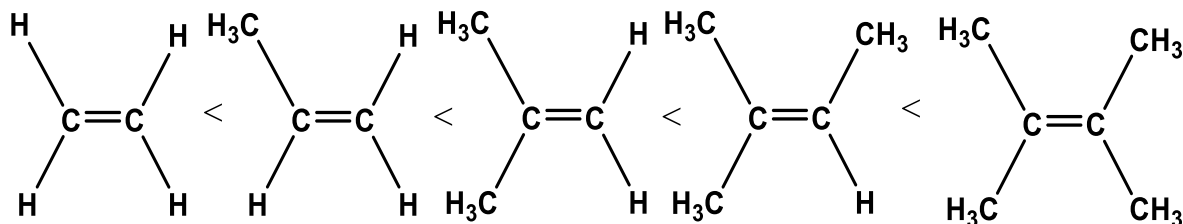
2) Stability of alkenes:

A general rule is that, the stability of alkenes increases with increase in the number of alkyl groups (containing hydrogen) on the double bond. It is due to increase in the number of contributing no bond resonance structures.

For example, 2-butene is more stable than 1-butene. This is because in 2-butene, there are six hydrogens involved in hyperconjugation whereas there are only two hydrogens involved in case of 1-butene. Hence the contributing structures in 2-butene are more and it is more stable than 1-butene.



The increasing order of stability of alkenes with increases in the number of methyl groups on the double bond is depicted below.

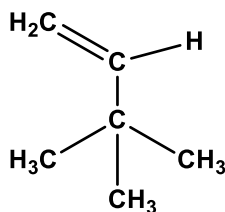


The heat of hydrogenation data of these alkenes supports the order. The values of heats of hydrogenation decrease with increase in the stability of alkenes.

In addition, the heats of formation of more substituted alkenes are higher than expected.

However, it is important to note that the alkyl groups attached to the double bond must contain at least one hydrogen atom for hyperconjugation. For

example. In case of the following alkene containing a tert-butyl group on doubly bonded carbon. The hyperconjugation is not possible.

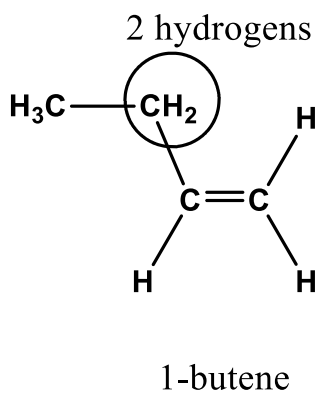
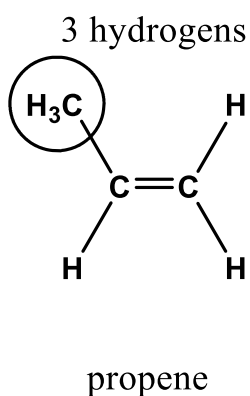


No H atoms on α carbon
Hence no hyperconjugation

It is also important to note that the effect of hyperconjugation is stronger than the inductive effect.

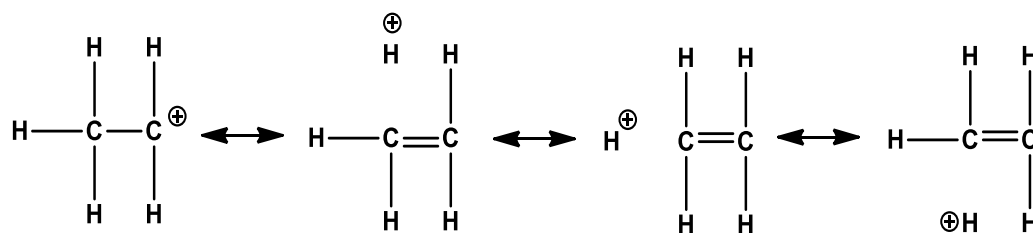
For example, the positive inductive effect of ethyl group is stronger than that of methyl group, hence based on inductive effect, 1-butene is expected to be more stable than propene.

However, propene is more stable than 1-butene. This is because there are three hydrogens on α -methyl group involved in hyperconjugation. Whereas, in 1-butene there are only two hydrogen atoms on $-\text{CH}_2$ group that can take part in hyperconjugation.



3) Stability of carbocations (carbonium ions):

The ethyl carbocation, $\text{CH}_3\text{-CH}_2^+$ is more stable than the methyl carbocation, CH_3^+ . This is because, the α -CH bond in ethyl group are delocalization into the empty p-orbital of the positive carbon center and thus by giving rise to “no bond resonance structures” as shown below, whereas hyperconjugation is not possible in methyl carbocation and hence is less stable.

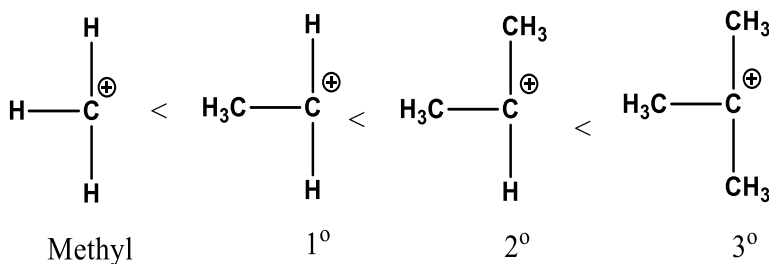


hyperconjugation in ethyl carbonium ion

In general, the stability of carbonium ions increases with increase in the number of alkyl groups (containing hydrogen) attached to the positively charged carbon due to increase in the number of contributing structures to hyperconjugation.

Note: this type of hyperconjugation can also referred to as isovalent hyperconjugation since there is no decrease in the number bonds in the no bond resonance forms.

Thus the increasing order of stability of carbocations can be given as: methyl < primary < secondary < tertiary as depicted below:



4) Stability of free radicals:

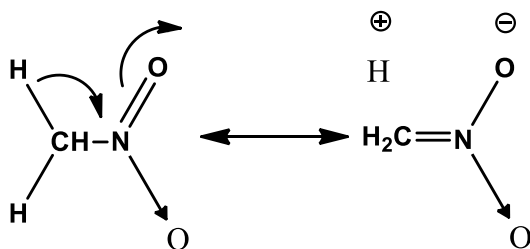
The stability of free radicals is influenced by hyperconjugation as in case of carbonium ions. The δ -electrons of α -carbon-H bond can be delocalized into the p-orbital of carbon containing an odd electron.

Due to hyperconjugation, the stability of free radicals also follow the same order as that of carbonium ions i.e., methyl < primary < secondary < tertiary.

5) Dipole moment & bond length:

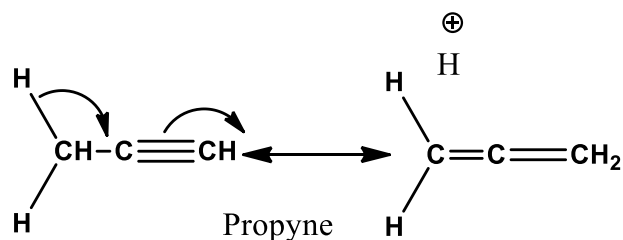
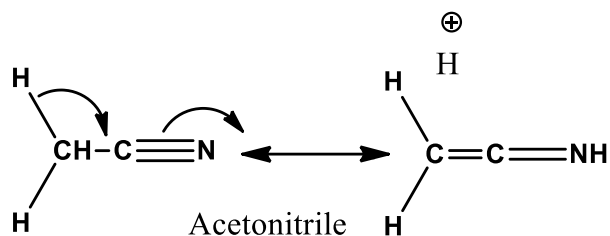
- The dipole moment of the molecules is greatly affected due to hyperconjugation since the contributing structures show considerable polarity.
- The bond lengths are altered due to change in the bond order during hyperconjugation. The single bond may get partial double bond character and vice versa.

e.g. the observed dipole moment of nitro methane is greater than the calculated value due to hyperconjugation. The observed C-N bond length is also less than the expected value due to same reason.



Hyperconjugation in nitromethane

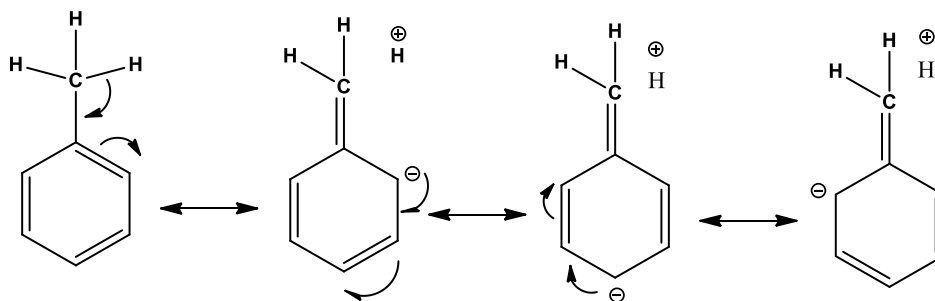
The same arguments can be applied to shortening of C-C bond adjacent to $\text{C}\equiv\text{N}$ in acetonitrile and the C-C bond adjacent to the $\text{C}\equiv\text{C}$ in propyne. Also, note that the observed dipole moments are again different from their expected values.



6) Reactivity & orientation of electrophilic substitution on benzene ring:

In Toluene, the methyl group release towards benzene ring partly due to inductive effect and mainly due to hyperconjugation. Thus, the reactivity of the ring towards electrophilic substitution increases and the substitution is directed at ortho and para positions to the methyl group.

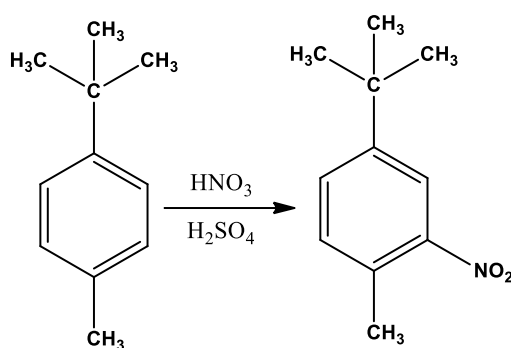
The no bond resonance forms of toluene due to hyperconjugation are shown below.



Hyperconjugation in toluene

From the above diagram, it can be seen clearly that the electron density on benzene ring is increased especially at ortho and para positions.

Since the hyperconjugation overpowers the inductive effect of the substitution (e.g nitration) on the following, disubstituted benzene occurs ortho to the methyl group. In the tert-butyl group. There are no hydrogens on the carbon directly attached to the benzene ring. Hence, it cannot involve in hyperconjugation.



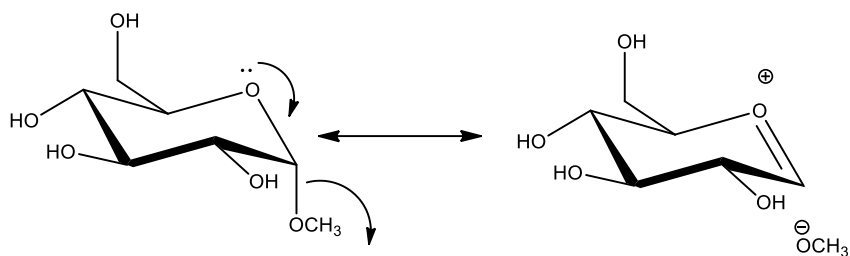
Also, note that the tert-butyl group is bulky and hinders the approach of electrophile.

7) Anomeric effect:

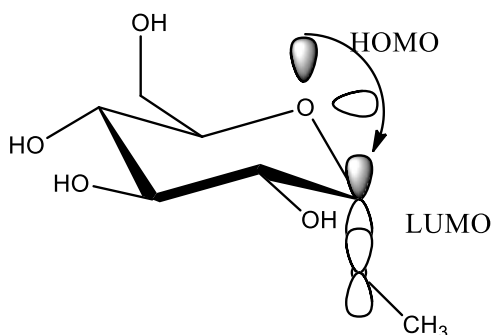
The general tendency of anomeric substitution to prefer an axial position is called Anomeric effect.

For example, the α -methyl glucoside is more stable than the β -methyl glucoside due to hyperconjugation.

In the α -methyl glucoside, the non-bonding HOMO with a pair of electrons on the ring oxygen is antiperiplanar to the antibonding LUMO of C-O bond in methoxy group. This allows hyperconjugation between them and thus by stabilizing the α -form.



Hyperconjugation in α -D-methylglucoside

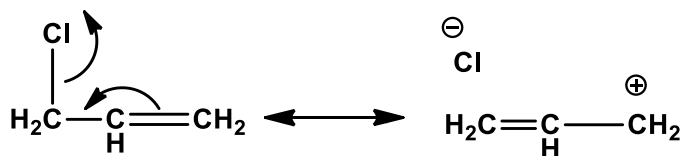


Anti periplanar arrangement is only possible in α -form

Whereas, in β -methyl glucoside the methoxy group is at equatorial position and cannot involve in hyperconjugation since it is not antiperiplanar to the lone pair on ring oxygen. Therefore, β -methyl glucoside is less stable than the α -methyl glucoside.

8) Reverse hyperconjugation:

In case of α -halo alkene, the delocalization of electrons occurs towards halogen group through hyperconjugation mechanism. It is referred to as reverse hyperconjugation. The dipole moments of α -halo alkenes are argued due to this phenomenon.



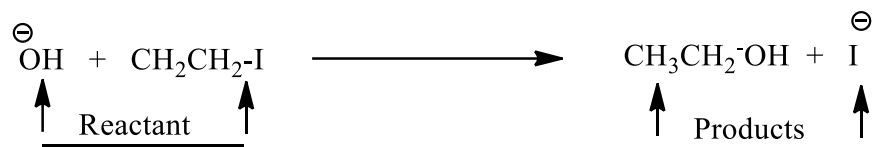
reverse hyperconjugation

Chapter 4

CLASSIFICATION OF REACTIONS AND REAGENTS

Introduction:

When iodomethane warmed with aqueous sodium hydroxide, the main product is ethanol. The reaction may be summarized in equation form as follow:



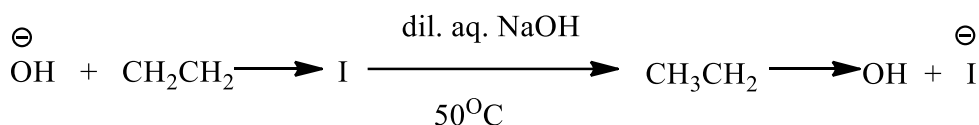
The molecule-attacked iodomethane, is referred to as **substrate**, and the species doing the attacking, the hydroxide ions, are called the **attacking reagent**. Sodium ions are also present, but since they are not directly involved in the reaction, they are often called spectator ions and are normally omitted from equation.

Equations summarizing organic reactions are usually written with an arrow ($\longrightarrow$) indicating the direction of the reaction and implies the equilibrium lies well to the right. Conversely the symbol ($\nrightarrow$) means that no appreciable reaction occurs under the given conditions.

- Frequently, **the reaction conditions** such as temperature, solvent, catalyst, etc., **are shown above and below the arrow** application of

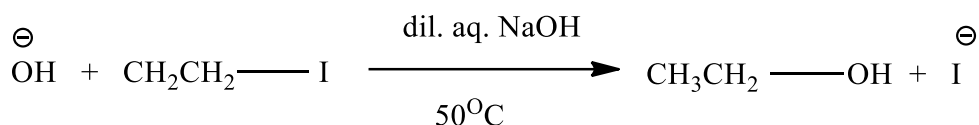
heat is indicated by stating the temperature, by the word reflux or by the symbol Δ

Oxidation by an unspecified agent is shown as {O}, and reduction likewise by {H}. An equation, labeled in this way is called annotated equation. For the above reaction, it might be:



- **Classification of reagents:**

All organic reaction involve breaking and reformation of covalent bonds. For example, in the substitution reaction:



The bond between the carbon and iodine atom has to be broken and a new bond formed between the carbon and oxygen atoms in the product. In principle, there are two different ways in which the covalent bond in a substrate could be broken, depending on the relative electronegativity of the bonded atoms and the experimental conditions.

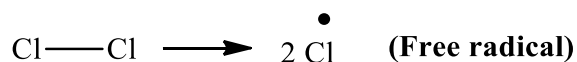
- The breaking of covalent bonds is termed ***bond cleavage or bond fission***. It takes place in two ways:
 - Hemolytic fission or hemolysis***: symmetrical breaking.
 - Heterolytic fission or heterolysis***: unsymmetrical breaking.

- **Hemolysis:**

This involves the breaking of bond in such a way that each separate atom carries one electron. The individual parts after cleavage are called **radicals**.

For example:

I. Breaking of Cl₂ molecule:



Here each chlorine atom will be a radical.

II. Breaking (fission) of ethane molecule:



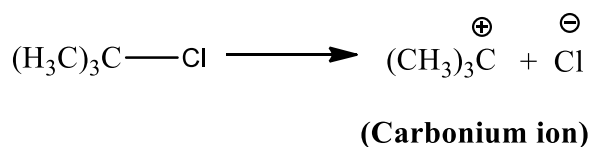
Both methyl groups are called **radical**.

- It is important to note that hemolytic fission of a covalent bond takes place when the electronegativity of the bonded atoms are equal or nearly equal. Hemolysis result in the formation of free radicals. Which are generally formed in the gaseous phase?
- The reactions, which proceed through homolytic fission, are known as **free radical reactions**.

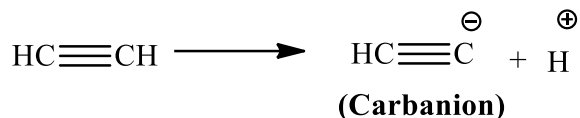
- **Heterolysis:**

- This involves the breaking of a bond in such a way that one of the separate atoms carries both bonding electrons. The product formed because of electron fission is termed as ions. For example:

I. Breaking of C-Cl bond in t-butyl chloride:



II. Breaking of C-H bond in acetylene:



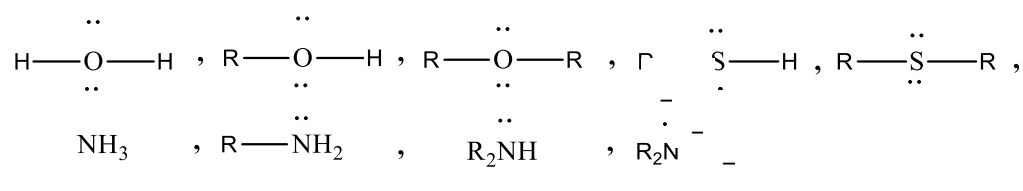
- The group, which contains positively charged carbon atom as in (i) is called carbonium ion, while, the group, which contains negatively charged carbon atom as in (ii) is called carbanion.
- Such reaction, which proceeds through heterolytic fission, is called **polar reaction**.
- Heterolytic fission occurs most readily with polar compounds in polar solvents.
- **Types of reagents in polar reactions:**
The formation of the new covalent bond takes place in two different ways:
 - i. The reagent **donates an electron pair** to the substrate.
 - ii. The reagent **accepts an electron pair** from the substrate.
- **Types of reagents in polar reactions:**

A reagent, which **capable of donating a pair of electrons to the substrate**, to form a new covalent bond is known as nucleophilic reagent or **nucleophile (nucleus loving)**.

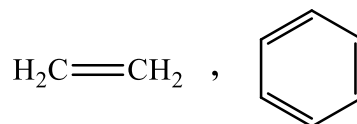
- It is evident that since the nucleophiles are nucleus loving. In a given chemical reaction, they **would seek (attack) a position of low electron density** in substrate.
- In general, nucleophiles include all those anion and molecules with unshared electron pair. Some typical nucleophiles are:
 - 1- Anions:

$\overline{\text{NH}_2}$, $\overline{\text{OH}}$, $\overline{\text{OR}}$, $\overline{\text{CN}}$, $\overline{\text{H}}$, $\overline{\text{X}}$ (halides), $\overline{\text{SH}}$, $\overline{\text{SR}}$, $\overline{\text{HSO}_3}$, $\overline{\text{RCOO}}$, $\overline{\text{CH}(\text{COOR})_2}$.

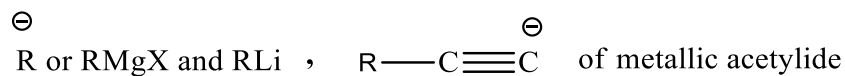
2- Lewis bases (molecules which contain atom with unshared electron pairs):



3- Unsaturated carbon of olefins and aromatic compounds::



4- Hydrocarbons resulted from organometallic compounds:



5- Reducing agents: Fe^{2+} .

- **Electrophilic reagents:**

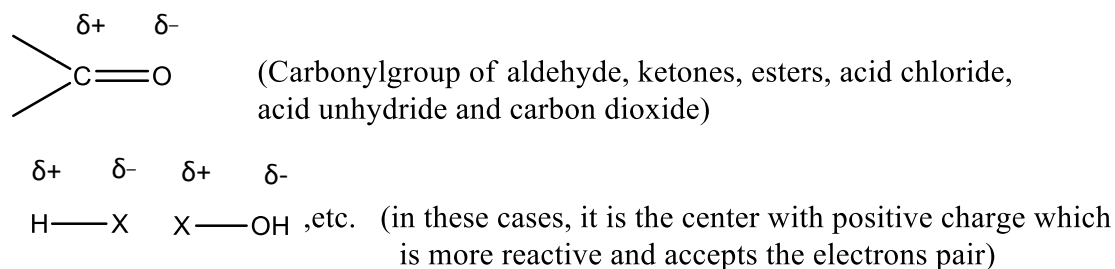
A reagent which **capable of accepting (sharing) a pair of electrons to the substrate**, to form a new covalent bond is known as nucleophilic reagent or an **electrophile (electron loving)**.

Since electrophiles are electron loving, therefore, in a given reaction, they would seek a position of high electron density in the substrate, in general, electrophiles include all cations dipolar molecules or molecules that can be readily polarized Lewis acids, some typical electrophile are:

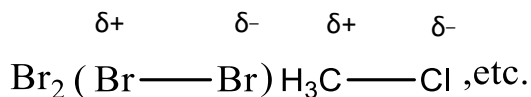
1- Cations:

+ + + + + + + +
H, H₃O, NO, NO₂, SO₃, X (halides), C₆H₅N₂, R, etc.

2- Dipoles:



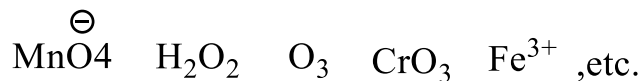
3- Molecules that get readily polarized:



4- Lewis acids: (molecules having atom with incomplete valence octet)



5- Oxidizing agents:



The concept of electrophilic reagent will occur in the study of mechanism of organic reactions. Let us summarize their characteristics.

<u>Nucleophiles</u>	<u>Electrophiles</u>
1. Electron rich 2. Provides as electron pair. 3. Attack on electron-deficient atom. 4. Possess an unshared pair of electrons, which are not too strongly held to the atomic nucleus (usually atoms of groups V and VI of the periodic table. 5. Are often anions.	1. Electron deficient. 2. Accept an electron pair. 3. Attack on electron rich atoms. 4. Possess an empty orbital to receive the electron pair from the nucleophile. 5. Are often cations.

- **Types of Organic reactions:**

Compound can be classified into four main types:

1. Substitution or displacement reaction.
2. Addition reactions.
3. Elimination reactions.
4. Rearrangement reactions.
5. Polymerization reactions.
6. Condensation reactions.

1- Substitution or displacement reactions:

There are also called displacement reactions. These are the organic reactions in which one atom or group in a molecule is substituted

(replaced) by another atom or group with the help of a suitable reagent.

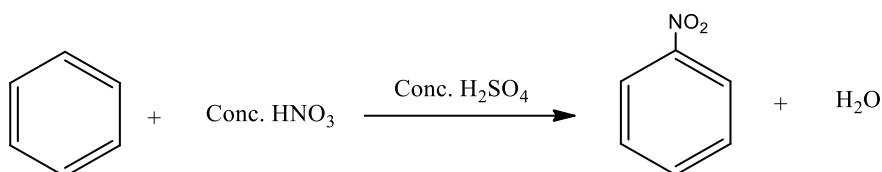
- Depending upon the nature of the attacking reagent, substitution reactions may be further classified as:

- I. Electrophilic substitution reactions.
- II. Nucleophilic substitution reactions.
- III. Free-radical substitution reactions.

2- Substitution or displacement reactions:

When a substitution reaction involves the attack by an electrophile (an electrophile indicates the reaction), the reaction is referred to as electrophilic substitution.

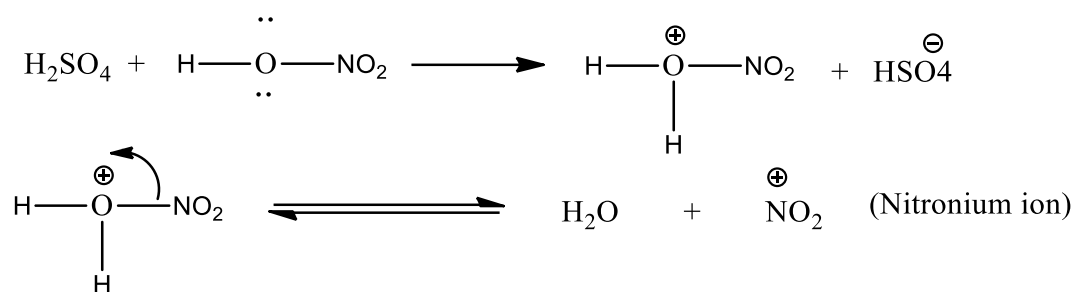
The nitration of benzene is an example of electrophilic substitution reaction:



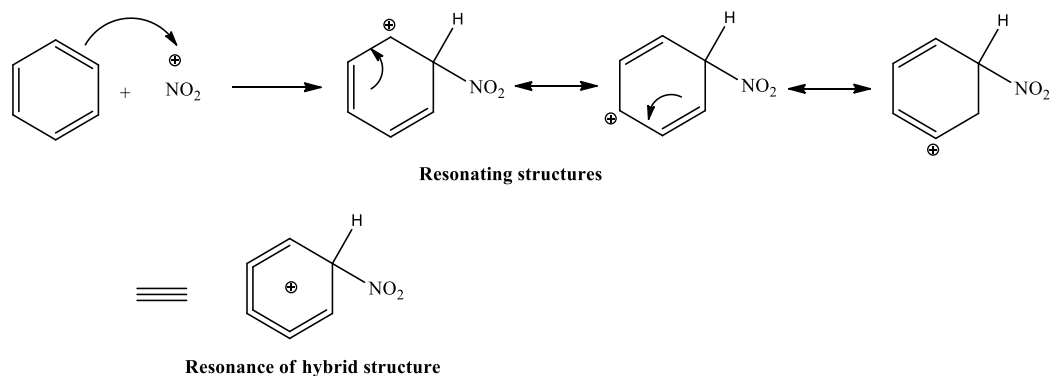
• The mechanism:

The mechanism of the above reaction involves the following steps:

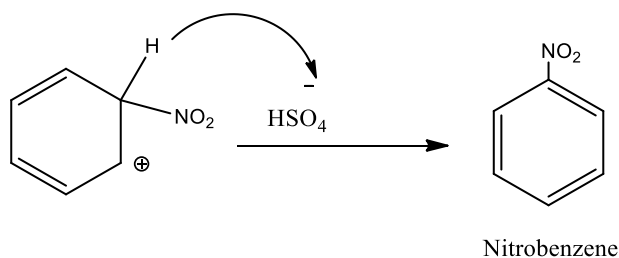
- I. Formation of the electrophile (nitronium ion, NO_2^+) by protonation of nitric acid by sulphuric acid:



II. The electrophile (NO_2^+) attacks the benzene ring to form a resonance stabilized carbonium ion:

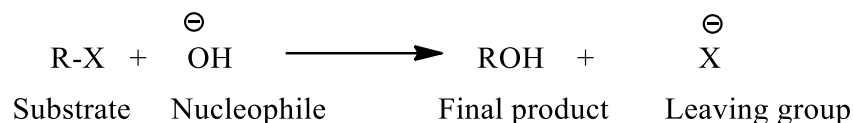


III. Elimination of proton to give nitrobenzene:



3- Nucleophilic substitution reactions:

When a substitution reaction involves the attack by a nucleophile (nucleophile indicates the reaction), the reaction is referred to as nucleophilic substitution. So (S stand for substitution and N for nucleophile), the hydrolysis for alkyl halides by aqueous NaOH is an example of nucleophilic substitution reactions.



The nucleophilic substitution reactions are divided to two types:

- i- S_{N}^1 reactions.
- ii- S_{N}^2 reactions.

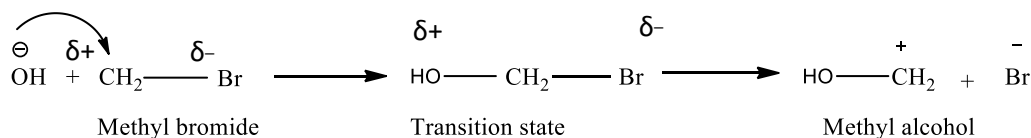
S_{N}^2 reaction stated for the bimolecular nucleophilic substitution.

When the rate of the nucleophilic substitution reaction depends on the concentration of both the substrate and the nucleophile, the reaction is of second order and is represented as S_{N}^2 .

$$\text{Rate} \propto [\text{Substrate}] [\text{Nucleophile}]$$

The rate-determining step involves the participation of both the substrate and the nucleophile.

Consider the hydrolysis of methyl bromide by aqueous KOH. The reaction and the transition state are represented as follows:



The hydroxide ion approaches the substrate carbon from the side opposite the bromine atom (**Back attack**). This is because both hydroxide ion and the bromine atom are electron rich.

The transition state (T.S.) may be pictured as a structure in which both OH and Br are partially bonded to the substrate carbon (α -carbon). In addition, the C-Br bond is not completely cleaved and C-OH bond is not completely formed. Hydroxide ion has a diminished negative charge because it has started to share its electrons with

substrate carbon. The bromine atom also carries a partial negative charge because it has started removing its shared pairs of electron from the carbon atom.

The energy needed for the cleavage of C-Br bond is partially provided by the energy liberated by the C-OH bond formation.

In the course of the reaction, the configuration of the carbon is ***inverted***.

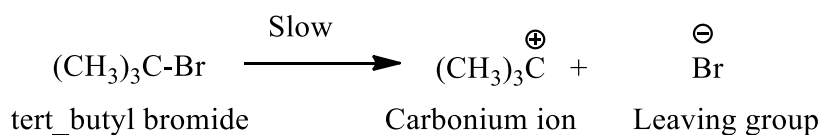
S_N¹ reaction stated for the unimolecular nucleophilic substitution.

When the rate of the nucleophilic substitution reaction depends only on the concentration of the substrate (alkyl halide), the reaction is of first order and is represented as S_N¹.

$$\text{Rate} \propto [\text{Substrate}]$$

Consider the hydrolysis of t-butyl bromide. The reaction consists of two steps:

- i- The alkyl halide ionized to give the carbonium ion. This is the rate-determining step.



The carbonium ion is planar. This is because the central positively charged carbon atom is SP² hybridized.

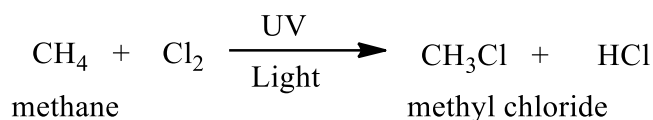
- ii- The nucleophile can attack the planar carbonium ion from either side to give t-butyl alcohol.

- **Remember that:**
- Primary alkyl halides undergo hydrolysis by S_N² mechanism.
- Tertiary alkyl halides undergo hydrolysis by S_N¹ mechanism.

- Secondary alkyl halides may undergo hydrolysis by either S_N^1 or S_N^2 mechanism.

4- Free Radical substitution Reactions:

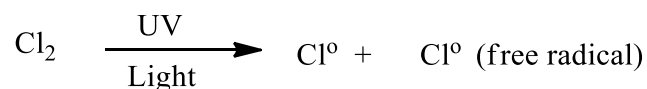
These reactions are initiated by free radicals. The chlorination of methane in the presence of ultraviolet light is an example of free radical substitution.



The mechanism of the above reaction involves the following steps:

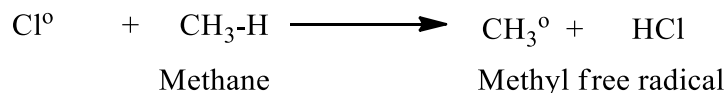
i- Initiation step:

A chlorine molecule undergoes homolytic fission in the presence of ultraviolet light to give chlorine free radicals.



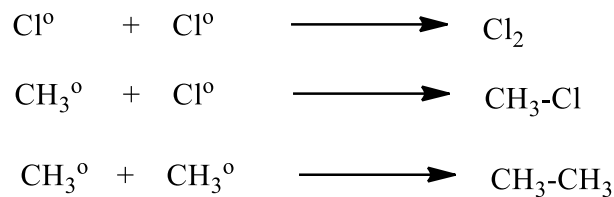
ii- Propagation step:

A chlorine free radical attacks the methane molecule to give methyl free radical and hydrogen chloride.



iii- Termination step:

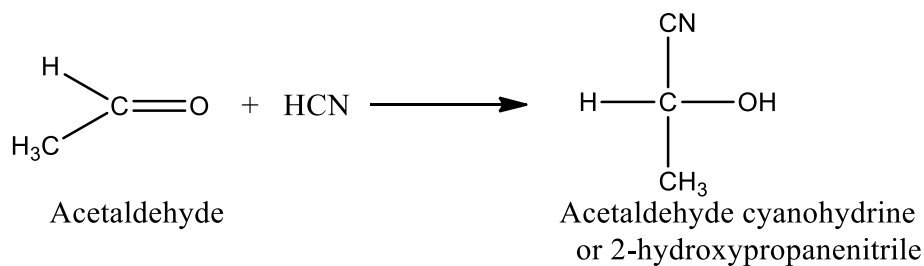
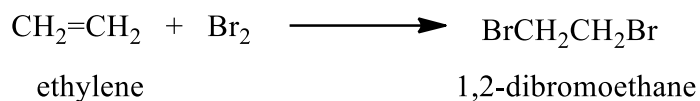
These involve the formation of stable molecules by combination of free radicals.



5- Addition Reactions:

Addition reactions are those in which atoms or groups of atoms are simply added to double or triple bond without elimination of any atom or other molecules.

In these reactions, at least one pi bond is lost while two new sigma bonds are formed. Double bonds become saturated, and the triple bonds are converted into double bonds or may become saturated by further addition. For example:



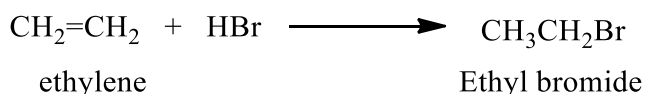
Base on the nature of attacking reagent, addition reaction are further classified as:

- i- Electrophilic addition reaction.
- ii- Nucleophilic addition reaction.
- iii- Free radical addition reaction.

1- Electrophilic addition reaction.

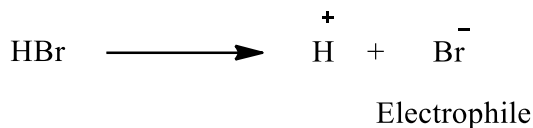
When an addition reaction involves the initial attack by an electrophile, the reaction is referred to as electrophilic addition reaction.

The addition of HBr to ethylene is an example of electrophilic addition reaction.

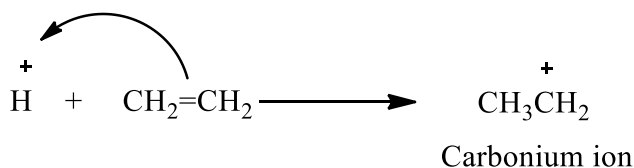


The mechanism of the above reaction involves the following steps:

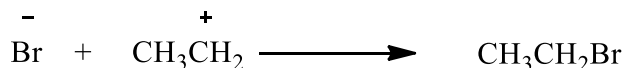
- i- Hydrogen bromide (HBr) gives a proton (H^+) and bromide (Br^-).



- ii- The proton (electrophile attacks the pi bond of ethylene to give a carbonium ion).



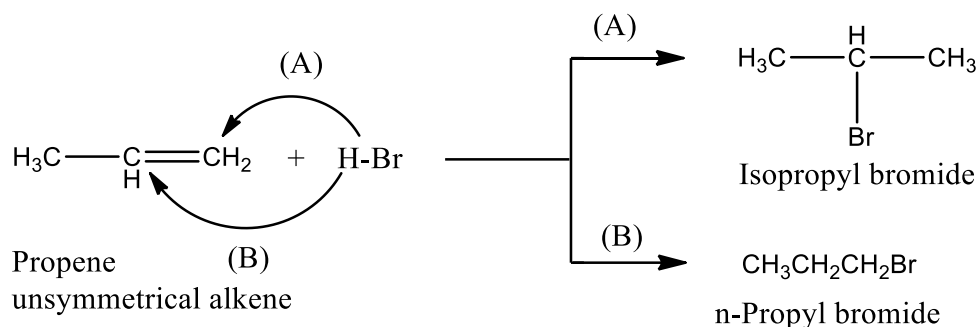
- iii- The bromine ion (nucleophile) attacks the carbonium ion to give the addition product.



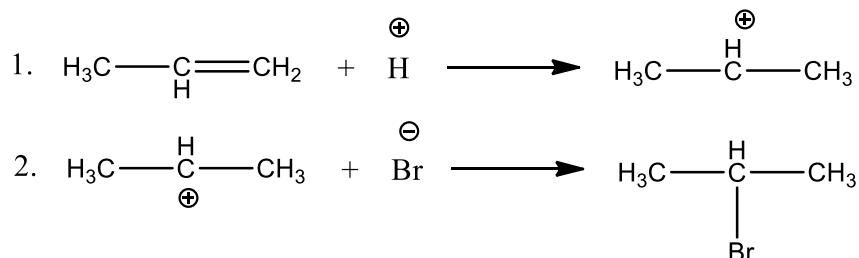
Other reagents like HCl, HOCl, H_2SO_4 , Br_2 , Cl_2 , etc. add to the alkenes similarly.

When the alkene is symmetrical about the double bond, as ethylene, the product formed in addition reaction is the same.

If, however, both the alkene and the adding reagent are unsymmetrical, two alternatives are possible:

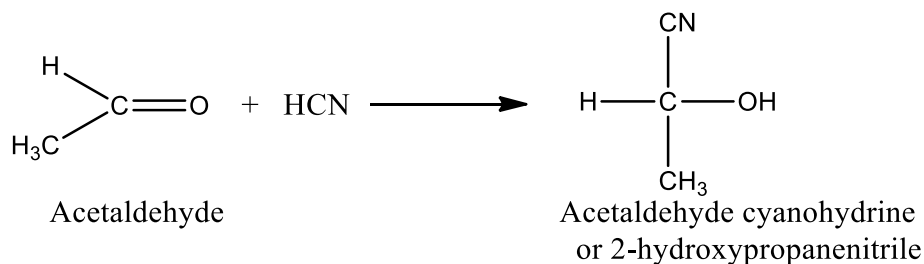


Experimentally it has been found that isopropyl bromide is the major product. Thus, when a symmetrical reagent adds to an unsymmetrical double bond, the positive part of the reagent becomes attached to the double bond carbon atom, which bears the greatest number of hydrogen atoms.



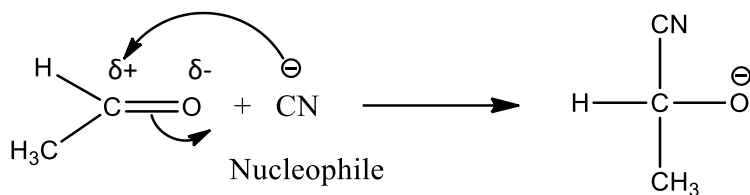
2- Nucleophilic addition reaction.

When an addition reaction involves the initial attack by a nucleophile, the reaction is referred to as nucleophilic addition reaction. Aldehydes and ketones, which contain carbon-oxygen double bond, undergo such reaction.

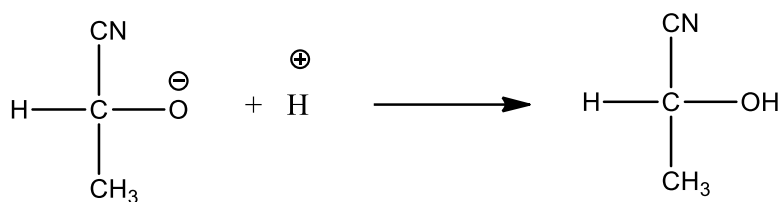


- The mechanism of the above reaction involves the following steps:

- i. Hydrogen cyanide (HCN) gives a proton (H^+) and cyanide ion (CN^-).
- ii. The cyanide ion (CN^-) (Nucleophile) attacks the positive charged carbonyl carbon to give the corresponding anion.



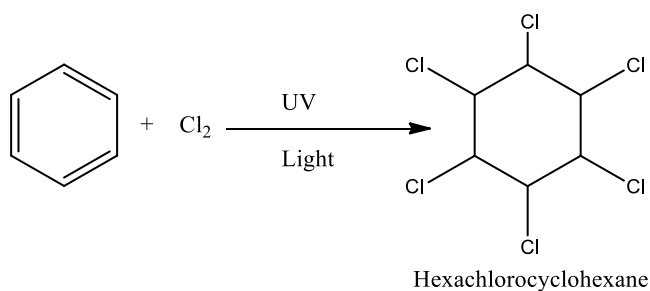
- iii. The proton (electrophile) combine with the anion to form the addition product.



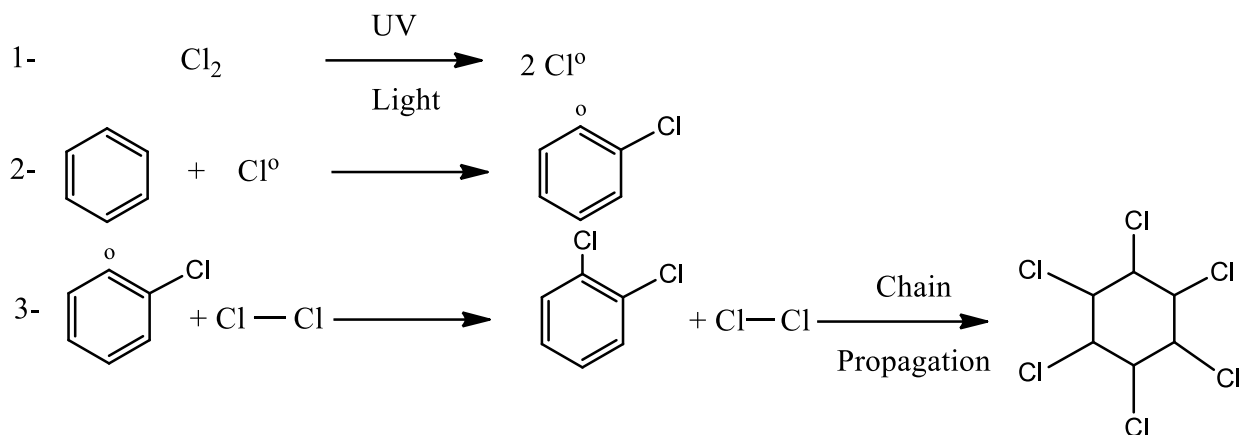
Acetaldehyde cyanohydrine

3- Free-Radical addition reaction.

These reactions are initiated by the free radical. Thus, benzene reacts with chlorine or bromine in presence of ultraviolet light to form benzene hexachloride.



The above reaction involves a free radical mechanism.

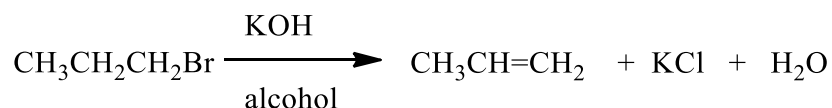


4- Elimination reaction.

Elimination reaction involve the removal of a small molecule or group of atoms from two adjacent atoms in the substrate molecules to form a multiple bond.

Elimination reactions may be regards as a reverse of addition reaction. In these reactions, two sigma bonds are lost and a new pi bond is formed. Saturated compounds become unsaturated.

For example, the dehydrohalogenation of alkyl halides with alcoholic alkalis:



These reactions like substitution reactions are also divided into two classes:

i- E₂ Reaction.

ii- E₁ Reaction.

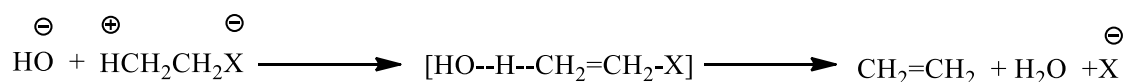
i- E₂ Reaction.

E₂ Reaction stands for **bimolecular elimination**, whereas the rate of an eliminsation reaction depends upon the concentration of the

substrate and the **nucleophile**, the reaction is **second order** and is represented as **E₂ Reaction**.

E₂ as if S_N² is also **one-step** process in which the attack of a nucleophilic base on the β-carbon atom followed by a simultaneous loss of a halide ion from the α-carbon atom.

The mechanism of such a reaction is represented as follows:

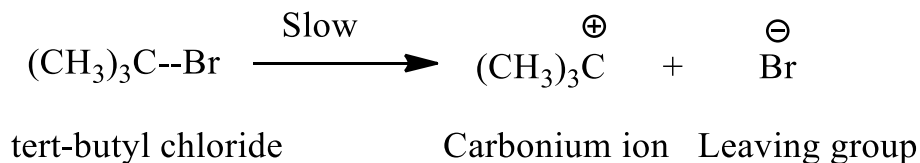


i- **E₁ Reaction**.

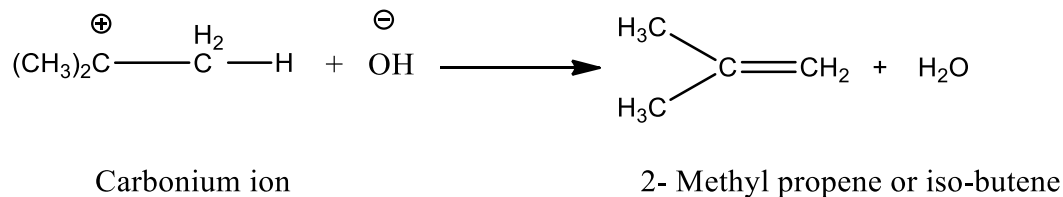
E₁ Reaction stands for **unimolecular elimination**, whereas the rate of an elimination reaction depends upon the concentration of the **substrate**, the reaction is **first order** and is represented as **E₁ Reaction**.

E₁ as if S_N¹ is also **two-step** process:

- i- The alkyl halide ionizes to give the carbonium ion. This is the rate-determining step.



- ii- The proton is abstracted by the base from the adjacent β-carbon atom to give the alkene.

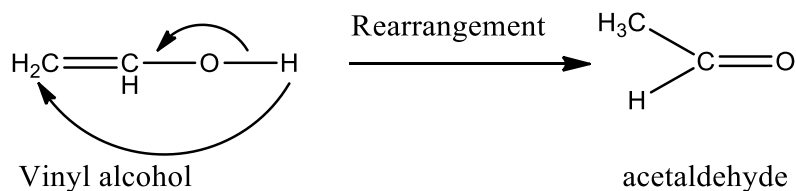


5- Rearrangement Reactions:

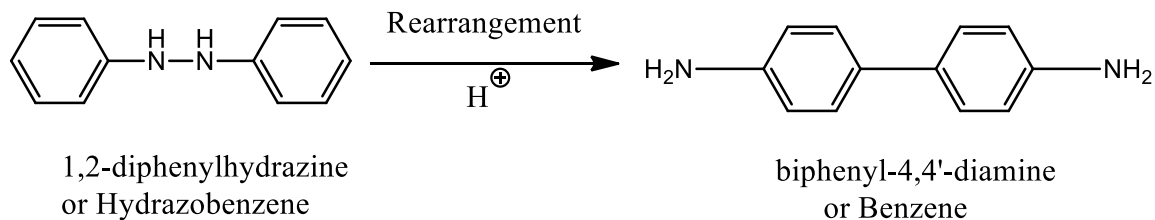
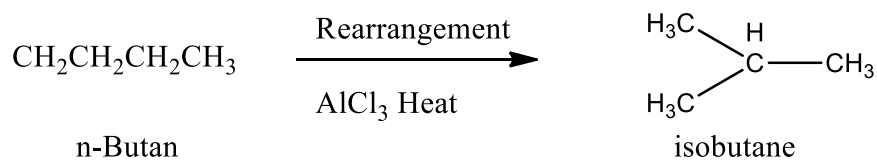
Rearrangement reaction involves the migration of an atom or group of atoms from one site to another within the same molecule to convert it into molecule, their molecules formulas remaining the same.

For example:

i- Vinyl alcohol is at once converted into acetaldehyde.



Also,



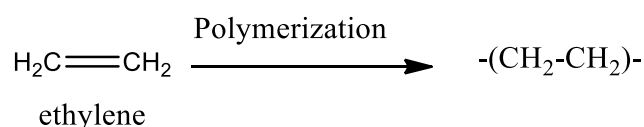
6- Polymerization Reactions:

The union of two or more molecules of a substance to form a large molecule is called polymerization reaction and the products thus obtained are called a polymer.



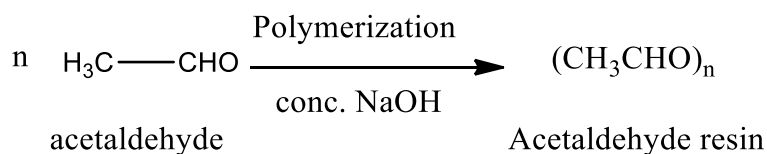
The simple molecules (M) are called monomers. And the products are named as dimers (M_2), trimers (M_3) and polymers (M_n) according to the number of molecules joining as the formation of the complex molecule joining in the formations of the complex molecule, 2,3, or n (many) respectively, for example:

i- Polymerization of ethylene:



ii- Resinification of aldehyde:

Aliphatic aldehydes on shaking with a conc. solution of a strong alkali salt NaOH (aq.) form a yellow resinous mass, which is a polymer of acetaldehyde. Thus,



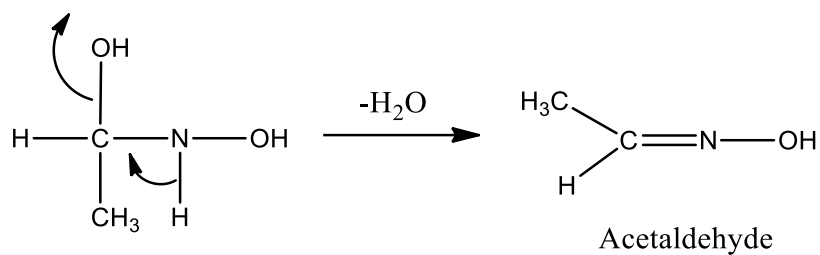
7- Condensation Reactions:

A *condensation reaction* is one in which *two* or *more molecules combine into a larger molecule with or without the loss of a small molecule (such as water)*.

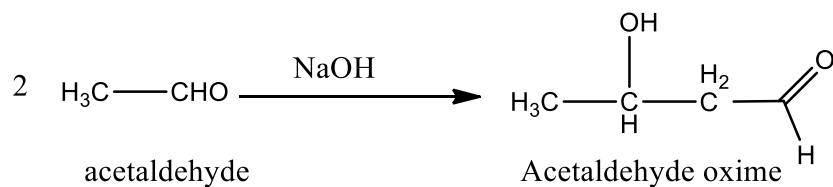
The **Aldol** condensation is an addition reaction in which no small molecule is lost.

- i- Hydroxylamine behave as nucleophile reagent since it has an unshared pair of electrons on nitrogen, it adds to the carbonyl group.

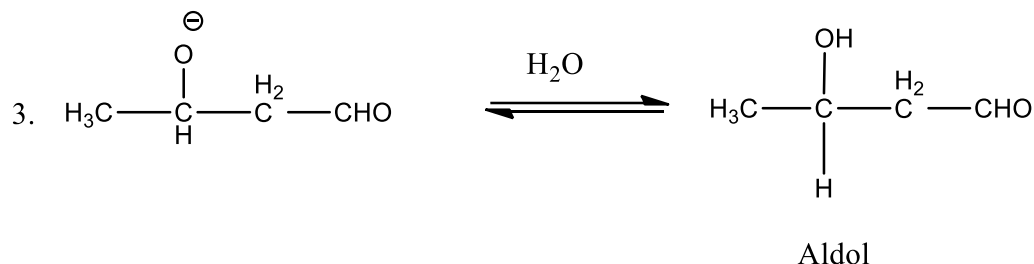
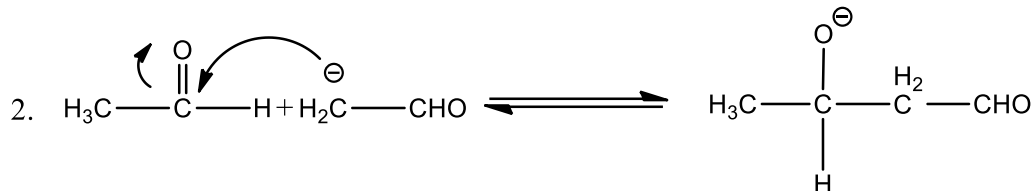
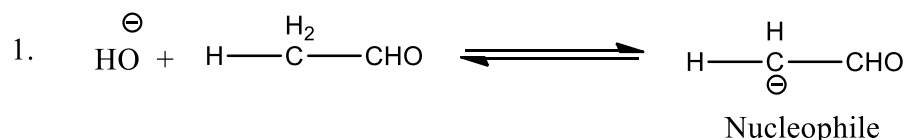
Addition product rapidly loses a molecule of water to give the final product.



- ii- Aldol condensation is condensation of two molecules of acetaldehyde in the presence of dilute alkali.



Mechanism:



- **Ionic and Free Radical Reaction:**

Organic reactions may be classified according to the nature of the reactive intermediates involved.

- i- **Ionic Reactions:**

A great majority of organic reactions are ionic reactions. Such reactions are usually favored with polar solvent, which helps to solvate the ionic species formed in the reaction.

- ii- **Free-Radical Reactions:**

Free radical reactions are usually reactions carried out in the presence of a free radical initiator or vapour phase reactions carried out at high temperatures.

The comparison between free radical reactions and polar reactions can be summarized as follow:

Free radical reaction	Ionic reaction
1. These occur in gas (vapour) phase or in non-polar solvent.	These occur only rarely in gas phase, but mainly in solutions of polar solvents, reaction is influenced by the polarity of solvent.
2. These reactions are initiated and catalyzed by light, high temperature, oxygen or peroxides.	These reactions are not affected by light, oxygen, or peroxides, but catalyzed by acids and bases. The reaction rate increases by increasing temperature.
3. These reactions are inhibited or prevented by the presence of free radical inhibitors (i.e. hydroquinone).	These are not affected by the presence of free-radical inhibitors.
4. During the reaction, one or more free radicals are involved and may result in the formation of a new intermediate free radical.	During the reaction, a pair of electrons transferred from the substrate neither to the reactant nor from the reactant to the substrate.
5. Often take place through chain mechanism.	Seldom take place through chain mechanism.

8- Condensation Reactions:

Heterolytic and homolytic bond fission result in the formation of short-lived fragments called reaction intermediates. Among the important reaction intermediates are carbonium ions, carbanions and free radicals.

- **Definitions:**

- 1- **Carbonium ion (Carbocation):**

An intermediate containing a positively charged carbon is carbocation (e.g. CH_3^+), such a species have one electron less than a free radical and was commonly referred to as carbonium ion, and the CH_3^+ species is called a methyl cation.

- 2- **Carbanion:**

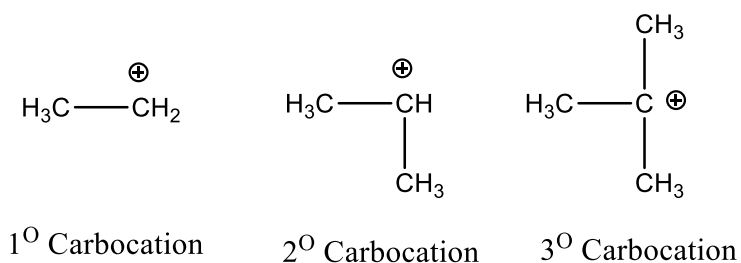
An intermediate in which a carbon is negatively charged carbon is carbanion (e.g. CH_3^-), such a species have one electron more than a free radical and was commonly referred to as carbanion ion, and the CH_3^- species is called a methyl anion.

- 3- **Free radical:**

An intermediate in which a carbon carries and odd electrons (e.g. $\text{CH}_3^\bullet$), such a species is a neutral species and is referred to as a free radical. The $\text{CH}_3^\bullet$ species is called a methyl radical.

- **Classification:**

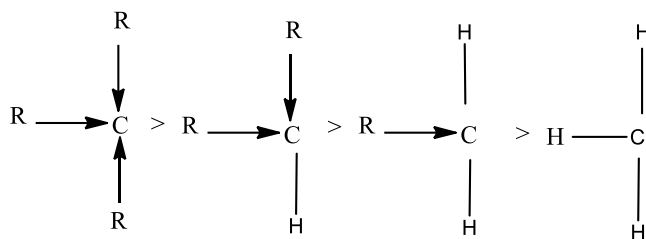
Carbonium ions, free radicals and carbanion may be classified as a primary (1°), secondary (2°) or tertiary (3°) depending on whether there are one, two or three carbon atoms attached to the carbon bearing the charge or odd electrons, for example:



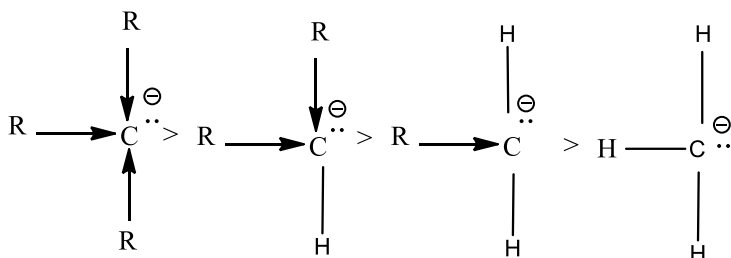
- **Stability and ease of formation:**



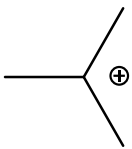
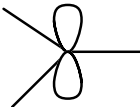
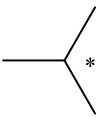
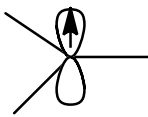
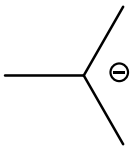
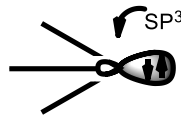
- The stability of carbonium ions (carbocations) is influenced by both resonance and inductive effect.
- E.g. Allyl ($\text{CH}_2=\text{CH}_2-\text{CH}_2^+$) and benzyl ($\text{C}_6\text{H}_5-\text{CH}_2^+$).
- Carbonium ions are stabilized by resonance.
- Electron releasing groups (+I) also stabilize carbonium ions by partial neutralization of the positive charge on carbon. Thus, 3^ocarbonium ion is the most stable because of the +I effect association with alkyl groups.



- Electron attracting group (-I group) like $-\text{NO}$, $-\text{Cl}$ will make a carbonium ion less stable.
- Stabilization of carbanion by inductive effects is in the opposite direction from the carbonium ions.
- Electron releasing group (+I) make the carbanions stable.
- Thus, a primary carbanion is the most stable because of +I effect associated with alkyl groups.

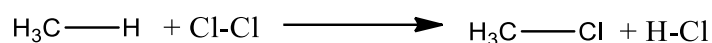


- Electron attracting group (-I groups) like $-\text{NO}_2$, $-\text{Cl}$ will stabilize carbanion ion by partial removal of the negative charge on the carbon.
- Like carbonium ions, a 3° free radical is more stable than 2° , which in turns is more stable than 1° .

Intermediate	Classification	Stereochemistry	
	Carbocation	SP ² carbon, planar with no electron in the empty p-orbital	
	Free radical	SP ² carbon, probably planar with one electron in the p-orbital	 P-orbital with one electron
	Carbanion	SP ³ carbon, pyramidal, with two electrons in a non-bonding orbital	

- **ENERGY CHANGE IN ORGANIC REACTIONS:**

The energy change accompanying a chemical reaction is in the form of heat absorbed or heat released. The heat of reaction (ΔH reaction) can be evaluated from the bond dissociation energy. E.g., in the reaction.



The total energy required to break the CH₃-H and Cl-Cl bond is:

$$\Delta H = (+104) + (+58) = 162 \text{ K cal/mole}$$

The total energy liberated due to the formation of CH₃-Cl and H-Cl bonds is:

$$\Delta H = (-84) + (-103) = -187 \text{ K cal/mole}$$

Therefore:

$$\Delta H = (104+58) - (84+103) = 162-187 = -25 \text{ Kcal/mole.}$$

- **Exothermic and endothermic reaction:**

An exothermic reaction is one in which heat is liberated ($\Delta H = -ve$).

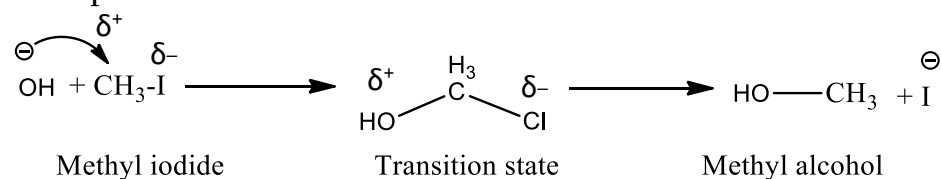
An endothermic reaction is one in which heat is absorbed ($\Delta H = +ve$).

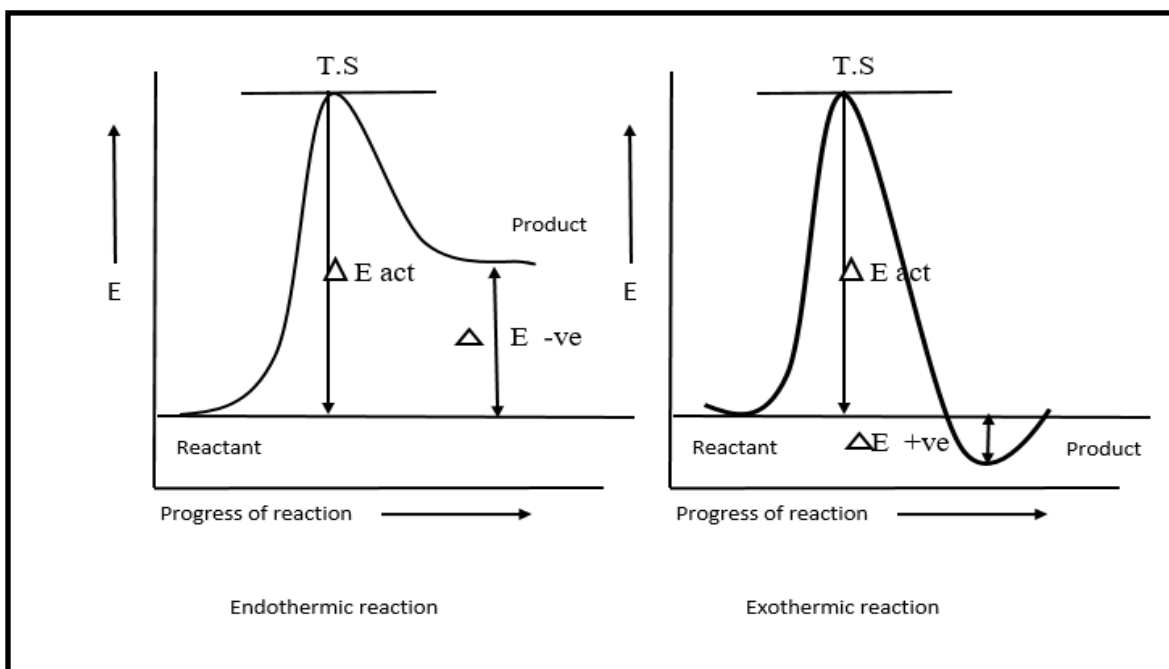
- **One step reaction:**

One-step reaction occur according to the following scheme:

Reactants $\longrightarrow$ Transition state (T.S.) $\longrightarrow$ product
or activated complex

the transition state (T.S.), formed through the collision of reacting molecules, possessing a definite geometry and charge distribution and represents the most energetic atomic aggregation in rate from the reactants to the products. For example:

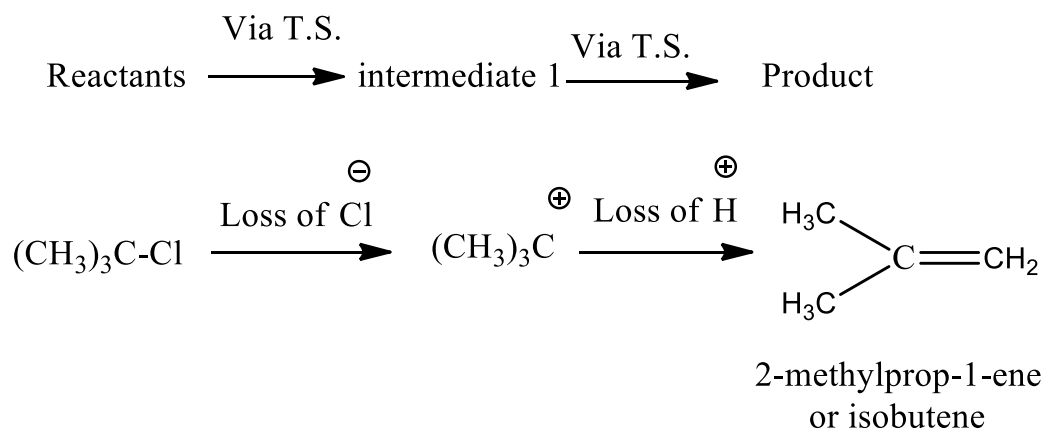


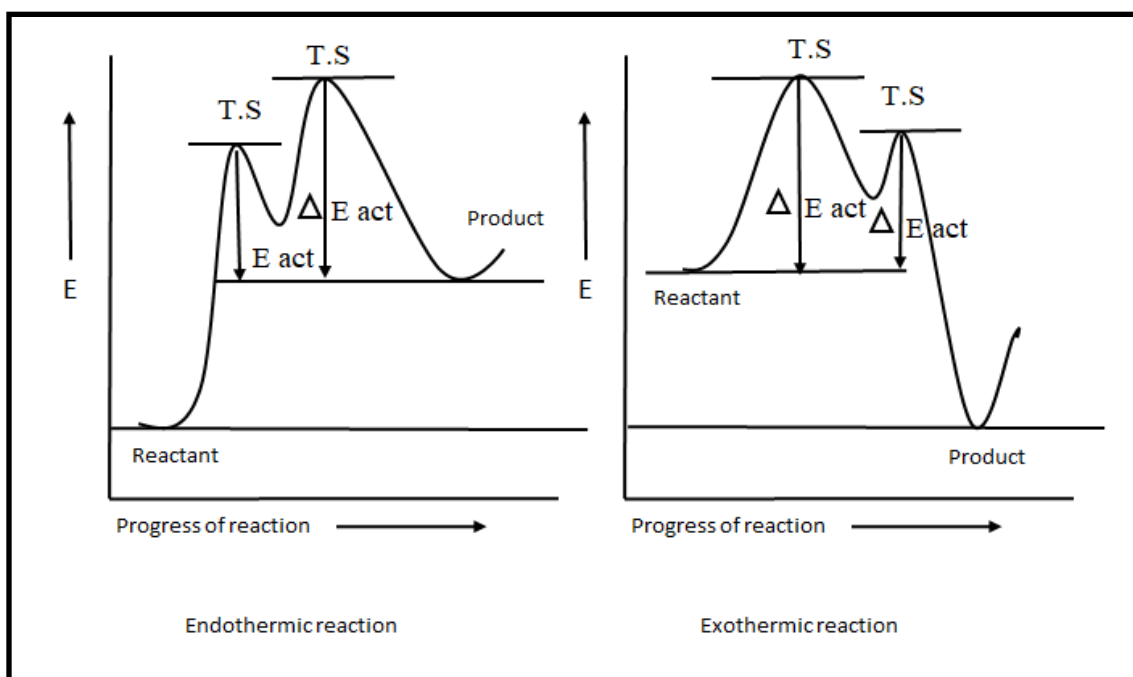


Energy profile of one-step reaction

- Two step reactions:**

Reactions involving an intermediate are two-step reactions that take place by the following scheme:





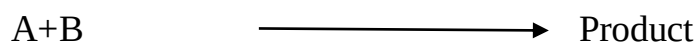
The energy profile diagram for such a reaction would show two maximum and minimum as shown.

- **Rate Dependence:**

A study of reaction is called **Chemical Kinetics**. The rate of an organic reaction is dependent upon a number of factors:

a- The rate of a reaction varies directly with the **concentration of reactants**.

For reaction:



$$\text{Rate} = K [A] [B]$$

Where [A] and [B] are concentrations of A and B expressed in moles/liter, and K is the specific rate constant.

- b- The rate of a reaction varies **directly** with the **temperature** but **inversely** with the **activation energy**.

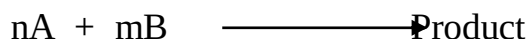
$$K = Ae^{-E_{act}/RT}$$

- **Activation energy:**

Is the minimum amount of energy that must be provided by collisions of the reacting molecules for the reaction to occur is known as **activation energy** (E_{act}).

- **Order and Molecularity:**

- c- General rate equation for:



Where, n and m are powers for concentration of reactants A, B.

- d- Oxidation of reaction is the sum of the concentration exponents (n+m) in the rate equation.
- e- Molecularity of the reaction represents the number of molecular species involved in the rate-determining step of the reaction. For many reactions, the molecularity of the reaction is the same order as the order of the reaction, although expectations are known.

Inductive and Mesomeric Effect –Summary

Inductive Effect	Mesomeric Effect
Electrostatic (Coulomb forces)	Delocalization of π -electrons (mesomeric or resonance structures)
Distance dependent	Independent from distance if conjugated double bonds, π -system must be in plane.
-I: attraction of bond electrons by substituent stronger than H.	-M: substituent decreases electron density in π -system (become negatively charged)
-I: attraction of bond electrons by substituent weaker than H.	-M: substituent increases electron density in π -system (become positively charged)
-I: $\equiv > \text{C}_6\text{H}_5 > =$ -NR ₂ < -OR < -F -NR ₂ ⁺ < -OR ₂ ⁺	-M: =NR < =NR ₂ ⁺ -NO ₂ , -NO =CR ₂ < =NR < =O
+I: -O < -NR ₂ -CH ₃ < -CH ₂ -CH ₂ < -CH(CH ₃) ₂	+M: -F < -OR < -NR ₂ -OR < O.