ORGANIC CHEMISTRY
(DCHE03)
(MSC CHEMISTRY)

ACHARYA NAGARJUNA UNIVERSITY

CENTRE FOR DISTANCE EDUCATION

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UNIT – 1

1. Nature of Bonding in Organic Molecules :

Delocalized Chemical Bonding :

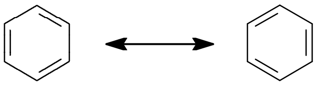
Some compounds contain one or more bonding orbitals that are not restricted to two atoms, but that are spread out over three or more. Such bonding is said to be delocalized bonding. This delocalised chemical bonding can be explained by Valence bond method and Molecular orbital method.

In the valence bond method, several Lewis structures or canonical forms are drawn and the molecule taken to be a weighted average of them.

$$\psi = C_1\psi_1 + C_2\psi_2 + ...$$

In this equation each ψ represents one of these structures. This representation of a real structure as a weighted average of two or more canonical forms is called resonance.

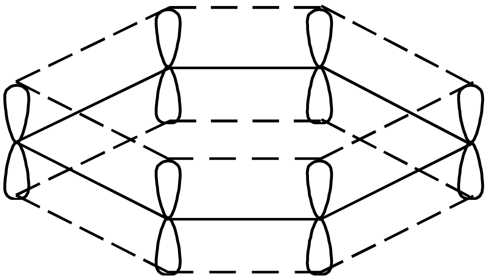
Ex.: Benzene



The above two forms are canonical forms of benzene. The energy of the actual molecule is obviously less than that of any one Lewis structure, since otherwise it would have one of those structures. The difference in energy between the actual molecule and the Lewis structure of lowest energy is called resonance energy.

The resonance picture is often used to describe the structure of molecules, but quantitative valence – bond calculations become much more difficult as the structures become more complicated. Therefore molecular orbital method is used much more often for the solution of wave equations.

Molecular orbital method can be best explained by taking the benzene as an example. In benzene each carbon atom is connected to three other atoms. It uses sp^2 orbitals to form σ bonds so that all 12 atoms are in one plane. Now each carbon has a 'p' orbital with one electron and each of these can overlap equally with the two adjacent 'p' orbitals. This overlap of six orbitals produces six new orbitals, three of which are bonding and three antibonding. As a result of the overlapping of six orbitals, a torus shaped electron cloud called aromatic sextet is produced. The C – C bond order for benzene, calculated by this method is 1.667.



Overlapping of 'p' orbitals in Benzene

For planar unsaturated and aromatic molecules, molecular orbital calculations have been made by treating the σ and π electrons separately. In these calculations π orbitals can be treated as delocalised bonds. First such calculations were made by Hucckel, and they are called Huckel Molecular Orbital calculations. Because electron – electron repulsions are either neglected or averaged out in the Huckel Molecular Orbital (HMO) method, another approach, the self consistent field (SCF) method was devised.

Although these methods give many useful results, they are often unsuccessful for other molecules. It could be better if both the σ and π electrons to be included in the calculations. The development of modern computers has now made this possible.

Both the Valence bond and Molecular orbital methods show that there is delocalization in benzene. Since each method is useful for certain purposes, we shall use one or the other as appropriate.

Kinds of Molecules having Delocalized bonds :

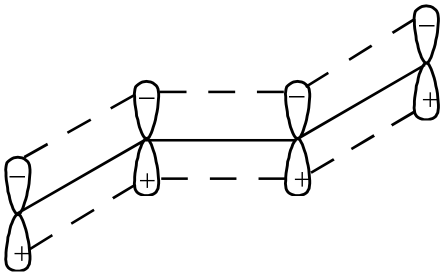
There are three main types of structures that exhibit delocalization. They are :

1. Double bonds in conjugation :

Butadiene is the best example for this. In the molecular orbital picture, the overlap of four orbitals gives two bonding and two antibonding orbitals. The energies of four orbitals are $\alpha + 1.618\,\beta$, $\alpha + 0.618\,\beta$, $\alpha - 0.618\,\beta$, $\alpha - 1.618\,\beta$ and the total energy is $4\alpha + 4.472\,\beta$. Since the energy of two isolated double bonds is $4\alpha + 4\beta$, resonance energy is 0.472 β.

The possible resonance structures are as follows :

$$H_2C = CH - CH = CH_2 \longleftrightarrow H_2\overset{\oplus}{C} - CH = CH - \overset{\ominus}{C}H_2 \longleftrightarrow H_2\overset{\ominus}{C} - CH = CH - \overset{\oplus}{C}H_2$$



Overlaping of '4p' orbitals of Butadiene

Bond lengths in Butadiene are 1.34A° for double bonds and 1.48 A° for single bond. But the typical single bond distance of a bond adjacent to an unsaturated group is 1.53 A°. This shortening can be explained by resonance.

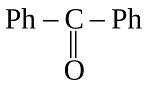
Resonance energies for butadiene, calculated from heats of combustion or hydrogenation are only about 4 K.cal./mol. and these values may not be entirely attributed to resonance. It may be that some of the already small value of 4 K.cal./mol. is not resonance energy, but arises from differing energies of bonds of different hybridisation.

Though bond distances fail to show it and the resonance energy is low, the fact that butadiene is planar shows that there is some delocalization. Similar delocalization is found in other conjugated systems.

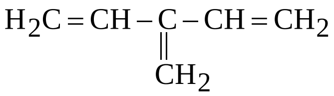
2. Cross conjugation :

In a cross conjugated compound, three groups are present two of which are not conjugated with each other, although each is conjugated with the third.

Ex.

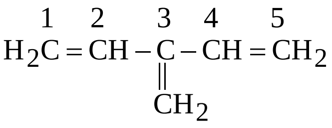


$Ph-\underset{\underset{O}{\|}}{C}-Ph$,



$H_2C=CH-\underset{\underset{CH_2}{\|}}{C}-CH=CH_2$

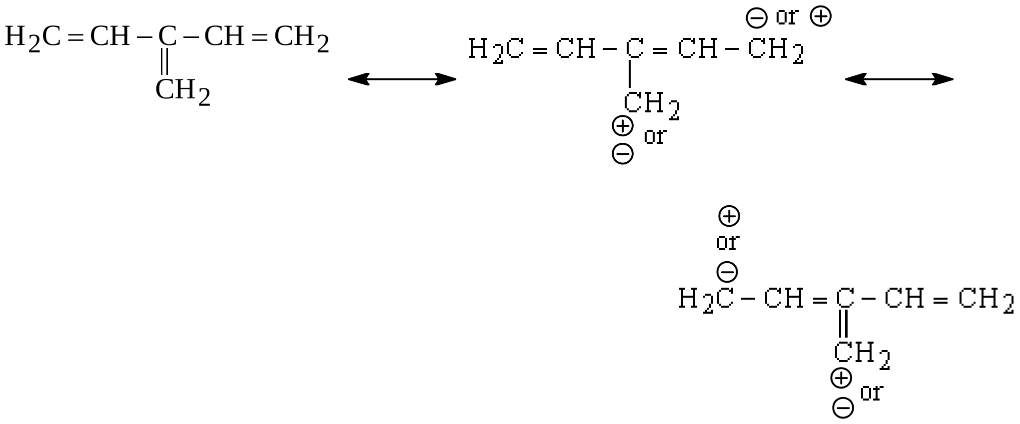
It can be best explained by taking the following example.



$$\overset{1}{H_2C}=\overset{2}{CH}-\overset{3}{\underset{\underset{CH_2}{\|}}{C}}-\overset{4}{CH}=\overset{5}{CH_2}$$

In the above compound we find that overlap of six 'p' orbitals gives six molecular orbitals of which three are bonding and three are antibonding. The total energy of the bonding orbitals is $6\alpha + 6.900\beta$. Since the energy of three isolated double bonds is $6\alpha + 6\beta$, the resonance energy for this molecule is $0.900\,\beta$.

Bond orders are 1.930 for C–1, C–2, bond, 1.859 for C–3, C–6 bond and 1.363 for C–2, C–3 bond. We see that C–1, C–2 bond contains more and C–3, C–6 bond has less double bond character than the double bonds in butadiene. The resonance phenomena supports this conclusion.



$$H_2C=CH-\underset{\underset{CH_2}{\|}}{C}-CH=CH_2 \longleftrightarrow H_2C=CH-\underset{\underset{\underset{\oplus\text{ or }\ominus}{CH_2}}{|}}{C}=CH-\overset{\ominus\text{ or }\oplus}{CH_2} \longleftrightarrow \overset{\oplus\text{ or }\ominus}{H_2C}-CH=\underset{\underset{\underset{\oplus\text{ or }\ominus}{CH_2}}{\|}}{C}-CH=CH_2$$

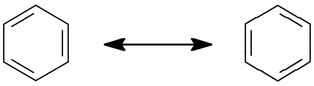
In these resonance structures C–1, C–2 bond is double in three of the five canonical forms, while the C–3, C–6 bond is double in only one.

In most cases it is easier to treat cross conjugated molecules by the molecular – orbital method than by the valence – bond method.

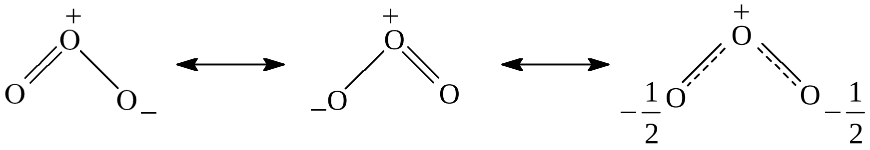
Resonance :

Resonance may be defined as the phenomenon is which two or more structures, involving identical position of atoms, can be written for a particular compound.

Ex.: Benzene



To deal with circumstances such as bonding in ozone, the notion of resonance between Lewis structures was developed. According to resonance concept, when more than one Lewis structure may be written for a molecule, a single structure is insufficient to describe it. Rather, the true structure has an electron distribution that is a hybrid of all possible Lewis structures that can be written for the molecule.



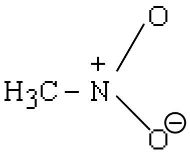
Resonance attempts to correct a fundamental defect in Lewis formulas. Lewis formulas show electrons as being localized. They either are shared between two atoms in a covalent bond or are unshared electrons belonging to a single atom. In reality, electrons distribute themselves in the way that leads to their most stable arrangement. This sometimes means that a pair of electrons is delocalized or shared by several nuclei.

Rules of Resonance :

In drawing canonical forms and deriving the true structures from them, we are guided by certain rules which are as follows.

1. Atomic positions must be the same in all resonance structures. Only the electron positions may vary among the various contributing structures.

Ex.:



(A)

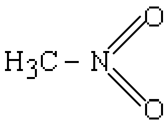
$H_3C-O-N=O$

(B)

These structural formulas represent different compounds, but not different resonance forms of the same compound. 'A' is the structure for nitromethane and 'B' is methyl nitrite.

2. Lewis structures in which second row elements share more than eight valence electrons are especially unstable and make no contribution to the true structure.

Ex.:



This compound has 10 electrons around nitrogen. Hence it is not a permissible Lewis structure for Nitromethane and so cannot be a valid resonance form.

3. When two or more structures satisfy the octet rule, the most stable one is the one with the smallest seperation of oppositely charged atoms.

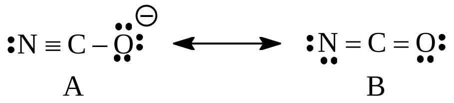
Ex.: $H_3C-O-N=O \longleftrightarrow H_3C-\overset{+}{O}=N-\overset{\ominus}{O}$

(A) (B)

The two Lewis structures A and B of methyl nitrite satisfy the octet rule. Structure A has no seperation of charge and is more stable than B.

4. Among structural formulas in which the octet rule is satisfied for all atoms and one or more of these atoms bears a formal charge, the most stable resonance form is the one in which negative charge resides on the most electronegative atom.

Ex.:

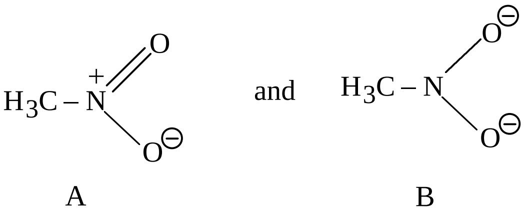


$:N\equiv C-\overset{\ominus}{\ddot{\underset{..}{O}}}: \longleftrightarrow :\underset{..}{N}=C=\underset{..}{O}:$

The most stable Lewis structure for cyanate ion is A because the negative charge is on its oxygen. In B negative charge is on nitrogen. Oxygen is more electronegative than nitrogen and can better support a negative charge.

5. Each contributing Lewis structure must have the same number of electrons and the same net charge although the formal charges of individual atoms may vary among the various Lewis structures.

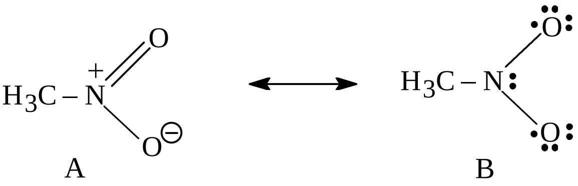
Ex.:



The two structures are not resonance forms of one another. Structure A has 24 valence electrons and a net charge of 0. 'B' has 26 valence electrons and a net charge of –2.

6. Each contribution Lewis structure must have the same number of unpaired electrons.

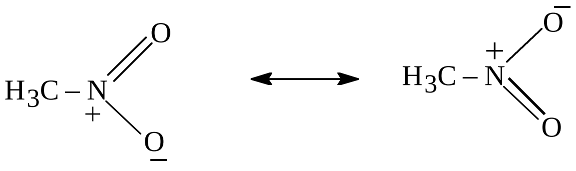
Ex.:



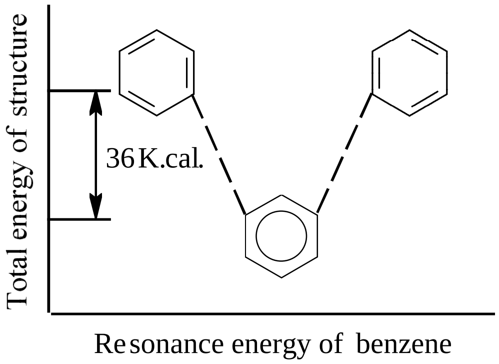
A is Lewis structure of nitromethane, B is not, even though it has the same atomic positions and the same number of electrons. Structure B has two unpaired electrons. Structure A has all its electrons paired and is a more stable structure.

7. Electron delocalization stabilizes a molecule. A molecule in which electrons are delocalized is more stable than implied by any of the individual Lewis structures that may be written for it.

Ex.:



Nitromethane is stabilised by electron delocalization more than methyl nitrite.
The difference in energy between the resonance hybrid and the most stable canonical structure is referred as the resonance energy of the molecule.

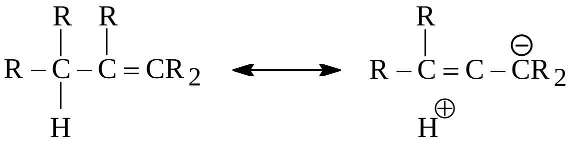


Hence Resonance energy for Benzene is 36 K.cal/mole.

HYPERCONJUGATION :

Alkly groups with at least one hydrogen atom on the σ – carbon atom when attached to an unsaturated carbon atom are able to release electrons by a mechanism known as Hyperconjugation.

Ex.:

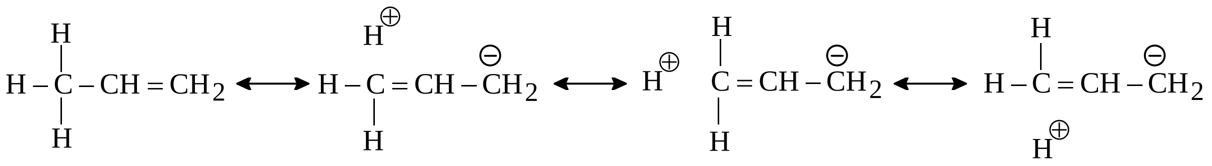


$$R-\underset{H}{\overset{R}{C}}-\overset{R}{C}=CR_2 \longleftrightarrow R-\underset{H^{\oplus}}{\overset{R}{C}}=C-\overset{\ominus}{C}R_2$$

The phenomenon of hyperconjugation may be considered in terms of resonance as well as molecular orbital theory.

i **Resonance :** Hyperconjugation may be interpreted in terms of resonance.

Ex.:



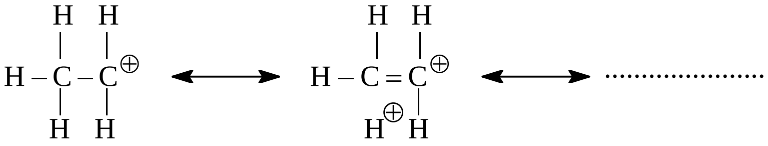
$$H-\underset{H}{\overset{H}{C}}-CH=CH_2 \longleftrightarrow H-\underset{H}{\overset{H^{\oplus}}{C}}=CH-\overset{\ominus}{C}H_2 \longleftrightarrow \overset{\oplus}{H}\ \underset{H}{\overset{H}{C}}=CH-\overset{\ominus}{C}H_2 \longleftrightarrow H-\underset{H^{\oplus}}{\overset{H}{C}}=CH-\overset{\ominus}{C}H_2$$

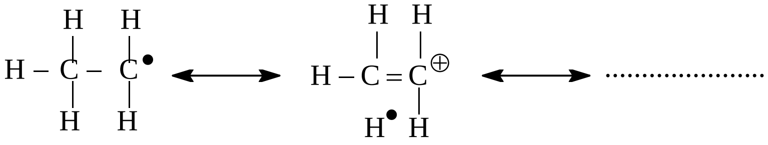
Since in the above resonating structures, there is no definite bond between one of the carbon atoms and one of the hydrogen atoms, hyper conjugation is also known as "No bond resonance".

ii. **Molecular Orbital Treatment :**

While considering the molecular orbital treatment, hyperconjugation may be regarded as an overlap of σ orbital of the C–H bond and π orbital of the C–C bond.

For carbocations and free radicals and for excited states of molecules, there is evidence that hyper conjugation is important. In hyperconjugation in the ground state of neutral molecules, which Muller and Mulliken call sacrificial hyperconjugation, the canonical forms involve not only no–bond resonance but also a charge separation not possessed by the main form. In free radicals and carbocations, the canonical forms display no more charge seperation than the main form. Muller and Mulliken call this as "isovalent hyperconjugation".





Effects of Hyperconjugation :

Hyperconjugation is used to interpret molecular properties in terms of structural formulae. It can affect both Physical and Chemical properties of molecules which is evident from the following examples.

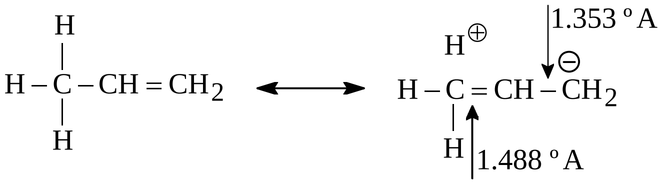
i. **Heats of Hydrogenation :**

For compounds of similar structure, smaller the heat of hydrogenation, more stable is the compound. The heat of hydrogenation of ethylene and propylene are 32.8 and 30.1 K.cal/mol. respectively. The more stability of propylene is due to hyperconjugation.

ii. **Bond length :**

Hyperconjugation also affects bond lengths, because during the process, the single bond in question acquires some double bond character and vice versa.

Ex.:



actual C – C bond length is 1.543 A° and C=C is 1.334 A°.

iii. **Dipole moments :**

Since hyperconjugation causes the development of charges, it also affects the dipole moment of the molecule.

Ex.: For $H_3C-CH=CH_2$ dipole moment is 0.4 D.

iv. **Ionization Potential :**

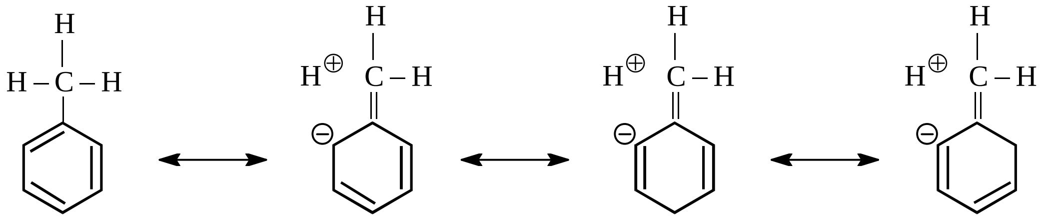
Since hyperconjugation increases the electron density on olefinic carbon atoms, ionization potential of olefins decreases with the increase in hyperconjugation.

Ex.: For $H_3C-CH=CH_2$ ionization potential is 9.76.

For cis $H_3C-CH=CH-CH_3$ ionization potential is 9.34.

v. Orienting influence of Methyl group :

The O, P – directing influence of methyl group in methyl benzenes is partly due to inductive effect and partly due to hyperconjugation.



Orienting influence of methyl group due to hyperconjugation.

Bonding in Fullerenes :

In 1984 Smalley had developed a method for the laser induced evaporation of metals at very low pressure and was able to measure the molecular weights of various clusters of atoms produced. When the experiment was carried out, in 1985 he found that under certain conditions a species with a molecular formula of C_{60} was present in amounts much greater than any other.

They concluded that its most likely structure is the spherical cluster of carbon atoms and named as buckminster–fullerene. Other carbon clusters, some larger than C_{60} and some smaller, were also formed in the experiment and the general name Fullerene refers to such carbon clusters.

DIAGRAM

All the carbon atoms in Fullerene are equivalent and are sp^2 hybridized. The strain caused by distortion of the rings from coplanarity is equally distributed among all of the carbons.

In 1990 a team of scientists successfully prepared Fullerene in amounts sufficient for its isolation, purification and detailed study. The aromaticity associated with its 20 benzene rings is degraded by their non planarity and the accompanying angle strain. It is now clear that C_{60} is a relatively reactive substance, reacting with many substances toward which benzene itself is inert. Many of these reactions are characterised by addition to Fullerene, converting sp^2 – hybridised carbons to sp^3 – hybridised ones and reducing the overall strain.

There are another group of compounds called single – walled nanotubes which are considered as stretched fullerenes. Thus the imporance of carbon cluster chemistry has been in the discovery of new knowledge. Many scientists feel that the earliest industrial applications of the fullerenes will be based on their novel electrical properties.

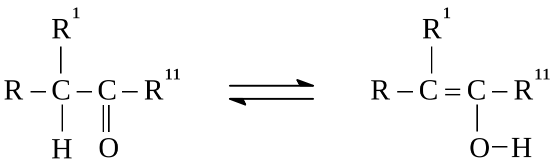
Buckminster fullerene is an insulator, but has high electron affinity and is a super conductor in its reduced form.

Tautomerism :

Tautomerism can be defined as "The phenomenon by which a single compound exists in two or more readily interconvertible structures that differ markedly in the relative positions of at least one atomic nucleus, generally hydrogen".

The tautomeric forms are quite chemically distinct entities and can be seperated and characterised. In tautomers, the position of an ion differs by several angstrom units.

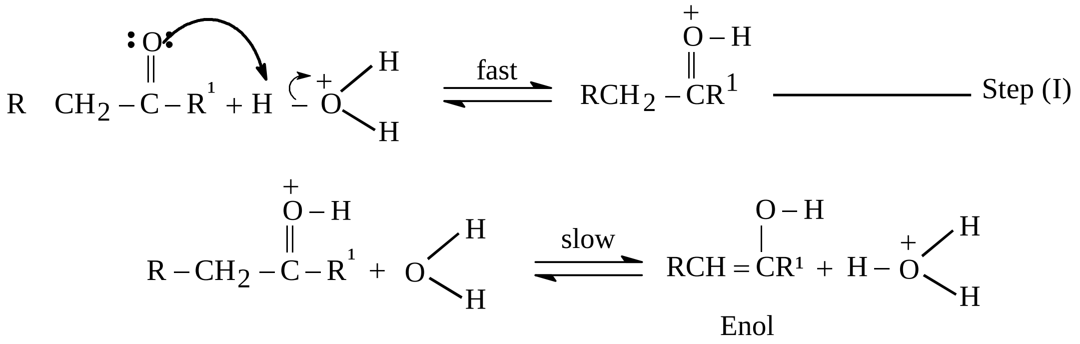
A very common form of tautomerism is that between a carbonyl compound containing an α – hydrogen atom and its end form which is known as Keto – Enol Tautomerism. It can be shown as follows.



$$R-\underset{H}{\overset{R^1}{C}}-\underset{O}{\overset{}{\underset{\|}{C}}}-R^{11} \rightleftharpoons R-\overset{R^1}{C}=\underset{O-H}{C}-R^{11}$$

Keto form Enol form

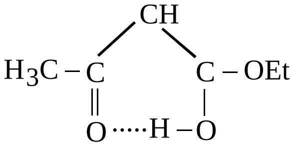
The mechanism of Keto – enol tautomerism involves the sequence of proton transfers. It is relatively slow in neutral media. The rate of enolization is catalysed by acids. In aquesous acid, a hydronium ion transfers a proton to the carbonyl oxygen in step – I and a water molecule acts as a Bronsted base to remove a proton from the α – carbon atom in step – II. The II – step is slower than I – step.



The Keto form has C – H, C – C, C = O bonds whose total bond energy is 359 K.cal./mol and enol form has C = C, C – O, O – H bonds whose total energy is 347 K.cal./mole. Therefore Keto form is thermodynamically stable by about 12 K.cal./mol. and enol form cannot be normally isolated. However there are some stable enols which can be shown as :

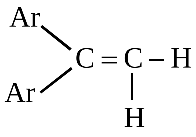
i. Molecules in which the enolic double bond is in conjugation with another double bond.

Ex.:



ii. Molecules that contain two or three bulky aryl groups.

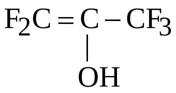
Ex.:



$$\mathrm{Ar_2C=\underset{\mathrm{H}}{\underset{|}{C}}-H}$$

iii. Highly fluorinated enols.

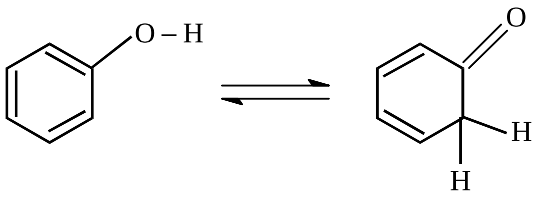
Ex.:



$$\mathrm{F_2C=\underset{\mathrm{OH}}{\underset{|}{C}}-CF_3}$$

In all the above cases enol form is more stable than the corresponding keto form. In addition to keto enol tautomerism there are some other tautomeric forms. They are

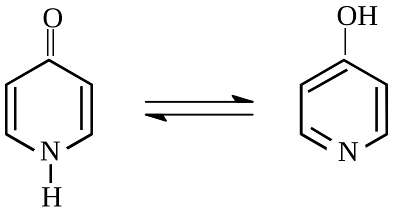
1. **Phenol – Keto tautomerism :**



Phenol Cyclohexadienone

For phenol itself there is no evidence for the existence of keto form. However keto form becomes important and may predominate when certain groups like second –OH or N = O groups are present. It is also found in heterocyclic systems, fused aromatic rings.

Ex.:



2. **Nitroso – Oxime tautomerism :**

$$\mathrm{R_2CH-N=O} \rightleftharpoons \mathrm{R_2C=N-OH}$$

Nitrosoform Oxime form

This equilibrium lies far to right, and as a rule nitroso compounds are stable only when there is no α –hydrogens.

3. **Imine – Enamine tautomerism :**

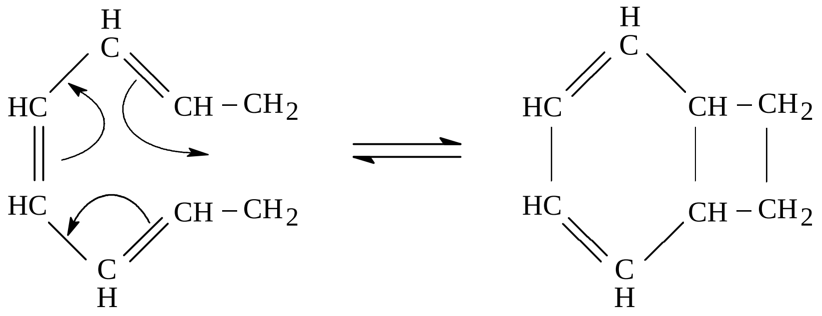
$$\mathrm{R_2CH-CR=NR} \rightleftharpoons \mathrm{R_2C=CR-NHR}$$

Imine Enamine

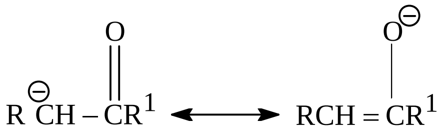
4. **Valence tautomerism :**

In valence tautomerism, the two forms differ only in the redistribution of the valencies.

Ex.:



The proton – transfer equilibrium that interconverts a carbonyl compound and its enol can be catalysed by bases as well as by acids. As in acid – catalysed enolization, protons are transferred sequentially rather than in a single step. The base abstracts a proton from the α – carbon atom to yield an anion. This anion is a resonance stabilized species. It's negative charge is shared by the α –carbon atom and the carbonyl oxygen.



$$R\overset{\ominus}{C}H-\overset{\overset{O}{\|}}{C}R^1 \longleftrightarrow RCH=\overset{\overset{O^{\ominus}}{|}}{C}R^1$$

Protonation of this anion can occur either at α – carbon or at oxygen. Protonation of α – carbon forms starting ketone while protonation of oxygen forms enol. This anion is called enolate ion ; which is a key intermediate in this process.

AROMATICITY

In the nineteenth century it was recognised that aromatic compounds differ greatly from unsaturated aliphatic compounds. These aromatic compounds are characterised by a special stability and they undergo substitution reactions more rapidly than addition reactions. The aromatic properties of benzene ring are related to the presence of a closed loop of electrons i.e., aromatic sextet.

With the help of NMR technique, it is possible to determine experimentally whether a compound contains a closed loop of electrons or not. With this technique, the concept of aromaticity can be defined as the ability to sustain an induced ring current. A compound with this ability is called diatropic. It can be shown as follows.

DIAGRAM

In duced π electron ring current in Benzene.

When external magnetic field is applied to an aromatic ring in an NMR instrument, the closed loop of π electrons begins to circulate in a plane at right angles to the direction of the applied field. This electron circulation generates an induced magnetic field which opposes the applied field in the region of π electron cloud and reinforces the latter in the peripheral region. Thus the proton lying in the former region are shielded while those lying in the latter region are deshielded. The hydrogens of benzene ring are located at about 7 to 8 δ where as normal olefinic hydrogens at 5 to 6 δ.

Aromaticity in Benzenoid Compounds :

The compounds which contain benzene ring in their structure are called Benzenoid compounds.

Benzene and other organic compounds which resemble benzene in certain characteristic properties are called aromatic compounds. These properties are called aromatic properties which are as follows :

i. **Unusual stability :** Aromatic compounds are highly stable due to the low heats of hydrogenation and low heats of combustion.

ii. **Substitution rather than addition reactions :** Aromatic compounds although possess double bonds, they donot undergo addition reactions. But they undergo electrophilic substitutions like nitration, sulphonation etc.

iii. **Resistent to oxidation :** These compounds are resistent to oxidation by aq. $KMnO_4$ and other mild oxidising agents.

iv. **Cyclic flat molecules :** These compounds generally contain six membered rings and are found to be cyclic flat structures.

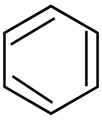
On the basis of molecular orbital treatment aromatic compounds must fullfill the following requirements.

i. It must have cyclic clouds of delocalised π electrons above and below the plane of the molecule.

DIAGRAM

These compounds must contain a total of (4n + 2) π electrons, where 'n' is an integer. This rule is known as Huckel rule. Thus according to Huckel rule, the no.of π electrons in an aromatic compound may be 2, 6, 10, 12 etc.

Ex.:

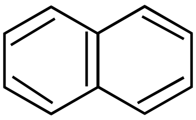


Benzene

n = 1

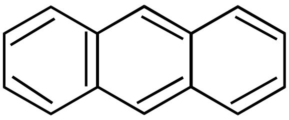
$4n + 2 = 4 + 2 = 6\pi$ electrons.

In systems of fused six membered aromatic rings. They obey Huckel's rule which can be shown as follows.



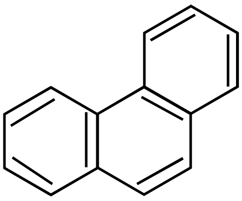
Napthalein
n = 2

$4n + 2 = 10\,\pi e^-$



Anthracene
n = 3

$4n + 2 = 14\,\pi e^-$

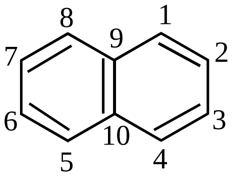


Phenanthrene
n = 3

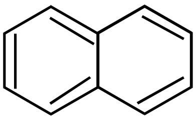
$4n + 2 = 14\,\pi e^-$

All these compounds follows the Huckel's rule and are aromatic.
In these systems, the principal canonical forms are usually not all equivalent.

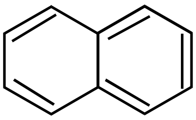
Ex.:



(I)



(II)

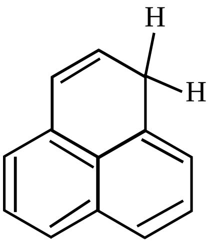


(III)

In the above examples I has a central double bond and different from II and III which are equivalent to each other. Molecular orbital calculations shows that bond orders and bond distances between 1, 2 & 2, 3 bonds are different. This non equivalency of bonds called partial bond fixation is found in nearly all fused aromatic systems.

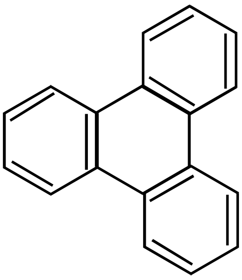
The resonance energies of the fused systems increase as the number of principal canonical forms increases. Resonance energies for fused systems can be estimated by counting canonical forms.

Not all the fused systems can be fully aromatic.
Ex.:



Phenalene

In a fused system there are not six electrons for each ring. In Naphthalein one of the ring has 6 π electrons and other has four, and hence one is aromatic system and other resembles butadiene system. As a result of this the reactivity of the compound increases and this effect becomes extreme in case of triphenylene.



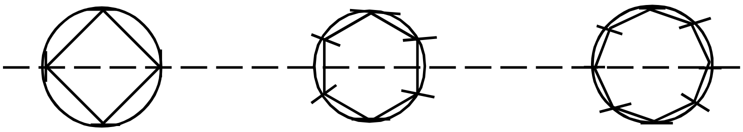
Triphenylene

In this compound there are 18 π electrons which were distributed so as to give each of the outer rings a sextet, while the middle ring is empty. Since none of the outer rings need share any electron with an adjacent ring, they are as stable as benzene. Unlike other fused aromatic systems it has low reactivity. This phenomenon, where some rings in fused systems give up part of their aromaticity to adjaint rings is called annellation.

Huckel's rule :

"Among planar, Mono cyclic, fully conjugated polyenes only those possessing (4n + 2) π electrons, where 'n' is a whole number, will have special stability; that is, be aromatic".

This statement is nothing but Huckel's rule. Thus the group of hydrocarbons with 2, 6, 10, 14 .... π electrons will be aromatic. Benzene, cyclobutadiene and cyclocta tetraene provide clear examples of Huckel's rule. Benzene, with 6 π electrons is a (4n + 2) system and is predicted to be aromatic by the rule. The π energy levels for these 3 compounds can be shown as



Cyclobutadiene Benzene Cyclooctatetraene

This pattern of orbital energies provides a convincing explanation for why benzene is aromatic while square cyclobutadiene and planar cyclo octatetraene are not. While counting the π electrons, cyclobutadiene has four, benzene six and cyclo octatetraene has eight. These π electrons are assigned to M.O's in accordance with the usual rules lowest energy orbitals first, a maximum of two electrons per orbital.

In Benzene the 6 π electrons are distributed in pairs among its three bonding π M.O's, giving a closed–shell electron configuration. All the bonding orbitals are filled and electron spins are paired..

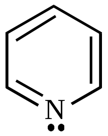
Cyclobutadiene has one bonding π M.O two equal energy non bonding π M.O's and one antibonding π * M.O. After the bonding M.O. is filled, the remaining two electrons are assigned to different non bonding M.O's in accordance with Hund's rule. This results a diradical. It lacks closed – shell electron configuration and not stabilised.

Six of the 8 π electrons of planar cyclo octatetraene occupy three bonding orbitals. The remaining two π electrons occupy one each, the two equal – energy non bonding orbitals. Like cyclobutadiene is should also be a diradical.

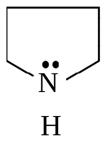
An important conclusion from MO diagrams is that the geometry required for maximum π electron delocalisation, a planar ring with 'p' orbitals aligned and equal C – C bond distances.

Applications of Huckel's rule :

i. Huckel's rule is applied to heterocyclic systems showing aromatic behaviour.
Ex.:



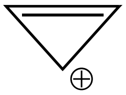
Pyridine



Pyrrole

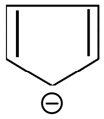
In Pyridine the ring contains 6 π electrons and the lone pair of electron remain on nitrogen. But in Pyrrole Nitrogen gives its lone pair to the ring to attain sextet configuration. In both the cases (4n + 2) rule is satisfied and hence they exhibits aromaticity.

This rule is applied to other systems as follows :



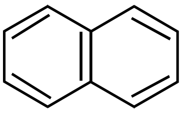
n = 0

$4n + 2 = 2 \pi e^-$

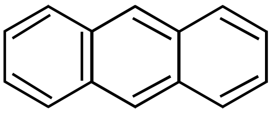


n = 1

$4n + 2 = 6 \pi e^-$



$4n + 2 = 10 \pi e^-$



$4n + 2 = 14 \pi e^-$

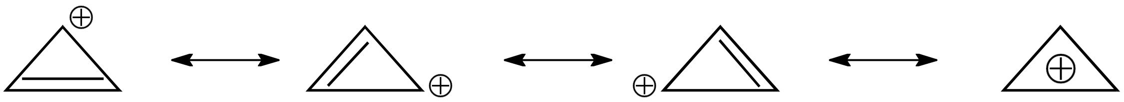
Since all the above compounds whether ions or neutral species obeys Huckel's rule they exhibit aromaticity.

Aromaticity in Non benzenoid compounds :

A non benzenoid aromatic compound is defined as a compound which although does not contain a benzenoid ring yet exhibit a degree of aromatic character typical of benzene. Some of them are as follows :

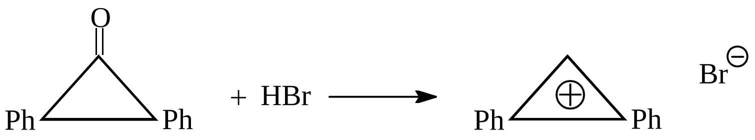
1. **Three membered carbocyclic compounds :**

According to Huckel's rule, the simplest aromatic system should contain only two π electrons, an example of which is cyclopropenyl cation. This cations shows 3 different canonical forms in which +ve charge is delocalized over 3 carbons. They are as follows :



Resonance hybrid

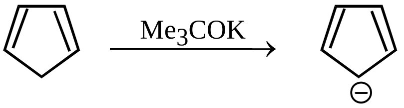
Hence cyclopropenyl cation should be stable. In practice several cyclopropenium salts have been prepared.
Ex.:



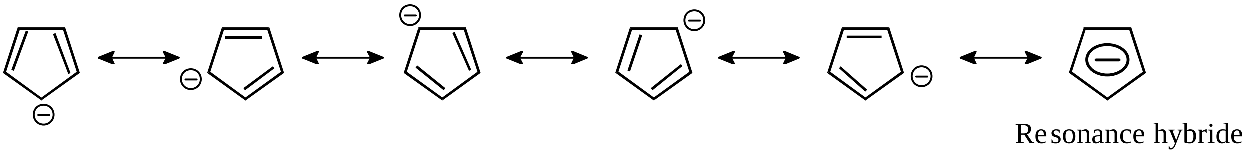
2. Five membered rings :

Cyclopentadiene is a typical diene and lacks aromatic characters. But, however if one of the atoms of cyclopentadiene has an unshared pair of electrons, the system can also have aromatic sextet and shows aromaticity.

A strong base is required to form cyclopenta diene anion which shows the predicted aromaticity.

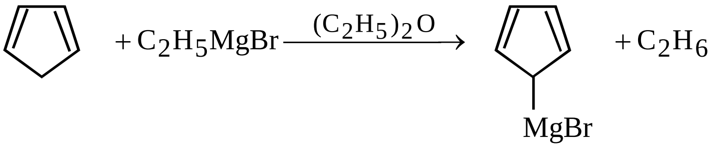


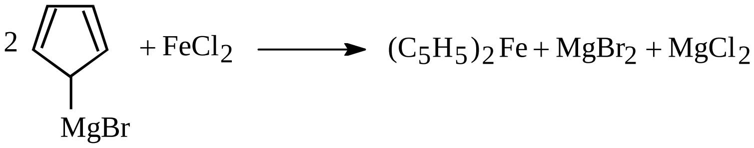
This cyclopenta dienyl anion is stabilised by resonance.



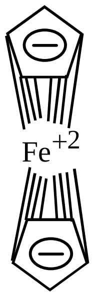
The resonance in cyclopentadienyl anion is proved by tracer technique. The aromatic characteristic of cyclopentadienyl anion is confirmed by isolation and the stability of its salts like Ferrocene and Fulvenes.

i. **Ferrocene :** This is the most important example of non benzenoid compounds. It can be prepared as follows :





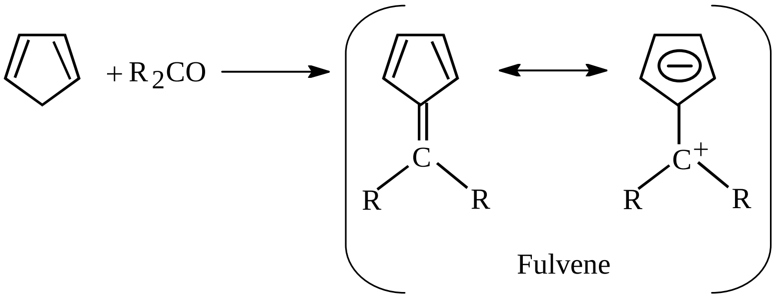
This Ferrocene is an organic solid and its structure is established by x – ray crystallography.



Ferrocene

This structure of Ferrocene is proved by its zero dipole moment.

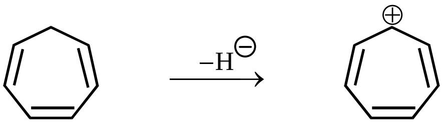
ii. **Fulvenes :** These Fulvenes are obtained by condensation of cyclopentadiene with carbonyl compounds.



In Fulvenes aromaticity is due to cyclopentadiene ring which acquires a stable six π electron arrangement in the ylide form.

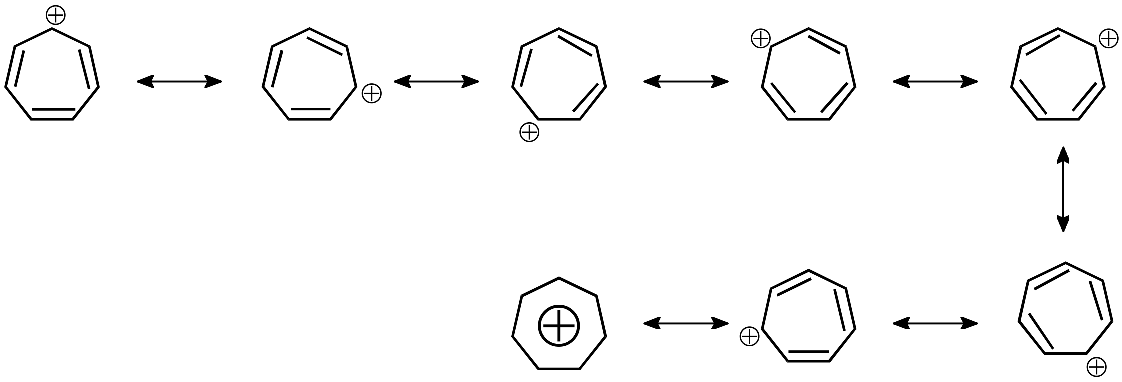
3. **Seven membered carbocyclic compounds :**

Cyclohepta triene behaves like a typical triene which has very low resonance energy which is nearly of the same order as that of the open chain conjugated triene. Removal of a hydride ion leads to the formation of a carbonium ion known as Tropylium cation.



Tropylium cation

This +ve charge on tropylium cation is not restricted to any one carbon. But it is delocalized over seven carbon which results in the formation of following canonical forms.



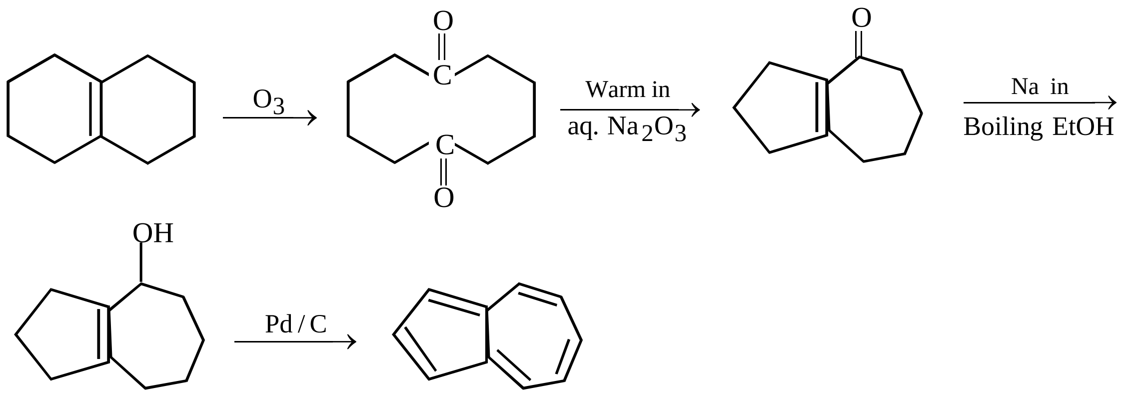
Resonance hybrid

This tropylium cation is planar and contains highly symmetrical six π electron structure.

Azulenes :

Azulenes are a group of deep blue compounds found in certain essential oils. Since these are basic in nature, these are extracted from essential oils with phosphoric acid followed by dilution with water.

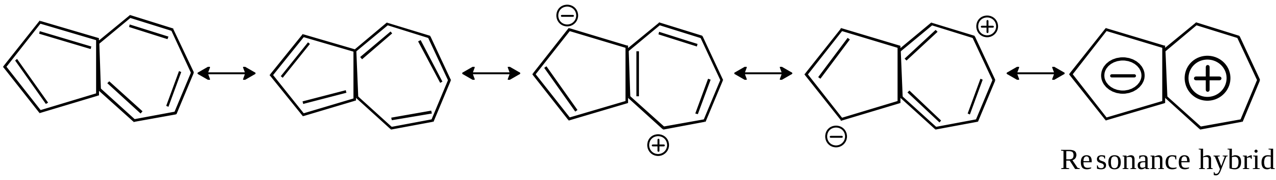
Plattner and StPfau Synthesised azulene in 1937 from 9 – octalin.



Azulene

It is a polycyclic non–benzenoid aromatic compound which is isomeric with Naphthalein. It is less stable than the Naphthalein.

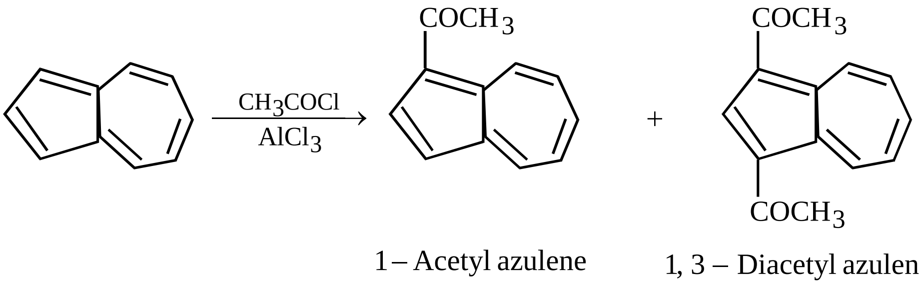
The canonical forms of azulene can be written as :



Resonance hybride

Thus azulene can be written as fused cyclopentadiene and cycloheptatriene rings neither of which alone is aromatic. The important aromatic characters of azulene are :

i. They do not undergo auto oxidation and do not polymerise.
ii. Like Naphthalein they form molecular compounds with picric acid.
iii. Azulene does not behave as a diene in Diel's – Alder reaction.
iv. They undergo electrophilic substitution like acylation, nitration, halogenation etc.

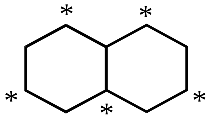


1 – Acetyl azulene 1, 3 – Diacetyl azulene

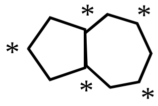
Alternant and Non alternant Hydrocarbons :

Aromatic hydrocarbons can be divided into two types. In alternant hydrocarbons, the conjugated carbon atoms can be divided into two sets such that no two atoms of the same set are directly linked.

Napthalein is an alternant hydrocarbon and azulene is a non alternant hydrocarbon.



Naphthalein

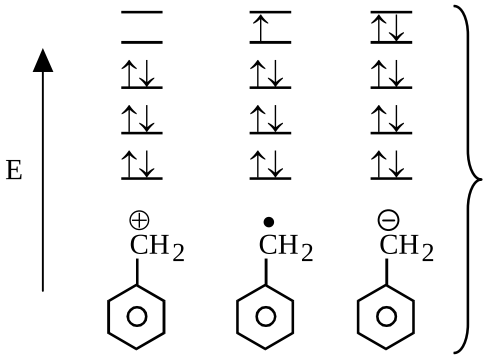


Azulene

In alternant hydrocarbons bonding and antibonding orbitals occur in pairs. Even – alternant hydrocarbons are those with an even number of conjugated atoms. For these hydrocarbons all the bonding orbitals are filled and the π electrons are uniformly spread over the unsaturated atoms.

Allylic system is an example for odd – alternant hydrocarbons. When odd no.of orbitals overlap, an odd no. is created. In benzylic system the cation has an unoccupied non bonding orbital, the free radical has one electron there and the carbanion two.

With allylic systems, all the three species have the same bonding energy. The charge distribution over the entire molecule is also same for the three species and can be calculated by a relatively simple process.



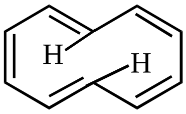
Energy levels for benzyl cation, radical carbanion.

Annulenes :

Conjugated monocyclic polyenes containing C_nH_n formula are called annulenes. Usually they contain 10 or more carbon atoms in a ring. They are named as [n] annulenes. Ex.: Benzene is [6] – annulene.

The prospect of observing aromatic character in conjugated polymers having 10, 14, 18 and so on π electrons spurred efforts towards the synthesis of higher annulenes. A problem immediately arises in the case of all cis isomer of [10] annulene.

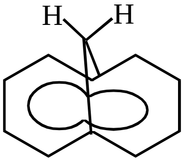
Ex.:



[10] – annulene

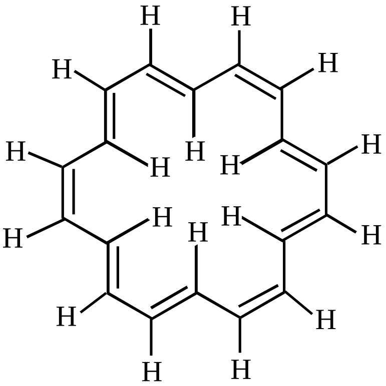
This compound contains trans double bonds, but due to interference between 1, 6 hydrogens it cannot attain coplanarity and does not exhibit aromaticity.

Later Vogeletal replaced 1, 6 hydrogens by a methylene bridge to permit π electron delocalization and the development of aromaticity as predicted by the Huckel's rule. It's structure is as follows :



1, 6 – Methano cyclo decapentane

When the ring contains 18 carbon atoms, it is large enough to be planar while still allowing its interior hydrogens to be far enough apart that they do not interfere with one another. Hence [18] annulene is planar.



[18] – annulene

Although its structure and resonance energy attest to the validity of Huckel's rule, which predicts special stability for [18] – annulene, its chemical reactivity does not. [18] – annulene behaves more like a polyene than like benzene in that it is hydrogenated readily, undergoes addition rather than substitution with bromine, and forms a Diels – Alder adduct with maleic anhydride.

Planar annulenes with 4n π electrons are antiaromatic. A member of this group [16] – annulene has been prepared. It is non planar and shows long bonds typical of a non aromatic cyclic polyene.

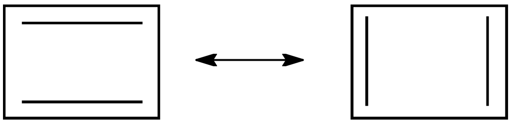
STRUCTURE

[16] – Annulene

Antiaromaticity :

Planar cyclic conjugated species less stable than corresponding acyclic unsaturated species are called antiaromatic. Molecular orbital calculations have shown that such compounds have 4n π electrons. Such cyclic compounds which have 4n π electrons are called antiaromatic and this characteristic is called antiaromaticity.

Thus although two equivalent contributing structures can be written for 1, 3 cyclobutadiene, it is extremely unstable antiaromatic compound, because it has 4n π electrons.



This shows that the ability to write equivalent contributing structures is not sufficient to predict stability. It has experimentally been shown that conjugated rings with 2, 6, 10 and 14 π electrons are aromatic, while those with 4, 8, 12, 16, 20 are not aromatic.

It can also be explained with NMR spectral data. In [16] – annulene which is antiaromatic, outside protons are more shielded and inside protons are less shielded. But in Benzene and [18] – annulene outside protons are less shielded and inside protons are more shielded. This reversal of shielding and dishielding regions in going form [18] to [16] annulene can only mean that the directions of their induced magnetic fields are reversed.

Thus [16] – annulene which is antiaromatic, not only lacks an aromatic ring current, its π electrons produce exactly the opposite effect when placed in a magnetic field.

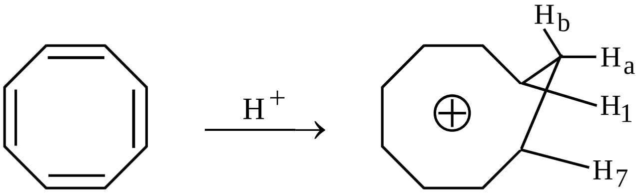
STRUCTURE

[16] – annulene

Homo – Aromaticity :

The compounds that contains one or more sp^3 – hybridised carbon atoms in a conjugated cycle are known as homo aromatic compounds and the phenomenon is known as Homoaromaticity.

When cyclooctatetraene is dissolved in conc. H_2SO_4 a proton adds to one of the double bonds to form the homotropylium ion.

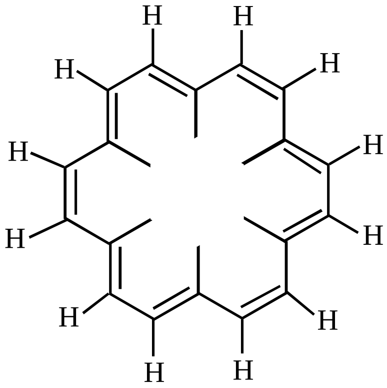


In this ion an aromatic sextet is spread over seven carbons as in the tropylium ion. The eighth carbon is an sp^3 carbon and so cannot take part in the aromaticity. NMR spectra show the presence of a diatropic ring current. H_b is found at δ = – 0.3 H_a at δ == 5.1 ppm.

In order for the orbitals to overlap most effectively so as to close a loop, the sp^3 atoms are forced to lie almost vertically above the plane of the aromatic atoms. In homotropylium ion H_b is directly above the aromatic sextet and so is shifted far upfield in the NMR.

All homoaromatic compounds so far discovered are ions, and it is questionable as to whether homoaromatic character can exist in uncharged systems. Homoaromatic ions of two and ten electrons are also known.

Pseudo Aromaticity :



Pseudo means half or semi. This compound 18 – Annulene is showing the pseudoaromaticity. i.e. 50% aromatic character.

This 18 – Annulene is solid. Thus it is probably planar obeys the Huckel rule. i.e. it has 4n + 2 π electrons n = 4. But this compound shows the olefinic characters.

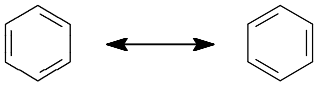
It is readily hydrogenated to the corresponding cycloalkane and react with metallic anhydride and bromide.

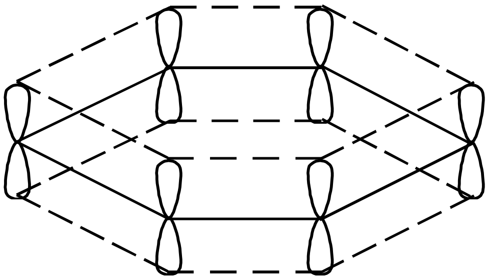
It will not undergo nitration or sulphonation.

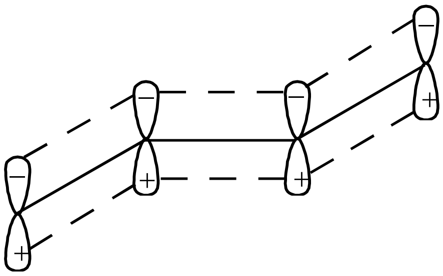
This compound is higher member of the Acene series, but highly reactive and unstable.

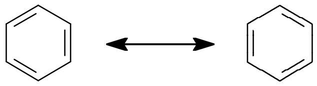
Eventhough this compound obey Huckel rule but shows non aromatic characters.

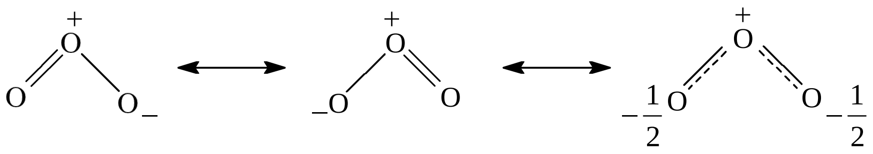
So, it is called as Pseudo aromatic compound.

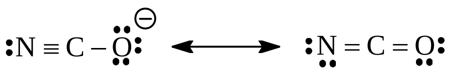




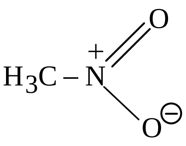






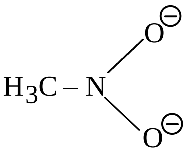


A B

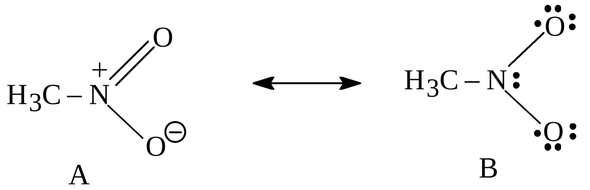


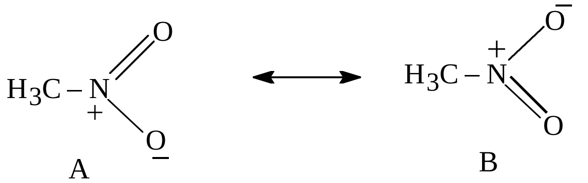
A

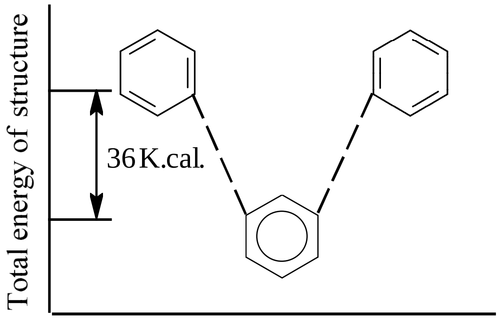
and



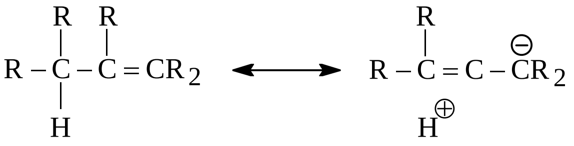
B



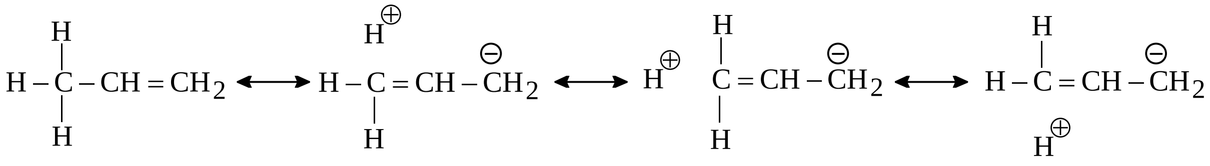




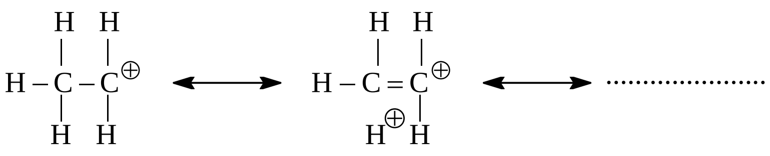
Resonance energy of benzene



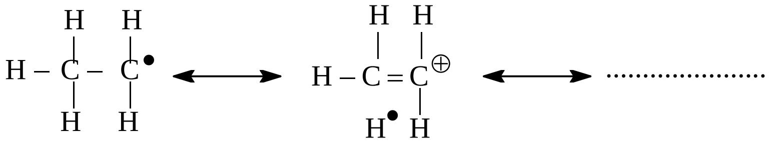
$$R-\underset{H}{\overset{R}{C}}-\overset{R}{C}=CR_2 \longleftrightarrow R-\underset{H^{\oplus}}{\overset{R}{C}}=C-\overset{\ominus}{C}R_2$$



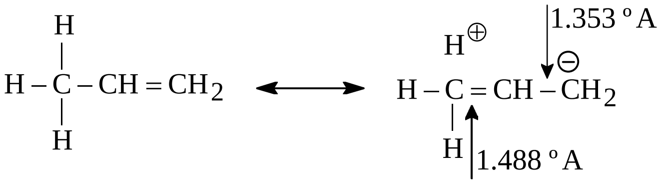
$$H-\underset{H}{\overset{H}{C}}-CH=CH_2 \longleftrightarrow H-\underset{H}{\overset{H^{\oplus}}{C}}=CH-\overset{\ominus}{C}H_2 \longleftrightarrow H^{\oplus}\ \underset{H}{\overset{H}{C}}=CH-\overset{\ominus}{C}H_2 \longleftrightarrow H-\underset{H^{\oplus}}{\overset{H}{C}}=CH-\overset{\ominus}{C}H_2$$

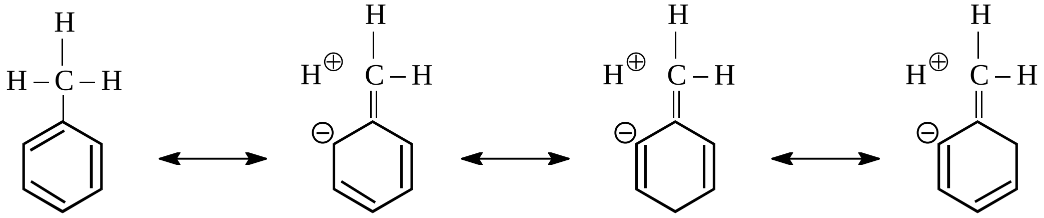


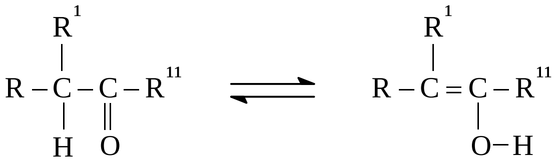
$$H-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}^{\oplus} \longleftrightarrow H-\underset{H^{\oplus}}{\overset{H}{C}}=\underset{H}{\overset{H}{C}}^{\oplus} \longleftrightarrow \cdots\cdots\cdots\cdots$$

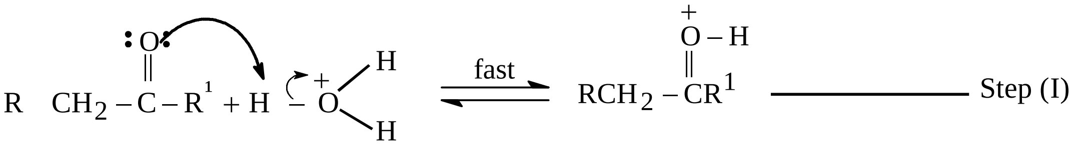


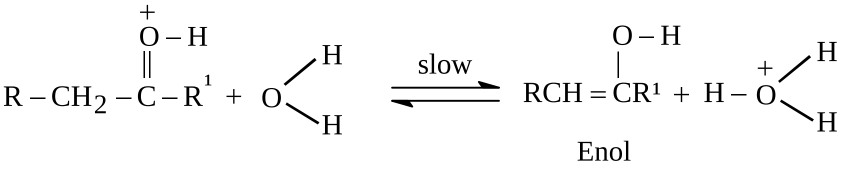
$$H-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}^{\bullet} \longleftrightarrow H-\underset{H^{\bullet}}{\overset{H}{C}}=\underset{H}{\overset{H}{C}}^{\oplus} \longleftrightarrow \cdots\cdots\cdots\cdots$$

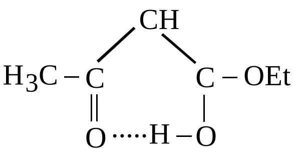

1.353 ° A
1.488 ° A

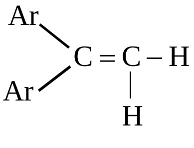


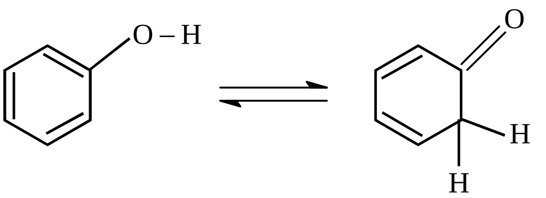



fast
Step (I)


slow
Enol

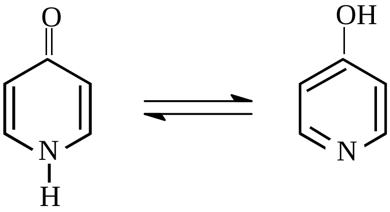


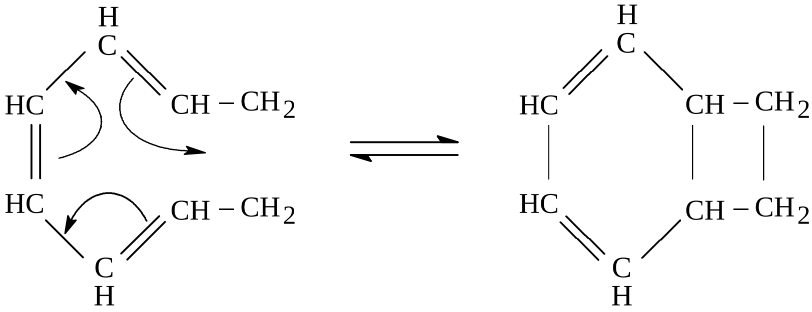


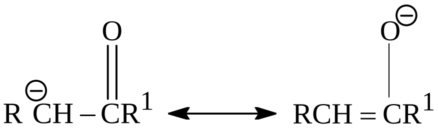


Phenol

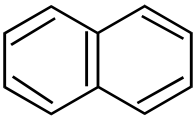
Cyclohexadienone

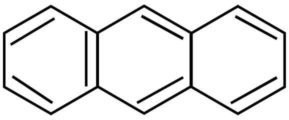


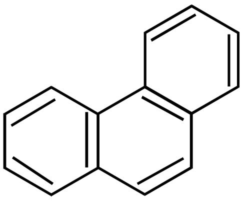


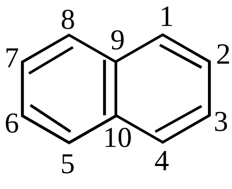


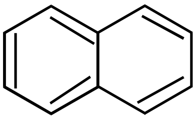
$$R\overset{\ominus}{C}H-\overset{\overset{O}{\|}}{C}R^1 \longleftrightarrow RCH=\overset{\overset{O^{\ominus}}{|}}{C}R^1$$

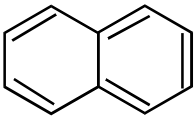


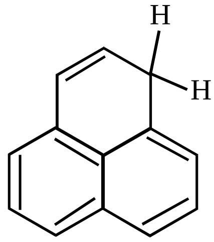


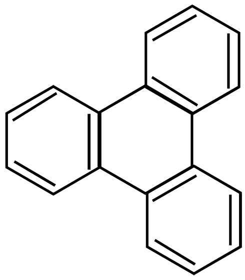


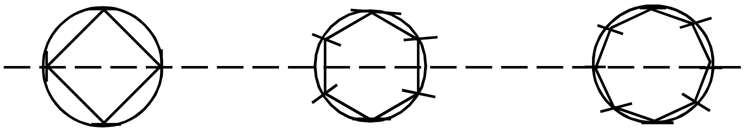


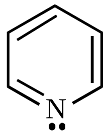





H
H



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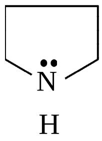
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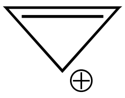
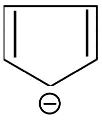
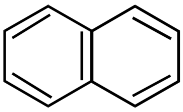
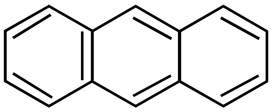
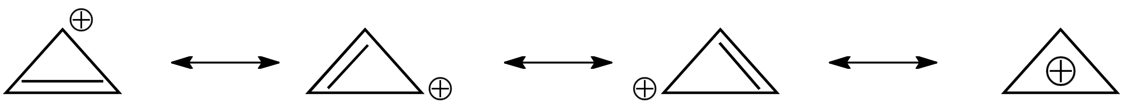
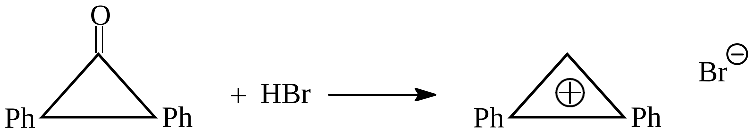


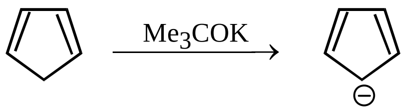


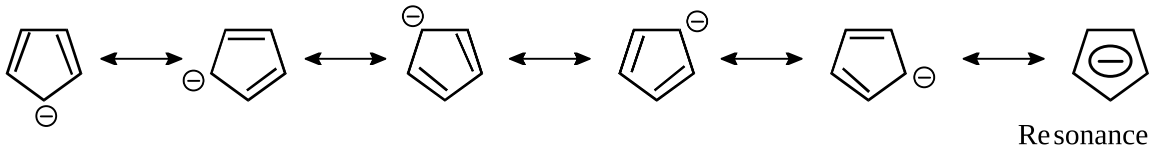




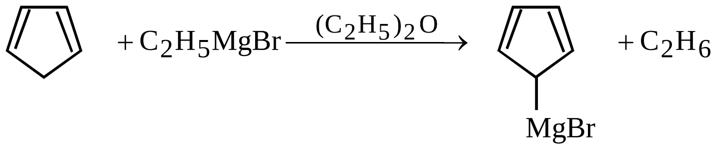


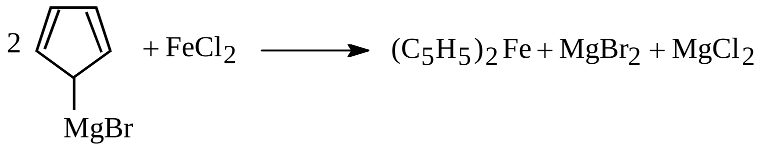

O
Ph
Ph
+ HBr
Ph
Ph
Br

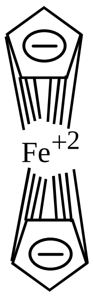




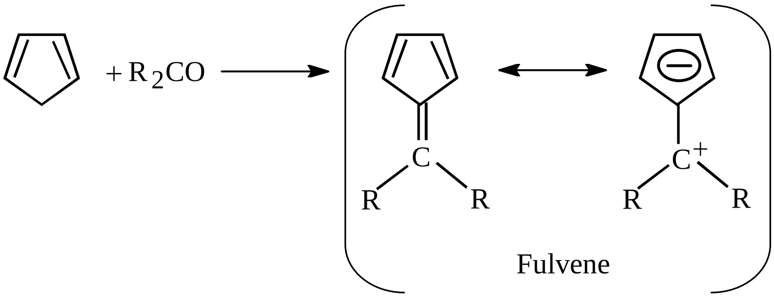
Resonance hybride



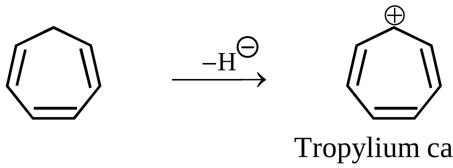




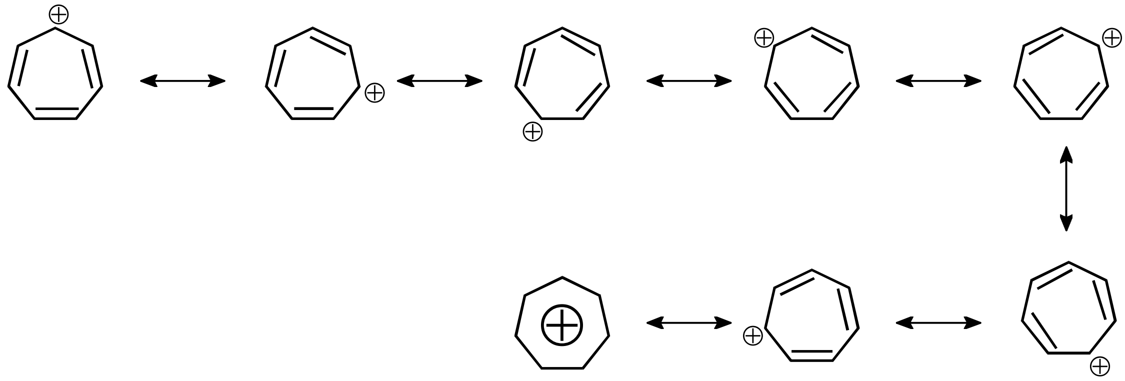
Ferrocene



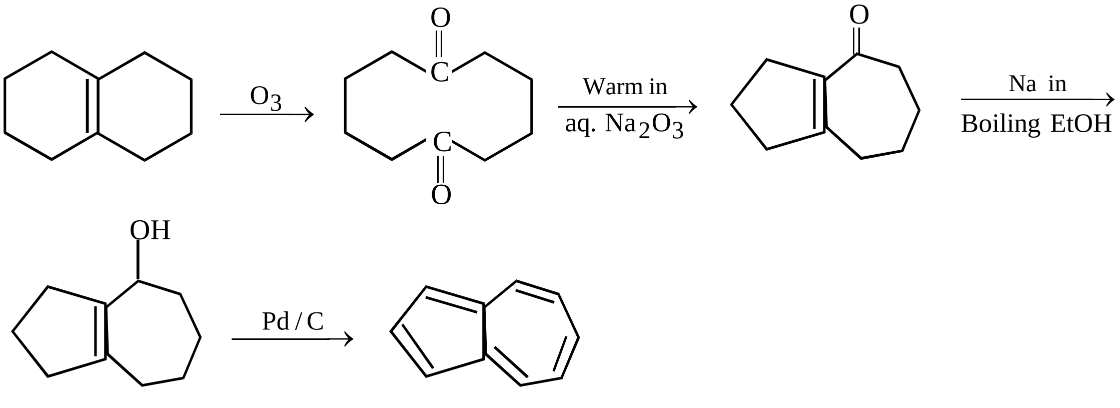
Fulvene



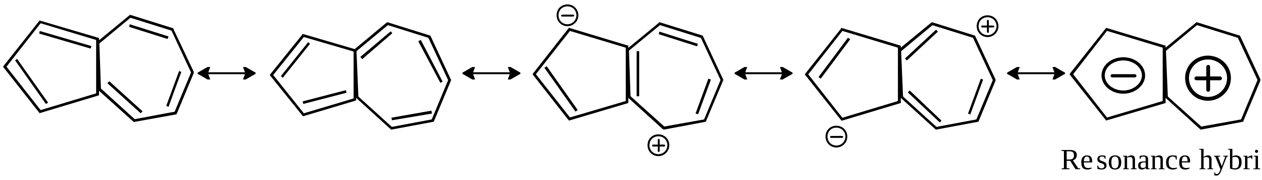
Tropylium cation



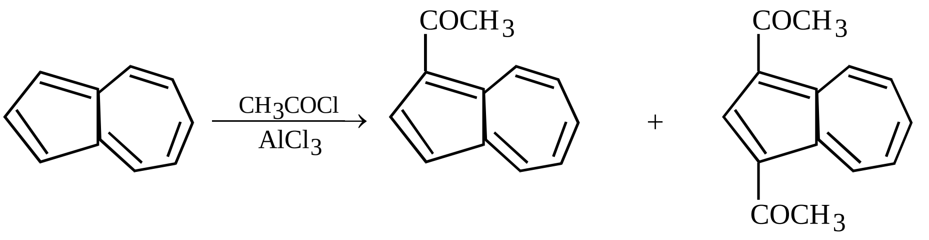
Resonance hybrid



Azulene

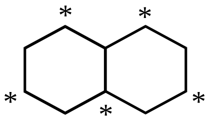


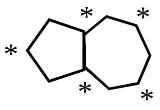
Resonance hybride

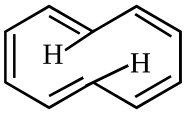


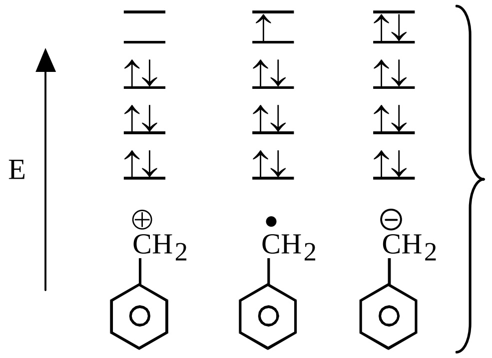
1 – Acetyl azulene

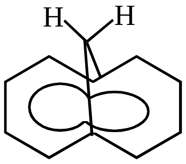
1, 3 – Diacetyl azulene

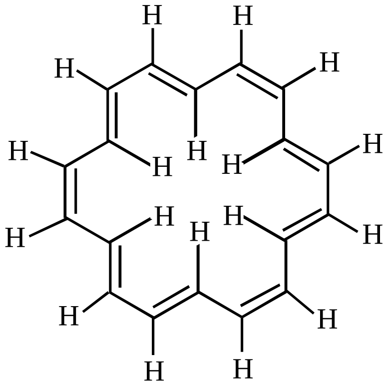


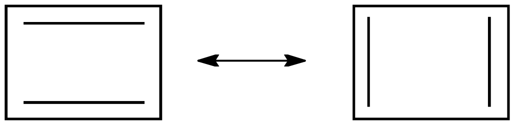


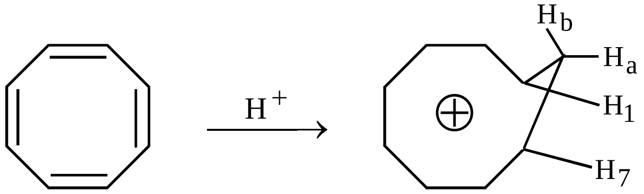

H
H

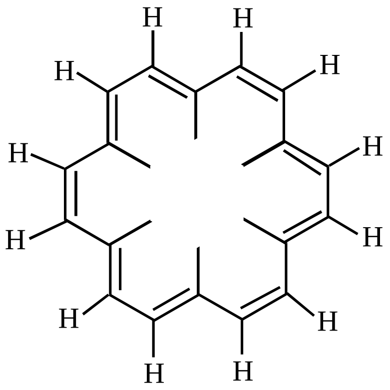

E
CH2
CH2
CH2


H
H






H+
Hb
Ha
H1
H7



UNIT - II
SYLLABUS

3. REACTION MECHANISM : STRUCTURE AND REACTIVITY

LESSON -1

Types of mechanisms - Methods of determining mechanisms - Types of reactions - Broad classification - Kinetics - Thermodynamic and Kinetic requirements - Kinetic and thermodynamic control - Potential energy diagrams - Transition states - Effect of structure and reactivity- Resonance and field effects - Steric effects - Quantitative treatment - Hammett equation and linear free energy relationship, substituent and reaction conditions.

LESSON -2

Intermediates - Generation - Structure - Stability and reactivity of carbocations, Crabonions, Free-radicals, Carbenes and nitrenes.

4. ALIPHATIC NUCELOPHILIC SUBSTITUTION

LESSON -3

The S_N^2, S_N^1 and S_N^2 mechanisms -The neighbouring group mechanisms -The neighbouring group participation, anchimeric assistance. The S_N^i mechanism.
Nucleophilic substitution at an allylic, aliphatic trigonal and a vinylic carbon.

LESSON - 4

Classical and non-classical carbocations - Phenonium ions - Common carbocation rearrangements - Reactivity effects of substrate structure - Attacking nucleophile - Leaving group and reaction medium - Ambident nucleophile regioselectivity.

UNIT - II

REACTION MECHANISM : STRUCTURE AND REACTIVITY

LESSON - 1

2.1 (i) Most organic reactions proceed in several steps. The study of a particular reaction is incomplete without knowing the mechanism. When the reaction is in process, bonds are either cleaved or new bonds formed. Stepwise description or the cleavage of formation of a bond, the probable pattern and the actual path way by which a reaction is likely to proceed is called mechanism.

A study of the reaction mechanism serves as an aid to understand the chemical reactivity of different types of organic compounds. A mechanistic study brings credibility and thereby predicts and if possible, classify the probable way by which the reaction is likely to proceed.

To determine the mechanism, the order in which the bonds are broken or formed, whether bond breaking preceded bond formation or otherwise or whether both proceed simultaneously are to be considered. There is no yard stick for a particular reaction to proceed in a particular way. Reactions are known to proceed by different mechanisms under different conditions. It is particularly true of substitution reactions. The same reaction may proceed exclusively by $S_N{}^1$ or $S_N{}^2$. With the change of reaction conditions, the reverse may be the case and may even proceed either way. Also known are reactions that proceed by mixed $S_N{}^1$ and $S_N{}^2$ mechanisms (in aliphatic nucleophilic substitution).

Depending on how the covalent bonds are broken, organic reactions may be categorised under three heads for the specific purpose of determining the mechanism namely

01. Homolytic or free radical reactions in which each atom retains one electron forming highly reactive species-radicals.
02. Heterolytic reactions in which both the electron are retained on one atom (electrons are always paired)-ions.
03. Pericyclic reaction in which the electrons move in a closed ring involving neither of the intermediates radicals or ions.

Examples followed by explanation for the above three categories are discussed at appropriate places.

Number of organic compounds isolated so far run into hundreds of thousands. Still they fit into any one of the four types namely Addition, Substitution, Elimination or rearrangement as far as the process of mechanism is concerned.

Electrophile (reagent that seeks electron pair), Nucleophile (reagent that donates electron pair) or a free-radical may add to carbon-carbon multiple bonds by two step process or the attack at the two carbon atoms of the double or triple bond may be simultaneous.

Substitution may also be processed through electrophilic, nucleophilic or free-radical (Ch 4 & 5) β – or 1,2 elimination reactions may take place either by hetero cyclic or pericyclic mechanisms (Ch 9)

Rearrangements involve migration of an atom or a group from one atom to another. Migrations are common with nucleophiles and free-radicals but rare with electrophiles. (Ch 4 & Ch6).

The above broad classification is of general nature nature and the reader may go through relevant chapters for further study .

The possible movement of electrons are represented by curved arrows.

Curved arrow   movement of electrons

Tail of arrow - Source of electrons

Head of the arrow - ultimate destination of the electron-pair.

2.1.(ii) Kinetics provides the most general and useful method for determining the reaction mechanism. The study of kinetics is concerned with the rate of reaction. It depends among other things mostly on mostly of concentration. Some reversible reactions proceed in such a way that the mechanism is the same under certain conditions except that it proceeds exactly the opposite way (principle of microscopic reversibility). These reactions of course are not influenced by kinetic studies.

Ordinarily when a reaction is carried out, it is but natural to presume the possible or likely product. Presumption is again based on

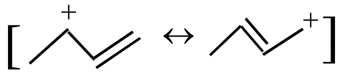
i) formation of stable product and ii) the fastness with which the other product is formed.

If stability of the product is the concern, the factors to be considered are ΔH values, entropy effect etc explained p. From them, the equilibrium constant between the reactants and products is determined. Based on the ratio of equilibrium constants, the ratio of products is determined. The reaction, however, is carried out under conditions that make it readily reversible. Reactions such as these are called thermodynamically controlled reactions. The most stable product is said to be the thermodynamically controlled product.

If , on the other hand, the quantity of each possible product is determined by the fastness with which each product is formed, the reaction is said to be kinetically controlled. These are more common.

Kinetic versus thermodynamic control :

Addition of HBr to 1,3 butadiene forms a mixture of 1,2 and 1,4 addition products. The former predominates (80%) at lower temperature (-80°C) where the equilibrium is not attained rapidly. The more stable 1,4-addition product, predominates (80%) at higher temperature (40°C) where equilibrium is attained more rapidly. The competition between 1,2 and 1,4 additions is typical of conjugated dienes and is an apt example of kinetic versus thermodynamic control. The reaction that occurs fastest produces the preferred 1,2 addition product -kinetic control. Higher temperature-more stable product-thermodynamic control. It is interesting to note that both the products are derived from the common intermediate.



Equilibrium free energy charge , thermodynamic and kinetic requirements :

A reaction is said to be in equilibrium if it takes place without alteration in the concentration of reactants and products. Equilibrium constant (k) for the chemical equilibrium of the reactions $A \rightleftharpoons B$

$$K = \frac{[B]}{[A]}$$

$$A+B \rightleftharpoons C \quad K=\frac{[C]}{[A][B]} \text{ and } A+B \rightleftharpoons C+D \quad K=\frac{[C][D]}{[A][B]}$$

K is determined by the change in free energy (G) Gibbs free energy change in a reaction is given by the equation $G = H - TS$ where T is is the absolute temperature. The change (Δ) in free energy of reactants and products is represented by ΔG. The negative value of ΔG indicates that certain amount of energy is released (when the reaction is completed) and that the free energy of the products lower than that of the free energy of the reactants. Free-energy is made up of two components, enthalpy H and entropy S. The free energy change in reaction is given by

$$\Delta G = \Delta H - T\Delta S$$

$\Delta G =$ (Free energy of products) - (Free energy of reactants).

$\Delta H =$ (enthalpy of products) - (enthalpy of reactants)

$\Delta S =$ (entropy of products) - (entropy of reactants).

The enthalpy changes relate to the difference in bond energies between the reactants and the products.

Enthalpy change $\Delta H =$ [Sum of the bond energies of the bonds formed] - [Sum of the bond energies of the bonds broken] + changes in resonance, strain, solvation energies, if any.

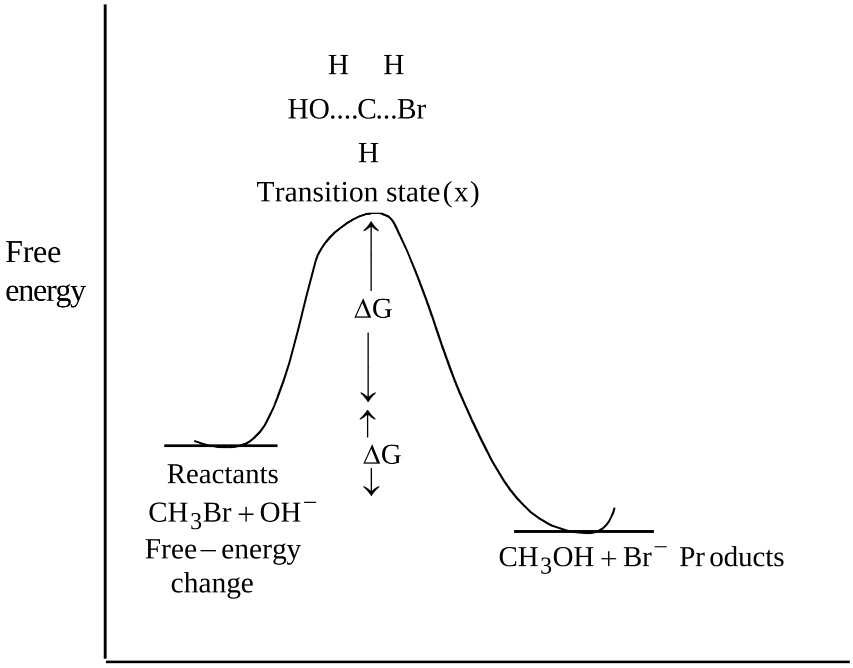
Entropy changes, on the other hand refer to the disorder of the system. Reactions tend to favour greater entropy. Low enthalpy and high entropy are the preferred conditions in nature. In any reacting system, enthalpy spontaneously decreases while entropy spontaneously increases. Spontaneity with which the reaction takes place in most cases is determined by enthalpy. Entropy effects though small, still dominate in certain types of reactions. The guiding factors are

1. The order of entropies are gases > liquids > solids. If, in a reaction, all the reactants are liquids and one or more of the products is a gas, the reaction is thermodynamically favored by the increased entropy.
2. In reactions where the reactant and product molecules are the same, $A + B \rightarrow C + D$ the entropy effects are small. When the product molecules are more $A \rightarrow B + C$ gain in entropy is noticed and the reaction is thermodynamically favoured. When the reactant molecules are more $A + B \rightarrow C$, decrease in entropy noticed.
3. Entropy becomes more and more important as is evident from the equation $\Delta G = \Delta H - T\Delta S$. Acyclic molecule e.g. hexane has more entropy than a similar cyclic molecule. (cyclohexane)

Kinetic requirements for a reaction:

From the preceding discussion, it is clear that the -ve value for ΔG is a necessary but not a sufficient condition for a reaction to occur spontaneously. This, however, does not give an idea of the fastness with which the reactant molecules are converted to products. A student is introduced to chemistry by citing the reaction between Hydrogen and Oxygen to give water. It is a fact that the reaction does proceed. But not until a tiny spark or say a flicker of flame is introduced to start the explosive reaction. H_2 and O_2 can be kept for any length of time at room temperature with no significant reaction taking place. Thus there is a barrier for the reaction to take place. The barrier has to be overcome and the transition state (has to be) attained. Energy therefore must be added to the reactants. This energy, the difference between the free energy of the reactants and the transition state, is the free energy of activation ΔG^* that must be added which incidentally governs the rate of a chemical reaction.

The profile of the reaction may be brought about by pictorial representation by energy profile diagrams. The following is the energy profile diagram for a single step reaction that does not involve intermediates illustrated with the alkaline hydrolysis of CH_3Br. fig. 2.1



Reaction co-ordinate
Fig. 2.1

x (Transition state or activated complex -possesses definite geometry and charge distribution but no finite existence).

ΔG Free energy change

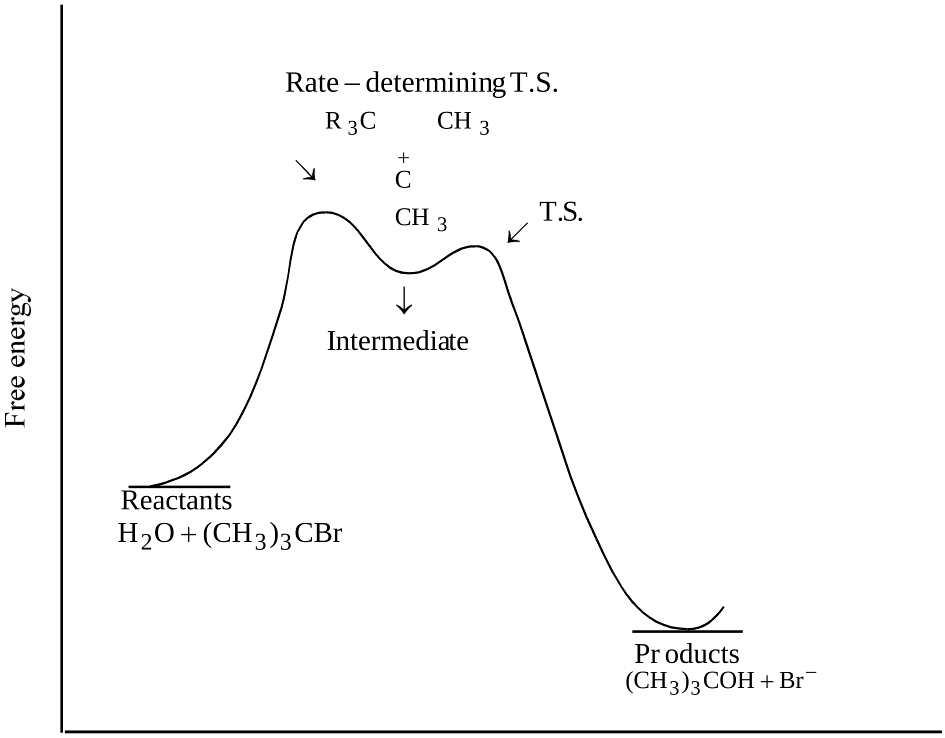
The height of the barrier ((ΔG^*) in the above figure is called free energy of activation and is made up of enthalpy and entropy components.

$$\Delta G^* = \Delta H^* - T\Delta S^*$$

ΔH^* is the enthalpy of activation. It is the difference in bond energies that include strain, resonance and solvation energies between the starting compound and the transition state. The bonds are either cleaved fully or partially broken before reaching the transition state.

Entropy of activation ΔS^* is the difference in entropy between the starting compounds and the transition state.

A study of the mechanism of alkaline hydrolysis of $CH_3Br(S_N{}^2)$ is explained later p. The energy profile diagram of $S_N{}^1$ reaction involving hydrolysis of t-butyl halides may be represented as follows fig. 2.2.



Reaction co - ordinate

Fig. 2.2.

2.1 (iii). Effect of structure on reactivity :

Organic compounds are characterised by functional groups. A compound may contain one or more functional groups (same or different). The introduction of yet another functional group is likely to affect the rate of reaction, the position of equilibrium. The course and the type of mechanism is also likely to be changed. Hence a trial is to be made to coordinate structure and reactivity. In a broad sense the two effects that play a major role to study the effect of structure on reactivity are

i) electrical and ii) steric effects.

Resonance and field affects (difficult to be separated) are grouped together and are called electrical effects. Field effect is turn associates itself with inductive effect and their separation is also not easy. The independent contribution of inductive and field effects, resonance (mesomeric) and steric effects all buy important to cohelate structure and reactivity. Over all factors will them be taken into consideration whereby a relationship can be established between structure and reactivity.

Inductive and field effects :

The C-C bond in alkanes, say ethane is not polar since it connects two equivalent atomic with chloroalkanes, the situation is different. The electronegative chlorine atom makes all the difference and C-C bond is polrisation.

$$H_3\overset{\delta\delta\delta+}{C} \rightarrow \overset{\delta\delta+}{CH_2} \longrightarrow \overset{\delta+}{CH_2} \rightarrow \overset{\delta^-}{Cl}$$

The electron pair forming the covalent bond between the chlorine atom C, will be displaced towards the chlorine atom. C_1 atom, therefore is deprived of some of its electron density. Hence C_1 acquires +ve charge. This is turn attracts the electron pair formly the covalent bond between C_1 and C_2. The process continues and $C_2 a_5 C_3$ acquires +ve charge. However the +ve charges are the order $C_1 > C_2 > C_3$.This type of electron displacement is called inductive effect. The electron pairs through permanently displaced, remain in the same valency shell. In addition to the inductive effect, there is the other effect that operates not through bones but directly through spare or solvent molecules . Field effect also decreases with increases distance as is the case with inductive effect called effect. It is rather difficult to separate the two kinds of effect. Field effect takes place independently of the electronic system in the molecule and depends on the geometry of the molecule while the inductive effect depends only on the nature of bond. Inductive effects may be due to atoms or groups. Functional groups may be classified as electron attracting or electron withdrawing (-I) and electron donating or electron releasing (+I). Hydrogen is chosen as reference in the molecule.

The student has to hear in mind that there is no lateral donation or withdrawal of electrons. NO_2 group is electron attracting conveys the meaning that it is no when compound with hydrogen.

Field effects of various groups relative to hydrogen in the order of decreasing strength.

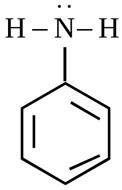
$$+ I, O^-, COO^-, (CH_3)_2C, (CH_3)_2CH, CH_3, CH_2, CH_3$$

$$- I\,NR_3^+, SR_2^+, NH_3^+, NO_2, SO_2R, CN, COOH, F, Cl, Br, I, OR, OH\,\cdot$$

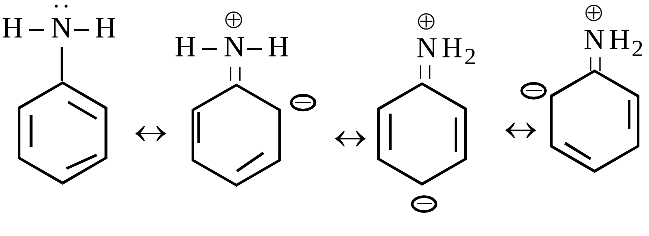
The field effect order of alkyl groups attached to unsaturated systems is tertiary>secondary>primary> CH_3. The order is not consistent when connected to saturated system.

Resonance Effect :

This is a stabilizing effect. It involves delocalisation of electrons like electron withdrawal from a negativity charged centre and electron release to positively charged centre. Aniline, when represented by



gives an indication that the two unshared electrons reside on nitrogen atom alone. This actually is not the case and the hybrid following canonical structures is the real structure of aniline.



It is therefore, clear that the electron density of the unshared pair is not merely concentrated on nitrogen but spread over the ring (unsaturated system). The decrease in electrodensity at one position is followed by corresponding increase else where is called the resonance or mesomeric effect.

Groups such as NH_2 are electron-releasing by resonance effect (+H groups). Groups that have a multiple bonded electronegative atom directly connected to unsaturated system are (-M) group.

E.g. NO_2 group.

+M groups $O^-, S^-, NH_2, NHR, NR_2, NHCoR, OR, OH, OCoR, SR, SH, Br, I, Cl, F, Ar$

-M groups $O^-, S^-, NH_2, NHR, NR_2, NHCoR, OR, OH, OCoR, SR, SH, Br, I, Cl, F, Ar.$

The resonance effect works only when the group is directly attached to the unsaturated system.

To draw a subtle distinction between field and resonance effects, the former operates through space, solvent molecules or the σ bonds of a system while the latter operates through π electrons.

Steric effect :

Organic reactions proceed through transition states in general. For a study of the reactions mechanism the geometry of the initial and transition states are to be considered. The speed of the reaction is certainly affected by steric factors. If the reaction is slowed down by steric effects, it is said that the reaction is subjected to steric hindrance and if specified up, the reaction is said to be subjected to steric acceleration.

Steric hydrauxine may be illuminates by taking SN^2 ethanolysis of certain alkyl halides the rate decreases with increasing β branch and reaches a very covalence for neopentyl bromide. This in the relative rates of reaction of RBr with ethanol, while the relative rate of CH_3Br is 17.6 that of $(CH_3)_3CCH_2Br$ is $4.2 x 10^{-6}$. Thus the increase of number of methyl groups on the central carbon atom increases steric retardations. In SN^2 reaction, there will be crowding in the transition state, bulkier the groups, the greater will be the compressive energy. Consequently the reaction will be hindered sterically.

In SN^1 mechanism, when the molecule containing the bulky groups is ionised, it can relieve the steric strain. $C^{\oplus}$ formed is flat. There is more room for accommodating the three alkyl groups. Thus there is steric accelerates.

E.g. Ozolysis of tertiary halides

$$R_3C - X \xrightarrow{H_2O} R_3C^{\oplus} + X^-.$$

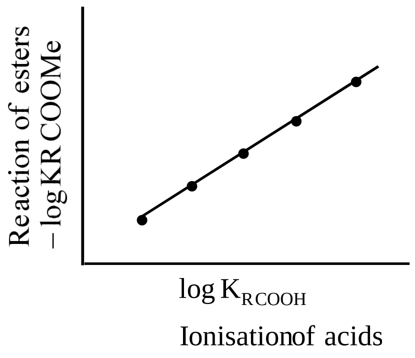
2.2 (iv) Hammett equation -Linear Free Energy Relationship :

Introduction of a substituent may

1. Change the position of equilibrium e.g. acetic acid becomes strongly acidic with the replacement of hydrogen at the $\alpha -$ position by chlorine.
2. Alter the rate of reaction.

   e.g. Nitration of toluene is rapid compared to benzene .

The equilibrium and rate constants are each related to free-energy changes. The correlation of relationship between the logarithms of rate or equilibrium constants is a linear free energy relationship LFER as is shown in the fig.2.3 given below.

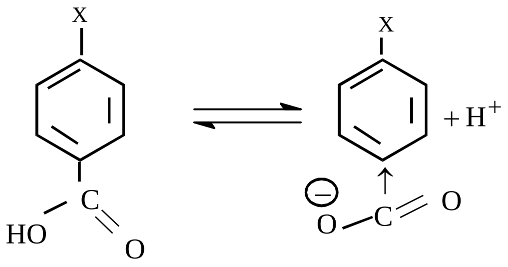


Hammett studied the acidities of a series of m- and p- substituted benzoic acids and correlated the structure and reactivity on a quantitative basis. The ionisation of these acids in aqueous media at 25°C is taken as the standard.

reference : The measurements were accurate and data available from literature.

Hammett equation is $\log \frac{K}{K_o} = P\sigma$

K and K_o represent the equilibrium constants for substituted and unsubstituted compounds. 'σ' the substituent constant depends on the nature of the position of the substituent in the ring. The strength of a series of substituted benzoic acids are compared with benzoic acid itself σ for each substituent is given by the equation .



$$\text{Log}\left[\frac{K_a(X.C_6H_4COOH}{K_a(C_6H_5\,COOH}\right] = P^{ka}(C_6H_5COOH) - PK_a(XC_6H_4COOH) = \sigma$$

A +ve σ value indicates an electron attracting group and a -ve σ value indicates electron donating group σ is generally independent of the nature of the reaction and is a quantitative measure of the polar effects in a given reaction by a m- or p-substituent relative to hydrogen.

The following table summarizes σ values for different meta and para substituents

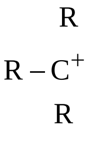
Substituent	σ_m	σ_p
H	O	O (by definition)
NH_2	-0.16	-0.66
CH_3	-0.07	-0.17
MeO	+0.12	-0.27
H O	+0.12	-0.37
F	+0.34	+0.06
I	+0.35	+0.18
Cl	+0.37	+0.23
Br	+0.39	+0.23
CN	+0.56	+0.66
NO_2	+0.71	+0.78

The reaction constant ρ is dependent on the nature of the reaction and conditions. The value of ρ indicates the sensitivity of a reaction or an equilibrium to a particular substituent. For a reaction assisted by electron attracting substituents, ρ is +ve. -ve ρ values indicate that the reaction is aided by high electron density at the reaction site.

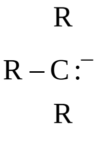
LESSON -2

2.2 (i) Intermediates :

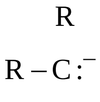
It was indicated earlier that organic reactions proceed step-wise. The step-wise process is known to take place through intermediates. The intermediates are usually very short-lived. They may not even be isoluble at times and detected by trapping experiments. Yet their study is important to have an overall idea of the complete nature of the reaction. Intermediates formed are prone to transform to stable molecules. The four types of intermediate carbon species are

1) Carbocations (carbonium ions) 

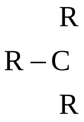
$R-\overset{R}{\underset{R}{C^{+}}}$

2) Carbon anions (carbanions) 

$R-\overset{R}{\underset{R}{C}}:^{-}$

3) Carbenes  and

$R-\overset{R}{C}:^{-}$

4) Free-radicals 
$R-\overset{R}{\underset{R}{C}}$

A glance at the structures of the above species brings to light the variation in the valency of carbon.

Nitrenes $R-\ddot{N}$ are the analogues of carbenes.

In the coming pages an attempt is made to infuse into the minds of the students, the generation, structure stability and reactivity of the above mentioned species.

2.2 (ii) Carbonium ions :

Suppose the bond $-C-X$ suffers a heterolytic cleavage to give a positively charged carbon residue. This carbon cation (1) is called carbonium ion. The remaining three valencies assume sp^2 hybridised state and the carbonium ion assumes a planar configuration(2).

Formation of carbonium is unlikely if the planarity is prevented by structural or steric factors.

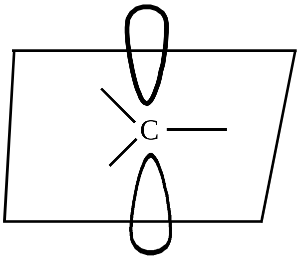
$-C-X \rightarrow -C^{+}+X^{-}$

(1)

120^{o} C^{+}

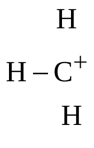
$C-$

(2)



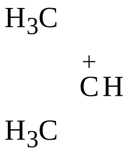
(2)

Following are some typical examples

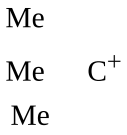

$H-\overset{H}{\underset{H}{C^{+}}}$

$CH_3\overset{\oplus}{C}H_2$

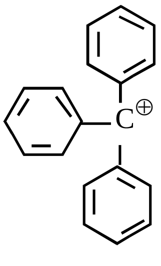
(Primary)(ethyl)


$\overset{H_3C}{\underset{H_3C}{}}\overset{+}{C}H$

Secondary(isopropyl)


$\overset{Me}{\underset{Me}{Me}}\;C^{+}$

tertiary(t – butyl)



Triphenyl methyl

$H_2C=CH-\overset{\oplus}{C}H_2$ allyl

$C_6H_5-\overset{\oplus}{C}H_2$ Benzyl

These carbonium ions are unstable, usually identified in solution half life period around fraction of a second. Following are some of the crystalline salts.

$(C_6H_5)_3C^+AlCl_4^-, (C_6H_5)_3C^+ ClO_4^-, (CH_3)_3C^+ SbF_6^-$

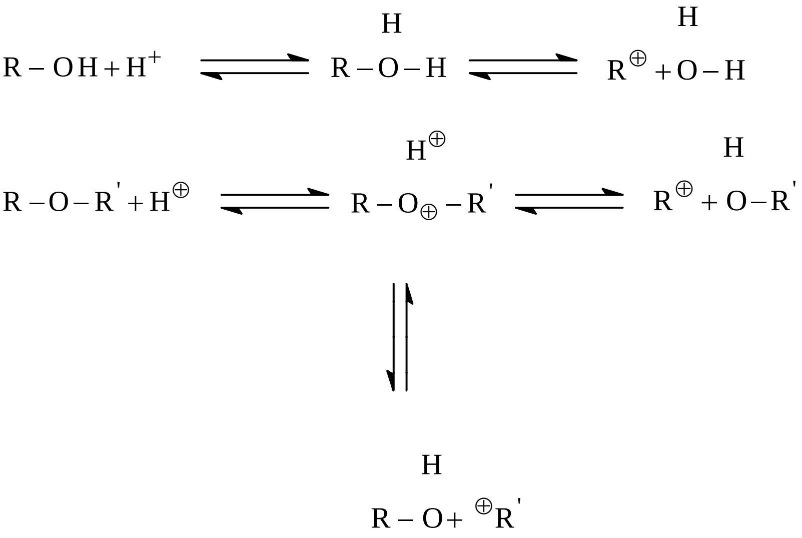
Generation :

Alkyl halides, alcohols, ethers and unsaturated systems like olefins and carbonyl compounds are some of the sources.

I. $R\ \ Cl + AlCl_3 \rightleftharpoons R^{\oplus} + AlCl_4^-$

$R-X \rightleftharpoons R^+ + X^-$ (Direct ionization in which the group attached to carbon atom leaves with its pair of electrons).

II.



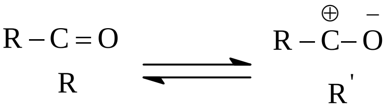
$$R-OH+H^+ \rightleftharpoons R-\overset{H}{O}-H \rightleftharpoons R^{\oplus}+\overset{H}{O}-H$$

$$R-O-R'+H^{\oplus} \rightleftharpoons R-\overset{H^{\oplus}}{O_{\oplus}}-R' \rightleftharpoons R^{\oplus}+\overset{H}{O}-R'$$

$$\downarrow\uparrow$$

$$R-\overset{H}{O}+{}^{\oplus}R'$$

$R-CH=CH-R+H^{\oplus} \longrightarrow R-CH-\overset{\oplus}{C}HR$



$$R-\underset{R}{C}=O \rightleftharpoons R-\underset{R'}{\overset{\oplus}{C}}-\overset{-}{O}$$

$R' = H,$ alkyl, aryl, hydroxyl, alkoxyl, aroxyl, acetoxyl etc).

Unequivocal evidence for the presence of carbonium ions was secured from a study of

a) Crystal structure of the solids salts

b) Cryoscopic behaviour of solutions

c) Conductivity of solutions and

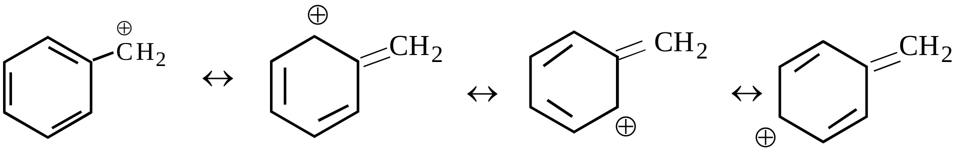
d) Spectroscopic methods -proton NMR in particular furnished valuable evidence -eg. butyl cation from the butyl fluorides in excess SbF_5

Stability :

The readiness with which a carbonium is formed depends on its stability . The stability in turn is connected with its generation. The relative rate of formation of carbonium ion as also its stability follows the order tertiary>secondary>primary > $\overset{+}{C}H_3$. The resonance energies of t-butyl,isopropyl and ethyl carbonium ions are 84,66 and 36 k.cal/mole respectively. Stability of t-butyl carbonium ion is attributed to the nine different possible hyper conjugation structures.

In allylic and benzylic cations, the charge on the carbon is quickly delocalised within the ion

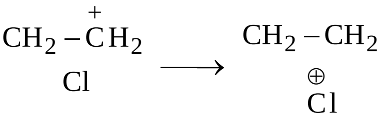
$$CH_2 = CH - \overset{+}{C}H_2 \rightleftharpoons \overset{+}{C}H_2 - CH = CH_2$$



Canonical forms of benzylic cations.

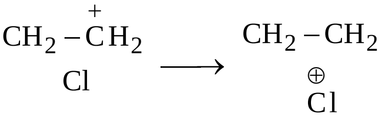
Diaryl and triaryl methyl cations are more stable than the benzylic carbonium ions. Stability is further increased when the electron donating substituents are in O-or p-positions.

Hetero atoms like halogens, nitrogen, oxygen and sulphur lend the lone pair of electron and stabilise the carbonium ion. In the process, a cyclic system arises.



$$\underset{Cl}{CH_2} - \overset{+}{C}H_2 \longrightarrow CH_2 - CH_2 \quad \overset{\oplus}{Cl}$$

Reactions of carbonium ions are summarised and represented in the following table.



$$\underset{Cl}{CH_2} - \overset{+}{C}H_2 \longrightarrow CH_2 - CH_2 \quad \overset{\oplus}{Cl}$$

Reactions of carbonium ions are summarised and represented in the following table.

2.2 (iii) Carbanions :

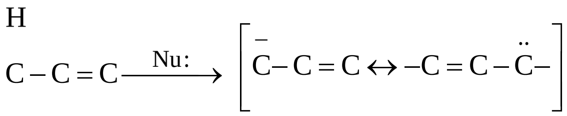
Carbanions are negatively charged ions. They possess an unshared pair of electrons and hence basic in nature. They are produced by the cleavage of carbon-hydrogen or carbon-metal bonds, (under the impact of a nucleophile) metal alkyls, Grignard reagents.

$$R-H \rightarrow \overset{..-}{R} + H^{\oplus}$$

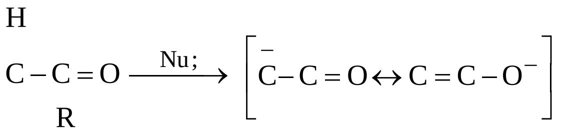
$$C-Li \rightleftharpoons C^{-} + Li^{\oplus}$$

$$C-MgX \rightleftharpoons C^{-}:+Mg^{\oplus}X$$

Loss of proton to a nucleophile (Nu:) from α – methyls of alkyl and carbonyl compounds results in the formation of carbanions.

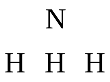


$$\overset{H}{C}-C=C \xrightarrow{Nu:} \left[\bar{C}-C=C \leftrightarrow -C=C-\ddot{C}-\right]$$



$$\overset{H}{C}-\underset{R}{C}=O \xrightarrow{Nu;} \left[\bar{C}-C=O \leftrightarrow C=C-O^{-}\right]$$

Its molecular picture resembles that of ammonia (1). It assumes the formation of a pyramid. The central carbon is sp^3 hybridised in its tetrahedral form. The unshared pair of electrons occupies one apex of the tetrahedron.



(1)

(2)

(3)

Stability :

More reactive unsaturated group such as carbonyl, nitrile etc. activate adjacent C-H bonds by higher conjugation. carbanions derived from them are more stable than those derived from the alkyl group. The stability order among alkyl carbanions is methyl >ethyl>isopropyl>t-butyl. With the increase of electron donating alkyl groups -ve charge on carbanion increases thereby decreasing the stability.

In unsaturated systems stability follows the increase in 's' character at the carbanion carbon. Electrons in 2s orbitals are closer to the nucleus than those in a 'p' orbital hence of lower energy and the stability order is $R_1 \equiv C^{-} > R_2C=\bar{C}H > R_3C\bar{C}H_2$. In the case of alkyl and benzylic carbanions the unshared pair overlaps with the π electrons of the double bond and the ion is stabilised.

If the carbanion is in conjugation with carbon-oxygen or carbon-nitrogen multiple bonds, the stability would be even more. This is obviously influenced adversely if carbonyl is attained to an electron releasing group and the case of formation of carbanion decreases in the order aldehydes ketones esters and free carboxylic acids.

In compounds where the methylene group is flanked by two polar groups such as malonic eser, acetoacetic ester, cyanoacetic ester, cyclic diones such as cyclopentadiene etc, the carbanion formed is a resonance hybrid of three or more forms and hence possess greater stability.

Carbanions are reactive nucleophiles. They take part in nucleophilic displacements

a) Alkylation b) Wrutz reaction c) Haloform reaction etc.

Additions :

a) Aldol condensation b) Perkins reaction c) Claisen condensation and related types

d) Michael addition e) Knoevenagel reaction etc.

Rearrangments :

a) Stevens b) Wittig c) Favorskie d) Sommelet rearrangements etc.

Mechanism of reactions included in the syllabus will be explained at appropriate places.

2.2.(IV) Carbenes :

Carbenes are highly reactive Parent species methylene is a short lived and bivalent carbon compound. It exists in two different forms, spectrally designated as singlet and triplet methylenes. In singlet methylene the unshared electrons are paired $\overset{H}{H:C:}$ and approximately sp^2 hybridized. The non-bonded electrons are not paired $H:\dot{C}:H$ in triplet methylene and the carbon is sp hybridised. It is a bi-radical.

Depending on how the carbenes are generated, some of them react as singlets, some as triplets and some others as singlets or triplets. The triplet is more stable than the singlet by about 20 K.cal $mole^{-1}$.

Disintegration of compounds like ketones and diazomethanes give carbenes,

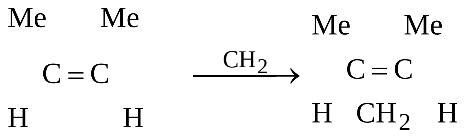
$$CH_2 = C = O \xrightarrow{\text{photolysis}} \overset{-}{C}H_2 + Co$$

$$CH_2 = \overset{+}{N} = \overset{-}{N} \xrightarrow[\text{CuCl}]{h\nu\Delta\text{ or}} \overset{-}{C}H_2 + N_2$$

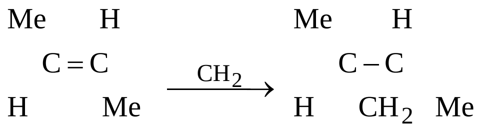
Reactions : Unusual reaction with carbene is 'insertion'.

1 Insertion reaction occur mainly in the C-H bonds and have little relevance since a mixture of products formed. $CH_3 - CH_2 - CH_3 \xrightarrow{CH_2} CH_3CH_2CH_2CH_3 + CH_3\underset{CH_3}{CH}CH_3$. Dihalocarbenes, however, do not give insertion reaction and are used to formylate aromatic rings. Riemer-Tiemann reaction is a very good example.

2 They add to unsaturated compounds such as cis and trans 2-butenes giving cis and trans cyclopropanes. The addition is stereospecific.



$$\underset{H\quad\quad H}{\overset{Me\quad\quad Me}{C = C}} \xrightarrow{CH_2} \underset{H\quad CH_2\quad H}{\overset{Me\quad\quad Me}{C = C}}$$



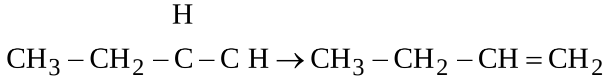
$$\overset{Me}{\underset{H}{}}C=C\overset{H}{\underset{Me}{}} \xrightarrow{CH_2} \overset{Me}{\underset{H}{}}C-C\overset{H}{\underset{Me}{}}\ (CH_2)$$

3 Dimerize : $R_2\bar{C} + R_2\bar{C} \rightarrow R_2C = CR_2$

4 Triple bonded compounds react with carbenes to give cyclopropanes which rearrange to allenes.

$$MeC \equiv CMe + 2\ddot{C}H_2 \rightarrow Me - Me$$

5 Rearrangement : Alkyl carbenes undergo rearrangement.



$$CH_3 - CH_2 - \overset{H}{C} - C\ H \rightarrow CH_3 - CH_2 - CH = CH_2$$

Rearrangement of acyl carbenes (Wolff rearrangement) and rearrangements leading to ring expansion (addition of carbenes to the double bonds of aromatic rings are also known. The order of reactivity among carbenes is $CH_2 > CHCl > CC_2 > CBr_2 > CF_2$

2.2 (V) Nitrenes :

The species that can exist with sextet of electrons on a nitrogen atom are called nitrenes. They are the nitrogen analogues (R-N) of carbenes. They are too reactive to be isolated under ordinary condition nitrenes can be generated in singlest (R-N) and triplet states (R- N).

Generation :

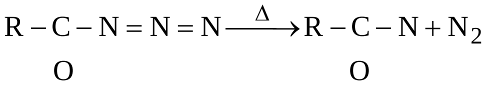
1. Photolysis of hydrazoic acid

$$HN_3 \xrightarrow{h\nu,Hg} H - N + N_2$$

2. Pyrolytic or thermal decomposition of azides.

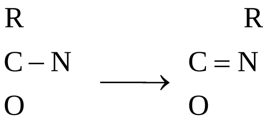
$$R - N = N^{\oplus} = N^{-} \xrightarrow{\Delta \text{ or } h\nu} R - N + N_2$$

3. Decomposition of acyl azides to acyl nitrenes.



$$R - \underset{O}{C} - N = N = N \xrightarrow{\Delta} R - \underset{O}{C} - N + N_2$$

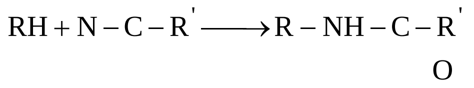
Acyl nitrenes are highly unstable and undergo rapid rearrangement to an isocyanate $(R - N = C = O)$, the nitrogen analogue or ketone.



$$\underset{O}{\overset{R}{C}} - N \longrightarrow \underset{O}{\overset{R}{C}} = N$$

Reactions are similar to carbenes :

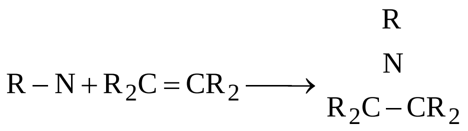
1. Insertion : Acyl nitrites in particular can insert into C-H and certain other bonds.



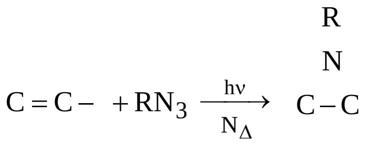
$$RH + N-C-R' \longrightarrow R-NH-\underset{O}{C}-R'$$

As in carbenes, this reaction in not useful since mixtures of products are formed.

2. Addition to $C=C$ bonds

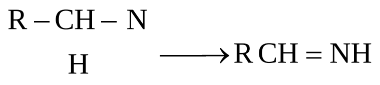


$$R-N + R_2C=CR_2 \longrightarrow \overset{\overset{R}{N}}{R_2C-CR_2}$$



$$C=C- \ + RN_3 \xrightarrow[N_\Delta]{h\nu} \overset{\overset{R}{N}}{C-C}$$

3. Rearrangement : In the case of alkyl nitrene, the rearrangement is very rapid and the formation of nitrene and migration are simultaneous.



$$R-\underset{H}{CH}-N \longrightarrow RCH=NH$$

4. Dimenzation : Formation of azobenzene from aryl nitrenes

$$2Ar-N \longrightarrow ArN=NAr$$

Nitrenes can also add to aromatic rings to give expansion products (as in carbenes).

Schmidt degradation and curtius , Hofmann, Neber rearrangements proceed through nitrene intermediates.

2.2 (VI) Free Radicals :

When a bond is broken homolytically, each fragment carries one electron called free-radicals or radicals in short. They are unstable and reactive. The weak bonds like O-O as in organic peroxides or C-C bonds influenced by steric factors are vulnerable for this type of fission.

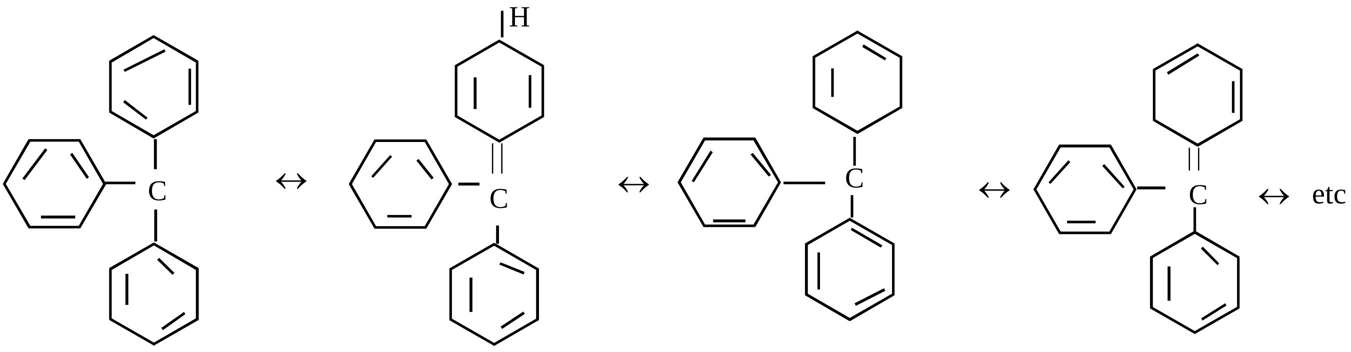
$$A-B \rightarrow A^{o} + {}^{o}B$$

$$-O-O- \rightarrow -O^{o} + {}^{o}O-$$

$$C-C \rightarrow C^{\cdot} + C^{\cdot} -$$

Stability :

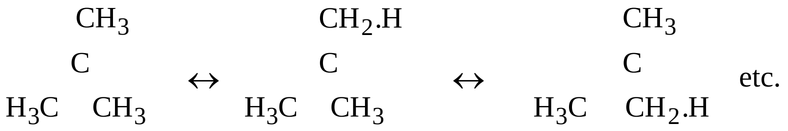
As in carbonium ions and cations, the radicals are also stabilised through extensive delocalisation of the free electrons. Thus triphenyl methyl radial is greatly stabilised by resonance (note 9 resonance structures can be drawn(as in the accompanying structures.



In the case of methyl or ethyl radicals, delocalisation is not feasible hence less stable and thereby dimerise to form stable products.

The higher the bond dissociation energy value less stable the radical R will be. The D value for the bond $CH_3 - H$ is 102 K.cal/mole at 25^oC while that of $(C_6H_5)_3C - C(C_6H_5)_3$ is 11 k.cal/mole.

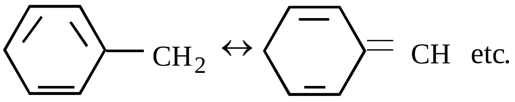
The order of stability among alkyl radical is T>S>P. The t-butyl radical is stabilised by hyper configuration as shown below.



$$\begin{array}{c}CH_3\\C\\H_3C\quad CH_3\end{array} \leftrightarrow \begin{array}{c}CH_2.H\\C\\H_3C\quad CH_3\end{array} \leftrightarrow \begin{array}{c}CH_3\\C\\H_3C\quad CH_2.H\end{array} \text{ etc.}$$

The stability of allyl and benzyl free radicals over simple alkyl radicals is also attributed to resonance.

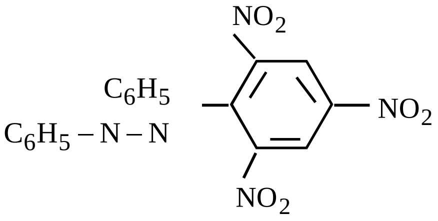
$CH_2 = CH - CH_2 \leftrightarrow CH - CH = CH_2$



Electron with drawing groups like NO_2 in a phenyl cause powerful delocalisation generating stable free-radicals with long life.

Some radicals, in which the unpaired electron is on a heteroatom are still more stable.

e.g. Diphenyl picryl hydrazyl is a solid that can be kept for several years.



Structure simple allyl radicals might have sp^2 or sp^3 bonding. In the former, the radical has a planar structure with the odd electron in the p-orbital. In the latter, the radical can assume a pyramidal structure with the odd electron in a sp^3 orbital. Further proof for the planar structure was obtained from kinetic evidence from iodine exchange reaction and also the evidence from the eser sectra. In short simple alkyl free-radicals prefer planar structure. The radicals is which the carbon is connected to atoms of high electronegativity.
e.g. CF_3 prefer pyramidal shape. Further study of free-radicals is included in chapter 6.

LESSON - 3

2.3 (i) Allyphatic nucleophilic substitution :

Organic reactions in which the nucleophile brings an electron pair to the substrate is called nucleophilic substitution (S_N).

This is characteristic of alkyl halides. The reaction of alkyl halide with nucleophilic may be represented as

Alkyl group Leaving group
(nucleofuge)

$$R - X \quad + : Y \xrightarrow{\text{solvent}} R - Y + : X$$

(substrate neutral
or +vely charged)

Nucleophile or
attacking agent or
nucelophilic agent
(-vely charged or neutral)

leaving group

Y must contain unshared pair of electrons. If Y itself is the solvent, the reactions are called solvolysis reactions. Water, ethanol and acetic acid are some of the specific solvents and produce hydrolysis, ethanolysis and acetolysis respectively. Though there is no broad division as such and make out a particular case, the reactions in general are characterised as S_N (unimolecular), S_N (bimolecular) S_Ni (substitution nucleophilic internal) and border - line behaviour caused by simultaneous operation (mixed S_N^1 and S_N^2). The main components required, are substrate, nucelophile and solvent.

Let us study the hydrolysis reactions of methyl bromide and t-butyl bromide. Both are substitution reactions in which bromine is replaced by the hydroxyl nucleophile.

$$CH_3Br + OH^- \rightarrow CH_3OH + Br^- \quad .... (1)$$

$$(CH_3)_3CBr + \overline{O}H \rightarrow (CH_3)_3COH + Br^- \quad ....(2)$$

The reactions appear to be simple but the mechanism is complex and can be understood by a study of kinetics.

In reaction (1) the rate depends on the concentration of $[CH_3Br]$ and the nucleophile $[OH^-]$. The rate of reaction was shown to be proportional to the concentration of both the bromide and the nucleophile.

Rate = $k[CH_3Br][\overline{O}H]$ k = specific rate constant.

It follows second order kinetics (S_N^2).

But in reaction (2) , the rate of reaction was found to be proportional to the concentration of alkyl bromide only and follows the first order kinetics.

$$\text{Rate} = k\left[(CH_3)_3CBr\right]$$

The rate of reaction is independent of $[OH^-]$ and called S_N^1.

2.3. (ii) S_N^2 mechanism :

The reaction is believed to take place in one step. The substrate and the nucelophile form a transition complex and decompose to give the products.

$$HO^- + C - Br \longrightarrow [HO....C.....Br]^- \longrightarrow HO - C \ + Br^-$$

The carbon is partially bonded to both to the attacking OH group and the leaving Br as shown in the transition complex. Neither the formation of C-OH bond nor the breakage of C-Br is complete in the transition state. The unstable transition complex decomposes with the formation of a new bond. The old bond with the leaving group is completely severed.

The S_N^2 reaction can take place at a hetero atom like N,O or S.

Ex :

$$CH_3CH_2I + (CH_3CH_2)_3N \longrightarrow (CH_3CH_2)_4 N^{\oplus} + I^-$$

$$CH_3S^{\oplus}(CH_3)_2 + \overset{-}{O}C_2H_5 \longrightarrow CH_3OC_2H_5 + S(CH_3)_2$$

$$CH_3OSO_2\, C_6H_5 + \overset{-}{O}H \longrightarrow CH_3OH + OSO_2C_6H_5{}^-$$

Stetreochemistry :

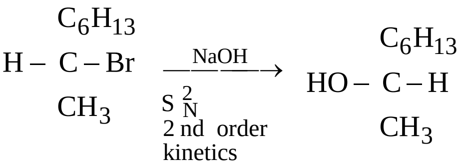
The two simple ways in which the reaction of CH_3Br with hydroxide ion can be effected are

i) The hydroxide ion might attack methyl bromide directly at the site where bromine is attached (front side attack).

ii) The hydroxide ion might attack from behind (rear-side or backside approach).

In optically active compounds, the rearward (backside) approach is conclusively established in S_N^2 mechanism when the substrate is optically active.

Ex :



$$H-\underset{CH_3}{\overset{C_6H_{13}}{C}}-Br \xrightarrow[\substack{S_N^2 \\ \text{2 nd order} \\ \text{kinetics}}]{NaOH} HO-\underset{CH_3}{\overset{C_6H_{13}}{C}}-H$$

(−) 2-bromooctane (+) 2- octanol

From the above reaction , it can be inferred that the configuration of the product is opposite to that of the reactant (look at the Br and OH groups). The S_N^2 reaction proceeds with complete stereochemical inversion.

Steric hindrance :

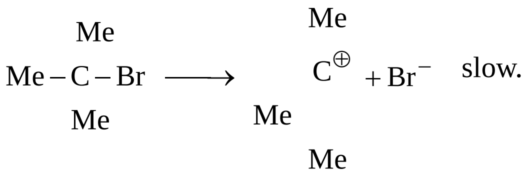
The reactivity of alkyl halides in S_N^2 reaction follows the order $\mathrm{Me > Et > Isopropyl > t.butyl}$ bromide. With the replacement of hydrogens in CH_3Br by Methyls, crowding around carbon is increased. The inaccessibility of the rearer side of the molecule increases. The reaction rates are due to steric factors and are dependent on the bulkiness of the groups.

2.3. (iii) Kinetics, stereochemistry and the effect of structure on reactivity form the basis for the study of S_N^2 mechanism.

$S_N{}^1$: As already stated, the formation of t-butyl alcohol from t-butyl bromide and hydroxide ion follows first order kinetics. The rate depends on the concentration of t-butyl bromide only and not on hydroxide ion.

Step I :

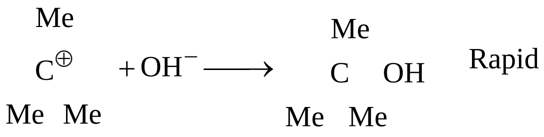
Formation of carbonium ions slow rate determining step.



$$\mathrm{Me}-\overset{\mathrm{Me}}{\underset{\mathrm{Me}}{\mathrm{C}}}-\mathrm{Br} \longrightarrow \mathrm{Me}\;\overset{\mathrm{Me}}{\underset{\mathrm{Me}}{\mathrm{C}^{\oplus}}} + \mathrm{Br}^- \quad \text{slow.}$$

Step II :

Neutralisation of carbonium ion by the nucleophilic fast step.



$$\overset{\mathrm{Me}}{\underset{\mathrm{Me}\quad\mathrm{Me}}{\mathrm{C}^{\oplus}}} + \mathrm{OH}^- \longrightarrow \overset{\mathrm{Me}}{\underset{\mathrm{Me}\quad\mathrm{Me}}{\mathrm{C}}}\;\mathrm{OH} \quad \text{Rapid}$$

The nucleophile can approach the planar carbonium ion from either side consequently there is no preferential formation for any one of the optical isomers. A Racemic mixture results.

Formation of phenyl ethyl alcohol from (-) or ± phenyl ethyl chloride results in 98% racemisation and 2% inversion.

The stereochemistry of the $S_N{}^1$ reaction and its product depends on

i) the nature of the leaving group

ii) stabilization of the carbonium ion intermediate

iii) the nature of the solvent

The larger the size of the leaving group, greater are the chances for racemisation

E.g. Tosyloloxyls.

With the increase of size of the alkyl substituents on the tertiary carbon, the rate of hydrolysis is increased. Thus the rate of hydrolysis of tri isopropyl methyl chloride is almost seven times that of t-butyl chloride.

This is due to the excessive back strain in the tri isopropyl methyl chloride. Chlorine is squeezed out at the first opportunity. The space released is occupied by bulky groups and the carbonium ion assumes a stable configuration. The back strain is referred to as B strain. The students may bring out the characteristic features of S_N^2 and S_N^1 mechanisms.

2.3 (iv) Mixed S_N^1 and S_N^2 mechanism :

S_N reactions are shown to be proceeding through S_N^2 or S_N^1 way or both depending on the substituent and reacting conditions. But there are certain reactions which seem to proceed in between -a border line region. There are two views to explain this phenomenon. According to one view the intermediates in mixed S_N^1 and S_N^2 mechanism follow neither of the two exclusively and proceed in between. The other view holds that the border line behaviour is caused by simultaneous operation of both S_N^1 and S_N^2 with no intermediate mechanism. Some molecules rear by S_N^1 and others by S_N^2 though the reaction was carried out in the same container.

According to seen, the S_N^1 and S_N^2 reactions of the alkyl halides proceed through the intermediate ion-pair followed by conversion to products.

$$RX \overset{k_1}{\rightleftharpoons} R^+X \overset{k_2}{\rightleftharpoons} \text{products .}$$

In S_N^1 the formation of ion pair (k_1) is rate determining. In S_N^2 mechanism its destruction (k_2) is rate determining. When the rate of formation and destruction of the ion-pair are of the same magnitude, border line behaviour is noticed. It was generally believed that the normal S_N^2 mechanism operates at high pressures and the cation molecule mechanism at lower pressures. Some believe that the key to the problem is perhaps the varying degrees of nucleophilic solvent assistance to ion formation.

Hydrolysis of 4-methoxy benzyl chloride in 70% aqueous acetone forming 4-methoxy benzyl alcohol is studied and following are the observations.

1. Conversion to the corresponding alcohol proceeds by S_N^1.
2. Addition of azide ion results in the formation of 4-methoxy benzyl azide in addition to 4-methoxy benzyl alcohol.
3. The addition of azide ions increases the rate of ionization and decreases the rate of hydrolysis.
4. The rate of ionization is less than the total rate of reaction indicating that azide formation to some extent proceeds by S_N^2 mechanism.

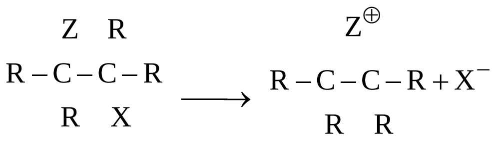
5. To conclude, $S_N{}^1$ and $S_N{}^2$ mechanism operate simultaneously and the mechanism expected is partial racemization and partial inversion.

2.3 (V) Neighbouring group mechanism :

In this mechanism, the neighbouring group Z with an unshared pair of electrons acts as in internal nucleophile. The reaction proceeds in two types.

Step I

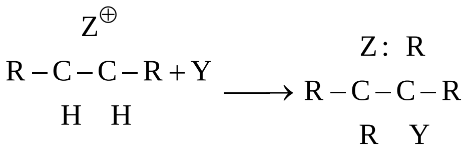
The neighbouring group helps push out the leaving group but still retains attachment to the molecule.



$$R-\underset{R}{\overset{Z}{C}}-\underset{X}{\overset{R}{C}}-R \longrightarrow R-\underset{R}{\overset{Z^{\oplus}}{C}}-\underset{R}{C}-R+X^{-}$$

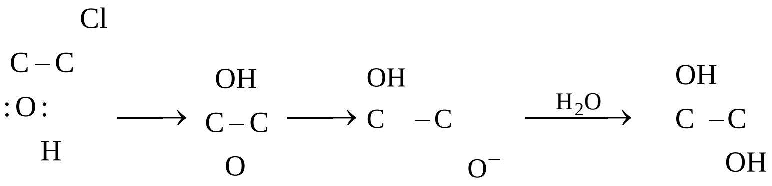
Step 2

The external nucleophile (y:) displaces the neighbouring group by rear-side approach.



$$R-\underset{H}{\overset{Z^{\oplus}}{C}}-\underset{H}{C}-R+Y \longrightarrow R-\underset{R}{\overset{Z:}{C}}-\underset{Y}{\overset{R}{C}}-R$$

$\beta-$halohydrins, $\alpha-$ halogenated carboxylic acids or $\alpha-$ aminohalogenated compounds during the substitution reaction exhibit retention of configuration. Kinetics is of first order and racemisation not noticed.



$$\underset{\underset{H}{:O:}}{C}-\overset{Cl}{C} \longrightarrow \overset{OH}{C}-\underset{O}{C} \longrightarrow \overset{OH}{C}\;-\underset{O^{-}}{C} \xrightarrow{H_2O} \overset{OH}{C}\;-\underset{OH}{C}$$

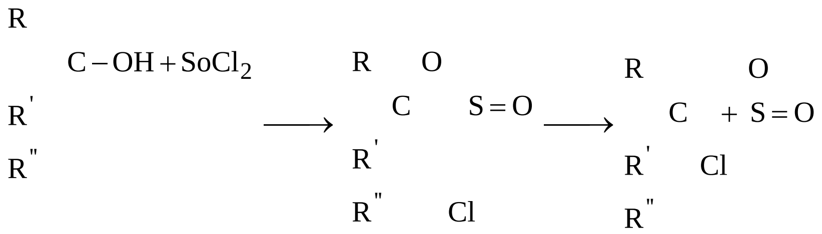
In the above example OH acts as an internal nucelophile and assists the halogen to escape as halide by rearward attack and gives rise to oxonium ion. This assistance is called anchimeric assistance or neighbouring group participation. Two inversions through two rearward attacks are noticed second one neutralising the inversion of the first, finally resulting in the retention of configuration.

Groups that lend active anchimeric assistance are $OH, -SR, NH_2$ etc that possess lone pair of electrons.

2.3 (VI) $S_N{}^i$ Mechanism : (Substitution nucleophilic internal) :

In this mechanism the part of the leaving group attacks the sub rate and in the process detaches itself from the rest of the leaving group.

Ex: Replacement of OH by Cl by thionyl chloride in phenyl alkyl carbinols.

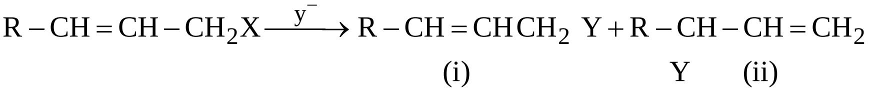


Step 1 : The hydrogen of the OH is displaced to give chlore sulphonic ester C-O bond is not broken and there is no change in configuration.

Step 2 : The attack by Cl takes place from the same side of the carbon atom and configuration retained. The final attack takes place internally (rearrangement followed by decomposition). This is called $S_N i$. Carbonium ion is not separated in this reaction.

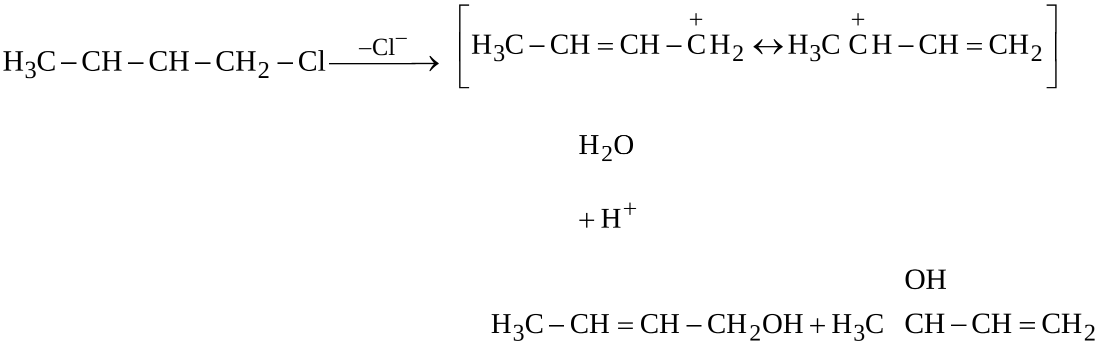
2.3 (vii) Nucleophilic substitution (S_N) at an allylic carbon.

If the S_N reactions of allyl halides are carried out under conditions that favour $S_N{}^1$ a mixture of two products are formed i) the normal substituted product and ii) the rearrangement product



$$R-CH=CH-CH_2X \xrightarrow{y^-} \underset{(i)}{R-CH=CHCH_2\,Y} + \underset{Y\quad(ii)}{R-CH-CH=CH_2}$$

ii). the rearranged product is an example of allylic rearrangement and the mechanism $S_N i$. It is believed to proceed through a resonance hybrid (ambidient)



$$H_3C-CH-CH-CH_2-Cl \xrightarrow{-Cl^-} \left[H_3C-CH=CH-\overset{+}{C}H_2 \leftrightarrow H_3C\overset{+}{C}H-CH=CH_2\right]$$

$$\xrightarrow[+H^+]{H_2O} H_3C-CH=CH-CH_2OH + H_3C\overset{OH}{CH}-CH=CH_2$$

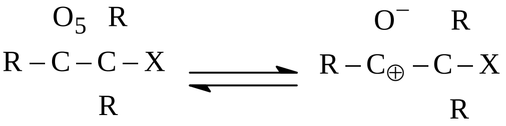
Methyl vinyl carbinol 2-butene-1-ol

Two different carbonium ions are produced and hence two different substitution products possible. However, shift of the double bond is noticed in one of the products. This is called allylic shift. Two mechanisms are in operation $S_N{}^1$ (no rearrangement). $S_{N1}{}^1$ (rearrangement). Both, ofcourse proceed through a common intermediate ambidient cation. S_N at allylic carbon can take plane $S_N{}^2$ way generally allylic arrangement does not takes place by $S_N{}^2$ mechanism.

2.3 (viiii) Nucleophilic substitution S_N at trigonal carbon :

S_N at trigonal carbon takes place more readily than at sp^3 carbon. It is especially true when the carbon is double bonded to oxygen, sulphur or nitrogen. Thus S_N takes place in much more facile manner at an acyl carbon than at a saturated carbon. Acid chlorides are more reactive than alkyl chlorides and acid amides more reactive than alkyl amines in S_N. It is the carbonyl group that make all the difference. The mechanism proceed svia tetrahedral intermediate. This sequence is not possible at a saturated carbon. The carbonyl is unsaturated the weak π bond breaks the requirement for the attachment of the nucleophile and oxygen ready to accept the negative charge.

Carbonyl compounds halogenated in the α – position proceed through $S_N{}^2$ mechanism since the carbonyl polarisation should favour $S_N{}^2$.

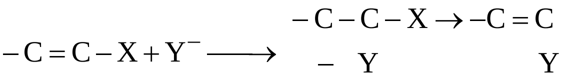


$$\begin{array}{c} O_5\ \ R \\ R-C-C-X \\ R \end{array} \rightleftharpoons \begin{array}{c} O^-\ \ \ R \\ R-C_{\oplus}-C-X \\ R \end{array}$$

2.3 (ix) Nucleophilic substitution at Vinylic carbon :

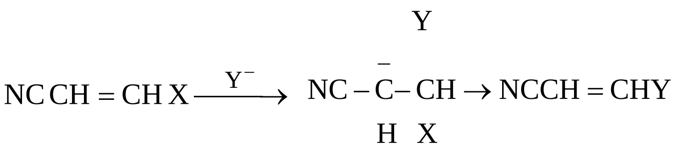
The S_N at vinylic carbon is difficult. Vinyl halides in general are inert towards $S_N{}^1$ and $S_N{}^2$ reactions. The carbon-halogen bond strength in vinyl halides is more compared to alkyl halides. Hence vinyl halides are much less reactive.

$$\left[> C = C - X \leftrightarrow C^- - C = X^+ \right]$$



$$-C=C-X+Y^- \longrightarrow \begin{array}{c} -C-C-X \\ -\ \ Y \end{array} \rightarrow \begin{array}{c} -C=C \\ \ \ \ Y \end{array}$$

In vinyl chloride, there is extensive delocalisation of the π electrons with the lone pair on the halogen atom. Separation of charges, therefore prevented. C-Cl bond possesses even partial double bond character and hence does not hydrolyse under the usual conditions with any base. If the substrate contains electrons attracting groups, the substitution however, is enhanced. Substituents in β group stabilise the carbanion.



$$NCCH=CHX \xrightarrow{Y^-} \begin{array}{c} Y \\ NC-\bar{C}-CH \\ H\ \ X \end{array} \rightarrow NCCH=CHY$$

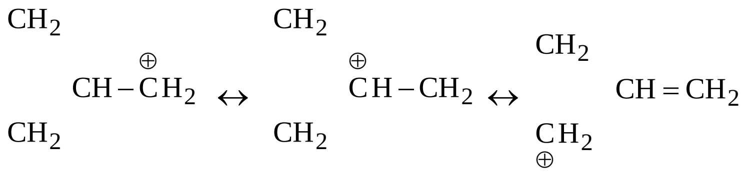
LESSON -4

2.4 (i) Classical and non-classical carbocations :

It was earlier pointed out that the nucleophilic attack involves an atom with unshared pair of electrons in the neighbouring group mechanism and proceeds through non-classical (bridged) intermediates carbocations.

In classical carbocations the positive charge is localised on one carbon atom. Also noticed was the delocalisation by resonance involving unshared pair of electrons. In alternate, the delocalisation in double bond in the allylic position noticed. The positive charge is delocalised in a non-classical carbonium also, but not in the allylic position or σ – bond.

e.g. : Cyclopropyl methyl cation :



The discussion may be extended to 7-norbornenyl cation, a homoallylic cation and also the nor bormyl cation formed through σ and π routes.

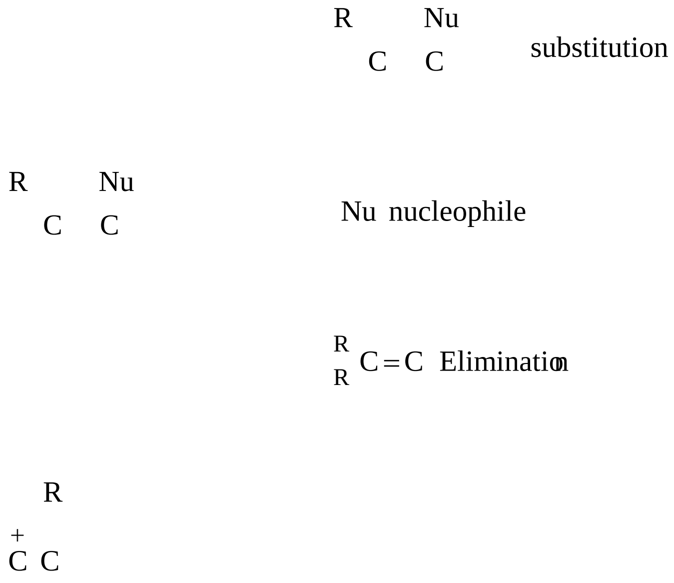
2.4 (ii) Carbonium ion rearrangements :

Formation carbonium ion may be followed

i. by neutralisation resulting in a substituted product.

ii. by elimination of a proton from the neighbouring carbon to produce olefine.

iii. yet another possibility is alkyl or aryl group or even hydroxide may migrate with its bonded electron pair from the α carbon atom to the carbonium ion (1,2 shifts) creating a new carbonium ion. The latter may follow a substitution or elimination or rearrangement depending upon the conditions of the reaction and the structure of the new carbonium ion.



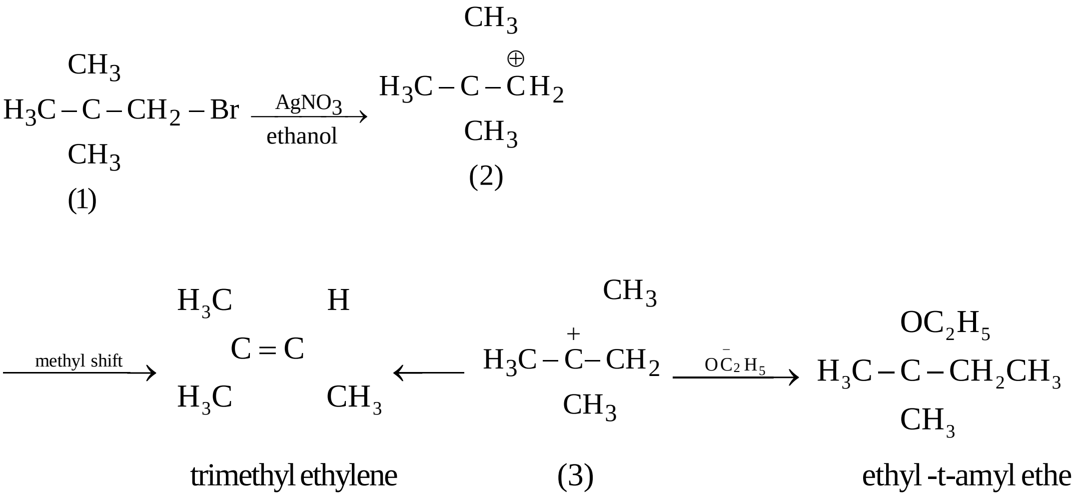
$R = H$, alkyl or aryl

The carbonium in rearrangement may involve 1,2 or 1,3 shifts of the group R or hydride structurally, compounds containing tertiary carbons α to the carbonium ion leads to these rearrangements.

2.4(iii) Wagner - Meerwein and related rearrangements :

Rearrangements of alcohols and halides under acidic conditions are generally known as Wagner-Meerwein rearrangements. Rearrangement in arnuries is known as Demjanow's rearrangement. Besides alkyl or aryl group migration, ring expansion, ring contraction or even ring closure may take place. These rearrangements proceed through classical or non-classical carbonium ions.

Solvolysis of neopentyl bromide i) in ethanol is an example in which the methyl group migrates with its bonding pair of electrons to give tertiary neopentyl carbonium ion (2)

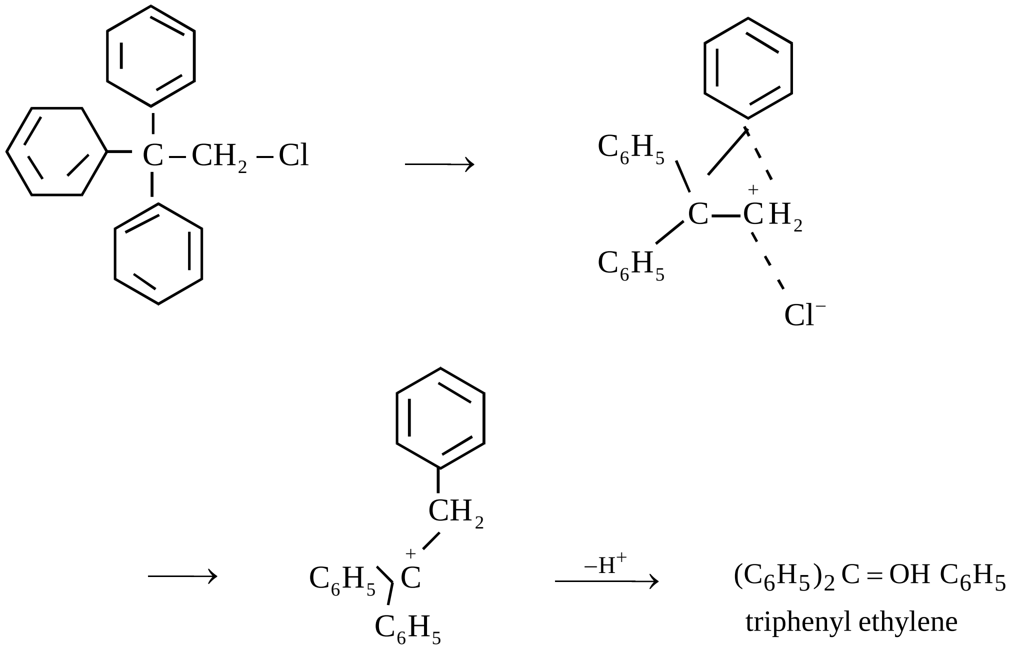


$$\underset{(1)}{H_3C-\overset{CH_3}{\underset{CH_3}{C}}-CH_2-Br} \xrightarrow[\text{ethanol}]{AgNO_3} \underset{(2)}{H_3C-\overset{CH_3}{\underset{CH_3}{C}}-\overset{\oplus}{C}H_2}$$

$$\xrightarrow{\text{methyl shift}} \underset{\text{trimethyl ethylene}}{\overset{H_3C\qquad H}{\underset{H_3C\qquad CH_3}{C=C}}} \longleftarrow \underset{(3)}{H_3C-\overset{CH_3}{\underset{CH_3}{\overset{+}{C}}}-CH_2} \xrightarrow{\bar{O}C_2H_5} \underset{\text{ethyl -t-amyl ether}}{H_3C-\overset{OC_2H_5}{\underset{CH_3}{C}}-CH_2CH_3}$$

Formation of high energy primary carbonium ion(3) is the rate determining step.

Solvolysis of neopentyl chloride (4) in HCOOH proceeds atleast 60,000 times faster than an alkyl group The rate determining step is the formation of lower energy bridged phenonium ion(5).



Migration is caused by the neighbouring group participation by phenyl. Phenyl group provides anchimeric assistance. This is not noticed if stable carbonium ion is formed by direct ionisation of the compound.

Examples are also known where two or even more 1,2, shifts occur.

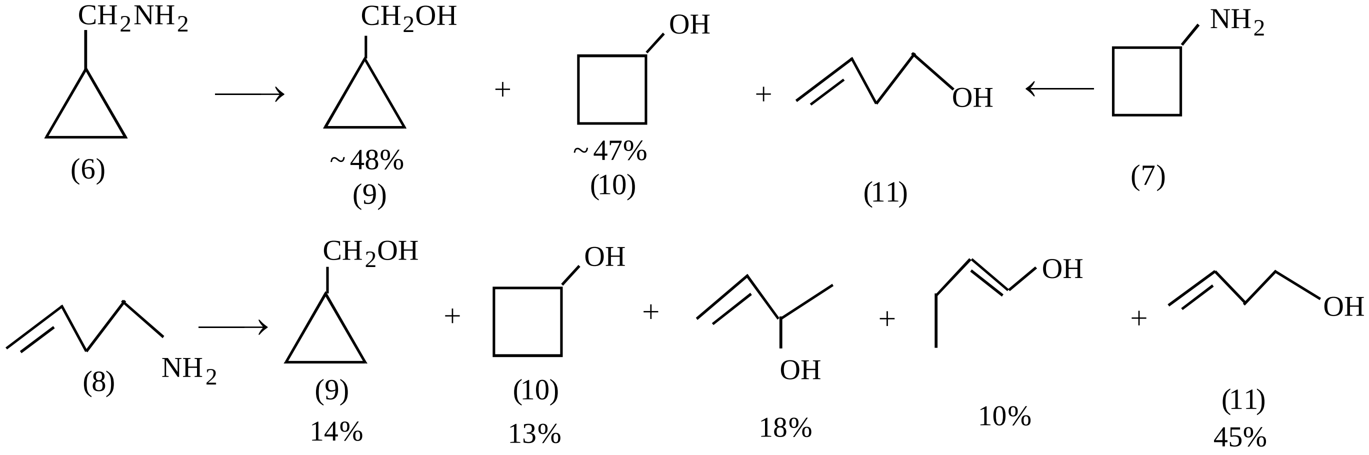
E.g. :

1. Formation of olefine from diethyl cyclobutyl carbinol in presence of an acid.
2. Rearrangement of camphane to isobornyl chloride (bicyclic system).

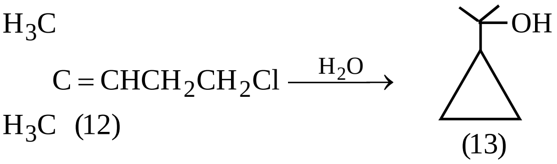
2.4(iv) Demjanow's rearrangement

e.g. for ring expansion or ring contraction.

The aqueous deaminations of cyclopropyl methyl amine (6), cyclobutyl amine (7) and allyl amine(8) gives a mixture of an unrearranged alcohol cyclopropyl methanol (9), cyclobutanol (10) and allyl alcohol(11).



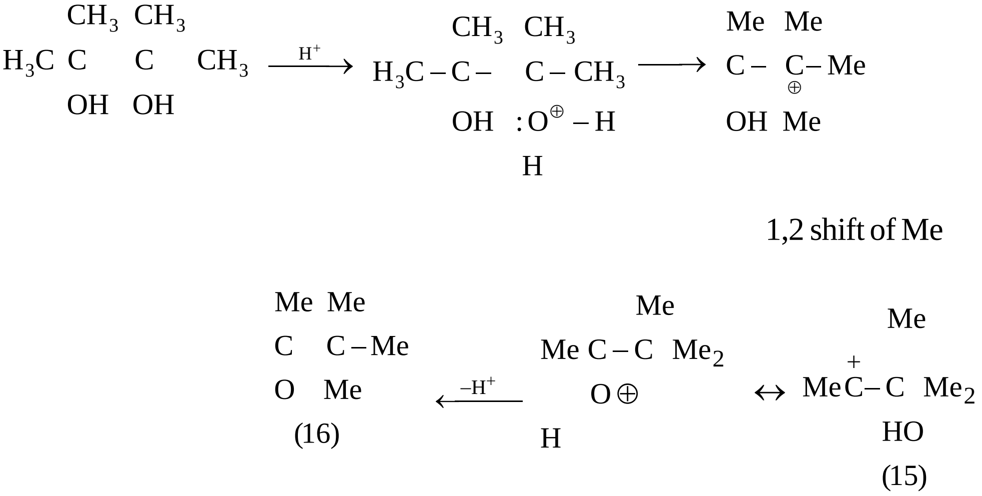
Hydrolysis of 5-chloro-2-methyl 2-pentene(12) to cyclopropyl dimethyl carbinol (13) in which the carbonium ion undergoes ring closure with the double bond.



(12) (13)

2.4(v) Pinacol pinaclone rearrangement :

Vicinal diols like pinacol (1,1,2,2 tetramethyl glycol) (14) when treated with acids rearrange to give substituted ketones. The mechanism involves a 1, 2 shift. The new carbonium ion (15) that carries a hydroxyl looses a proton from the hydroxyl to give ketone pinacolone (16).

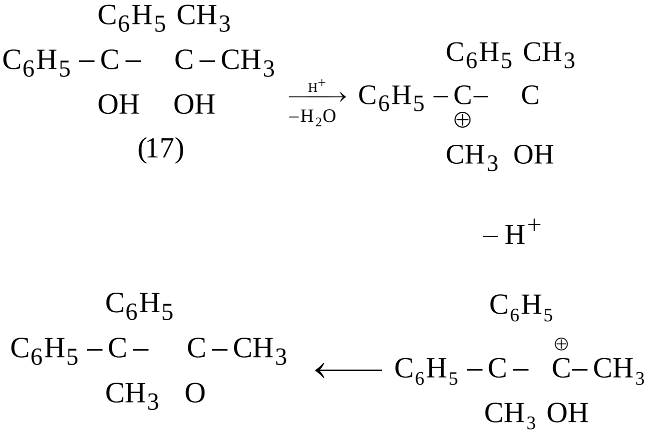


(16) (15)

If the groups attached are not the same, migratory aptitude decides the order of preference.

Migratory aptitudes among aryl, alkyl and hydrogen follows the order aryl>alkyl>hydrogen.

The stability of the carbonium ion outweighs even the greater migratory aptitude in the course of rearrangement. Thus in the case of 1,1, dimethyl 2, 2 diphenyl glycol (17) the hydroxyl group that leaves behind the more stable carbonium ion departs first.



(17)

2.4 (vi) Reactivity :

The effect of substrate structure. It is rare with tertiary substrates. Primary and secondary substrates react by $S_N{}^2$ mechanism while tertiary substrates proceed through $S_N{}^2$. However, elimination predominates if $\beta-$hydrogen is present. $S_N{}^2$ reactions of simple alkyl derivatives follow the order pri > sec > ter. Steric hindrance plays a notable role in determining the $S_N{}^2$ reaction rate. The rate is decreased with the branching at either α or β carbons. Neopentyl halides are very $S_N{}^2$ unreactive in reactions because of the steric hindrance by the methyl groups on the β carbon.

In the case of $S_N{}^1$ reactions, the rate is independent of nucleophilic and hence steric hindrance has a little role to play. The rates of $S_N{}^1$ reactions of alkyl derivatives follow the order tertiary >secondary >primary .This is in complete contrast to $S_N{}^2$ reactions.

Mechanism of reactions containing vinyl and substrates of the type $RCOX$ in which there is unsaturation at the $\alpha-$carbon were discussed earlier. Also it was pointed out that allyl and benzylic substrates in which a double bond was present in the β position, the cation is stabilised by resonance and the $S_N{}^2$ rates enhanced. This is because of the resonance possibilities in the transition complex. The effect of electron donating and electron attracting groups can be learnt in detail in aromatic substitution.

2.4 (vii) Effect of attacking nucleophile :

In $S_N{}^1$ reactions, the rate is independent of nucleophile of species that contains lone pair of electrons. However, a negatively charged nucleophile is always more powerful than its conjugate acid.

e.g. OH^- more powerful nucleophile than $H-\underset{H}{O}$ and $NH_2{}^-$ than $\underset{H}{H-N-H}$. The ability to donate an electron pair to carbon is nucleophilicity OH^-, a strong base is a good nucelophile. A very weak base I^- may also be a good nucleophile. The reactivity sequence is $I^- > Br^- > Cl^-$ as against the expected $Cl^- > Br^- > I^-$. It may perhaps be associated with the solvation energies of the ions. Smaller negatively charged nucleophiles are more solvated by the usual polar prootic solvents.

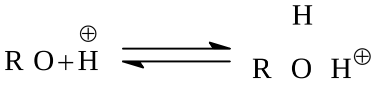
The approximate order of nucleophilicity is $N\overline{H}_2 > R\overline{O} > O\overline{H} > R_2NH$. The more the nucleophilic reactivity of the reagent, the more the participation of $S_N{}^2$ compared to $S_N{}^1$ mechanism. Also more free the nucelophile is, the greater is the rate.

2.4 (viii) The effect of the leaving group :

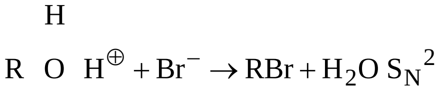
01. At a saturated carbon : Whether it be $S_N{}^1$ or $S_N{}^2$ reaction, there is a correlation between the reactivity of $R-X$ and the strength of H-X. The reactivity of alkyl derivative RX is partly determined by the leaving group, X. The best leaving groups are the weakest bases. Thus among halides the best leaving

group is iodide. S_N^2 reactions require powerful nucleophiles and take place under basic or neutral conditions. Most of the S_N^1 reactions take place under acidic conditions.

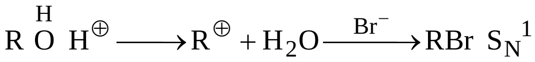
OH^- is a poor leaving group. A strong acid catalyst is needed for alcohols to react in the S_N^2 reaction and the OH is protonated. Hydroxyl group is thus transformed into a better leaving group. (H_2O in place of $\overline{OH}$)



$$R\,O + \overset{\oplus}{H} \rightleftharpoons R\,\overset{H}{O}\,H^{\oplus}$$



$$R\,\overset{H}{O}\,H^{\oplus} + Br^- \rightarrow RBr + H_2O \quad S_N^2$$

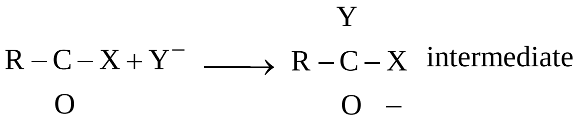


$$R\,\overset{H}{O}\,H^{\oplus} \longrightarrow R^{\oplus} + H_2O \xrightarrow{Br^-} RBr \quad S_N^1$$

NH_2, NHR and NR_2 are extremely poor leaving groups. However, the leaving group ability of NH_2 may be increased if the primary amine RNH_2 converted to the detosylate.

02. At a carbonyl carbon :

It was already pointed out earlier that tetrahedral mechanism operates at carbonyl carbon.



$$R - \underset{O}{C} - X + Y^- \longrightarrow R - \overset{Y}{\underset{O^-}{C}} - X \quad \text{intermediate}$$

In the above intermediate X and Y compete. If X is a poor leaving group compared to Y, then naturally Y prefers to leave and the intermediate reverts to the starting compound. The order of decreasing stability $RCOCl > RCOOR' > RCONH_2$ etc.

2.4 (viii) The effect of the medium:

The medium plays a very important role. The ionising power of a solvent depends on two factors. 1) Dielectric constant 2) Solvation. Increase of the dielectric constant increases ionising strength. The more polar the solvent is, the greater is the rate of S_N^1 reactions. The increase of polarity however retards the reaction in S_N^2 mechanism. The same reaction may proceed by S_N^1 in one solvent and S_N^2 or S_N^1 and S_N^2 in other solvent.

E.g. The alkaline hydrolysis of benzyl chloride in aqueous acetone proceeds both by S_N^2 and S_N^1 mechanism. If water is the solvent S_N^1 mechanism predominates. This is because the dipole moment of water is more than that of aqueous acetone.

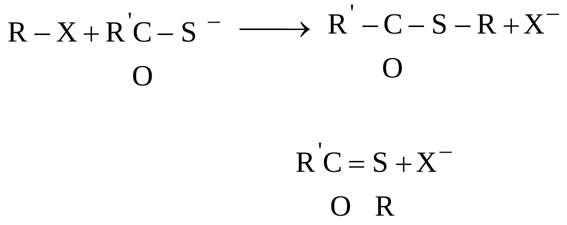
With neutral substrates, with the increase of polarity of the solvent the reaction proceeds faster. In the case of positively charged substrates, the speed of the reaction is decreased with the increase of polarity of the solvent. The addition of small amount of salts like LiBr, $LiClO_4$ (external salt effect) also increase or decrease the rate of reaction.

E.g. Acetolysis of some alkyl tosylates.

2.4(x) Ambidient Nucleophiles Regioselectivity :

Substrates that can be attacked at two or more positions are called ambidient substrates. Multiatomic nucleophile with more than one nucleophilic center are called ambidient ions. The nucelophile in such cases may attack in two or more different ways and form different products called ambidient nucleophiles. Attachment of the nucleophile to the alkyl group by different atoms lead to mixed products.

E.g : Reaction between salts of thioacids and alkyl and halides to give both thiol esters and thione esters.

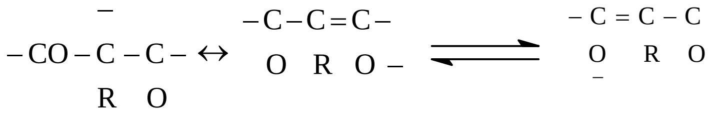


$$R-X+R'\underset{O}{C}-S^{-} \longrightarrow R'-\underset{O}{C}-S-R+X^{-}$$

$$R'\underset{O}{C}=\underset{R}{S}+X^{-}$$

On the other hand, the nucleophile NCO^{-} though potential enough to give more than one structural isomer produces only isocyanates RNCo but not cyanates. The reaction is said to be regioselective. Ambidient nucelophiles.

1. Ions formed by the removal of proton from malonic ester in which C-alkylation or O-alkylation may result



$$-CO-\underset{R}{\overset{-}{C}}-\underset{O}{C}- \leftrightarrow -\underset{O}{C}-\underset{R}{C}=\underset{O-}{C}- \rightleftharpoons -\underset{\underset{-}{O}}{C}=\underset{R}{C}-\underset{O}{C}$$

2. Formation of a dicarbanion from a β -keto ester.

$$CH_3-CO-CH_2-CO- \xrightarrow[\text{a base}]{\text{2 moles of}} {}^{-}CH_2-CO-\overset{-}{C}H-CO-$$

3. The $C\overline{N}$ ion in which the nucleophile can give nitriles $RC\equiv N$ or isonitriles $RN\equiv C$.
4. The nitrite ion may form nitrite esters R-O-N=O or nitro compounds $R\,NO_2$ (not an ester)

There seen to be two major factors

i) Polarizability of the nucelophile and ii) solvation effects to find out which atom of an ambidient nucelophile attacks the given substrate. Ambidient nucelophile is likely to attack with its less electronegative atom when the reaction changes its mode from $S_N{}^1$ like to $S_N{}^2$ like. The position of attack is influenced more by the solvent. A change from prootic to a polar aprotic solvent often increases the attack by the more electronegative atom.

E.g. : Sodium β naphthoxide attacks benzyl bromide by O-alkylation 95% (D MSO solvent) and 85% C-alkyltation (2,2,2 trifluoro ethanol).

Steric effects may also govern the regioselectivity. Deeper study leads us to conclude that many exceptions are there and no particular rule prevails. It can generally be inferred that the position of attack depends also on the nature of the nucleophiles, the solvent, the leaving group and conditions prevailing at the time of reaction

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ORGANIC CHEMISTRY PAPER III UNIT III
AROMATIC ELECTORPHILIC SUBSTITUTION

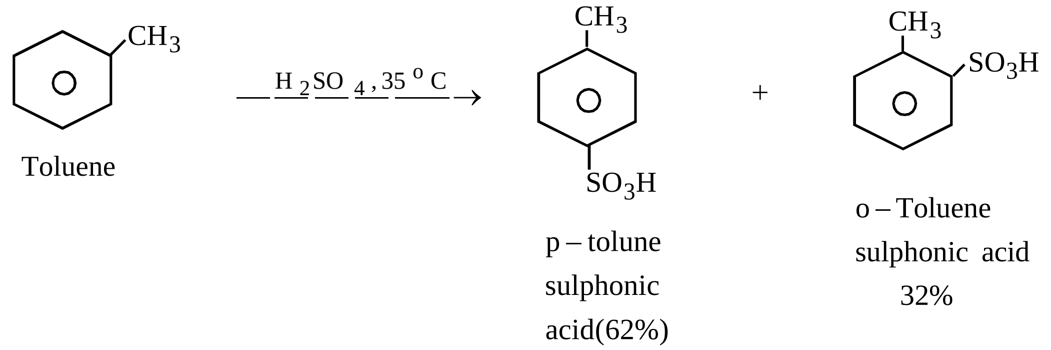
The chief reactions of benzene are those in which benzene ring serves as a source of electrons that is as a base. Electrophilic reagents react with benzene and are said to be electrophilic substitution reactions.

Electrophilic aromatic substitution include a wide variety of reactions, nitration, halogenation, sulphonation, Friedel-Craft's reactions, Diazo coupling reactions are shown by highly reactive aromatic compounds.

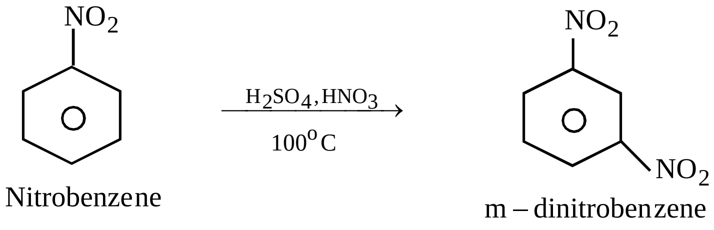
Effect of substituent groups :

Like, benzene toluene undergo electrophilic aromatic substitution giving two of the three possible products ortho- and para-isomers. It was found experimentally that toluene reacts much faster than benzene in any of the electrophilic substitution reactions.Methyl group makes the ring to be more reactive than benzene itself and directs the attacking reagent to ortho- and para- positions of the ring.

Ex :



On the other hand nitrobenzene reacts slowly than benzene and give chiefly meta isomer.



Any group attached to a benzene ring affects the reactivity and orientation of substitution. A group that make the ring more active than benzene is called an activating group and that makes ring less reactive are called deactivating group.

A group that causes the attack to occur chiefly at ortho- and para- positions to it is called ortho- para directing. A group that causes the attack to occur chiefly at positions meta to it is called meta-directing group.

Ortho- para directing groups : $-OH, -NHCOCH_3, -CH_3$

$-F, -Cl, -Br, -I$

meta-directing groups : $-\mathrm{NO_2},\ -\overset{+}{\mathrm{N}}(\mathrm{CH_3})_3$

$-\mathrm{COOH},\ -\mathrm{CHO},\ -\mathrm{SO_3H}$

A given group causes same general kind of orientation, whatever the electrophilic reagent is involved.

A group is called an activating group if that group makes the ring to be more reactive than benzene. If the group decreases the activity than that of benzene is called deactivating group.
Activating (ortho- para directors)

$-\mathrm{NH_2},\ -\mathrm{NHR},\ -\mathrm{NH_2},\ -\mathrm{OR}$

$-\mathrm{NHCOCO_3},\ -\mathrm{C_6H_5},-\mathrm{R}$

Deactivating (meta directors)

$-\mathrm{NO_2},-\overset{+}{\mathrm{N}}(\mathrm{CH_3})_3,-\mathrm{CN},$ $\quad -\mathrm{COOH},-\mathrm{COOR}$

$-\mathrm{SO_3H},\ -\mathrm{CHO}$ $\quad -\mathrm{COR}$

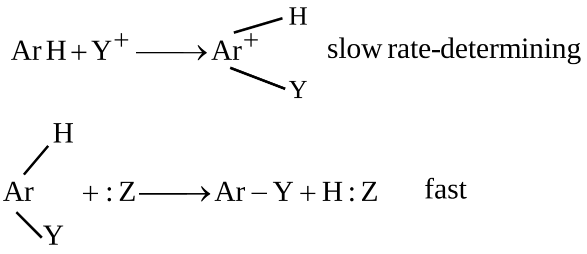
Deactivating (ortho-para directors)

$-\mathrm{F},-\mathrm{Cl},-\mathrm{Br},-\mathrm{I}$

Mechanism of electrophilic aromatic substitution two step mechanism.

The two essential steps involved are

i) Attack by an electrophilic reagent upon the ring to form a carbocation
ii) Abstraction of proton from this carbocation by some base.



i) $\mathrm{Ar\,H} + \mathrm{Y}^{+} \longrightarrow \mathrm{Ar}^{+}\!\begin{array}{l}\diagup \mathrm{H}\\ \diagdown \mathrm{Y}\end{array}$ slow rate-determining

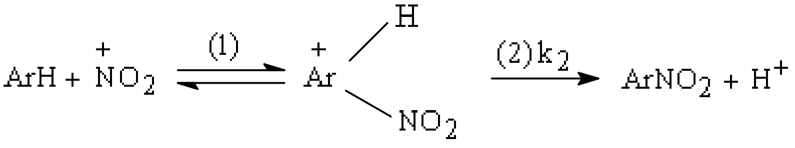
ii) $\mathrm{Ar}\!\begin{array}{l}\diagup \mathrm{H}\\ \diagdown \mathrm{Y}\end{array} + :\mathrm{Z} \longrightarrow \mathrm{Ar}-\mathrm{Y} + \mathrm{H}:\mathrm{Z}$ fast

The evidence that the first step is much slower than the second is obtained by carrying out reaction with deuterium labelled benzene (i.e. $\mathrm{C_6D_6}$) .In nitration, bromination, and Friedel-Crafts alkylation no significant isotopic effect was observed, indicating that the breaking of C-H or C-D bond in the second step is not the rate-determining step.

The rate of overall substitution is determined by the slow attack of the electrophilic reagent to the aromatic ring to form the carbocation. Once formed carbocation rapidly loses hydrogen or deuterium to form the products.

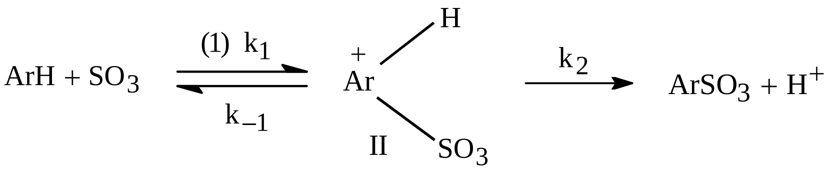
Absence of isotropic effect establish not only that reaction involves two steps, but also the first step is the rate determining step.

Energy profile diagram-Nitration



$k_2 >> k_{-1}$

However, sulphonation shows a moderate isotope effect. Ordinary hydrogen is displaced from an aromatic ring about twice as fast as deuterium. This is explained by considering the reaction to be reversible (i.e) the carbocation formed lose SO_3 to form the hydrocarbon.



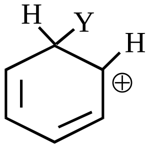
$k_2 \sim k_{-1}$

The reaction (2) is not much faster than the reverse reaction of (1) In sulphonation, the energy barriers on either sides of the carbocation (II) must be roughly the same height. whether the carbocation is II(D) or II(H) the barrier to the left is the same height. But to climb the borrower to the right, the barrier is higher for II (D) than for II (H). Hence the deuterated benzene reacts much slower than benzene itself and in sulphonation thus shows isotopic effect.

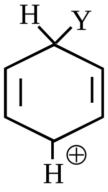
Reactivity and orientation :

We have already learnt that certain groups activate the ring in electrophilic substitution reactions and some groups deactivate the ring. As the rate of reaction is determined by slow step, any difference in rate of substitution must therefore be due to differences in the rate of this step.

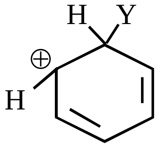
The difference the rate is largely determined by the stability of transition state. In electrophilic aromatic substitution the intermediate carbocation is a hybrid of structures I,II adn III.



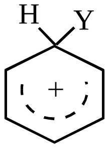
(I)



(II)



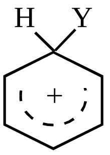
(III)



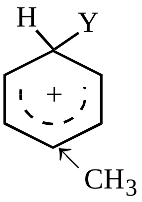
A group already present in the benzene ring should affect the stability of carbocations which depends on whether the group is electron releasing or electron with drawing.

Theory of reactivity :

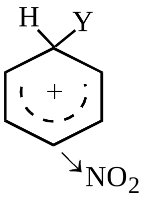
The rate of substitution reactions in benzene, toluene and nitrobenzene can be compared by considering the structures of carbocation formed from three compounds.



(I)



(II)



(III)

Methyl group tends to neutralise the positive charge of the ring,and stabilise the carbocation. The $-NO_2$ on the other hand tends to increase the positive charge and destabilize the carbocation and thus causes a slower reaction.

Theory of orientation :

An activating group, activates all positions of benzene ring. It directs ortho and para because it activates the ortho and para positions much more than it does the meta.

A deactivating group deactivates all positions in the ring. It directs meta because it deactivates ortho and para-even more than it does the meta.

Effect of halogen on electrophilic aromatic substitution :

Halogens in benzene ring are deactivating and are ortho-para directing. This unusual behaviour is explained by considering that halogens deactivate the ring through inductive effect and release the electrons through resonance effect.

Through its resonance effect halogen tends to release electrons and this to stabilise the intermediate carbocation. The electron release is effective only for attack at the positions ortho and para to the halogen.

The inductive effect is stronger than the resonance effect and causes net electron withdrawal-and hence deactivation for attack at all positions.

Reactivity is thus controlled by the stronger inductive effect, and orientation is controlled by the resonance effect.

Ortho para ratio :

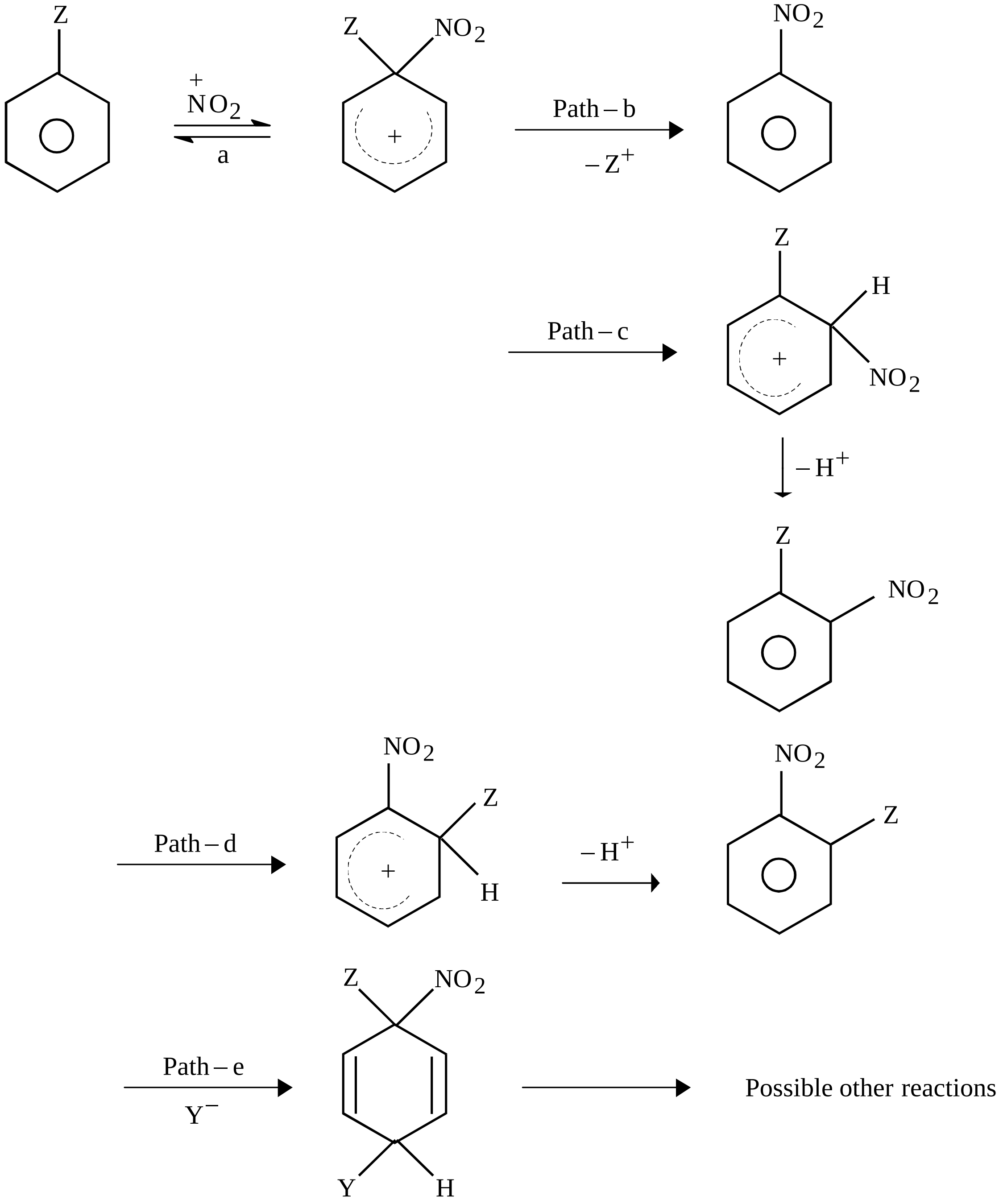
If all conditions are equal then an o-p directing group would be expected to give an o/p ratio of 2 : 1. Due to number of factors this ratio was always less. The factors which effect the ratio are polar effects of substituents inductive (I) and resonance (R)) its size (steric effect), the size of the entering group solvent effects, temperature effects and electrostatic forces acting between substrate and electrophile as these approach.

For example in the nitration of alkyl benzene the change in the o/p ratio was found to be Me (1.57) > Et (0.93) > $Me_2CH(0.48) > Me_3C(0.22)$. The trend is likely to be largely due to the steric effect of the alkly substituents.

Ipso Attack :

It is already discussed that in monosubstituted benzene, the orientation of attack by newly entering electrophile may be either ortho / para or meta positions. However it is observed in recent times that in certain reaction the attack of the electrophile takes place at the position wearing the substituent (called ipso position).

Ipso attack has been studied for nitration. When nitronium $(\overset{+}{N}O_2)$ attacks at the ipso position, the resulting arenium ion has five possible modes for the reaction to give products.



Path – a : The arenium ion can lose $\overset{+}{N}O_2$ and revert to the starting compound. The result is no net reaction.

Path – b : The arenium ion can lose Z^+, resulting in simple aromatic substitution in the leaving group is Z^+.

Path – c : The electrophile $\overset{+}{N}O_2$ can undergo 1, 2 – migration followed by loss of proton, resulting in the formation of ortho substituted compound.

Path – d : The ipso substituent (Z) can undergo 1, 2 – migration followed by loss of proton, resulting in the formation of ortho substituted compounds.

Path – e : A nucleophile may attack on the arenium ion, resulting in cyclohexadiene derivative, further reactions from this product may take place.

Quantitative treatment of reactivity in the substrate :

Quantitative rate studies in aromatic substitutions can be understood from the study of partial rate factor. Partial rate factor for a given group and a given reaction is defined as the rate of substitution at a single position relative to a single position in benzene. This can be understood by examination of the partial rate factors for the acetylation of toluene.

i) For ortho position $O_f^{Me} = 4.5$

ii) For meta position $M_f^{Me} = 4.8$

iii) For para position $P_f^{Me} = 749.0$

Toluene is acetylated 4.5 times as fast as a single position in benzene (or) 0.75 times as fast as the overall rate of acetylation of benzene.

A partial rate factor greater than one for a given position indicates that the group activates the position for given reaction.

If the partial rate factors are known it is possible to predict the proportion of isomers to be obtained when two or more groups are present on a ring, if the assumption is made that the effect of substituents is additive.

Calculated and experimental isomer distributions in the acetylation of m – xylene *

Position	Cal.	Obse.
2	0.30	0
4	99.36	97.5
5	0.34	2.5

* Data from Advanced organic chemistry by J. March.

Some aromatic substitution reactions :

(1) Nitration :

Aromatic compounds can be nitrated using a wide variety of nitrating agents. For less reactive aromatic systems, a mixture of concentrated nitric acid and sulphuric acid is used. For reactive systems nitration can be carried out with nitric acid alone, or in water or acetic acid or acetic anhydride. If anhydrous conditions are required nitration can be carried out with N_2O_5 in CCl_4 in presence of P_2O_5. Nitronium salts like $\overset{+}{N}O_2\overset{-}{B}F_4, \overset{+}{N}O_2\overset{-}{P}F_6$ etc. can also be used.

The formation of electrophile $\overset{+}{N}O_2$, under different conditions can be explained as follows :

i) In concentrated sulphuric acid, nitric acid acting as the base

$$HNO_3 + 2H_2SO_4 \rightleftharpoons \overset{+}{N}O_2 + 2H\overset{-}{S}O_4 + H_3\overset{+}{O}$$

ii) When concentrated nitric acid alone used, one molecule acts as acid and other acts as a base.

$$2HNO_3 \rightleftharpoons \overset{+}{N}O_2 + \overset{-}{N}O_3 + H_2O$$

iii) N_2O_5 in CCl_4, spantaneous dissociation results in the formation of $\overset{+}{N}O_2$.

$$N_2O_5 \rightleftharpoons \overset{+}{N}O_2 + \overset{-}{N}O_3$$

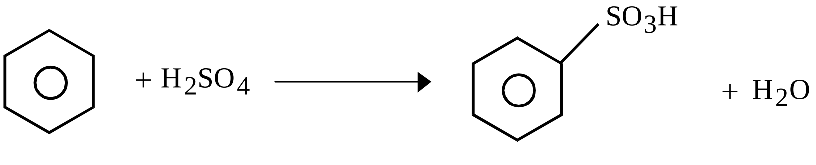
iv) When nitronium salts are used, $\overset{+}{N}O_2$ is present to participate in the reaction.

Evidence for the formation of nitronium ion is obtained from Raman spectra, of the mixture of nitric acid and sulphuric acid. Depression of freezing point on addition of nitric acid to sulphuric acid is also an evidence for the formation of $\overset{+}{N}O_2$ species.

The rate of reaction with most reagents is proportional to concentration of $\overset{+}{N}O_2$. In concentrated and aqueous mineral acids the order of reaction was found to be second order – first order each in aromatic substrate, and in nitric acid. In organic solvents like nitromethane, acetic acid, the kinetics are first order in nitric acid alone and zero order in substrate because the formation of $\overset{+}{N}O_2$ is the rate determining step.

(2) Sulphonation :

Benzene reacts with concentrated sulphuric acid to give benzene sulphonic acid.



All aromatic systems can be sulphonated. Sulphonation can also be carried out with fuming sulphuric acid, SO_3, chlorosulphonic acid ($ClSO_3H$). The sulphonation reaction reaction is a reversible reaction and can be carried out at low temperature to get maximum yield of the product, as the reverse reaction is slow at low temperature.

Different types of species were proposed to be formed in the reaction depending upon the nature of solution.

At concentrations below 85% H_2SO_4, the electrophile is thought to be $H_3S\overset{+}{O}_4$ (a combination of SO_3 and $H_3\overset{+}{O}$).

At higher concentrations $H_2S_2O_7$ was considered to be formed (a combination of H_2SO_4 and SO_3).

When pure SO_3 is the reagent in aprotic solvent, SO_3 itself acts as electrophile.

(3) Halogenation :

Aromatic compounds can be chlorinated or brominated using chlorine or bromine in presence of a catalyst iron. The actual catalyst in these reactions is ferric chloride or ferric bromide formed by reaction between iron and halogen. Lewis acid can be used as catalysts. For active substrate, use of catalyst is not necessary. For examples phenols and amines react so rapidly when bromination is carried out with dilute solution of bromine. Chlorine is more reactive than bromine.

Other reagents used are HOCl, HOBr, N–chloro and N–bromoamides. In all these cases the reaction is catalysed by acids.

When Lewis acid is used as catalyst the attacking species formed may be Cu^+ or Br^+ by the reaction.

$$Cl_2 + FeCl_3 \rightarrow \overset{-}{Fe}Cl_4 + Cl^+$$

$$Br_2 + FeCl_3 \rightarrow \overset{-}{Fe}Cl_3Br + Br^+$$

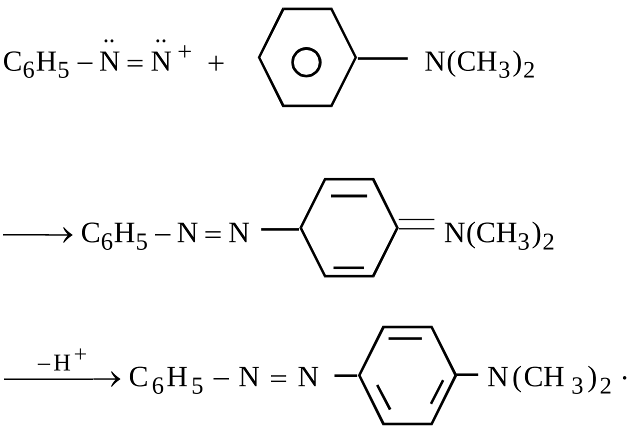
The Cl^+ or Br^+ can attack on aromatic system in a rate determining step and subsequent loss of proton in a fast leads to the formation of chloro or bromo substituted products.

Diazonium compling reactions :

A detailed study of the compling reaction has shown that the mechanism is electrophilic substitution, the electrophile being the diazonium cation and substitute being highly reactive benzene ring e.q. free amine or the phenoxide ion.

$$C_6H_5 - \overset{+}{N} \equiv N \leftrightarrow C_6H_5 - \ddot{N} = \ddot{N}^{+}$$

(I) (II)



The phenoxide ion also undergoes similar reaction.

Structure (II) is the reactive species and any factor that increases its contribution will increase the reactivity of that diazonium cation. Electron with drawing groups favour (II) and electron donating group would favour (I). This was found to be time that the p-nitrobenzenediazonium cation is more reactive than corresponding p-methoxy compound (about 10,000 times) under same conditions.

Introduction of more number of electron-withdrawing groups makes the diazonium cation to be highly reactive. For example 2,4,6-trinitrobenzene diazonium cation that it couples with certain hydrocarbons.
e.g. mesitylene.

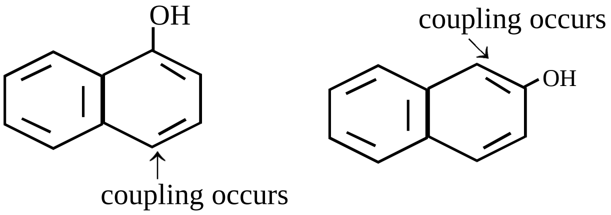
The mechanism given above gains evidence from the following facts.

i) Primary, secondary, tertiary amines undergo coupling in weakly acid solutions. The rate of coupling decreases as pH changes from 6 to 2. As pH decreases, the amine forms salt and thus ring is deactivated by –I effect of the ammonium cation.

ii) Phenols couple very readily in weakly alkaline solution, the rate of coupling increases as pH changes from 5 to 8. This is due to the fact that ring is activated by phenoxide in than neutral phenol molecule.

Coupling occurs preferentially in the p-position to the hydroxyl or amino group. If this is blocked o-coupling occurs.

1- and 2- napthols in alkaline solution couples with diazonium salts respectively in 4- and 1- position.



Gattermann-Koch aldehyde synthesis :

The reaction is useful for the preparation of aromatic aldehyde. Benzaldehyde is prepared by bubbling a mixture of carbon monoxide and hydrogen chloride through a solution of nitrobenzene or ether containing benzene and a catalyst aluminium chloride and a small amount of cuprous chloride.

$$C_6H_6 + CO + HCl \xrightarrow{AlCl_3} C_6H_5CHO + HCl \cdot$$

It is considered that formyl cation is the active species.

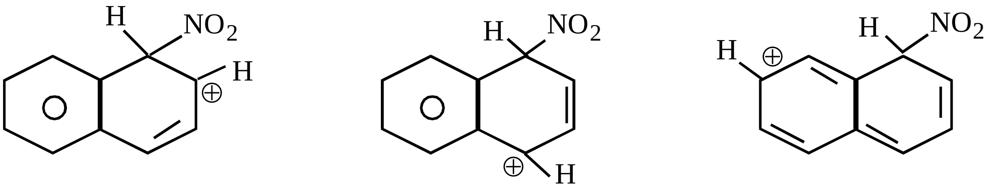
$$CO + HCl + AlCl_3 \longrightarrow [H\overset{+}{C} = O \leftrightarrow H - C \equiv O]^+ + AlCl_4^- \cdot$$

The formyl cation attacks on the benzene carbon atom followed by subsequent elimination of proton gives the product. The reaction is not applicable to phenols and their ether or when the substituents in benzene ring are strongly deactivating .

Electrophilic substitution in naphthalene :

Like benzene, polynuclear hydrocarbons typically undergo electrophilic substitution. For example in napthalene, nitration and halogenation occurs mainly in the α -position.

Attack by nitronium ion at the α -position of naphthalene yields an intermediate carbocation that is a hybrid of structures I and II in which positive charge is accommodated by the ring under attack, and several structures like (III) in which the charge is accommodated by the other ring.



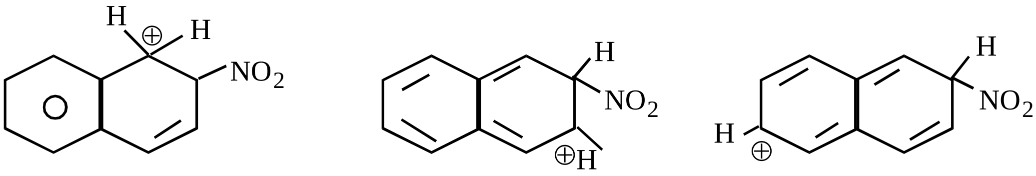
I
More stable

II
More stable

III
less stable

Alpha Carbon - Attack

Attack at the β -position yields an intermediate carbocation that is a hybrid of IV and V and several structures like (VI) in which the positive charge is accommodated by the other ring.



IV
More stable

V
less stable

VI
less stable

Beta Carbon Attack

In structures I,II and IV, the aromatic sexet is preserved in the ring that is not under attack.

In structures III, V and VI, the aromatic sexet is disrupted in both rings. Clearly it is understood that structures like I, II and IV are much more stable.

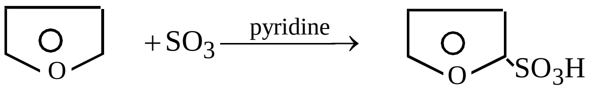
Two of the contributing structures are for the attack at the $\alpha-$ position, only one for attack at the $\beta-$ position. On this basis it is expected that the carbocation resulting from attack at α - position is much more stable than the carbocation resulting from the attack at the β-position.

Hence, nitration would therefore occur much more rapidly at the α-position.

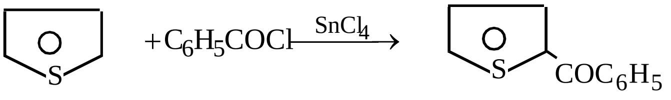
Electrophilic substitution in pyprole, furan, and thiophene ; Reactivity and orientation.

The five membered heterocylic compounds pyrrole, furan and thiophene undergo electrophilic substitution like nitration, halogenation, sulphation, and Friedel-Crafts alkylation. These are much more reactive than benzene in undergoing such reactions as the Reimer-Tiemann reaction, nitrosation, and coupling with diazonium salts.

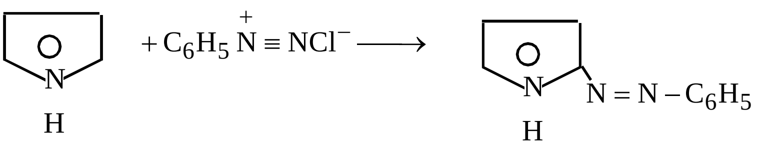
Reaction takes place predominantly at the 2- position.



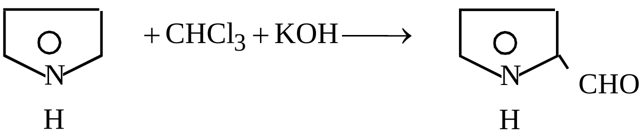
Furan 2 – Furansulphonic acid



Thiphene 2 – Benzoylthiophene



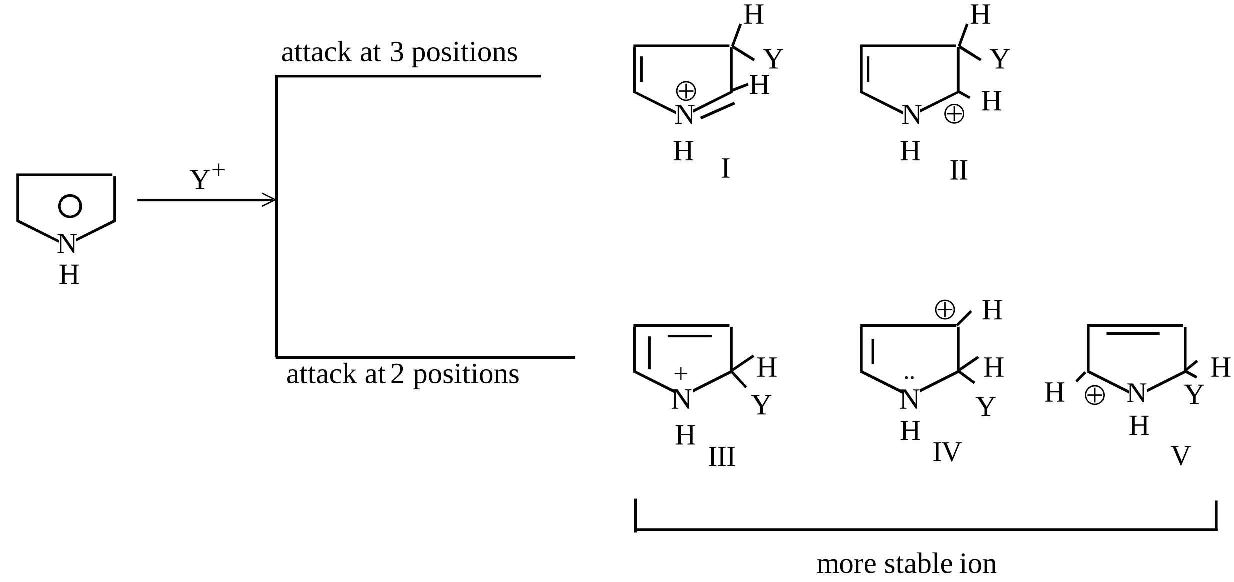
Pyrrole 2 – (phenylazo)pyrrole



Pyrrole 2 – pyrrole carboxyldehyde

In the study of the electrophilic aromatic substitution we learnt that the attack of the electrophilic reagent in the rate controlling step which takes place in such a way to yield most stable intermediate carbocation. The same may be applied for aromatic substitution in the heterocyclic compounds.

Let us apply this approach to the reactions of pyrrole.

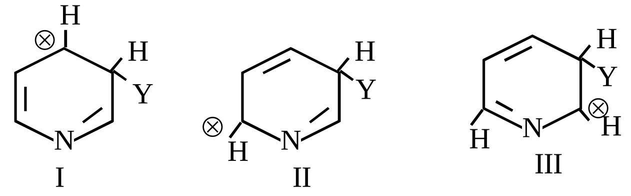


Attack at 3-position yields carbocation that is a hybrid of structures I and II. Attack at 2 positron yields a carbocation that is hybrid of three structures III, IV and V. This leads to extra stabilisation of carbocation. Also, attack at 2-positron is faster because the developing positive charge is accommodated by three atoms of the ring instead of by only two.

Pyrrole is highly reactive, compared with benzene, because of contribution from the relatively stable structure III. In III every atom has an octet of electrons.

Orientation of substitution in furan and thiophene, as well as their high reactivity can be explained in a similar way .

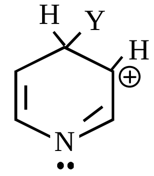
Electrophile substitution in pyridine :



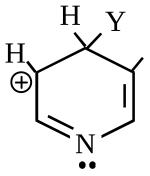
Pyridine resembles highly deactivated benzene derivative towards electrophilic substitution. It under goes nitration, sulphonation and halogenation but does not under go Friedel-Crafts reaction.

Electrophilic substitution mainly takes place at 3 position which results in the formation of stable carbocation than resulting from the attack at 4-position (2-position resembles 4-position)

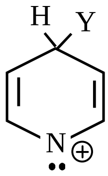
Electrophilic attack at 3-position :



IV



V



VI
highly unstable
nitrogen has sexet

Electrophilic attack at 4-position

All the structures are less stable than the corresponding ones for attack on benzene because of the electron withdrawal by nitrogen atom. As a result pyridine undergoes substitution more slowly than benzene.

FREE RADICAL REACTIONS

3.2.i Introduction :

Free radicals are the species having one or more unpaired electrons. Homolytic fission of a bond produces free radicals.

$$R_3C - X \rightleftharpoons R_3C^{\bullet} + {}^{\bullet}X$$

Homolytic fission of an R_3CX bond is, in the gas phase always requires less energy than heterolytic fission.

Reactions involving radicals occur widely in the gas phase. Radial reactions also occur in solution if carried out in non–polar solvent and if catalysed by light, or decomposition of substances known to produce radicals eg. organic peroxides.

Radicals once formed in solution are generally found to be less selective in their attack on other species.

Radical reactions once initiated, they often proceed with great rapidity, owing to the establishment of chain reaction.

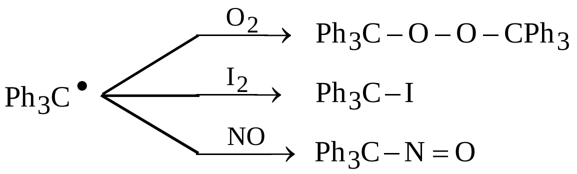
Radical reactions can be inhibited by the introduction of substances those react rapidly with radicals. (inhibitors).

Ex.: Phenol, quinones, diphenylamine, iodine etc.

The first free radical that identified was triphenyl methyl ($Ph_3C^{\bullet}$).

When Ph_3CCl in benzene treated with finely divided silver metal, there obtained an **Yellow solution**.

$$Ph_3CCl \xrightarrow{Ag} Ph_3C - CPh_3 \rightleftharpoons 2Ph_3C^{\bullet}$$



$$Ph_3C^{\bullet} \xrightarrow{O_2} Ph_3C - O - O - CPh_3$$

$$Ph_3C^{\bullet} \xrightarrow{I_2} Ph_3C - I$$

$$Ph_3C^{\bullet} \xrightarrow{NO} Ph_3C - N = O$$

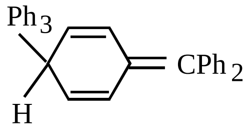
The radical reacted with halogens to form triphenylmethyl halide.

On exposure to O_2 formed triphenyl methyl peroxide.

On reaction with ‘NO’ formed triphenyl methyl nitrosomethane.

The yellow solution is in equilibrium with colourless dimer. On removal of solvent dimer was obtained.

The dimer was shown by proton n.m.r. spectroscopy to be



3.2.ii Production of free radicals :

Most important methods are

1. Photolysis
2. Thermolysis
3. Redox reactions by inorganic ions, metals or electrolysis involving one electron transfer.

3.2.iii Photolysis :

The requirement for this method is the ability of the molecules to absorb radiation in the UV or visible region.

Acetone in vapour phase is decomposed by light having a wave – length of 3200A°. $(\equiv 375\ \text{KJ mole}^{-1})$

$$\text{MeCOMe} \xrightarrow{h\nu} \overset{\bullet}{\text{Me}} + \text{CH}_3\overset{\bullet}{\text{C}}\text{O} \longrightarrow \text{CO} + \overset{\bullet}{\text{Me}}$$

Other species that undergo ready photolysis are alkylhypochlorites, nitrites.

$$\text{ROCl} \xrightarrow{h\nu} \text{R}\overset{\bullet}{\text{O}} + \overset{\bullet}{\text{Cl}}$$

$$\text{RONO} \xrightarrow{h\nu} \text{R}\overset{\bullet}{\text{O}} + \overset{\bullet}{\text{N}}\text{O}$$

Another useful homolytic fission by photolysis is that of halogen molecule.

$$\text{Cl}_2 \xrightarrow{h\nu} 2\overset{\bullet}{\text{Cl}}$$

$$\text{Br}_2 \xrightarrow{h\nu} 2\overset{\bullet}{\text{Br}}$$

There halogen radicals are useful for halogenation of alkanes or addition to alkenes.

The advantage of photolysis over thermolysis is

(a) It is possible to cleave strong bonds that do not break readily at reasonable temperatures.

Ex.: $\text{R} - \text{N} = \text{N} - \text{R} \xrightarrow{h\nu} \text{R}^1 + \text{N}_2 + {}^\bullet\text{R}$

(b) Energy at only one particular level is transferred to a molecule so that it is more specific method of effecting homolysis than pyrolysis.

Ex.: Cleavage of diacyl peroxide occurs clearly on photolysis.

$$R-COO-OCOR \xrightarrow{h\nu} 2RCOO^{\bullet} \longrightarrow 2R^{1} + 2CO_2$$

Another technique for radical generation is flash photolysis, which employs, a very intense pulse of radiation (visible or U.V.) of very short duration.

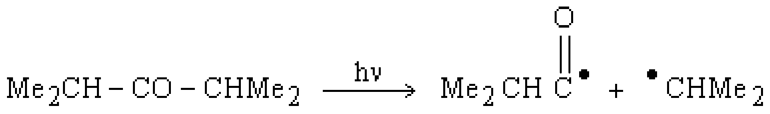
This produces a very high immediate concentration of radicals.

Photolysis of iodophenyl acetylene in benzene solution gives the following radicals.

$$C_6H_5-C\equiv C-I \xrightarrow{h\nu} C_6H_5C\equiv C^{\bullet} + I^{\bullet}$$

Photolysis of some more substances.

i)



$$Me_2CH-CO-CHMe_2 \xrightarrow{h\nu} Me_2CH\overset{O}{\overset{\|}{C}}{}^{\bullet} + {}^{\bullet}CHMe_2$$

ii) $MeCOCH_2Cl \xrightarrow{h\nu} MeCO\overset{\bullet}{C}H_2 + \overset{\bullet}{Cl}$

iii) $Me_2CHCHO \xrightarrow{h\nu} Me_2CH^{\bullet} + {}^{\bullet}CHO$

iv) $CH_3COCOCH_3 \xrightarrow{h\nu} 2CH_3\overset{\bullet}{C}O$

Radicals may also be generated by irradiation of neutral molecules with X – rays or with γ –rays (radiolysis).

3.2.iv Thermolysis :

Alkyl radicals of short life were produced in the vapour phase through decomposition of metal alkyls.

$$PbR_4 \rightleftharpoons Pb + 4R^{\bullet}$$

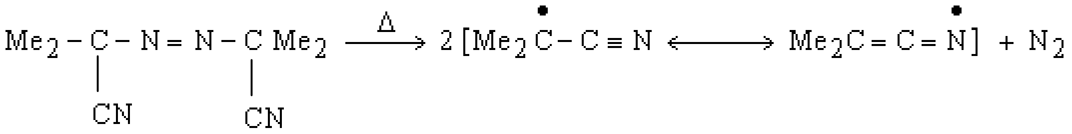
Radicals may be generated in solution in inert solvents, as well as in vapour phase by thermolysis of weak bonds (Having energy < 165 KJ (40 Kcal.)).

The major sources of radicals in solution are the thermolysis of peroxides (– O – O –) and azo compound (C – N).

Stable radicals are obtained when the radicals formed are stabilised by substituents present on the radicals.

Ex.: $(Me_3.COO)_2$ has half life of $\approx$ 200 hr. at 100ºC.

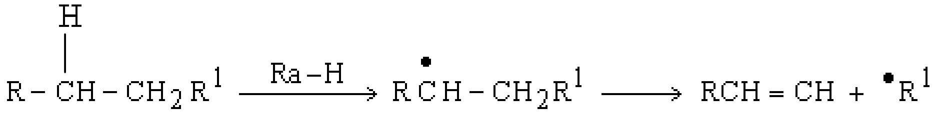
$(PhCOO)_2$ has on $\approx$ 0.5 hr. at the same temperature.



$$Me_2-\underset{\displaystyle CN}{\underset{|}{C}}-N=N-\underset{\displaystyle CN}{\underset{|}{C}}\,Me_2 \xrightarrow{\Delta} 2\,[Me_2\overset{\bullet}{C}-C\equiv N \longleftrightarrow Me_2C=C=\overset{\bullet}{N}] + N_2$$

Radical formation through carbon – carbon bond fission is seen in radical induced cracking at $\approx$ 600º of long chain alkanes.

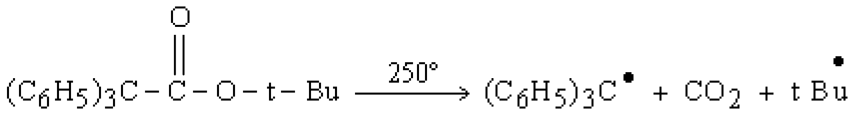
$\overset{\bullet}{Ra}$



$$R-\overset{\displaystyle H}{\overset{|}{C}}H-CH_2R^1 \xrightarrow{Ra-H} R\overset{\bullet}{C}H-CH_2R^1 \longrightarrow RCH=CH + {}^{\bullet}R^1$$

Some representative examples of thermal decomposition of azo, diazo compounds t – butyl triphenylacetale, alkyl nitrites.

$$(CH_3)_3C-N=N-C(CH_3)_2 \xrightarrow{180-200^{o}} 2(CH_3)_3C^{\bullet} + N_2$$



$$(C_6H_5)_3C-\overset{\displaystyle O}{\overset{\|}{C}}-O-t-Bu \xrightarrow{250^{o}} (C_6H_5)_3C^{\bullet} + CO_2 + t\,\overset{\bullet}{Bu}$$

$$(CH_3)_3C-O-NO \xrightarrow{180^{o}} (CH_3)_3C-O^{\bullet} + \overset{\bullet}{N}O$$

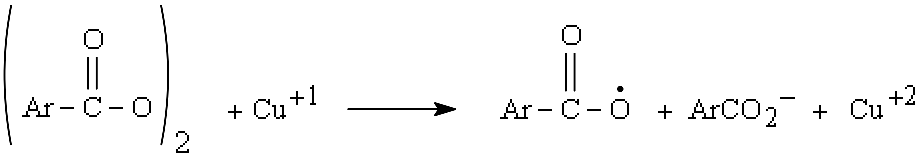
Most commonly used radical initiators are peroxides, benzyl and acyl peroxides and azo bis isobutylnitrile (AIBN).

An initiator may be describe as a substance which furnishes sufficient number of radicals to start the reaction.

3.2.v Redox reactions :

These reactions involve one – electron transfer in generating the radicals and hence metal ions such Fe^{+2}/Fe^{+3} and Cu^{+}/Cu^{+2} are involved.

Cu^{+1} ions are found to accelerate greatly the decomposition of acyl peroxides.



$$\left(Ar-\overset{\displaystyle O}{\overset{\|}{C}}-O\right)_2 + Cu^{+1} \longrightarrow Ar-\overset{\displaystyle O}{\overset{\|}{C}}-\overset{\bullet}{O} + ArCO_2^{-} + Cu^{+2}$$

Cu^+ is also involved in the conversion of diazonium salts $Ar\overset{-}{N}_2Cl^-$ to $ArCl + N_2$, where $Ar^\bullet$ is probably formed as an intermediate.

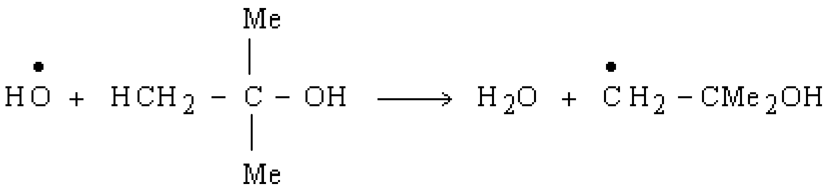
$$Ar\overset{+}{N}_2 + Cu^+ \longrightarrow \overset{\bullet}{Ar} + N_2 + Cu^{+2}$$

Fe^{+2} is used to catalyse the oxidation reactions of aqueous hydrogen peroxide solution.

$$H_2O_2 + Fe^{+2} \longrightarrow H\overset{\bullet}{O} + \overset{-}{O}H + Fe^{+3}$$

This mixture is known as Fenton's reagent.

$H\overset{\bullet}{O}$ useful to abstract H, and can be used to generate the resultant radical.



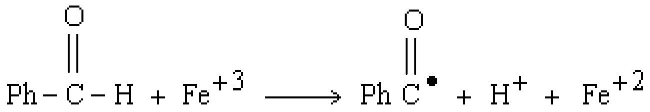
$$H\overset{\bullet}{O} + HCH_2 - \underset{Me}{\overset{Me}{C}} - OH \longrightarrow H_2O + \overset{\bullet}{C}H_2 - CMe_2OH$$

$$\longrightarrow \underset{\text{Dimer}}{HO\,CMe_2 - CH_2CH_2\,CMe_2OH}$$

Direct reduction of carbocation has been used.

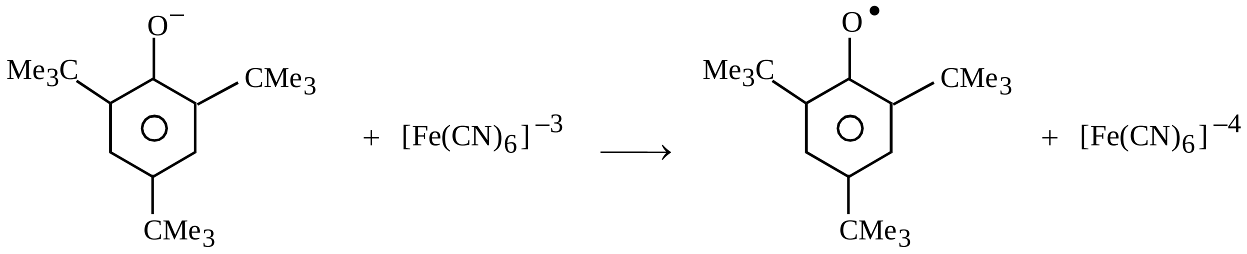
$$Ph_3C^+ + V^{2+} \longrightarrow Ph_3\overset{\bullet}{C} + V^{3+}$$

Generation of radical through an oxidative process probably occurs in the initiation of the auto oxidation of benzaldehyde, catalysed by heavy metal ion capable of one electron transfers Fe^{+3}.



$$Ph - \overset{O}{\overset{\|}{C}} - H + Fe^{+3} \longrightarrow Ph\,\overset{O}{\overset{\|}{C}}^{\bullet} + H^+ + Fe^{+2}$$

Stable phenoxy radical is generated by one – electron oxidation by $[Fe(CN)_6]^{-3}$.



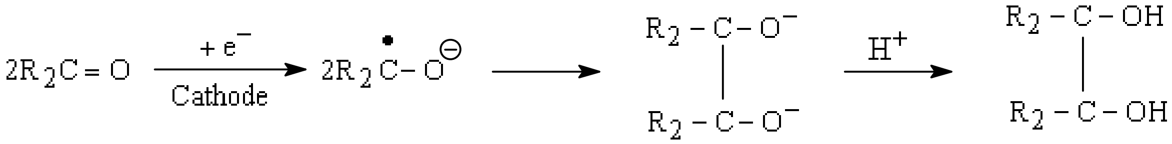
Oxidation of carbanions

$$2(MeCO)_2CH^- \xrightarrow{I_2} 2(MeCO)_2\overset{\bullet}{C}H \longrightarrow (MeCO)_2CH\,CH(COMe)_2$$

Anodic oxidation of carboxylate anions.

$$RCO_2^- \xrightarrow[\text{anode}]{-e^-} 2R\dot{C}O_2 \xrightarrow{-CO_2} 2R^\bullet \longrightarrow R-R \text{ (Kolbe's electrolysis)}$$

Electrolysis of ketones, results in their cathodic reduction to radical anions which dimerise to the dianions of pinacols.



$$2R_2C=O \xrightarrow[\text{Cathode}]{+e^-} 2R_2\dot{C}-O^{\ominus} \longrightarrow \begin{array}{c} R_2-C-O^- \\ | \\ R_2-C-O^- \end{array} \xrightarrow{H^+} \begin{array}{c} R_2-C-OH \\ | \\ R_2-C-OH \end{array}$$

Alkyl or aryl radicals may be produced by electrolysis of grignard reagents in ether.

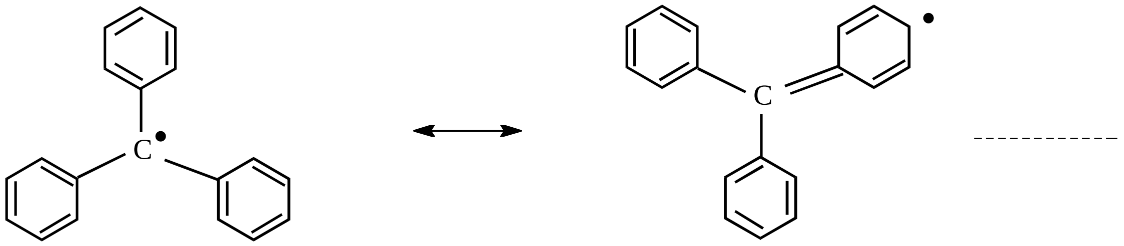
$$RMgBr \xrightarrow{-e^-} R^\bullet + MgBr^+ \longrightarrow R-R$$

Tripositive titanium with hydroxylamine in acid solution appears to generate amide radicals.

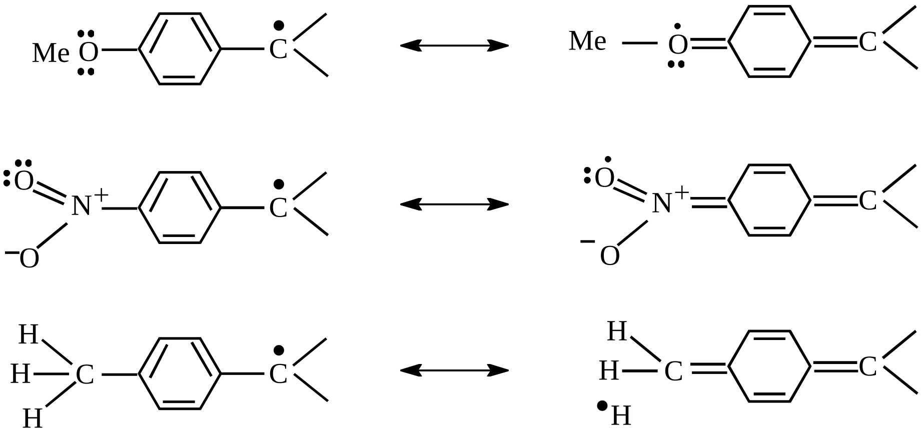
$$Ti^{+3} + HO-NH_2 \longrightarrow TiOH^{+3} + {}^\bullet NH_2$$

3.2.vi Stability of free radicals :

Unusal stability of triaryl methyl radicals in the capacity of the three benzene rings to delocalise the unpaired electron.



Substitutents at the ortho and para positions may further delocalise the unpaired electron by electron donation, by electron with drawal or by hyperconjugation.



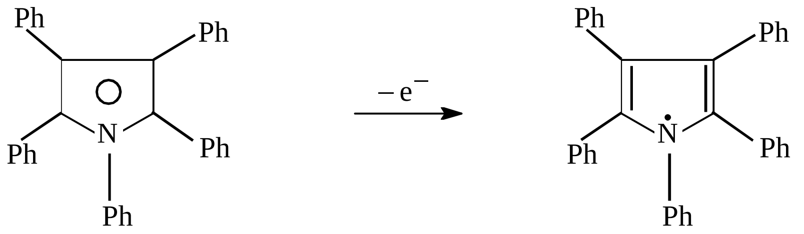
Two features are favouring the dissociation of a hydrocarbon radicals.

1) Excessive crowding in the hydrocarbon itself.
2) Delocalisation of the unpaired electron over a large area in the radical.

Careful oxidation of triphenylamine tetraphenyl hydrazine, pentaphenyl pyrrole yield ammonium ion radicals.

$$Ph_3\ddot{N} \xrightarrow{-e^-} Ph_3\dot{N}$$

$$Ph_2N - NPh_2 \longrightarrow [Ph_2N - \dot{N}Ph_2]^+$$



3.2.vii Detection of short – lived free radicals :

Paneth and his coworkers studied the thermal decomposition of certain volatile organometallics (Me_4Ph, $(PhCH_2)_4Sn$). When passed through a glass tube, and if small area of the tube when vigorously heated, a metallic mirror was deposited in the inside of tube at the point of heating.

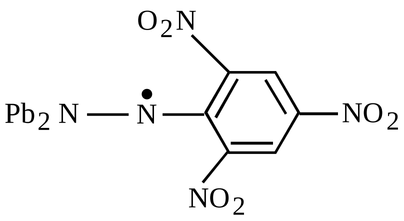
The gaseous decomposition products were found to remove the original mirror as they passed over it.

It was inferred that the decomposition of organometallic compound yielded the parent metal and free alkyl radical. The free radicals reacted with original metal mirror, converting this mirror to a volatile organometallic compound.

This method is used to detect alkyl radicals, from decomposition of aliphatic azocompounds from pyrolysis of paraffin hydrocarbons, from photolysis of aldehydes and ketones. And from action of sodium vapour on alkyl or aryl halides. Paneth technique is not applicable to reactions in liquid phase.

Radical consuming reagents whose disappearance may be measured quantitatively are useful for detection of free radicals in soltion.

Ex.: Diphenyl picrylhydrozyl whose consumption



may be followed by fading of its characteristic “**violet colour**”.

$FeCl_3$ which often transfers chlorine atoms to active free radicals yielding readily tritable $FeCl_2$.

Another useful and sensitive test is the initiation of polymerisation. Polymerisation of acrylonitrile and methyl methacrylate.

Most useful method for detection of radicals is e.s.r spectroscopy.

The electron spin can have one of two values $+\frac{1}{2}$ or $-\frac{1}{2}$ and in presence of an applied magnetic field. These corresponds to different energy levels, transitions are possible between them resulting in a characteristic and detectable absoption spectrum.

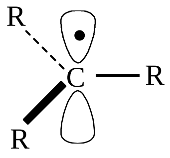
In e.s.r. spectroscopy, the interaction (splitting) occurs between the unpaired electron and neighboring magnetic nuclei – especially 'H'.

Radicals have been detected by e.s.r. spectroscopy, in the low concentration of $10^{-8}M$.

3.2.viii Radical shape :

It is the question whether simple radicals of the type R_3C, the unpaired electron is accommodated in p–orbital (sp^2) or sp^3 hybrid orbital.

Direct physical evidence for $\dot{C}H_3$ comes from esr spectrum of $^{13}\dot{C}H_3$ that $\dot{C}H_3$ radical is essentially planar. The same conclusion was derived from U.V. and I.R.



The 's' character of the half filled orbital s found to increase across the series

$$\dot{C}H_3 < \dot{C}H_2F < \dot{C}HF_2 < \dot{C}F_3$$

being sp^3 in $\dot{C}F_3$, this radical is pyramidal.

3.2.ix Types of free radical reactions and some characteristics :

Two types of reactions are of interest

1) Radical displacement
2) Radical addition

Radical displacements seldom take place on carbon atoms. Most often they occur on hydrogen or halogen atoms.

Ex.: $\overset{\bullet}{\mathrm{Cl}} + \mathrm{H-CMe_3} \longrightarrow \mathrm{Cl-H} + \overset{\bullet}{\mathrm{C}}\mathrm{Me_3}$

$\overset{\bullet}{\mathrm{C}}\mathrm{H_3} + \mathrm{Br-CCl_3} \longrightarrow \mathrm{CH_3Br} + \overset{\bullet}{\mathrm{C}}\mathrm{Cl_3}$

Substitutions are generally the result of two independent reactions.

$\overset{\bullet}{\mathrm{Cl}} + \mathrm{H-CMe_3} \longrightarrow \mathrm{Cl-H} + \overset{\bullet}{\mathrm{C}}\mathrm{Me_3}$

$\overset{\bullet}{\mathrm{C}}\mathrm{Me_3} + \mathrm{Cl-Cl} \longrightarrow \mathrm{Me_3C-Cl} + \overset{\bullet}{\mathrm{Cl}}$

In most radical additions, it is a carbon atom that suffers attack by the radical (not on a π – electron system)

There are two processes of importance Radical Coupling.

$$\mathrm{R}\bullet + \bullet\mathrm{R} \longrightarrow \mathrm{R-R}$$

Radical disproportionation

$$\mathrm{2CH_3}\overset{\bullet}{\mathrm{C}}\mathrm{H_2} \longrightarrow \mathrm{CH_2=CH_2} + \mathrm{CH_3-CH_3}$$

In all reactions, which proceed through active free radicals, the concentration of radical at ordinary temperature is much less than those of reactants.

In favourable instances, free radicals may undergo eliminations, decarboxylations, rearrangements.

$$\mathrm{Br_2CH-}\overset{\bullet}{\mathrm{C}}\mathrm{HBr} \longrightarrow \overset{\bullet}{\mathrm{B}}\mathrm{r} + \mathrm{BrCH=CHBr}$$

$$\mathrm{CH_3}\overset{\bullet}{\mathrm{C}}\mathrm{OO} \longrightarrow \overset{\bullet}{\mathrm{C}}\mathrm{H_3} + \mathrm{CO_2}$$

$$\mathrm{Me_2CPh-}\overset{\bullet}{\mathrm{C}}\mathrm{H_2} \longrightarrow \mathrm{Me_2}\overset{\bullet}{\mathrm{C}}\mathrm{-CH_2Ph}$$

Radical reactions follow chain reactions and sequence may continue until the radicals one destroyed.or the reactants are completely consumed.

Thus a single radical may bring about the successive formation and destruction of thousands of radicals, and hence bring about changes in thousands of molecules.

Radical chain reactions may be retarded or halted by inhibitors or chain breakers.

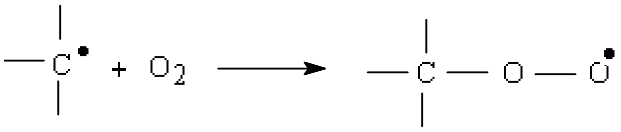
Ex.: Chain breakers : $\mathrm{I_2}$, aromatic sulphides.

$\mathrm{R^\bullet} + \mathrm{I-I} \longrightarrow \mathrm{RI} + \mathrm{I^\bullet}$ (less action)

$\mathrm{R^\bullet} + \mathrm{Ar-S-S-Ar} \longrightarrow \mathrm{RSAr} + \mathrm{ArS^\bullet}$ (less action)

Nitric oxide, diphenyl picryl hydrazide are also the retarders.

Oxigen also acts as inhibitor. Oxygen reacts with carbon radicals to yield peroxy radicals.



$$\overset{|}{\underset{|}{-C^{\bullet}}} + O_2 \longrightarrow \overset{|}{\underset{|}{-C}}-O-O^{\bullet}$$

Peroxy radicals are relatively less reactive. Hence, it was found that number of free – radical reactions exhibit an induction period if oxygen is not rigorously excluded.

Such reactions begin sluggishly but their rates suddenly increase when all of the oxygen has been consumed.

“Induction period and inhibition by retarders are two features that distinguish homolytic from heterolytic reactions.

Heterolytic reactions are not accelerated by light, whereas homolytic reactions are frequently accelerated by light.

Homolytic reactions are much less subject to acid or base catalysis.

Rates of homolytic reactions are less sensitive to changes in solvent polarity and ionic strength.

Relation between structure and reactivity is some what more clear cut than for homolytic reactions.

The kinetic treatment of free radical reactions tends to be more complex than that of most heterolytic reactions.

PAPER – III :: UNIT – III
LESSON – 3

3.3.i Radical reactions :

Free radical halogenation :

Chlorination of alkane is a typical free radical reaction, for it may initiated photochemically or by such initiators as benzoyl peroxide, tetraethyllead, and azomethane.

$$Cl-Cl \xrightarrow{h\nu} \overset{\bullet}{Cl} + \overset{\bullet}{Cl}$$

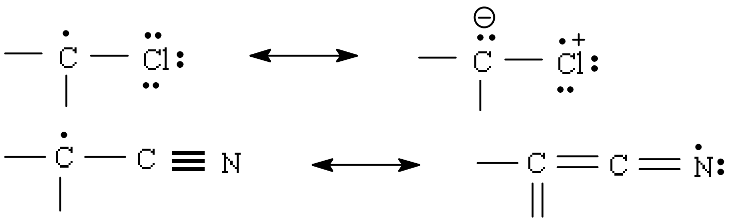
$$RH + \overset{\bullet}{Cl} \longrightarrow R^{\bullet} + HCl$$

$$R^{\bullet} + Cl_2 \longrightarrow RCl + \overset{\bullet}{Cl}$$

It has long been recognised that tertiary hydrogens are removed readily in free radical chlorination than are secondary, than are primary.

The reactivities of primary, secondary, tertiary hydrogens are in the ratio 1 : 3 : 4.

We except introduction of chloro or cyano substituents facililate radical attack at the α –carbon atom, for resonance stabilised radicals should be obtained by removal of an α –hydrogen.



We might therefore predict that alkyl chlorides and nitriles would undergo free radical chlorination at the α –position. But, it is now known that homolytic chlorination takes place at β or γ – carbon atoms.

The radical is an electrophile and seeks electron – rich site in the substrate for preferential attack.

Thus +I groups facililate chlorination where –I groups retard it.

The side chain chlorination of toluene has been found to be retarded by electron–attracting substituents in the benzene ring.

The relative amount of substitution at the four different carbon atoms in 1 – chlorobutane on photochemical chlorination at 35° is

$CH_3 - CH_2 - CH_2 - CH_2 - Cl$

25% 5% 17% 3%

Free radical chlorination generally becomes less selective as the reaction temperature is increased.

Ex.: Chlorination of alkyl chlorides, the yield of 1, 2 – dichloro compounds falls very nearly zero at temperatures above 375ºC.

Propene on chlorination at about 450ºC, substitution occurs to the total exclusion of addition.

The allyl radical obtained by H – atom abstraction is stabilised by delocalisation.

$$\dot{C}H_2-CH=CH_2 \longleftrightarrow CH_2=CH-\dot{C}H_2$$

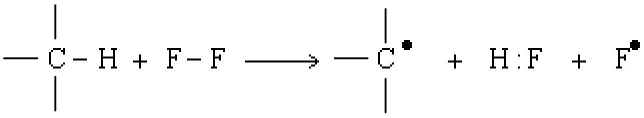
Cyclohexene undergoes analogous allylic chlorination.

Elemental fluorine reacts violently with most organic compounds under ordinary circumstances.

Flurorination may be studied in the gas phase by diluting with N_2, on in liquid phase by dilution with inert solvents $CCl_3.CF_3$.

Fluorination often occurs in the dark at low temperatures and in the absence of initiators.

It has been suggested that fluorine radicals are formed together with alkyl radicals when an energetic fluorine molecule colloides with a hydrogen atom of a hydrocarbon chain.



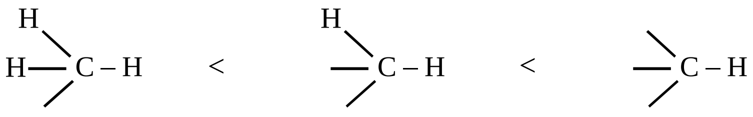
$$-\overset{|}{\underset{|}{C}}-H + F-F \longrightarrow -\overset{|}{\underset{|}{C}}^{\bullet} + H:F + F^{\bullet}$$

This is favoured thermodynamically by the low F – F bond energy (37 Kcal.) and very high H–F bond energy (135 Kcal.).

Bromination is slower than chlorination H–abstraction by $\dot{Br}$ is endothermic.

So endothermic in case of $I^{\bullet}$ and that direct iodination of alkanes does not normally takes place.

Bromination is much more selective than chlorination.

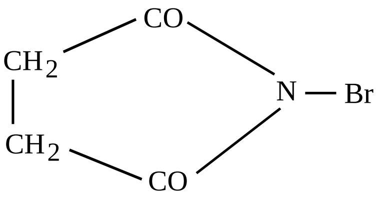


Primary : Secondary : Tertiary

1 : 80 : 1600

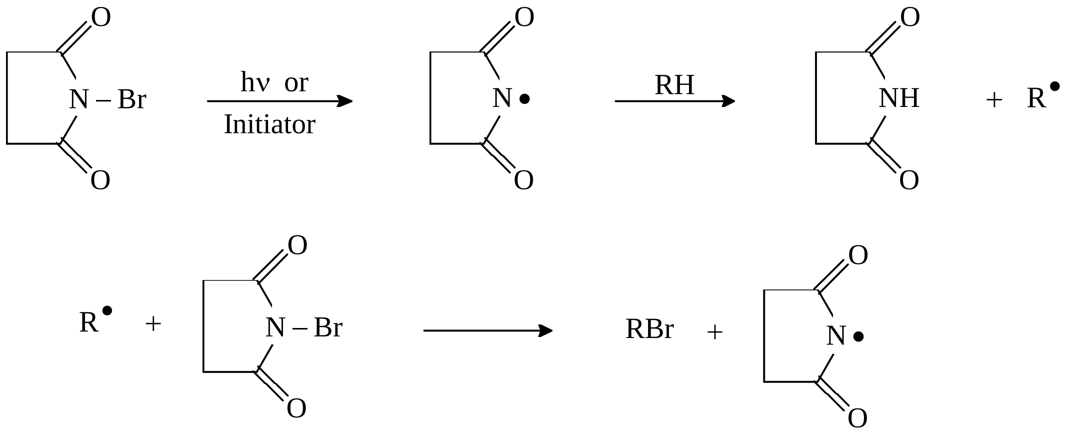
$(CH_3)_3CH$ found to yield $(CH_3)_3CBr$ only.

Free radical halogenation may be carried out using reagents other than the molecular halogens. Most familiar is N–Bromosuccinimide.

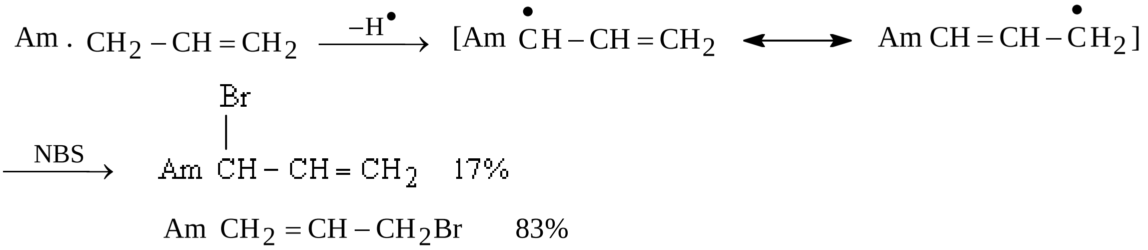


This often an agent for allylic carbons. In presence of efficient initiators, it brominates saturated compounds as well.

Bromination probably takes place as follows



If $R^\bullet$ is allylic, it may react with second molecule of NBS at one of two sites, leading to a mixture of bromides.



$$\text{Am}\,.\,CH_2-CH=CH_2 \xrightarrow{-H^\bullet} [\text{Am}\,\overset{\bullet}{C}H-CH=CH_2 \longleftrightarrow \text{Am}\,CH=CH-\overset{\bullet}{C}H_2]$$

$$\xrightarrow{\text{NBS}} \text{Am}\,\overset{\overset{\text{Br}}{|}}{C}H-CH=CH_2 \quad 17\%$$

$$\text{Am}\,CH_2=CH-CH_2Br \quad 83\%$$

If there are two non – equivalent allylic hydrogens in the substrate, four different allylic bromides be formed in the resulting mixture.

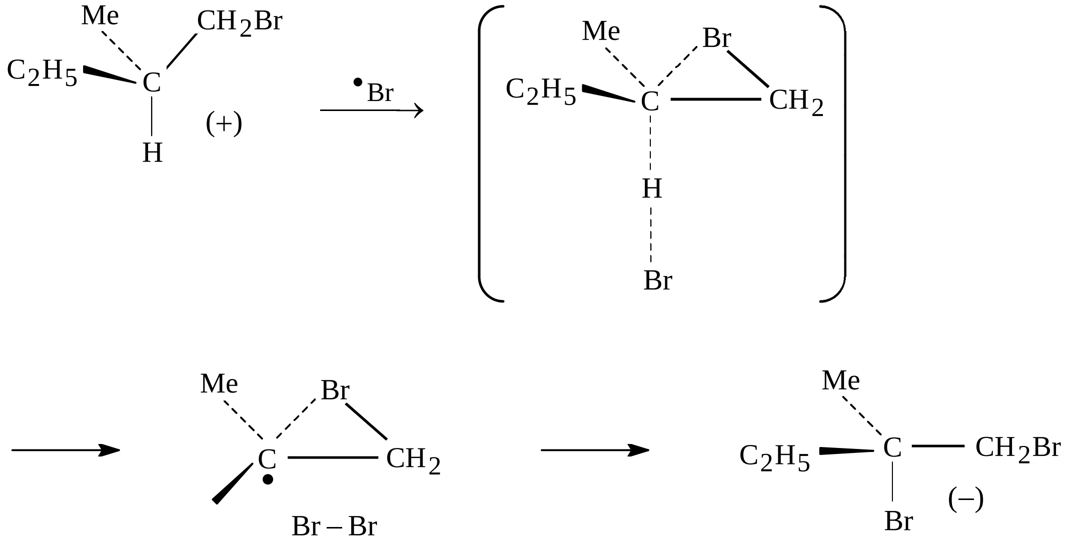
Halogenation of an optically active form of a chiral alkane $R\,R^1\,R^{11}\,CH$ found to yield $(\pm)$ halide. Racemisation would be observed with either planar or rapidly inverting pyramidal structure.

Bromination of (+) 1 – bromo – 2 – methyl butane is found to yield active bromide (–) 1, 2 – dibromo – 2 – methyl butane.

(ie.) Overall substitution occurs with retention of configuration.

This is the result of the original 1 – bromo substituent interacting with one side of the intermediate radical, the one opposite to that from which H been abstracted.

– promoting attack by Br_2 on the other, leading to retention of configuration.

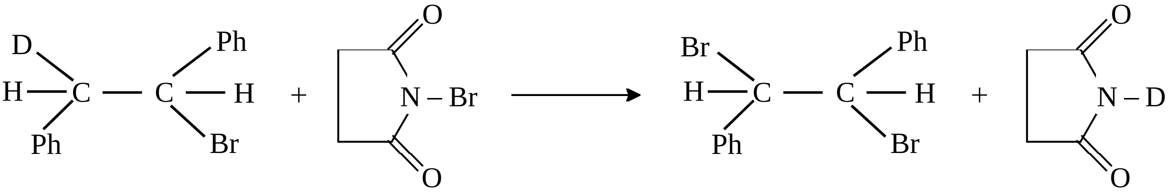


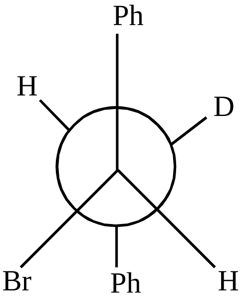
Bromination of an optically active form of the corresponding chloro compound.

1 – chloro – 2 – methylbutane also result in an optically active product, with retention of configuration.

Halogenation with more reactive chlorine is found to lead wholly to racemisation.

When erythro form of deuterated bromide PhCHD – CHBrPh is treated with NBS. Deuterium atoms are found to be removed from the substrate nearly twice as rapidly as are hydrogen atoms.



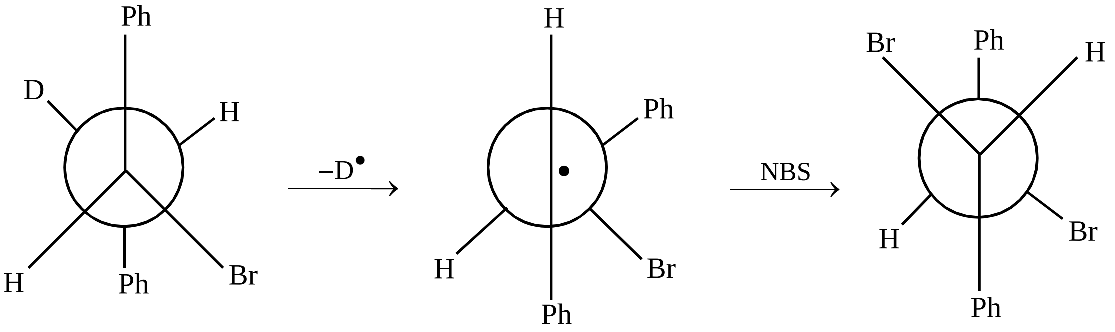


This unsual isotopic effect is partially a steric phenomenon. Removal of H requires that the radial should approach on the more crowded side in the above.

Whereas remove of deuterium atom the radical approches on the less crowded side.

Polar effects also favour the removal of deterium atom. It would be expected that the electronegative nitrogen atom in the attacking succinimido radical would keep as far as possible from the electronegative bromine in the substrate.

The resulting dibromide is meso form indicating that the formation of new C – Br is also stereospecific.



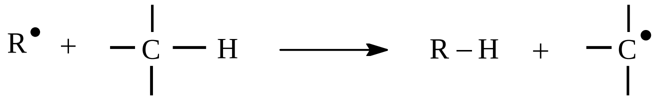
(I) (II) (III)

The favoured conformation of radical is II, in which phenyl groups lie as far apart as it is possible. NBS, approaches the radical from the less crowded side of the radical.

3.3.ii Auto - oxidations :

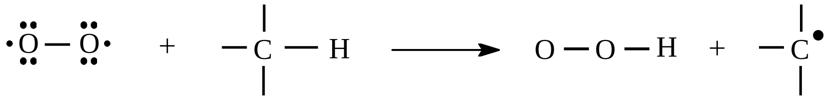
The reaction of organic compounds with elemental oxygen under mild conditions are referred to as auto-oxidations. These reactions takes place by thermselves when the substrate is exposed to atmosphere.

Under mildest condition, (temperature below 100°C) (in presence of free radical initiator), oxygen attacks on hydrocarbons to form alkyl hydroperoxides.



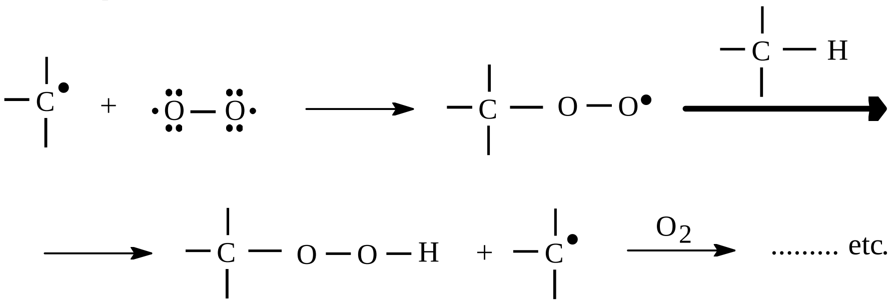
$$R^\bullet + -\overset{|}{\underset{|}{C}}-H \longrightarrow R-H + -\overset{|}{\underset{|}{C}}{}^\bullet$$

(or)



$$\cdot\ddot{\underset{\cdot\cdot}{O}}-\ddot{\underset{\cdot\cdot}{O}}\cdot + -\overset{|}{\underset{|}{C}}-H \longrightarrow O-O-H + -\overset{|}{\underset{|}{C}}{}^\bullet$$

The propagation sequence is



$$-\overset{|}{\underset{|}{C}}{}^\bullet + \cdot\ddot{\underset{\cdot\cdot}{O}}-\ddot{\underset{\cdot\cdot}{O}}\cdot \longrightarrow -\overset{|}{\underset{|}{C}}-O-O^\bullet \xrightarrow{-\overset{|}{\underset{|}{C}}-H}$$

$$\longrightarrow -\overset{|}{\underset{|}{C}}-O-O-H + -\overset{|}{\underset{|}{C}}{}^\bullet \xrightarrow{O_2} \text{......... etc.}$$

One of the termination reactions is the coupling of alkyl radicals to form alkane with twice the number of carbons.

Attack of a C – H bond with R – O – $O^{\bullet}$ radicals proceeds more readily in the order.

Tertiary > Secondary > Primary hydrogens

Removal of hydrogen from an allylic or benzylic carbon is still easier.

It may be noted that in formation of hydroperoxides by auto - oxidation, attack occurs at alpha to a double bond, alpha to a benzene ring or at a tertiary carbon.

In the absence of added initiators, the auto - oxidations of many hydrocarbons are autocatalytic.

Hydroperoxides may act as free – radical initiators.

The preparation of hydroperoxides in high yield from hydrocarbons have some serious difficulties.

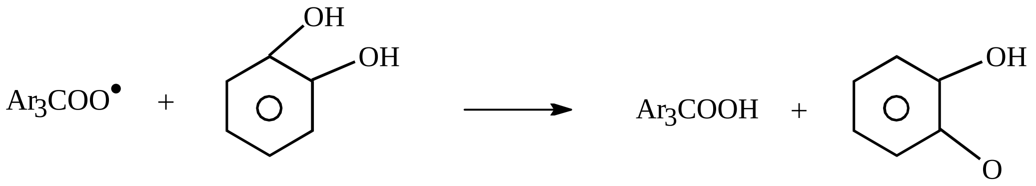
1) Temperature, if too low chain reaction becomes slow.
2) At higher temperatures homolytic decomposition of the hydroperoxide may greatly reduce the yield.
3) Hydroxides when formed with unsaturated hydrocarbons, can attack the double bonds of the remaining hydrocarbon molecules.

The auto - oxidations of hexaarylethanes occur readily in the absence of outside initiators.

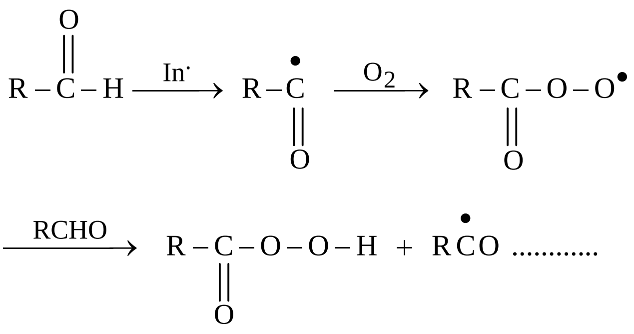
$$Ar_3C-CAr_3 \xrightarrow{slow} Ar_3\overset{\bullet}{C} \xrightarrow{O_2} Ar_3C-O-\overset{\bullet}{O} \xrightarrow{Ar_3C-CAr_3}$$

$$Ar_3C-O-O-C-Ar_3 + Ar_3\overset{\bullet}{C} \text{ .... etc.}$$

In presence of inhibitors, (catechol), $Ar_3C^{\bullet}$ formed hydroperoxide.



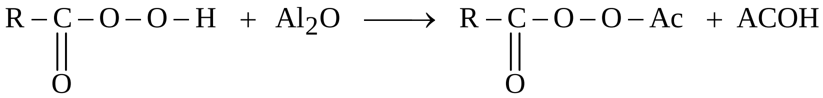
The auto - oxidation of aldehydes proceeds with ease, even at room temperatures.



$$R-\overset{\overset{O}{\|}}{C}-H \xrightarrow{In^{\cdot}} R-\underset{\underset{O}{\|}}{\overset{\bullet}{C}} \xrightarrow{O_2} R-\underset{\underset{O}{\|}}{C}-O-O^{\bullet}$$

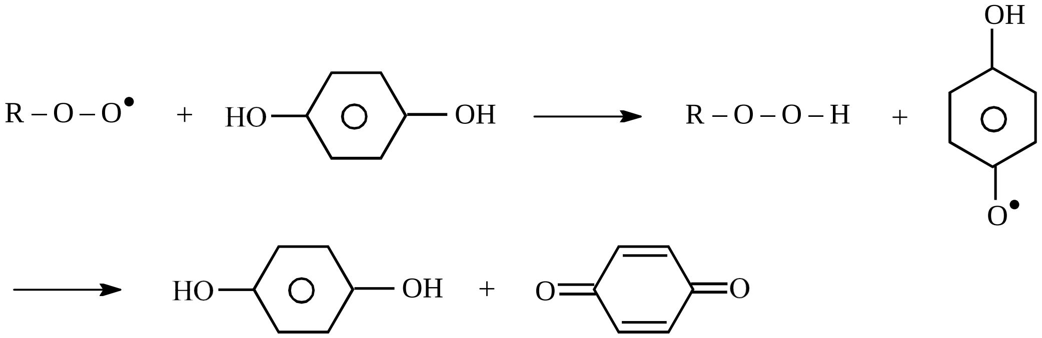
$$\xrightarrow{RCHO} R-\underset{\underset{O}{\|}}{C}-O-O-H + R\overset{\bullet}{C}O \text{ ....}$$

Here the product is peroxy acid $(R-\dot{C}O+\dot{O}OH)$ peroxy acid reacts with AC_2O to give diacyl peroxide.


$$R-\underset{\underset{O}{\|}}{C}-O-O-H + Al_2O \longrightarrow R-\underset{\underset{O}{\|}}{C}-O-O-Ac + ACOH$$

The substances that are known to be most effective in inhibiting auto - oxidations are phenols, Aromatic amines.

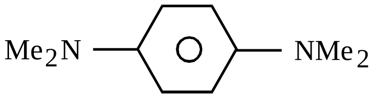
These inhibitors are believed to react with peroxy radicals rather than alkyl or acyl radicals.



Deuterated amines like Ph.NDMe and Ph_2ND were found to inhibit the auto oxidation of cumene as effectively as undeuterated amines.

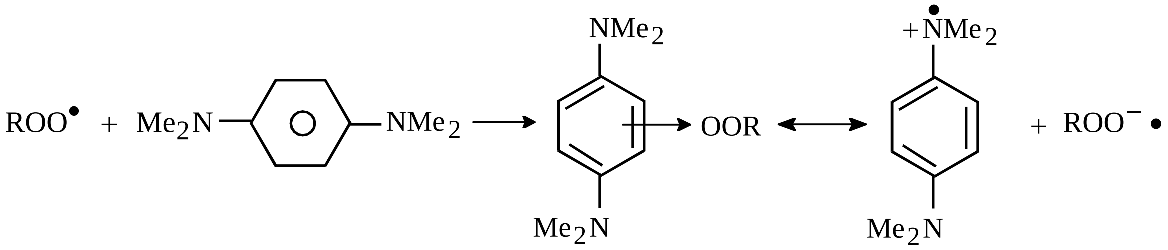
If the inhibition process begins with a breakage of N – H or N – D bonds, deuterated compounds less effective.

The auto - oxidation is similarly inhibited by tetramethyl p – phenylene diamine



in which there are no N – H bonds.

Hence, it is believed that auto - oxidation action of aromatic amines is due not to hydrogen atom transfer but rather to formation of complex with peroxy radical.



Auto - oxidations are catalysed by traces of metal salts. The salt should be derived from a metal having at least two readily accessible oxidation states **differing by one unit**.

(Fe, Co, Cu, V, Mn)

Peroxides react with both upper and lower oxidation states of these metals.

$$Fe^{+2} + ROOH \longrightarrow Fe(OH)^{+2} + OR^{\bullet}$$

$$Fe(OH)^{2+} + ROOH \longrightarrow Fe^{+2} + HOH + ROO^{\bullet}$$

Salt having the metal in the lower valence state is added to a solution containing peroxide, the metal ion will be oxidised, then reduced, then oxidised etc.

Each of these changes generate radical capable of removing a hydrogen atom from a molecule of hydrocarbon or aldehyde.
Hence, these metal salts enhance the effectiveness of peroxy compounds as radical initiators.

Since such salts, decompose the peroxides, yields of peroxides obtained from such accelerated auto - oxidations are generally decreased.

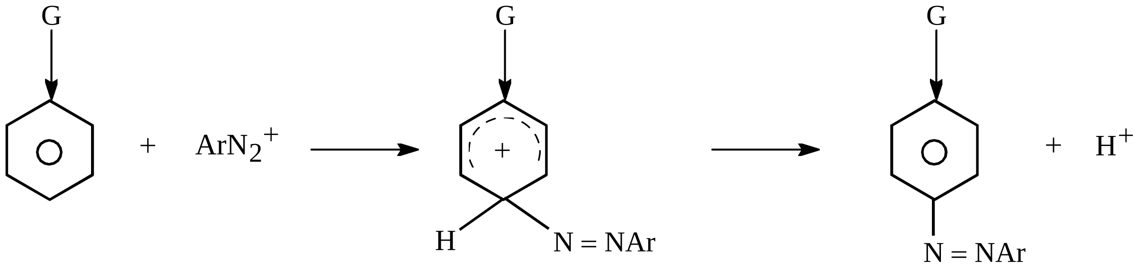
3.3.iii Coupling of diazonium salts :

Diazonium salts react with certain aromatic compounds to give products having the general formula $Ar - N = N - Ar^1$ called azo compounds. Such reactions are known as coupling reactions. The nitrogen of the diazonium group is retained in the product.

$$ArN_2^+ + Ar^1H \longrightarrow \underset{\text{an azo compound}}{Ar - N = N - Ar^1}$$

The aromatic ring (Ar^1H) undergoing attack by the diazonium ion must contain a powerful electron releasing group generally –OH, $-NR_2$, –NHR or $-NH_2$. Substitution occurs para to the activating group. Generally coupling with phenols is carried out in mildly alkaline solution, and with amines in midlly acidic condition.

Evidence from the kinetic studies indicates that the coupling is electrophilic aromatic substitution in which the diazonium ion is the attacking reagent.

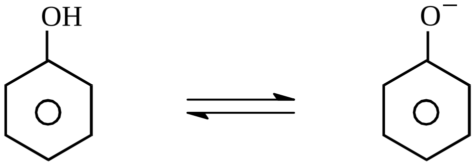


ArN_2^+ is a weak electrophile and can attack only very active aromatic rings. Coupling reactions are not observed even with benzene and other less electron releasing groups containing benzene rings.

The coupling reactions are susceptible to the solvent condition. Proper acidity or alkalinity must be maintained for better yields of the product.

For example, the reaction of aniline with diazonium salts was found to decrease with increase in acidity of the medium. This is because in high acid condition, aniline is converted into its salt ($-NH_2 + H^+ \longrightarrow -NH_3^+$) and group $-NH_3^+$ deactivating group and the compound becomes unreactive towards weakly electrophilic reagents (ie.) ArN_2^+.

In case of phenol which is appreciably acidic ionise in aqueous solution and exists in equilibrium with phenoxide ion.



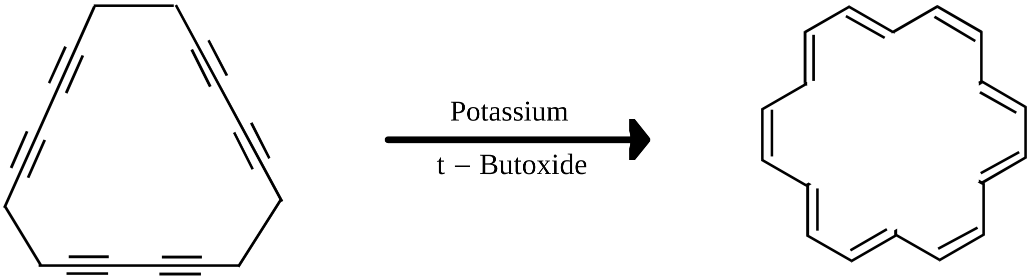
Fully developed $-O^-$ is more powerful electron releaving than –OH. If the acidic nature of medium is increased, higher proportion of phenol becomes un – ionised and thereby lowers the rate of coupling. Hence, proper condition of the medium must be maintained so as the reaction to take place to give better yields of diazo compounds.

3.3.iv Coupling of alkynes :

Terminal alkynes on heating with stoichiometric amounts of cupric salts in pyridine or a similar base gives diyne in high yield. This reaction is called Coupling of alkynes.

$$2R-C\equiv CH \xrightarrow[\text{Pyridine}]{CuX_2} R-C\equiv C-C\equiv C-R$$

This reaction is known Eglinton reaction. This reaction is useful to prepare large – ring annulenes of Sondheimer et.al. by rearrangement and hydrogenation of cyclic polyynes, by coupling of terminal diynes.



The mechanism of Eglinton reaction is initiated by loss of proton. The last reaction is the coupling of two free radicals.

$$2R-C\equiv C^{\circ} \longrightarrow R-C\equiv C-C\equiv C-R$$

The anion is converted into radical, depends on the oxidising agent.

Sandmeyer Reaction :

The conversion of aromatic diazo compounds to aryl halides by use of Cu_2Cl_2 appear to proceed through aryl radicals.

The reaction is first order in diazonium ion and in cuprous chloride (actually $CuCl_2^-$).

$$ArN_2^+ + CuCl_2^- \longrightarrow Ar^\bullet + N_2 + CuCl_2$$

The reaction is retarded by large excess of added HCl, suggesting that complex $CuCl_4^{-3}$ is ineffective in converting diazonium ion into aryl radical. Univalent copper is not consumed in the overall reaction.

(ie.) Copper oxidised in the rate determining step must be reduced in a subsequent step.

$$ArN_2^+ + Cl-Cu-Cl^- \xrightarrow{\text{Slow}} Ar^\bullet + Cl-Cu-Cl + N_2$$

$$\xrightarrow{\text{fast}} ArCl + CuCl + N_2$$

Addition of hydrogen halides :

The addition of HBr to olefins in non – polar solvents in presence of oxygen or peroxide or with the aid of illumination, the direction of addition is reversed.

$$R-O-O-R \longrightarrow 2R\overset{\bullet}{O} \xrightarrow{2HBr} 2ROH + 2\overset{\bullet}{Br}$$

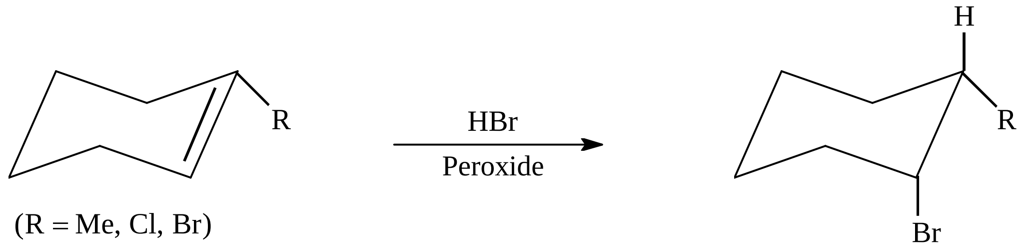
The addition of Bi radical takes place in the formation of stable carbon free radical

$$CH_3-CH=CH_2 \xrightarrow{{}^\bullet Br} CH_3-\overset{\bullet}{C}H-CH_2Br$$

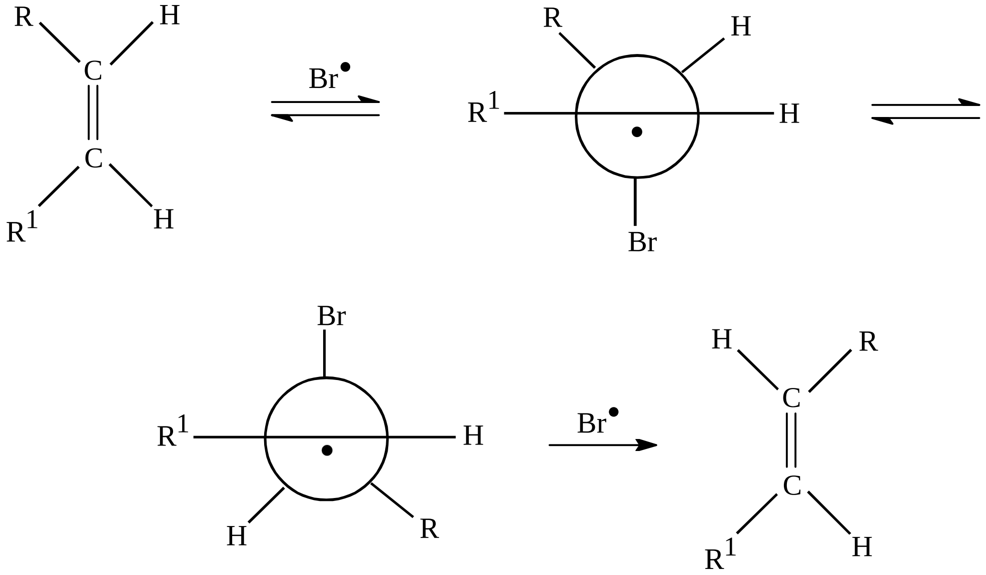
$$CH_3-\overset{\bullet}{C}H-CH_2Br+HBr \longrightarrow CH_3CH_2CH_2Br + {}^\bullet Br$$

Peroxide effect is observed in addition of HBr, but not for addion of HCl or HI.

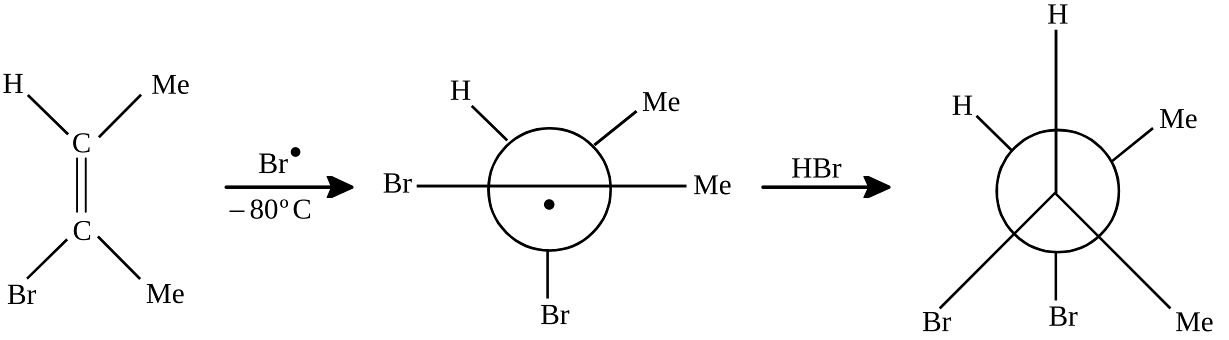
Homolytic addition of HBr to substituted cyclohexanes are stereospecific trans – addition. Addition to 1–methyl cyclohexene gives cis – 1 – bromo – 2 – methyl cyclohexane.



The holytic addition of HBr to non – cyclic olefins at room temperature and above is non stereospecific.



At low temperatures, rotation about C = C bond in the radical intermediate becomes much less free, if large of excess of HBr is taken, stereospecificity may be restored.



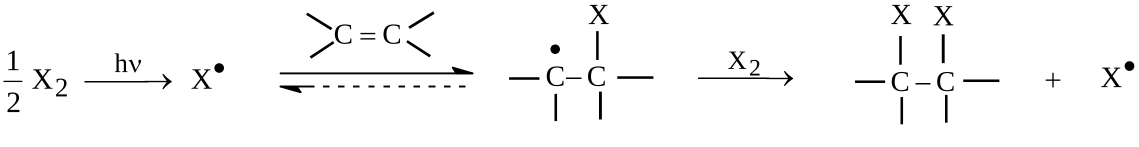
Meso 90%

Cis olefins gives Meso isomer.

Trans - olefins gives corresponding d, ℓ compounds.

Homolytic halogen addition :

Usual chain mechanism for halogen addition

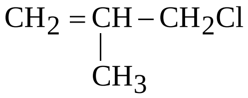


Addition chlorine and Bromine proceed with ease. Addition of I_2 is sluggish with fluorine, violent reaction takesplace. Addition of $Cl^{\bullet}$ to ordinary C = C double bonds appears irreversible at temperature below 200ºC.

Reversibility becomes increasingly important as the temperature is raised.

The rate of hydrogen abstraction likewise increases and at temperatures above 450ºC, substitution at allylic position over shadow halogen addition.

Ex.: Isobutene is converted into methyl chloride at about 600ºC.



$$\underset{\displaystyle CH_3}{CH_2 = \underset{|}{C}H - CH_2Cl}$$

The addition of $Br^{\bullet}$ is often reversible at room temperature.

This reversibility is the ability of bromine radicals to bring about Cis – trans isomerization.

Elemental iodine when heated or irradiated in solution also catalyse isomerisation of olefins indicating that addition of iodine atoms to C = C is also reversible.

Rearrangements of free radicals :

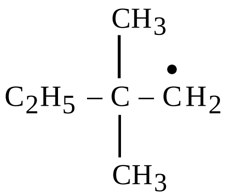
β, β, β – triphenyl ethyl radical formed by the decomposition of the corresponding aldehyde in presence of peroxide rearranges to give a new radical and the product is obtained accordingly.

$$Ph_3CCH_2CHO \xrightarrow{tBu\overset{\bullet}{O}} Ph_3C\,CH_2 - \overset{\bullet}{C} = O \xrightarrow{-CO} Ph_3 - \overset{\bullet}{C}H_2 \xrightarrow{Ph,\ shift}$$

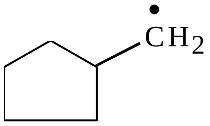
$$Ph_2\overset{\bullet}{C} - CH_2Ph \xrightarrow{Ph_3C\,CH_2CHO} Ph_2CH - CH_2Ph \; + \; Ph_3CCH_2\overset{\bullet}{C}O$$

(The product Ph_3CCH_3 was not obtained)

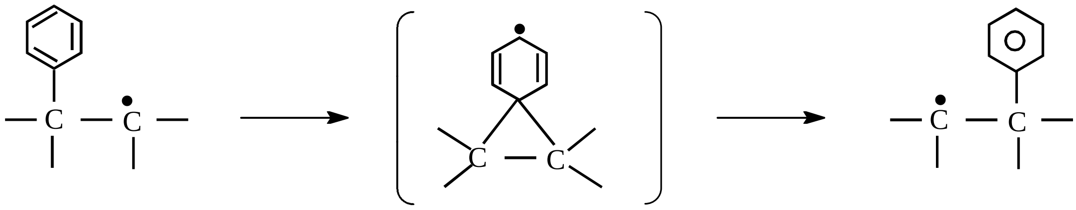
However non – phenylated radicals suffer no rearrangement.



$$C_2H_5 - \underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{C}} - \overset{\bullet}{C}H_2$$



The fact that aryl groups, but not alkyl groups may shift in rearrangements of free radicals suggests that such rearrangements proceed through bridged activated complex.



Such aryl shift generally does not occur unless there is considerable crowding at C_β .

Thus, no migration of aryl group is observed in reactions of radicals of the type $Ar_2-CH\overset{\bullet}{C}H_2$.

The formation of bridged radical intermediates is not easy as the formation of carbonium ions.

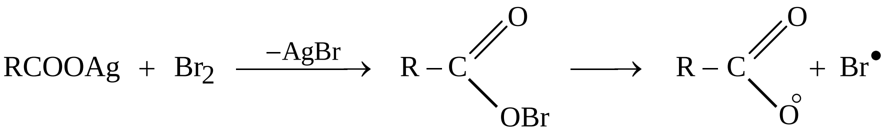
Radical displacements on carbon are rare and presumably require considerable activation energy, whereas the electrophilic displacement on aromatic carbon takes place easily.

Hunsdiecker reaction :

Silver salts of carboxylic acids may be converted to alkyl or aryl halides by treatment with elemental bromine or iodine in an inert solvent. This reaction is known as Hunsdiecker reation. It is believed that the reaction takes place by free radical mechanism.

$$C_6H_5CH_2COOAg + Br_2 \xrightarrow[76^\circ C]{\text{dry } CCl_4} C_6H_5CH_2Br + AgBr + CO_2$$

The mechanism involves the formation of carboxylate radical through decomposition of an acyl hypobromite intermediate.



$$RCOOAg + Br_2 \xrightarrow{-AgBr} R-C(=O)OBr \longrightarrow R-C(=O)\overset{\circ}{O} + Br^\bullet$$

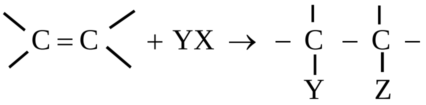
$$\longrightarrow R^\bullet + CO_2 + Br^\bullet \longrightarrow RBr + CO_2$$

The first step is not free radical process, acyl hypohalite is considered to be the intermediate though it was never isolated from the reaction mixture.

ADDITION REACTIONS OF CARBON – CARBON DOUBLE BONDS

The functional group present in alkenes is carbon – carbon double bond. It is this functional group which determines the characteristic reactions of alkenes. Alkenes mainly undergo addition reactions.

Double bond consists of a strong σ – bond and a weak π – bond. Reactions take place by breaking of the weak π –bond. When π –bond is broken, two strong σ – bonds are formed in its place.



$$>C=C< + YX \rightarrow -\underset{Y}{\overset{|}{\underset{|}{C}}}-\underset{Z}{\overset{|}{\underset{|}{C}}}-$$

A reaction in which two molecules combine to give a single molecule of product is called an addition reaction.

Carbon – carbon double bond act as a source of electrons (i.e.) it acts as a base. Electron deficient molecules or species (i.e) acids react with alkenes. These acidic reagents that are seeking a pair of electrons are called electrophilic reagents. The typical reaction of an alkene is electrophilic addition.

Reactions which generally take place are

i. addition of hydrogen (H_2)
ii. addition of hydrogen halides (HX)
iii. addition of halogens (X_2)
iv. addition of hypohalites (HOX)

Addition of hydrogen halides, Markovnikov's rule. Regioselective reactions.

An alkene react with hydrogen halide to give alkyl halide.

$$-C=C- + \quad HX \longrightarrow -\underset{H}{\underset{|}{C}}-\underset{X}{\underset{|}{C}}-$$

alkene (HX=HCl, HBr, HI) Alkyl halide

The reaction is carried out by passing the dry gaseous hydrogen halide directly into the alkene. Polar solvents are used in certain cases which dissolve both hydrogen halide and alkene.

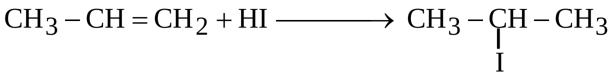
Ethylene reacts with hydrogen iodide to give ethyl iodide

$$CH_2=CH_2+HI \longrightarrow CH_3CH_2I$$

The reactivity of hydrogen halides towards alkene is

$$HI > HBr > HCl > HF$$

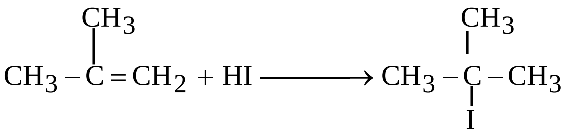
Propene ($CH_3-CH=CH_2$) reacts with hydrogen halide to give two products, n – propyl halide and isopropyl halide depending upon the orientation of addition. Actually, only the isopropyl halide is formed.



$$CH_3-CH=CH_2+HI\longrightarrow CH_3-\underset{\displaystyle I}{\underset{|}{C}}H-CH_3$$

Isopropyl iodide

In the same way isobutene could give two products, isobutyl halide or t–butyl halide. Actually, only t–butyl halide is formed.



$$CH_3-\overset{\displaystyle CH_3}{\overset{|}{C}}=CH_2+HI\longrightarrow CH_3-\underset{\displaystyle I}{\underset{|}{\overset{\displaystyle CH_3}{\overset{|}{C}}}}-CH_3$$

t–Butyl iodide

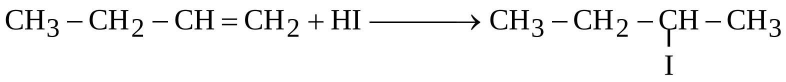
On examination of a large number of such additions, Markovnikov observed that where two isomeric products are formed one of them is the predominant product.

The orientation of addition was enuntiated by Markovnikov and is known as Markovikov's rule.

In the addition of hydrogen halide (or an acid) to the carbon – carbon double bond of an alkene, hydrogen is bonded to the carbon atom already having greater number of hydrogens. This is known as Markovnikov's rule.

Using this rule one can correctly predict the principal product of many reactions.

Examples :



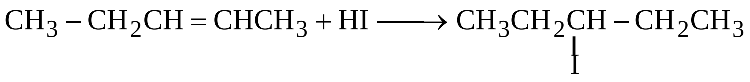
$$CH_3-CH_2-CH=CH_2+HI\longrightarrow CH_3-CH_2-\underset{\displaystyle I}{\underset{|}{C}}H-CH_3$$

1 – Butene 2 – iodobutane

$$CH_3-\overset{\displaystyle CH_3}{\overset{|}{C}}=CH-CH_3+HI\longrightarrow CH_3-\underset{\displaystyle I}{\underset{|}{\overset{\displaystyle CH_3}{\overset{|}{C}}}}-CH_2-CH_3$$

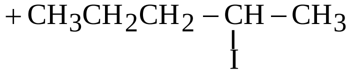
2 – Methyl – 2 – butene 2 – iodo – 2 – methyl butane

However, the Markovnikov's rule is not applicable in respect of such compounds like 2 – pentene. In this case neither product predominates, equal quantities of two isomers are obtained.



$$CH_3-CH_2CH=CHCH_3+HI\longrightarrow CH_3CH_2\underset{\displaystyle I}{\underset{|}{C}}H-CH_2CH_3$$

2 – pentene 3 – iodopentane



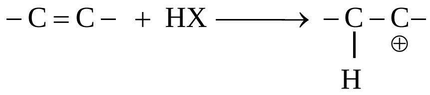
$$+CH_3CH_2CH_2-\underset{\displaystyle I}{\underset{|}{C}}H-CH_3$$

2 – iodopentane.

Reactions in which orientation of addition is such that one of the possible isomeric product is exclusively formed are called "regioselective" reactions.

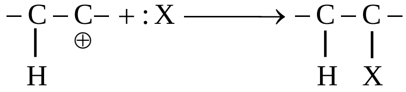
Electrophilic addition : Mechanism :

Addition of acidic reagents like HX to an alkene involves two steps.

i. 

$$-C=C- + HX \longrightarrow -\underset{H}{C}-\underset{\oplus}{C}- \quad \text{(slow)}$$

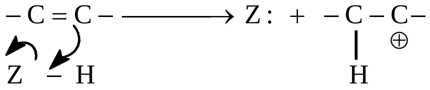
(HX = HCl, HBr, HI)

ii. 

$$-\underset{H}{C}-\underset{\oplus}{C}- + :X \longrightarrow -\underset{H}{C}-\underset{X}{C}- \quad \text{(fast)}$$

(Z = Cl^-, Br^-, I^-)

In step (i) hydrogen is transferred to alkene (i.e.) without its electrons, to give a carbocation.

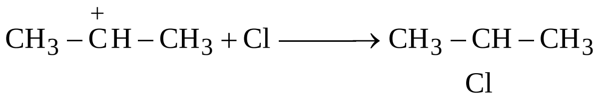


$$-C=C- \longrightarrow Z: + -\underset{H}{C}-\underset{\oplus}{C}-$$

Electrophilic addition

Step (i) is slow and difficult step and its rate controls the overall rate of addition. This step involves the attack by an electron–seeking reagent (i.e.) electrophilic reagent and hence the reaction is an example of electrophilic addition.

Example : $CH_3-CH=CH_2+HCl \longrightarrow CH_3-\overset{+}{C}H-CH_3+\overset{-}{Cl}$



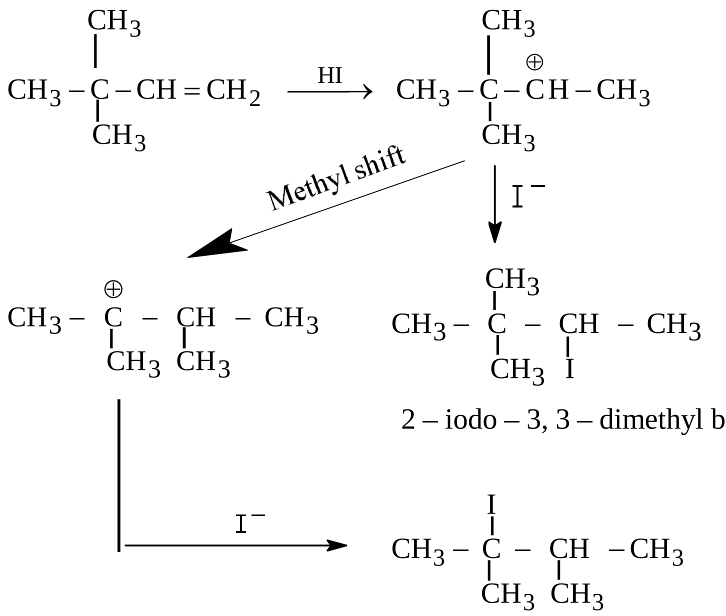
$$CH_3-\overset{+}{C}H-CH_3+Cl \longrightarrow CH_3-\underset{Cl}{CH}-CH_3$$

The rate of reaction depends on the concentration both alkene and hydrogen halide.

Electrophilic addition : Rearrangement

The addition of hydrogen halide to an alkene is accompanied by rearrangement depending upon the structure of the carbocation formed in the first step of the reaction.

For example, addition of hydrogen iodide to 3, 3 – dimethyl – 2 – butene gives not only 2 – iodo – 3, 3 – dimethyl butane, but also 2 – iodo – 2, 3 – dimethyl butane.



2 – iodo – 3, 3 – dimethyl butane

2 – iodo – 2, 3 – dimethyl butane

The initially formed secondary carbocation rearranges to give more stable tertiary carbocation by methyl shift.

Electrophilic addition : Orientation and Reactivity :

It was already mentioned that addition of hydrogen chloride to three types of alkenes takes place according to Markovnikov's rule.

This reaction follows two steps mechanism.

i. Propene gives 2 – chloropropane.
ii. Isobutene gives tert – butyl chloride.
iii. 2 – methyl – 2 – butene gives tert – pentyl chloride.

The orientation of addition depends upon the relative rates of formation of one carbocation or other. In the electrophilic addition the rate of formation of carbocation follows the sequence.

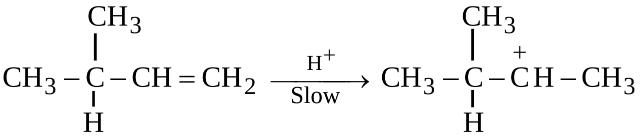
Rate of carbocation formation : $3^o > 2^o > 1^o > \overset{+}{C}H_3$

This is the same as the order of stability of cabocations.

It is now possible to define Markovnikov's rule as : electrophilic addition to a carbon – carbon double involves the intermediate formation of more stable carbocation.

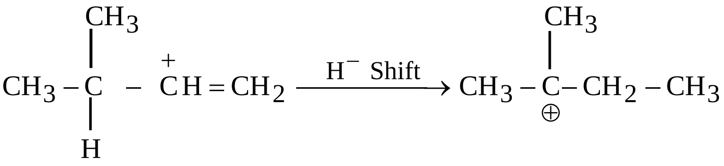
In certain alkenes, the initially formed carbocation by the addition of hydrogen rearranges to form more stable carbocation by either methyl shift or hydride shift.

Ex.: Addition of HCl to 3 – methyl – 1 – butene

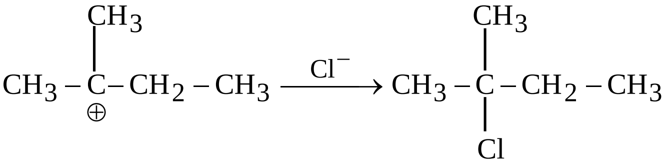


$$CH_3-\underset{H}{\overset{CH_3}{C}}-CH=CH_2 \xrightarrow[\text{Slow}]{H^+} CH_3-\underset{H}{\overset{CH_3}{C}}-\overset{+}{C}H-CH_3$$

(Secondary carbocation)



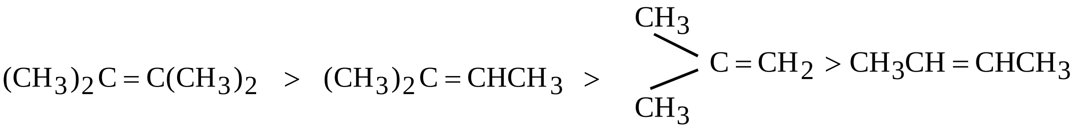
$$CH_3-\underset{H}{\overset{CH_3}{C}}-\overset{+}{C}H=CH_2 \xrightarrow{H^-\ \text{Shift}} CH_3-\underset{\oplus}{\overset{CH_3}{C}}-CH_2-CH_3$$



$$CH_3-\underset{\oplus}{\overset{CH_3}{C}}-CH_2-CH_3 \xrightarrow{Cl^-} CH_3-\underset{Cl}{\overset{CH_3}{C}}-CH_2-CH_3$$

Rate of addition of hydrogen ion to a double bond depends on the stability of carbocation being formed. This factor not only determines the orientation of addition, but also relative reactivities of alkenes.

Relative reactivity of alkenes towards hydrogen halides is



$$(CH_3)_2C=C(CH_3)_2 > (CH_3)_2C=CHCH_3 > \begin{matrix}CH_3\\ CH_3\end{matrix}\!\!>C=CH_2 > CH_3CH=CHCH_3$$

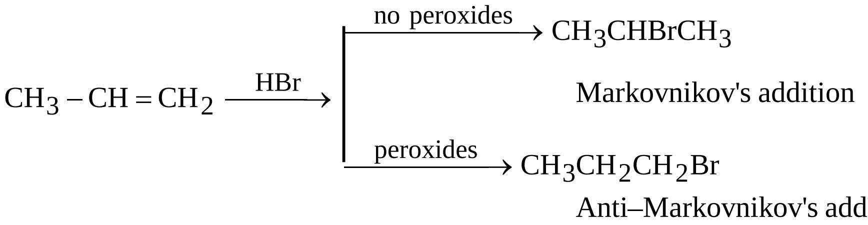
$$> CH_3CH=CH_2 > CH_2=CH_2 > CH_2=CHCl$$

In the above series vinyl chloride was found to react very slowly because the electron withdrawing group (chlorine) increases the positive charge on carbon atom and hence destabilises the carbocation.

Addtion of hydrogen bromide : Peroxide effect :

Kharasch and Mayo discovered the orientation of addition of hydrogen bromide to an alkene in presence of peroxide.

In the absence of peroxide all the three types of hydrogen halides were found to give products according to Markovnikov's rule. However, the addition of HBr in presence of peroxide was found to give product exactly opposite to that of the Markovnikov's product. Hence, the reaction of HBr to alkene is also termed as Anti–Markovnikov's addition.



$$CH_3-CH=CH_2 \xrightarrow{HBr} \begin{cases} \xrightarrow{\text{no peroxides}} CH_3CHBrCH_3 \\ \xrightarrow{\text{peroxides}} CH_3CH_2CH_2Br \end{cases}$$

Markovnikov's addition

Anti–Markovnikov's addition

The reversal of the orientation of addition in presence of peroxides is known as peroxide effect.

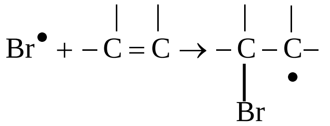
Free radical addition :

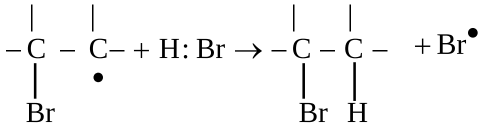
In presence of peroxides, the addition of HBr to an alkene takes place through free radical mechanism. Peroxides initiate the free radical reaction.

The mechanism of the addition can be understood from the following sequence of steps.

1. Peroxide $\longrightarrow$ Radicals
2. Radicals + H : Br $\longrightarrow$ Rad : H + $Br^{\bullet}$

} Chain initiating steps

3. 
$Br^{\bullet} + -\overset{|}{C}=\overset{|}{C} \rightarrow -\overset{|}{\underset{Br}{C}}-\overset{|}{\underset{\bullet}{C}}-$

4. 
$-\overset{|}{\underset{Br}{C}}-\overset{|}{\underset{\bullet}{C}}- + H{:}Br \rightarrow -\overset{|}{\underset{Br}{C}}-\overset{|}{\underset{H}{C}}- + Br^{\bullet}$

} Chain propagation steps

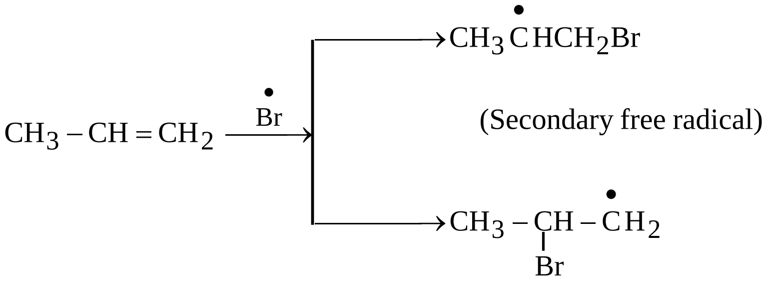
Orientation of free – radicals addition :

Free – radical addition of HBr to propene gives 1–bromopropane. In the chain propagation step (3), Br is added to a double bond to produce a carbon free radical. It is the stability of this free radical determines the orientation of addition.

The stability of free radicals is

$$3^{o} > 2^{o} > 1^{o} > \dot{C}H_3$$

Addition of $\dot{Br}$ takes place in such a way so as to give more stable free radical.



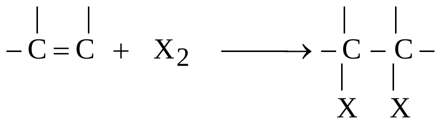
(Secondary free radical)

(Primary free – radical)

Being secondary free radical more stable the final product obtained in the above reaction is n – propyl bromide, but not isopropyl bromide.

Addition of Halogens :

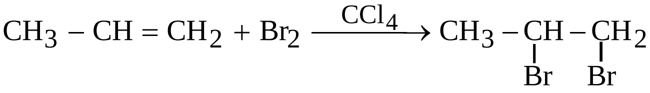
Alkenes readily react with chlorine or bromine to give saturated compounds containing two halogen atoms bonded to adjacent carbon atoms (vicinal halide) Iodine fails to react.



$$-\overset{|}{C}=\overset{|}{C} + X_2 \longrightarrow -\underset{X}{\underset{|}{\overset{|}{C}}}-\underset{X}{\underset{|}{\overset{|}{C}}}-$$

(Br_2, Cl_2)

The reaction can be carried out in an inert solvent like carbon tetrachloride. The addition takes place rapidly at room temperature.



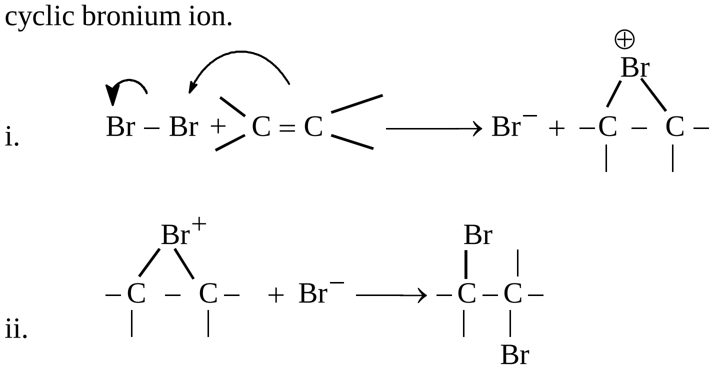
$$CH_3-CH=CH_2+Br_2 \xrightarrow{CCl_4} CH_3-\underset{Br}{\underset{|}{CH}}-\underset{Br}{\underset{|}{CH_2}}$$

Propene 1, 2 – dibromopropane

Addition of bromine in carbon tetrachloride is generally used for detection of unsaturation in the given organic compounds. Unsaturated compounds rapidly decolourise the reddish colour of bromine.

Mechanism of addition of halogens :

Addition of halogens to alkenes is believed to be electrophilic involving two steps. The first step involves the formation of halonium ion. If bromine is used as reagent for addition, it results in the formation of cyclic bronium ion.



Alkene acting as a nucleophile attaches itself to one of the bromine and pushes the other bromine out as bromide ion. The mechanism proposed is based on certain experimental observation made

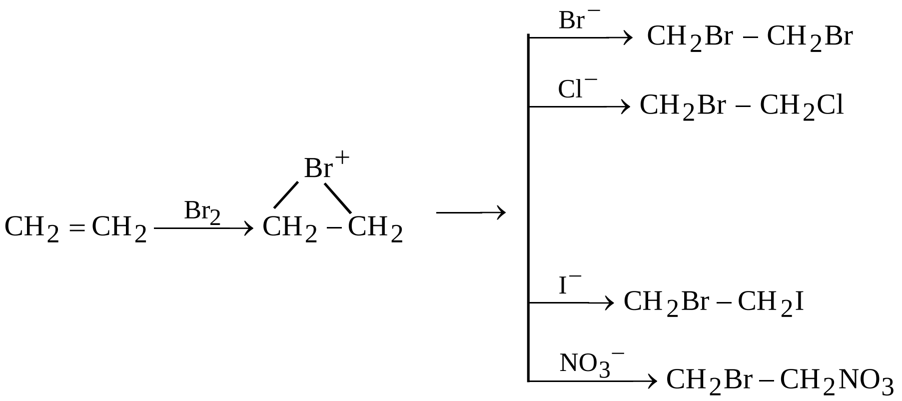
1. The effect of structure of the alkene on reactivity.
2. The effect of added nucleophiles
3. Complete stereo electivity and in the anti addition.

Effect of structure on alkene reactivity :

Alkenes show the same order of reactivity towards halogens as towards acids. Electron – releasing substituents activate the alkene. This support the idea that alkenes acts as electron source and halogen acts as acid.

Effect of added nucleophiles :

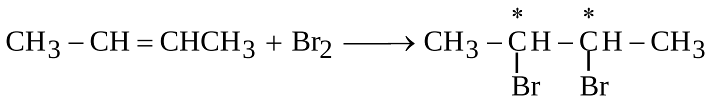
The bromonium ion formed in the reaction of bromine with ethylene, should be able to react not only with bromide ion, but also other nucleophile added into the reaction mixture. In fact the products were also isolated in which the added nucleophiles are bonded to the alkene carbon atom.



Stereochemistry of Addition of halogens to alkenes :

Addition of bromine to 2 – butene is useful example to study the sterochemistry of addition to an alkene.

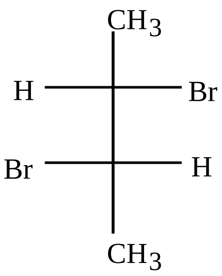
Addition of bromine to 2 – butene gives 2, 3 – dibromobutane. Two chiral centres are generated in this reaction.



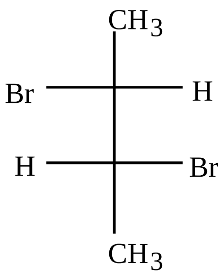
$$CH_3-CH=CHCH_3+Br_2 \longrightarrow CH_3-\underset{\mathrm{Br}}{\overset{*}{C}}H-\underset{\mathrm{Br}}{\overset{*}{C}}H-CH_3$$

(* indicates chiral centre)

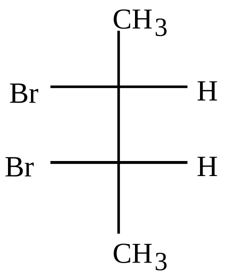
The product can exist as a pair of enantiomers (I and II) and a meso compound (III).



(I)

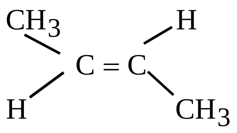


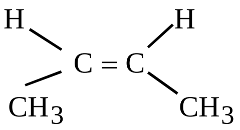
(II)



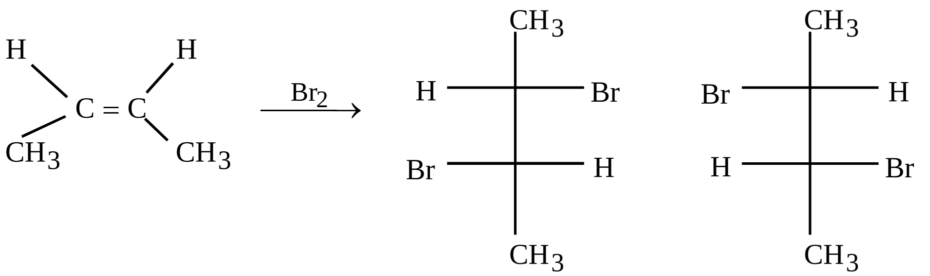
(III) (Meso)

2 – butene exists in two geometrical isomers, Cis and trans.





Cis – 2 – butene on reaction with bromine gives only racemic 2,3 – dibromobutane I and II, but none of the meso compound.

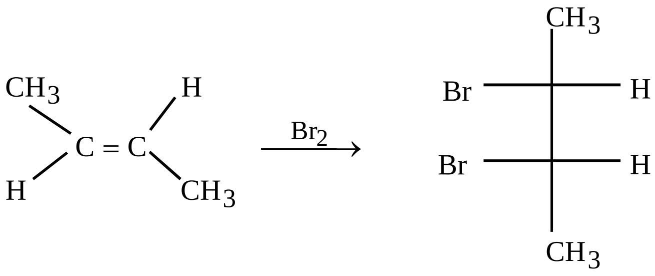


(I) (II)

Only product

A reaction that gives predominantly one stereoisomer of several possible diastereoisomers is called stereoselective reaction.

However, trans – 2 – butene reacts with bromine to give meso product(III) only but none of the compounds I and II



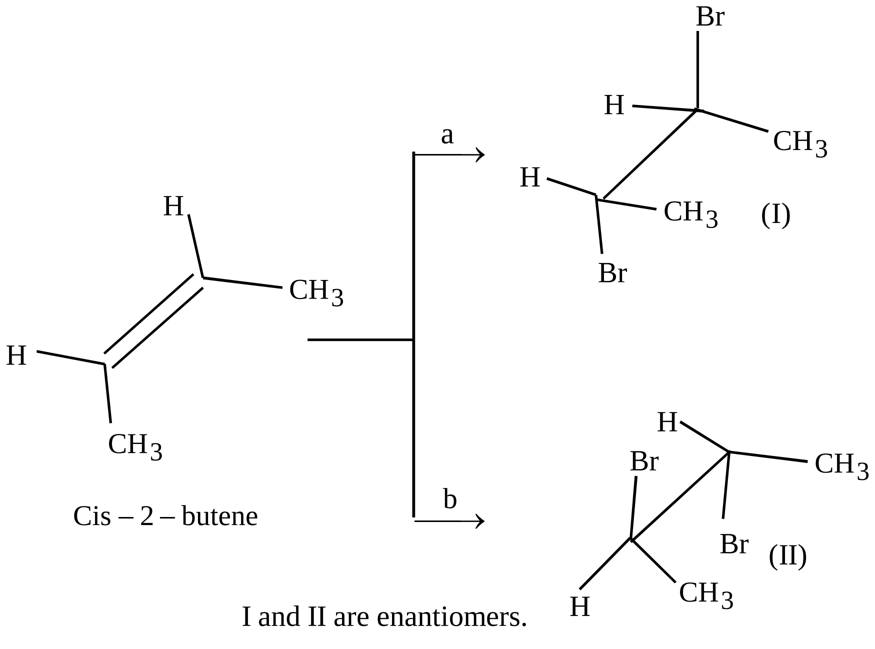
(III)

III Meso only product

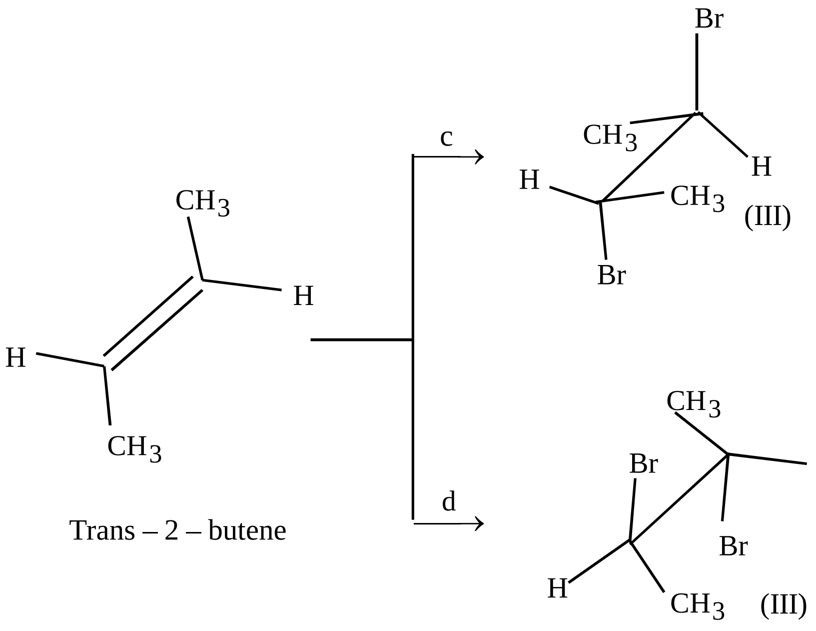
A reaction in which sterochemically different molecules react differently is called stereospecific reaction.

Addition of bromine to alkene is both stereoselective and stereospecific.

Addition of bromine to 2 – butene involves anti – addition



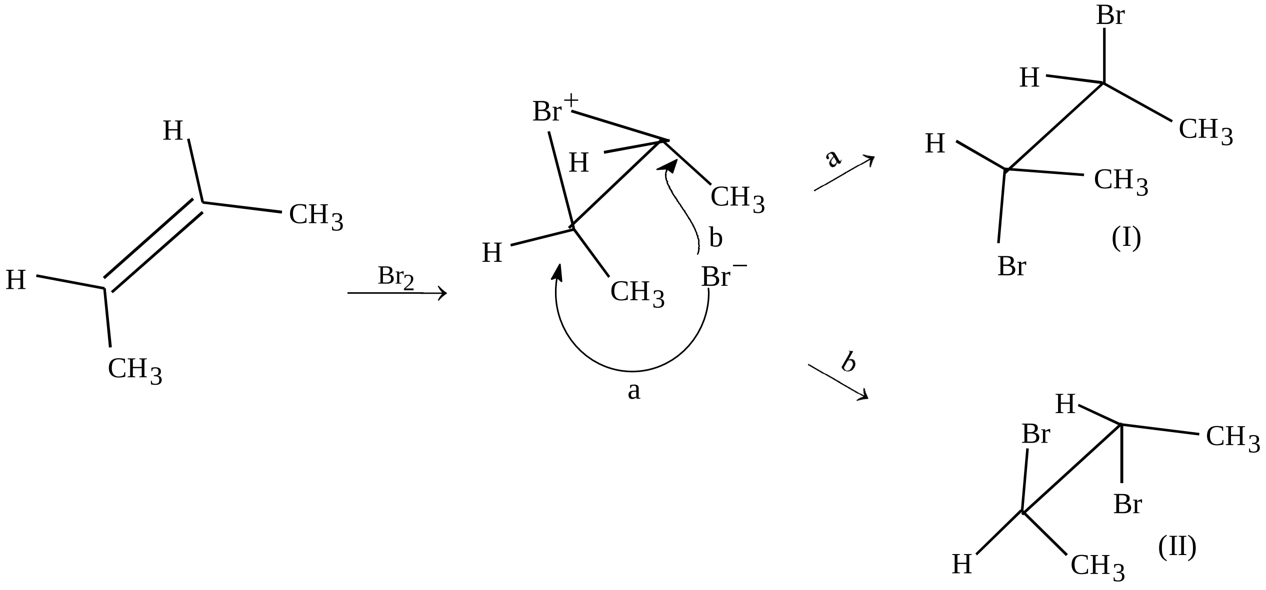
I and II are enantiomers.

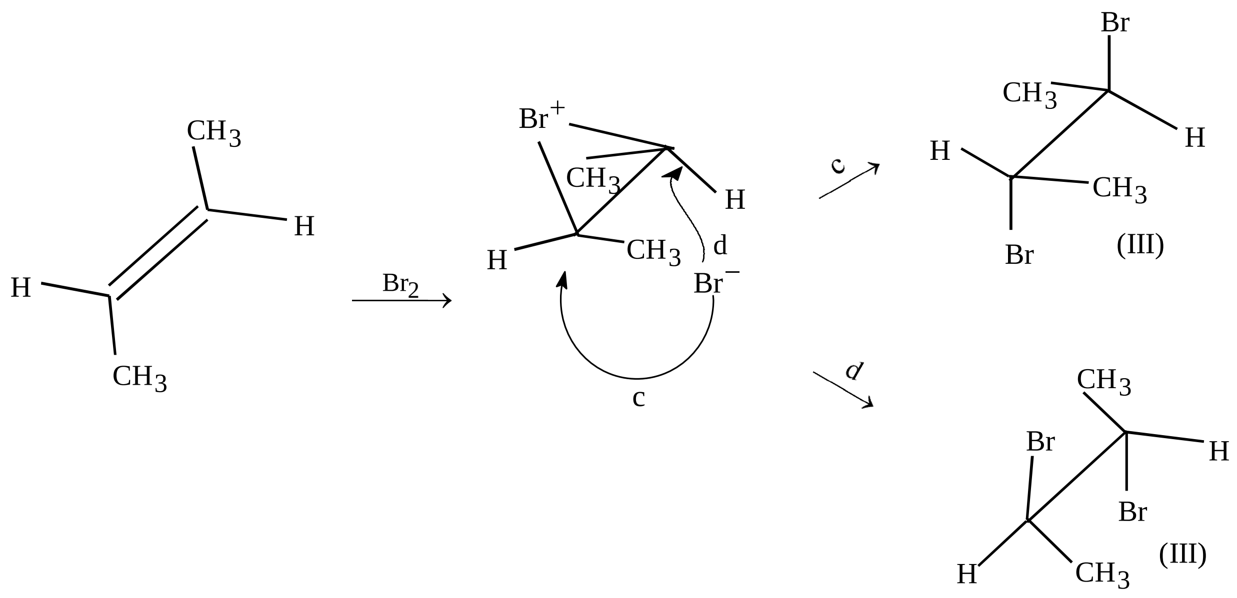


III is meso compound

Anti – addition is the general rule for the reaction of bromine or chlorine with simple alkenes.

The anti – addition products mentioned in the above reaction can be conveniently be explained with the help the mechanism already proposed (i.e.) mechanism involving halonium ion formation in the first step of addition.





Addition of bromine via cyclic bromonium ion.

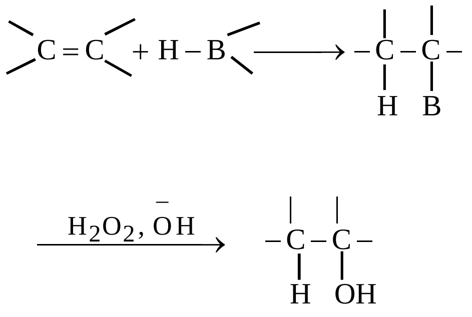
Hydroboration – Oxidation :

Diborane (B_2H_6) reacts with alkenes to form alkylborane. This reaction is known as hydroboration. Alkylboranes on oxidation give alcohols.

$$6CH_2{=}CH_2 + (BH_3)_2 \longrightarrow 2(CH_3CH_2)_3B$$

$$(CH_3CH_2)_3B + 3H_2O_2 \xrightarrow{\bar{O}H} 3CH_3CH_2OH + B(OH)_3$$

The reaction procedure is simple and high yields of the products are obtained. Hydroboration involves the addition of BH_3 to the double bond, with hydrogen atom bonded to one doubly bonded carbon atom and boron to the other.



$$>C=C< + H-B< \longrightarrow -\underset{H}{\overset{|}{C}}-\underset{B}{\overset{|}{C}}-$$

$$\xrightarrow{H_2O_2,\ \bar{O}H} -\underset{H}{\overset{|}{C}}-\underset{OH}{\overset{|}{C}}-$$

The two stage process of hydroboration followed by oxidation, involves the addition a molecule of H_2O across the double bond.

Orientation of hydroboration :

Hydroboration – oxidation converts alkenes into alcohols. Addition is highly regioselective. The products obtained are opposite to one formed in the acid catalysed hydration.

Examples :

a) $CH_3-CH=CH_2 \xrightarrow{(BH_3)_2} (CH_3-CH_2-CH_2)_3B$

$\xrightarrow{H_2O_2,\ \overset{-}{O}H} CH_3CH_2CH_2OH$

n – propyl alcohol

b) $CH_3-CH_2-CH=CH_2 \xrightarrow{(BH_3)_2} \xrightarrow{H_2O_2,\ \overset{-}{O}H}$

$CH_3CH_2CH_2CH_2OH$

n – butyl alcohol

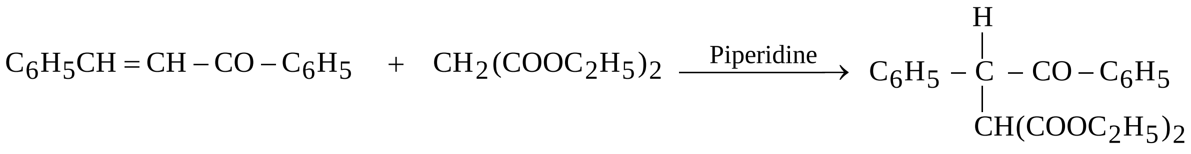
The reaction gives products corresponding to anti – Markovinkov's addition of water to the carbon – carbon double bond. One of the important advantages of this reaction that no rearrangement in the carbon skeleton occurs.

Michael addition :

Nucleophilic addition of carbanion to α, β – unsaturated carbonyl compounds resulting in the formation of a new carbon – carbon bond is known as **Michael addition**.

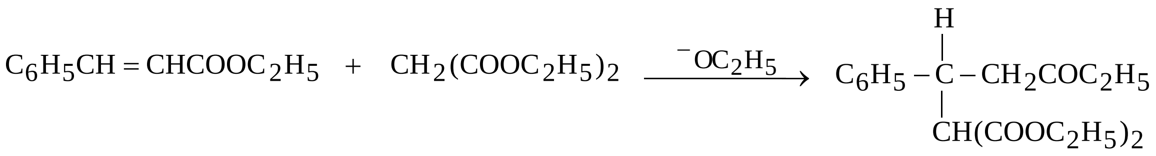
Ex.:

i.



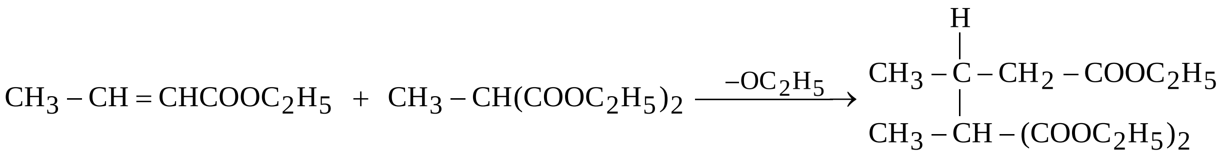
$$C_6H_5CH=CH-CO-C_6H_5 \quad + \quad CH_2(COOC_2H_5)_2 \xrightarrow{\text{Piperidine}} \begin{array}{rl} & H \\ & | \\ C_6H_5 - & C - CO-C_6H_5 \\ & | \\ & CH(COOC_2H_5)_2 \end{array}$$

ii.



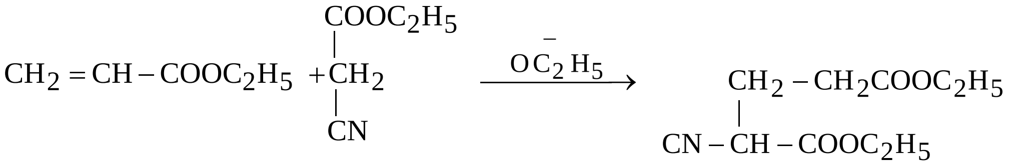
$$C_6H_5CH=CHCOOC_2H_5 \quad + \quad CH_2(COOC_2H_5)_2 \xrightarrow{^{-}OC_2H_5} \begin{array}{rl} & H \\ & | \\ C_6H_5 - & C - CH_2COC_2H_5 \\ & | \\ & CH(COOC_2H_5)_2 \end{array}$$

iii.



$$CH_3-CH=CHCOOC_2H_5 \quad + \quad CH_3-CH(COOC_2H_5)_2 \xrightarrow{-OC_2H_5} \begin{array}{rl} & H \\ & | \\ CH_3 - & C - CH_2-COOC_2H_5 \\ & | \\ CH_3 - & CH-(COOC_2H_5)_2 \end{array}$$

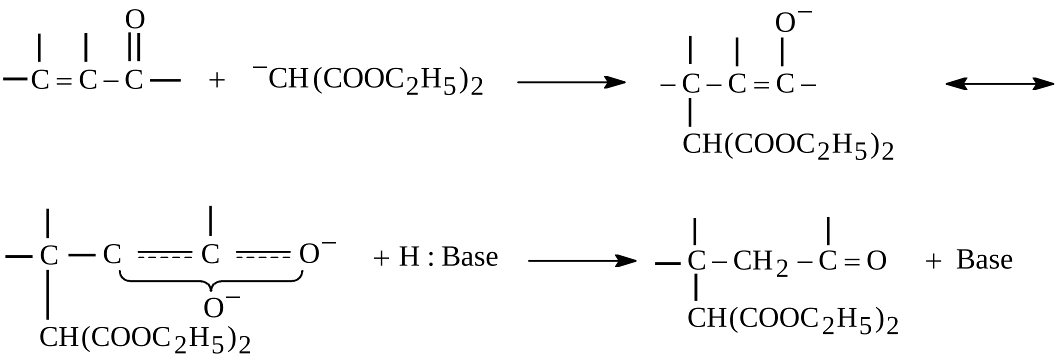
iv.



$$CH_2=CH-COOC_2H_5 + \underset{\displaystyle CN}{\overset{\displaystyle COOC_2H_5}{CH_2}} \xrightarrow{\bar{O}C_2H_5} \begin{array}{l} \quad CH_2-CH_2COOC_2H_5 \\ \quad | \\ CN-CH-COOC_2H_5 \end{array}$$

Mechanism :

$$CH_2(COOC_2H_5)_2 + \text{Base} \longrightarrow {}^{-}CH(COOC_2H_5)_2 + \text{H Base}$$



$$-\overset{|}{C}=\overset{|}{C}-\overset{\overset{\displaystyle O}{||}}{C}- + {}^{-}CH(COOC_2H_5)_2 \longrightarrow \underset{\displaystyle CH(COOC_2H_5)_2}{-\overset{|}{C}}-\overset{|}{C}=\overset{\overset{\displaystyle O^{-}}{|}}{C}- \longleftrightarrow$$

$$\underset{\displaystyle CH(COOC_2H_5)_2}{-\overset{|}{C}}-\underbrace{C \;{=\!=}\; \overset{|}{C} \;{=\!=}\; O^{-}}_{O^{-}} + \text{H : Base} \longrightarrow \underset{\displaystyle CH(COOC_2H_5)_2}{-\overset{|}{C}}-CH_2-\overset{|}{C}=O + \text{Base}$$

The function of the base is to generate carbanion by abstracting proton from malonic ester.

This carbanion acts as nucleophile, which attacks on the conjugated system.

Such compounds having active methylene groups in them easily generate carbanions in presence of base.

Compounds like ethyl cyanoacetate, ethyl acetoacetate can also be used.

Hydrogenation of double bonds :

Hydrogenation is the addition of hydrogen to a multiple bond. A simple example of this reaction is addition of hydrogen to ethylene to give ethane.

$$CH_2=CH_2+H_2 \longrightarrow CH_3-CH_3$$

The bonds in the product are stronger than in the reactants. The overall reaction is exothermic and the heat evolved on hydrogenation of alkenes is defined as its heat of hydrogenation.

The uncatalysed addition of hydrogen to an alkene, although exothermic is slow. The rate of hydrogenation increases tremendously in presence of certain finely divided metal catalysts. Platinum, palladium, nickel, rhodium are generally used. Metal catalysed reactions are very rapid at room temperature and good yield of the products are obtained.

The solvent used in a catalytic hydrogenation is chosen as to dissolve the alkene. Generally acetic acid, ethanol and hexane are used. The metal catalysts are insoluble in these solvents. Two phases, the solution and the metal are present. The reaction takes place at the interface between them. Such reactions are known as heterogeneous reactions.

Heats of hydrogenation :

Heats of hydrogenation have been used to assess the relative stabilities of alkenes. Catalytic hydrogenation of 1–butene, cis – 2 – butene and trans – 2 – butene give same product butene. Measured heats of hydrogenation reveal that trans – 2 – butene is 4 KJ/mole lower in energy than cis – 2 – butene and cis – 2 – butene is 7 KJ/mole is lower in energy than 1 – butene.

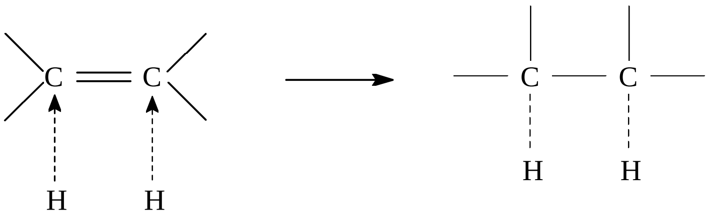
The following order will give the stability of alkenes.

$CH_2 = CH_2$, $RCH = CH_2$, $RCH = CHR$, $R_2CH = CHR$, $R_2C = CR_2$

$$\xrightarrow[\text{Increasing stability of double bond}]{\text{Decreasing heat of hydrogenation}}$$

Stereochemistry of alkene hydrogenation :

Hydrogenation of alkenes in presence of a metal catalyst takes place in which both the hydrogen atoms are added to the double bond from the same side of the alkene.

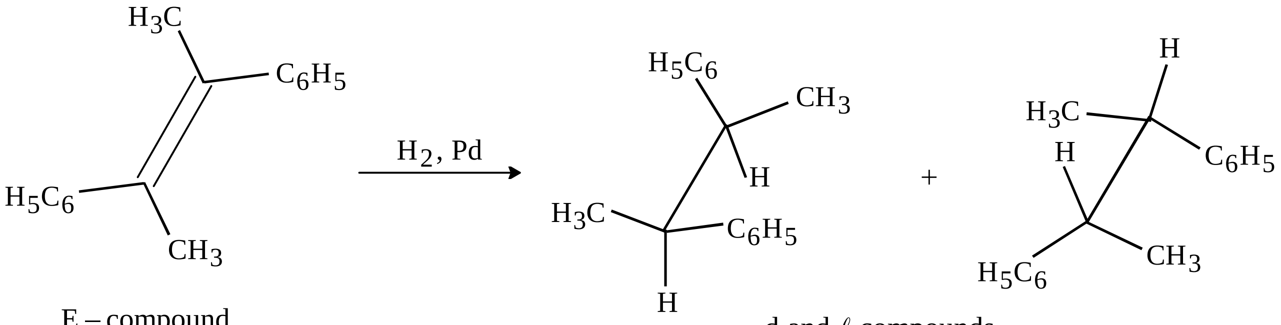


Syn – addition

The term syn – addition is used to for such addition reactions.

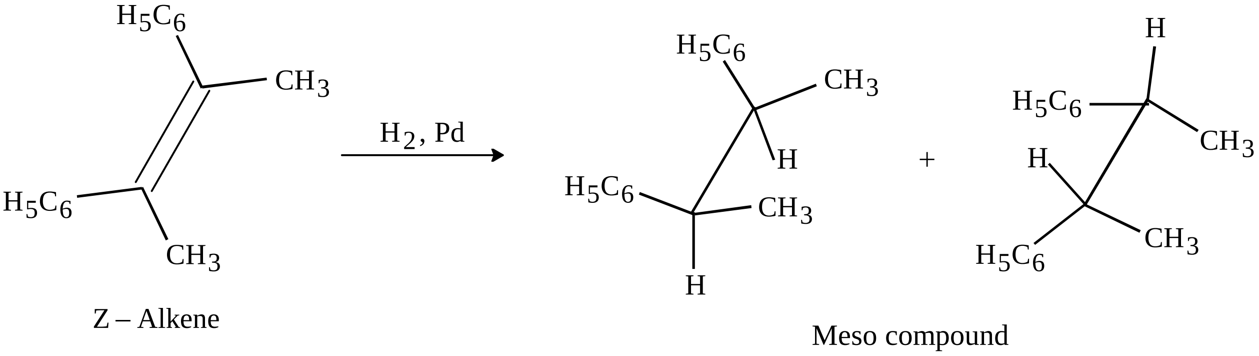
Example :

Hydrogenation of E – stilbene derivative gives a racemic mixture where as Z – stilbene derivative gives meso isomer.



E – compound

d and ℓ compounds



Hydrogenation of triple bonds :

The conditions of hydrogenation of alkynes are similar to those of alkenes. In presence of finaly divided catalysts two molar equivalents of hydrogen add to the triple bond of an alkyne to give alkane.

$$R-C\equiv CR^1+2H_2 \longrightarrow RCH_2-CH_2R^1$$

Substituents effect the heat of hydrogenation in the same way they effect alkenes.

Alkyl groups release the alkyne and decrease heat of hydrogenation.

	$CH_3CH_2C\equiv CH$ 1 – Butyne	$CH_3-C\equiv C-CH_3$ 2 – Butyne
$-\Delta H$	292 KJ/mole	275 KJ/mole

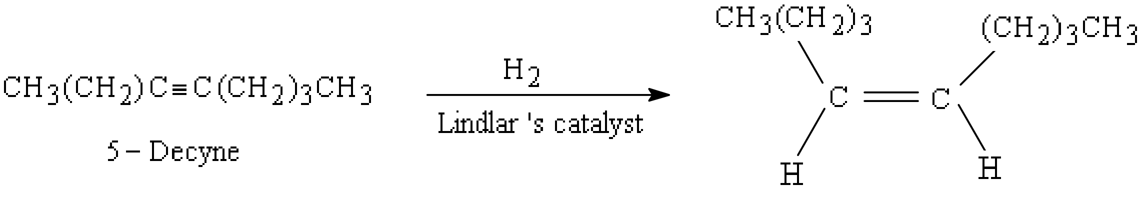
Alkenes are the intermediates in the hydrogenation of alkynes to alkanes.

$RC\equiv C-R \xrightarrow{H_2} RCH=CHR$ .... First addition

$RCH=CHR \xrightarrow{H_2} RCH_2-CH_2R$ .... Second addition

Partial hydrogenation provide a useful method for the synthesis of alkenes. This is most frequently affected by using Lindlar's catalyst. Palladium on calcium carbonate combination to which lead acetate or quinoline is added is known as Lindlar's catalyst. These substances partly deactivate the catalyst making it a poor catalyst for alkene hydrogenation while it can act as catalyst for hydrogenation of alkynes.

Hydrogenation of alkynes to alkene is highly stereoselective and give cis (or Z) alkenes by syn addition to triple bond.

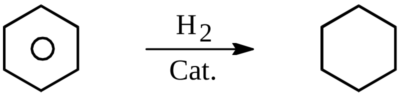


(Z) 5 – Decene (87%)

Hydrogenation of aromatic rings :

Aromatic systems are considered to be most stable systems. Hydrogenation of such systems by catalytic methods generally require higher temperature (100 to 200ºC) than ordinary double bonds.

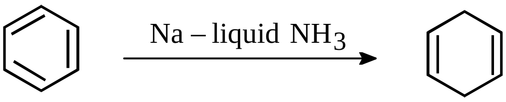
Though the reaction is usually carried out with heterogeneous catalysts, homogeneous catalysis have also been used, conditions are much milder.



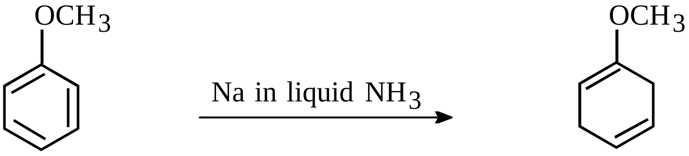
Many functional groups such as –OH, O^-, $-COOH$, $-COOR$ $-NH_2$ etc. do not interfere with the reaction but some groups may be reduced. Among these is $-CH_2OH$ which undergo hydrogenolysis to CH_3. Phenols may be reduced to cyclohexanones. Heterocyciclic compounds can be reduced. For example, furan on hydrogenation gives tetrahydrofuran.

Benzene on hydrogeneration does not stop only after hydrogenation of one or two double bonds. Thus one mole of benzene with one mole of hydrogen does not give cyclohexadiene or cyclohexene but $^1\!/_3$ rd mole of cyclohexane and $^2\!/_3$ rd moles benzene. This is not true for all aromatic systems. Phenanthrene on hydrogenation give 9, 10 – dihydro compounds.

When aromatic rings are reduced by sodium in liquid ammonia in presence an alcohol 1, 4 – addition of hydrogen takes place to give unconjugated cyclohexadiene. This reaction is known as Birch reduction.



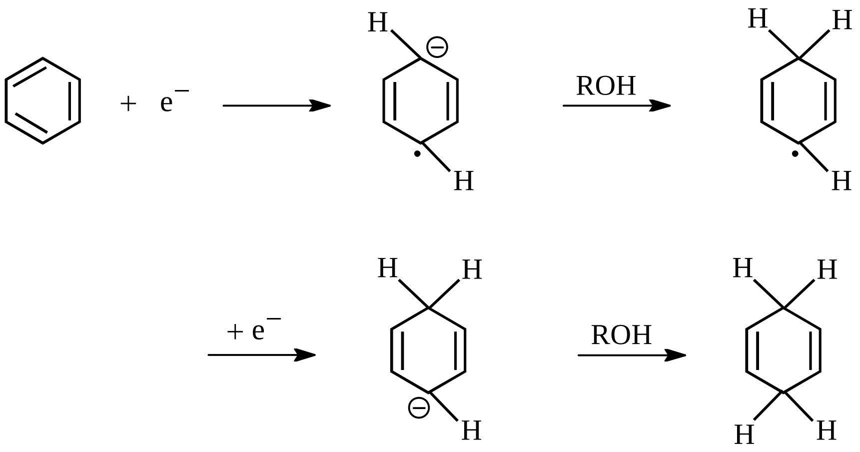
When substituted aromatic compounds are subjected to the Birch reduction, electron donating groups decrease the rate of reaction and are generally found on the non reduced position of product. For example, anisole on Birch reduction gives 1 – methoxy – 1, 4 cyclohexadiene.



On the other hand, electron withdrawing groups such as –COOH or $-CONH_2$ increase the reaction rate and are found on the reduced position of the product.

Mechanism :

Mechanism involves the direct transfer of electron from sodium to the ring producing a radical ion. The radical ion accepts a proton from the solvent to give a radical which is reduced to a carbanion by another sodium atom and proton is accepted to form the product.



Ordinary olefins are usually unaffected by Birch – reduction. Aromatic systems containing unconjugated double bonds are not affected by Birch reduction.

UNIT – III

MODEL QUESTIONS

1. “Markovnikov’s rule is based on the stability of intermediate carbocation” explain with an example.
2. What are the possible products of bromination of 1, 3 – butadiene which compound is formed in major amount ?
3. Give an example for chemoselectivity in electrophilic addition to alkene.
4. Discuss on the regioselectivity of electrophilic addition reactions.
5. What is general mechanism of an electrophilic substitution in benzene ?
6. Discuss briefly about the influence of a substituent about the orientation of substitution in benzene system.
7. What do you understand by ipso attack, explain with an example ?
8. What are free radicals ? How they are generated ? Write with suitable examples.
9. Discuss briefly about the free radicals addition of HX to an alkene.
10. What are diazocompounds ? How they are obtained ?
11. Write short notes on Sandmeyer reaction.
12. “Hundiecker reaction is useful to prepare alkyl halide”. Explain with an example.
13. What is meant by hydroboration ?
14. Write short notes on Michael reaction.
15. Coupling reaction are an important class of reactions for synthesis of azo compound. Explain briefly.

UNIT – IV :: Lesson – 1
ADDITION TO CARBON – HETERO MULTIPLE BONDS

4.1 Metal hydride reductions :

The most important reagents used for metal hydride reductions are aluminium alkoxide, lithium aluminium hydride and sodium borohydride.

4.1.i Meerwein – Pondorff – Verely reduction : (MPV reduction) :

The reduction of carbonyl compounds to alcohols with aluminium isopropoxide is called MPV reduction. The reaction is easily effected by heating the components in isopropyl alcohol. The product is obtained by distilling off acetone as it is formed.

The reaction is considered to proceed by transfer of hydride ion from the isopropoxide to the carbonyl compound through a six membered transition state.

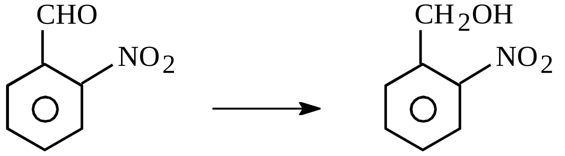
Aldehydes are reduced to primary alcohol, while ketones are reduced to give secondary alcohols. The advantage of this reaction is carbon – carbon double bonds and other unsaturated groups are unaffected.

Examples :

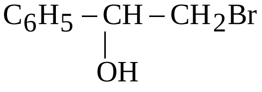
i) $C_6H_5CH = CHCHO \rightarrow C_6H_5CH = CHCH_2OH$

Cinnamaldehyde → Cinnamyl alcohol

ii)



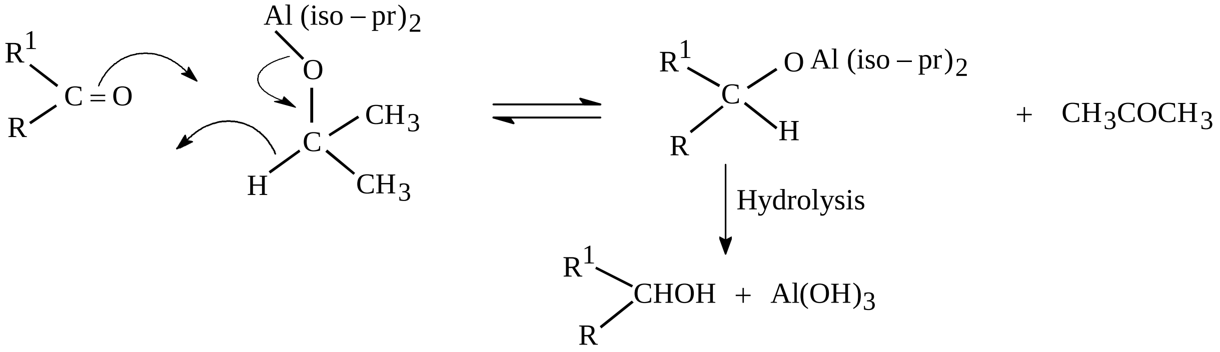
iii) $C_6H_5COCH_2Br \rightarrow$



$C_6H_5 - \underset{|}{\overset{}{CH}}\!\!\underset{OH}{} - CH_2Br$

Phenacyl bromide → Styrene bromohydrin

Mechanism :



4.1.ii Reduction with lithium aluminium hydride and sodium borohydride :

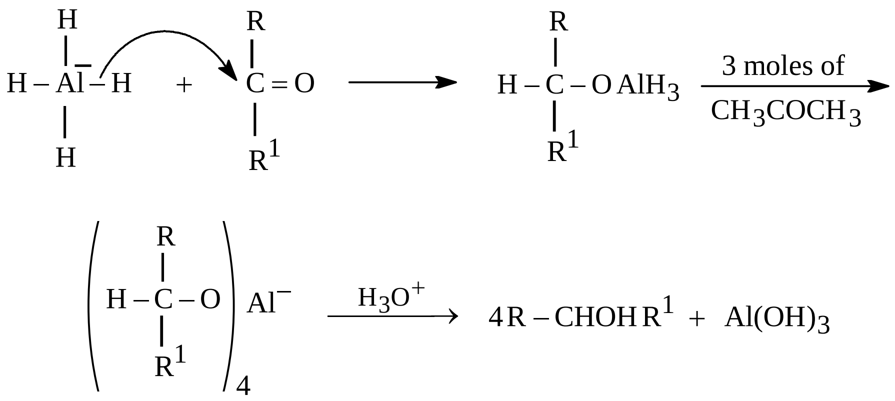
Lithium aluminium hydride ($LiAlH_4$) and sodium borohydride $(NaBH_4)$ are considered mixed hydrides.

$$LiH + AlH_3 \rightarrow LiAlH_4$$

$$NaH + BH_3 \rightarrow NaBH_4$$

The compounds on ionisation produce AlH_4^- and BH_4^- which act as nucleophiles and attack polarised multiple bonds such as C = O, $C \equiv N$ by transfer of hydride ion to the more positive atom. They do not reduce isolated C = C or $C \equiv C$.

All the four hydrogen atoms may be used for reduction, being transferred in a stepwise manner.

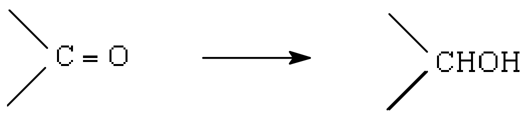


$$H_3\bar{Al}H + RR^1C{=}O \longrightarrow H{-}C(R)(R^1){-}OAlH_3 \xrightarrow[CH_3COCH_3]{\text{3 moles of}}$$

$$\left(H{-}C(R)(R^1){-}O\right)_4 Al^- \xrightarrow{H_3O^+} 4R-CHOHR^1 + Al(OH)_3$$

For reduction with $LiAlH_4$, each successive transfer of hydride ion takes place more slowly than one before.

$LiAlH_4$ is the most powerful reducing agent than $NaBH_4$ and reduces most common functional groups.



$$>C=O \longrightarrow >CHOH$$

$-COOR \longrightarrow -CH_2OH + ROH$

$-COOH \longrightarrow -CH_2OH$

$-C \equiv N \longrightarrow -CH_2NH_2$

$LiAlH_4$ reacts most readily with water and other compounds containing hydrogen atoms. Hence, the reduction with $LiAlH_4$ must be carried out under anhydrous conditions, and in non – hydroxylic solvents.

(ie.) ether, tetrahydrofuran (THF) are commonly used as solvents.

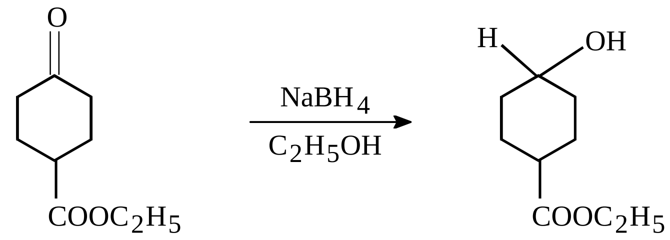
$NaBH_4$ reacts slowly with water and most alcohols at room temperature. Reduction is often effected in ethanol solution.

At room temperature, $NaBH_4$ readily reduces aldehydes and ketones, but it does not generally attack esters or amides.

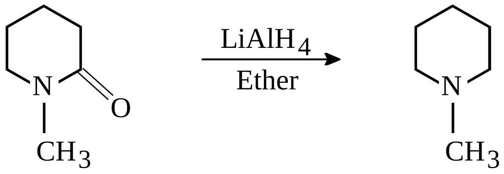
Examples :

i) $$CH_2 = CH - CH = CH - CHO \xrightarrow[NaBH_4]{LiAlH_4\ (or)} CH_2 = CH - CH = CH - CH_2OH$$

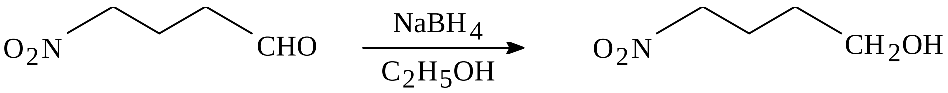
ii)



iii)



iv)

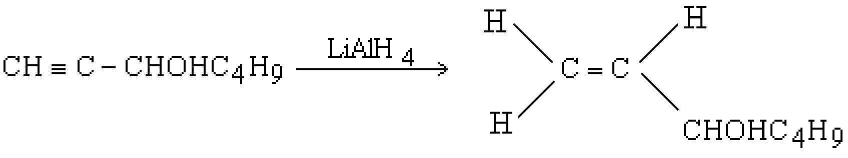


An exception to the general rule that carbon – carbon double bonds are not attackd by hydride reducing agents is found in the reduction of β – aryl – α, β – unsaturated carbonyl compounds with $LiAlH_4$.

$$C_6H_5CH = CH - CHO \xrightarrow[Ether\ \ 35°C]{LiAlH_4} C_6H_5CH_2CH_2CH_2OH$$

$$C_6H_5CH = CH - CHO \xrightarrow[\substack{LiAlH_4 \\ Ether\ \ -10°C}]{NaBH_4\ (or)} C_6H_5CH = CH - CH_2OH$$

Triple bonds flanked by hydroxyl groups are reduced.

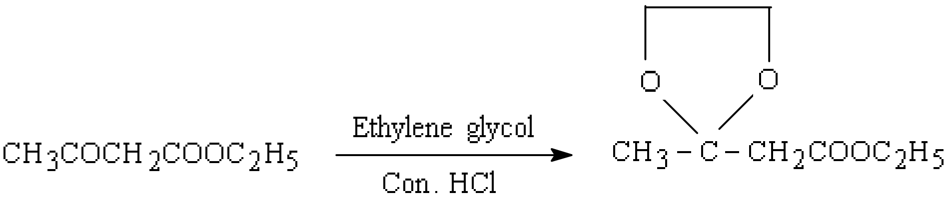


Aldehydes, ketones, carboxylic acids, ester amides can be reduced smoothly to corresponding alcohols under mild conditions.

$$CH_3COCH_2COOC_2H_5 \xrightarrow[\text{Ether}]{LiAlH_4} CH_3CHOHCH_2CH_2OH$$

$$\xrightarrow[\text{Ethanol}]{NaBH_4} CH_3CHOHCH_2COOC_2H_5$$

In order to reduce ester group in presence of a keto group in the molecule with $LiAlH_4$, the keto group must be protected. This can be done by reaction of the compound with ethylene glycol to produce a cyclic ketal, which then can be reduced and hydrolysis give ketone containing alcohol.



$$CH_3COCH_2COOC_2H_5 \xrightarrow[\text{Con. HCl}]{\text{Ethylene glycol}} CH_3-\overset{O\quad O}{C}-CH_2COOC_2H_5$$

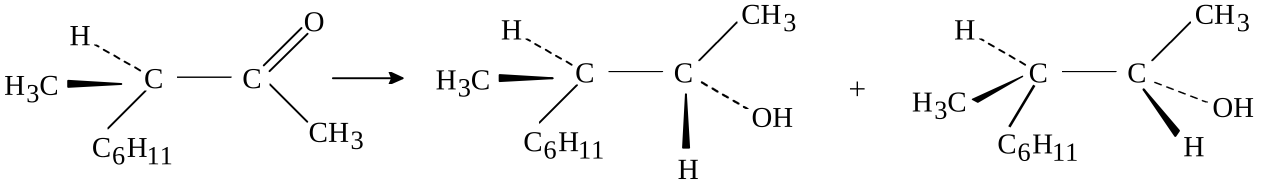
$$\xrightarrow[\text{(ii) } H_3O^+]{\text{(i) } LiAlH_4,\ \text{ether}} CH_3COCH_2CH_2OH$$

The reducing properties of $NaBH_4$ are substantially modified by the presence of certain salts. For example, in presence Ce(IV), selective reduction of a diketone can be effected.

– less reactive carbonyl group is reduced before the other.

Ketones can be reduced in the presence of aldehydes by reaction with one equivalent of $NaBH_4$ in aqueous ethanol in presence of cerium (IV) chloride. This reason for this is that the aldehyde group is protected as the hydrate, which is stabilised by complexation with the cerium ion.

Reduction of carbonyl groups of unsymmetrical ketone such as ethyl methyl ketones leads to the racemic mixture. Ketones in which an assymmetric carbon is present on the adjacent carbonyl carbon, the carbinols are not produced in equal amounts.

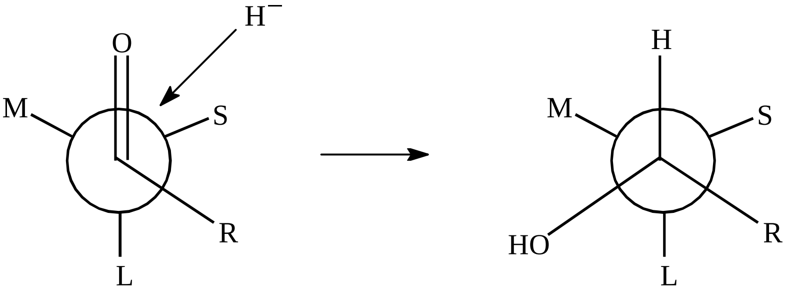


Threo (72%)

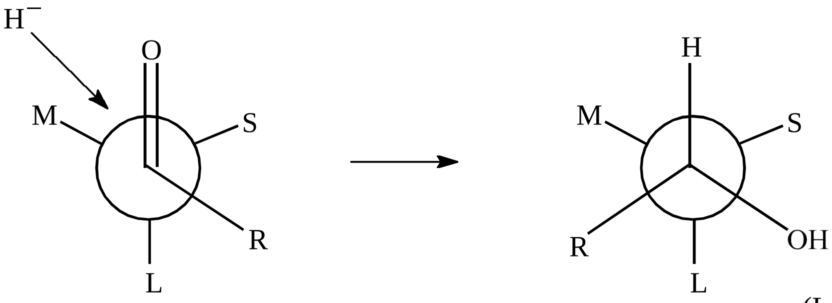
Erythro (28%)

The main compounds formed in these reactions can be predicted on the basis of **Cram's rule**.

According to Cram's rule, the diastereoisomer predominates in the product which is formed by the approach of the reagent to the less hindered side of the carbonyl group, when the rotational conformation of the molecule is such that the carbonyl group is flanked by two less bulky groups on the adjacent chiral centre.



(Predominant)



(Less predominant)

L – Large size group
M – Medium size group
S – Small size group

4.1.iii Reduction of carboxylic acids to alcohols :

$$\mathrm{RCOOH} \xrightarrow{\mathrm{LiAlH_4}} \mathrm{RCH_2OH}$$

Carboxylic acids are usually reduced to primary alcohols by $\mathrm{LiAlH_4}$. The reaction does not step at aldehyde stage. The reduction takes place under mild conditions at room temperature. The reduction of –COOH groups takes place without affecting carbon – halogen bonds in the same molecule.

Reduction of carboxylic esters with $\mathrm{LiAlH_4}$ give ethers.

$$\mathrm{RCOOR^1} \xrightarrow{\mathrm{LiAlH_4}} \mathrm{RCH_2OR^1}$$

The more usual course of reaction is two produce two alcohols (ie.) $\mathrm{RCH_2OH}$ and $\mathrm{R^1OH}$.

Sodium borohydride reduces phenolic esters, containing electron – withdrawing groups.

Reduction of cyanides produce amines.

$$\mathrm{RCN} \xrightarrow{\mathrm{LiAlH_4}} \mathrm{RCH_2NH_2}.$$

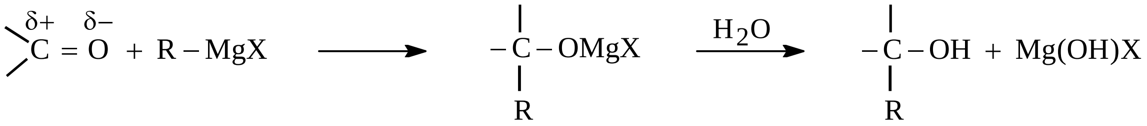
4.1.iv Addition of Grignard reagent to Carbonyl compounds

This reaction is very much useful for the preparation of primary, secondary and tertiary alcohol by appropriately selecting the carbonyl compound and Grignard reagent. Grignard reagents are prepared by treating magnesium metal with an alkyl halide in dry ether. Absolutely dry condition must be maintained for good yield of Grignard reagent.

$$RX + Mg \xrightarrow{\text{dry ether}} RMgX$$

Of the alkyl halides iodides reacts much faster than bromides which in turn react faster than chlorides.

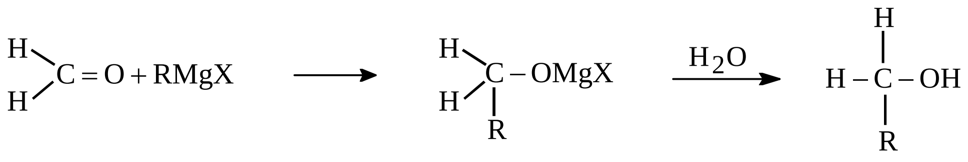
The carbon – magnesium bond of the Grignard reagent is highly polar bond, carbon being negative relative to electropositive magnesium. In the addition to carbonyl compounds, the organic group becomes attached to carbon and magnesium to oxygen.



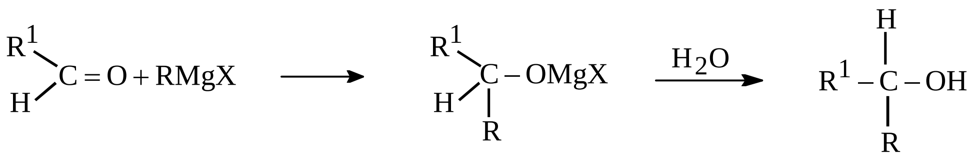
The product is the magnesium salt of the weakly acidic alcohol and can be easily converted into alcohol by the addition of the water.

4.1.v Products of the Grignard synthesis :

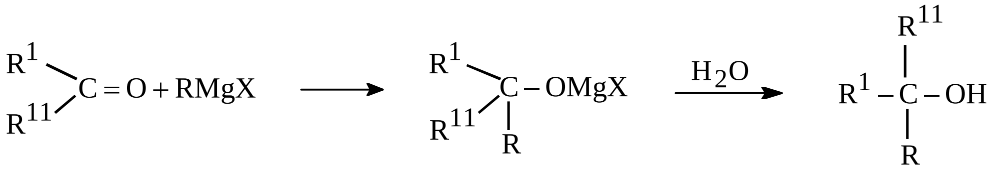
The class of alcohol obtained from Grignard synthesis depends upon the type of carbonyl compounds used. Formaldehyde (HCHO) yields primary alcohols, other aldehydes, (RCHO) yield secondary alcohols and ketone (R_2CO) yield tertiary alcohols.



Primary alcohol

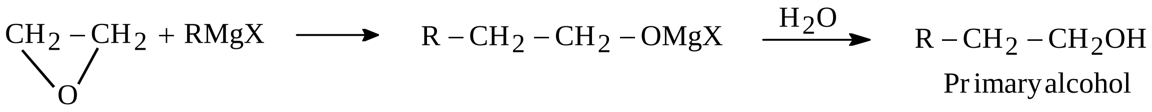


Secondary alcohol



Tertiary alcohol

Ethylene oxide reacts with Grignard reagent to give primary alcohol.

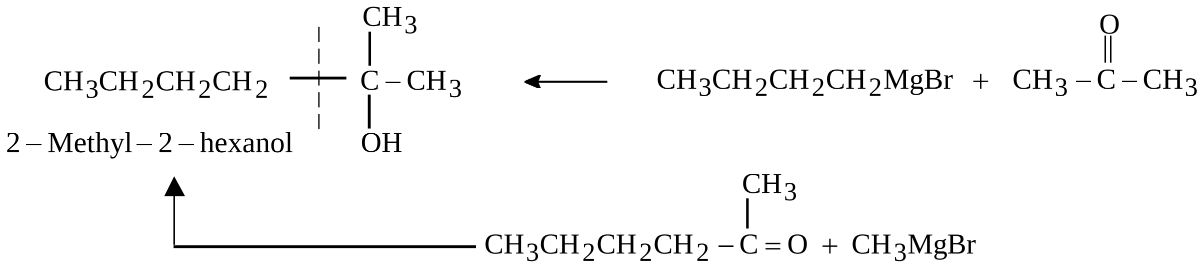


$$\underset{\text{O}}{CH_2-CH_2} + RMgX \longrightarrow R-CH_2-CH_2-OMgX \xrightarrow{H_2O} \underset{\text{Primary alcohol}}{R-CH_2-CH_2OH}$$

4.1.vi Planning a Grignard synthesis :

It is always necessary to identity what carbonyl compound and Grignard reagent must be selected in order to prepare a required alcohol in the laboratory. A look at the structure of the required alcohol reveal that, the groups bonded to the carbon atom bearing –OH group, one must come from the Grignard reagent, the other two (including any hydrogens) must come from the carbonyl compound.

Let us consider the synthesis of 2 – methyl – 2 – hexanol. This alcohol can be prepared from more than one combination of the reagents.



$$\underset{\text{2 – Methyl – 2 – hexanol}}{CH_3CH_2CH_2CH_2-\overset{CH_3}{\underset{OH}{C}}-CH_3} \longleftarrow CH_3CH_2CH_2CH_2MgBr + CH_3-\overset{O}{\overset{\|}{C}}-CH_3$$

$$\uparrow\ CH_3CH_2CH_2CH_2-\overset{CH_3}{C}=O + CH_3MgBr$$

4.1.vii Limitation in Grignard synthesis :

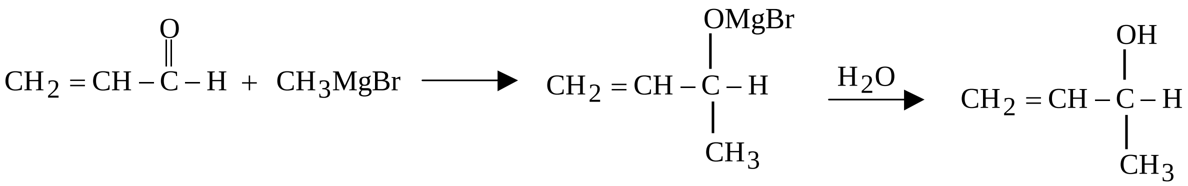
Grignard reagents are extremely reactive compounds and react readily with water to produce alkanes. In the same way any compound containing hydrogen attached to electronegative elements like oxygen, nitrogen, sulphur or even triply bonded carbon decompose Grignard reagent.

Alkyl halides, carbonyl compound and the ether used as solvent must be scrupulously dried. During the experiments contents of the reaction must be protected from moisture. It is not possible to prepare Grignard reagents from such compounds containing –OH groups.

4.1.viii Addition of Grignard reagents to α, β – unsaturated carbonyl compounds :

1, 2 – Addition of Grignard reagent :

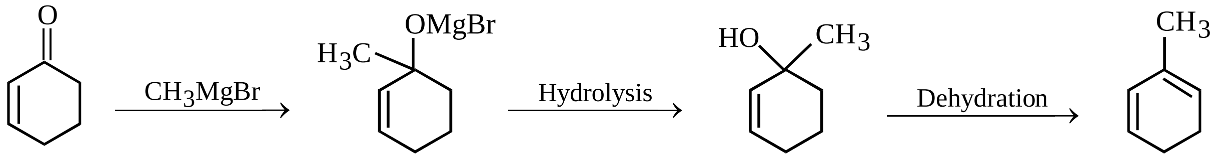
Grignard reagents undergo 1, 2 – addition to α, β – unsaturated carbonyl compounds to give an addition product which on acid hydrolysis give corresponding alcohol.



$$CH_2=CH-\overset{O}{\overset{\|}{C}}-H + CH_3MgBr \longrightarrow CH_2=CH-\overset{OMgBr}{\underset{CH_3}{C}}-H \xrightarrow{H_2O} CH_2=CH-\overset{OH}{\underset{CH_3}{C}}-H$$

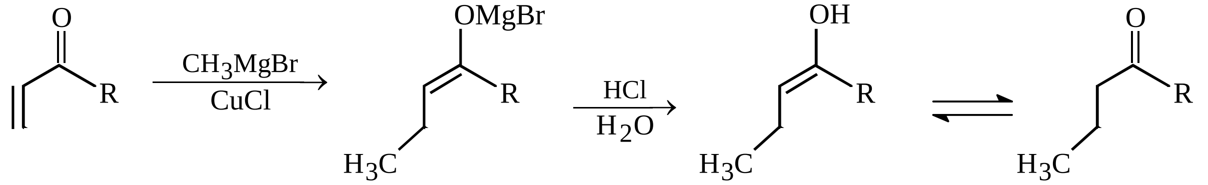
This reaction is widely useful in organic synthesis. For example conjugated dienes useful in Diels – Alder addition can be readily obtained from this reaction.

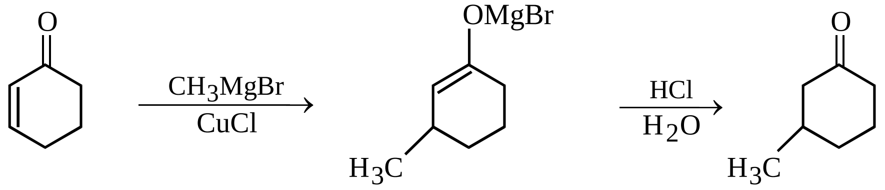
Example :



4.1.ix 1, 4 – addition of Grignard reagent :

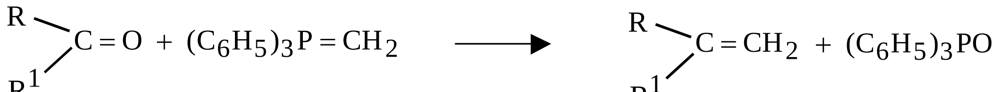
In pressure of copper salts as catalysts the nucleophilic carbon of the Grignard reagent add to the β – carbon of an α, β – unsaturated carbonyl compound to give an addition product which on hydrolysis give a product of 1, 4 – addition.





4.1.x Wittig reaction :

Wittig reaction is an important reaction for synthesis of alkenes from aldehydes or ketones. The reaction involves the treatment of an aldehyde or ketone with alkylidenetriphenyl phosphoranes (Wittig reagents)

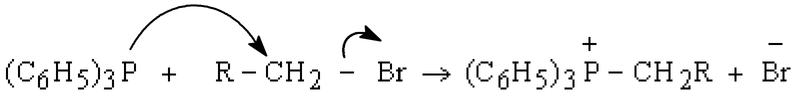


$$R(R^1)C=O + (C_6H_5)_3P=CH_2 \longrightarrow R(R^1)C=CH_2 + (C_6H_5)_3PO$$

Triphenylphosphine oxide

Before going to study the mechanistic aspects of Wittig reaction, it is necessary to understand as to how the Wittig reagents are obtained.

Alkylidenetriphenyl phosphoranes are usefully prepared by treating triphenyl phosphine with an alkyl halide and then abstracting the alpha hydrogen from the resultant phosphonium salt by the action of strong base such as sodamide or sodium hydride.



$$(C_6H_5)_3P + R-CH_2-Br \rightarrow (C_6H_5)_3\overset{+}{P}-CH_2R + \overset{-}{Br}$$

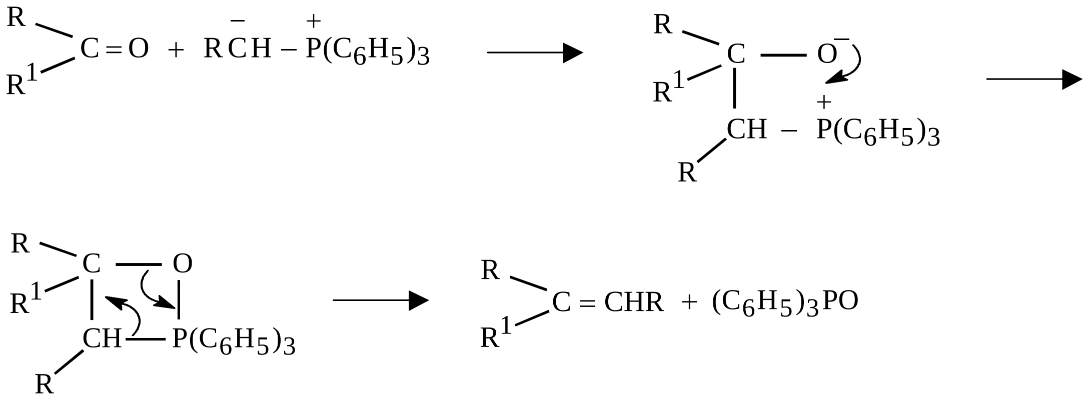
$$(C_6H_5)_3\overset{+}{P}-CH_2-R \xrightarrow{\text{Base}} (C_6H_5)_3P=CHR$$

(Wittig reagent)

Mechanism :

$$(C_6H_5)_3 = CHR \longleftrightarrow (C_6H_5)_3\overset{\oplus}{P} - \overset{\ominus}{C}HR$$

Phosphorane form   Ylide form



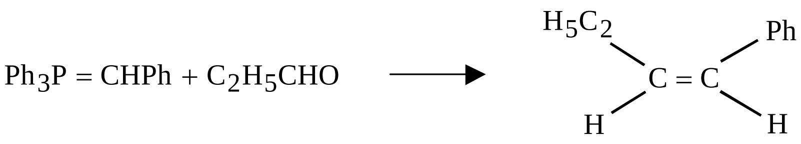
The main step in the reaction is the nucleophilic attack on carbonyl carbon of the aldehyde or ketone by the alkylidenetriphenylphosphorane (a carbanion stabilised by resonance with d - orbitals of adjascent phosphonium cation). The initial addition product formed subsequently decompose to produce an alkene and triphenyl phosphine oxide via four membered cyclic transition state.

Wittig reaction is accelerated by the presence of electron withdrawing groups in the carbonyl compounds.

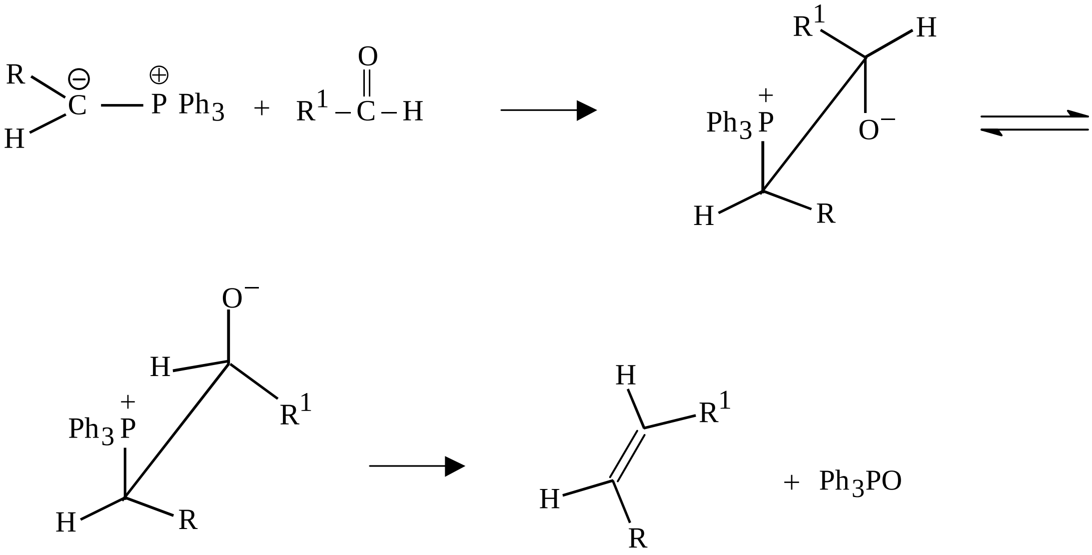
This reaction involves the conversion of C = O into C = C. The reaction has an advantage in that the position of double bond is the position in which C = O group is present and no other alkene products are obtained.

4.1.xi Stereoselectivity in Wittig reaction :

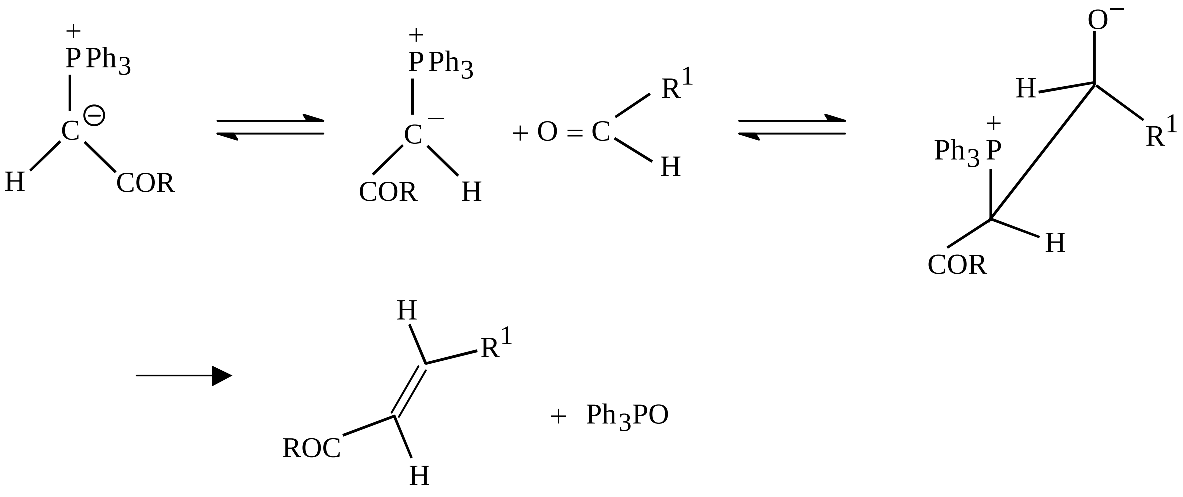
It was found in general that unstabilised phosphoranes give predominantly Z – alkenes in presence of polar solvents. For example, the Wittig reagent gives below react with propanal to give 95% of Z – alkene in presence of dimethyl formamide and lithium iodide.



The reasons for the selectivity are based on the steric effects develop when the carbonyl compound and the reagent approach. On the case of unstabilised reagent, the formation of betaine is irreversible and betaine which is formed determines the major product. Polar solvent in this reaction solvate the betaine. Further, the elimination of triphenyl phosphine oxide is syn, and hence predominant amount of Z – alkene is obtained.



In case of stabilised phosphoranes, the formation of the intermediate betaine is reversible and this allows the formation of the more stable stereoisomeric form of betaine. Thus reaction proceeds through the more stable betaine and syn – elimination of triphenylphosphine oxide results in the formation of E – alkene.



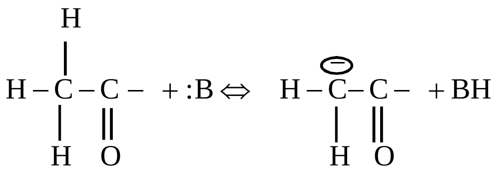
(E – alkene)

UNIT – IV :: Lesson – 2

MECHANISM OF CONDENSATION REACTIONS INVOLVING ENOLATE ANION

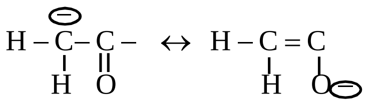
4.2 Any molecule having a carbonyl group with an α – hydrogen atom can exists in two tautomeric forms called keto-enol tautomerism. The α – hydrogen with the influence of carbonyl group behaves like an acidic hydrogen and in presence of a base, a proton can be extracted to form a carbanion.

This carbanion is stabilised by the carbonyl group.



$$H-\overset{H}{\underset{H}{C}}-\underset{O}{\overset{\|}{C}}- + :B \Leftrightarrow H-\overset{\ominus}{\underset{H}{C}}-\underset{O}{\overset{\|}{C}}- + BH$$

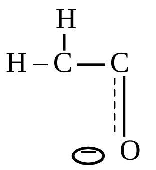
I



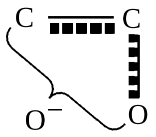
$$H-\overset{\ominus}{\underset{H}{C}}-\underset{O}{\overset{\|}{C}}- \leftrightarrow H-\underset{H}{C}=\underset{O^{\ominus}}{C}$$

I II

The resonance hybrid of enolate can be represented as



III



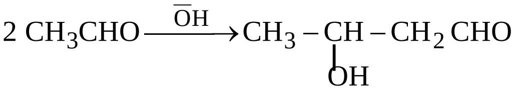
I is called as carbanion and it is the conjugate base of carbon acid that is, an acid which loses a proton from carbon.

The carbanion like this stabilised by the adjacent carbonyl group and is called enolate anion. It is this enolate anion that will participate in reaction.

The carbonyl group occurs in aldehydes, ketones, esters. These groups make the α – hydrogens acidic and this acids in the formation of carbanions. These carbanions are extremely reactive species and behave like nucleophiles. These nucelophiles can attack on other electrophilic carbon atoms to form a carbon-carbon bond.

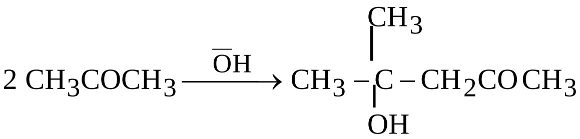
4.2.i Aldol condensation :

In presence of dilute base two molecules of an aldehyde or a ketone combine to form a β – hydroxy aldehyde or β – hydroxy ketone. This reaction is known as aldol condensation.



$$2\,CH_3CHO \xrightarrow{\overline{O}H} CH_3-\underset{OH}{\underset{|}{CH}}-CH_2CHO$$

3 – hydroxy butanal



$$2\ CH_3COCH_3 \xrightarrow{\overline{O}H} CH_3-\underset{OH}{\overset{CH_3}{C}}-CH_2COCH_3$$

4 – hydroxy – 4methyl pentanal

If aldehyde or ketone does not have an $\alpha-$ hydrogen, aldol condensation cannot take place.

Ex : Aryl aldehydes ArCHO
Formaldehyde HCHO
Trimethyl acetaldehyde $(CH_3)_3C.CHO$
Aryl ketone ArCO Ar
These compounds do not undergo aldol condensation.

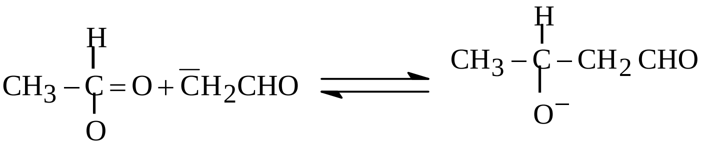
Mechanism :

Step (1)

$$CH_3CHO+\overline{O}H \rightleftharpoons H_2O+\overline{C}H_2\,CHO$$

(IV)

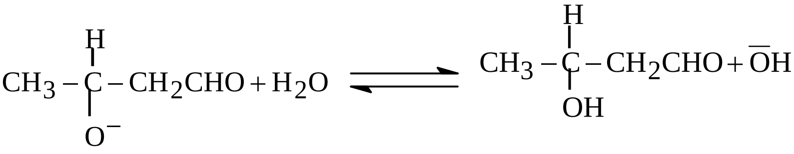
Step (2)



$$CH_3-\underset{O}{\overset{H}{C}}=O+\overline{C}H_2CHO \rightleftharpoons CH_3-\underset{O^-}{\overset{H}{C}}-CH_2\,CHO$$

(v)

Step (3)



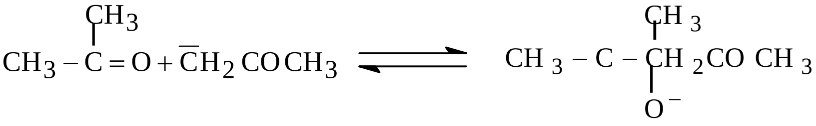
$$CH_3-\underset{O^-}{\overset{H}{C}}-CH_2CHO+H_2O \rightleftharpoons CH_3-\underset{OH}{\overset{H}{C}}-CH_2CHO+\overline{O}H$$

(vi)

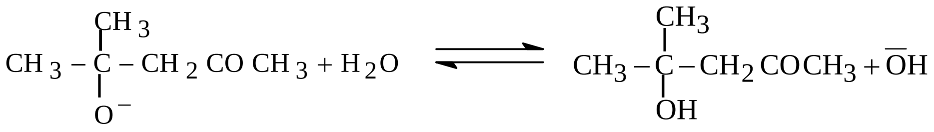
In step (1), base abstracts a proton from the $\alpha-$ carbon atom of the aldehyde to form carbanion IV. This carbanion IV attacks (step 2) carbonyl carbon to form ion V. Ion V abstracts a hydrogen ion from water to form $\beta-$hydroxyaldehyde VI, regenerating hydroxide ion.

In a similar way the compound in aldol condensation using acetone can be represented as

$$CH_3COCH_3+\overline{O}H \Leftrightarrow \overline{C}H_2COCH_3+H_2O$$



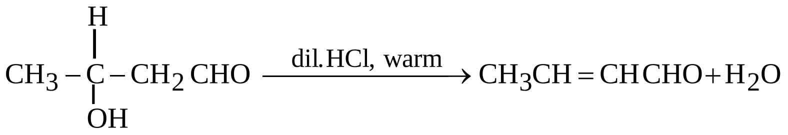
$$CH_3-\overset{CH_3}{C}=O+\overline{C}H_2COCH_3 \rightleftharpoons CH_3-C-\underset{O^-}{\overset{CH_3}{C}}H_2CO\,CH_3$$



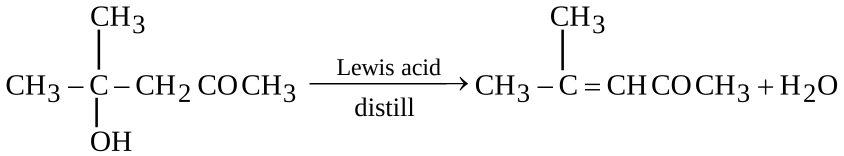
$$CH_3-\overset{CH_3}{\underset{O^-}{\overset{|}{\underset{|}{C}}}}-CH_2COCH_3+H_2O \rightleftharpoons CH_3-\overset{CH_3}{\underset{OH}{\overset{|}{\underset{|}{C}}}}-CH_2COCH_3+\overline{O}H$$

4.2.ii Dehydration of aldol products :

The products obtained in aldol condensation can be dehydrated very easily to get α,β -unsaturated carbonyl compounds.

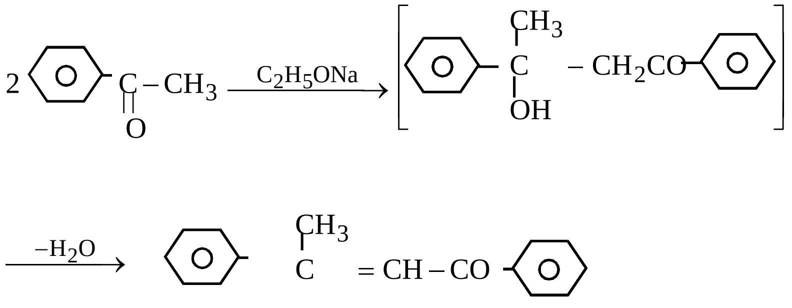


$$CH_3-\overset{H}{\underset{OH}{\overset{|}{\underset{|}{C}}}}-CH_2CHO \xrightarrow{\text{dil.HCl, warm}} CH_3CH=CHCHO+H_2O$$



$$CH_3-\overset{CH_3}{\underset{OH}{\overset{|}{\underset{|}{C}}}}-CH_2COCH_3 \xrightarrow[\text{distill}]{\text{Lewis acid}} CH_3-\overset{CH_3}{\overset{|}{C}}=CHCOCH_3+H_2O$$

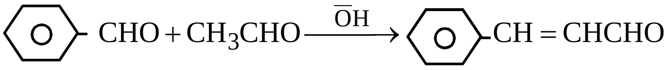
Elimination of water takes place easily because the alkene obtained is stable due to presence of carbon-oxygen double bond in conjugation with the carbon-carbon double bond formed. When aromatic ketones are used the product finally obtained is dehydrated one, as the alkene is particularly stable due to its conjugation with aromatic ring. The same can be explained by the following example in which the aldol condensation of acetophenone results in the formation of an alkene.



4.2.iii Crossed aldol condensation :

A aldol condensation between two different carbonyl compounds is called crossed aldol condensation. The reaction is generally not conducted in the laboratory, because a mixture of four products are obtained when two different carbonyl compounds are used. However, exclusive aldol product can be obtained when one of the carbonyl compounds contains no $\alpha-$ hydrogen.

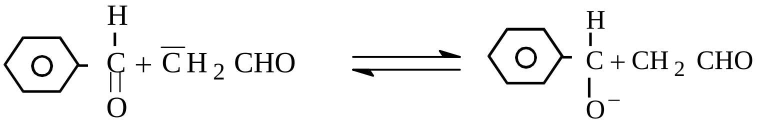
For example an aldol condensation between benzaldehyde and acetaldehyde is crossed aldol condensation reaction . As there is no $\alpha-$ hydrogen in benzaldehyde self condensation cannot takes place. The carbanion can be produced only from acetaldehyde which can attack on carbonyl carbon of benzaldehyde.



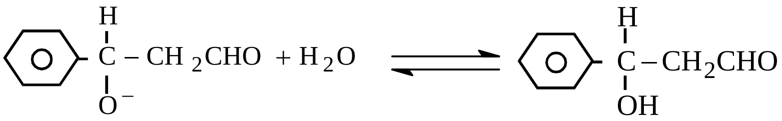
Mechanism:

Step (1) $$CH_3CHO + \overline{O}H \rightleftharpoons \overline{C}H_2CHO + H_2O$$

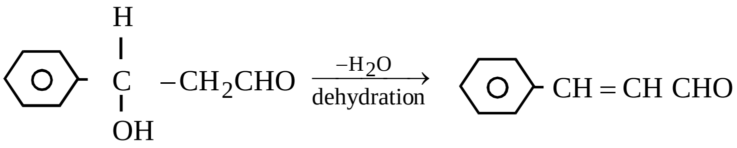
Step (2)



Step (3)



Step (4)

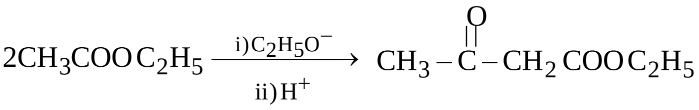


A similar aldol condensation can also be considered for reaction between formaldehyde and acetaldehyde.

4.2.iv Claisen condensation :

An $\alpha-$ hydrogen in an ester also behaves like acidic hydrogen and in presence of base a carbanion can be produced. Claisen condensation involves the condensation of two molecules of an ester to give a $\beta-$ keto ester. Carbanion formed from one molecule of ester acting as a nucleophile can attack on the carbonyl group in the other ester molecule resulting in a substitution reaction.

When ethyl acetate is treated with sodium ethoxide, followed by acidification gives acetoacetic ester

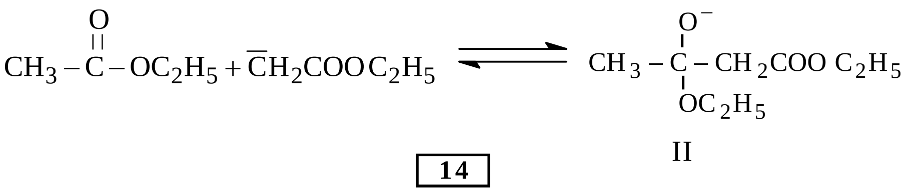


$$2CH_3COOC_2H_5 \xrightarrow[ii)H^+]{i)C_2H_5O^-} CH_3-\overset{\overset{\Large O}{||}}{C}-CH_2COOC_2H_5$$

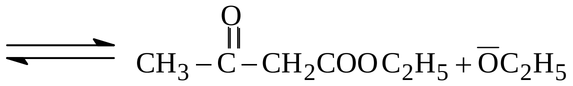
Mechanism :

Step (1) $$CH_3COOC_2H_5 + C_2H_5O^- \rightleftharpoons \underset{I}{\overline{C}H_2COOC_2H_5} + C_2H_5OH$$

Step (2)



$$CH_3-\overset{\overset{O}{||}}{C}-OC_2H_5 + \overline{C}H_2COOC_2H_5 \rightleftharpoons \underset{II}{CH_3-\underset{OC_2H_5}{\overset{O^-}{\overset{|}{\underset{|}{C}}}}-CH_2COOC_2H_5}$$

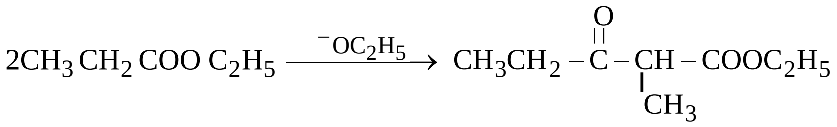


$$\rightleftharpoons CH_3-\overset{\overset{\displaystyle O}{||}}{C}-CH_2COOC_2H_5+\bar{O}C_2H_5$$

III

In step (1) ethoxide ion abstracts a proton from $\alpha-$carbon atom of the ester to form a carbanion (I). This carbanion being a nucleophile can attack on carbonyl carbon of another molecule of ester to displace ethoxide ion to give acetoacetic ester.

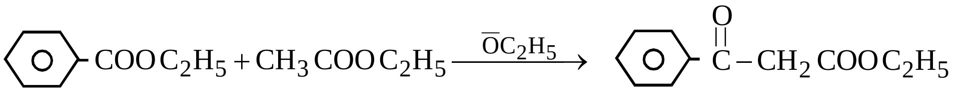
If ethyl propionate is used in Claisen condensation the product obtained again a $\beta-$ keto ester.



$$2CH_3CH_2COOC_2H_5 \xrightarrow{^-OC_2H_5} CH_3CH_2-\overset{\overset{\displaystyle O}{||}}{C}-\underset{\underset{\displaystyle CH_3}{|}}{CH}-COOC_2H_5$$

4.2.v Crossed Claisen condensation :

Like crossed aldol condensation, crossed Claisen condensation is generally feasible only when one of the esters does not contain $\alpha-$hydrogen. For example condensation between ethylbenzoate (no $\alpha-$hydrogen) and ethyl acetate the product is ethyl benzoyl acetate.



4.2.vi Knoevenagel reaction :

Condensation of an aldehyde or a ketone with compounds having active methylene group in presence of a base to give $\alpha,\beta-$unsaturated compound is called Knoevenagel reaction. The generally used bases in this reaction are primary amines, secondary amines, tertiary amines. For example aniline (or) dialkyl amines (or) trialkyl amines (or) pyridine or piperidine etc.

$$C_6H_5CHO + CH_2(COOR)_2 \xrightarrow{\text{Pyridine}} C_6H_5CH = C(COOR)_2$$

Benzaldehyde   Malonic ester

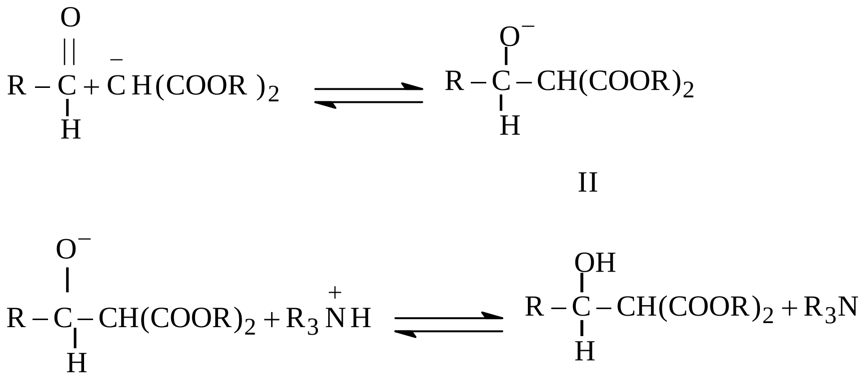
$$\xrightarrow[\text{ii) heating}]{\text{i) hydrolysis}} C_6H_5CH = CHCOOH$$

cinnamic acid

Mechanism

Step (1) $R_3\ddot{N}+CH_2(COOR)_2 \rightleftharpoons R_3\overset{+}{N}H+\overset{-}{C}H(COOR)_2$

I



Step (2)

$$R-\overset{\overset{\displaystyle O}{||}}{\underset{\underset{\displaystyle H}{|}}{C}}+\overset{-}{C}H(COOR)_2 \rightleftharpoons R-\overset{\overset{\displaystyle O^-}{|}}{\underset{\underset{\displaystyle H}{|}}{C}}-CH(COOR)_2$$

II

Step (3)

$$R-\overset{\overset{\displaystyle O^-}{|}}{\underset{\underset{\displaystyle H}{|}}{C}}-CH(COOR)_2+R_3\overset{+}{N}H \rightleftharpoons R-\overset{\overset{\displaystyle OH}{|}}{\underset{\underset{\displaystyle H}{|}}{C}}-CH(COOR)_2+R_3N$$

Step (4) $\xrightarrow[\text{ii) heating}]{\text{i) hydrolysis}} RCH=CH-COOH$

In the first step base removes a proton from active methylene group to generate a carbanion. The carbanion then attacks on the carbonyl carbon of the aldehyde (or ketone) to give II (step 2), which abstracts the proton to form a hydroxy compound III, (step 3). III on hydrolysis and decarboxylation gives an $\alpha,\beta-$unsaturated acid.

The reaction is given by both aromatic as well as aliphatic aldehyde. In this reaction ketones are less reactive than aldehyde due to steric and electronic effects.

Knoevenagel reaction is useful for preparation a number of $\alpha,\beta-$unsaturated acids like

Crotonic acid $CH_3CH=CHCOOH$

Cinnamic acid $C_6H_5CH=CHCOOH$ etc.

4.2.vii Perkin reaction :

A condensation reaction between an aromatic aldehyde with an acid anhydride (having at least two $\alpha-$hydrogen atoms) in presence of sodium or potassium salt of the corresponding acid, to gives $\alpha,\beta-$unsaturated compound is called Perkin reaction.

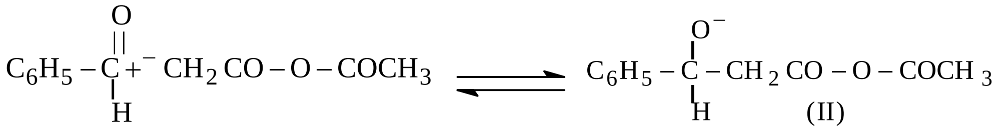
$$C_6H_5CHO+(CH_3CO)_2O \xrightarrow[170\text{–}180^oC]{CH_3COONa} C_6H_5CH=CHCOOH+CH_3COOH$$

Mechanism :

Step (1) $CH_3CO-O-COCH_3+CH_3CO\overline{O} \rightleftharpoons CH_3COOCO\overline{C}H_2+CH_3COOH$

acetic hydride

I

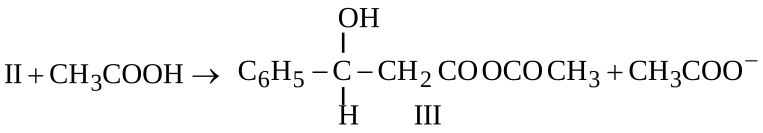


Step (2)

$$C_6H_5-\overset{\overset{\displaystyle O}{||}}{\underset{\underset{\displaystyle H}{|}}{C}}+\overset{-}{C}H_2CO-O-COCH_3 \rightleftharpoons C_6H_5-\overset{\overset{\displaystyle O^-}{|}}{\underset{\underset{\displaystyle H}{|}}{C}}-CH_2CO-O-COCH_3$$

(II)

Step (3)



$$II + CH_3COOH \rightarrow C_6H_5-\underset{\displaystyle H}{\overset{\displaystyle OH}{\underset{|}{\overset{|}{C}}}}-CH_2COOCOCH_3 + CH_3COO^-$$

III

Step (4) $$III \xrightarrow[-H_2O]{170^o} C_6H_5-CH=CH.COOCOCH_3$$

IV

Step (5) $$IV \xrightarrow{\text{hydrolysis}} C_6H_5-CH=CHCOOH + CH_3COOH$$

V

Acetate ion acting like a base abstracts a proton from the anhydride to form a carbanion (I).

The carbanion (I) attacks on the carbonyl carbon atom of aromatic aldehyde to give (II) which interms takes up proton from acetic acid to give (III). III undergoes dehydration on heating to give IV which on hydrolysis gives Cinnamic acid (V).

The reaction is specific for aromatic aldehydes which cannot undergo self condensation in presence of base.

4.2.viii Mannich Reaction :

The condensation of a compound containing active hydrogen with formaldehyde in presence of ammonia or primary, secondary amines to form amino methyl or substituted amino methyl derivative is known as Mannich reaction. The base called Mannich base is usually isolated as its hydrochloride. Aryl amines do not normally respond in this reaction.

$$C_6H_5COCH_3 + HCHO + (CH_3)_2NH.HCl \longrightarrow C_6H_5COCH_2CH_2N(CH_3)_2HCl + H_2O.$$

With ammonia or primary amines the reaction may proceed further since the first formed Mannich base still contains hydrogen on nitrogen atom.

$$CH_3COCH_3 + HCHO + CH_3NH_2.HCl \longrightarrow CH_3COCH_2CH_2NH.CH_3.HCl + H_2O$$

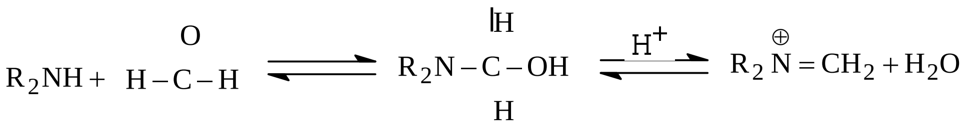
$$\xrightarrow{HCHO} (CH_3COCH_2CH_2)_2N.CH_3.HCl + H_2O\cdot$$

Hence, secondary amines are generally preferred for this reaction.

The active hydrogen containing compound which participate in this reaction are aldehydes, ketones, esters, phenols, nitroalkanes, etc.

Mechanism :

In the first step amine and formaldehyde condense to form iminium cation.



$$R_2NH + H-\overset{\displaystyle O}{\overset{\|}{C}}-H \rightleftharpoons R_2N-\underset{\displaystyle H}{\overset{\displaystyle H}{\overset{|}{C}}}-OH \overset{H^+}{\rightleftharpoons} R_2\overset{\oplus}{N}=CH_2 + H_2O$$

It is then attacked by the enolate anion of the active hydrogen compound to from Mannich base.

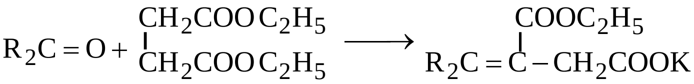
$$R'CO\overset{-}{C}H_2 + R_2\overset{+}{N}=CH_2 \rightleftharpoons \underset{\text{Mannich base}}{R'COCH_2CH_2NR_2}$$

4.2.ix Stobbe condensation :

Aldehydes and ketones condense with the diester of succinic acid in presence of base to give the salts of $\alpha,\beta-$ unsaturated half esters is known as Stobbe condensation.

Carbonyl compounds generally used are aliphatic, and $\alpha,\beta-$unsaturated aldehydes aliphatic aromatic, alicyclic ketones.

The bases generally used are : Sodium ethoxide (C_2H_5ONa), Potassium tert-butoxide (Me_3COK) or sodium hydride (NaH).

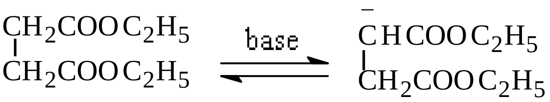


$$R_2C=O+\begin{array}{l}CH_2COOC_2H_5\\ |\\ CH_2COOC_2H_5\end{array} \longrightarrow R_2C=\begin{array}{l}COOC_2H_5\\ |\\ C-CH_2COOK\end{array}$$

The reaction is specific for succinic ester.

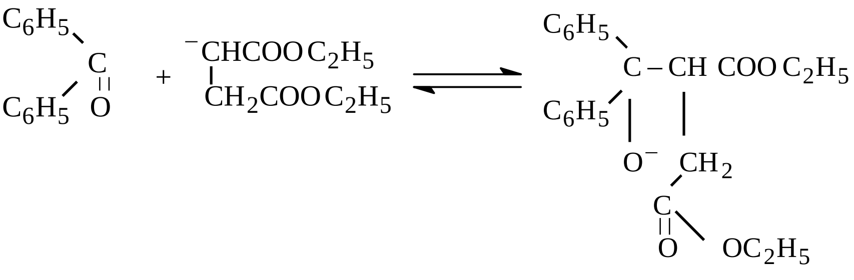
Mechanism :

The base abstracts a proton from succinic ester to give carbanion in the first step.

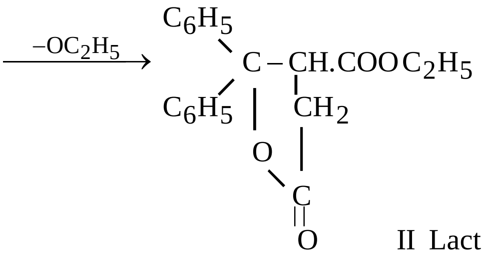


$$\begin{array}{l}CH_2COOC_2H_5\\ |\\ CH_2COOC_2H_5\end{array} \xrightleftharpoons{\text{base}} \begin{array}{l}\overset{-}{C}HCOOC_2H_5\\ |\\ CH_2COOC_2H_5\end{array}$$

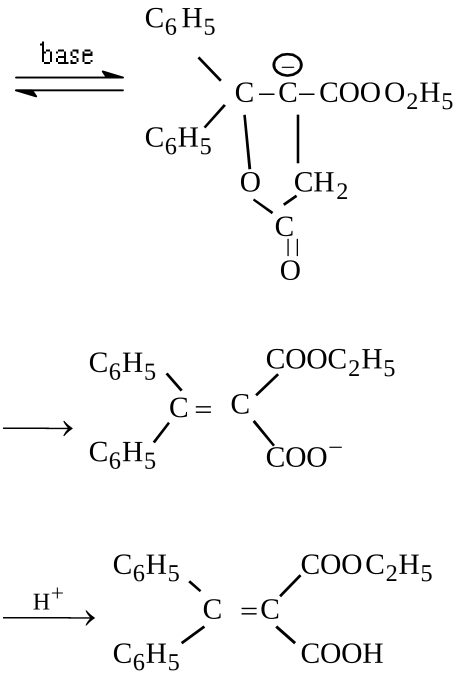
The carbanion then attacks on the carbonyl carbon to give (I)



I

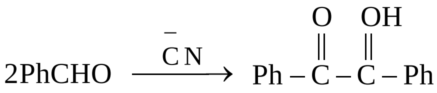


II Lactone



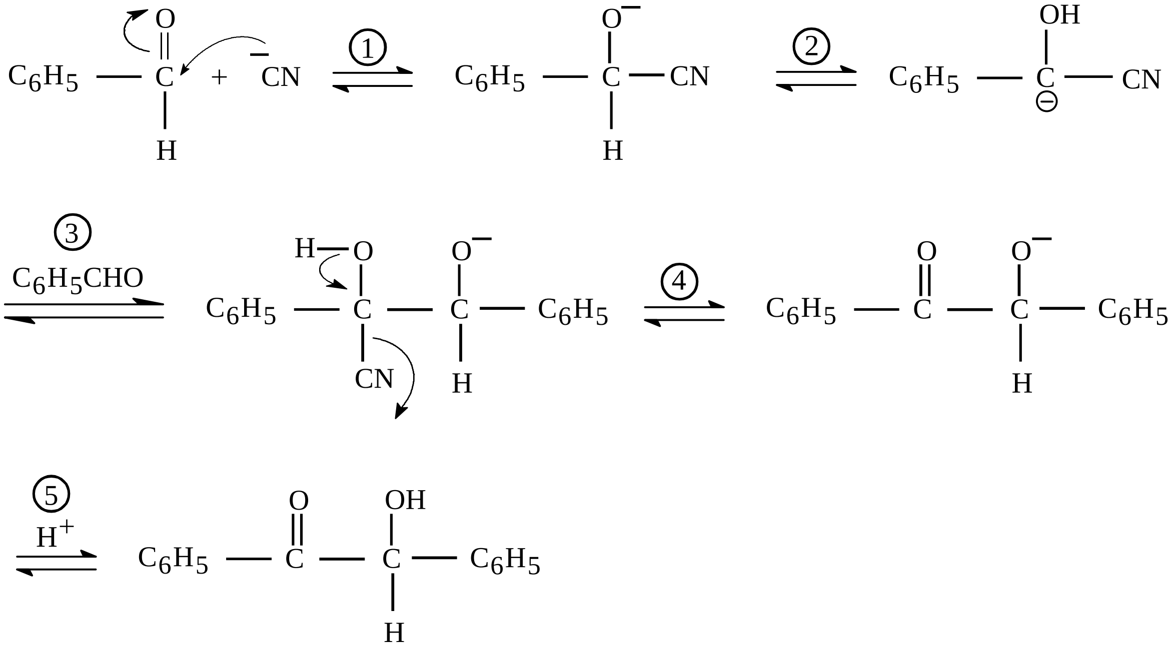
4.2.x Benzoin condensation : Intermolecular condensation of two aromatic aldehydes in presence of cyanide ion gives an acyloin is known as benzoin condensation.

The condensation of benzoin gives benzoin.



$$2PhCHO \xrightarrow{\bar{C}N} Ph-\overset{\overset{O}{\|}}{C}-\overset{\overset{OH}{\|}}{C}-Ph$$

Mechanism :



In the first step , the cyanide ion attacks on carbonyl carbon of the aldehyde molecule to give an addition product. The cyanide ion increases the acidic character of hydrogen and thus enhances the loss of this hydrogen as proton resulting in the formation of a carbanion.

The carbanion acting as nucleophile attacks on the carbonyl carbon atom of another aldehyde molecule and subsequant loss of cyanide ion gives final product benzoin.

Cyanide ion is used as catalyst in this reaction due to the following reasons.

a) It acts as a good nucleophile.
b) It will increase the acidic character of hydrogen attached to carbonyl carbon atom in the addition.
c) It also stabilises the carbanion.
d) It also acts as a good leaving group. (good nucleofuge)

The benzoin condensation fails in cases where the aromatic aldehyde contains electron donating groups like $-NMe_2$ in para – position to aldehyde group. This is because the electron donating group decrease the electrophilic nature of carbonyl carbon and attack of cyanide will not take place easily.

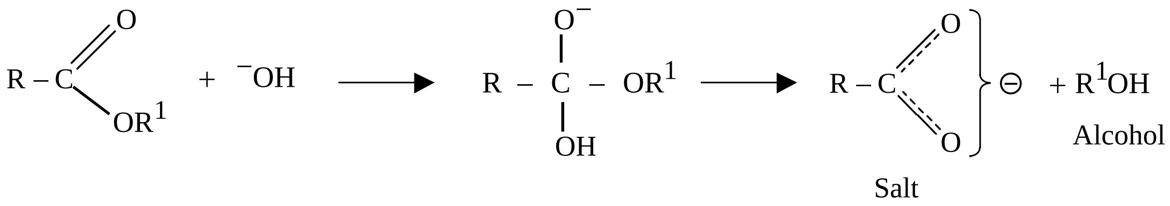
Benzoin condensation does not take place when strongly electron withdrawing groups are present in benzene ring. Thus p – nitrobenzaldehyde does not undergo this reaction. This is because the nitro group with draws the electron density on carbanion and carbanion becomes less nucleophilic to attack on second aldehyde molecule. Though the first step takes place much more easily.

Hydrolysis of Esters :

A carboxylic ester is hydrolysed to a carboxylic acid and an alcohol or phenol when heated with aqueous acid or base. In alkaline condition, carboxylic acid salt is obtained from which acid can be obtained by addition of mineral acid.

4.2.xi Base catalysed hydrolysis :

Base promotes hydrolysis of esters by providing the strongly nucleophilic reagent ^{-}OH . The reaction is essentially irreversible, since a resonance stabilised carboxylate anion shows little tendency to react with an alcohol.



The reaction involves the attack on the ester by hydroxide ion, hence the rate of reaction depends on the concentration of both ester and hydroxide ion hence is a second order reaction. This is inconsistent with the experimental observation.

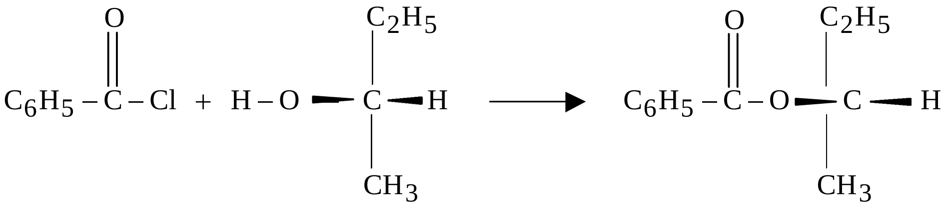
This is followed by subsequent cleavage of bond between oxygen and acyl group $RCO - OR^1$.

The evidence for acyl – oxygen cleavage is obtained from study of stereochemistry of the reaction.

Example :

Formation and subsequent hydrolysis of an ester of optically active sec – butyl alcohol is known as an example.

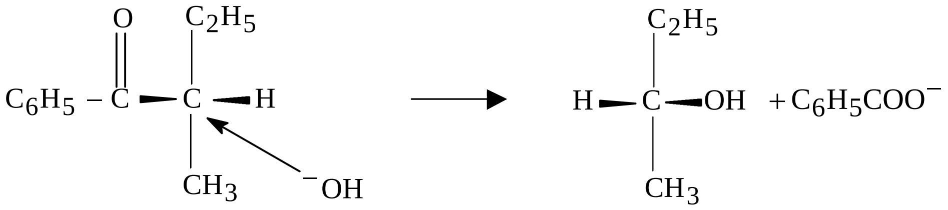
Reaction of (+) sec – butyl alcohol with benzoyl chloride must involve cleavage of the hydrogen – oxygen bond and hence cannot change the configuration about the chiral carbon atom.



$$C_6H_5-\overset{O}{\overset{\|}{C}}-Cl + H-O-\underset{CH_3}{\overset{C_2H_5}{C}}-H \longrightarrow C_6H_5-\overset{O}{\overset{\|}{C}}-O-\underset{CH_3}{\overset{C_2H_5}{C}}-H$$

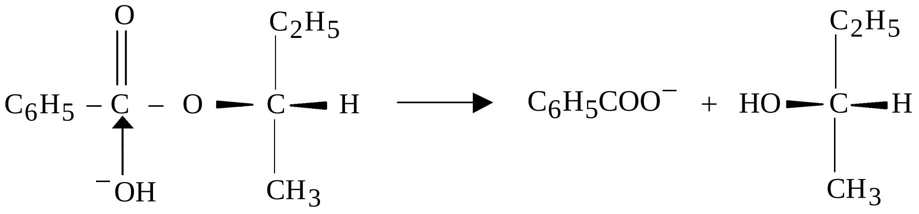
(+) sec–butylalcohol

If hydrolysis of this ester involves cleavage of the bond between oxygen and the sec – butyl group, it would result in the inversion of configuration.



$$C_6H_5-\overset{O}{\overset{\|}{C}}-\underset{CH_3}{\overset{C_2H_5}{C}}-H \quad {}^{-}OH \longrightarrow H-\underset{CH_3}{\overset{C_2H_5}{C}}-OH + C_6H_5COO^{-}$$

If on the other hand, the bond between oxygen and sec – butyl group remains infact during hydrolysis, then we would expect to obtain sec – butyl alcohol of the same configuration as the starting material.

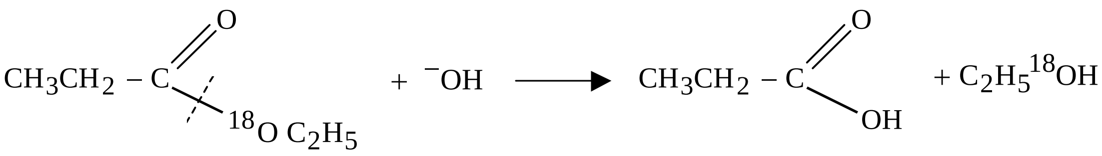


$$C_6H_5-\underset{\uparrow\, {}^{-}OH}{\overset{O}{\overset{\|}{C}}}-O-\underset{CH_3}{\overset{C_2H_5}{C}}-H \longrightarrow C_6H_5COO^{-} + HO-\underset{CH_3}{\overset{C_2H_5}{C}}-H$$

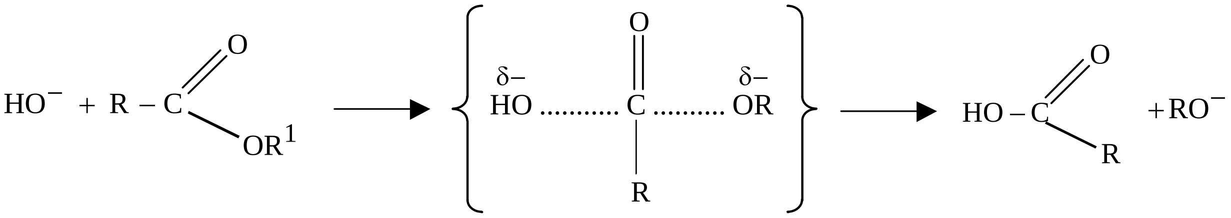
(+) sec–butyl alcohol

When the sec – butyl alcohol having rotation of +13.8° was converted into ester and hydrolysis of ester with alkali, there was obtained sec – butyl alcohol of rotation +13.8°. The complete retention of configuration clearly indicates that bond cleavage occurs between oxygen – acyl group.

Another evidence is obtained from tracer studies also. When ethyl propionate labeled with ^{18}O was hydrolysed by base in ordinary water, the ethanol produced was found to be enriched in ^{18}O, and propionic acid contained only ordinary ^{16}O.

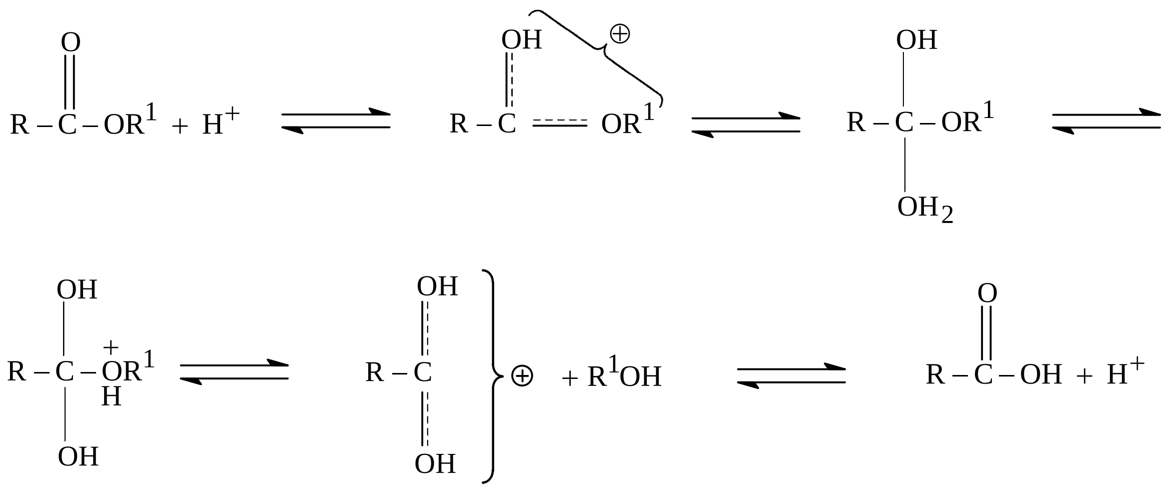


Hence, it is considered that the mechanism of hydrolysis of esters by alkali involves two steps. The first step is the formation of tetrahedral transtion state followed by subsequent cleavage of acyl – oxygen fission gives acid and alcohol.



4.2.xii Acid catalysed hydrolysis :

Acid catalysed hydrolysis of esters is a reversible reaction and mechanism for acid – catalysed hydrolysis and esterification s given as follows.

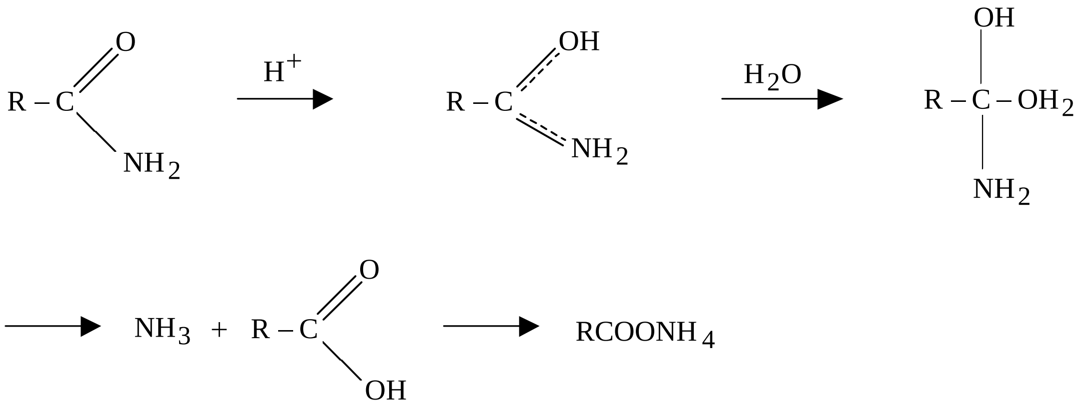


Mineral acid speeds up both processes by protonating carbonyl oxygen and thus rendering carbonyl carbon more susceptible to ncleophilic attack. In hydrolysis, the nucleophilic is water and leaving group is alcohol.

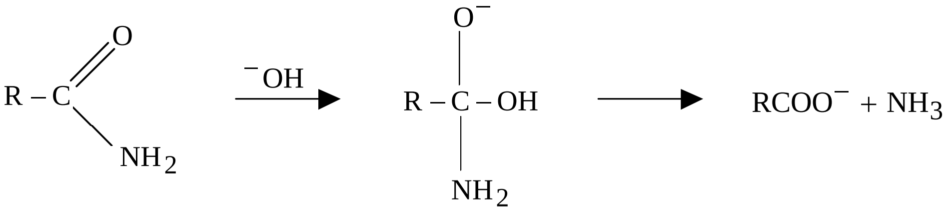
The evidence fr the mechanism is much te same as in alkaline hydrolysis. The position of cleavage $RCO\text{–}OR^1$ and $RCO - OH$ has been shown by ^{18}O studies of both hydrolysis and esterification.

4.2.xiii Hydrolysis of amides :

Hydrolysis of amides involves the nucleophilic substitution in which $-NH_2$ group is replaced by –OH. Under acidic conditions hydrolysis involves attack by water on thr protonated amide.

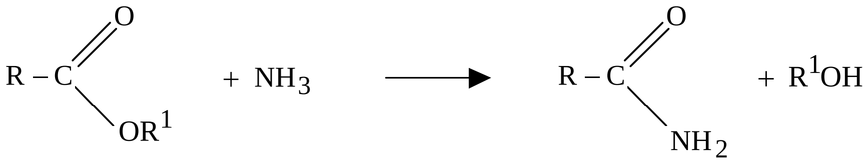


In alkaline conditions, hydrolysis involves attack by the strongly nucleophilic hydroxide ion on the amide itself.



4.2.xiv Ammonolysis of Esters :

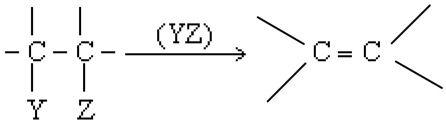
Reaction of an ester with ammonia, generally in ethyl alcohol solution yields an amide. This reaction involves nucleophilic attack by a base, ammonia on the electron – deficient carbon; the alkoxy group $-OR^1$ is replaced by $-NH_2$.



UNIT – IV :: Lesson – 3

Elimination reactions :

Elimination reactions are an important class of reactions which are widely used in the preparation of alkenes. In these reaction a piece of molecule is eliminated from adjacent carbon atoms of the reactant to form a double bond between them.



Such elimination reactions are called 1, 2 – elimination or β–elimination reaction. Also known are 1, 1 – elimination and 1, 3 – elimination reaction, but less commonly. Depending upon the molecule eliminated the names of the reactions are given.

The eliminated molecule is HX, it is called dehydrohalogenation.

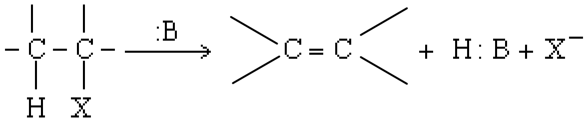
The eliminated molecule is X_2, it is called dehalogenation.

The eliminated molecule is H_2O, it is called dehydration.

The eliminated molecule is H_2, it is called dehydrogenation.

Dehydrohalogenation of alkyl halides : 1, 2 – elimination :

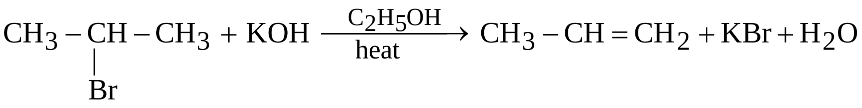
Dehydrohalogenation involves the elimination of halogen atom and a hydrogen atom from adjacent carbon atoms. The reagent required is a base, whose function is to abstract the hydrogen as a proton.



The bas :B can be neutral or negatively charged.

Example :

When isopropyl bromide is treated with hot concentrated alcoholic solution of potassium hydroxide, propene is obtained.



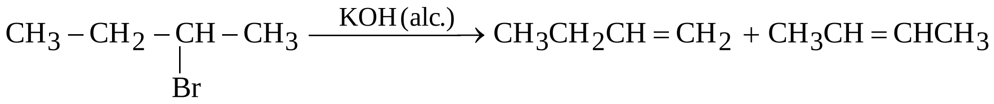
$$\underset{\text{Br}}{\underset{|}{CH_3 - CH - CH_3}} + KOH \xrightarrow[\text{heat}]{C_2H_5OH} CH_3 - CH = CH_2 + KBr + H_2O$$

In some cases, dehydrohalogenation yields a single alkene and in other cases gives a mixture of alkenes depending on the structure of the alkyl halide.

n – Butyl bromide gives only product 1 – Butene.

$$CH_3 - CH_2 - CH_2 - CH_2Br \xrightarrow{\text{KOH(alc.)}} \underset{\text{1 – Butene}}{CH_3CH_2CH = CH_2}$$

Secondary butyl bromide gives 1 – Butene (19%) and 2 – butene (81%).



$$CH_3-CH_2-\underset{\displaystyle Br}{\underset{|}{C}H}-CH_3 \xrightarrow{KOH(alc.)} CH_3CH_2CH=CH_2 + CH_3CH=CHCH_3$$

1 – Butene (19%) 2 – Butene (81%)

Elimination reactions are characterised by the following :

i. The substrate contains a leaving group, an atom or group that leaves the molecule, taking its electron pair with it.
ii. In a position beta to the leaving group the substrate contains an atom or group – generally hydrogen, can be extacted by base, leaving its electron pair behind.
iii. Reaction is brought about by the action of base.

Bases generally used are ethoxide $(\overset{-}{O}C_2H_5)$, hydroxide ion $(\overset{-}{O}H)$, tert – butoxide $(CH_3)_3C\overset{-}{O})$

Kinetics of dehydrohalogenation : Duality of mechanism :

Two kinds of kinetic behaviours were observed in elimination reactions. A first order reaction is observed with secondary and tertiary substrates and with a base which is either weak or in low concentration. The rate of elimination depends only on the concentration of alkyl halide and is independent of the concentration of base.

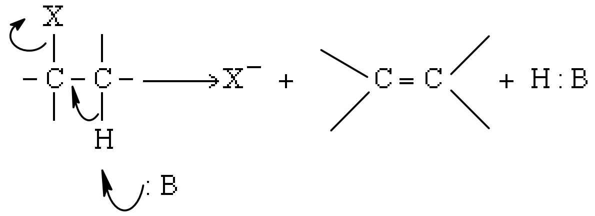
$$\text{Rate} = k\,[RX]$$

A second order reaction is observed with primary substrates and when base strong or concentrated. The rate of reaction depends on concentration of both alkyl halide and base.

$$\text{Rate} = k\,[RX]\,[:B]$$

To account for two types of kinetic behaviour two different mechanism have been proposed namely E_1 and E_2.

E_2 mechanism : The reaction proceeds by second – order kinetics. The reaction involves single step : base takes out a proton from the carbon, simultaneously halide ion departs and double bond forms.



As the electron pair from departing proton begins to form π bond, the carbon – halogen bond starts breaking (i.e) the halogen is pushed out. The rate determining step is the only step and the rate is proportional to the concentration of both reactants. Hence the mechanism was named E_2, elimination, bimolecular.

Evidence for E_2 mechanism :

i. The reaction follows second order kinetics.
ii. The reaction is not accompanied by rearrangements.
iii. Shows large isotopic effect.
iv. Are not accompanied by hydrogen exchange.
v. Show a large elemental effect.

Facts (i) and (ii) are as observed in E_2 mechanism involving only single step mechanism. Hence, there is no possibility for any rerrangement to occur.

E_2 – Mechanism : Isotope effect : E_2 reactions show large hydrogen isotopic effect. A difference in rate due to a difference in the isotope present in the reaction system is called isotope effect.

Isotopic effects due to the breaking of a bond to the isotopic atom are called primary isotopic effects. For example the bond to protium (H) is broken faster than a bond to deuterium (D).

$$\sim C-H+Z \xrightarrow{k^H} [\sim C \ldots\ldots\ldots H \ldots\ldots\ldots Z] \longrightarrow \sim + C + HZ$$

$$\sim C-D+Z \xrightarrow{k^D} [\sim C \ldots\ldots\ldots D \ldots\ldots\ldots Z] \longrightarrow \sim C + D:Z$$

K^H/K^D was found to about 5 to 8, that is to say, the reaction is about 5 to 8 times as fast as for ordinary hydrogen as for deuterium.

The isotopic effect in respect of E_2 mechanism can be explained by considering elimination reaction with two compounds $C_6H_5CH_2CH_2Br$ (I) (2 – phenyl ethyl bromide) and $C_6H_5CD_2CH_2Br$ (II).

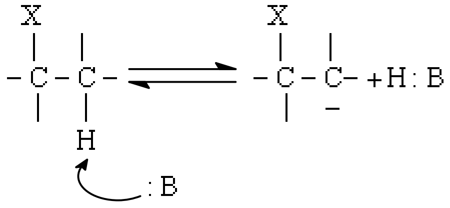
The second compound contains two deuterium atoms in the position from which it is to be eliminated.

The rates of dehydrobrominations by sodium ethoxide were measured. It was found that compound (I) reacted seven times faster than compound (II). This clearly indicates that breaking C – H bond is involved in the rate – determining step. This observation is consistent with the E_2 mechanism.

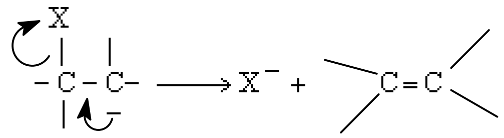
Evidence of E_2 mechanism : Absence of hydrogen exchange :

For elimination reaction, there is another reasonable mechanism in which a carbanion forms in the rate determining step by losing a proton and in the second step which is fast the halide is lost to give alkene.

i)



$$-\underset{|}{\overset{\overset{X}{|}}{C}}-\underset{\underset{H}{|}}{\overset{|}{C}}- \rightleftharpoons -\underset{|}{\overset{\overset{X}{|}}{C}}-\underset{-}{\overset{|}{C}}- + H:B$$

ii) 

Step (i) is an acid – base reaction, in which substrate acting as an acid. Elimination involving carbanion formation is often called E_1CB elimination, unimolecular, of the conjugate base.

To identify whether carbonion mechanism involved in elimination or not, experiments were carried out using deuterium as a label where deuterium acts as a tracer.

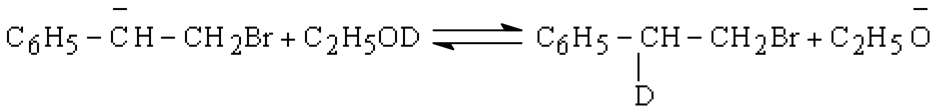
Consider the dehydrohalogenation of 2 – phenylethylbromide $C_6H_5CH_2CH_2Br$.

$$C_6H_5CH_2CH_2Br \xrightarrow[C_2H_5OH]{C_2H_5ONa} C_6H_5CH=CH_2$$

If the reaction follows a carbanion mechanism, the first step can be written as

$$C_6H_5CH_2-CH_2Br+C_2H_5O^- \rightleftharpoons C_6H_5\overset{-}{C}H-CH_2Br+C_2H_5OH$$

If the solvent is labeled ethanol C_2H_5OD, the deuterium atom should enter into the reactant in the reverse reaction



$$C_6H_5-\overset{-}{C}H-CH_2Br+C_2H_5OD \rightleftharpoons C_6H_5-\underset{\displaystyle D}{\underset{|}{C}}H-CH_2Br+C_2H_5\overset{-}{O}$$

Reaction was allowed to run until half the substrate had been converted into alkene. Reaction was interrupted and unconsumed 2 – phenyl ethyl bromide was recovered. It was found that no molecules containing deuterium were isolated, indicating that the reaction is not accompanied by hydrogen exchange.

The observation also rules out the mechanism involving the carbanion formation.

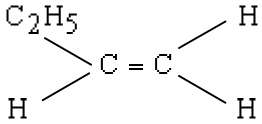
Evidence for E_2 – mechanism – The element effect :

The second – order eliminations show a large element effect. This involves that how the rate of reaction is effected by the presence of leaving group. Experimental observations indicate that the order of reactivity is greately influenced by the ease of breaking of carbon–halogen bond, iodides are more reactive than bromides than chlorides.

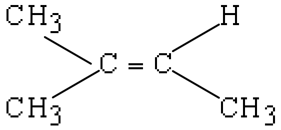
E_2 – Reaction : Orientation and reactivity :

Study of many reactions have shown that when there is possibility for the formation of two isomers, one isomer is obtained predominantly than the other. It is of course possible to predict the orientation of elimination on the basis of the molecular structure.

As already pointed that in the dehydrohalogenation of sec–butyl bromide 2 – butene was the predominant product.



2 – butene is a disubstituted alkene, whereas 1 – butene is monosubstituted alkene.



In other elimination reactions also disubtituted alkene is preferred over a monosubstituted alkene and a trisubstituted alkene is preferred over disubstituted alkene.

These observations were made by Saytzeff and formulated a rule which can be defined as

"In dehydrohalogenation, the preferred product is the alkene that has greater number of alkyl groups attached to the doubly bonded carbon atoms".

The ease of formation of alkenes is

$$R_2C = CR_2 > R_2C = CHR > R_2C = CH_2$$
$$\approx RCH = CHR > RCH = CH_2 > CH_2 = CH_2$$

The same is the order of stability of alkenes.

Alkene stability not only determines orientation of dehydrohalogenation, but also an important factor in determining the reactivity of alkyl halide towards elimination.

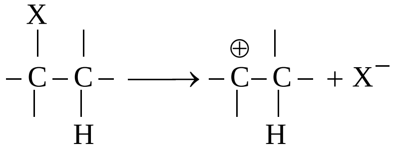
As one proceeds along a series of alkyl halides from 1° to 2° to 3° the order of reactivity of alkyl halides for E_2 dehydrohalogenation is $3^o > 2^o > 1^o$

E_1 – Mechanism :

The reaction proceed by first – order kinetics. In this mechanism, bond breaking and bond –making do not take place simultaneously, but one after another (i.e.) E_1 mechanism involves two steps.

In step (1) the substrate undergoes slow heterolysis to form halide ion and a carbocation.
In step (2) the carbocation rapidly loses a proton to the base and form the alkene.

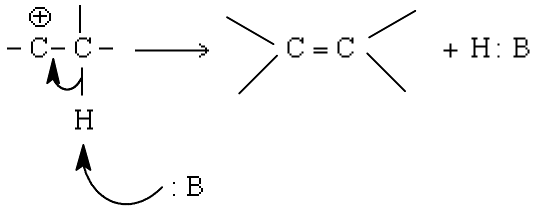
(1)



$$-\underset{|}{\overset{\overset{X}{|}}{C}}-\underset{\underset{H}{|}}{\overset{|}{C}}- \longrightarrow -\underset{|}{\overset{\oplus}{C}}-\underset{\underset{H}{|}}{\overset{|}{C}}- + X^-$$

slow

(2)



fast

The overall rate of reaction is determined only by the slow step and as the rate determining step involves only substrate, its rate depends only on the concentration of substrate. The rate of E_1 reaction is independent of force consentration elimination, unimolecular because in the rate – determining step only one molecule, substrate is involved.

$$\text{Rate} = k\,[RX]$$

Evidence for the E_1 – mechanism :

The E_1 elimination reactions :

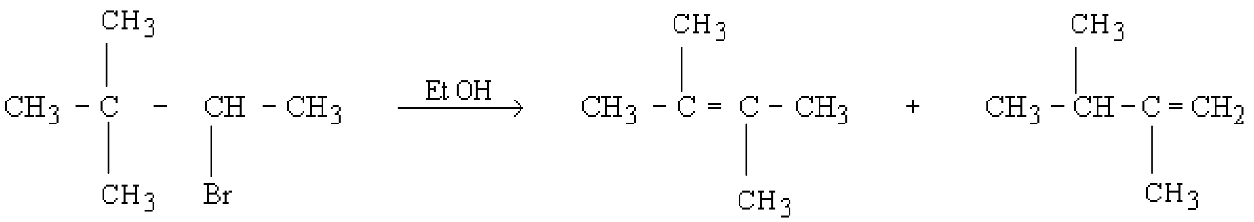
i. the reaction follows first order.
ii. are not accompanied by primary hydrogen isotope effect.
iii. show the same effect of structure on reactivity as SN^1 reactions.
iv. are accompanied by rearrangements.

Reactivity in E_1 $3^o > 2^o > 1^o$

Where structure permits, first – order eliminations are accompanied by rearrangement.

Examples :

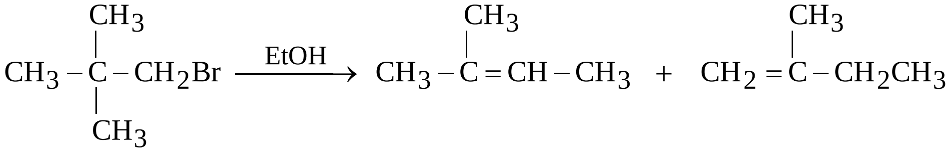
a.



$$CH_3-\underset{CH_3}{\overset{CH_3}{C}}-\underset{Br}{CH}-CH_3 \xrightarrow{Et\,OH} CH_3-\overset{CH_3}{C}=\underset{CH_3}{C}-CH_3 + CH_3-\overset{CH_3}{CH}-\underset{CH_3}{C}=CH_2$$

3, 3 – dimethyl – 2 – bromobutane 2, 3 – dimethyl – 2 – butene 2, 3 – dimethyl – 1 – butene

b.

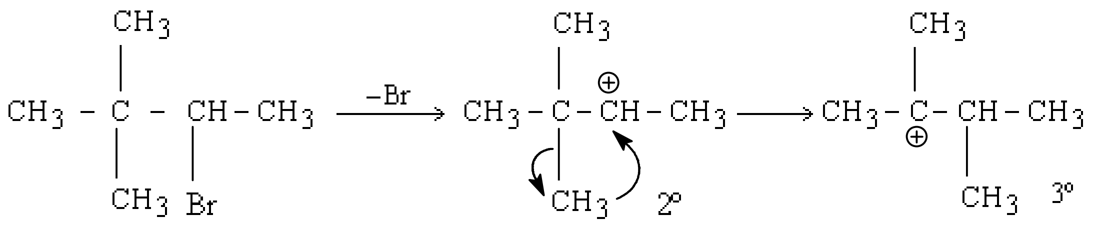


$$CH_3-\underset{CH_3}{\overset{CH_3}{C}}-CH_2Br \xrightarrow{EtOH} CH_3-\overset{CH_3}{C}=CH-CH_3 + CH_2=\overset{CH_3}{C}-CH_2CH_3$$

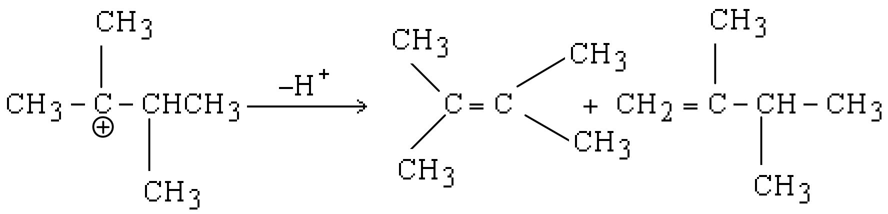
2–methyl –2–butene 2–methyl – 1 – butene

In the examples cited above the initially formed carbocation can rearrange by a 1, 2 – shift to form more stable carbocation.

a.



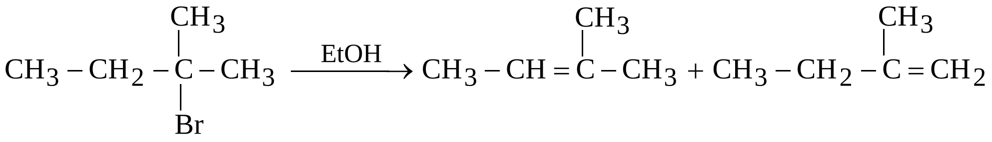
$$CH_3-\underset{CH_3}{\overset{CH_3}{C}}-\underset{Br}{CH}-CH_3 \xrightarrow{-Br} CH_3-\underset{CH_3}{\overset{CH_3}{C}}-\overset{\oplus}{CH}-CH_3 \;\; 2^\circ \longrightarrow CH_3-\underset{\oplus}{\overset{CH_3}{C}}-\underset{CH_3}{CH}-CH_3 \;\; 3^\circ$$



E_1 – Reaction – orientation :

Elimination by E_1 show strong Saytzeff orientation. That is to say when more than one alkene can be formed, more stable alkene is the preferred product.

Example :



$$CH_3-CH_2-\underset{Br}{\overset{CH_3}{C}}-CH_3 \xrightarrow{EtOH} CH_3-CH=\overset{CH_3}{C}-CH_3 + CH_3-CH_2-\overset{CH_3}{C}=CH_2$$

t – pentyl bromide

2–methyl – 2 – butene 82%

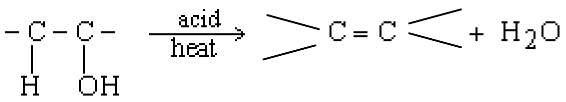
2–methyl –1–butene 18%

When rearrangement occurs in E_1, the orientation is predicted by Saytzeff rule, but we must consider the loss of β – protons from the rearranged cations as well as from the cations initially formed.

Dehydration of alcohols :

The dehydration of alcohols also come into the category of 1, 2 – elimination of course catalysed by acids. Fundamentally dehydration is not very different from dehydrohalogenation.

An alcohol is converted into alkene by dehydration : elimination of a molecule of water

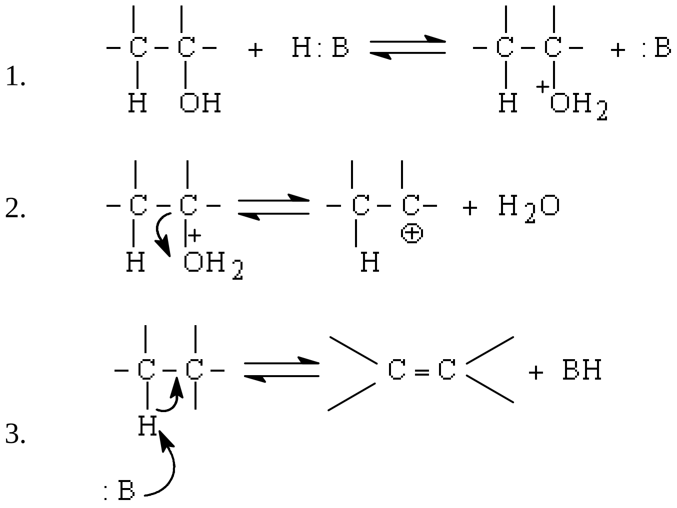


$$-\underset{H}{C}-\underset{OH}{C}- \xrightarrow[heat]{acid} >C=C< + H_2O$$

The reaction is brought about by heating with sulphuric acid or phosphoric acid or by passing alcohol vapours over alumina at high temperature.

The ease of dehydration of alcohols is $3^o > 2^o > 1^o$

Mechanism of dehydration :



Step (1) : A fast acid–base reaction between alcohol and catalysing acid to give protonated alcohol.

Step (2) : Protonated alcohol undergoes heterolysis to formed carbocation.

Step (3) : Carbocation loses a protan to the base to give alkene.

Where the structure of the alkyl group permits rearrangement take place as was observed in the case of E_1 eliminations.

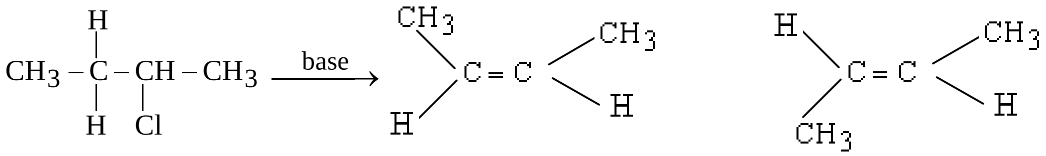
Where more than one alkene can be formed, the preferred product is the most stable one and it is strong Saytzeff orientation.

Stereochemistry of elimination :

Dehydrohalogenation : E_2 – elimination :

It was already pointed out that E_2 elimination reaction takes place in a single step, which is also the rate determining step. As the proton is abstracted by the base, the leaving group goes out with its bonding electron resulting in the formation of a carbon – carbon double bond. The elimination is always takes place following Saytzeff rule (i.e.) more stable alkene is the predominant product.

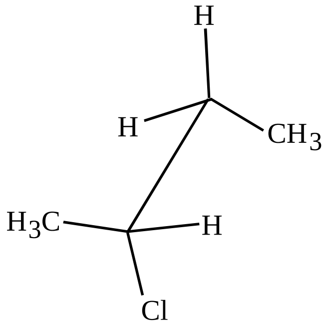
For E_2 elimination two important factors determine the course of reaction (i) Stereoelectronic factor (i.e.) the groups to be eliminated must be anti to each other. The other factor is steric factor (i.e.) the steric requirement of the groups will decide the rate of elimination reaction. These factors can be explained by considering the elimination of hydrogen chloride from 2–chlorobutane with a base. In this elimination reaction 2–butene is major compound obtained. However, as 2–butene exists in two geometrical isomers, it is to be considered whether which of two geometrical isomers will be obtained in large quantity over the other. The answer to this can be obtained by considering the two factors (i.e.) stereoelectronic factor and steric factor.



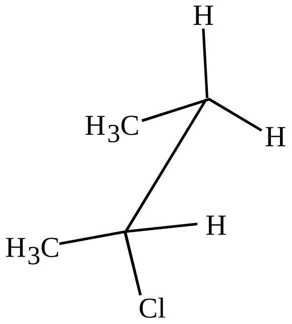
Cis

2–chlorobutane exists in a number of conformation about $C_2 - C_3$ bond. (about the bond between carbon atoms two and three).

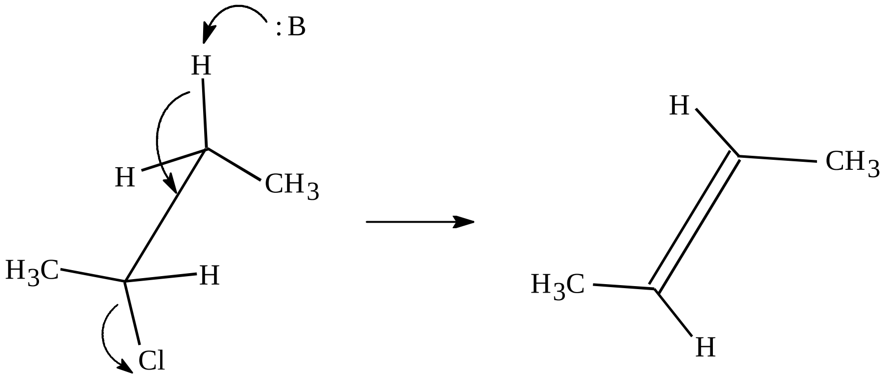
Of the number of possible conformations two are given below in which, it is deliberately written that chlorine on one carbon atom exactly anti to the hydrogen atom on the other.



(I)

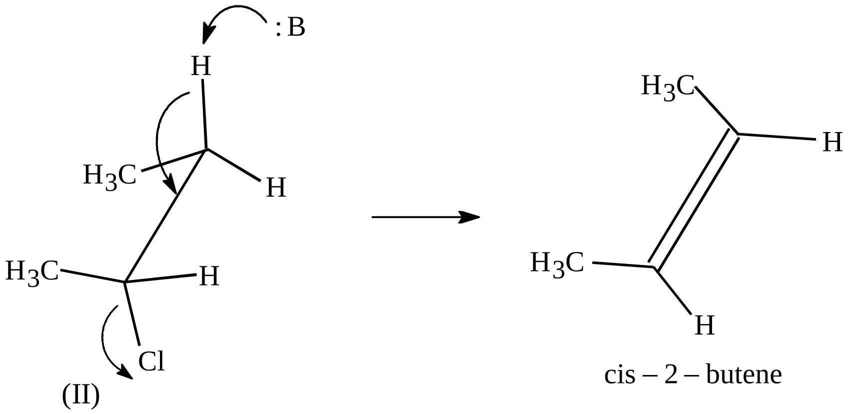


(II)



(I)

trans – 2 – butene



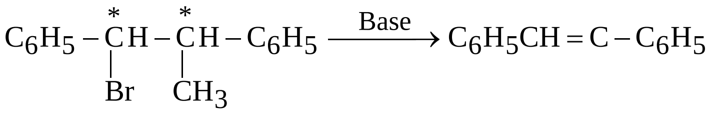
(II)

cis – 2 – butene

In conformation (I), two bulky methyl groups are for away from each other while in conformation (II), two bulky methyl groups are gauche to each other. Hence, it may be understood that more number of molecules will be in conformation (I) than (II) since steric crowding in (II) is more than in (I).

The population of the conformer (I) is more than (II). Hence, the more percentage of trans – 2 – butene is obtained than cis–2–butene.

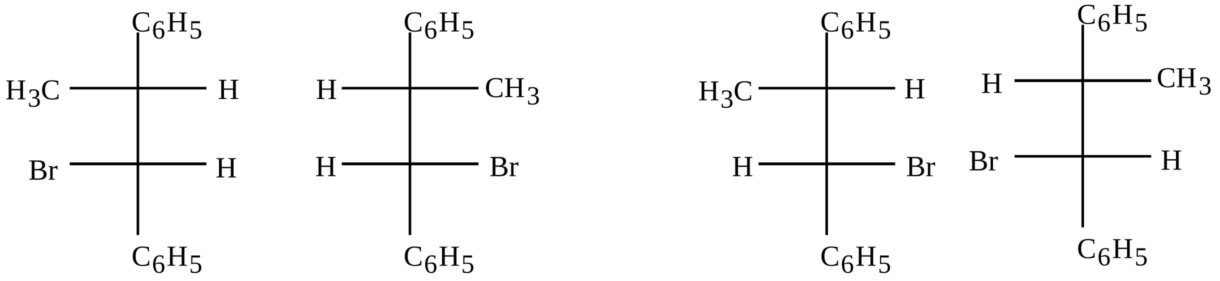
Consider the dehydrohalogenation of 1–bromo – 1, 2 – phenyl propane.



$$C_6H_5-\underset{\overset{|}{Br}}{\overset{*}{C}H}-\underset{\overset{|}{CH_3}}{\overset{*}{C}H}-C_6H_5 \xrightarrow{\text{Base}} C_6H_5CH=C-C_6H_5$$

1– Bromo – 1, 2 – diphenyl propane 1, 2 – diphenyl propene

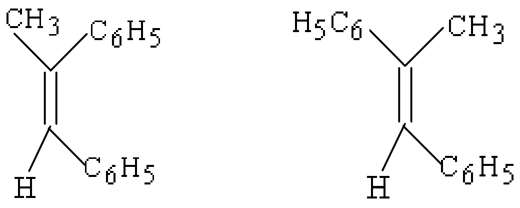
The compound contains two chiral centres and hence exists in two enantiomeric pairs I, II and III, IV.



(I) (II) (III) (IV)

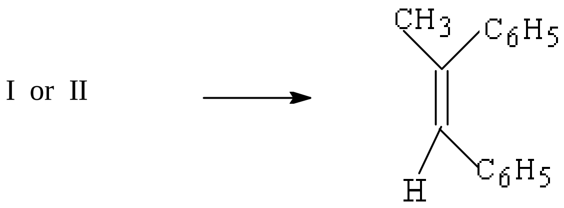
Erythro Threo

The product, 1, 2 – diphenyl propene exists two geometrical isomers.

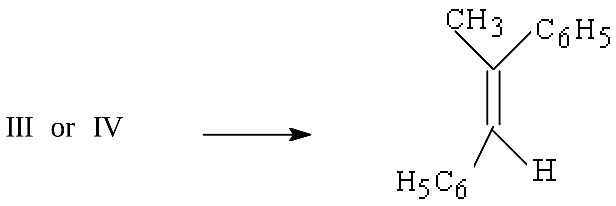


1, 2 – diphenyl propene

Experimentally, it was observed that erythro halides I and II, on dehydrobromination gave only Z – alkene.

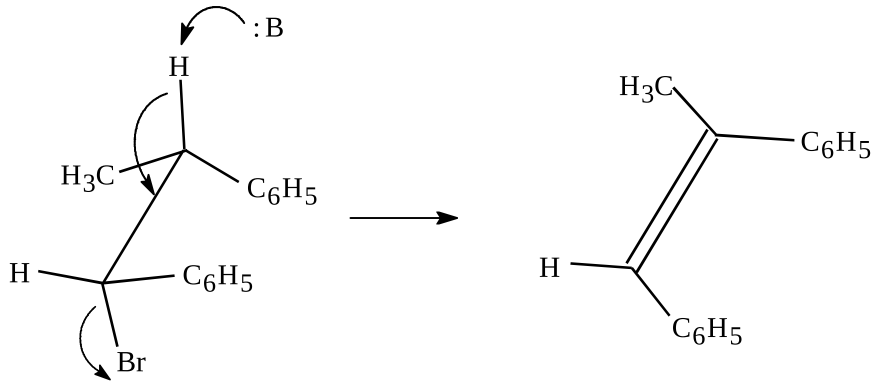


Whereas from threohalides III and IV, only E –alkene is obtained.



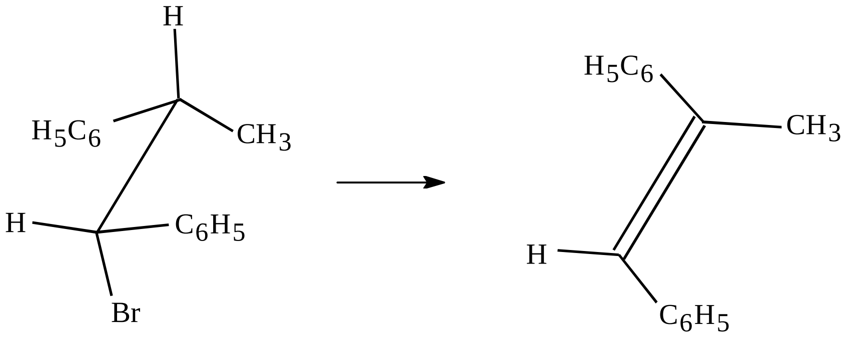
These experimental observations can be explained only on the basis that E_2 elimination always involves anti in the transition state the hydrogen and the leaving group bromine are in anti position.

I or II gave Z – alkene



(Z) – 1, 2 – diphenyl propene

III or IV gave E – alkene



(E) – 1, 2 – diphenyl propene

Pyrolytic eliminations :

Some compounds such as acetates, xanthates and amine oxides undergo thermal decomposition are known as pyrolytic elimination (pyro means heat. Any reaction which undergo on heating is known as pyrolytic reaction)

Characteristics of pyrolytic eliminations :

i. They involve unimolecular mechanism .

ii. Undergo concerted mechanism proceeding through a cyclic transition state.

iii. High temperature is needed in the absence of solvent.

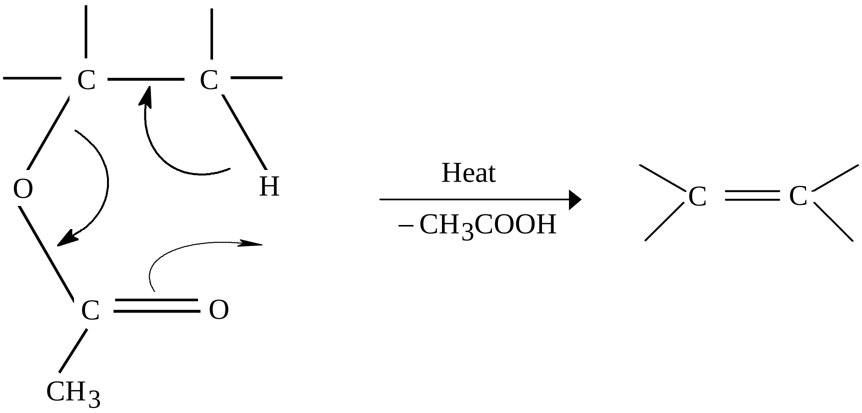
iv. Syn elimination of hydrogen atom and leaving group.

v. No catalyst (either acidic or basic).

Examples :

Pyrolysis of acetates :

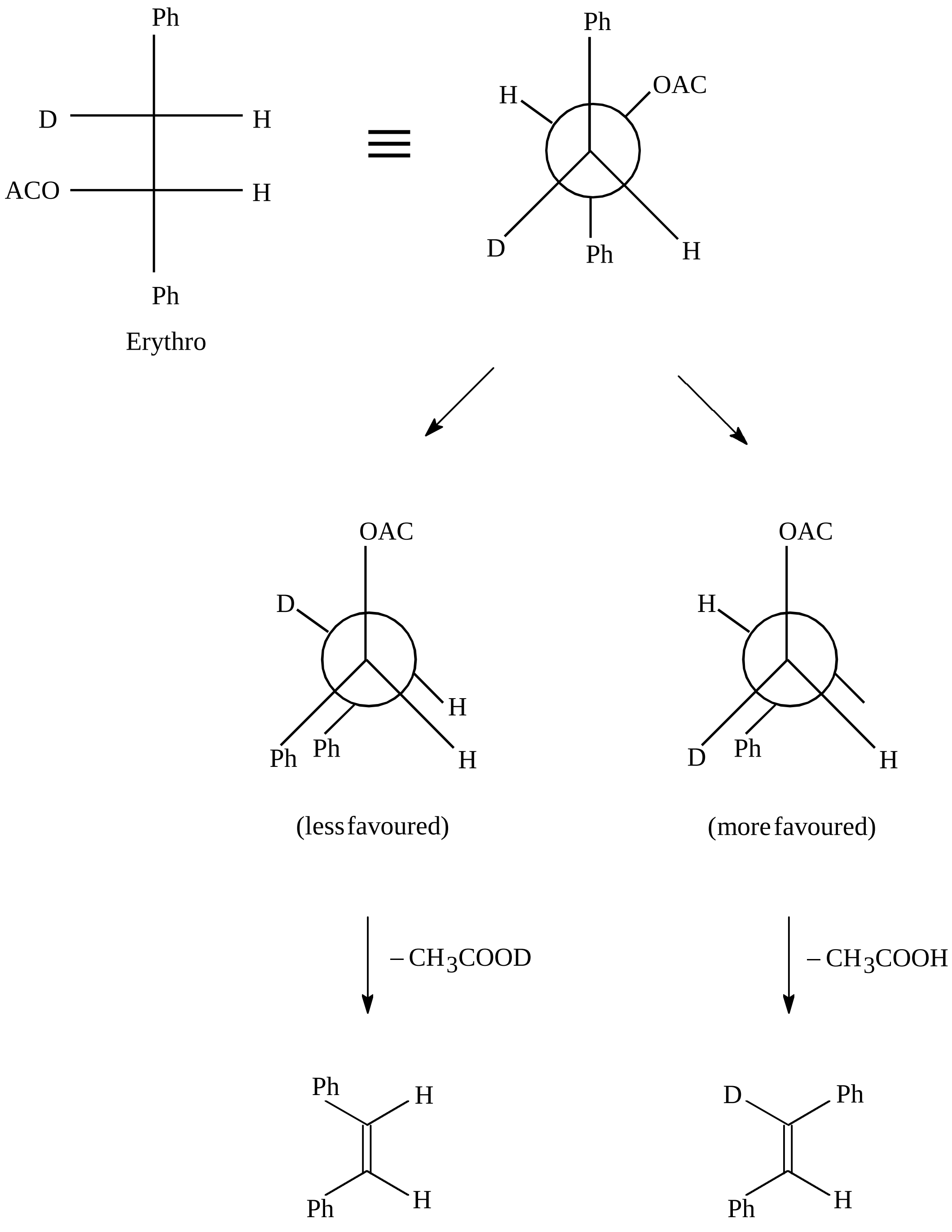
The mechanism involves six membered cyclic transition state. A general representation is given below.

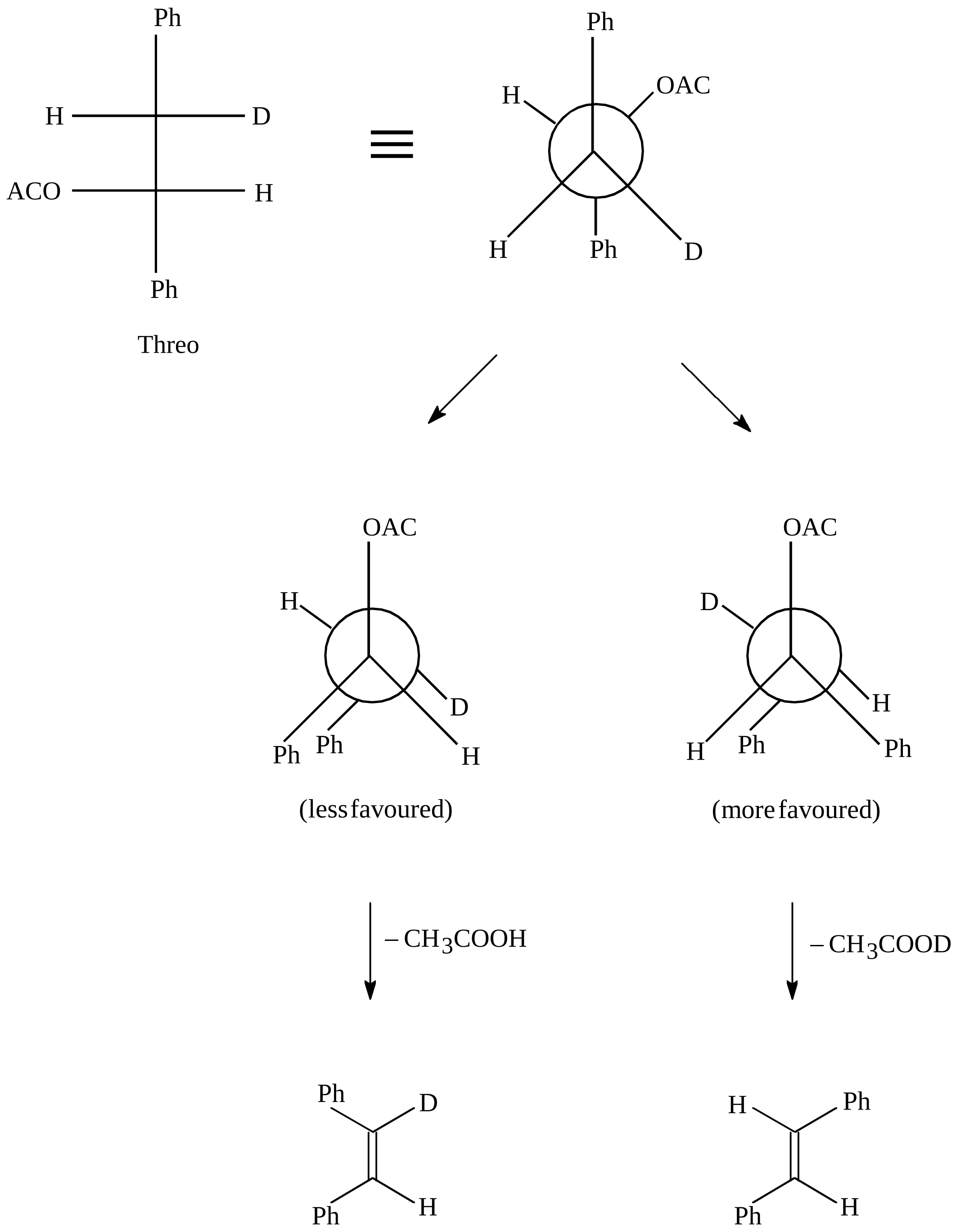


Orientation in pyrolytic eliminations :

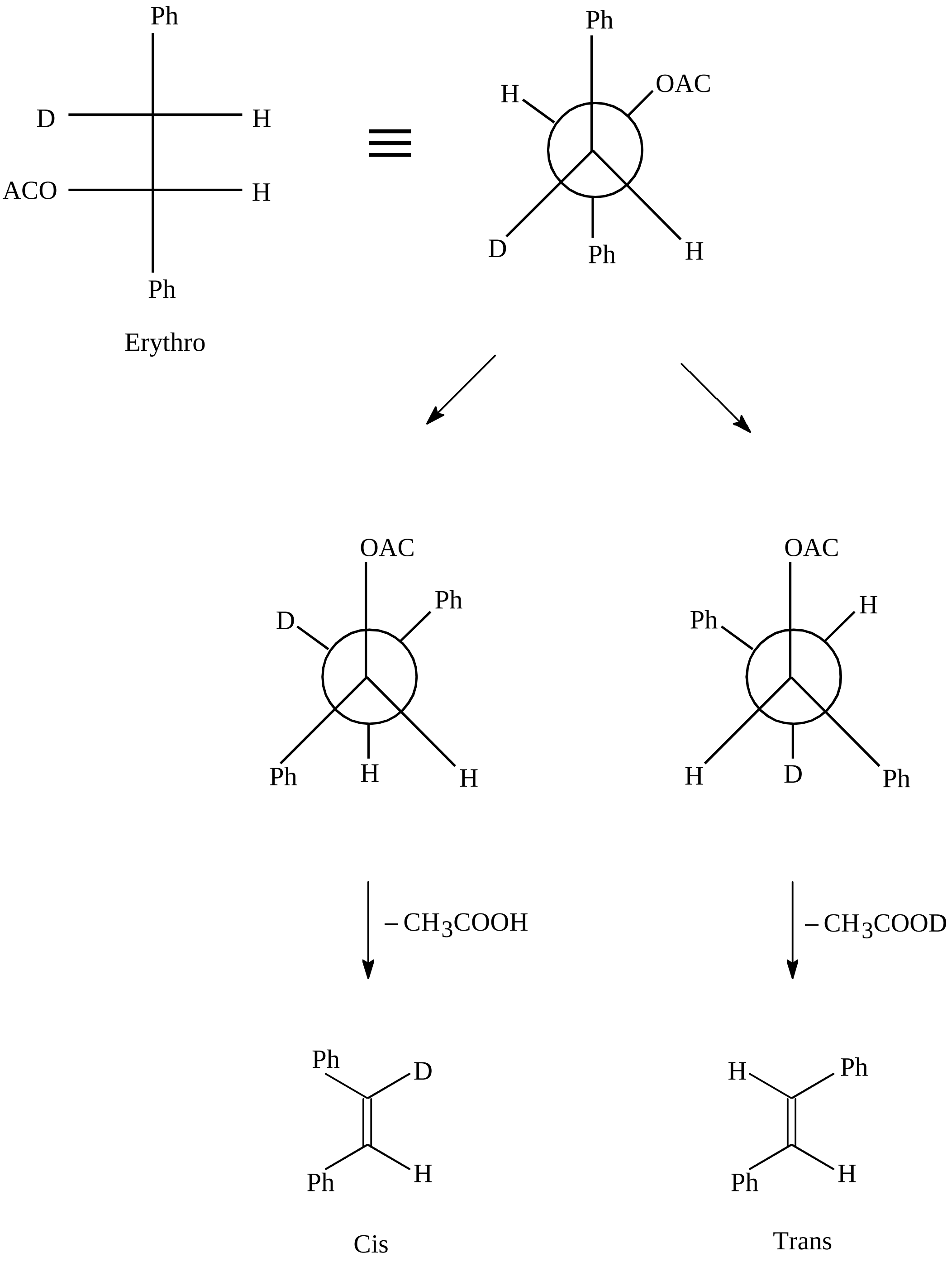
Pyrolysis of erythro and threo isomers of 1 – acetoxy – 2 – deutero – 1, 2 – diphenyl ethanes can be taken as example to study the orientation in pyrolytic eliminations. The products excepted for both syn and anti eliminations for the above isomers are given below. It is to be noted that above elimination may involve the loss of acetic acid or deuteroacetic acid.

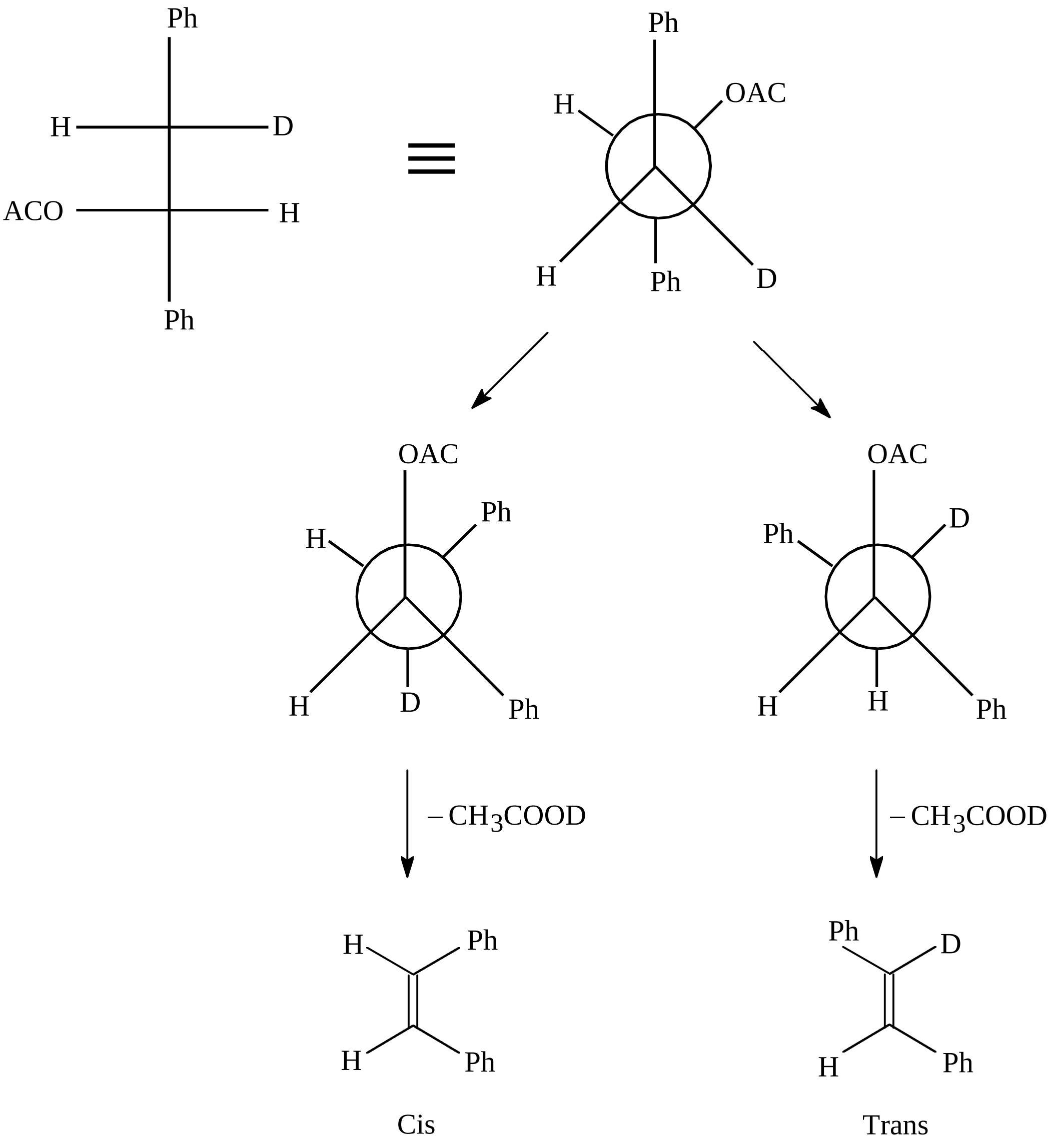
Syn – elimination :




Ph
H
D
ACO
H
Ph
Threo
Ph
H
OAC
H
Ph
D
OAC
H
D
Ph
Ph
H
(less favoured)
OAC
D
H
H
Ph
Ph
(more favoured)
– CH$_3$COOH
– CH$_3$COOD
Ph
D
Ph
H
H
Ph
Ph
H

Anti – elimination :





The following are the important observations from the above figures.

i. An erythro compound undergo syn elimination with a loss of CH_3COOD to give cis – stilbene without deuterium in the product.

ii. An erythro compound undergo syn elimination with a loss of CH_3COOH much more favourably than loss of CH_3COOD to give trans – stilbene with deuterium in the product.

iii. An Erythro compound on anti elimination results in the formation cis – stilbene in which a molecule of CH_3COOH is eliminated. The product however, contains deuterium in it.

iv. An erythro compound on anti elimination gives trans – stilbene with loss of CH_3COOD. The loss of CH_3COOD is much more favourable than loss of CH_3COOH. The product does not contain deuterium.

v. A threo compound on syn – elimination give trans stilbene with loss of CH_3COOD. This is more favourable than loss of CH_3COOH.

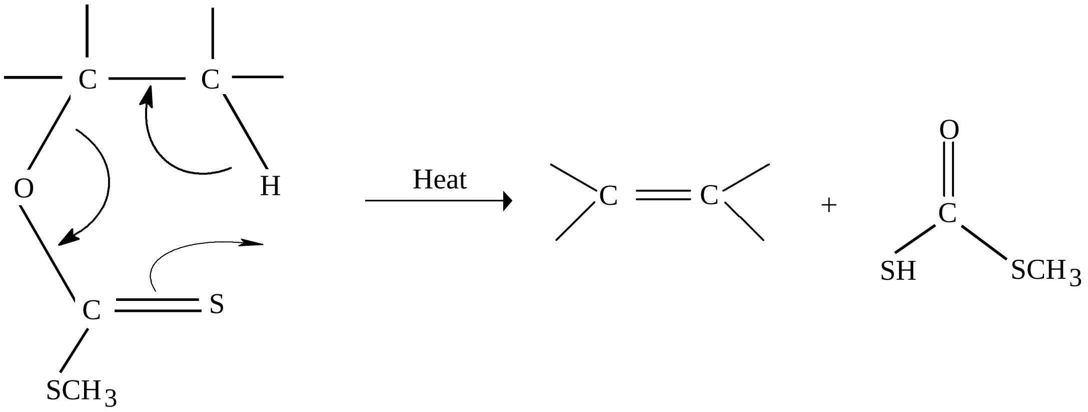
vi. A threo compound on syn – elimination involving loss of CH_3COOH is less favourable and gives cis – stilbene.

vii. A threo compound on anti – elimination of CH_3COOH is more favourable and produce trans – stilbene which contains deuterium in its structure.

viii. A threo compound on anti elimination involving loss of CH_3COOD gives cis – stilbene. However, this is less favourable.

Pyrolysis of Xanthates : Chugaev reaction :

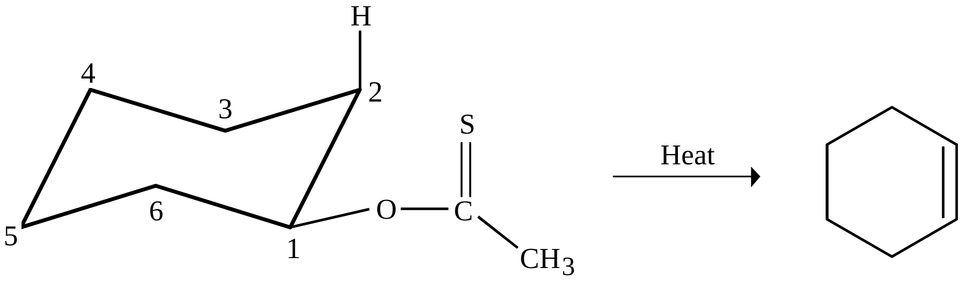
Xanthates undergo pyrolytic elimination similar to acetates involving six membered cyclic transition as shown below.



Xanthates or acetates undergo pyrolytic elimination via the conformation in which Xanthate group or acetate group and hydrogen are in gauche orientation to each other.

In case of cyclic systems, the stereochemical requirement for these eliminations is 1, 2 – cis orientation. For example in cyclohexane system the leaving groups must be in 1, 2 – positions in cis manner (i.e.) if one group is in axial orientation, the other must be in equitorial orientation.

In the pyrolysis of Xanthate given in the following example, Xanthate group is in equitorial position and hydrogen in the axial position will only be eliminated not the hydrogen in the equitorial position to give cyclohexene.



UNIT – IV

MODEL QUESTIONS

1. Write steps involved in E_1 mechanism with suitable examples.
2. What is the preferred stereo electronic requirement of E_2 reaction ? Explain.
3. What are the characteristic features of a pyrolytic elimination reaction ?
4. What is Wittig reagent ? How it is prepared ?
5. Write an example of intermolecular aldol condensation.
6. Discuss briefly about various mechanisms of β – elimination.
7. "Dehalogenation takes place via anti – conformation" Explain with suitable examples.
8. Write about orientation of double bond in elimation reactions.
9. Explain the mechanism involved in Metal hydride reduction.
10. Grignard reagents are useful to prepare any type of alcohol. Elaborate the statement.
11. Write the meachanism involved in Claisen reaction.
12. Write some examples with explanation about reactions involving enolates.
13. What are important effects of medium in an elimination reaction.
14. Wittig reaction is useful for synthesis of alkenes from carbonyl compounds. Explain with suitable examples.
15. Write mechanism involved in Wittig reaction.