Organic Reaction Mechanisms-II

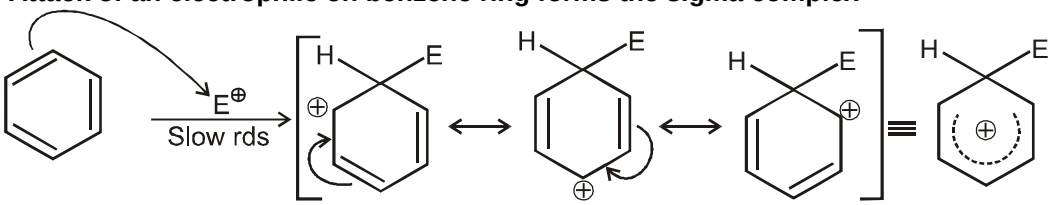
Section (A) : Electrophilic substitution reaction of aromatic compounds

Like an alkene, benzene has cloud of pi electrons above and below its sigma bond framework. Although benzene's pi electrons are in a stable aromatic system still they are available to attack with a strong electrophile to give a carbocation. This resonance-stabilized carbocation is called a **sigma complex** because the electrophile is joined to the benzene ring by a new sigma bond.

The sigma complex (also called an arenium ion) is not aromatic because the sp^3 hybrid carbon atom interrupts the ring of p orbitals. This loss of aromaticity contributes to the highly endothermic nature of thus first step. The sigma complex regains aromaticity either by a reversal of the first step (returning to the reactants) or by loss of the proton on the tetrahedral carbon atom, leading to the substitution product.

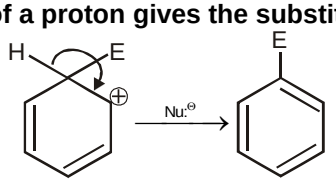
The overall reaction is the substitution of an electrophile $(\overset{\oplus}{E})$ for a proton $(\overset{\oplus}{H})$ on the aromatic ring so it is called **electrophilic aromatic substitution**.

Step 1 : Attack of an electrophile on benzene ring forms the sigma complex



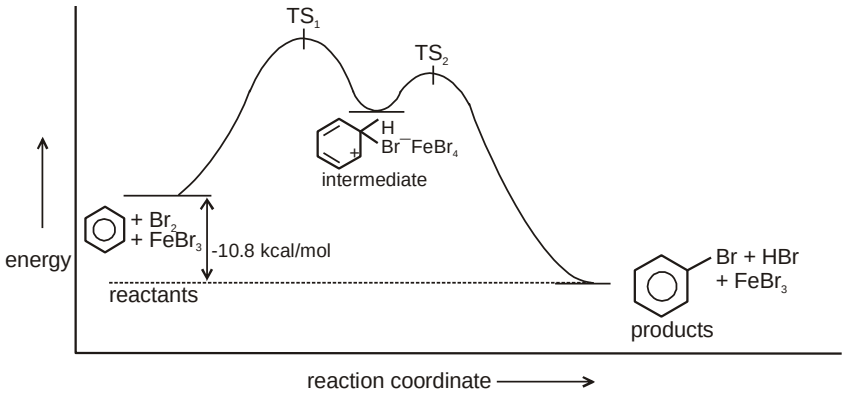
Resonance hybrid
[σ – complex]
Arenium Ion

Step 2 : Loss of a proton gives the substitution product.



+ Nu – H

Energy diagram : For bromination reaction, electrophile is bromonium ion (Br^+)



For an electrophilic aromatic substitution reaction to overcome the high activation energy that charaterizes the first step, the electrophile must be a fairly reactive one. Many of the electrophilic reagents that react rapidly with alkenes do not react at all with benzene. For example peroxy acids and diborane, fall into this category, others such as bromine react with benzene only in presence of catalysts that increases their electrophilicity.

Effect of substituent groups in monosubstituted benzene :

(A) Ortho-para directing and activating groups : All electron releasing groups (+m, +I) are ortho-para directing groups and activating towards electrophilic reactions.

(B) Ortho para directing but deactivating groups : Halogens are deactivating but ortho-para directing groups.

Reactivity of benzene decreases by –I effect of halogens and ortho-para directing nature is decided by +m effect of halogens.

(C) Meta directing and deactivating groups : Mostly electron withdrawing groups (–m, –I) are meta directing groups and deactivating towards electrophilic reactions.

	Substituent groups	Reactivity (effect on rate)	Directing nature (effect on orientation)
1.	$-O^- > -NH_2 > -NHR > -NR_2 > -OH$	Very strongly activating	Ortho-para directing
2.	$-OR > -NH-\overset{\overset{O}{\|\|}}{C}-R > -O-\overset{\overset{O}{\|\|}}{C}-R$	Strongly activating	Ortho-para directing
3.	$-R, -Ar, -CH=CH_2$	Activating	Ortho-para directing
4.	$-X(F, Cl, Br, I), -N=O, -CH_2X, -CHX_2$	Deactivating	Ortho-para directing
5.	$-CHO, -\overset{\overset{O}{\|\|}}{C}-R, -COOR, -COCl, -C\equiv N, -SO_3H$	Strongly deactivating	Meta directing
6.	$-NO_2, -\overset{+}{N}R_3, -\overset{+}{S}R_2, -CF_3$	Very strongly deactivating	Meta directing

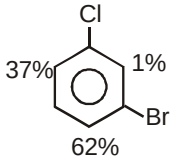
Effect of substituent groups in disubstituted benzene :

(1) If activating and deactivating both groups are present in a system then position of electrophile will be determined by activating group.

(2) If both groups present in a system are deactivator then position of electrophile will be determined by stronger deactivator.

(3) If both the groups are activating group then position of electrophile will be determined by stronger activator.

(4) There is often little substitution between two groups that are meta to each other.

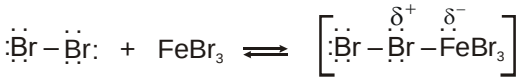
Ex. Nitration product of 

(% nitro product)

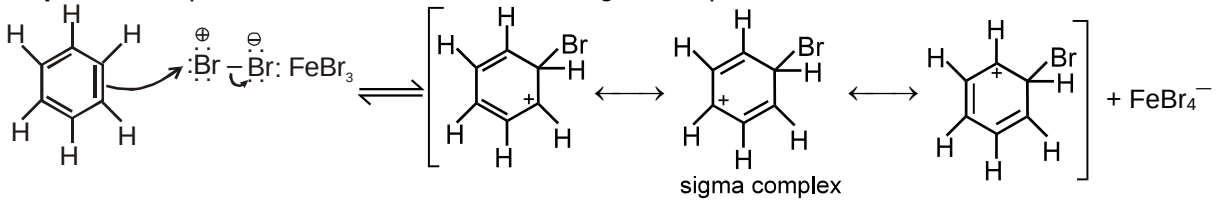
(i) Halogenation

Chlorine and bromine in presence of lewis acid (like $AlCl_3$, $FeCl_3$) react with benzene. Fluorination and iodination of benzene and other arenes rarely performed. Fluorine is so reactive that its reaction with benzene is difficult to control. Iodination is too slow and has an unfavourable equilibrium constant.

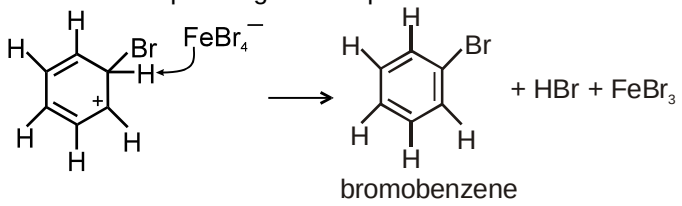
Step 1 : Formation of a stronger electrophile.



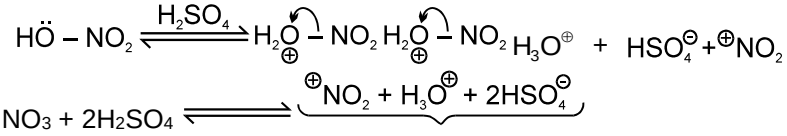
Step 2 : Electrophilic attack and formation of the sigma complex.



Step 3 : Loss of a proton gives the products.

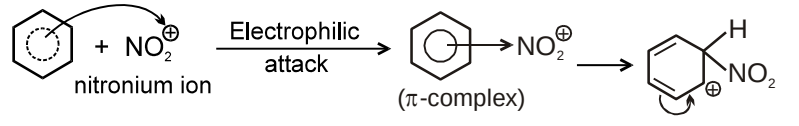


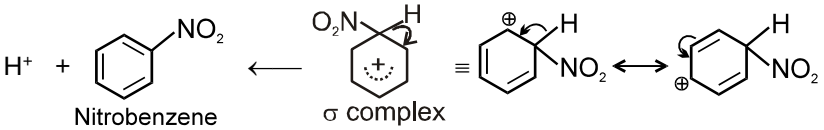
(ii) Nitration



$HNO_3 + 2H_2SO_4 \rightleftharpoons {}^{\oplus}NO_2 + H_3O^{\oplus} + 2HSO_4^{\ominus}$

HNO_3 act as a base in the above reaction.



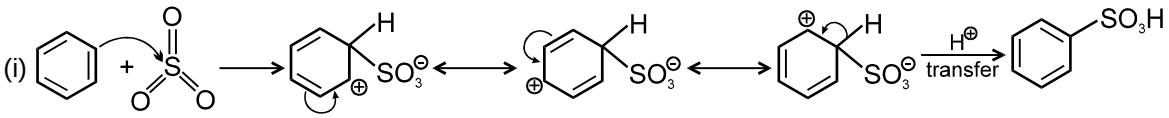


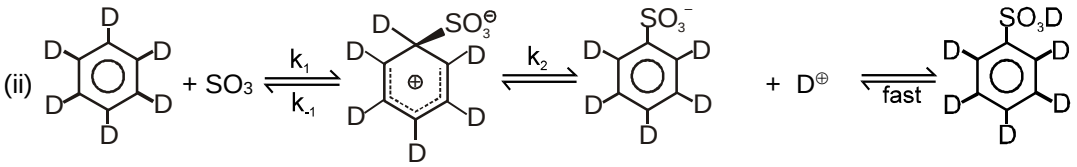
***** Purpose of sulphonic acid in the reaction is to increase the concentration of nitronium ion (NO^+_2)

(iii) Sulphonation

Sulphur trioxide in sulphuric acid is used as the sulphonation agent.

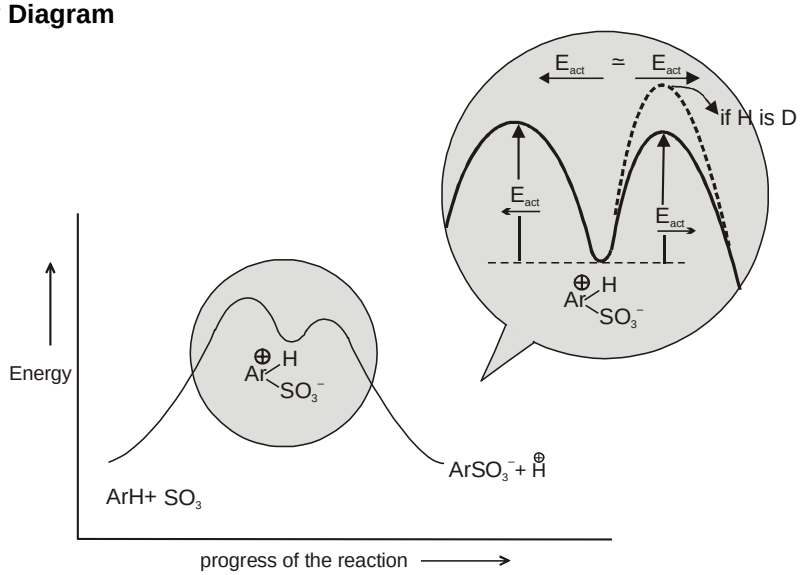
$2H_2SO_4 \rightleftharpoons SO_3 + H_3O^{\oplus} + HSO_4^{\ominus}$

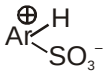
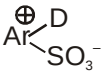




Sulphonation, is **reversible** and takes place in concentrated sulphuric acid. ($K_{-1} \simeq K_2$).

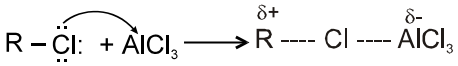
Energy Diagram

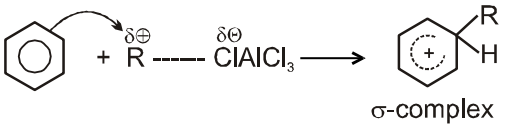


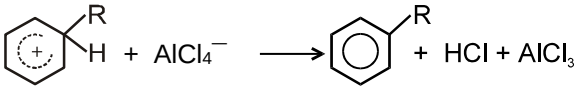
Some  or  go on to product, some revert to the starting material and decrease the rate of reaction. This effect is known as isotope effect.

(iv) Friedel Craft's reaction

(a) Alkylation : The mechanism for Friedel Craft's reaction involves the following steps.

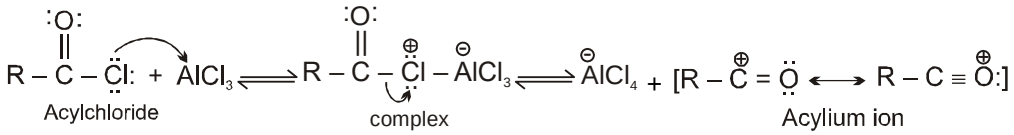
(i) 

(ii) 

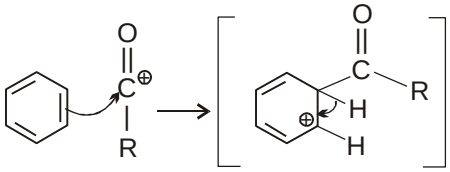
(iii) 

(b) Acylation : Acylation of benzene may be brought about with acid chlorides or anhydrides in presence of Lewis acids.

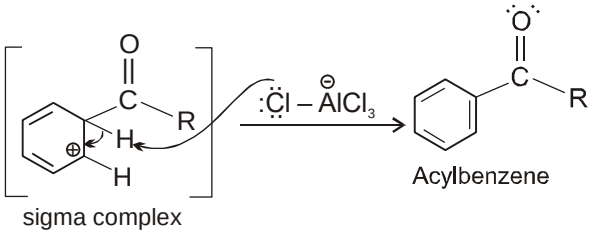
Step-1 : Formation of an acylium ion.



Step-2 : Electrophilic attack.



Step-3 : Loss of a proton. Complexation of the product.



Limitations of Friedel craft's reactions :

(i) Highly reactive rings like anililine and highly deactivated rings like nitrobenzene, cyanobenzene do not give friedel craft reactions.

(ii) Poly alkylation is possible but poly acylation is not possible.

(iii) Rearranged products may form in the friedel craft alkylation reactions.

(iv) Diketone also undergoes the Friedel Craft reaction with benzene.

Section (B) : Free radical substitution & Free radical addition reaction

(a) Free radical substitution reaction of alkanes

Characteristic reaction of alkanes is **free radical substitution** reaction, these reactions are generally chain reactions which are completed in three steps :

(i) chain initiation (ii) chain propagation. (iii) chain termination

Halogenation : $R–H + X_2 \xrightarrow[250^o–400^oC]{\text{UV Light or temp.}} R–X + HX$

Mechanism :

(i) Chain initiation : $X_2 \xrightarrow[250^o–400^oC]{\text{UV or temp.}} \dot{X} + \dot{X}$

(ii) Chain propagation : $\dot{X} + R – H \xrightarrow{rds} \dot{R} + HX$

$\dot{R} + X – X \longrightarrow R – X + \dot{X}$

(iii) Chain termination : $\dot{X} + \dot{X} \longrightarrow X_2$

$\dot{R} + \dot{R} \longrightarrow R – R$

$\dot{R} + \dot{X} \longrightarrow R – X$

Reactivity of X_2 : $F_2 > Cl_2 > Br_2 > I_2$
Reactivity of H : 3°H > 2°H > 1° H

Remarks : With F_2 alkanes react so vigorously that even in the dark and at room temperature, reactant is diluted with an Inert gas. Iodination is reversible reaction, since HI is formed as a by product and It is a strong reducing agent and reduces alkyl iodide back to alkane. Hence iodination can be done only in presence of strong oxidising agent like HIO_3, HNO_3 or HgO.

Ex. $CH_4 \xrightarrow[h\nu]{Cl_2} CH_3Cl \xrightarrow[h\nu]{Cl_2} CH_2Cl_2 \xrightarrow[h\nu]{Cl_2} CHCl_3 \xrightarrow[h\nu]{Cl_2} CCl_4$

$+ \quad + \quad + \quad +$

$HCl \quad HCl \quad HCl \quad HCl$

In a chain reaction following reagents are involved -

(i) Initiators : They initiate the chain reaction, Initiators are peroxide (R_2O_2), Perester's etc.

(ii) Inhibitors : A substance that slows down or stops the reaction is known as inhibitors

For example O_2 is a good inhibitor

$\dot{R} + O_2 \longrightarrow R – O – \dot{O} + \dot{R} \longrightarrow R – O – O – R$

all reactive alkyl free radicals are consumed so reaction stops for a period of time.

Halogenation of higher alkane :

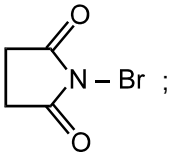
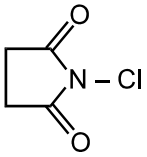
(a) $CH_3–CH_2–CH_3 \xrightarrow[\text{light, } 25^oC]{Cl_2} CH_3 – \underset{\displaystyle Cl}{\underset{|}{CH}} – CH_3 + CH_3 – CH_2 – CH_2 – Cl$

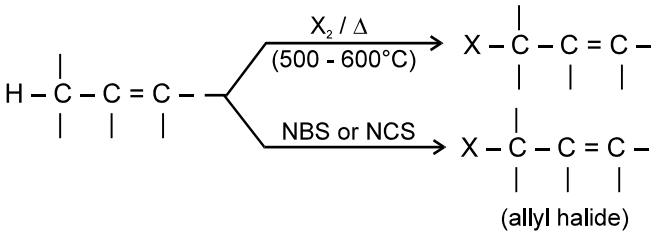
(b) $CH_3 – \underset{\displaystyle CH_3}{\underset{|}{CH}} – CH_3 \xrightarrow[\text{light, } 25^oC]{Cl_2} CH_3 – \underset{\displaystyle CH_3}{\underset{|}{CH}} – CH_2 – Cl + CH_3 – \underset{\displaystyle Cl}{\underset{|}{\overset{\displaystyle CH_3}{\overset{|}{C}}}} – CH_3$

(c) $CH_3-\underset{\underset{CH_3}{|}}{CH}-CH_3 \xrightarrow[\text{heat, 127°C}]{Br_2} \underset{\underset{CH_3}{|}}{CH_3-CH-CH_2Br}$ (trace) + $CH_3-\underset{\underset{CH_3}{|}}{\overset{CH_3}{\overset{|}{C}}}-Br$ (over 99%)

(b) Free radical allylic and benzylic substitution reaction :

Reagents: $Cl_2/h\nu$ or Δ , $Br_2/h\nu$ or Δ , NBS or NCS

NBS = N-Bromosuccinimide  ; NCS = N-Chlorosuccinimide 

General Reaction 

$X_2 = Cl_2, Br_2$

It is free radical substitution reaction.

(c) Free radical addition reaction of alkene & alkyne :

Reagents : HBr / R_2O_2, hν [Kharasch Effect or Peroxide Effect]

General Reaction :

$$R-CH=CH_2 + HBr \xrightarrow{R_2O_2/h\nu} R-CH_2-CH_2-Br$$

Mechanism :

(1) $R-O-O-R \xrightarrow{h\nu} 2RO^{\bullet}$

(2) $RO^{\bullet} + HBr \longrightarrow ROH + Br^{\bullet}$

.....Chain initiation steps

(3) $R-CH=CH_2 + Br^{\bullet} \longrightarrow R-\dot{C}H-CH_2-Br$ (major, $2^{o}\dot{R}$) + $R-CH(Br)-\dot{C}H_2$ (minor, $1^{o}\dot{R}$)

(4) $R-\dot{C}H-CH_2-Br + HBr \longrightarrow R-CH_2-CH_2-Br + Br^{\bullet}$

$Br^{\bullet}$ repeats step (3).

.....Chain propagating steps

Remarks :

(1) When HBr is added to an unsymmetrical alkene in presence of sunlight and peroxide. Then an **Anti Markovnikov's Addition Product is obtained.**

(2) It is a free radical chain reaction.

(3) In presence of peroxide and sunlight $Br^{\bullet}$ is formed in chain initiation step.

(4) $Br^{\bullet}$ forms more stable alkyl radical by homolysis of C=C π bond.

(5) In the last step alkyl radical abstracts $H^{\bullet}$ from HBr and Anti markownikov's product is obtained.

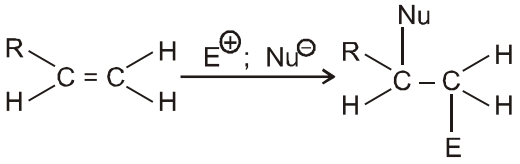
Section (C) : Electrophilic addition reaction

(a) Electrophilic addition reaction of Alkenes :-

Due to presence of weak π electrons in alkene and alkyne, it will go for electrophilic addition reaction.

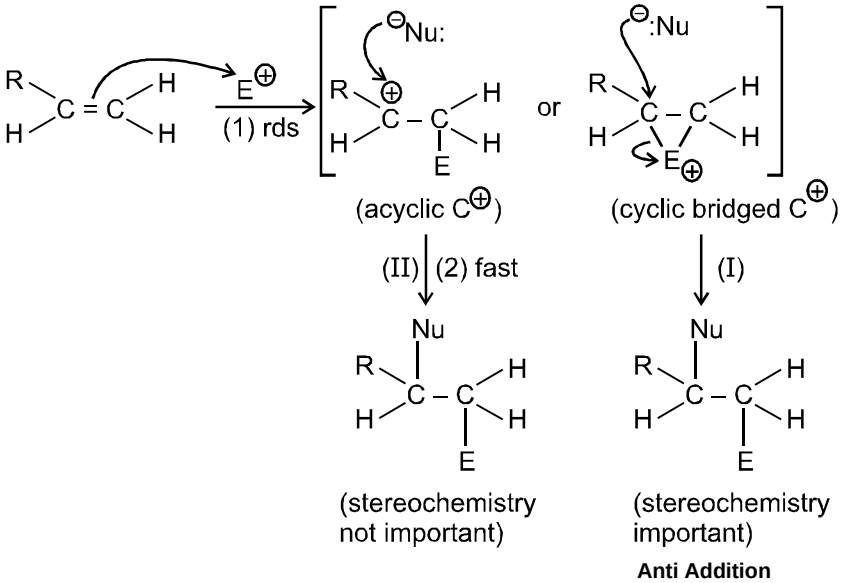
In electrophilic addition reactions one weak π-bond (251 KJ mol^{-1}) is broken and two strong σ bonds (2 × 347 = 694 KJ mol^{-1}) are formed. The overall reaction is accompanied by a release of about 694–251 = 443KJmol^{-1} of energy.

General Reaction of electrophilic addition :



..... Addition product.

The overall reaction mechanism can be visualised as followed :



Anti Addition

Remarks :

Alkenes, Alkynes and Alkadienes are electron rich species. So they function as $Nu:^{\ominus}$ species (due to loosely bound π-electrons)

These compounds mainly give electrophilic addition reactions. Due to nucleophilic nature of alkenes/alkynes having affinity for $E^{\oplus}$.

The reaction is initiated by an attack of $E^{\oplus}$.

Rate of reaction ∝ stability of carbocation

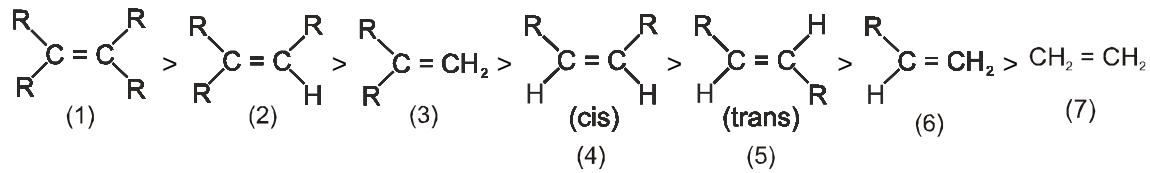
Reactivity of an Alkene :

(1) Presence of e^{-} releasing groups (+m, +I) at C = C increases nucleophilicity and reactivity.

(2) Presence of ERG stabilises the intermediate carbocation. (3) More stable $C^{\oplus}$, more is reactivity.

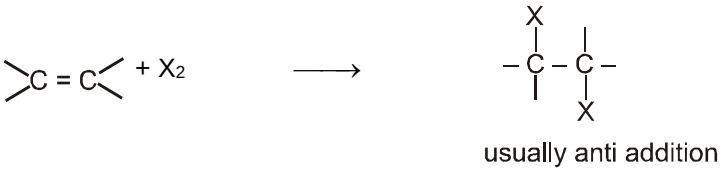
Examples of Reactivity Orders :

(i)



(ii) ERG – CH = CH_2 > CH_2 = CH_2 > EWG – CH = CH_2

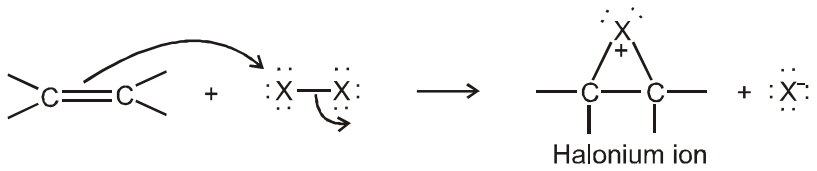
(i) ADDITON OF HALOGEN (HALOGENATION) :



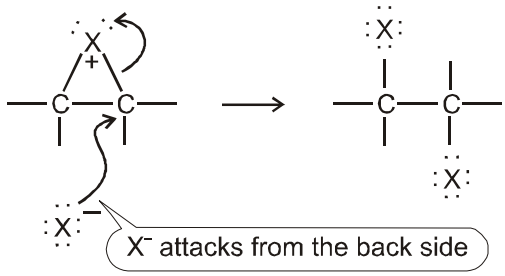
(X_2 = Cl_2, Br_2, but not F_2 and I_2)

Mechanism

Step 1 :



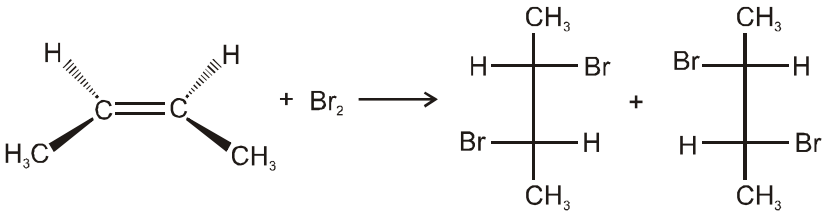
Step 2 :



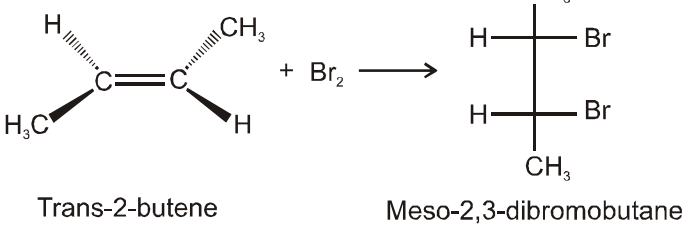
Remarks : Anti addition; No rearrangement; Bridged Carbocation; Markovnikoff's additions

The addition of bromine to cyclopentene is a stereospecific **anti addition.**

Ex.



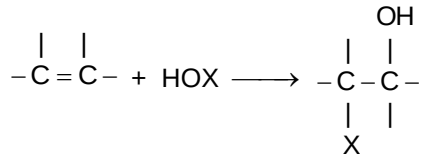
Ex.



(ii) ADDITION OF HOX :

Reagents : (i) $X_2 + H_2O \rightarrow HOX + HX$ or (ii) HOX , H^+

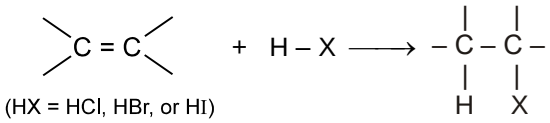
Electrophile : X^+ , Halonium ion ;



Remarks : Anti addition ; No rearrangement ; Bridged Carbocation ; Markovnikoff's additions

(iii) ADDITION OF HYDROGEN HALIDES (+ HX) :

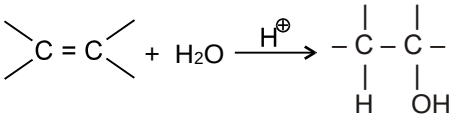
Reagents : HX; **Electrophile :** H^+



Remarks : Markovnikoff additon ; Intermediate carbocation ; Rearrangement may take place

(iv) ADDITION OF H_2O (HYDRATION REACTION)

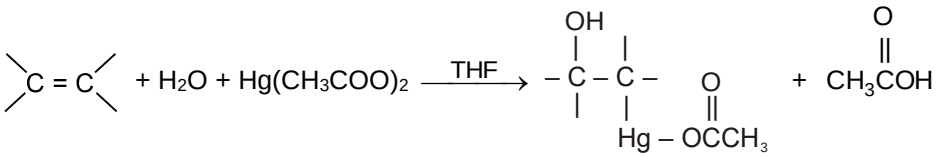
(a) Acid-Catalyzed Hydration of Alkenes : **Reagents :** Dilute H_2SO_4 or H_3O^+

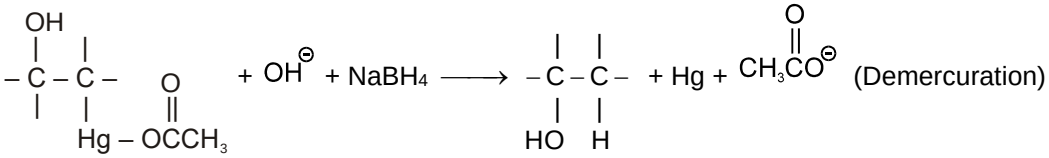


Remarks : Markovnikoff additon ; Intermediate carbocation ; Rearrangement may take place

(b) Oxymercuration-Demercuration : **Reagents :** (i) $Hg(OAc)_2$, H_2O (ii) $NaBH_4$

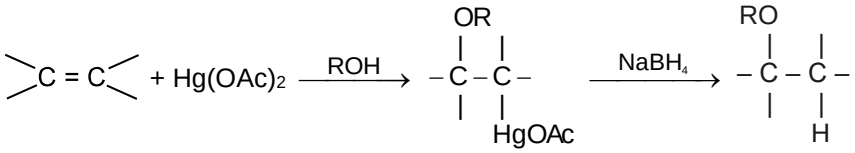
Electrophile : $\overset{+}{H}gOAc$



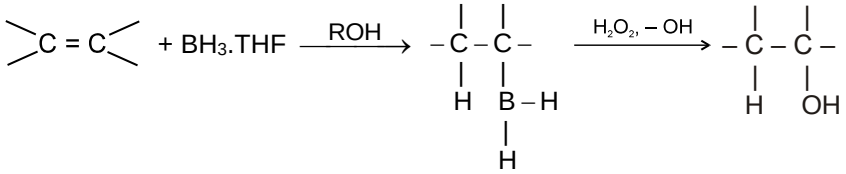


Remarks : No rearrangement ; Bridged Carbocation ; Markovnikoff's additions

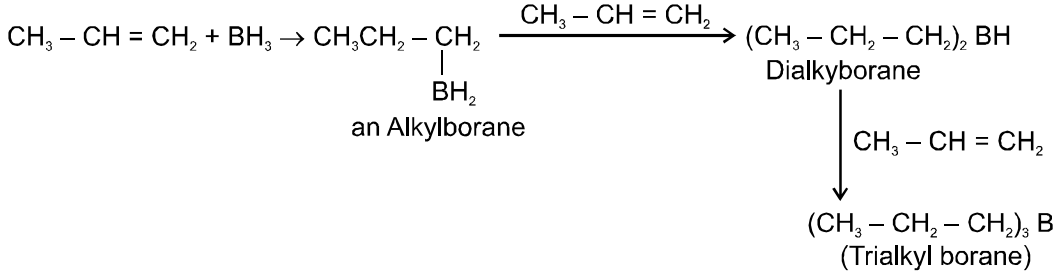
Alkoxymercuration - demercuration



(c) Hydroboration-oxidation : **Reagents :** BH_3,THF/H_2O_2,$^-$OH



Mechanism :



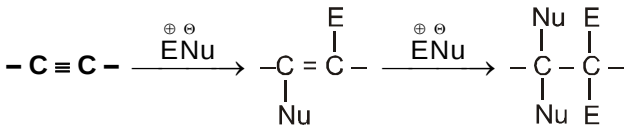
Remarks : Anti Markovnikov's addition ; Syn addition.

(b) Electrophilic addition reaction of Alkynes :

Many of the reactions of alkynes are similar to the corresponding reactions of alkenes. Like the pi bond of an alkene, the pi bonds of an alkyne are electron-rich, and they readily undergo addition reaction. The bond energy of the alkyne triple bond is about 226 kJ (54 kcal) more than the bond energy of an alkene double bond.

Since sigma bonds are generally stronger than pi bonds, the reaction is usually exothermic. Alkynes have two pi bonds, so upto two molecules can add across the triple bond.

We must consider the possibility of a double addition whenever a reagent adds across the triple bond of an alkyne. Some conditions may allow the reaction to stop after a single addition, while other conditions give double addition.

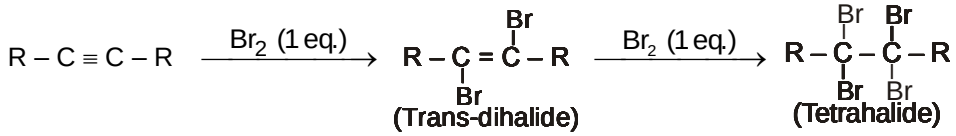
General Reaction : 

Common Reagents :

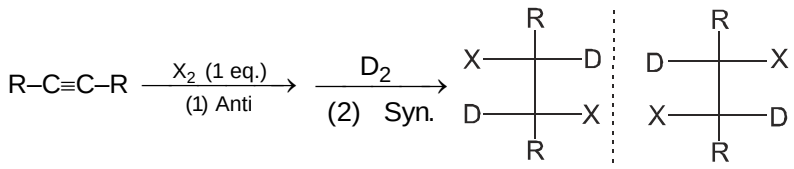
(i) + X_2 ($X^{\oplus}$) (ii) + HOX ($X^{\oplus}$) (iii) + HX ($H^{\oplus}$)

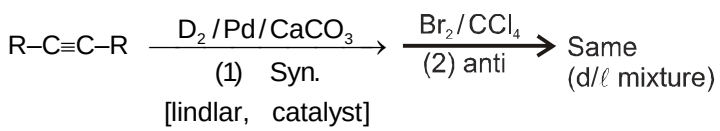
Markovnikov's rule of addition : In an electrophilic addition reaction to alkenes and alkynes the electrophile attacks in such a way that a more stable carbocation intermediate is formed on which nucleophile attacks in the next step.

(i) ADDITON OF HALOGEN (HALOGENATION) :



Remark : - Reaction is Anti in both step

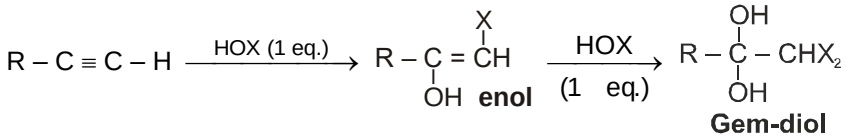




(ii) ADDITION OF HOX :

Alkynes + HOX $\longrightarrow$ α, α-dihaloketone + α-haloketone

(90% major) (10% minor)



10% (minor) 90% (major)

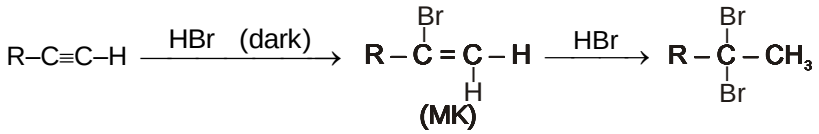
[α-Haloketone] [α, α-Dihaloketone]

Remarks :

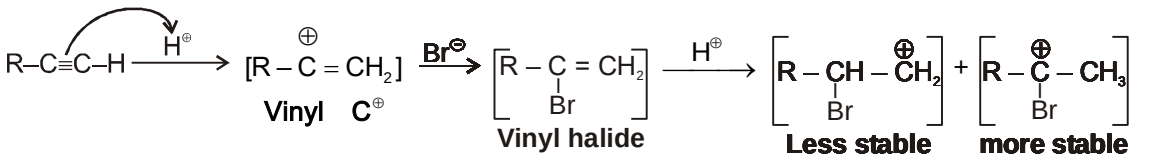
Two molecules of HOX can be added, the end product is α, α-Dihaloketone.

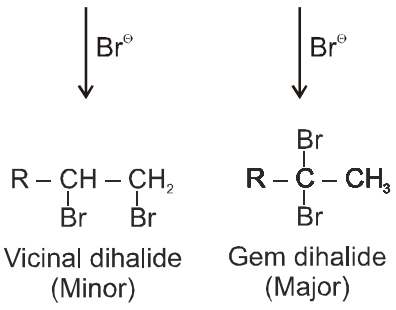
The intermediate product is an enol which gives a minor product α-haloketone.

(iii) ADDITION OF HYDROGEN HALIDES (+ HX) :



Mechanism :





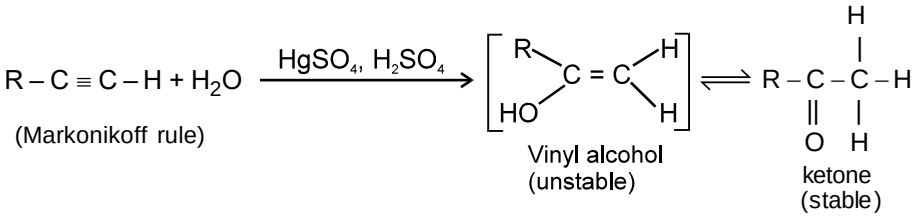
Remarks : (1) Markovnikov's Addition in both steps.

(2) If two moles of HX are added the final product is Gemdihalide.

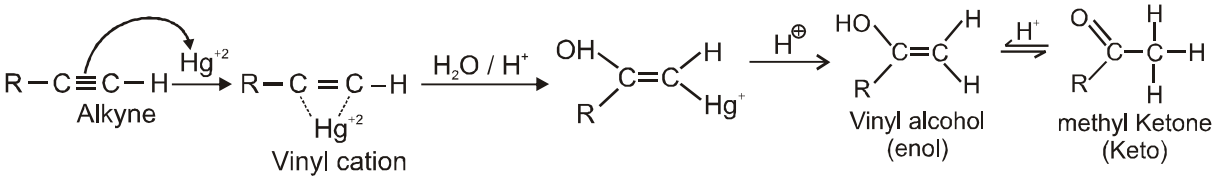
(3) **Electrophilic addition to terminal alkyne is regioselective.**

(iv) ADDITION OF H_2O (HYDRATION REACTION) :

(a) Mercuric ion catalyzed hydration :



Mech.



(b) Hydroboration Oxidation of Alkynes :

Alkadienes :