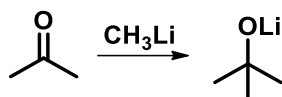


3.5. Organic Reaction Mechanisms

3.5.1. Categories

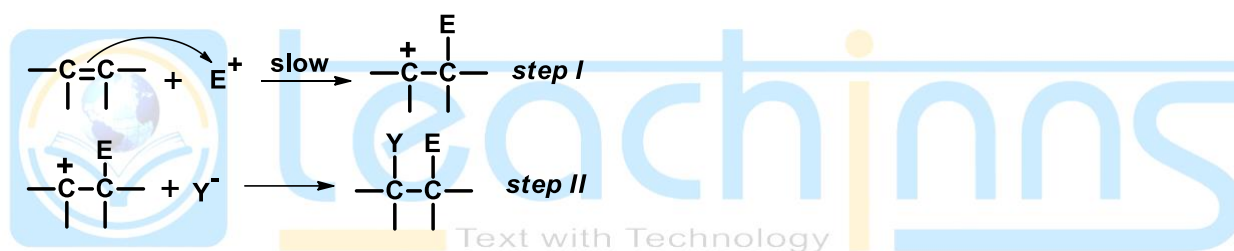
- Based on the reactants, products and side products organic reactions are classified into four categories, (a) Addition reaction, (b) Elimination reaction, (c) Substitution reaction and (iv) Rearrangement reaction.

3.5.1a. Addition reaction: These are the characteristics of compounds having unsaturation or multiple bonds (alkenes or alkynes). This reaction occurs very rapidly because sigma bonds are stronger than pi-bonds.



3.5.1a.I. Electrophilic addition reaction:

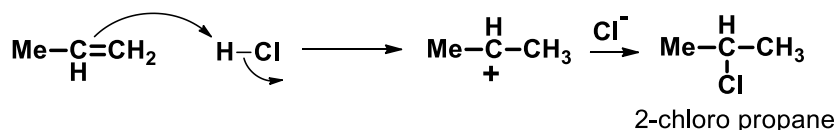
- It is the reaction between an electron deficient species with electron rich substrate. This reaction proceeds through two step mechanism.



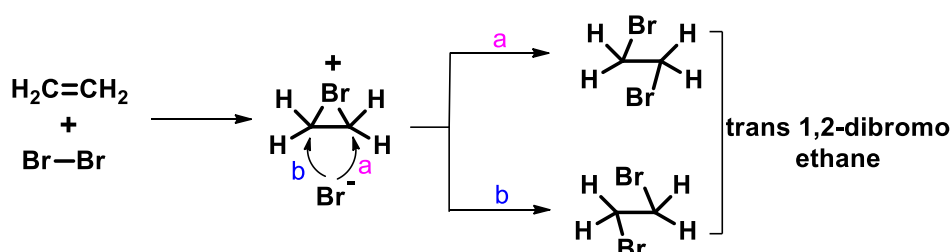
- Reaction of HCl with propene and Br₂ with ethane

The reaction of HCl with propene and Br₂ with ethane is completely different, the former reagent produces a mixture of products (cis- and trans isomer), however, the addition reaction of Br₂ with ethane produce only trans dibromo ethane.

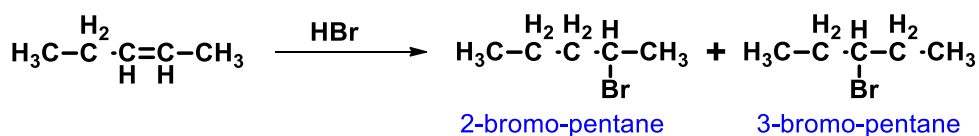
In case of HCl addition to propene, first a 2° carbocation is formed and then Cl⁻ attacks to the carbocation to form 2-chloro propane.



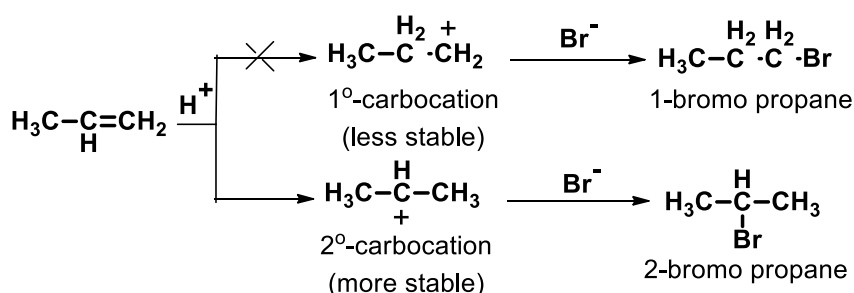
Whereas in case of bromine addition with ethane, first bromonium cation is formed and in the second step bromide ion attacks to the cation which proceeds from anti or para position. Therefore this reaction always affords trans dibromo ethane.



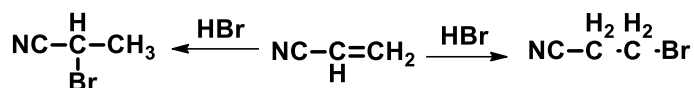
- The bromination of trans -2-butene produces meso-dibromide and the cis-2-butene affords racemic compounds (a pair of enantiomers) under the same reaction condition.
- In both the cases the reaction proceeds through bromonium cation (common intermediate).
- ❖ **Addition rule:** The addition reaction of unsymmetrical reagents to unsymmetrical alkenes or alkynes follows a rule which is known as **Markownikoff's rule**. This rule states that the negative end of the reagent goes/adds to the carbon atom which has least number of hydrogen atom or which is more substituted or which is sterically more hindered.
- ❖ When both the carbon atoms having same number of hydrogen atoms in an unsymmetrical alkene a mixture of products are formed.



The formation of these products can be explained by the stability of the carbocations formed.



- ❖ However, Markownikoff's rule is not applicable for those alkenes which contains electron withdrawing atoms or groups.

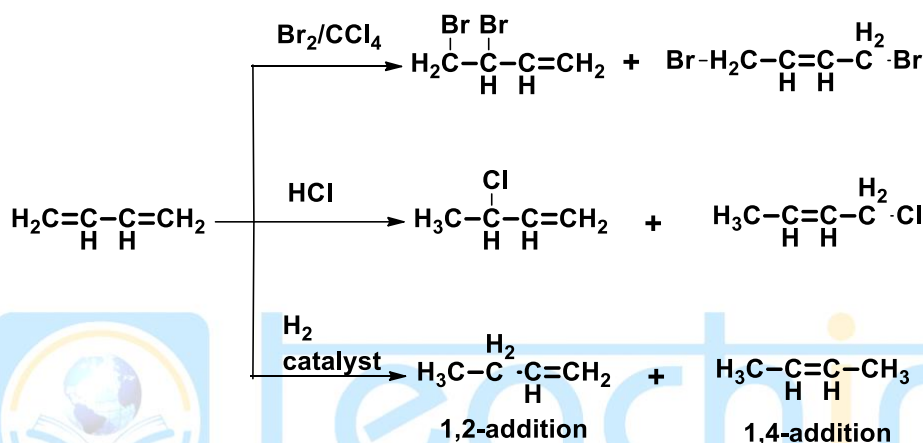


2-bromo propane nitrile
obtained from less
stable carbocation

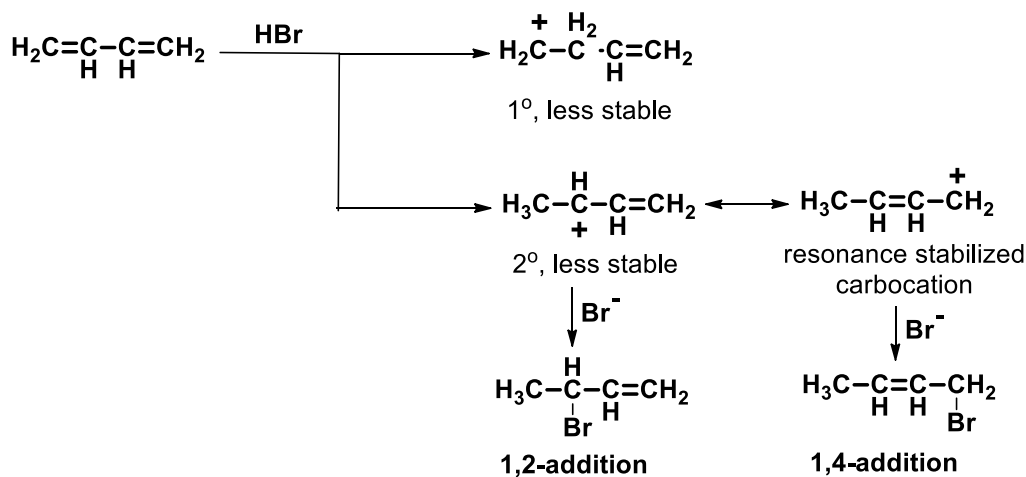
3-bromo propane nitrile
obtained from more
stable carbocation

❖ **Addition to conjugated dienes:**

- A conjugated diene (e.g. 1,3-butadiene) produces two types (1,2- and 1,4-) addition products.



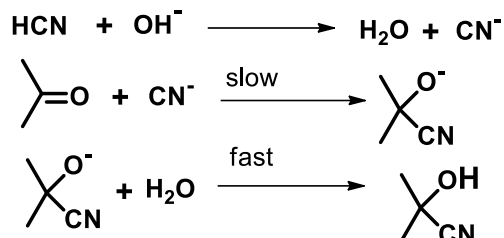
- The addition of HBr to 1,3-butadiene produces the following products



3.5.1a.II. Nucleophilic addition reaction

It is the reaction between electron rich reagents with electron deficient substrate.

Example: (i) Addition of HCN to carbonyl group

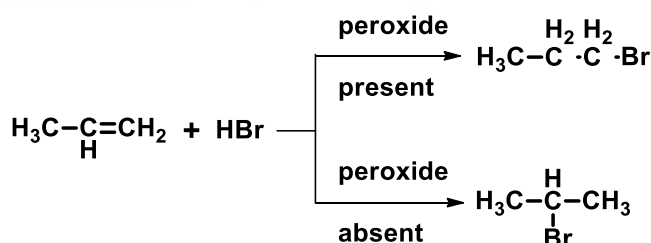


- Nucleophilic addition to activated carbon-carbon double bond

Due to presence of π -electron cloud on the carbon-carbon double bond nucleophilic attack is difficult, however, the presence of electron withdrawing group onto the carbon-carbon double bond facilitates the nucleophilic attack.

3.5.1a.III. Free radical addition:

The addition reaction of HBr to unsymmetrical alkene in presence of organic peroxide (benzoyl peroxide) does not obey Markownikoff's rule and hence produces anti Markownikoff addition product when the reaction is performed in presence of peroxide. This is known Kharash peroxide effect or peroxide effect.



The mechanism of anti-Markownikoff's or Kharash peroxide effect includes three steps.

- (i) chain initiating step, (ii) chain propagating step and (iii) chain terminating step.
- HCl and HF do not form free radical due to larger bond energy, hence peroxide effect is not shown in such cases.
- Although HI has minimum bond energy, very reactive, instead forms I_2 .

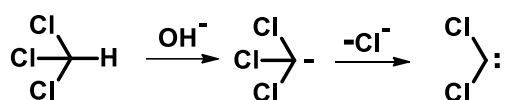
❖ **Cis-Trans addition:**

- Cis- addition on cis form results meso.
- Cis-addition on trans form produces racemic mixtures.
- Trans addition on trans form results meso.
- Trans addition on cis form yields racemic mixtures.
- Addition of Br₂ to the cis-alkene forms only the threo pair of enantiomers.
- Addition of Br₂ to the trans alkene forms only the erythro pair of enantiomers.

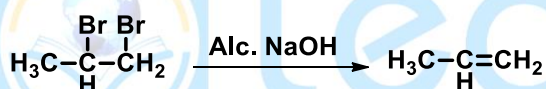
3.5.1b. Elimination reaction

3.5.1b.I. 1,1-(α)-Elimination reaction: When two groups or atoms are lost from the same carbon.

atom of the molecule, is called 1,1-or α-elimination reaction.



3.5.1b.II. 1,2-(β)-Elimination reaction: When two atoms or groups are lost from the two adjacent carbon atoms, the process is known as 1,2- or β-elimination reaction.



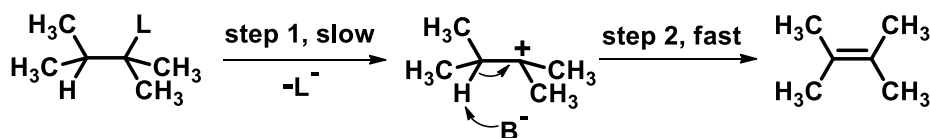
- In most of the organic elimination reaction, one of the eliminating group is hydrogen and the other one is a leaving group and thereby, the sp^3 carbon changes to sp^2 carbon.

3.5.1b.IIa. E1-elimination Reaction: E1-elimination reaction can be explained by the following mechanisms.

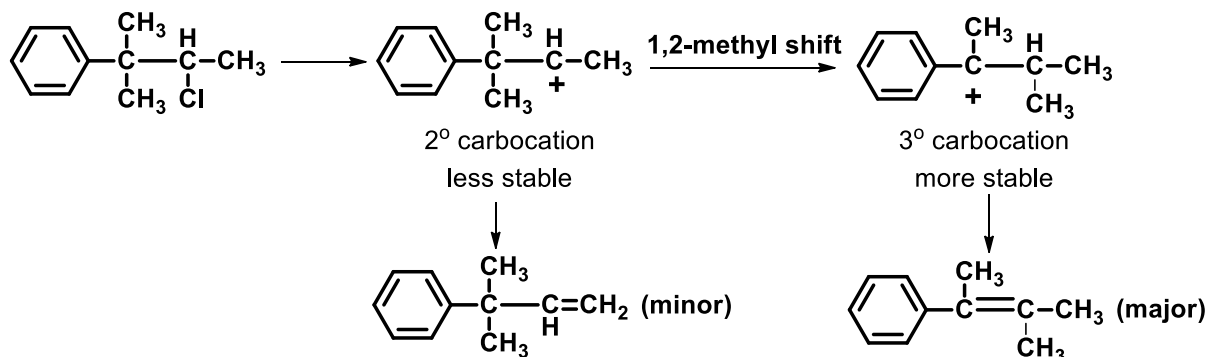
(i) E1 mechanism via carbocation

Step 1: The C-L (leaving group or atom) bond is cleaved heterolitically to form a carbocation.

Step 2: The carbocation loses a proton from the adjacent carbon to form a π -bond in presence of a nucleophile.



- Step 1 is the rate determining step (rds), hence it is called E1 (unimolecular elimination) reaction. In this reaction the intermediate is carbocation which can be rearranged to afford more stable carbocation before losing proton.

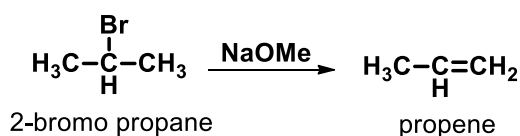


- When two elimination products can be obtained, the major product will be one which is formed following Saytzeff's rule (which states that hydrogen will be eliminated from the β -carbon which is bonded to the fewest hydrogens).
- E1 mechanism via cyclic transition state (TS) produces cis product.

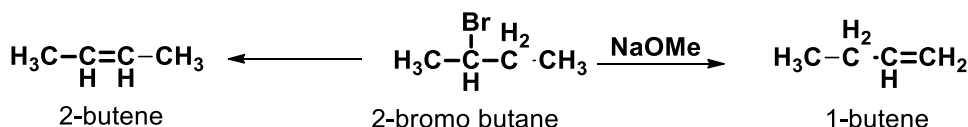
3.5.1b.IIb. E2-elimination Reaction:

- This is bimolecular reaction.
- The two groups or atoms are eliminated in a single step or concerted manner.
- The rate of reaction depends on the concentration of substrate and nucleophile.
- The reaction is of second order.

- ❖ 2-bromo propane has two β -hydrogens from which a proton can be eliminated in an E2 reaction, either of the two, anyone can be removed because of its symmetrical structure.



- ❖ However, 2-bromo butane which has structurally different two β -hydrogens, by removing the protons produces 1-butene and 2-butene. But, according to Saytzeff's rule, 2-butene will be predominant because more substituted alkene will be more stable.

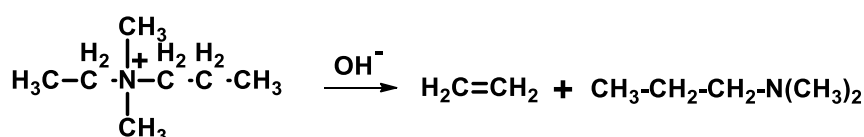


3.5.1b.IIc. E-1cB-elimination Reaction: This reaction proceeds via two steps

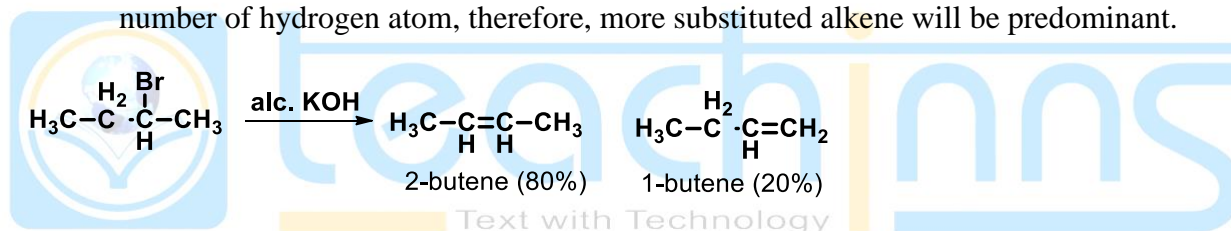
- (i) Step 1: It is the removal of proton by a base to form carbanion.
- (ii) Step 2: In the second step the carbanion loses a leaving group to form an alkene. It is the rds.

Orientation in elimination reaction: The orientation of the product formed is dependent on two rules, (a) Hofmann's rule and (b) Saytzeff's rule.

- (a) Hofmann rule: This rule is applicable for the substrate in which a-carbon atom is attached with a positively charged atom. This rule states that least substituted alkene will be major product.



- (b) Saytzeff's rule: This rule is applicable for unsymmetrical alkene. According to this rule, hydrogen atom will be eliminated preferably from that carbon atom which has less number of hydrogen atom, therefore, more substituted alkene will be predominant.



(c) Substitution reaction:

In this reaction an atom or a group of atoms in a molecule is replaced by another.

Substitution reaction may be classified by

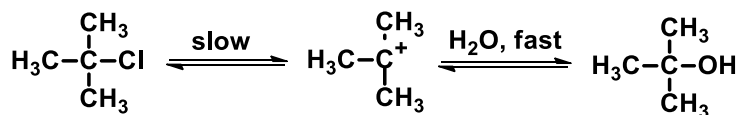
- (i) Replacement by nucleophile called Nucleophilic Substitution reaction (S_N).
- (ii) Replacement by electrophile called Electrophilic Substitution reaction (S_E).

❖ Nucleophilic Substitution reaction (S_N):

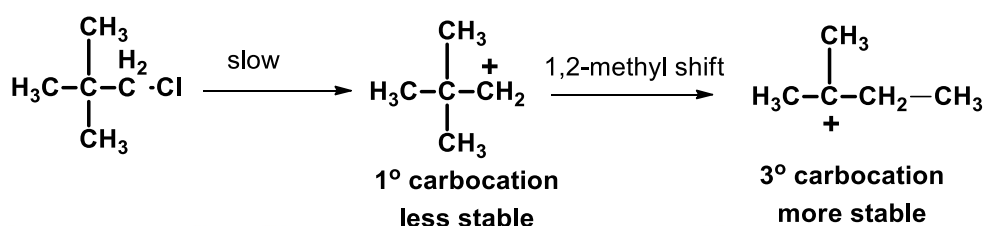
The compound on which substitution takes place is called substrate, and the group which is displaced from the carbon is called leaving group. Nucleophilic substitution reaction may be categorized as unimolecular ($\text{S}_\text{N}1$) and bimolecular ($\text{S}_\text{N}2$).

S_N1 (Substitution Nucleophilic Unimolecular): A S_N1 reaction proceeds in two steps, in the first step a carbocation is formed (rds) and in the second step carbocation is captured by nucleophile.

- In several cases, nucleophile is a solvent such as water, ammonia or alcohol (commonly known as solvolysis).



- Carbocation formed in the 1st step may undergo rearrangement and affords more stable carbocation before attacking the nucleophile.



- As a result of S_N1 reaction there can be racemization or retention of configuration as the carbocation formed is planar, so the nucleophile can approach from both the sides and ultimately resulted in racemization or inversion of configuration.

S_N2 (Substitution Nucleophilic Bimolecular): This reaction proceeds via a concerted step where the nucleophilic attack occurs simultaneously with the pushing out the leaving group. The rate of the reaction is proportional to the concentration of both the substrate and nucleophile.

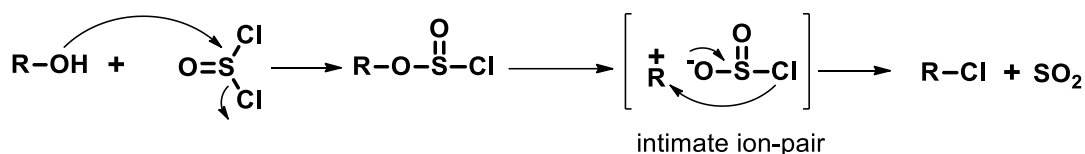
As a result of S_N2 reaction inversion is observed.

• **Factors affecting S_N1 and S_N2 reactions:**

- Polar effect** (I-effect, M-effect, R-effect and hyperconjugation): If polar effect stabilizes the carbocation, then S_N1 will be more probable than S_N2. Primary alkyl halide undergoes S_N2, secondary alkyl halide undergoes both S_N1 and S_N2, tertiary alkyl halide undergoes S_N1 reaction.
- Steric effect:** More steric hindrance restrict the S_N2 mechanism,
- Exception:** Although neopentyl halide is primary, but the tertiary butyl group is large enough to restrict the S_N2 reaction and hence undergoes S_N1 reaction.
- The nature of leaving group:** The rate of S_N1 reaction is dependent on the nature of the leaving group. The higher the stability of the leaving group, greater will be the stability of the carbocation and S_N1 reaction will be more favorable.

- (v) **Nature of nucleophile:** Strong nucleophile favors S_N2 mechanism whereas weak nucleophile favors S_N1 reaction.
- (vi) **Neighbouring group participation (NGP):** NGP increases the rate of the reaction.
- (vii) **Nature of solvent:** Polar solvents (protic) favour S_N1 reaction as they favour ionization of alkyl halide and thereby facilitate the formation of carbocation and stabilizes the carbocation. Whereas, S_N2 mechanism is favoured by aprotic solvents.
- Benzylic and allylic halides undergo S_N1 reaction due to stability of the carbocation by resonance.
- Vinyl and acrylate halide does not undergo S_N1 reaction because of the instability of the carbocation. Hence, these substrates undergo S_N2 reaction.

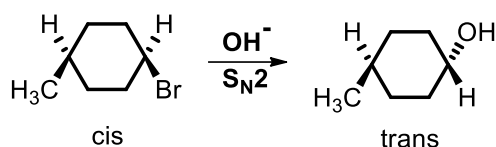
S_Ni (Substitution Nucleophilic Internal): In this process part of leaving group which attacks the substrate detaches itself from the rest of the leaving group.



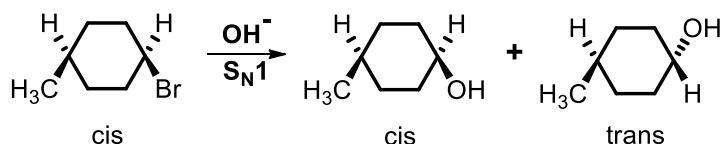
❖ Stereochemistry of S_N2 and S_N1 reaction:

In S_N1 reaction both the retention and racemization of configuration is observed, however in S_N2 reaction only inversion of configuration is obtained.

In case of cyclo compounds, S_N2 reaction produces only the trans product because the nucleophile attacks to the carbon atom from the back side of the leaving group.



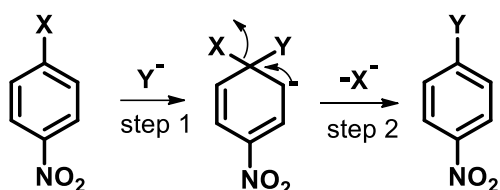
However, in case of S_N1 reaction, both the cis and trans products are formed because the nucleophile can attack the carbocation from either side.



❖ Nucleophilic Aromatic Substitution Reaction:

Benzene does not react with nucleophile under the reaction conditions because

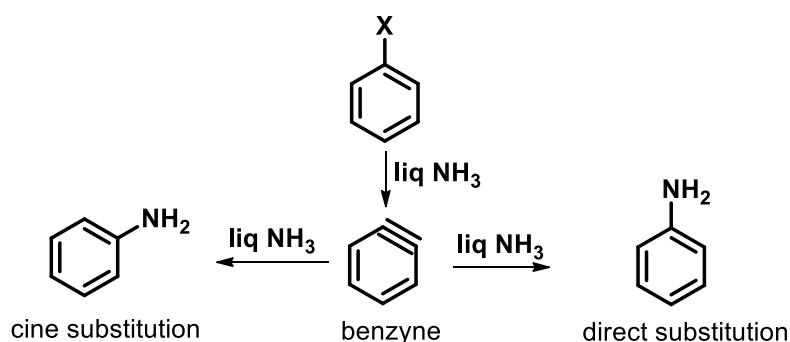
- (i) The π -electron cloud of the benzene ring results repulsion to the electrons of nucleophile.
- (ii) Leaving group H- (hydride) is a strong base, but a leaving group should be a weak base to show good result.
- (iii) If the benzene ring contains one or more electron withdrawing groups/substituents (such as nitro) in ortho or para position with respect to leaving group (such as halogen) then nucleophilic substitution reaction can take place.



- (iv) Sometimes aryl halides under nucleophilic substitution reaction in presence of strong base like NH_2^- , for this base the aromatic ring does not have to contain electron withdrawing substituent.



- (v) The reaction can take place via highly reactive benzyne intermediate, the incoming nucleophile attacks to the benzyne intermediate to form aniline, but there are two types of substitution reaction, (a) where the nucleophile attacks to the same carbon having leaving group or atom (this is called direct substitution) and (b) the nucleophile attacks to adjacent carbon with respect to the leaving group or atom (this is called cine substitution).



❖ Electrophilic Substitution Reaction

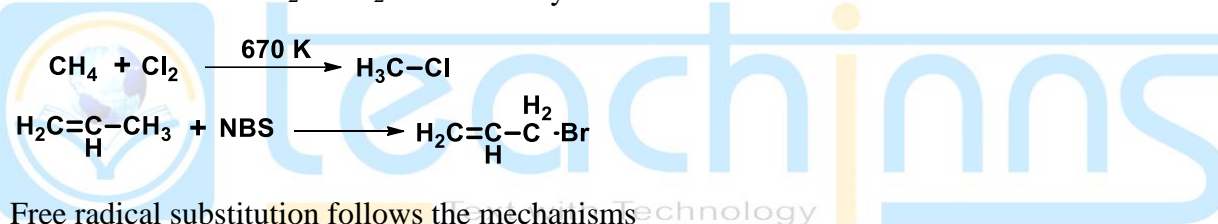
Electrophilic substitution reaction takes place in benzene ring because the π -electrons are highly delocalized. This reaction proceeds through the following mechanism.

- (i) **Generation of electrophile:** The substituting reagent gets ionized to generate an electrophile or electron deficient species.
- (ii) **Attack of electrophiles on π -electron system:** The electrophile attacks the benzene ring and a carbocation intermediate (benzenonium ion) is formed which is very unstable and can not be isolated, except in salt form in special cases.
- (iii) **Removal of proton by base:** In the last step a proton is removed from the benzenonium ion to restore the benzene ring and thus the aromatic character remains intact.

Example of electrophilic substitution: Nitration of benzene, chlorination of benzene, Friedel-Craft's alkylation, Friedel-Craft's acylation.

❖ **Free Radical Substitution Reaction:**

Alkanes react with Cl_2 or Br_2 to afford alkyl chlorides or bromides.



Free radical substitution follows the mechanisms

- (i) Initiation, (ii) Propagation and (iii) Termination