

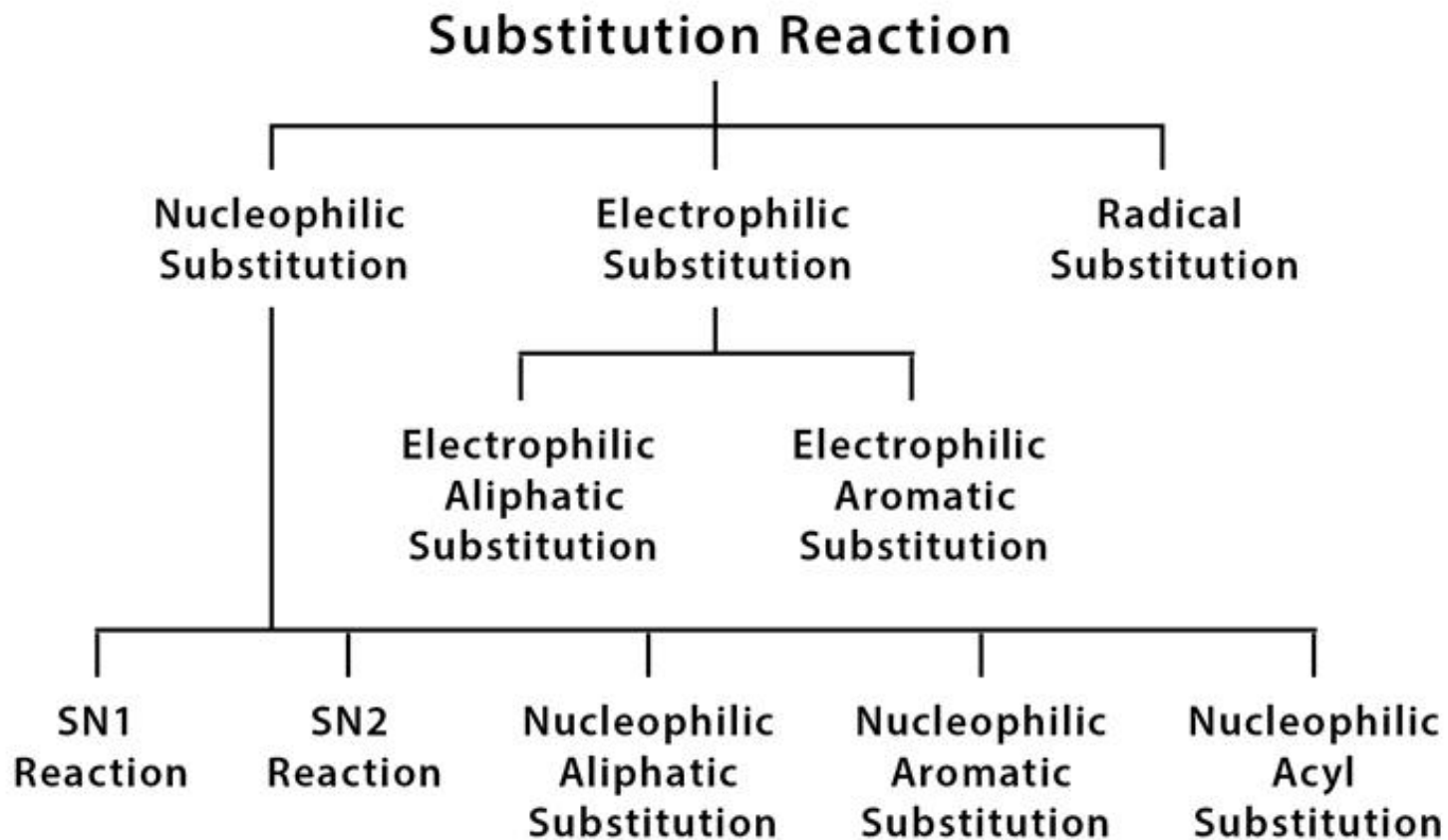
# UNIT-V- S3

## Introduction to reactions involving substitution

# Substitution reaction

A substitution reaction is a chemical reaction in which the functional group attached to a compound is replaced by another group (nucleophile or electrophile).

## Types of Substitution Reaction



# Nucleophilic reactions

What does the term "*nucleophilic substitution*" imply ?

- A **nucleophile** is an electron rich species that will react with an electron poor species
- A **substitution** implies that one group replaces another.

Nucleophilic substitution reactions occur when an electron rich species, the **nucleophile**, reacts at an electrophilic saturated **C** atom attached to an electronegative group, the **leaving group**, that can be displaced as shown by the general scheme:



The electrophilic C can be recognized by looking for the polar  $\sigma$  bond due to the presence of an electronegative substituent (esp. **C-Cl**, **C-Br**, **C-I** and **C-O**)

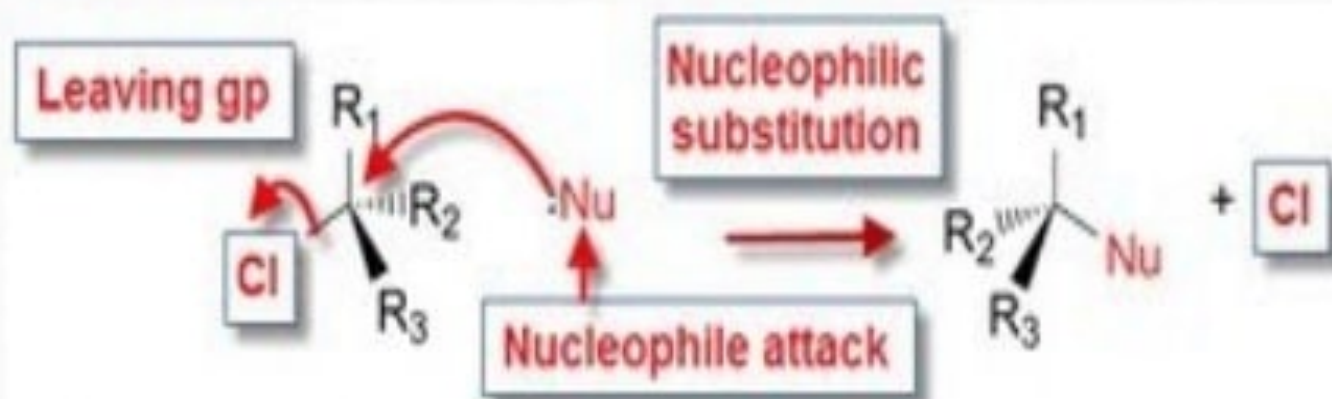
Nucleophilic substitution reactions are an important class of reactions that allow the interconversion of functional groups.

Of particular importance are the reactions of alkyl halides (**R-X**) and alcohols (**R-OH**)

For alcohols, the range of substitution reactions possible can be increased by utilizing the tosylates (**R-OTs**), an alternative method of converting the **-OH** to a better leaving group.

## Nucleophilic Substitution -

- **Nucleophile** (non bonding electron) attack the partial positive charge carbon (nucleus)
- **Chloride** (halogen) - **leaving group** and substituted by nucleophile
- **Nucleophile** replace/substitute the halogen

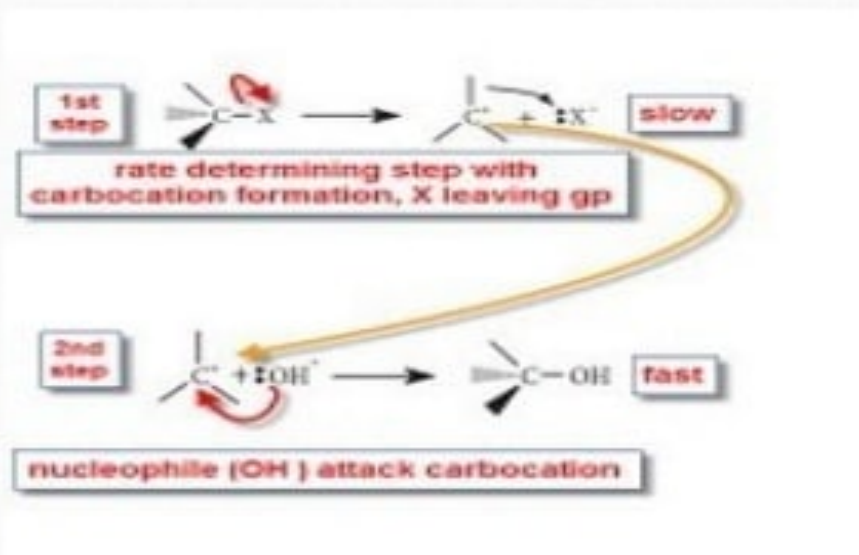


# Mechanism of Nucleophilic Substitution ( $S_N1$ and $S_N2$ )

## $S_{N1}$ - Substitution Nucleophilic Unimolecular

- $S_N1$  - 2 steps, unimolecular (first order)
- 1st step - slow/rds, Carbocation formation
- 2nd step - fast, Nucleophilic attack carbocation
- Rate =  $k$  [substrate], First order overall
- Rate depend on conc substrate  
NOT conc nucleophile
- Nature of the nucleophile doesn't affect the rate

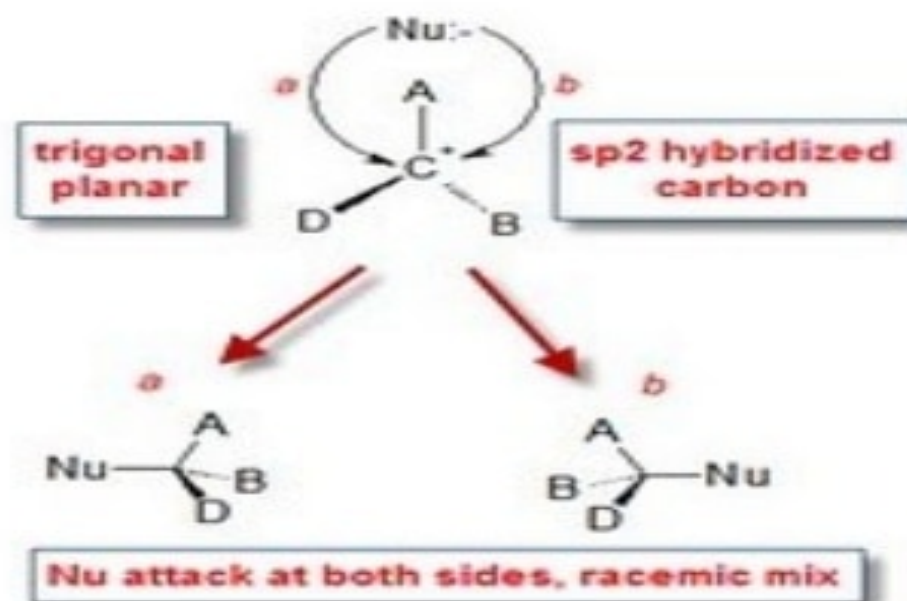
Click [HERE](#) for more info





## Stable Intermediate Carbocation

- $S_N1$  - produce intermediate carbocation
- Carbocation - positive charged on carbon
- Carbocation formation -  $sp^2$  hybrid (Trigonal Planar)
- Nucleophile attack from both sides
- Racemic Mixture



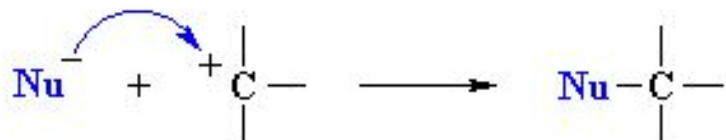
# $S_N1$ mechanism with an example

$S_N1$  indicates a **substitution, nucleophilic, unimolecular** reaction, described by the expression rate =  $k [R-LG]$ . This implies that the rate determining step of the mechanism depends on the decomposition of a single molecular species.

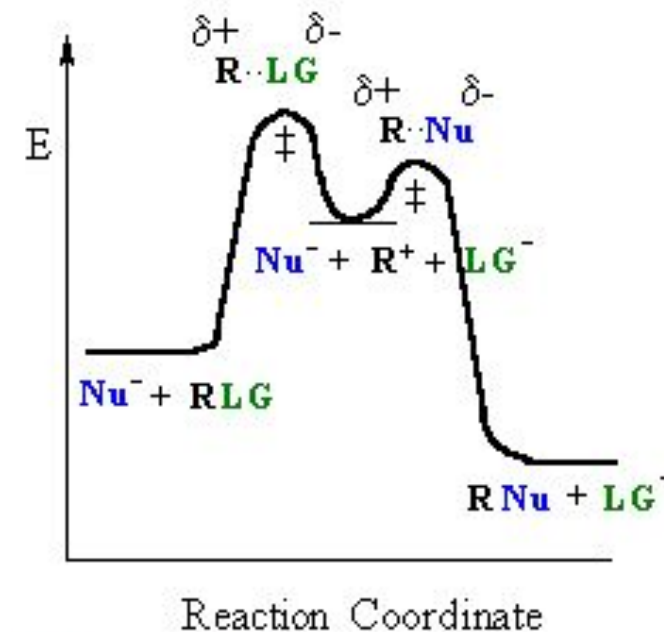
This pathway is a multi-step process with the following characteristics:



step 1: slow loss of the leaving group, **LG**, to generate a carbocation intermediate, then



step 2 : rapid attack of a nucleophile on the electrophilic carbocation to form a new  $\sigma$  bond



$S_N1$  reaction

## IB examples for $S_N1$ and $S_N2$ reactions

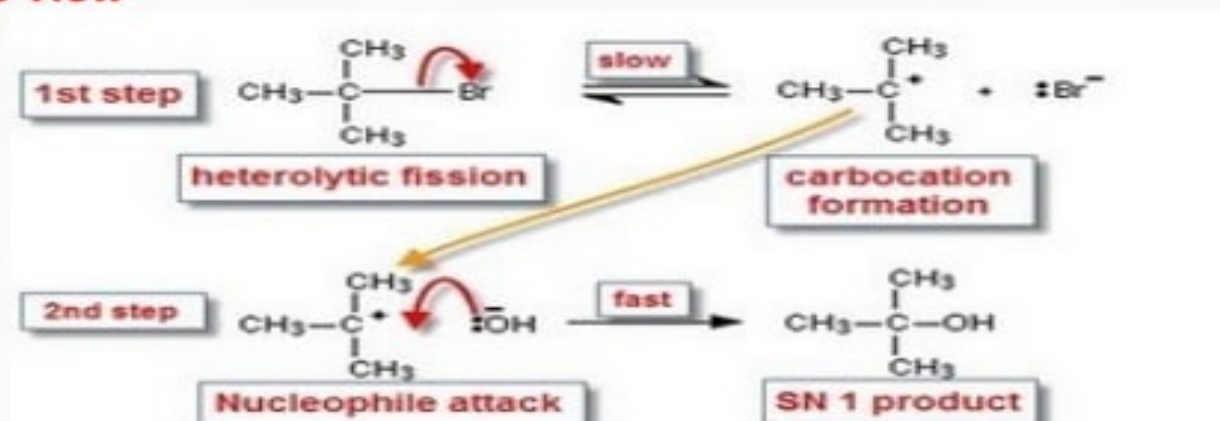
$S_N1$  reaction, Hydrolysis of 2-Bromo 2-Methylpropane with warm aq dil NaOH



Tertiary -  $S_N1$

- 2 steps mechanism
- 1st step, slow/rds, Heterolysis (breaking C-Br bond) forming carbocation
- 2nd step, fast, nucleophile  $OH^-$  reacts with carbocation

Click [HERE](#) to view



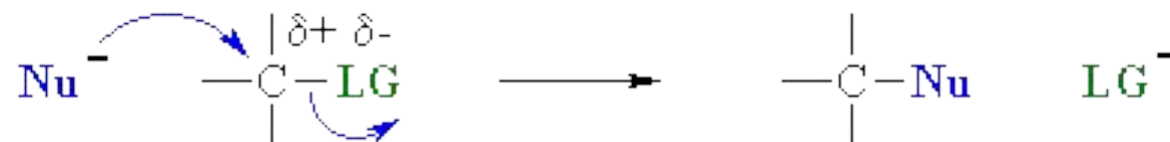


# $S_N2$ mechanism

$S_N2$  indicates a **substitution, nucleophilic, bimolecular** reaction, described by the expression rate =  $k [\text{Nu}][\text{R-LG}]$ .

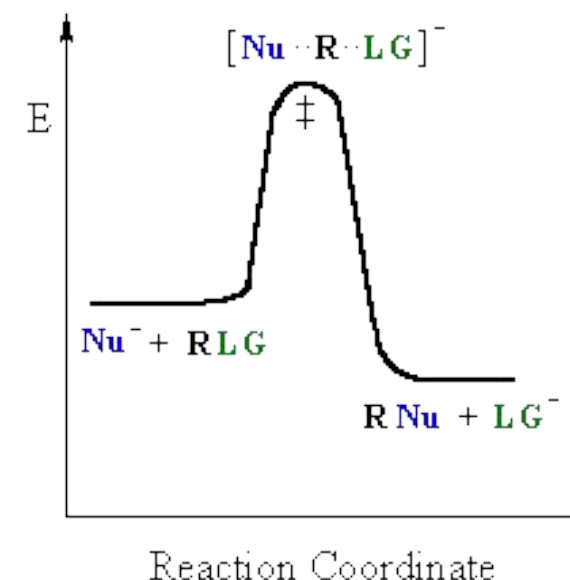
This implies that the rate determining step involves an interaction between two species, the nucleophile and the organic substrate.

This pathway is a concerted process (single step) as shown by the following reaction coordinate diagrams, where there is simultaneous attack of the nucleophile and displacement of the leaving group.



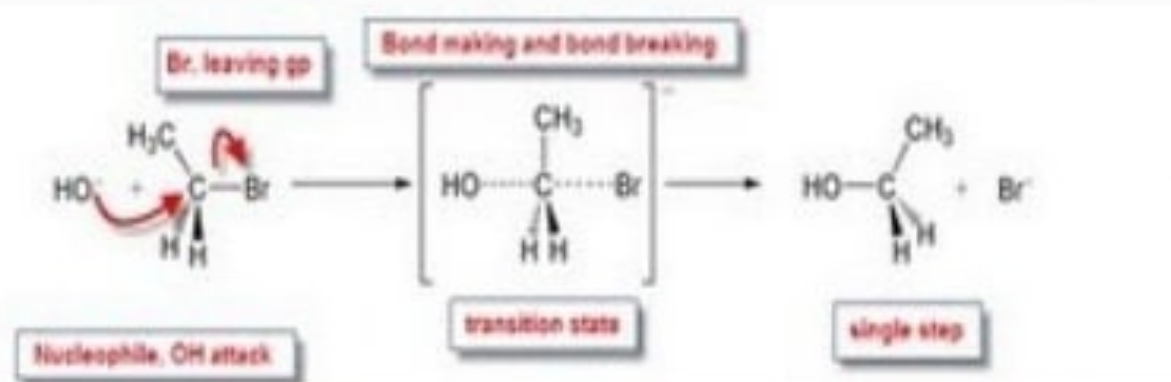
The nucleophile attacks at the carbon with the partial positive charge as a result of the polar  $\sigma$  bond to the electronegative atoms in the leaving group.

Single step reactions have no intermediates and a single transition state (TS). In an  $S_N2$  there is simultaneous formation of the carbon-nucleophile bond and breaking of the carbon-leaving group bond, hence the reaction proceeds via a TS in which the central C is partially bonded to five groups.



## $S_N2$ - Substitution Nucleophilic Bimolecular

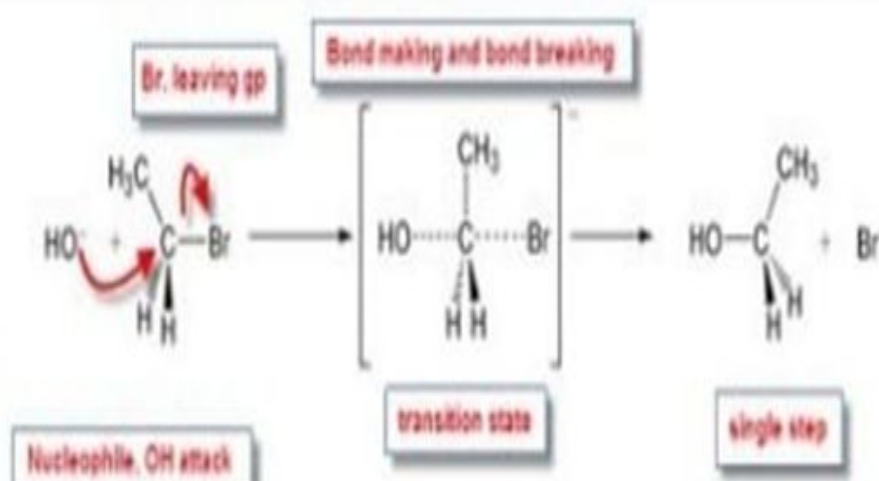
- 1 step mechanism, Bimolecular collision
- Rate =  $k[\text{substrate}][\text{nucleophile}]$ , Second order overall
- Rate depend on conc of substrate and nucleophile
- Bond making/breaking occur together result in trigonal bipyramidal shape
- Inverted configuration (backside attack by Nucleophile)



## $S_N2$ reaction, Hydrolysis of Bromoethane with warm aq NaOH



- Primary -  $S_N2$
- One step mechanism
- Bond making/breaking simultaneous in transition state



## Factor affecting rate of Nucleophilic Substitution ( $S_N1$ / $S_N2$ )

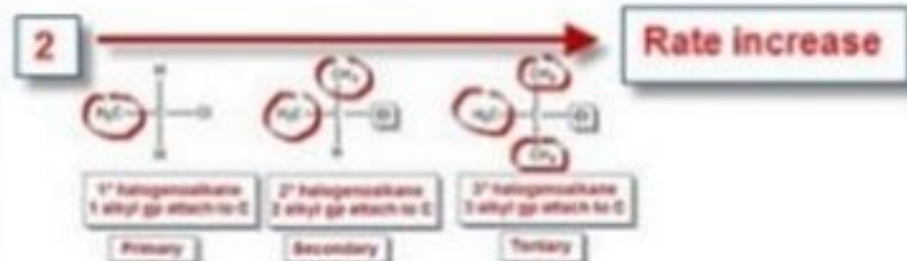
### 1. Nature of Halogen

• Bond length increase, Bond strength decrease from Cl to I, easier for nucleophile to attack by  $S_N2$



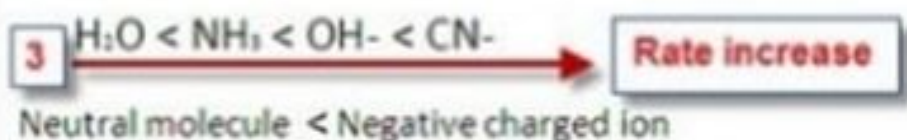
### 2. Nature of Halogenoalkane

• Tertiary ( $S_N1$ ) faster than Primary ( $S_N2$ )  
Formation Carbocation ( $S_N1$ ) faster than formation of transition state ( $S_N2$ )



### 3. Nature of Nucleophile

• Negatively charged more reactive than neutral nucleophile





## Comparison between S<sub>N</sub>1 and S<sub>N</sub>2 reaction mechanism



S <sub>N</sub> 2 reaction mechanism	S <sub>N</sub> 1 reaction mechanism
<b>One step</b> mechanism	<b>Two step</b> mechanism
<b>Bimolecular</b> reaction	<b>Unimolecular</b> reaction
Product formation takes place by <b>TS</b>	Product formation takes place by <b>carbocation intermediate</b>
<b>No carbocation rearrangement</b>	<b>Carbocation rearrangement</b>
Reaction is favoured by <b>polar aprotic solvents</b>	Reaction is favoured by <b>polar protic solvents</b>
Given mainly by <b>methyl halides</b>	Given mainly by <b>tertiary alkyl halides</b>
Reactivity of RX; <b>CH<sub>3</sub>X &gt; 1° &gt; 2° &gt; 3°</b>	Reactivity of RX; <b>3° &gt; 2° &gt; 1° &gt; methyl</b>
Mechanism is favoured when <b>nucleophile is an anion</b>	Mechanism is favoured when <b>nucleophile is neutral</b>
Reaction velocity depends on the concentration of nucleophile. <i>i.e.</i> , mechanism is favored by high concentration of nucleophile	Reaction velocity is independent of the concentration of nucleophile.
<b>Inversion of configuration</b>	<b>Racemisation</b>



# **Electrophilic substitution**

## **Electrophilic substitution reaction:**

**Electrophile: Electron loving (positively charged species)**

An electrophilic substitution reaction is a chemical reaction in which the functional group attached to a compound is replaced by an electrophile.

### **Types of Electrophilic Substitution Reactions**

- 1. Electrophilic aliphatic substitution reactions**
- 2. Electrophilic aromatic substitution**

## 1. Electrophilic aliphatic substitution reactions

In electrophilic aliphatic substitution reactions, an electrophile replaces the functional group (generally hydrogen) in an aliphatic compound.

**Ex:** Halogenation of ketone, Nitrosation

## 2. Electrophilic Aromatic Substitution Reaction

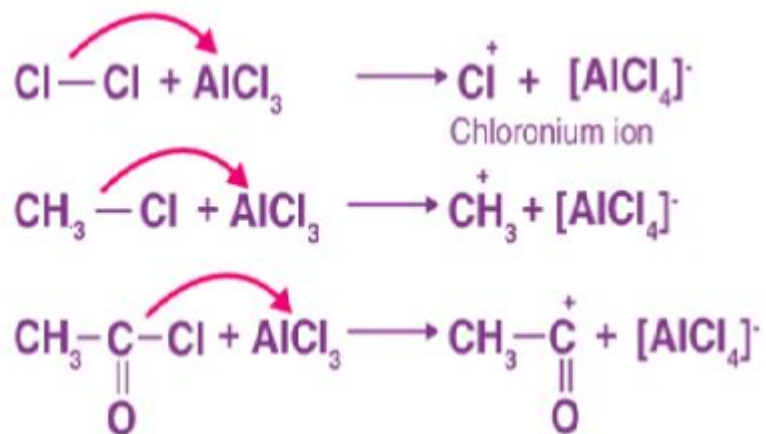
In electrophilic aromatic substitution reactions, an atom attached to an aromatic ring is replaced with an electrophile.

**Ex:** Aromatic nitrations, aromatic sulphonation, and Friedel-Crafts reactions.

# Mechanism of Electrophilic substitution reactions

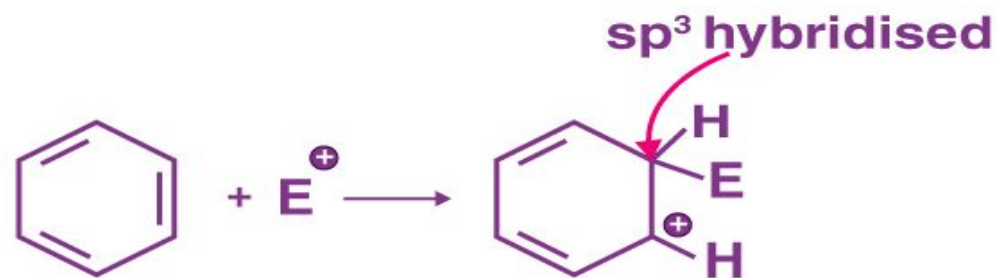
## Step 1: Generation of Electrophile

Anhydrous aluminium chloride is a very useful Lewis acid in the generation of electrophile for the chlorination, alkylation, and acylation of an aromatic ring.



## Step 2: Formation of Carbocation

The electrophile attacks the aromatic ring, forming a sigma complex or an arenium ion.

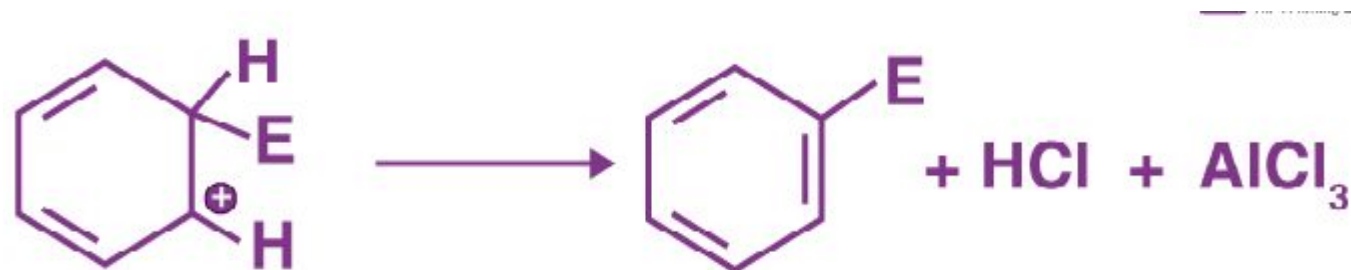


Sigma complex (arenium ion)

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## Step 3: Removal of Proton

The sigma complex releases a proton from the  $sp^3$  hybridized carbon when it is attacked by the  $[AlCl_4]^-$

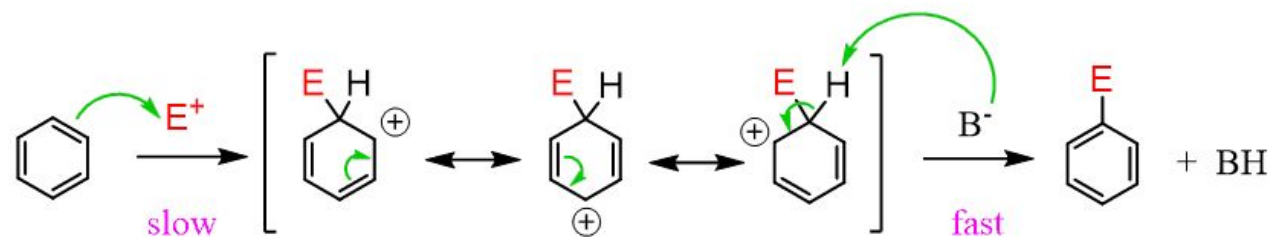


Thus, the electrophile replaces the hydrogen atom in the benzene ring.



# Mechanism

## The Mechanism of Electrophilic Aromatic Substitution

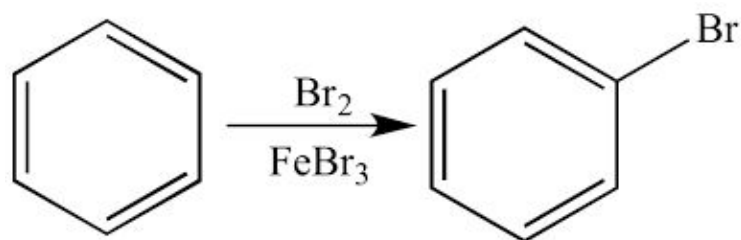


**Step 1.** Addition of the electrophile-  
Making the C-E bond

**Sigma Complex**

**Resonance stabilized Arenium ion**

**Step 2.** Proton transfer-  
Restoring Aromaticity

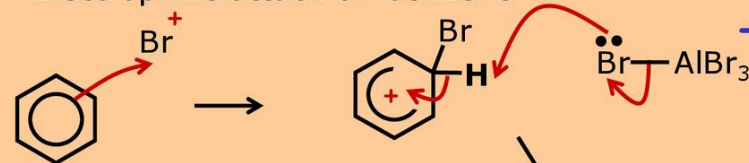


### Electrophilic substitution mechanism

1. Formation of the electrophile



2. Electrophilic attack on benzene



3. Forming the products  
and re-forming the catalyst

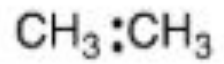


# Different electrophilic substitution reactions of benzene

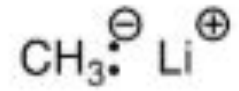
Types of reaction	Reagent used	Electrophile generated ( $E^+$ )	Product formed
Halogenation (Chlorination)	$Cl_2 + FeCl_3/AlCl_3$	$Cl^+$	Chlorobenzene
Bromination	$Br_2 + FeBr_3$	$Br^+$	Bromobenzene
Nitration	Conc. $HNO_3 + H_2SO_4$	$NO_2^+$	Nitrobenzene
Sulphonation	Fuming $H_2SO_4$ ( $H_2SO_4 + SO_3$ )	$SO_3$	Benzene sulphonic acid
Friedel-Crafts alkylation	$R-Cl + FeCl_3$	$R^+$	Alkyl benzene
Friedel-Crafts acylation	$R-COCl + FeCl_3$	$RCO^+$	Alkyl phenyl ketone

# Free radical

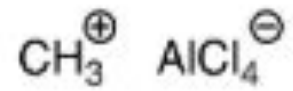
unpaired electron



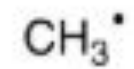
ethane  
(covalent bond)



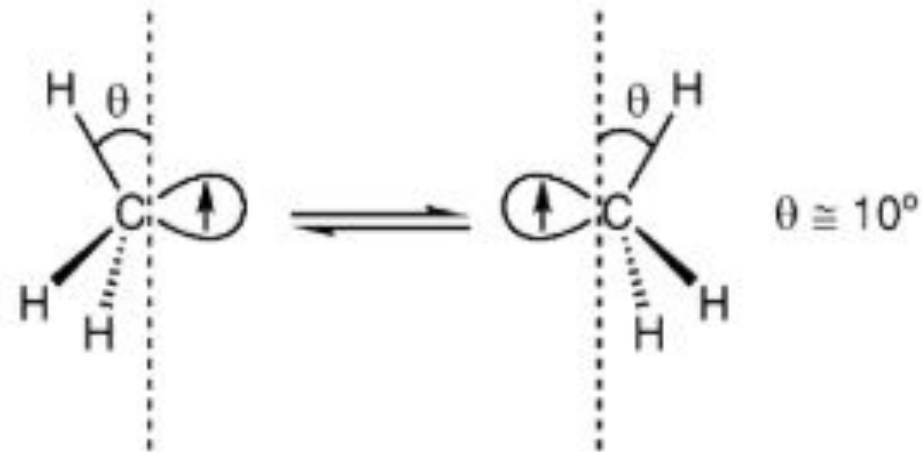
methyl anion  
(ionic bond)



methyl cation  
(ionic bond)



methyl radical  
(neutral species)



inversion of methyl radical

# Free radical Substitution reaction

## Free radical substitution

### chlorination of methane

i.e. homolytic breaking of covalent bonds

### Overall reaction equation



### Conditions

ultra violet light

excess methane to reduce further substitution

# Mechanism of free radical reaction

## Free radical substitution mechanism

ultra-violet



initiation step

