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### 4. Summary

## 1. Learning Outcomes

After studying this module, you shall be able to:

- Know how organic reactions proceed.
- Identify the different types of reaction mechanisms.
- Analyse the difference between each type of mechanism.

## 2. Introduction

**Reaction Mechanism:** Mechanism for any reaction is defined as collection of number of processes that explains the overall reaction.

- This is the actual method of completion of reaction as it gives the number of broken bonds and the number of steps involved.
- In a mechanism the positions of all atoms (stereochemistry), role of solvent molecules and the energy of the system is specified.
- It also helps in describing the reaction intermediate, activated complex and transition state involved in the whole reaction.
- A mechanism accounts for all the reactants used, the function of a catalyst, all products formed and their amount.
- From a mechanism the rate law can be deduced.

You are already familiar with some common terms frequently encountered while discussing any reaction mechanism as given below:

**Substrate:** In most reactions of organic compounds, one or more covalent bonds are broken. For most reactions, it is convenient to call one reactant the attacking reagent and the other the substrate.

**Nucleophile and Electrophile:** Reagent having an electron pair is known as nucleophile and the reaction is nucleophilic. A reagent that takes an electron pair is called an electrophile and the reaction is electrophilic.

**Leaving Group:** In a reaction in which the substrate molecule becomes cleaved, part of it (the part not containing the carbon) is usually called the leaving group. A leaving group that carries away an electron pair is called a nucleofuge. If it comes away without the electron pair, it is called an electrofuge.

**Reaction intermediates:** Intermediates are those chemical species which are short-lived and unstable. They are neither reactant nor product. They are said to be temporary products or reactants generally free radicals or ions.

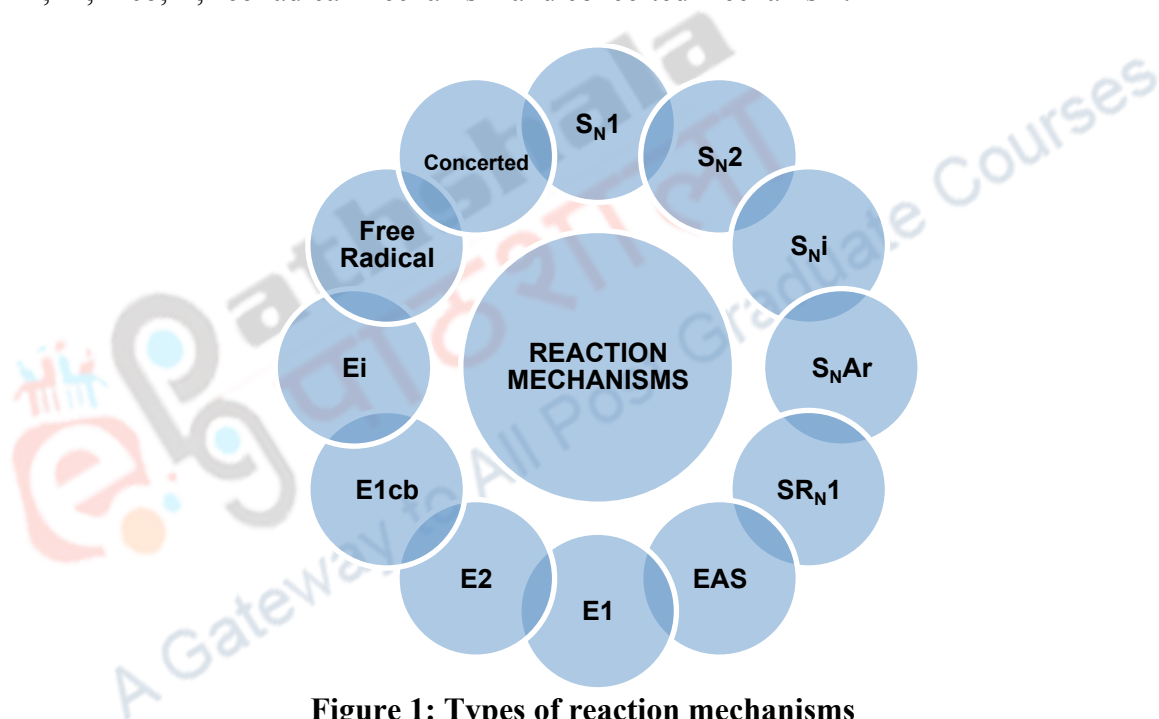
**Transition states:** It is an unstable intermediate molecular state with an unusual number of bonds and/or unstable geometry.

**Molecularity:** It is defined as number of colliding molecular entities involved in a single reaction step.

- Unimolecular reaction step involve only one molecular entity.
- Bimolecular reaction step involve two molecular entities.
- Termolecular reaction step involve three molecular entities.

### 3. Types of Reaction Mechanisms

Organic reactions proceeds via various mechanisms some common mechanisms are  $S_N1$ ,  $S_N2$ ,  $S_Ni$ ,  $S_NAr$  (addition-elimination, elimination-addition, aryl cation),  $SR_N1$ , EAS, E1, E2, E1cb, Ei, free radical mechanism and concerted mechanism.

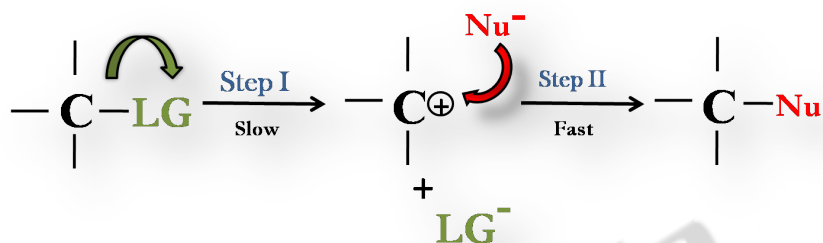


**Figure 1: Types of reaction mechanisms**

#### 3.1. Substitution Nucleophilic Unimolecular Mechanism ( $S_N1$ )

The reaction between tert alkyl halides (eg. *tert*-butylbromide) and water follows Substitution Nucleophilic Unimolecular Mechanism ( $S_N1$ ). Unimolecular means that only one molecule is involved in the rate-determining step.

The mechanism of  $S_N1$  reaction is as follows:



- $S_N1$  reaction proceeds in two steps.
- Step 1 is formation of carbocation.
- Step 2 is capture of carbocation by nucleophile.
- Follow first order kinetics. Because, the rate of the reaction depends on the concentration of only one reactant i.e. alkyl halide in this case, the reaction is a first-order reaction.
- Rate law is define as:

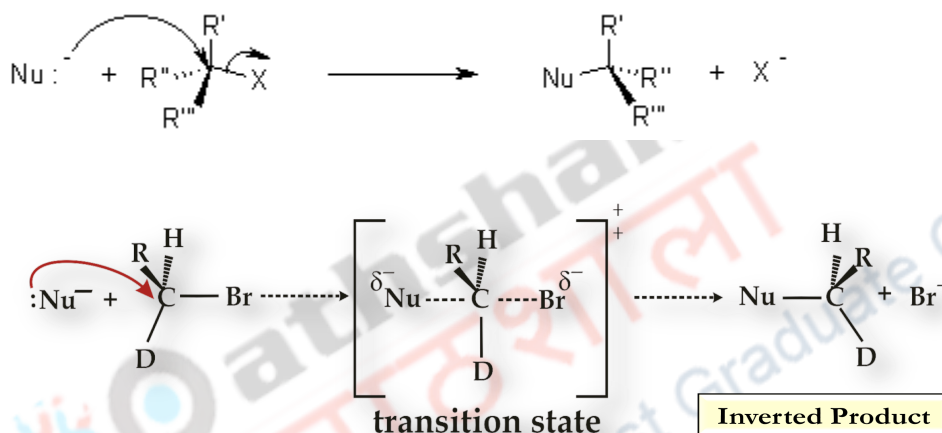
$$\text{Rate} = k [\text{RX}]$$

- Two stereoisomers are formed for an alkyl halide having asymmetric carbon. One of the products has the same relative configuration at the asymmetric carbon as the reacting alkyl halide while the other has inverted configuration..
- The order of reactivity for alkyl halides is  $3^\circ > 2^\circ > 1^\circ > \text{CH}_3\text{X}$
- As reaction proceeds through formation of carbocation there is possibility of rearrangement to form more stable carbocation.
- $S_N1$  is favoured in polar protic solvent and in the presence of weak nucleophile.

### 3.2 Substitution Nucleophilic Bimolecular Mechanism ( $S_N2$ )

The reaction of methyl bromide with hydroxide ion follows  $S_N2$  mechanism. When the transition state is reached, the central carbon atom has gone from its initial  $sp^3$  hybridisation to a  $sp^2$  state with an approximately perpendicular p orbital. There are two lobes of p-orbital, one overlaps with the leaving group and the other with nucleophile. During transition state the three non-reacting substituents and the central carbon are in a same plane. This inversion of configuration is called Walden inversion.

The mechanism of  $S_N2$  reaction is as follows:



- An alkyl halide having an asymmetric carbon results in the formation of only one stereoisomer and the inversion of configuration takes place.
- Reactions following  $S_N2$  mechanism occur in one step via formation of a transition state.
- The rate of the nucleophilic substitution depends upon the concentration of reactant, methyl bromide in this case, if the concentration of reactant doubles, the rate of the nucleophilic substitution reaction also doubles.
- The rate of the reaction also depends on nucleophile concentration. This means that both reactants are involved in the rate determining step.

Hence the rate law is:

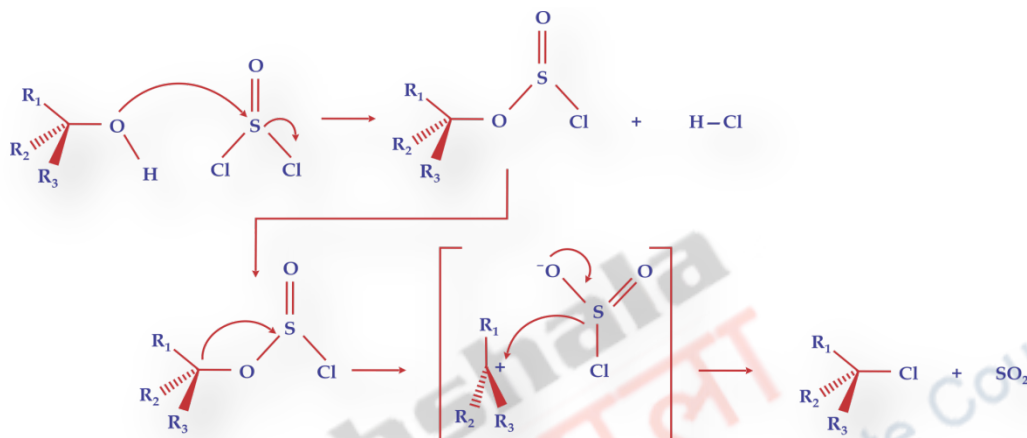
$$\text{Rate} = k [\text{RX}] [\text{Nu}]$$

- Polar aprotic solvents favour  $S_N2$ .

### 3.3 Substitution Nucleophilic Internal Mechanism ( $S_Ni$ )

Replacement of OH of alcohols by Cl in the presence of  $\text{SOCl}_2$  proceeds via  $\text{S}_{\text{N}}\text{i}$  mechanism. It follows second order rate law. This reaction proceeds with the retention of configuration.

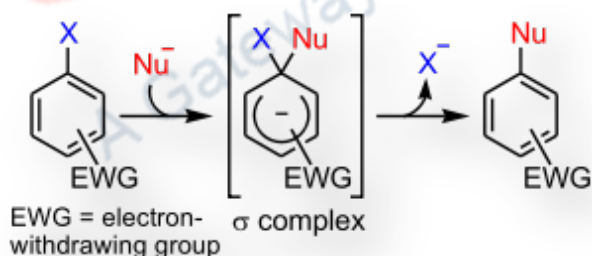
$$\text{Rate} = k [\text{ROH}] [\text{SOCl}_2]$$



### 3.4 Aromatic Nucleophilic Substitution Mechanism ( $\text{S}_{\text{N}}\text{Ar}$ )

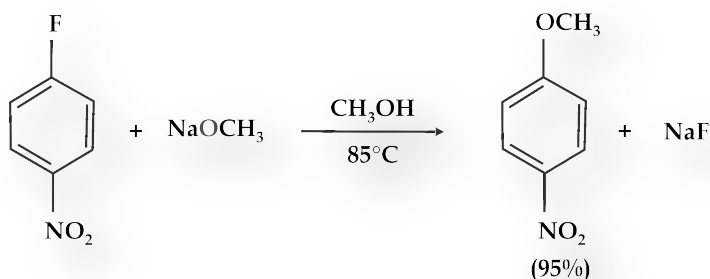
In aromatic nucleophilic substitution mechanism a strong nucleophile replaces a leaving group. It can be through an addition-elimination, elimination-addition or aryl cation mechanism.

#### 3.4.1 The $\text{S}_{\text{N}}\text{Ar}$ Addition-Elimination Mechanism



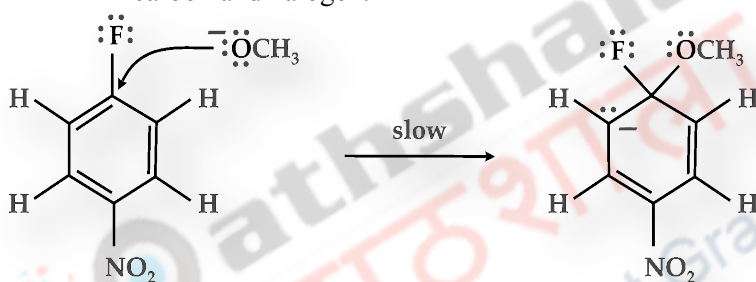
Here substitution takes place at ipso position. Presence of strong electron withdrawing group at ortho/para to leaving group favors addition-elimination mechanism. It uses one of the vacant  $\pi^*$  orbitals for bonding interaction with the nucleophile. This allows addition of nucleophile to the aromatic ring without displacing any substituent. Net substitution occurs in second step by elimination of leaving group.

Example of reaction undergoing through addition-elimination mechanism: Reaction of para-nitro fluoro benzene with sodium methoxide.



It is a two step mechanism and proceeds as shown:

- (i) Slow step: Aromaticity of ring is lost in this step. Nucleophile attacks on bond between carbon and halogen.



The intermediate formed is stabilised via resonance. Presence of electron withdrawing group at ortho or para position provides extra stabilisation.



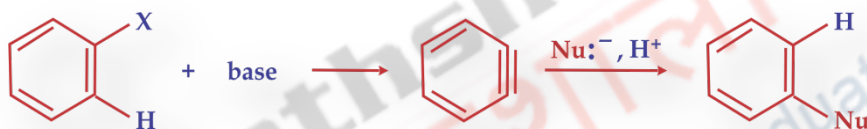
- (ii) Fast step: Aromaticity of the ring is restored in this step. Intermediate formed in first step loses fluoride.



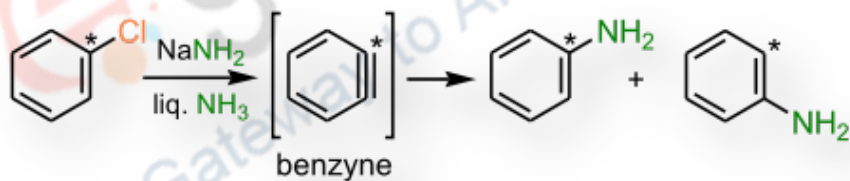


### 3.4.2 Elimination-Addition Mechanism (Benzyne Mechanism)

Elimination-addition mechanism involves a highly unstable intermediate called dehydrobenzene or benzyne.

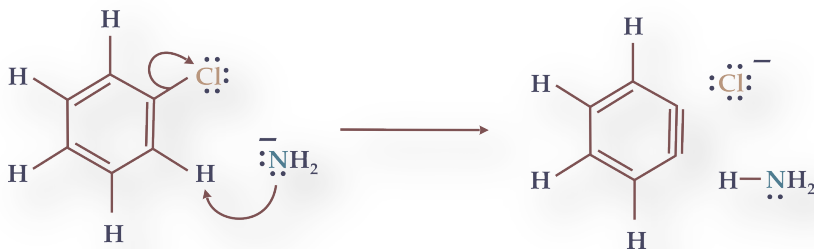


Example of elimination-addition mechanism: Reaction of chlorobenzene with soda amide in liquid ammonia. If the aryl halide contains two ortho substituents, the reaction should not occur.

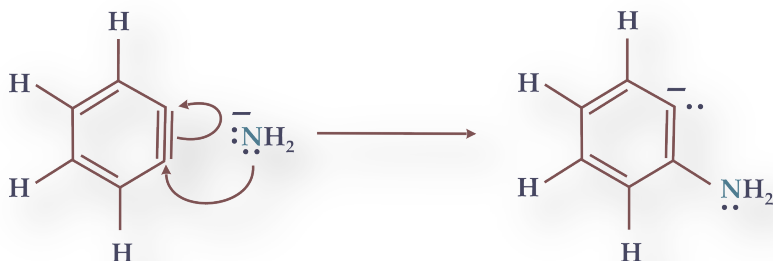


The mechanism of this reaction is shown below:

(i) First step is elimination of proton ortho to the substituent present and formation of benzyne.



(ii) Attack of amide ion on the benzyne intermediate.

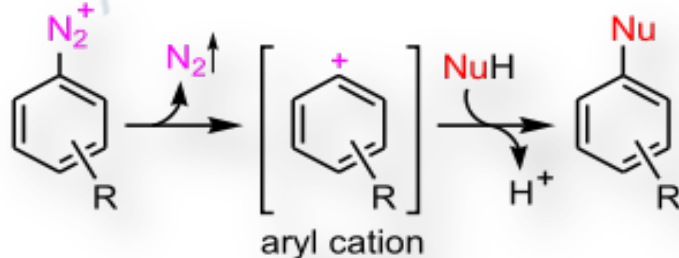


(iii) Abstraction of proton from ammonia.



### 3.4.2 Aryl Cation Mechanism

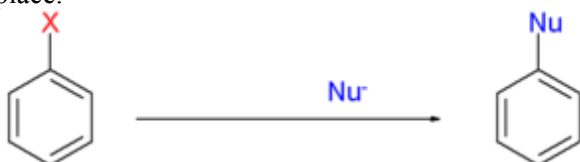
The aromatic aryl cation  $S_N1$  mechanism is encountered with diazonium salts. The reaction rate is first order in diazonium salt and independent of the concentration of nucleophile.



### 3.5 Substitution Radical Nucleophilic Unimolecular ( $S_{RN}1$ )

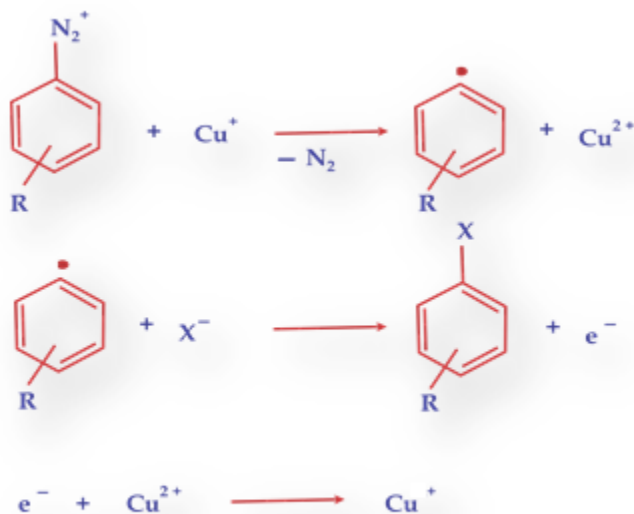
This was discovered in 1970 by Bunnett and Kim where,  $S_{RN}1$  stands for substitution radical-nucleophilic unimolecular as it is similar to aliphatic  $S_N1$  reaction.

$S_{RN}1$  is a substitution reaction in which nucleophilic substitution on aromatic compound takes place.



Where, X is a halide.

An example of this reaction type is the Sandmeyer reaction which involves synthesis of aryl halides from aryl diazonium salts via  $S_{RN}1$  mechanism.



### 3.6 Electrophilic Aromatic Substitution Mechanism (EAS)

It involves attack of  $\pi$ -system on electrophile and the stabilization of benzenonium ion through resonance and removal of proton by base.

Examples of reactions undergoing EAS mechanism are nitration, sulphonation, halogenations, Friedel and Craft reactions. Ions formed in this mechanism are known as Wheland intermediates,  $\sigma$  complexes or arenium ions.

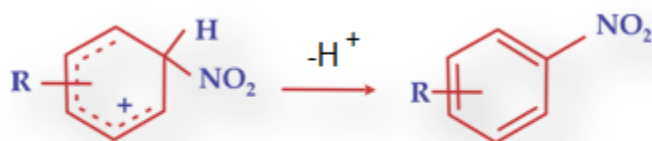
1. Generation of electrophile



2. Attack of electrophile on aromatic ring forming carbocation intermediate

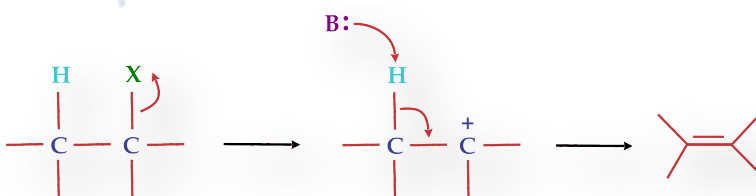


3. Deprotonation



### 3.7 Unimolecular Elimination Mechanism (E1)

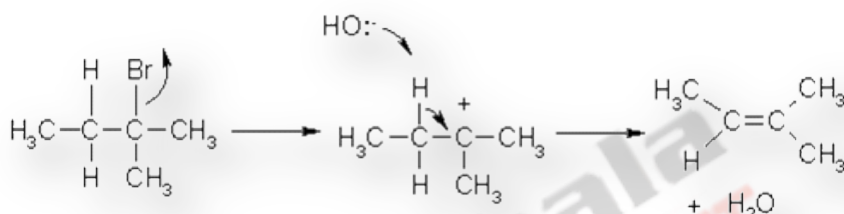
First step of a Unimolecular Elimination Mechanism (E1) is the loss of leaving group and formation of a carbocation which is a slow and rate limiting step. The overall elimination is completed by rapid removal of proton from adjacent carbon by attack of base (B:) leading to formation of a double bond between the two carbon atoms.



- Rate of elimination is dependent on the concentration of the substrate.  
i.e., Rate =  $k$  [RX].

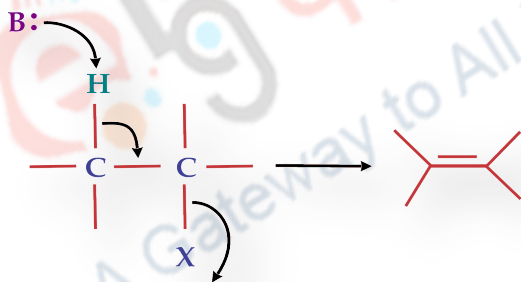
- Reaction is independent of nucleophile.
- Reaction is first order.
- It is favoured by protic polar solvent.
- Rearrangement may take place.
- A strong base not required.
- A good leaving group is required, such as a halide or a tosylate.
- The mechanism goes through carbocation intermediate, therefore rearrangement can take place.

Example of Unimolecular Elimination Mechanism (E1): Dehydrohalogenation of alkyl halide.



### 3.8 Bimolecular Elimination Mechanism (E2)

In the Bimolecular Elimination Mechanism (E2), a base ( $\text{B}^-$ ) abstracts a proton from a carbon adjacent to the carbon attached to the leaving group. The electron pair left on the carbon forces the leaving group to leave and create a double bond. All this occurs simultaneously in this mechanism.



- E2 is a one step process. C-H and C-X bond breaking takes place simultaneously in one step.
- Rate of elimination depends on concentration of substrate and base. It follows second order kinetics.

$$\text{Rate} = k [\text{RX}] [\text{B}]$$

- High concentration and strong base favours E2.
- It requires aprotic solvent.
- In E2 1,2-elimination takes place.

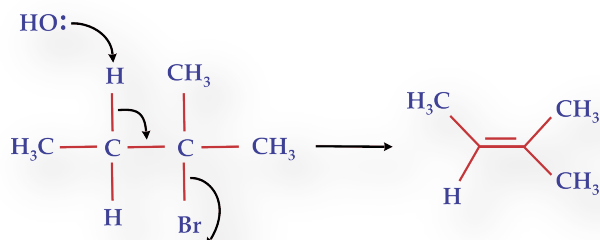
- A good leaving group is required, such as a halide or a tosylate.

Examples of Bimolecular Elimination Mechanism (E2):

(i) Acid catalysed dehydration of alcohols.

(ii) Hoffman degradation of quaternary ammonium hydroxides.

(iii) The base induced elimination of hydrogen halide from alkyl halide.

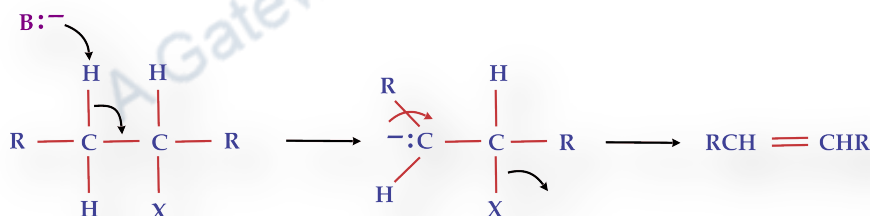


### 3.9 Conjugate Base Elimination Mechanism (E1cb)

In a Conjugate Base Elimination Mechanism (E1cb) the C-H bond breaks with formation of carbanion as intermediate. Formation of carbanion is fast and loss of leaving group is slow and rate limiting. The greatest likelihood of finding E1cb mechanism is in substrates that have a) poor nucleofuge b) an acidic hydrogen.

$$\text{Rate} = k [\text{RX}] [\text{B}]$$

The E1 mechanism requires formation of a primary carbocation, whereas the E1cb proceeds via a carbanion intermediate.

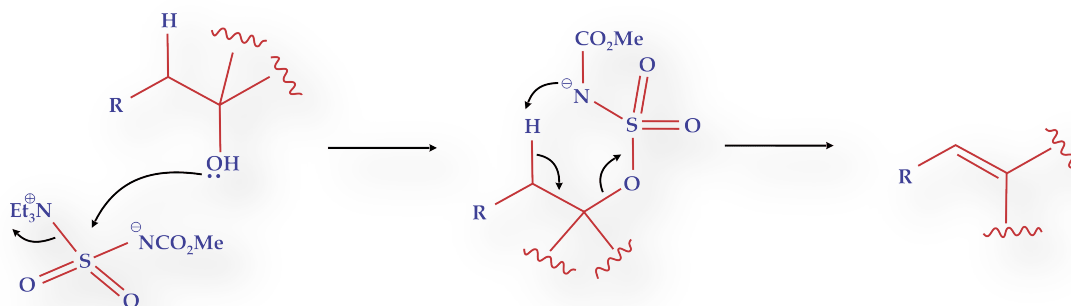


### 3.10 Elimination Internal Mechanism (Ei)

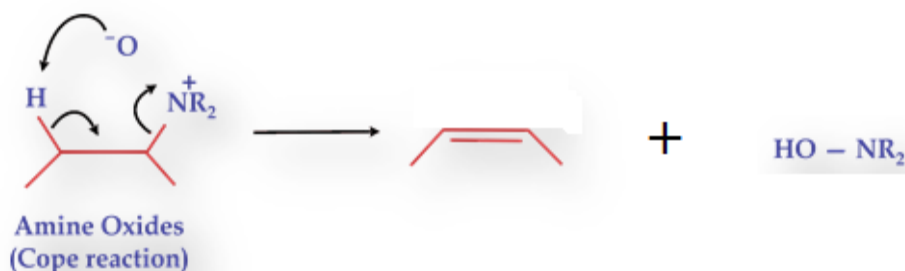
In Elimination Internal mechanism (Ei), two vicinal substituents on an alkane framework leave simultaneously in a single step and formation of alkene takes place in a syn elimination.

Examples of Ei mechanism:

(a) The Burgess Reagent or methyl *N*-(triethylammoniumsulfonyl)carbamate is a dehydrating reagent mild in nature. it involves the conversion of secondary and tertiary alcohol to alkenes in a syn-elimination.



(b) The Cope reaction is an elimination reaction involved in the formation of 5-membered cyclic (intramolecular) transition state. In this reaction, alkene and a hydroxylamine is formed.



### 3.11 Free Radical Mechanism

In radical mechanism hemolytic bond cleavage takes place. The free radicals are involved in chain reaction which leads to chain propagation. The final step chain termination involves combination of two radicals. Initiation may happen spontaneously or may be induced by heat or light.

**Initiation:**



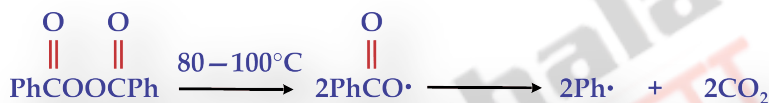
**Propagation:**



### Termination:



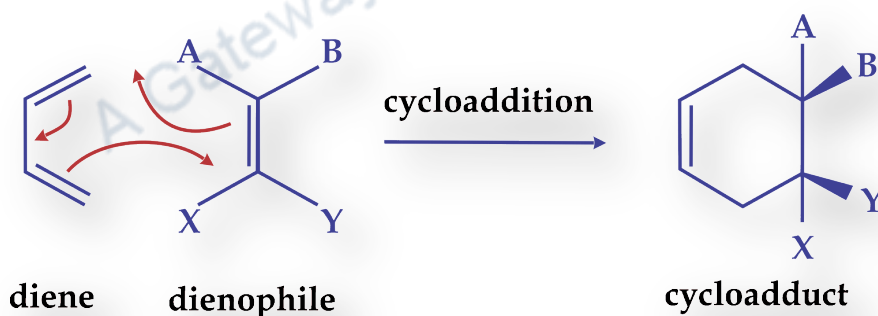
Peroxides such as benzoyl peroxide, dialkyl, diaryl and acyl peroxides are common source of radical initiators. The O-O bond in peroxides is weak and reaction generally occurs at low temperatures. Some organic compounds with low-energy bonds, such as azo compounds are also used. Molecules that are cleaved by light are most often chlorine, bromine and various ketones.



### 3.12 Concerted Mechanism

Concerted reaction mechanism occurs without any intermediate. The transition state involves bond breaking and bond formation. Reorganization of electrons via cyclic transition structures is the process of concerted pericyclic reactions.

Diels-Alder reaction between diene and dienophile is an example of concerted cycloaddition reaction.





#### 4. Summary

- Mechanism for any reaction is define as collection of number of processes that explains the overall reaction.
- The different types of mechanism via which an organic reaction may proceed are:
  - Substitution Nucleophilic Unimolecular Mechanism ( $S_N1$ )
  - Substitution Nucleophilic Bimolecular Mechanism ( $S_N2$ )
  - Substitution Nucleophilic Internal Mechanism ( $S_{Ni}$ )
  - Aromatic Nucleophilic Substitution Mechanism ( $S_{NAr}$ )
  - Substitution Radical Nucleophilic Unimolecular ( $SR_N1$ )
  - Electrophilic Aromatic Substitution Mechanism (EAS)
  - Unimolecular Elimination Mechanism (E1)
  - Bimolecular Elimination Mechanism (E2)
  - Conjugate Base Elimination Mechanism (E1cb)
  - Elimination Internal Mechanism (Ei)
  - Free Radical Mechanism
  - Concerted Mechanism