

# **CHEMISTRY PRESENTATION**

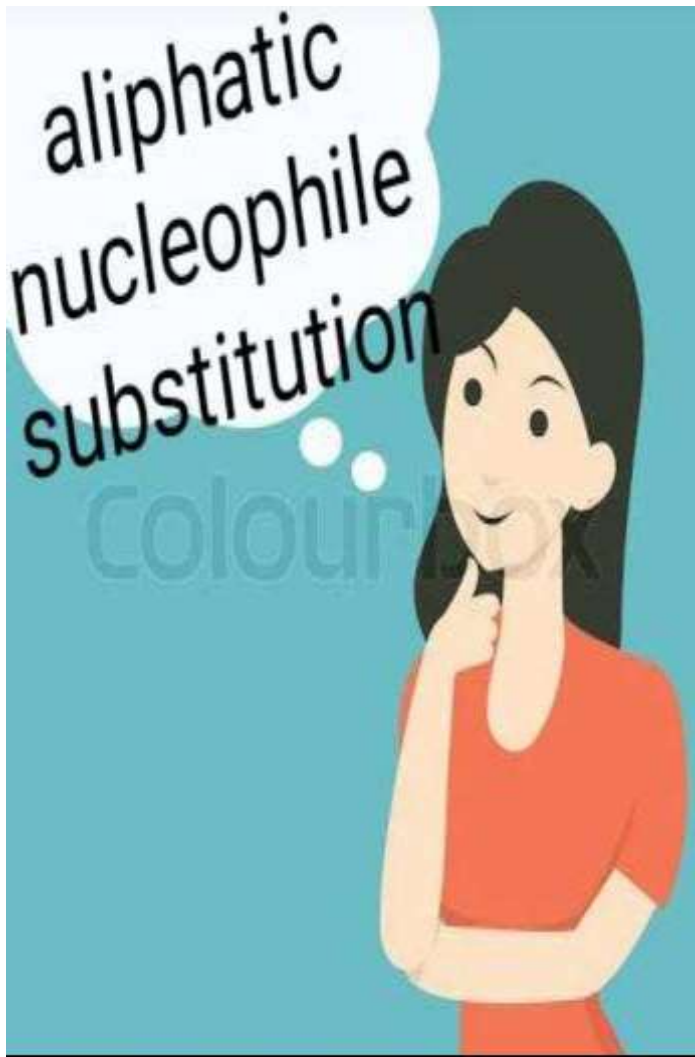
## **TOPIC: ALIPHATIC NUCLEOPHILIC SUBSTITUTION**

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## ALIPHATIC NUCLEOPHILIC SUBSTITUTION



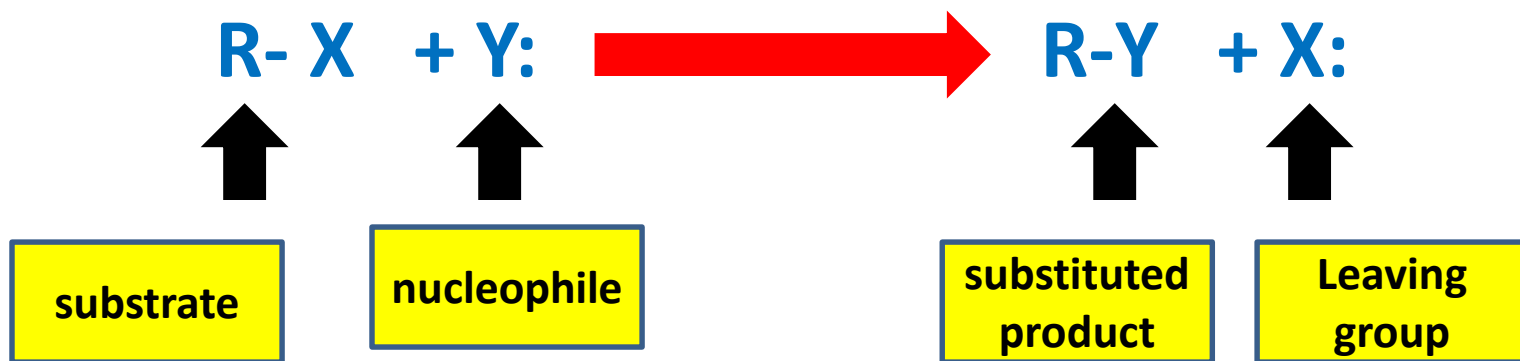
## SUBSTITUTION-

- replacement of an atom or group of atom by any other atom or group of atom.

## NUCLEOPHILE-

- At least one unshared pair of electron
  - Lewis base
- Attracted towards positively charged species.
- May be neutral or negatively charged.
- Example:  $\text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{I}^-$ ,  $\text{CN}^-$ ,  $\text{OH}^-$ ,  $\text{NH}_3$ ,  $\text{RNH}_2$ ,  $\text{H}_2\text{O}$ ,  $\text{ROH}$ , etc.

# General reaction-



- ❖ **Nucleophile Y: may be neutral or negatively charged.**
- ❖ **Substrate may be neutral or positively charged.**

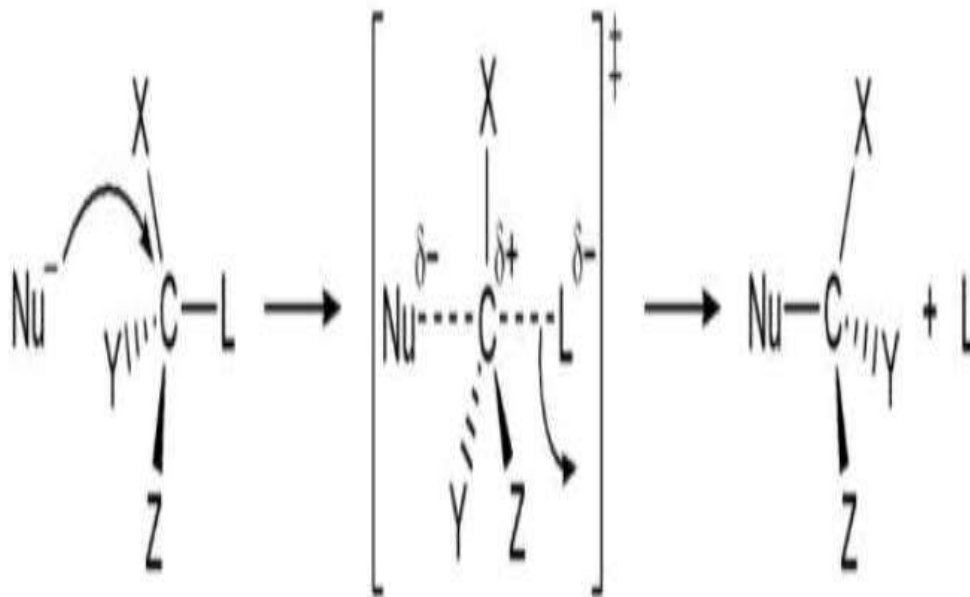
# Type of Nucleophilic Aliphatic substitution Reaction



# SN<sub>2</sub> MECHANISM

- SN<sub>2</sub> stands for substitution nucleophilic bimolecular.
- BACK SIDE ATTACK
- SINGLE STEP.
- Direct displacement.
- NO INTERMEDIATE FORMATION
- INVERSION OF CONFIGURATION
- The energy necessary to break the C-L bond is supplied by simultaneous formation of the C-Nu bond.
- GENERALLY YIELD SINGLE PRODUCT

## S<sub>N</sub>2 Reaction Mechanism



- L = Leaving group
- Nu<sup>-</sup> = Attacking Nucleophile

# Evidences for the S<sub>N</sub>2 mechanism:

## 1. Kinetics:

- rate expression,

**Rate=**

**k[substrate][nucleophile]**

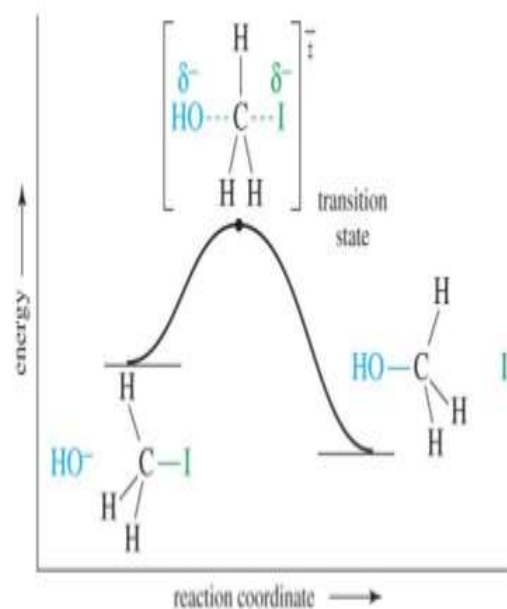
- If a large excess of nucleophile is present (i.e. solvolysis) –

**Rate= k [substrate]**

such kinetics are called

**pseudo-first order.**

## S<sub>N</sub>2 Energy Diagram

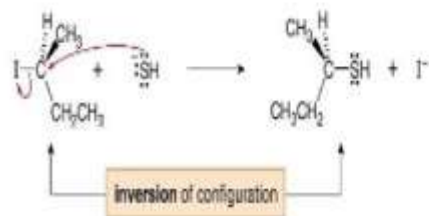
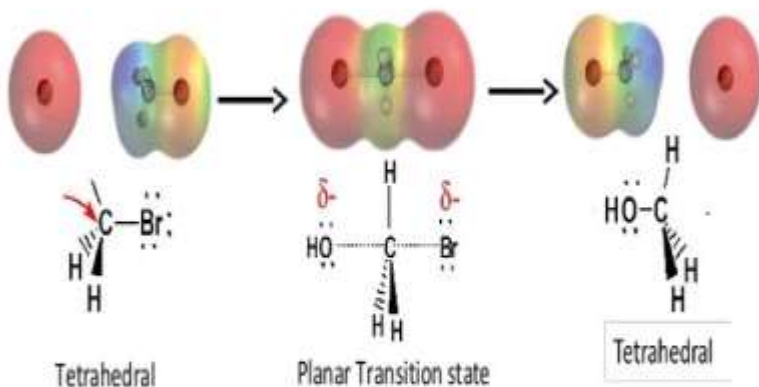


- The S<sub>N</sub>2 reaction is a one-step reaction.
- Transition state is highest in energy.

## 2. Stereochemistry:

### Stereochemistry

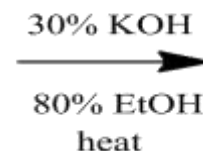
- The transition state of an  $S_N2$  reaction has a planar arrangement of the carbon atom and the remaining three groups
- Occurs with inversion of chiral center called **Walden Inversion**.



The bond to the nucleophile in the product is always on the **opposite side** relative to the bond to the leaving group in the starting material.

## 3. No substitution at bridgehead carbon

- Not be able to react by this mechanism, since the nucleophile cannot approach from **the rear**
- **REQUIREMENT FOR  $S_N2$ :**
- $S_N2$  mechanism requires the **backside attack** by the nucleophile, **inversion** of configuration and **coplanarity of three no-reacting groups in the transition state**.
- **REASON:** prevented at the bridgehead carbons **due to rigid cage like structures**



No Reaction



# SN<sub>1</sub>

## MECHANISM

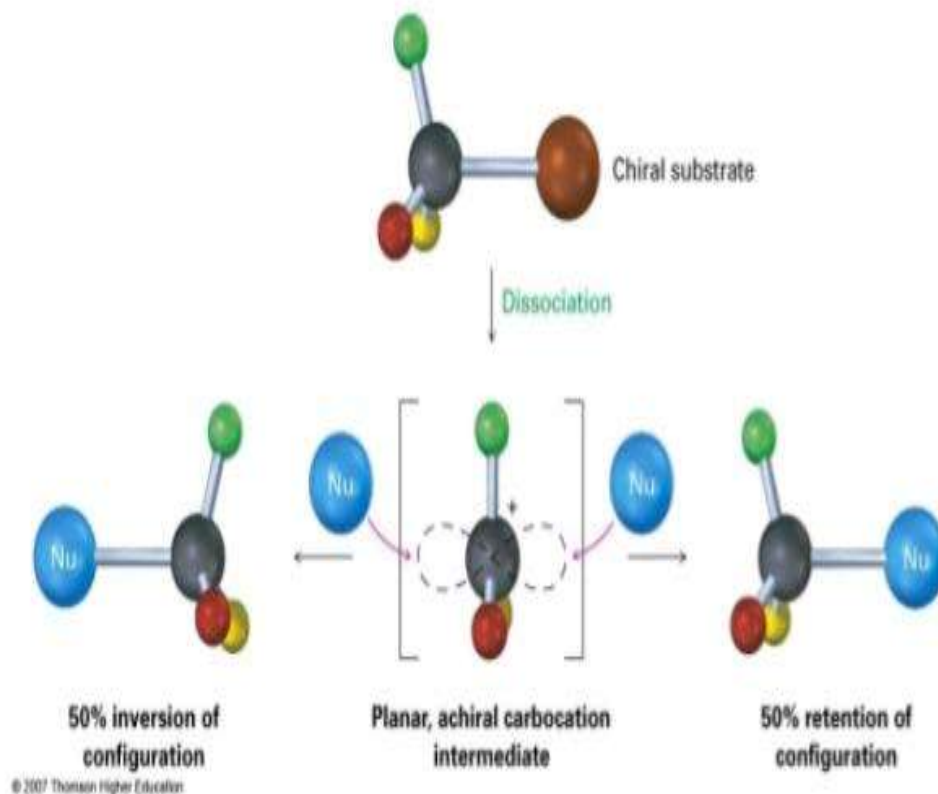
❖ SN<sub>1</sub> mechanism (substitution nucleophilic unimolecular)

❖ TWO STEP PROCESS

❖ The first step is a slow ionization of the substrate and is the rate-determining step

❖ The second is a rapid reaction between the intermediate carbocation and the nucleophile

❖ The ionization of a leaving group to form the carbocation is always assisted by the solvent, since the energy necessary to break the bond is largely recovered by solvation of CATION and of LEAVING GROUP.



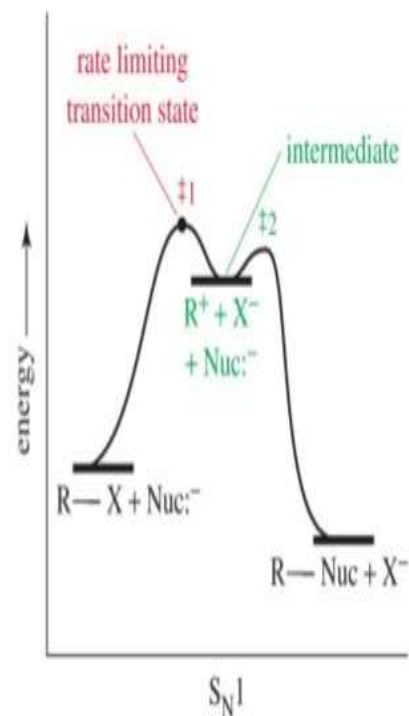
# EVIDENCES FOR THE $S_N1$ MECHANISM:

## 1. kinetics

- first-order reaction following the rate law:  
**RATE= k [RX]**
- solvent is necessary to assist in the process of ionization, it does not enter the rate expression, because it is present in large excess.

## $S_N1$ Energy Diagram

- Forming the carbocation is an endothermic step.
- Step 2 is fast with a low activation energy.

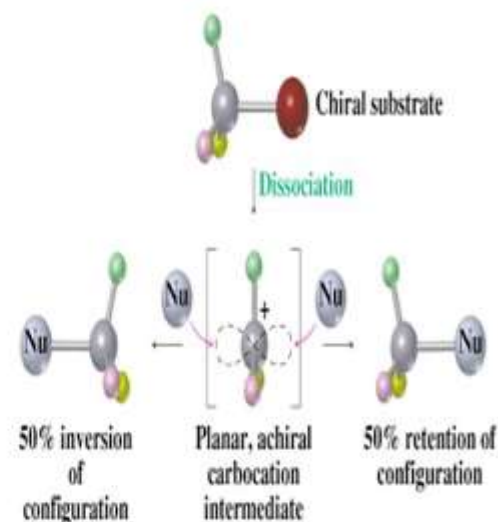


## 2. STEREOCHEMISTRY

- ❖ The stereo chemical evidence for the SN1 mechanism is **less clear-cut than it is for the SN2 mechanism.**
- ❖ First-order substitutions **do give complete racemisation**, many others do not. Typically there is 5–20% inversion.
- Some of the products are not formed from free carbocations but rather from **ion pairs**.

## Stereochemistry of S<sub>N</sub>1 Reaction

- The planar intermediate should lead to loss of chirality
  - A free carbocation is achiral
- Product should be racemic



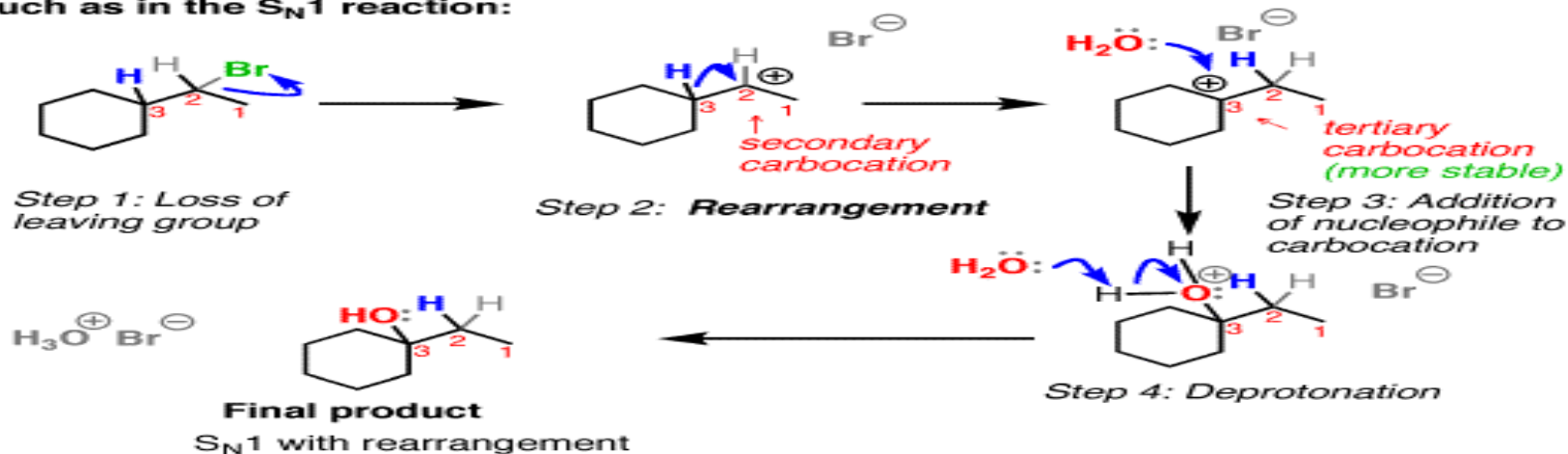
- **Role of ion pair:**



- Here is an intimate, contact, or tight ion pair; a loose or solvent-separated ion pair and the dissociated ions (each surrounded by molecules of solvent) are formed.
- The reaction products can result from attack by the nucleophile at any stage.
- Nucleophilic attack by a solvent molecule on tight ion pair thus leads to **inversion**. Attack on solvent separated ion pair leads to **racemisation**.

### 3. Formation of rearranged products:

Rearrangements can accompany reactions where carbocations are formed, such as in the S<sub>N</sub>1 reaction:



## 4. NO substitution at bridgehead carbons

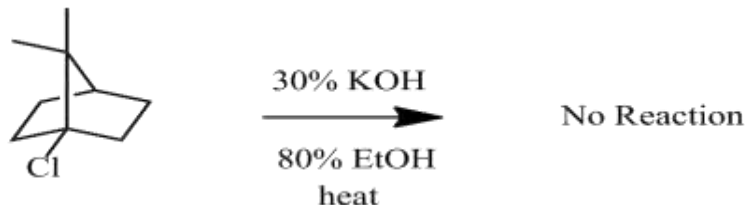
- Not be able to react by this mechanism, since the nucleophile

- **REQUIREMENT:**

SN1 proceed through carbocations which must be planar.

- **REASON:**

Because of **rigid cage like structure**, **bridgehead carbon atom cannot assume planarity**, hence **heterolysis leading to formation of carbocation is prevented**.



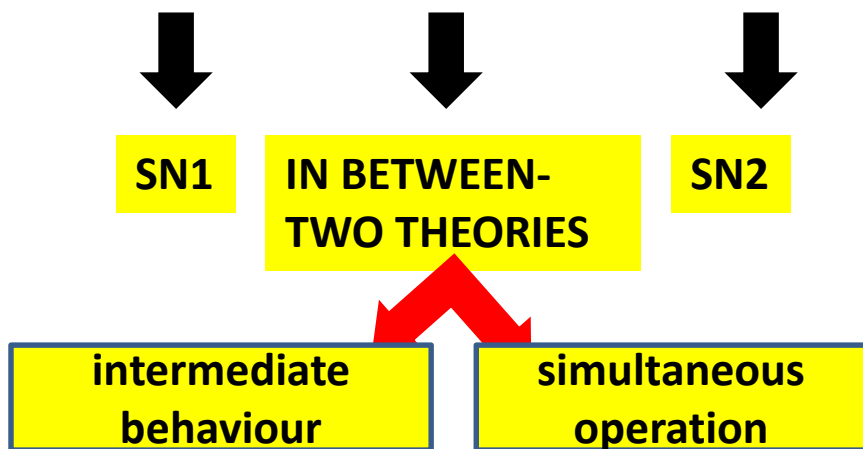
## THE SET MECHANISM (single-electron transfer).

- In some nucleophilic reaction, sn1 is highly probable.
- ESR detection of intermediate- free radicals are involved.
  - Carbocation- good electron acceptor
- Nucleophile- good electron donor.
- Mechanism- SET mechanism. For example, the reaction between the triphenylmethyl cation and t-butoxide ion:-



# Mixed SN1 AND SN2 MECHANISM:-

- Some reactions of a given substrate under a given set of conditions display all the characteristics of –



## : INTERMEDIATE BEHAVIOUR- GIVEN BY SNEEN –

- mechanism that is neither “pure” SN1 nor “pure” SN2, but some “in-between” type.
- all SN1 and SN2 reactions can be accommodated by one basic mechanism (the ion-pair mechanism).

- The substrate first ionizes to an intermediate ion pair that is then converted to products-

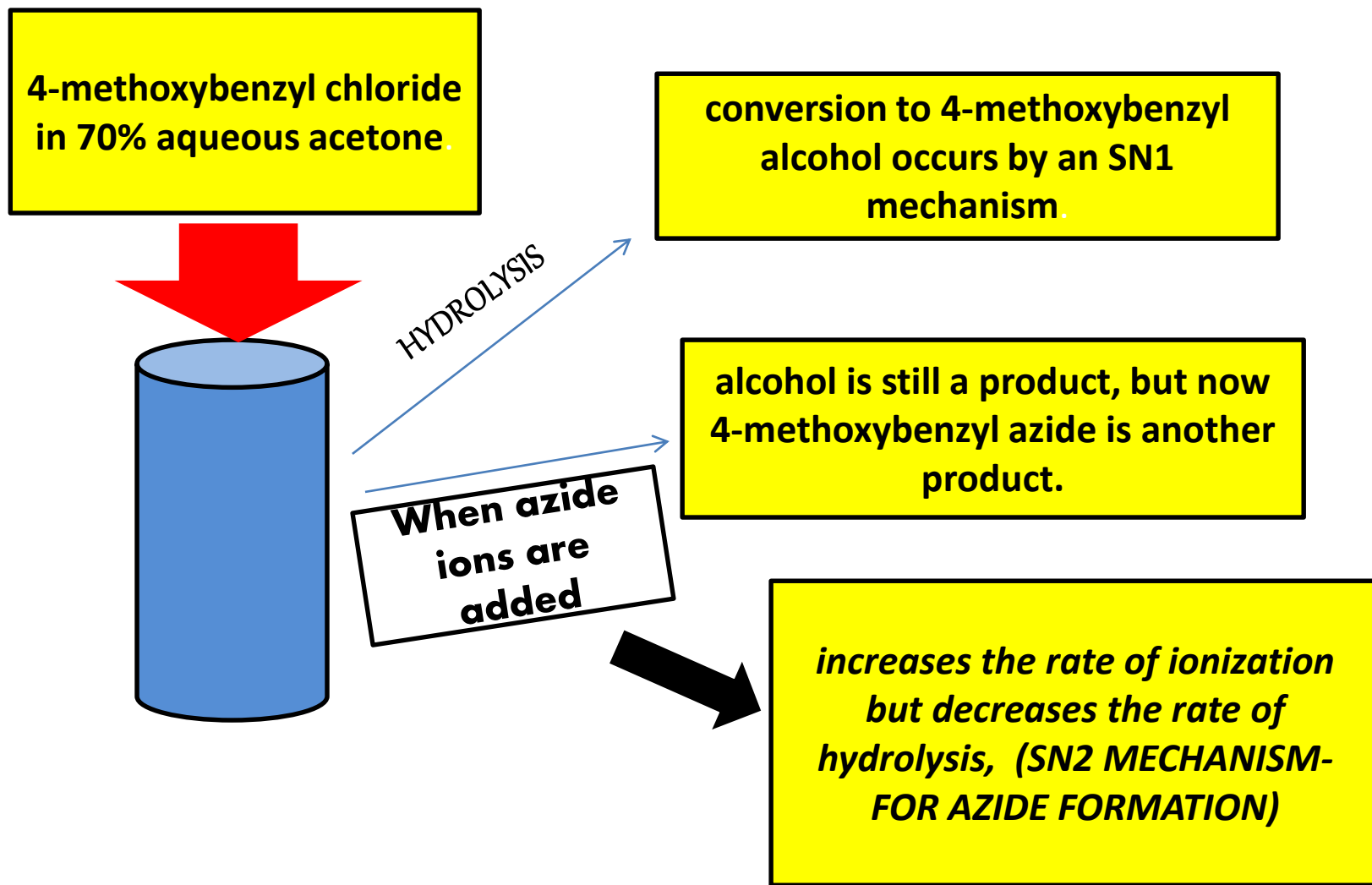


- If  $k_1 > k_2$  then mechanism is SN2, if
- $k_2 > k_1$  then mechanism is SN1
- Borderline behaviour is found where the rates of formation and destruction of the ion pair are of the same order of magnitude ( $k_1 = k_2$ ).

## 2: simultaneous operation:

- no intermediate mechanism at all, and borderline behaviour is caused by simultaneous operation.
- in the same flask, of both the SN1 and SN2 mechanisms; that is, some molecules react by the SN1, while others react by the SN2 mechanism.

- Among the experiments that have been cited for the viewpoint that borderline behaviour results from **simultaneous SN1 and SN2 mechanisms** is the behaviour of 4-methoxybenzyl chloride in 70% aqueous acetone.



# The S<sub>N</sub>i Mechanism

❖ (substitution nucleophilic internal)

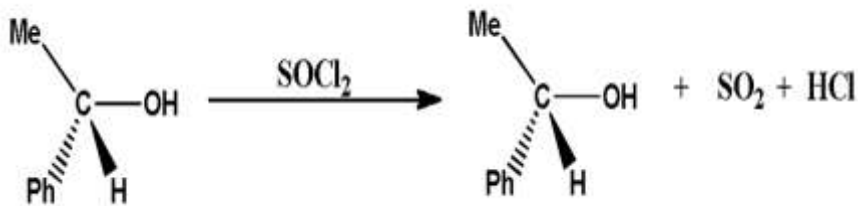
❖ In a few reactions, nucleophilic substitution proceeds with **retention of configuration**, even where there is **no possibility of a neighboring-group effect**.

❖ Follows **second order kinetics**

❖ **RARE**

❖ The reaction between alcohols and thionyl chloride has been studied exclusively.

❖ Example-  **$\alpha$ -phenyl alcohol and thionyl alcohol**



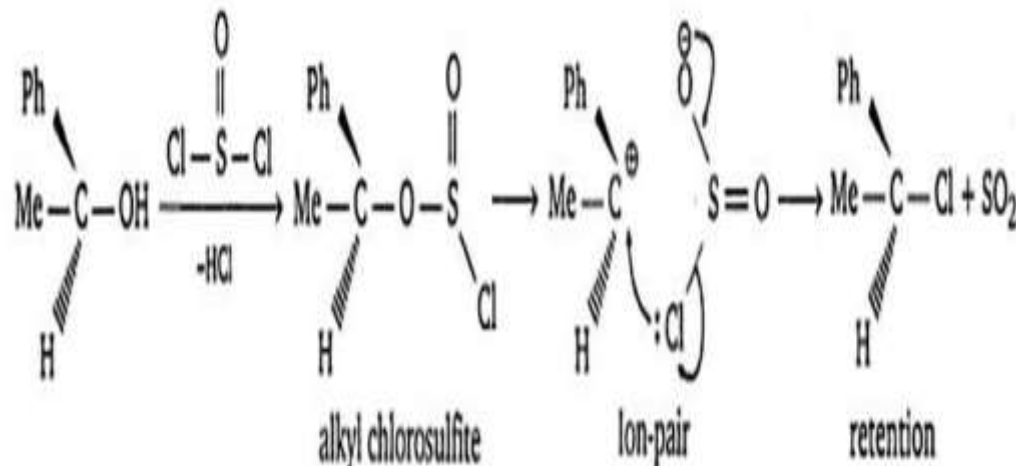
- It was found that product is formed with complete retention of configuration on the starting alcohol.
- The reaction proceeds with the formation of a chlorosulphite ester which collapses with elimination on  $\text{SO}_2$ .
- The chlorosulphite ester could form the product by  $\text{S}_{\text{N}}2$  with inversion, and  $\text{S}_{\text{N}}1$  with racemisation.



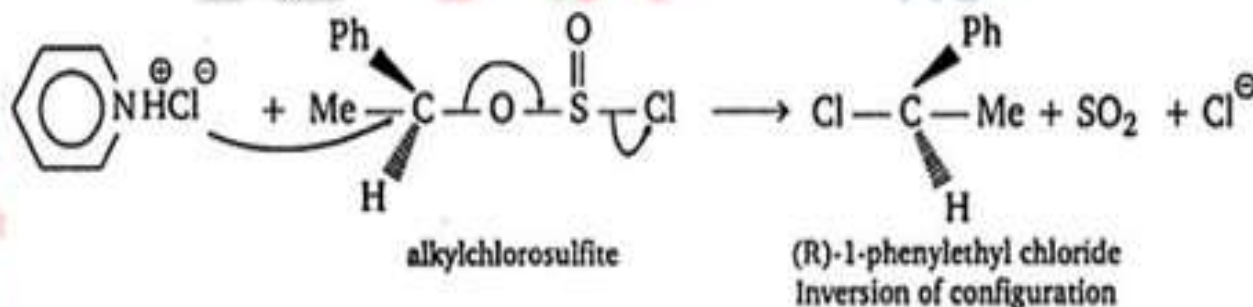
## MECHANISM OF S<sub>N</sub>i

on the basis of experimental fact-

- ❑ First step- formation of chlorosulphite (**intermediate**).
- ❑ Second step- **dissociation** of the chlorosulphite ester to form an ion –pair (not dissociated).
- ❑ Because of the geometry of the ion pair, the chlorine atom is forced to attach the carbonium ion from the side as original C-O bond of the alcohol (**internal attack**).



- If (S)-1-phenyl ethanol and SOCl<sub>2</sub> react in presence of a tertiary amine such as pyridine, the product is (R)-1-phenylethylchloride is obtained, i.e. Inversion of configuration occurs.
- The pyridine reacts with the HCl, produced in the first step of the pyridinium hydrochloric acid and Cl<sup>-</sup> being an effective nucleophile, attacks the alkyl chlorosulphite from the back via SN<sub>2</sub> reaction.

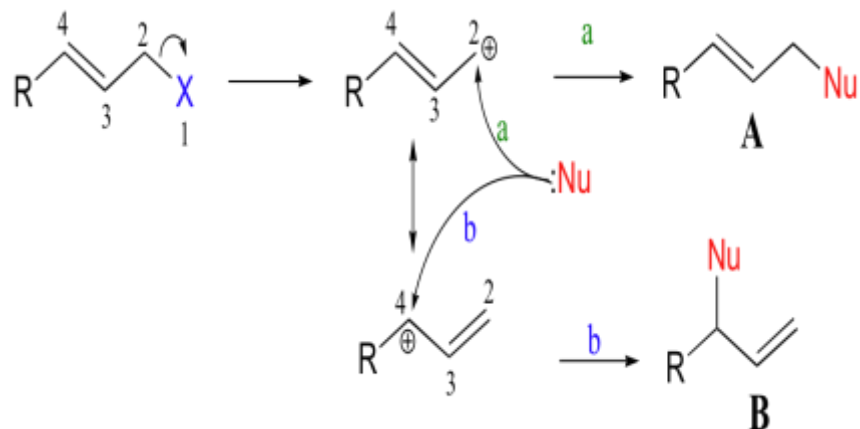


- Thus we can say in presence of pyridine, reaction follows the SN<sub>2</sub> mechanism and without it follows the SN<sub>1</sub> mechanism.
- **RATE OF REACTION-** both reactant plays crucial role in reaction. Therefore,  

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

# Nucleophilic Substitution at an Allylic Carbon

- ❖ **Allylic substrates** rapidly undergo nucleophilic substitution reactions .
- ❖ usually accompanied by a certain kind of rearrangement known as an **allylic rearrangement**.
- ❖ When allylic substrates are treated with nucleophiles under **SN1 conditions**, **two products** are usually obtained: **the normal one and a rearranged one**.

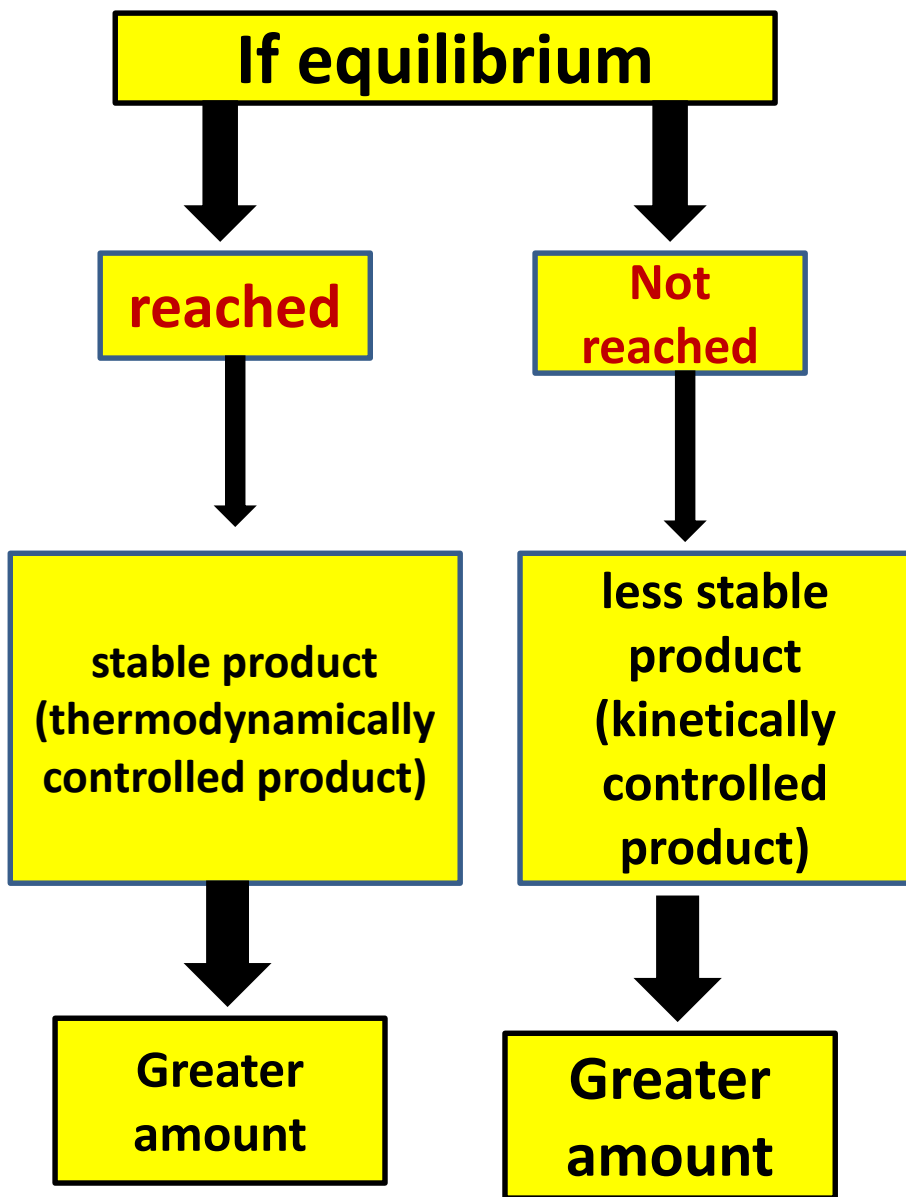


## • Reason-

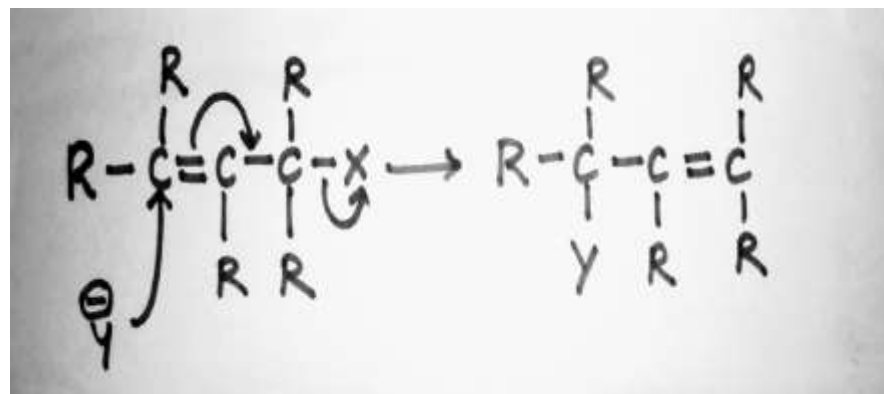
Two products are formed because an **allylic type of carbocation is a resonance Hybrid** so that **C-1 and C-3** each carry a **partial positive charge** and both are attacked by nucleophile resulting in the formation of two products:



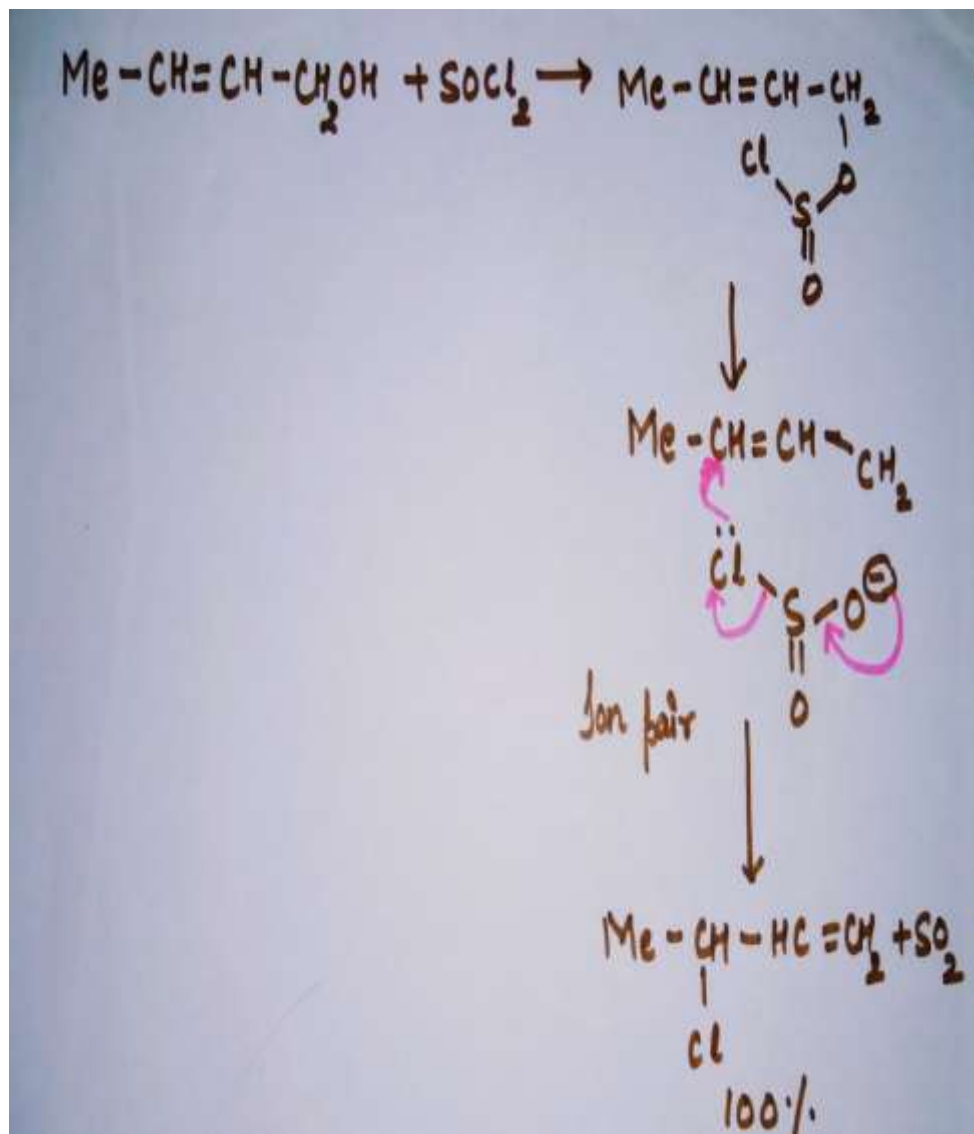
- This mechanism has been called the **SN1' mechanism**.



- Nucleophilic substitution at an allylic carbon can also take place by an **SN2 mechanism**, in which case **no allylic rearrangement** usually takes place.
- In which **the nucleophile attacks at the  $\gamma$  carbon** rather than the usual position. This mechanism is called **SN2' mechanism** and is an allylic substitution. **The SN2' mechanism takes place under SN2 conditions where  $\alpha$  substitution sterically retards the normal SN2 mechanism.**

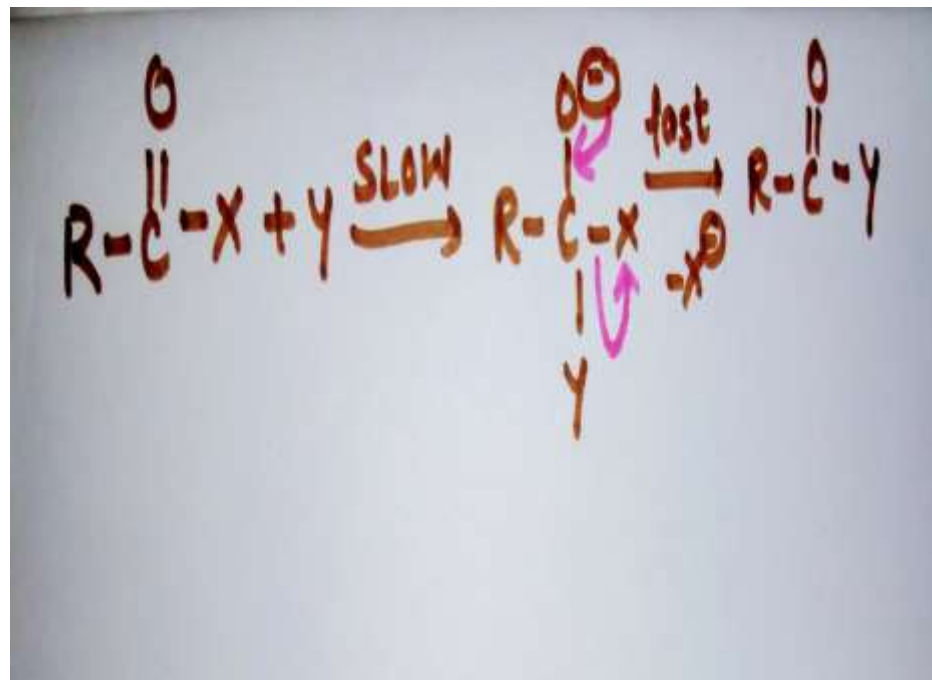


- When a molecule has in an allylic position a nucleofuge (leaving group) capable of giving the S<sub>N</sub>i reaction, it is possible for the nucleophile to attack at γ the position instead of the α position. This is called **the S<sub>N</sub>i' mechanism** and has been demonstrated on 2-buten-1-ol and 3-buten-2-ol, both of which gave 100% allylic rearrangement when treated with thionyl chloride in ether. Ordinary allylic rearrangements (S<sub>N</sub>1') or S<sub>N</sub>2' mechanisms could not be expected to give 100% rearrangement in both cases.

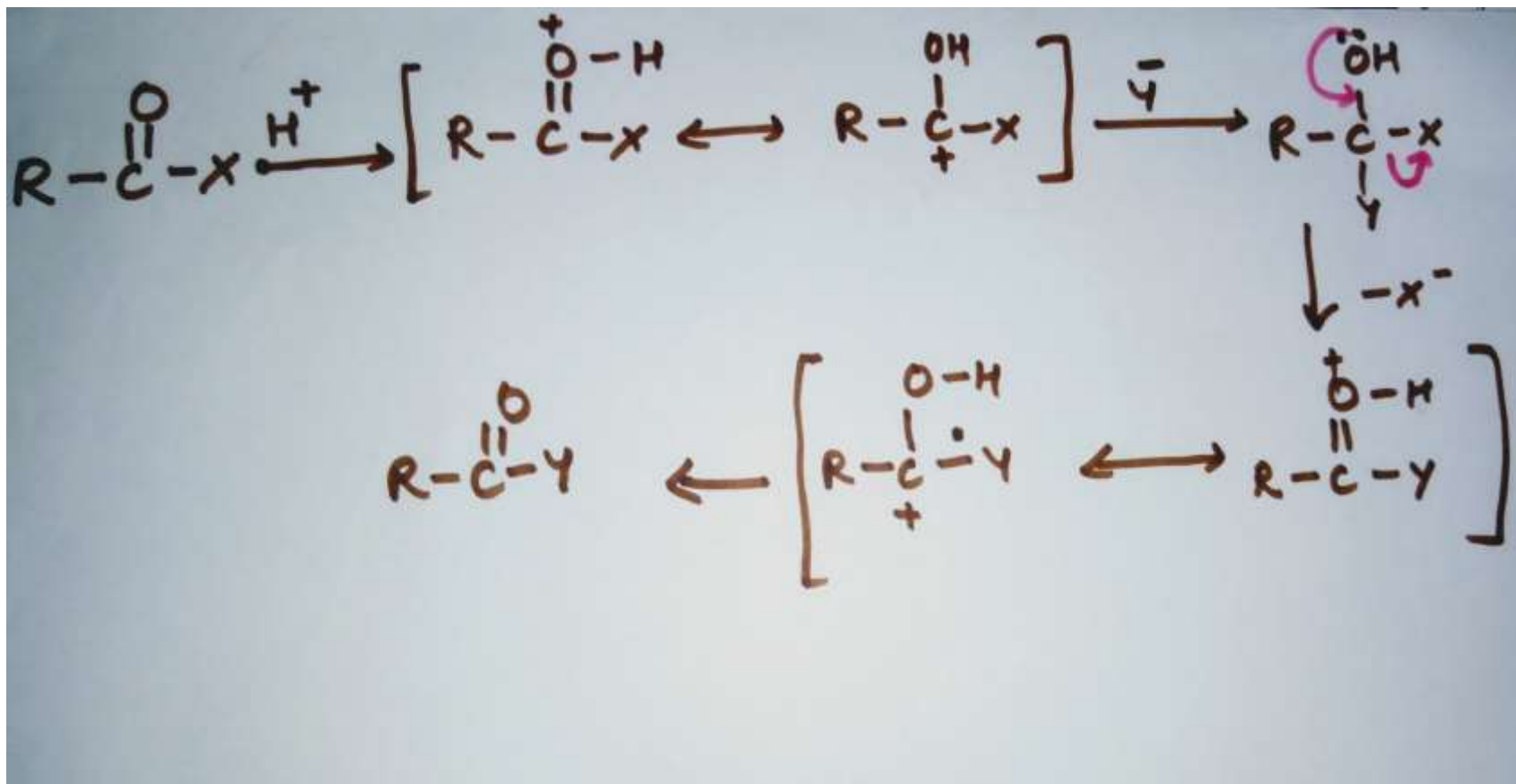


# Nucleophilic Substitution at an Aliphatic Trigonal Carbon

- The compounds containing a **trigonal carbons**, especially when the **carbon is double bonded to an oxygen, a sulphur, or a nitrogen** undergo nucleophilic substitution through **tetrahedral mechanism**, often reaction follows the **second order called addition-elimination**.
- In tetrahedral mechanism first the nucleophile attacks to give a tetrahedral intermediate and then the leaving group departs.



- As expected, this reaction is **catalysed by acid** because, **protonation decreases the electron density** at the carbon undergoing substitution, which **facilitates the attack of nucleophile**:



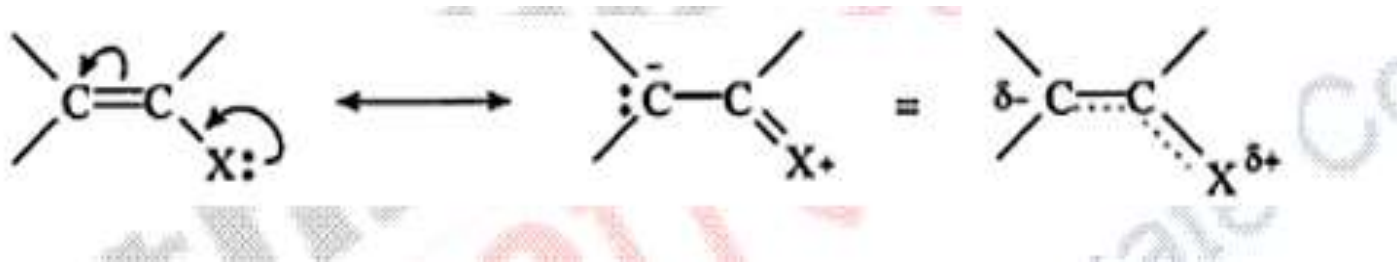
# Nucleophilic Substitution at a Vinylic Carbon

➤ Concerned with the nucleophilic substitution at unsaturated carbon such as vinylchloride ( $\text{CH}_2=\text{CHCl}$ ).

Nucleophilic substitution at a vinylic carbon is **difficult under normal condition** and is **extremely slow compared to substitution at saturated carbon**. The Vinyl chloride are essentially inert towards nucleophiles.

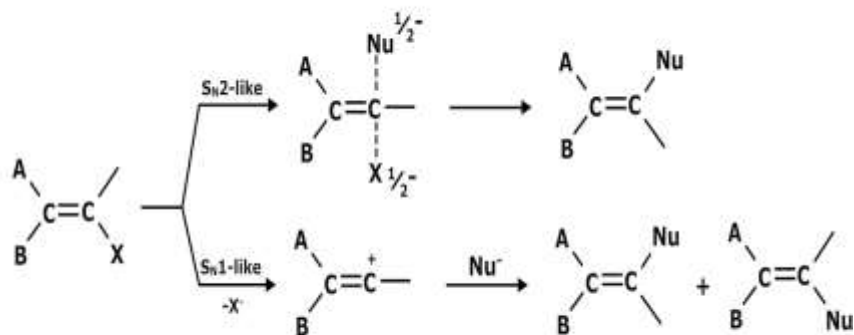
## Reason-

1. Vinyl C-X bond (x= halogen, oxygen, nitrogen) is stronger than the alkyl C-X bond because of a **resonance interaction** between the double bonds and an unsaturated pair on X. **This interaction also weakens and polarizes the pi bond**, which is why such compounds are **reactive towards the electrophilic addition**.





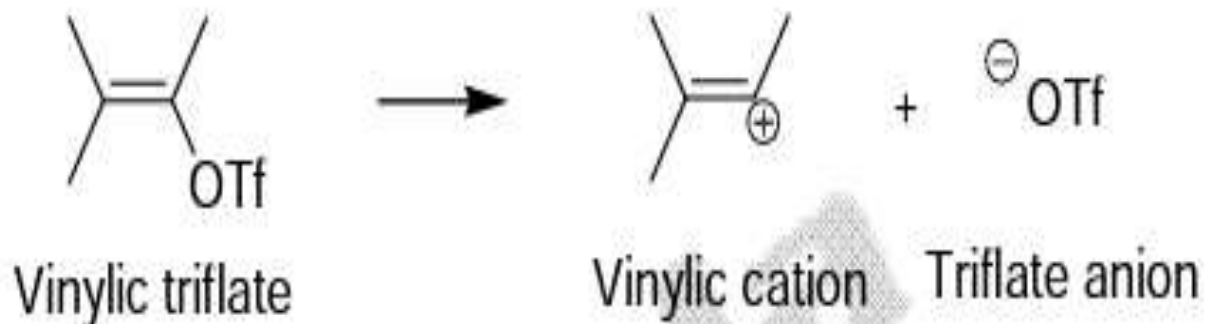
2. The  $sn_2$  transition state as well as  $sn_1$  intermediate (a vinyl cation) are **too high in energy to be readily accessible.**



▪ It takes 16-18 kcal **more energy to break a C-X bond in vinyl halide than corresponding alkyl halide.**

- Thus the **rate determining step involves the breaking of C-X bond.** The bond in vinyl halide is harder to break and **reaction is slow.**
- After a lot of reserch,
- The vinylic cation can readily made through by solvolysis of the SN1 kind if two conditions are met:
  1. The leaving group is extremely good one.
  2. The vinylic group contains electron releasing substituents.

Most commonly used for this purpose is the ***super leaving group – trifluoromethanesulfonate (-OSO<sub>2</sub>CF<sub>3</sub>) WHICH is known as TRIFLATE.***



The **powerful electron withdrawing F- ATOM**( through dispersal of negative charge) help to **stabalise the triflate anion**, and makes the parent acid CF<sub>3</sub>SO<sub>2</sub>OH one of the strongest LOWRY- BRONSTED ACID known, much stronger than known H<sub>2</sub>SO<sub>4</sub> AND HClO<sub>4</sub>.

# REFERENCE-

1. **Advanced organic chemistry: reaction mechanisms and structure by Jerry March; McGraw Hill**
2. **Advanced organic chemistry by Dr. Jagdamba singh and Dr. L.D.S.Yadav; pragati prakshan**
3. **Organic reactions and their mechanisms ( second edition) by P.S. KALSI**
4. **REACTION MECHANISM in organic chemistry by S.M. Mukhrjee and S.P. Singh and Macmillan.**

**THANK YOU**