

ADDITIONAL MODULE OF SUBSTITUTION REACTION (S_Nⁱ AND NGP) FOR 2ND SEMESTER STUDENTS

Part A: S_Nⁱ Substitution Reactions

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Nucleophilic Substitution SNⁱ (Nucleophilic Substitution Internal)

This kind of reaction is seen only in one situation.



The reaction follows the second order rate equation; Rate = k_2 [Substrate] [SOCl₂]

So, in SNⁱ reactions, we have **retention of configuration**.

But this is different from SN¹ reactions as there is no formation of a racemic mixture over here.

This is also different from SN² reactions as in SN², there is inversion of configuration, whereas over here, the stereochemistry of the reactant and the product is nearly the same.

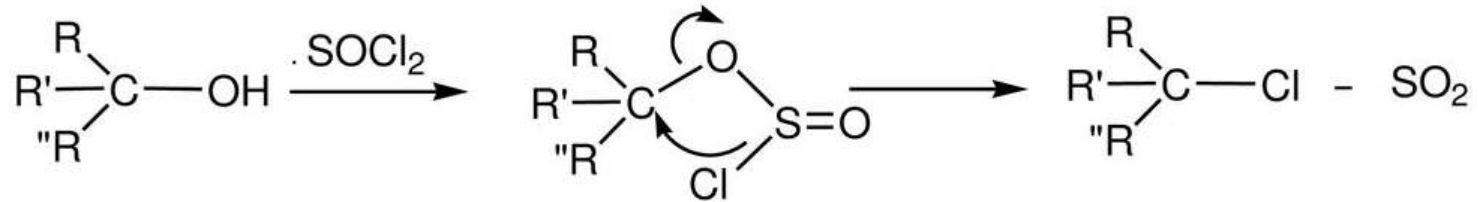
Hence this reaction can be explained **neither by SN¹ nor by SN²**.

Nucleophilic Substitution Internal

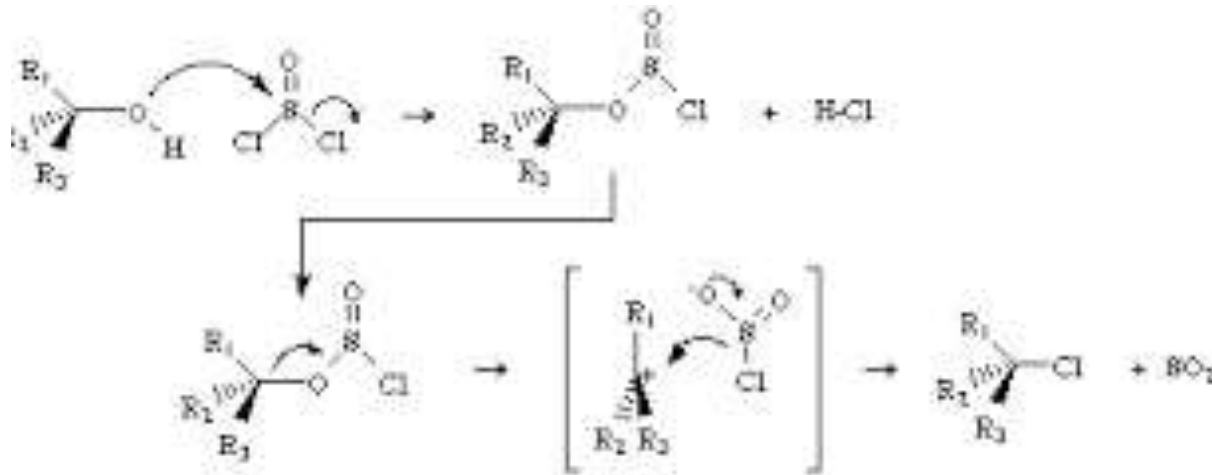
SNⁱ

Two proposed mechanism:

1. Concerted



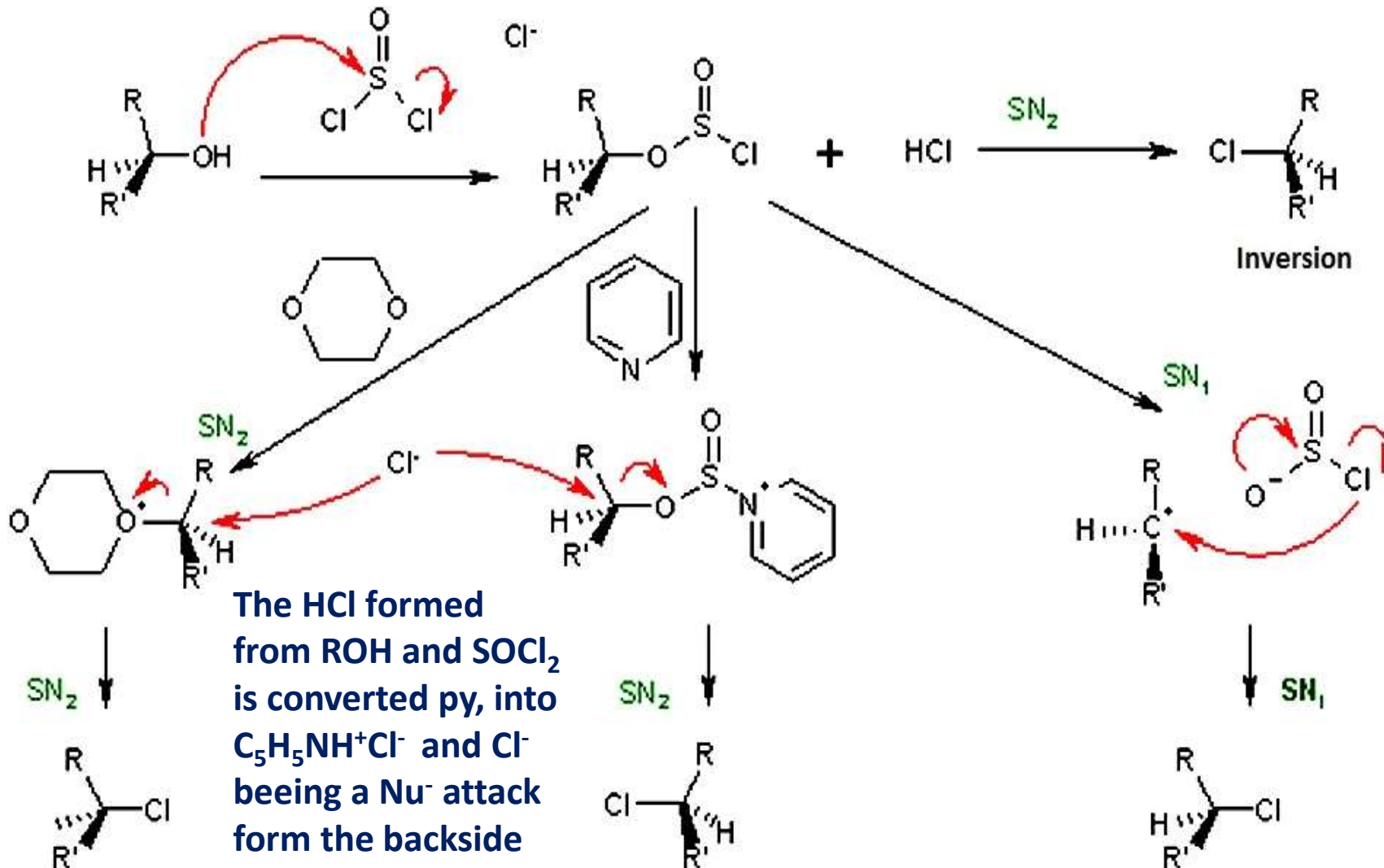
2. Through the formation of intimate ion pair (In intimate ion pair, an ion is completely shielded by the counter ion. There are no solvent molecule between two ions)



The intimate ion pair within a solvent cage is further attacked by Cl⁻ is likely to occur from the same side of the departing gr. ie. with retention of configuration

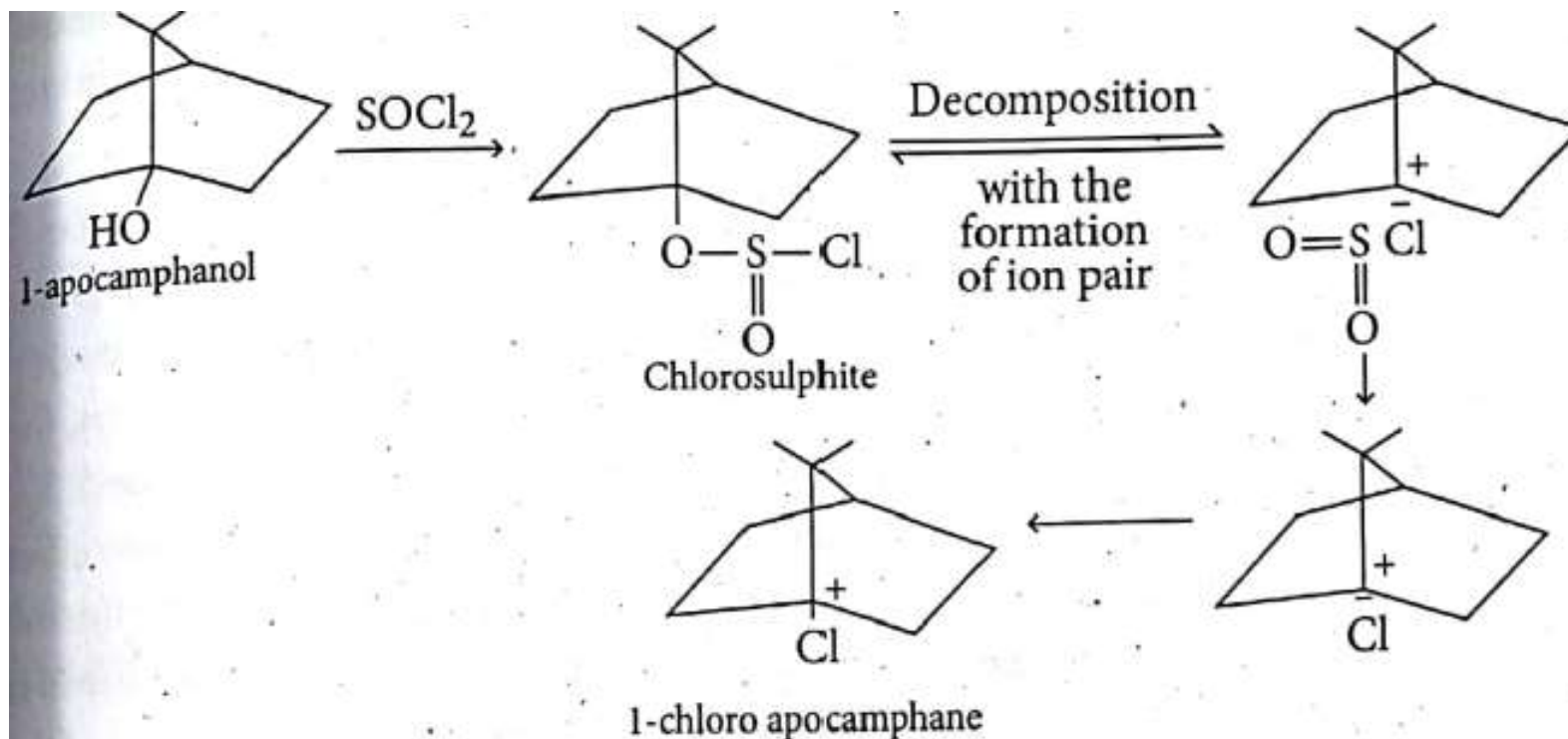
SNⁱ

SNi reaction in presence of different solvents:



The SNi reaction in presence of pyridine or dioxane occurs through the inversion of configuration of the substrate

SNi reaction for bridgehead Molecules:??



In case of such rigid molecule, formation of such non classical carbocation formation is unusual, but as ion pair formation does not involve formal carbocation, replacement of hydroxyl group can easily occur.

Hence we can draw **four** important inferences:

1. In ether medium, the reaction follows the rules of **SNⁱ** mechanism.
2. If pyridine is added as the medium solvent to this reaction, it will form a strong **nucleophile** in Pyridinium chloride, which will cause a **backward** attack on the system, eliminating Sulphur dioxide from it.
3. This type of reaction will be termed as SN² because there is **inversion** of configuration. In case of pyridine, the nature of the reaction changes from **SNⁱ** to **SN²**.
4. In case of SNⁱ reactions, the rate of the reaction is dependent on the concentration of both the alcohol and the thionyl chloride, i.e.,

$$\text{Rate } r \propto [\text{R} - \text{OH}] [\text{SOCl}_2],$$

as opposed to the case of SN¹ and SN² reactions.

SNⁱ

Part B: Neighbouring Group Participation (NGP)

Definition

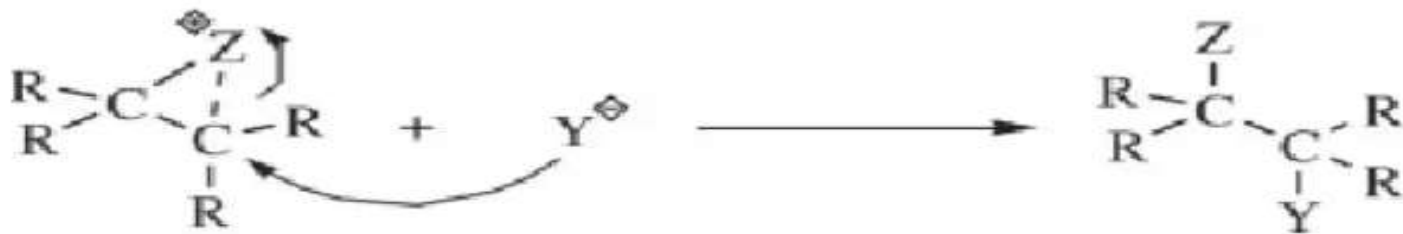
The direct interaction of the reaction centre with a lone pair of electrons of an atom or with the electrons of a sigma or pi bond contained within the parent molecule but not conjugated with the reaction centre.

Neighbouring Group Mechanism

- **Step 1** In the first step the neighbouring group act **Z** as a nucleophile and pushes the leaving group **X** but still remain attach to the molecule.

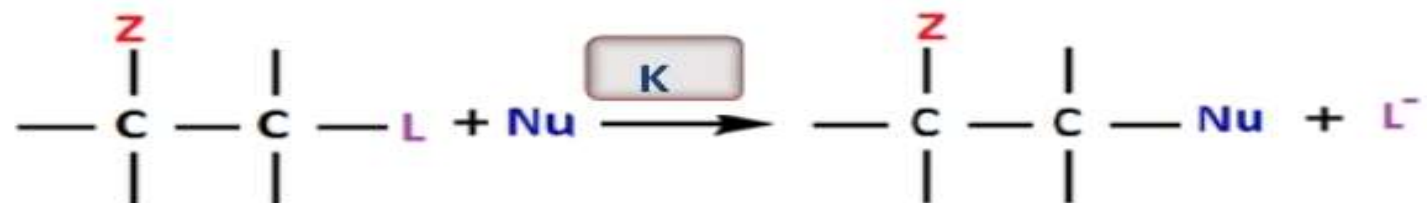


- **Step 2** In the second step the external nucleophile **Y** displaces the neighbouring group **Z** from the back side.



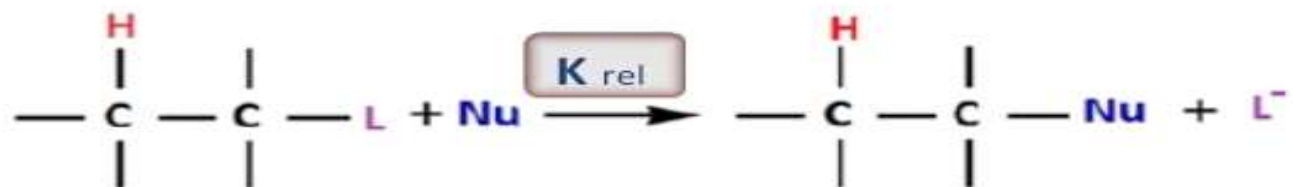
In the mechanism Z acted as a nucleophile.

Z = Electron pair donor



If there is no Nucleophile Z

i.e. Z = H



Where $K \gg K_{\text{rel}}$

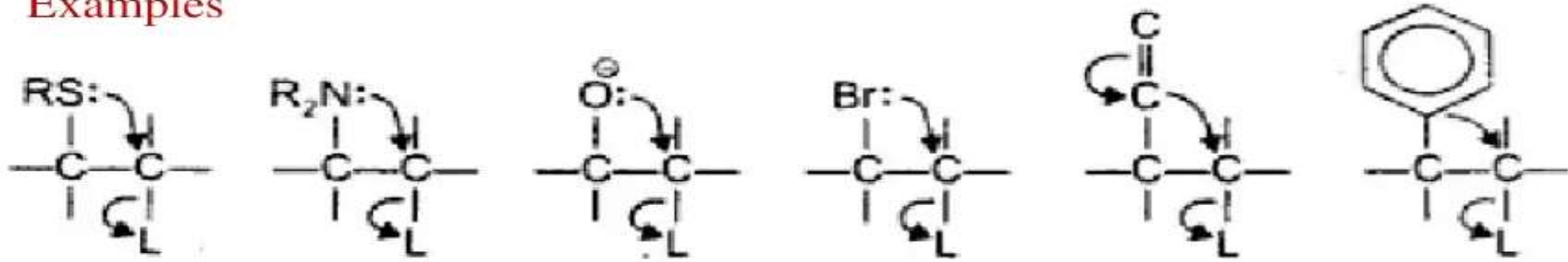
➤ Z (electron pair donor) helps in the removal of L (leaving group). So the rate of reaction increases many times.

Types of Groups which are expected to display in NGP

Any Group which has

- Lone pair
- Pi electron

Examples



Consequences of NGP

There are three consequences of NGP

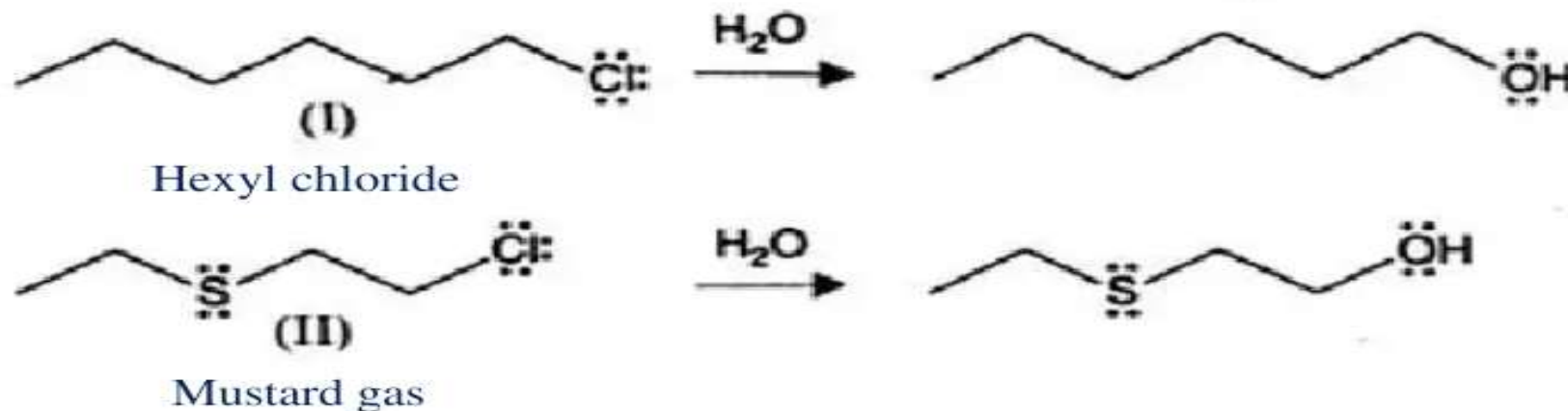
1. Anchimeric Effect
2. Retention of Configuration
3. Cine Substitution

1) Anchimeric Assistance

If the neighbouring group participation result in an abrupt increase in the rate of reaction ,then the phenomenon is known as Anchimeric Effect or Anchimeric Assistance

Example:

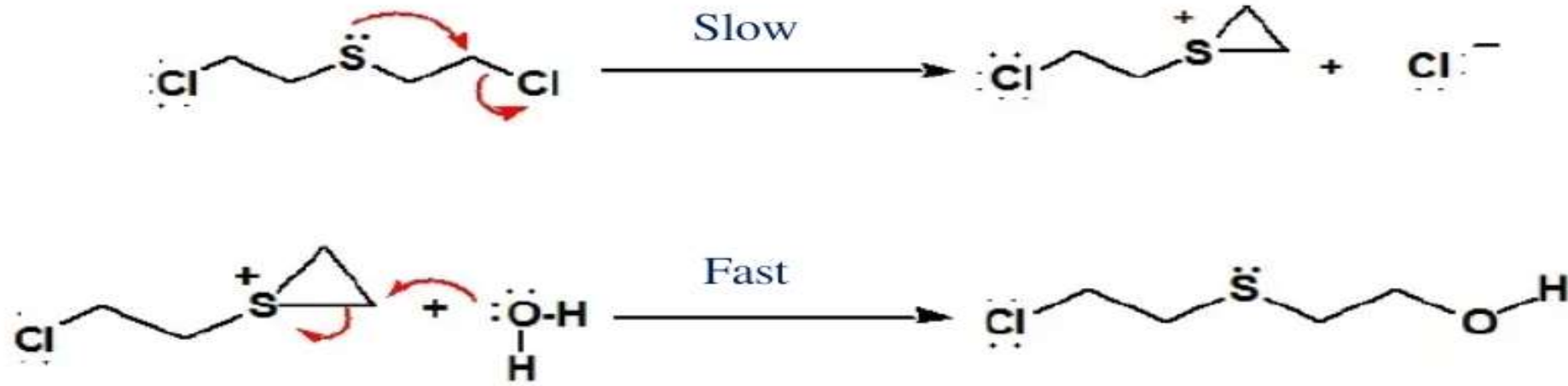
On reaction with water both hexyl chloride and mustard gas give there corresponding alcohols. However the rate of Sulfur containing compound is much greater than that of alkyl halide.



The rate of (II) is 700 times greater (I)

Cont..

An increase in the rate is observed when mustard gas is hydrolyzed because sulfur acts as a neighbouring group and displaces the leaving group, forming an intermediate which on hydrolysis gives the product.



2) Retention of Configuration

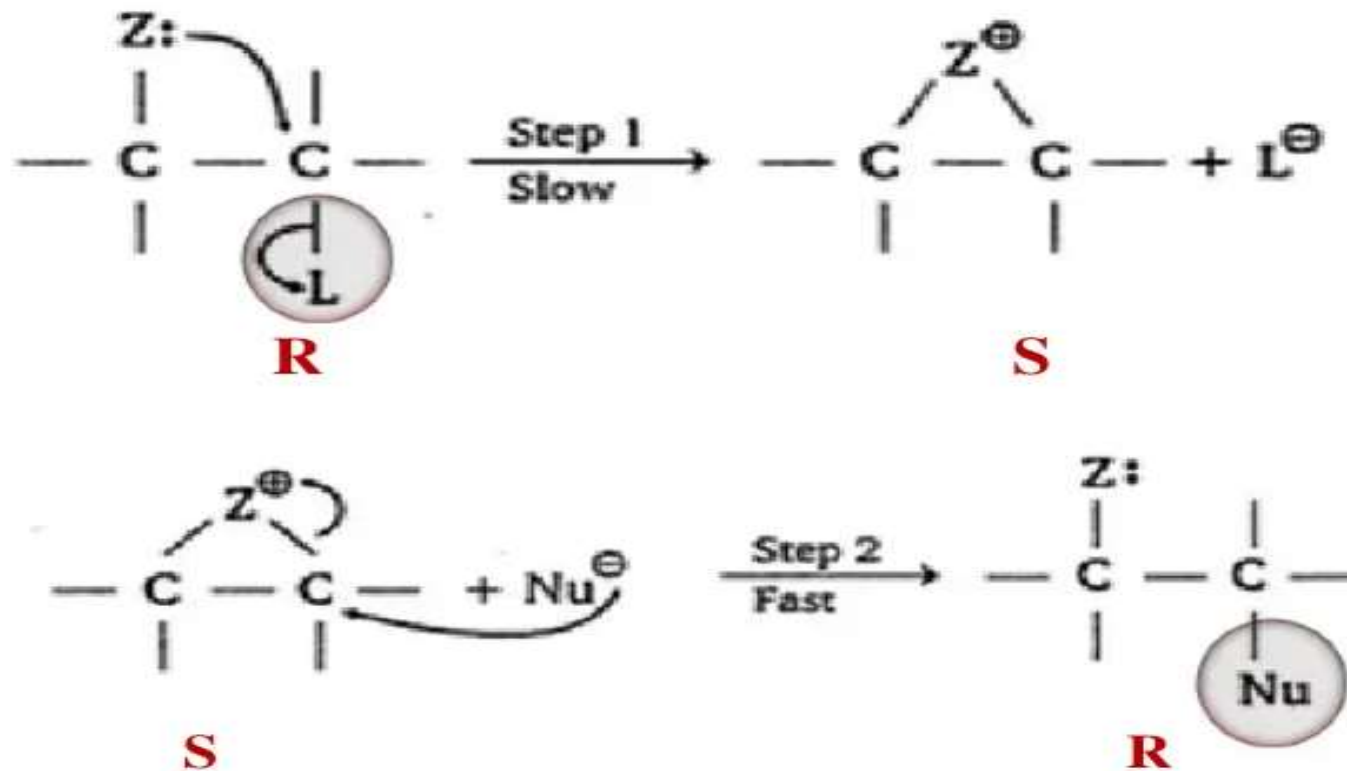
If the net change in a reaction is the replacement of a ligand on a chiral center in a reactant molecule, and, if in the product the attacking ligand occupies the same site on the chiral center as the replaced ligand, the reaction is said to occur with retention of configuration.

A number of reactions are known in which nucleophilic substitution occur with retention of configuration. One of the important factor which leads to retention of configuration is ***Neighbouring group participation***

Conti..

Such reaction involve **two *SN2* substitution** :

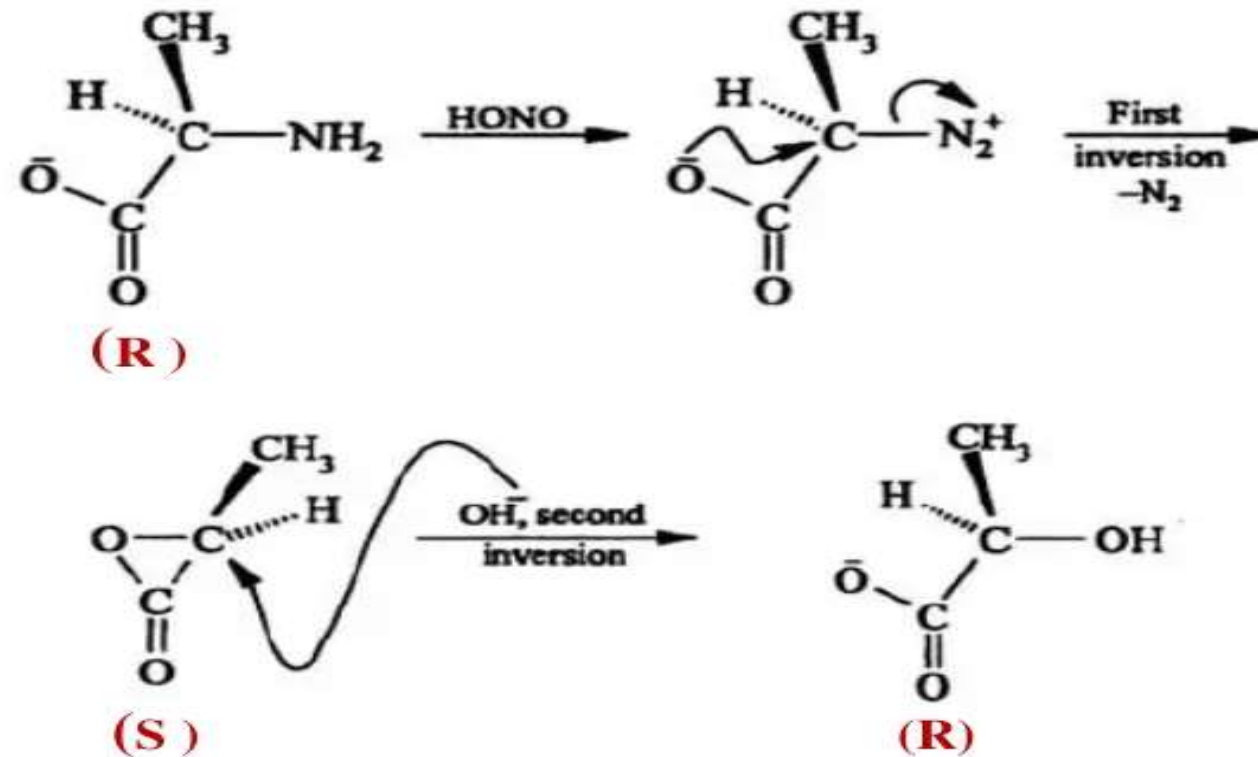
In the first step the neighbouring group Z attacks as a nucleophile and pushes out the leaving group L while the external nucleophile pushes out the neighbouring group in the subsequent step.



Conti..

Examples Of Stereochemical Consequences Of NGP:

Deamination of L-alanine to L-lactic acid by the way of an intermediate lactone formed by participation of the carbonyl group.



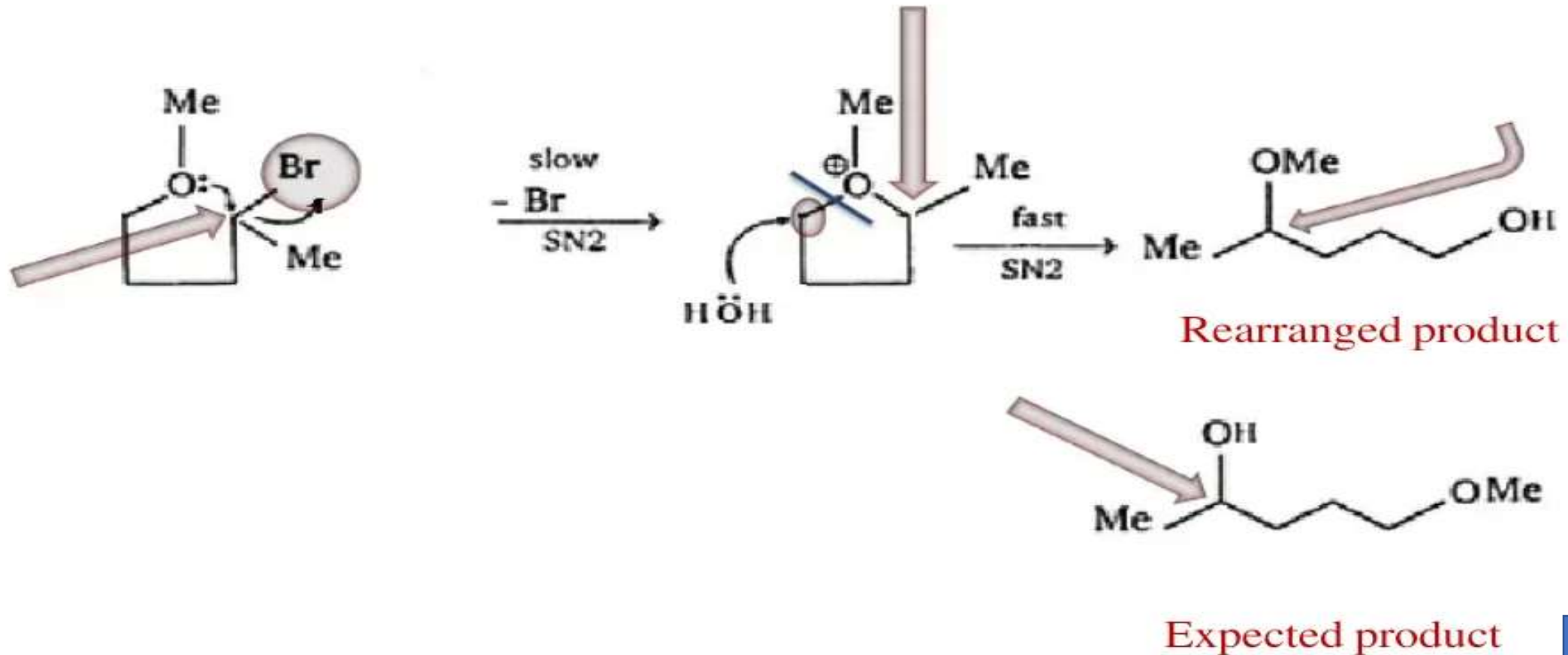
Retention of configuration

NGP

Conti..

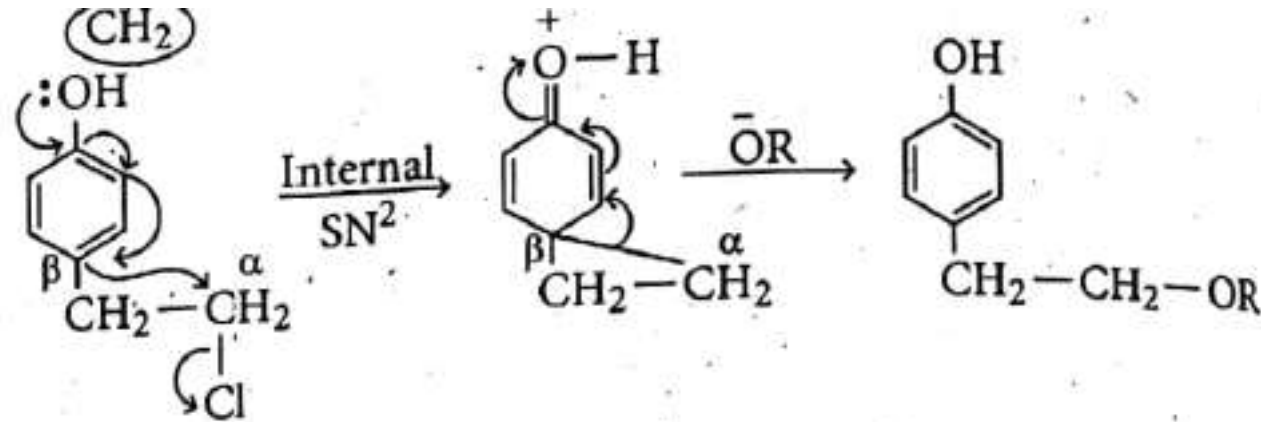
Example:

NPG may also involve in the formation of rearranged product called cine substitution.



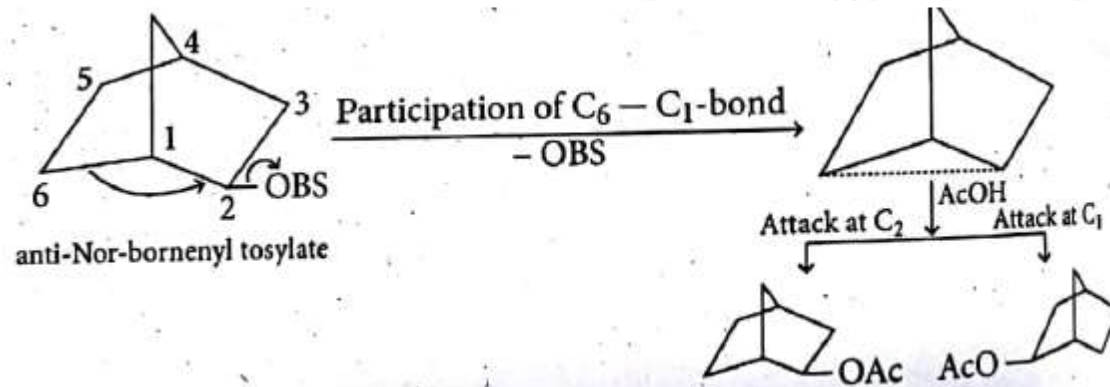
Some additional problems.....

1.



Example of π bond participation.

2.



Example of σ bond participation

Solve the following problems:

1. $\text{EtSCH}_2\text{CH}_2\text{Cl}$ is found to undergo hydrolysis 10^4 times faster than $\text{EtOCH}_2\text{CH}_2\text{Cl}$ -Explain
2. Base hydrolysis of 1,2 chlorohydrin is found to yield the 1,2 diol with retention of configuration- Explain
3. Give evidence in favor of concerted mechanism of $\text{S}_{\text{N}}\text{i}$ substitution reaction.