




FACTORS AFFECTING SUBSTITUTION REACTION

1. Effect of Substrate Structure
2. Effect of Nucelophile
3. Effect of Solvent
4. Effect of Leaving Group

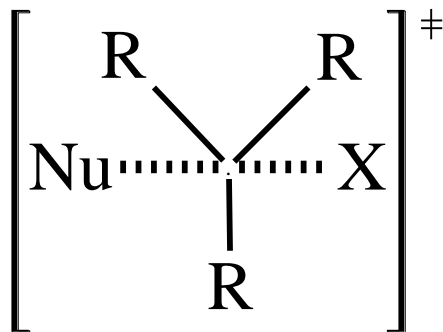
1. EFFECT OF SUBSTRATE STRUCTURE

(i) Steric Factor

- Steric hindrance to nucleophilic attack increases \longrightarrow

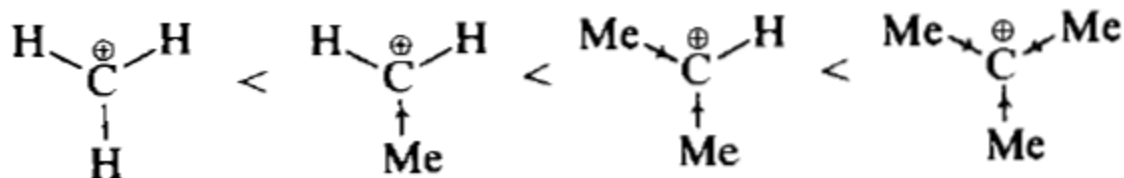
structure	$\text{Me}-\text{X}$			
type	methyl	primary	secondary	tertiary
$\text{S}_{\text{N}}1$ reaction?	no	no	yes	good
$\text{S}_{\text{N}}2$ reaction?	good	good	yes	no

- Steric repulsions in T.S. during nucleophilic attack also increases \longrightarrow



Least stable due to crowding/repulsions

(ii) Electronic Factor



- More branching at α -carbon, more chances of S_N1 reaction and vice versa
More branching at β -carbon, more chances of S_N1 reaction also, although effect is less.
- More stability of carbocation, more chances of S_N1 reaction and vice versa

Type of cation	Example 1	Example 2
simple alkyl	tertiary (good) <i>t</i> -butyl cation $\text{Me}_3\text{C}^{\oplus} = \text{Me}-\overset{\oplus}{\text{C}}(\text{Me})_2$	secondary (not so good) <i>i</i> -propyl cation $\text{Me}_2\text{CH}^{\oplus} = \text{H}-\overset{\oplus}{\text{C}}(\text{Me})_2$
conjugated	allylic 	benzylic
heteroatom-stabilized	oxygen-stabilized (oxonium ions) 	nitrogen-stabilized

Type of electrophilic carbon atom	S_N1 reaction	S_N2 reaction
methyl ($\text{CH}_3\text{-X}$)	no	very good
primary alkyl ($\text{RCH}_2\text{-X}$)	no	good
secondary alkyl ($\text{R}_2\text{CH-X}$)	yes	yes
tertiary alkyl ($\text{R}_3\text{C-X}$)	very good	no
allylic ($\text{CH}_2=\text{CH-CH}_2\text{-X}$)	yes	good
benzylic ($\text{ArCH}_2\text{-X}$)	yes	good
α -carbonyl ($\text{RCO-CH}_2\text{-X}$)	no	excellent
α -alkoxy ($\text{RO-CH}_2\text{-X}$)	excellent	good
α -amino ($\text{R}_2\text{N-CH}_2\text{-X}$)	excellent	good

2. EFFECT OF NUCLEOPHILE

$S_N1 \rightarrow$ Independent of Nucleophile (Rate= $k[\text{Substrate}]$)

$S_N2 \rightarrow$ Depends upon both conc. and nature of nucleophile

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

Rate \propto Nucleophilicity or Reactivity of nucleophile

- A negatively charged nucleophile is stronger than its conjugate acid
 $\text{HO}^- > \text{H}_2\text{O}$
- When nucleophilic atom is same, nucleophilicity parallels basicity
 $\text{RO}^- > \text{HO}^- > \text{H}_2\text{O}$
- When nucleophilic atom is in same row of periodic table, nucleophilicity parallels basicity
 $\text{R}_3\text{C}^- > \text{R}_2\text{N}^- > \text{RO}^- > \text{F}^-$
- When nucleophilic atom is in same group of periodic table, nucleophilicity is inverse of basicity
 $\text{I}^- > \text{Br}^- > \text{Cl}^- > \text{F}^-$

3. EFFECT OF LEAVING GROUP

S_N1 → Requires a good leaving group to generate a carbocation

S_N2 → Good leaving group increases the rate of reaction

Properties of good leaving groups

- Capable of independent existence after leaving e.g. $H_2O > ^-OH$
- Capable of better accommodate negative charge after leaving e.g. $PhO^- > RO^-$
- Leaving group ability is generally inverse of its basicity e.g. $I^- > Cl^-$
- Best leaving groups are generally weakest bases e.g. I^-

Poor Leaving Groups: ^-OH , $^-NH_2$

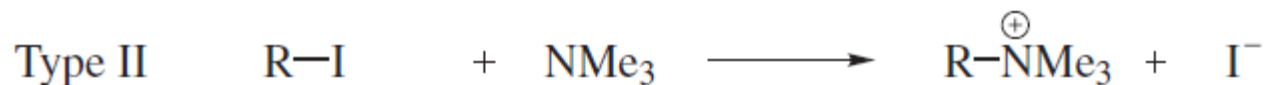
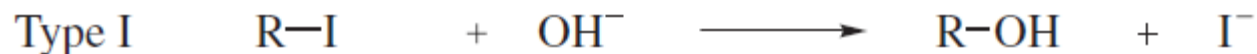
Good Leaving Groups: H_2O , NH_3 , TsO^- , PhO^- , I^- etc

4. EFFECT OF SOLVENT

The greater the polarity of solvent, the greater its ability to stabilize charged species.

S_N1 → Reactions which produce ions from neutral species are accelerated by polar solvent.

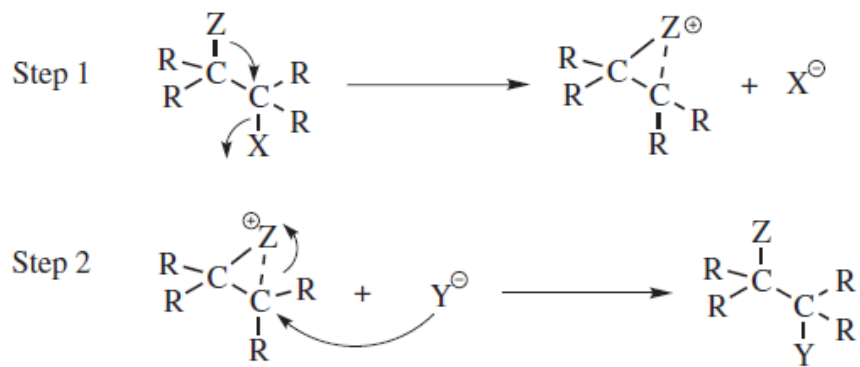
S_N2 → Effect of solvent depends on whether the initial charge is dispersed or decreased or increased in the rate-determining step.



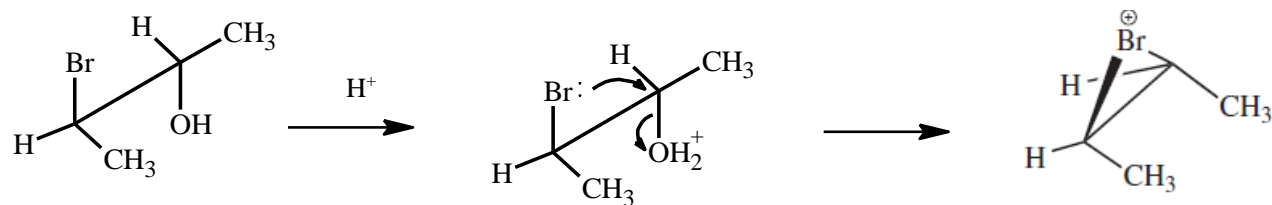
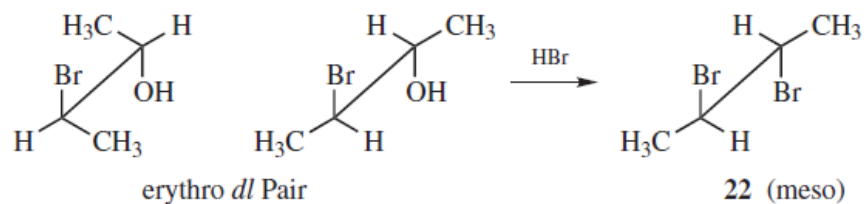
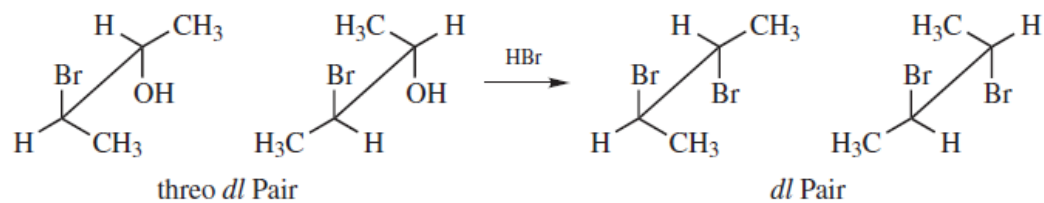
- Aprotic solvents like DMSO decreases the nucleophilicity of a nucleophile through solvation.
- Solvation in aprotic solvent (DMSO) is less than in protic solvent (H₂O)

NEIGHBOURING GROUP PARTICIPATION

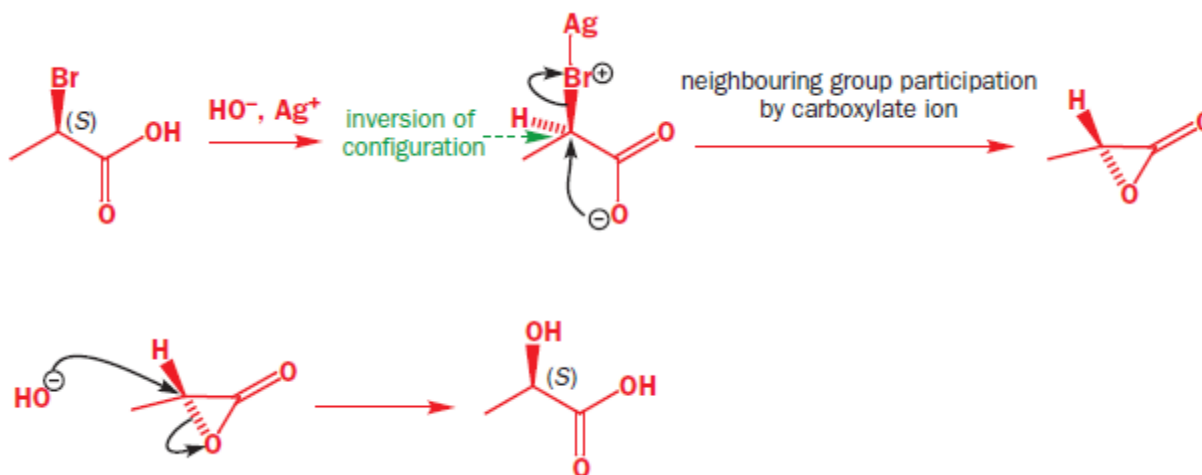
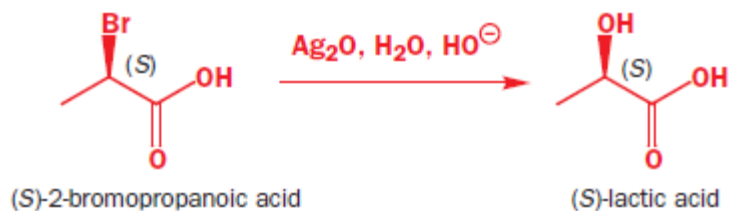
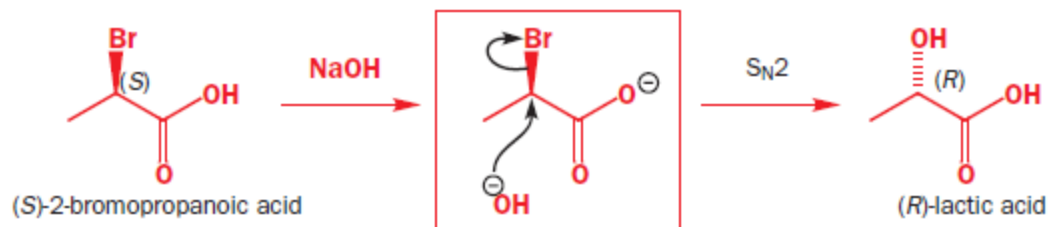
Neighbouring group participation is occasionally called anchimeric assistance (Greek anchi =neighbouring; mer = part).



Example-1: Stereochemistry is changed



Example-2: Stereochemistry is changed



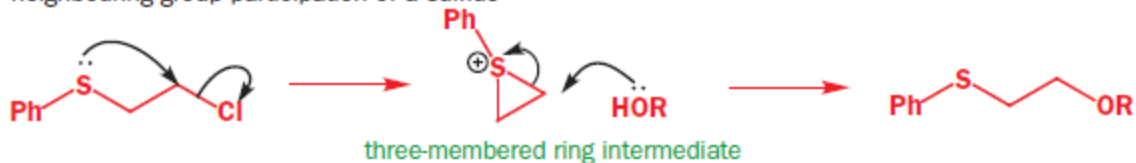
Example-3: Rate of reaction is increased

S_N1 reaction of ethoxymethyl chloride



Example-4: Rate of reaction is increased

neighbouring group participation of a sulfide

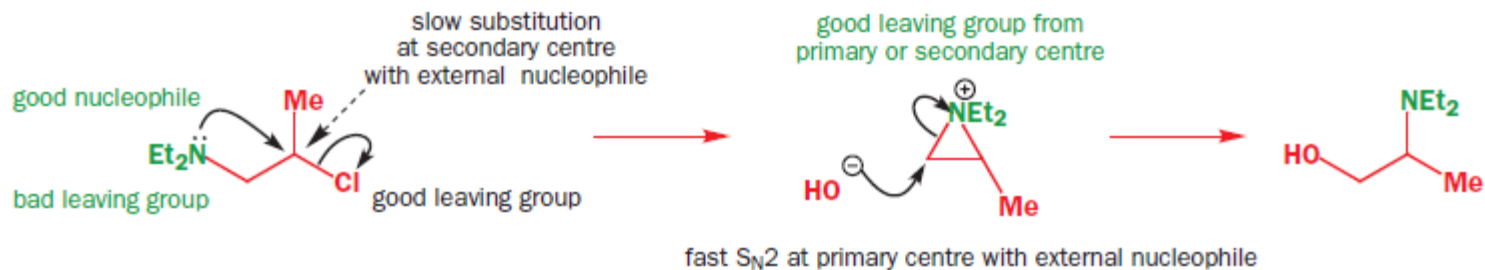


Example-5: Rate of reaction is increased



reacts with H_2O 600 times faster than CH3CH2CH2Cl

Example-6: Re-arrangement can occur and rate of reaction is also increased



Conclusion

Intramolecular reactions, including participation, that give three-, five-, or six-membered rings are usually faster than intermolecular reactions.