



Nucleophilic Substitution Reaction

(Part 1)

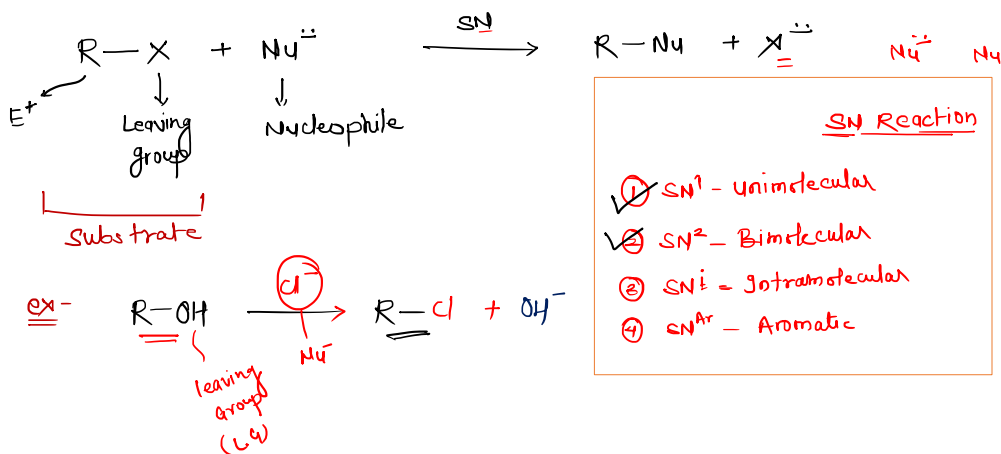
Nucleophiles/Leaving groups Tendency

B.Pharm. | POC-I | U 3 | L2

Nucleophilic Substitution Reaction



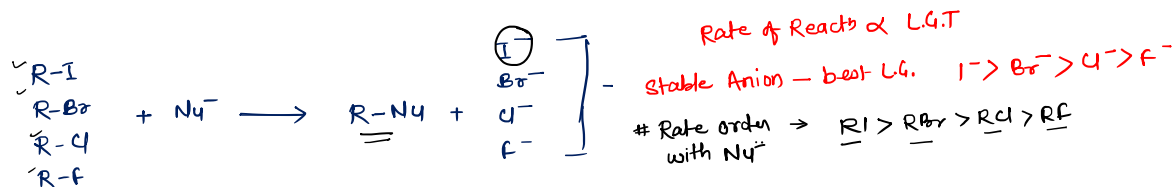
- A chemical reaction in which **an electron-rich nucleophile replaces** a functional group in an electron-deficient molecule.



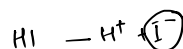
Nucleophilic Substitution Reaction



Leaving Group Tendency



For identify best LG- we can observe

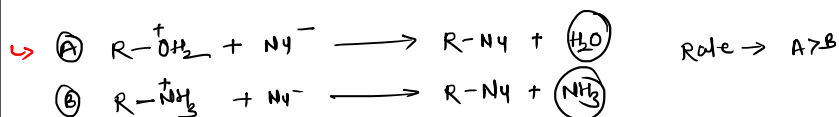
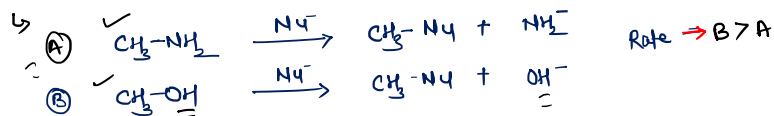
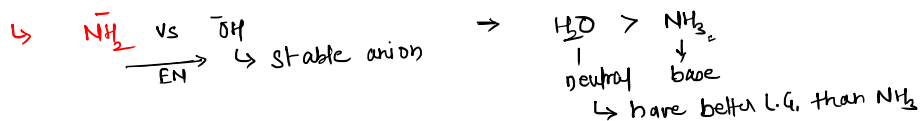


1. Formation of stable Anion
2. Strong Acid have good LG- $\text{HI} > \text{HBr} > \text{HCl} > \text{HF}$ -- Acidic order
3. Weakest Conjugated base is a good LG- $\text{I}^- < \text{Br}^- < \text{Cl}^- < \text{F}^-$
weakest conj. base

Nucleophilic Substitution Reaction



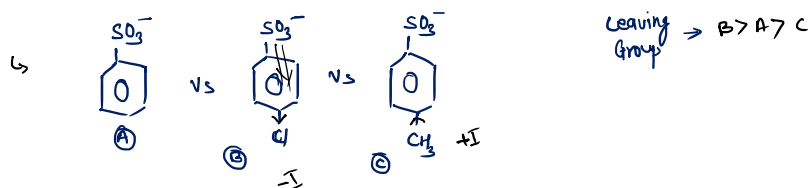
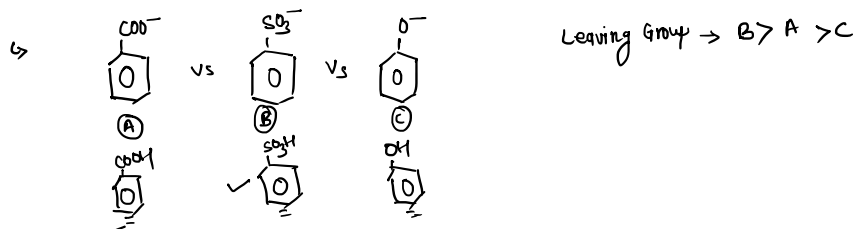
Leaving Group Tendency



Nucleophilic Substitution Reaction



Leaving Group Tendency



Nucleophilic Substitution Reaction

(Part 2)

S_N1 Reaction Mechanism

Factors affecting of S_N1

Stereochemistry

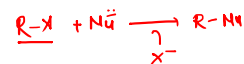
B.Pharm. | POC-I | U 3 | L2

SN1 Reaction

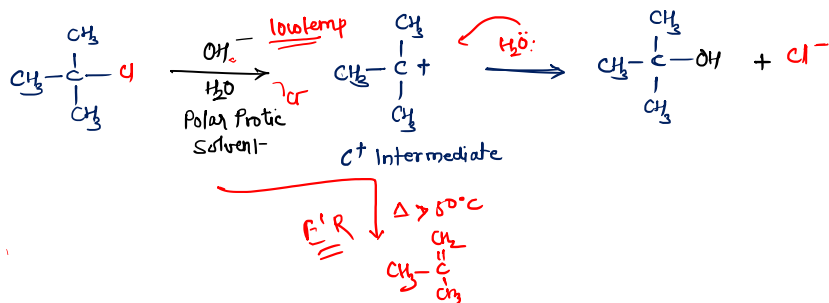


Substitution Nucleophilic Unimolecular Reaction

- In Rate Determining Step (RDS)- Involve only 1 Molecule
- Rate \propto [Substrate]¹, 1st Order Kinetic
- SN1- Carbocation Intermediate $3^\circ > 2^\circ > 1^\circ$
- Rate- depends on formation of stable Carbocation Before Rearrangement



Hydrolysis of Alkyl Halide:- Preferred in 3^o alkyl halide — SN1

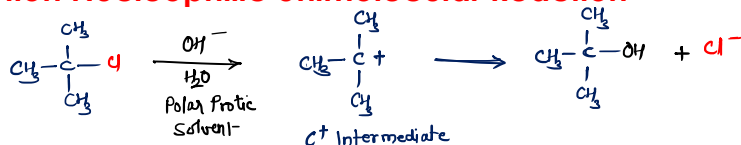


SN1 Reaction



Substitution Nucleophilic Unimolecular Reaction

Hydrolysis of Alkyl Halide:-

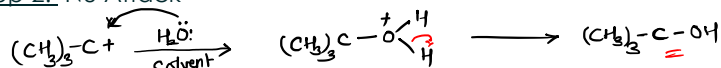


SN1 Reaction Mechanism:-

Step 1: Formation of Carbocation, Rearrangement Possible [1^o → 2^o → 3^o]



Step 2: Nu⁻ Attack



-H shift > phenyl shift > me. shift-

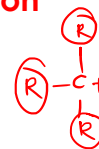
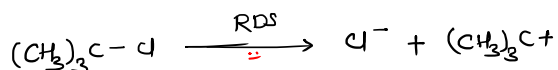
SN1 Reaction



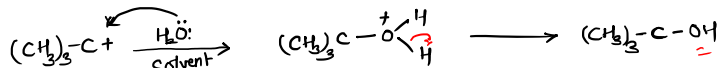
Substitution Nucleophilic Unimolecular Reaction

SN1 Reaction Mechanism-

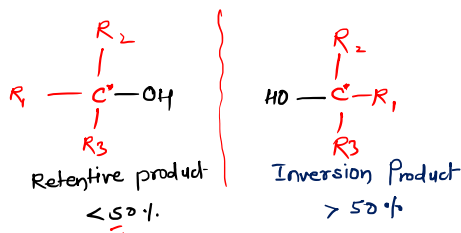
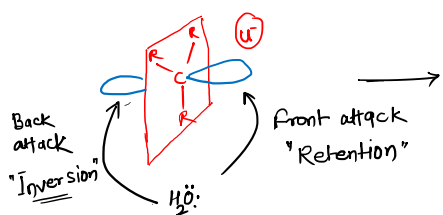
Step 1: Formation of Carbocation, Rearrangement Possible [1 → 2 → 3]



Step 2: Nu Attack



Carbocation → sp^2 , planar



SN1 Reaction



Imp Points & Factors of SN¹ Reaction

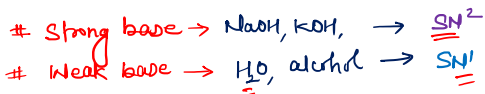
1. Kinetics- First Order Kinetics



$$\text{Rate} \propto [\text{RX}]^1 \quad \# \text{ Rate of SN}^1 \text{ React}^n \text{ depends on conc. of alkyl halide only}$$

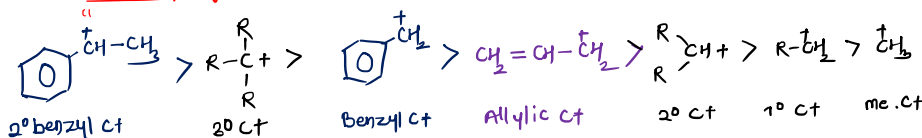
2. Conc. of Alkyl Halide: increase the rate of reaction with in conc. of alkyl halide

3. Conc. of Nucleophile: No effects, but depends on nature of Nucleophile



4. Nature of Alkyl Halide:

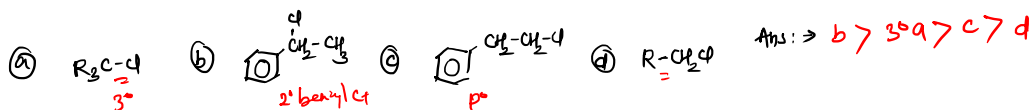
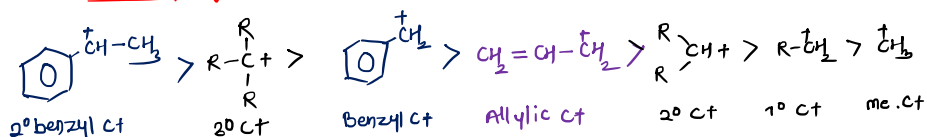
stability of C^+ →



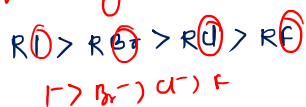
SN1 Reaction

Imp Points & Factors of SN¹ Reaction

4. Nature of Alkyl Halide:

Stability of C⁺ →

Nature of Leaving Group



SN1 Reaction

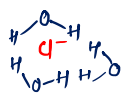
Imp Points & Factors of SN¹ Reaction

5. Nature of Solvent:

C-X

Polar Protic Solvent →

↳ To stabilise L.G.

↳ To break the R⁺-X⁻ bond

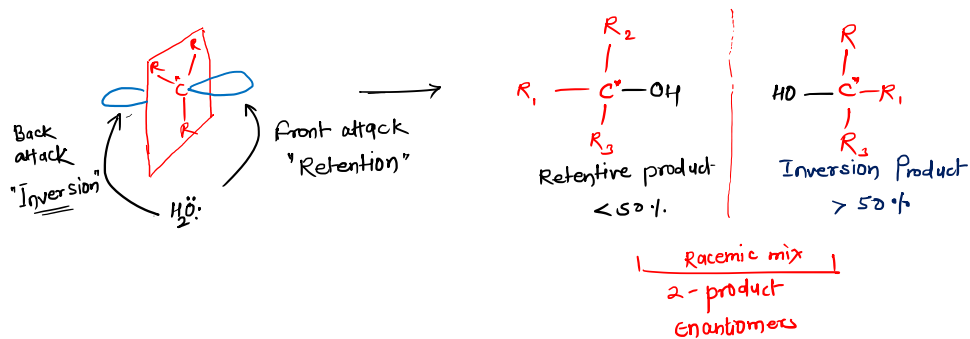
#	H ₂ O	C ₂ H ₅ OH	CH ₃ OH	React ⁿ Rate
Dielectric Constant	80	35	5	
Rate	1.5Lx	4x	1x	

6. Temp: SN1 → Exothermic- Release energy, occurs at Low temp

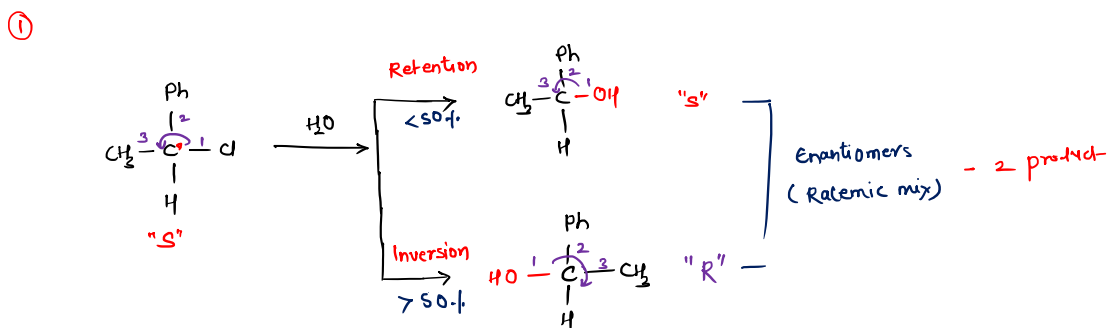
SN1 Reaction

Stereochemistry in SN¹ Reaction

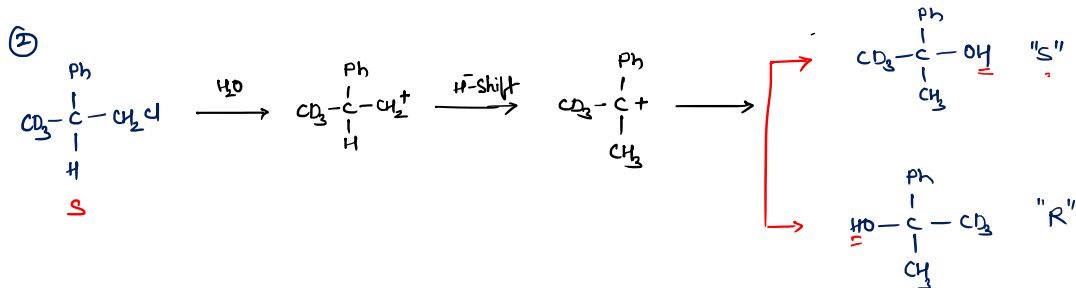
Carbocation \rightarrow sp², planar



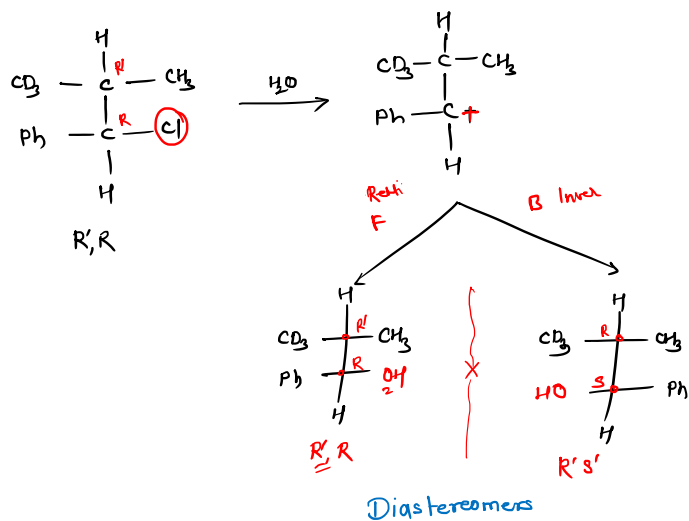
SN1 Reaction

Stereochemistry in SN¹ Reaction

SN1 Reaction

Stereochemistry in SN¹ Reaction

SN1 Reaction

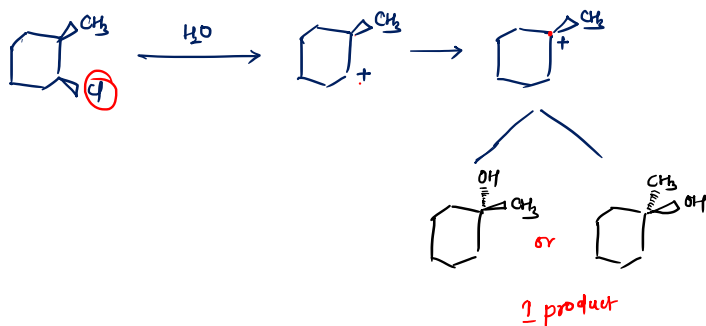
Stereochemistry in SN¹ Reaction

SN1 Reaction



Stereochemistry in SN¹ Reaction

④



Nucleophilic Substitution Reaction (Part 3)

SN² Reaction Mechanism

Factors affecting Rate of SN²

SN¹ vs SN²

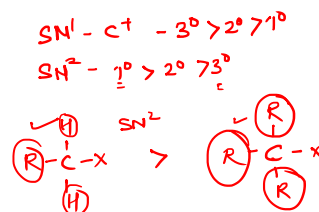
B.Pharm. | POC-I | U 3 | L3

SN2 Reaction

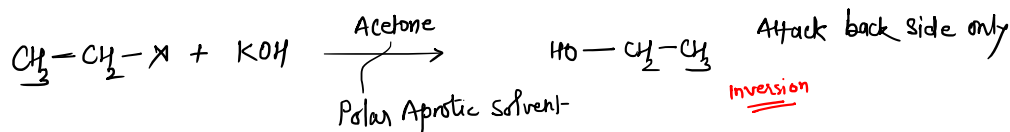


Bimolecular Substitution Nucleophilic Reaction

- In Rate Determining Step (RDS)- Involve 2 Molecule
- Rate \propto [RX] [KOH], 2nd Order Kinetic
- SN2- Transition Intermediate, Single Step
- Rate- depends on formation of stable transition state
- Rate \propto 1/Steric Hinderance



Hydrolysis of Alkyl Halide:- Preferred in 1° Alkyl Halide



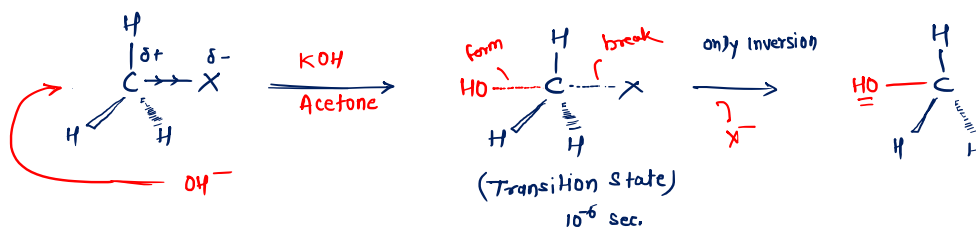
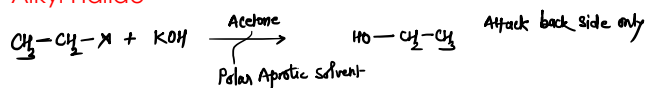
SN2 Reaction



Bimolecular Substitution Nucleophilic Reaction

Hydrolysis of Alkyl Halide:- Preferred in 1° Alkyl Halide

Reaction Mechanism

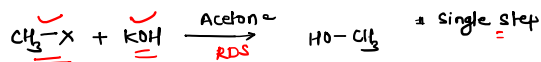


SN2 Reaction



Imp Points & Factors of SN² Reaction

1. Kinetics- Second Order Kinetics



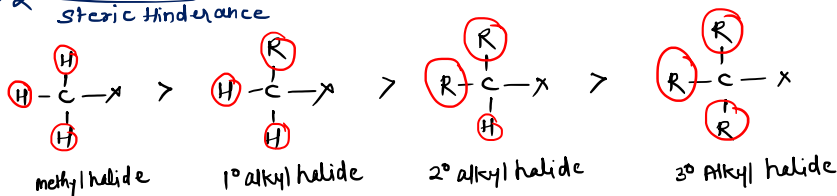
Rate $\propto [\text{RX}]^1 [\text{KOH}]^1$, $\#$ React^o Rate of SN² depends on conc of RX and KOH both

2. Conc. of Alkyl Halide: increase the rate of reaction with in conc. of alkyl halide

3. Conc. of Nucleophile/Base: increase the rate of reaction with in conc. of Strong Base

4. Nature of Alkyl Halide: $\#$ Rate $\rightarrow \text{RI} > \text{RBr} > \text{RI} > \text{RF} < \begin{matrix} \text{SN}^1 \\ \text{SN}^2 \end{matrix}$

Rate $\propto \frac{1}{\text{steric hindrance}}$

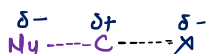


SN2 Reaction



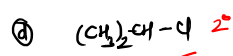
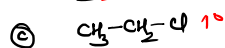
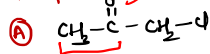
Important Points and Factor

$\#$ Rate \propto stability of Transition State



\rightarrow stability enhanced by presence of Electron Withdrawing Group (-I Effect)

Example \rightarrow



Rate $\rightarrow a > b > c > d$

$\#$ SN¹ - 3^o > 2^o > 1^o ✓

SN² - 1^o > 2^o > 3^o ✓

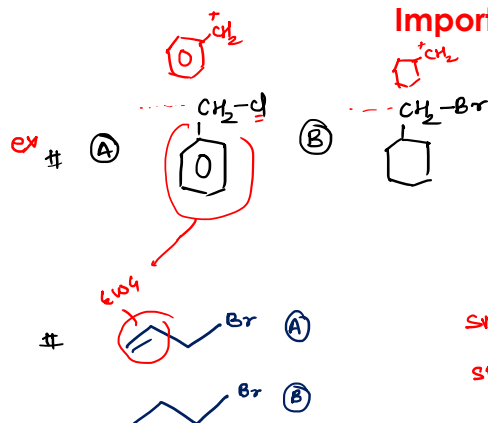
$\#$ जितने SN¹ Reactⁿ Fast होता है उतने SN² Reactⁿ slow होता है - Wrong statement Not Rule

$\#$ Impact on Rate EWG > steric hindrance

SN2 Reaction



Important Points and Factor



SN¹ Reactn order - $a > b$

SN² Reactn order - $A > B$

SN₁ A > B

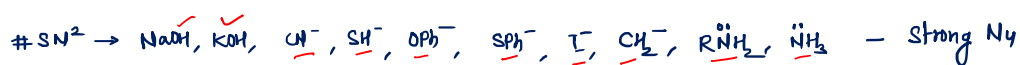
SN₂ A > B

SN2 Reaction



Imp Points & Factors of SN¹ Reaction

5. Nature of Nucleophile- High Conc and Strong Nu - Rate of Reaction



6. Nature of Solvent- Polar Aprotic Solvent -

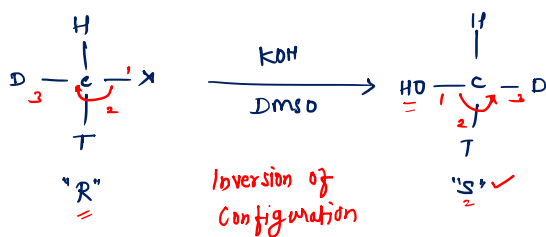
Acetone, DMSO (dimethyl sulfoxide), Ether, DMF (dimethyl formide)

7. Temperature- Exothermic, at low temp

SN2 Reaction



Stereochemistry



SN2 Reaction



Identify SN¹ or SN²

