

Mechanisms of Aliphatic Nucleophilic Substitution Reactions

(A) Bimolecular Nucleophilic Substitution Rxn

- S_N2 Reaction

→ 2nd order reaction

→ Rate depends upon both substrate & the nucleophile

→ It is bimolecular, since because the rate

determining step involves both substrate & nucleophile

→ Rate law

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

k → Rate constant



Substrate

Nucleophile

Product

leaving group

$$\text{Rate} = k [\text{CH}_3\text{Br}] [\text{OH}^-]$$

Mechanism (proposed by Hughes & Ingold)

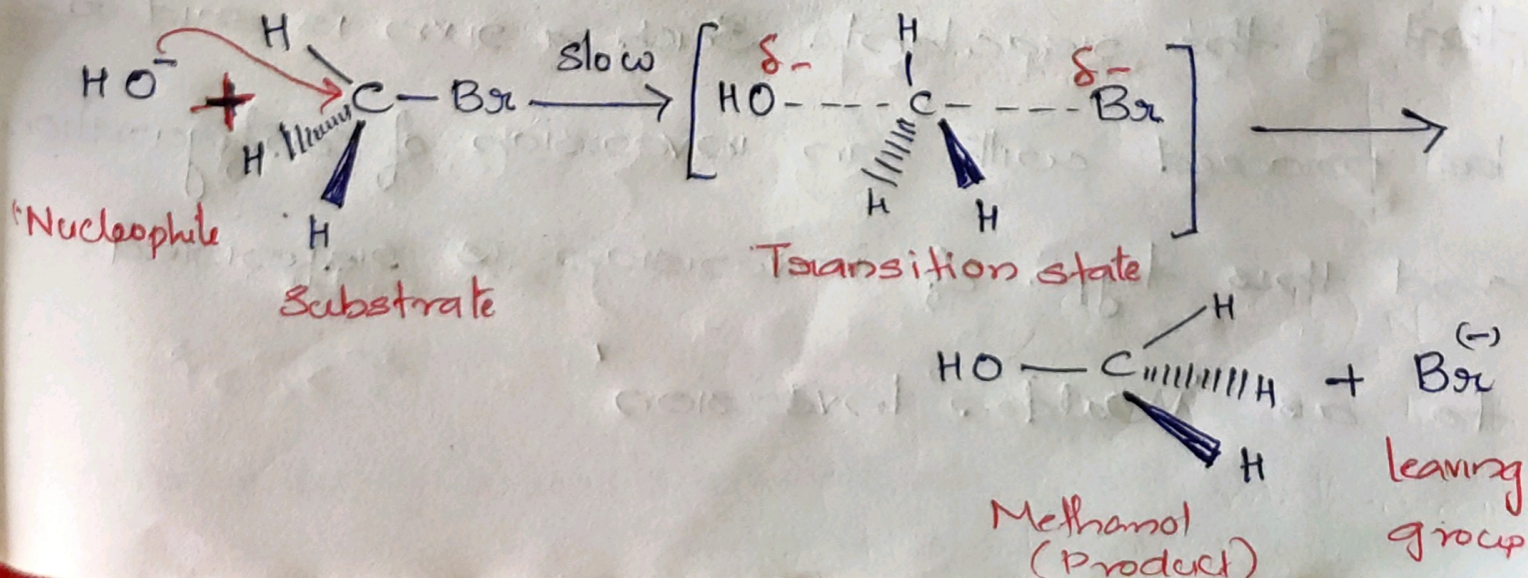
→ Involve single step

→ Without the ~~maximal~~ formation of intermediate

→ Direct displacement mechanism in which

bond breaking & bond forming occurs

simultaneously. $\text{OH}^- + \text{CH}_3\text{-Br} \longrightarrow \text{CH}_3\text{-OH} + \text{Br}^-$



→ Rxn proceeds through transition state in which C-OH bond is not completely formed & the C-Br bond is not yet completely broken.

→ Backside attack by the nucleophile will be reflected as an inversion of configuration (Walden Inversion) in the product.

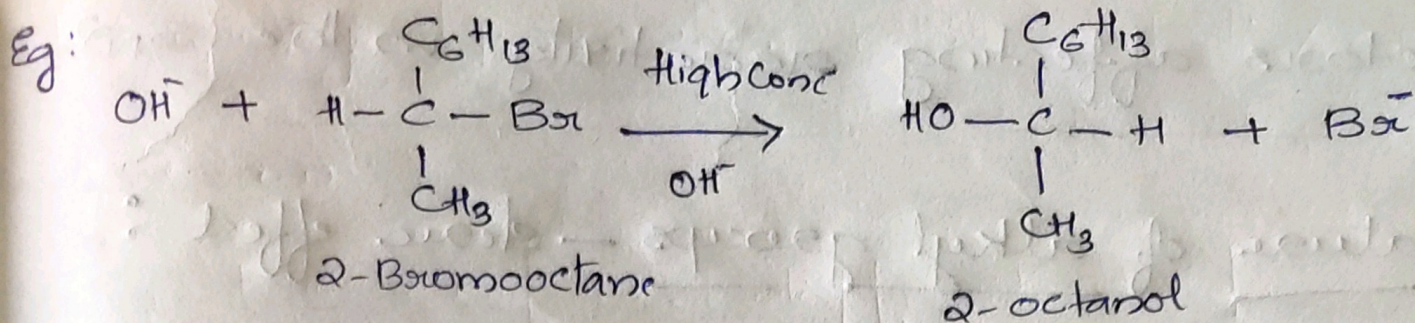
Kinetics

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

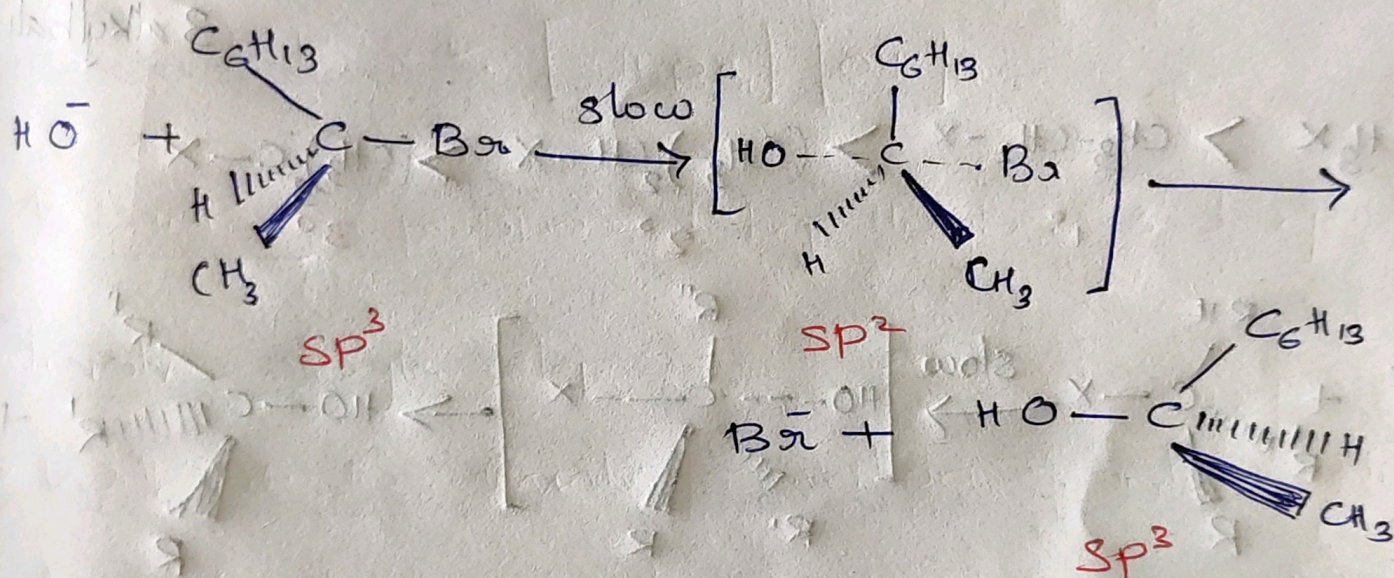
⇒ A second order process.

Stereochemistry of S_N2 reaction - Walden Inversion

The product has a configuration opposite to that of the reactant. Such a rxn is said to be proceed with an inversion of configuration and this type of inversion is referred to as 'Walden Inversion'.



→ this stereochemical inversion supports the view that the $\text{S}_{\text{N}}2$ mechanism involves a 'back-side attack' on alkyl halide



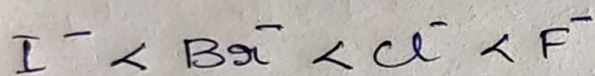
The state of hybridisation of C goes from sp^3 to sp^2 and then again to sp^3 .

→ As the nucleophile comes in one side of substrate & bonds to the carbon, & the halide departs from other side, configuration at the stereocentre obviously undergoes an inversion just as 'open umbrella turns inside out in a sudden gush of wind'.

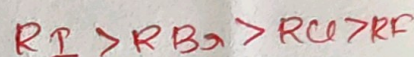
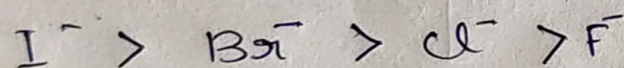
② Nature of leaving group

→ weakens the basicity of the group, better is its leaving ability — Because, weaker the base, weaker the bond with C atom, easier to break.

→ Relative basicity order



→ Relative leaving ability



③ Nature of nucleophile

→ Nucleophiles are Lewis base

→ 'strongest the bases are better Nucleophiles'

→ OH^- , CH_3O^- & NH_2^- are strong base &

hence better nucleophile than H_2O , CH_3OH , NH_3

→ Order of basicity $H_3C^- > H_2N^- > HO^- > F^-$

→ Greater Nucleophilicity of nucleophile, the greater is its S_N2 reactivity.

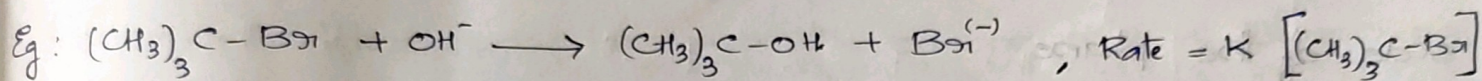
(B) UNIMOLECULAR NUCLEOPHILIC SUBSTITUTION REACTIONS - S_N1 Rxn

→ Kinetically 1st order reaction

→ Rate depends only on the substrate concentration

→ Unimolecular - because rate determining step involves only one molecule

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



tert-butyl bromide

Substrate

Nucleophile

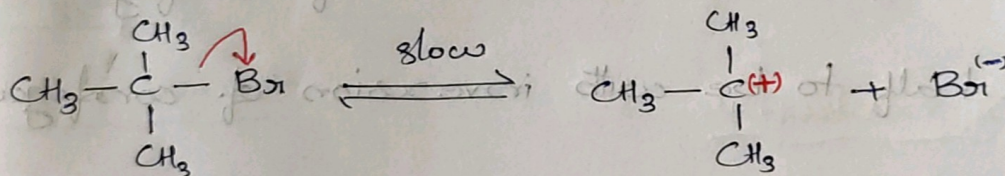
Product

leaving group

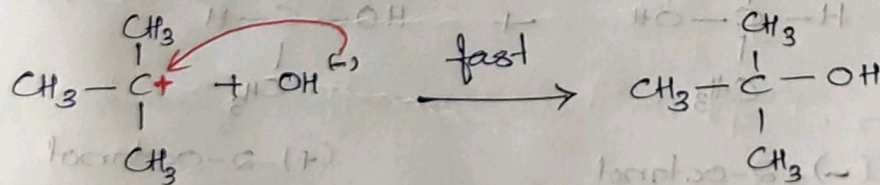
Mechanism:

→ Involves two steps

step 1: Leaving groups breaks away by heterolytic fission & forms a carbocation.



step 2: Carbocation rapidly reacts with nucleophile & yield product

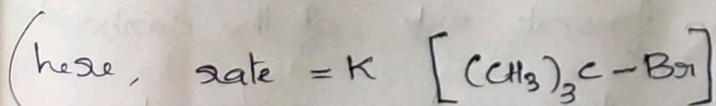


Kinetics:

→ 1st step is the rate determining step (because slow step)

→ Thus rate depend only on conc of substrate.

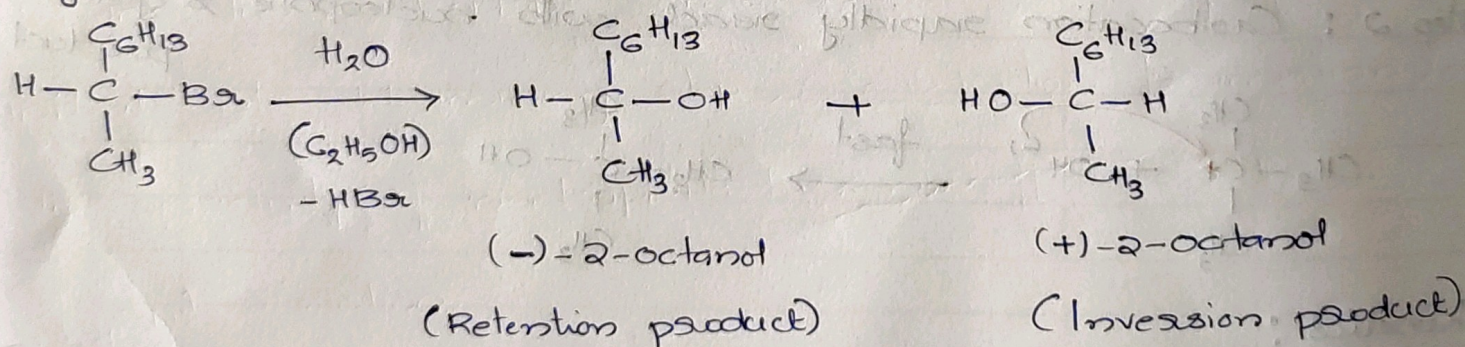
$$\text{rate} = k [\text{Substrate}]$$



Stereochemistry:

- Heterolytic cleavage of C-X bond lead to the formation of carbocation
- Carbocation has planar structure due to sp^2 hybridisation of +vely charged C atom
- Attack of nucleophile is equally probable from either side of the plane
- Front side attack would result in retention of configuration
- Back side attack would result in inversion of configuration
- Both are equally probable & would expect half of the product to be with retention of configuration & the other half to be with inversion of configuration.

→ Eg:



Mose

→ Why a greater proportion of inversion occurs can be explained as follows,

One side, which we call ~~front~~ front side, of the carbocation formed is not completely free ~~front~~ for some time

to react with the nucleophile, contrary to our expectations. This front side is shielded from the approaching nucleophile by the departing bromide ion for a period of time as it clings to the carbocation through electrostatic attraction. The combination is called an ion pair. During the life time of this ion pair, the nucleophile molecule can attack only from, giving rise to inversion. Afterwards, however the components of the ion pair are separated through the intervention of solvent layers; this makes both back-side & front-side attacks possible, yielding both the inversion product & retention product. The net result is the formation of a greater proportion of the inversion product.

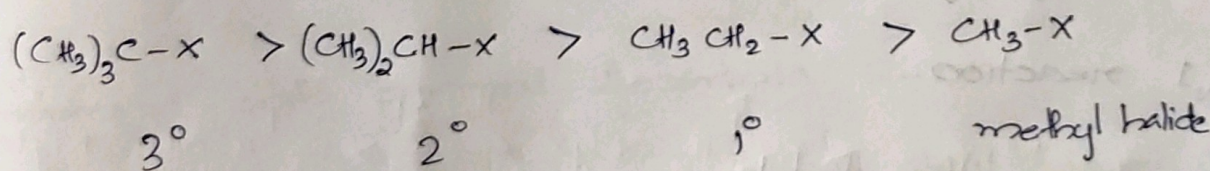
Factors affecting :

(a) Nature of substrate

(i) Nature of alkyl group:

→ Relative reactivity order: 3° alkyl halide $>$ 2° alkyl halide $>$ 1° alkyl halide

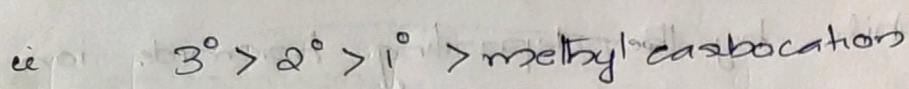
Eg: S_N1 reactivity decreases in the order,



→ This can be explained as : Since the first step of the mechanism involve carbocation formation.

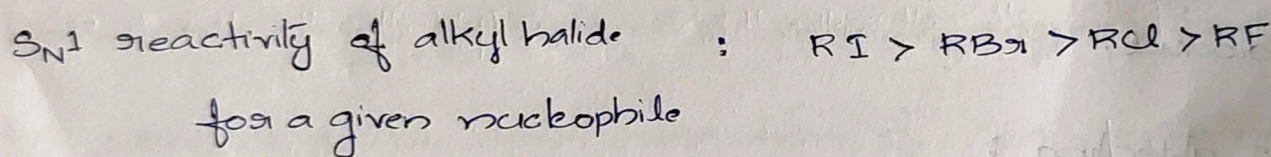
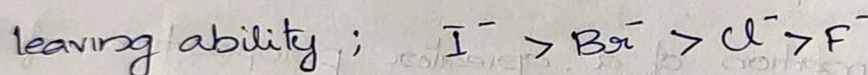
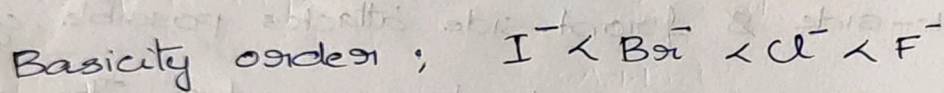
The greater the stability of carbocation that is to be formed in the first step of S_N1 reaction, the

greater would be the ease of its formation & thus the greater the S_N1 reactivity of the original alkyl halide.



(2) Nature of leaving group:

→ Weaker the basicity of the group, the better is its leaving ability. — Because weaker the base, the weaker is its bond with the stereocentral carbon and the easier it is to break it.



(B) Nature of nucleophile

Since the nucleophile comes into action only after the initial rate determining step, (Carbocation formation).

the reactivity of nucleophile has no effect on the rate of S_N1 reaction.

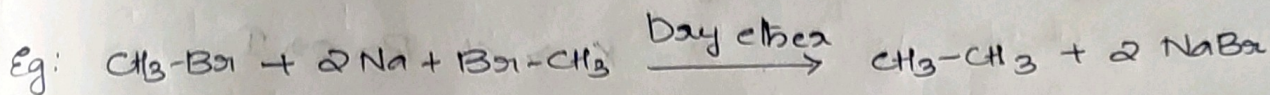
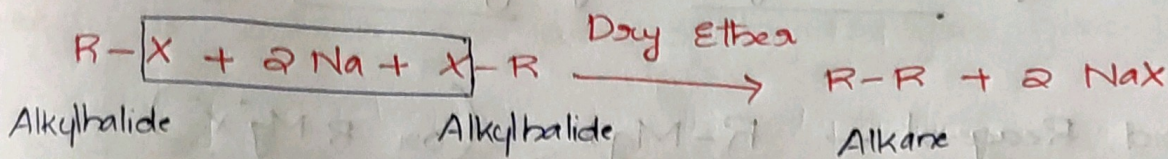
Note down the table.

Some other reactions

① Wurtz Reaction

Alkyl halides treated with Na metal in dry ether

solution to yield higher alkanes.



→ 3° alkyl halides fail to undergo wurtz reaction

② Wurtz-Fittig Reaction

Aryl halide is heated with an alkyl halide in the presence of Na in dry ether solution, alkylarenes are obtained.

