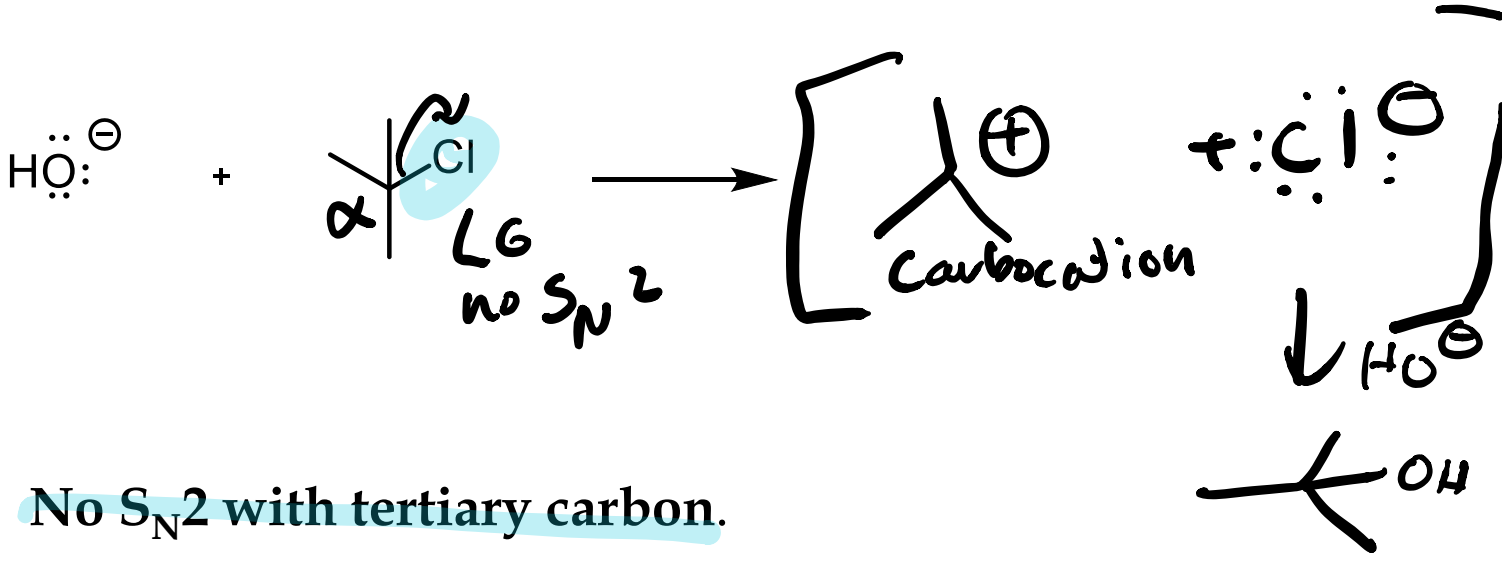
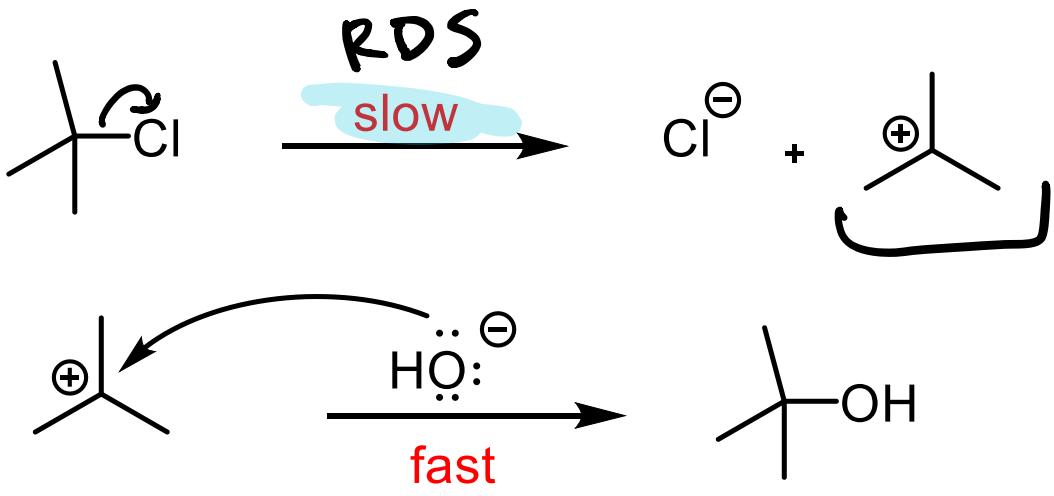
I- Nucleophilic Substitution Reactions S_N1



- **No S_N2 with tertiary carbon**.
- Bond breaks with the electrons moving to the more electronegative atom first (the Leaving Group)
- Nucleophile then reacts with the generated **carbocation**

S_N1 Reaction Mechanism



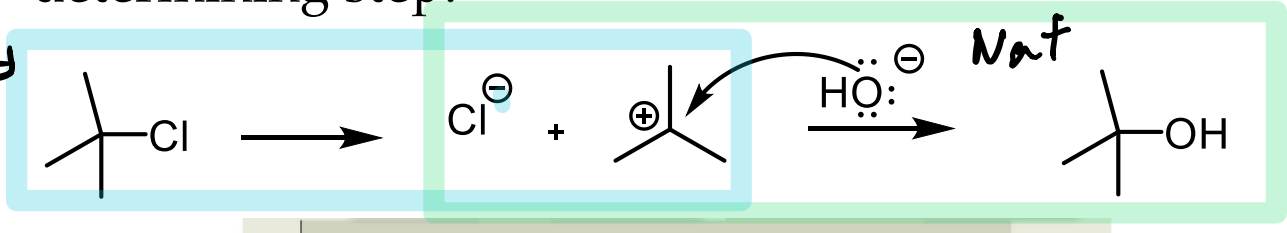
S_N1 proceeds via two-steps:

- Formation of the carbocation intermediate (slow)
- Reaction between the nucleophile and the intermediate (fast)

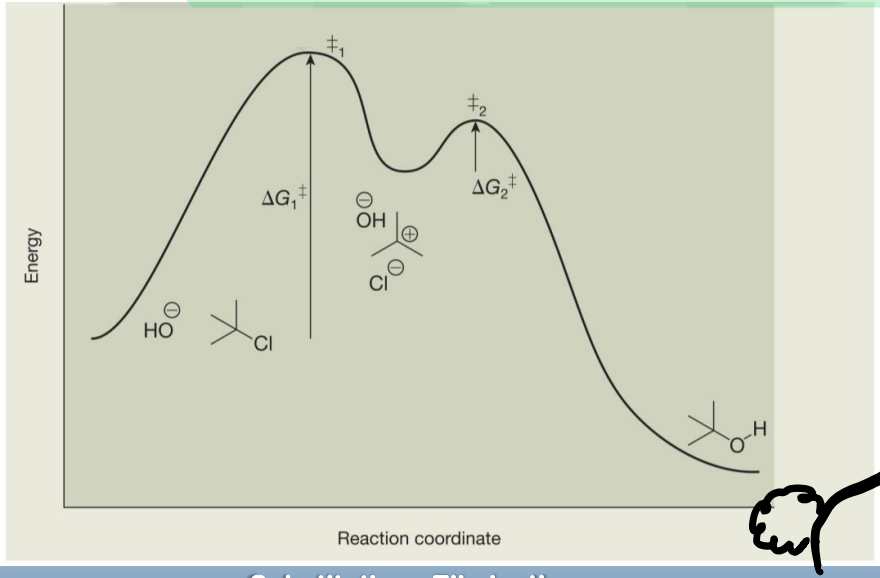
Energy diagram:

- Two steps, two transition states.
- The formation the carbocation is the rate-determining step.

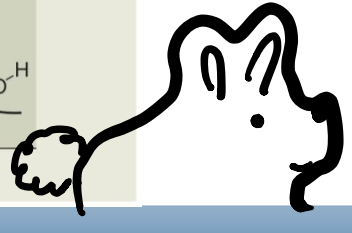
1st step



Nat



2 bumps bc 2 steps



S_N1 Reaction Rate - Kinetics

- S_N1 : Substitution Nucleophilic **unimolecular**.

- Rate depends only on the concentration of the electrophile:

$$\text{rate} = k\,[\text{R-X}]$$

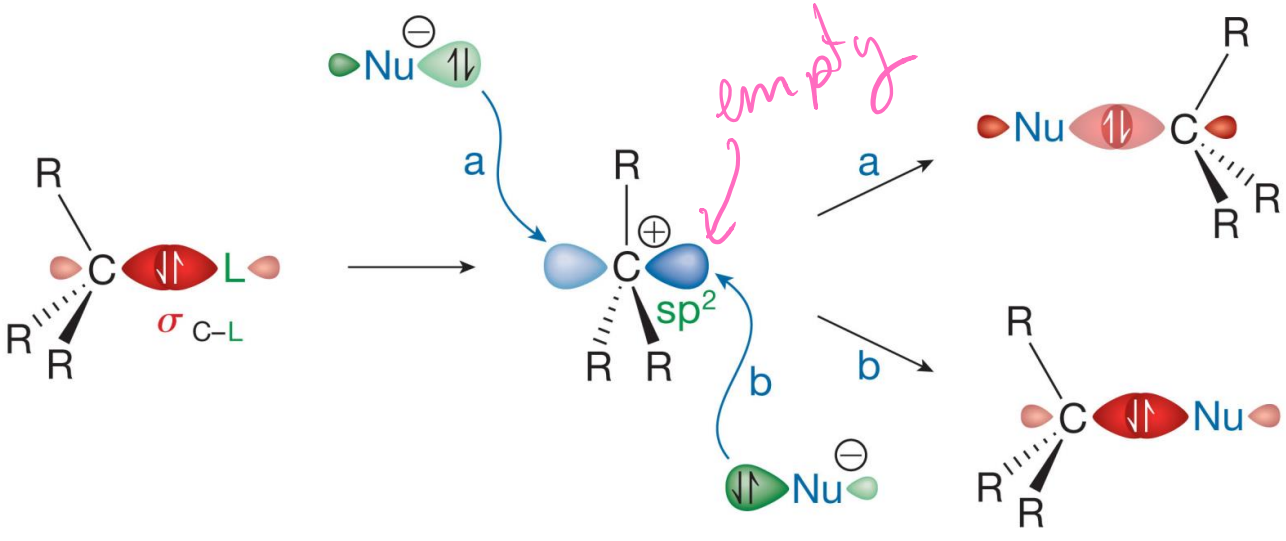
First-order Reaction

FIRST MIDTERM

S_N2, S_N1, E_2

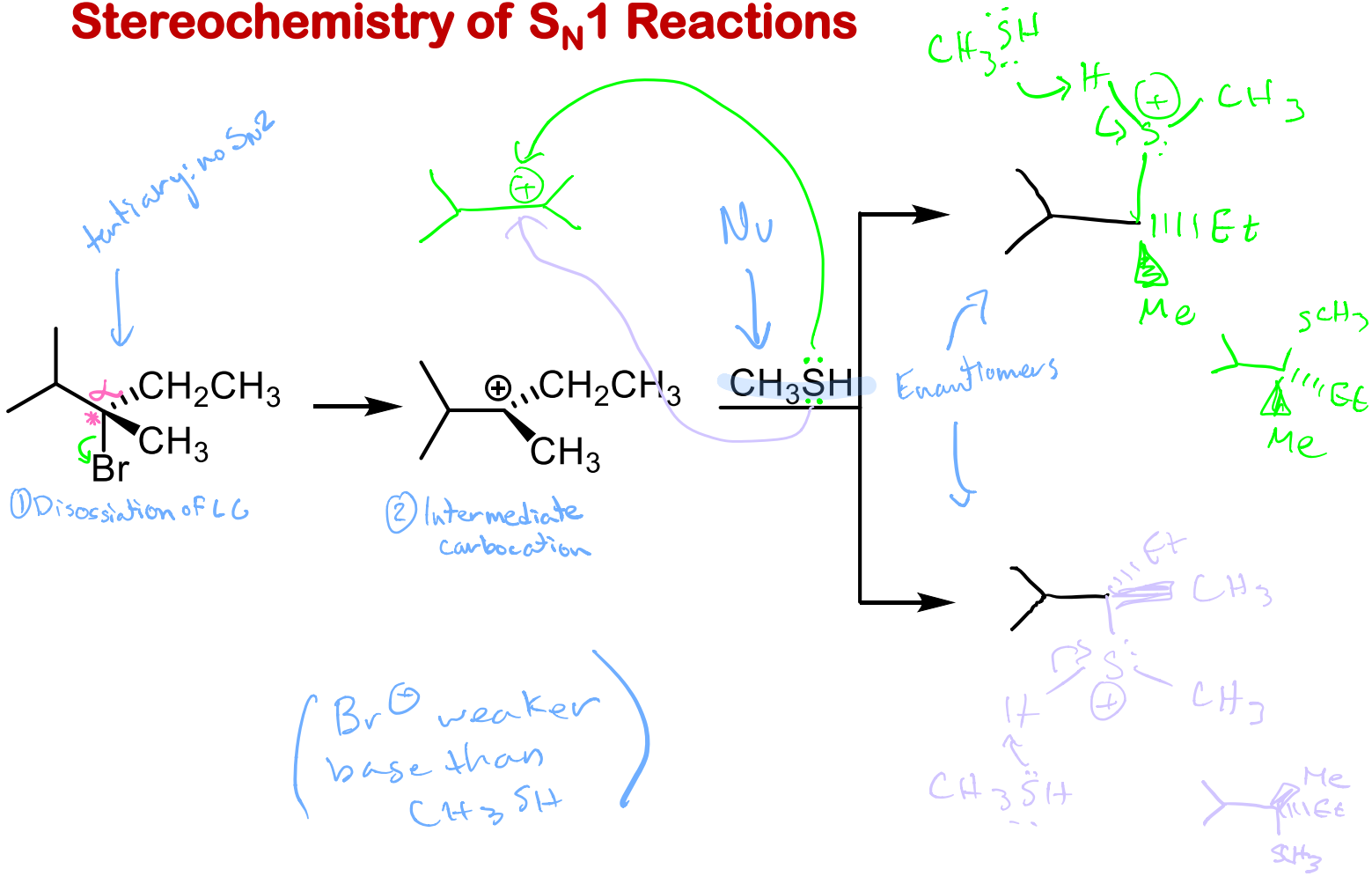
all of module 1.

Stereochemistry of S_N1 Reactions



- Carbocations are sp^2 hybridized trigonal planar (flat).
- Nucleophile are free to approach either side of the carbocation.
- Results: mixture of both enantiomers if chiral carbon.

Stereochemistry of S_N1 Reactions

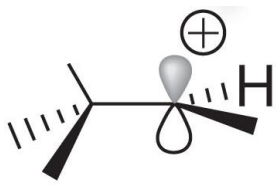


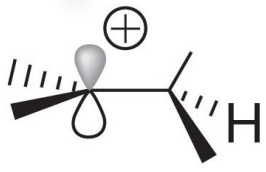
Carbocation Stability

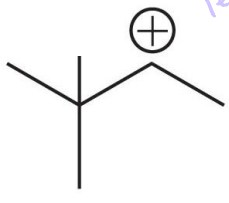
- The S_N1 reaction is heavily dependent on the ability of the α-carbon to stabilize a positive charge.

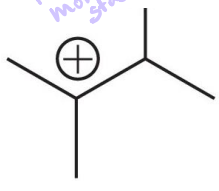
- Carbocations can be stabilized by:
  - ✓ **Hyperconjugation**
  - ✓ **Charge delocalization**

Carbocation Stabilized by Hyperconjugation



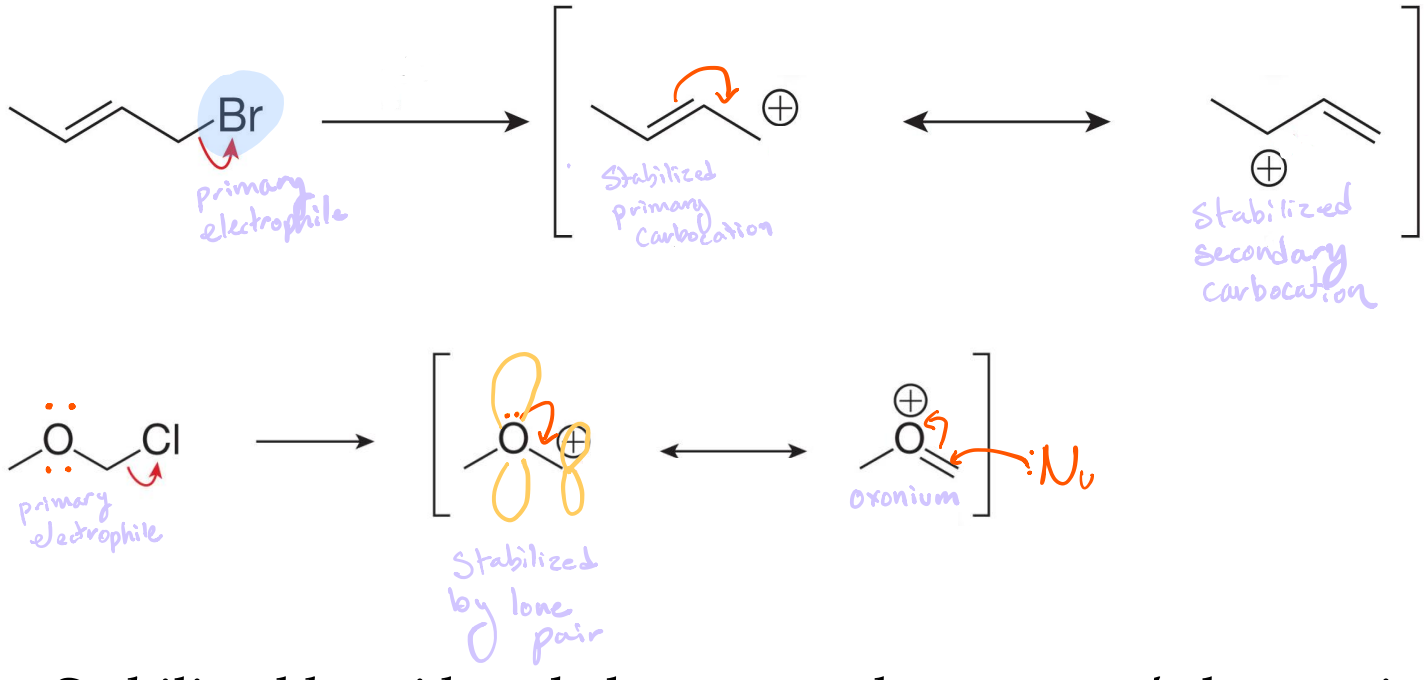






- Alkyl groups are electron donating groups.
- Partial overlap between shared σ bond electrons and carbocation p orbital.
- More alkyl groups, more stable is the carbocation.

Carbocation Stabilized by Charge delocalization



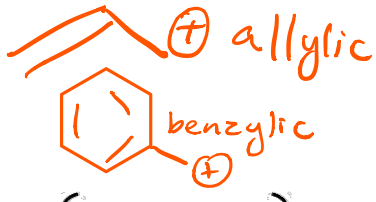
- Stabilized by pi bond electrons or heteroatom's lone pair

Carbocation Rearrangements

- Rearrangements are common in S_N1 reactions
- Rearrangements occur when a more stable carbocation can be formed.

hydride shift – $H^{\oplus}$ shift

alkyl shift → gives methyl



$$\text{methyl} < 1^\circ \text{ alkyl} < \begin{Bmatrix} 2^\circ \text{ alkyl} \\ 1^\circ \text{ allylic} \\ 1^\circ \text{ benzylic} \end{Bmatrix} < \begin{Bmatrix} 3^\circ \text{ alkyl} \\ 2^\circ \text{ allylic} \\ 2^\circ \text{ benzylic} \end{Bmatrix} < \begin{Bmatrix} 3^\circ \text{ allylic} \\ 3^\circ \text{ benzylic} \end{Bmatrix}$$

Increasing stability of carbocations

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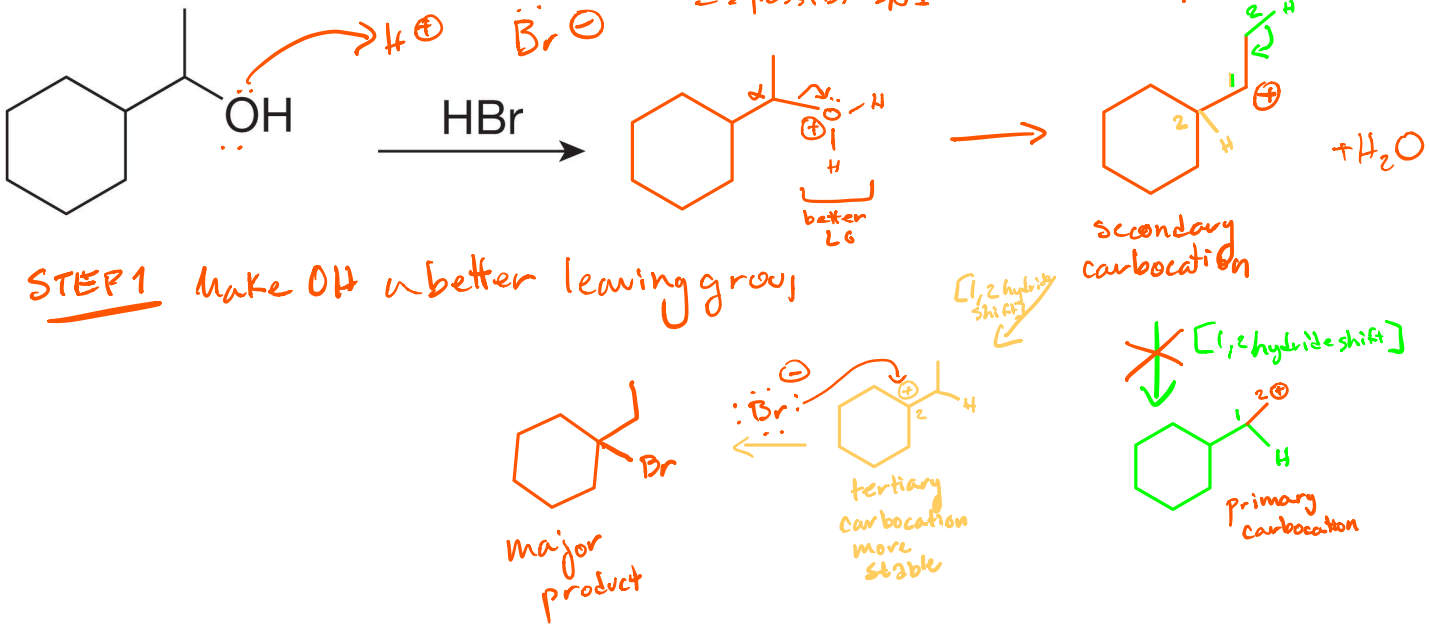
Possible Rearrangements: via 1,2 shift

always carbocation

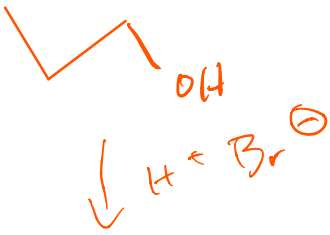
- [1,2]-hydride shift

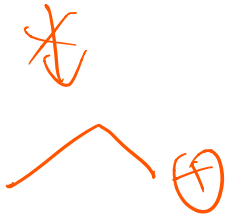
$H^{\oplus}$ ← not a proton



under acidic conditions ⇒ there's a high chance for an OH to be H_2O and leave.
if you're forming a stable carbocation

⇒ reaction will go through S_N1



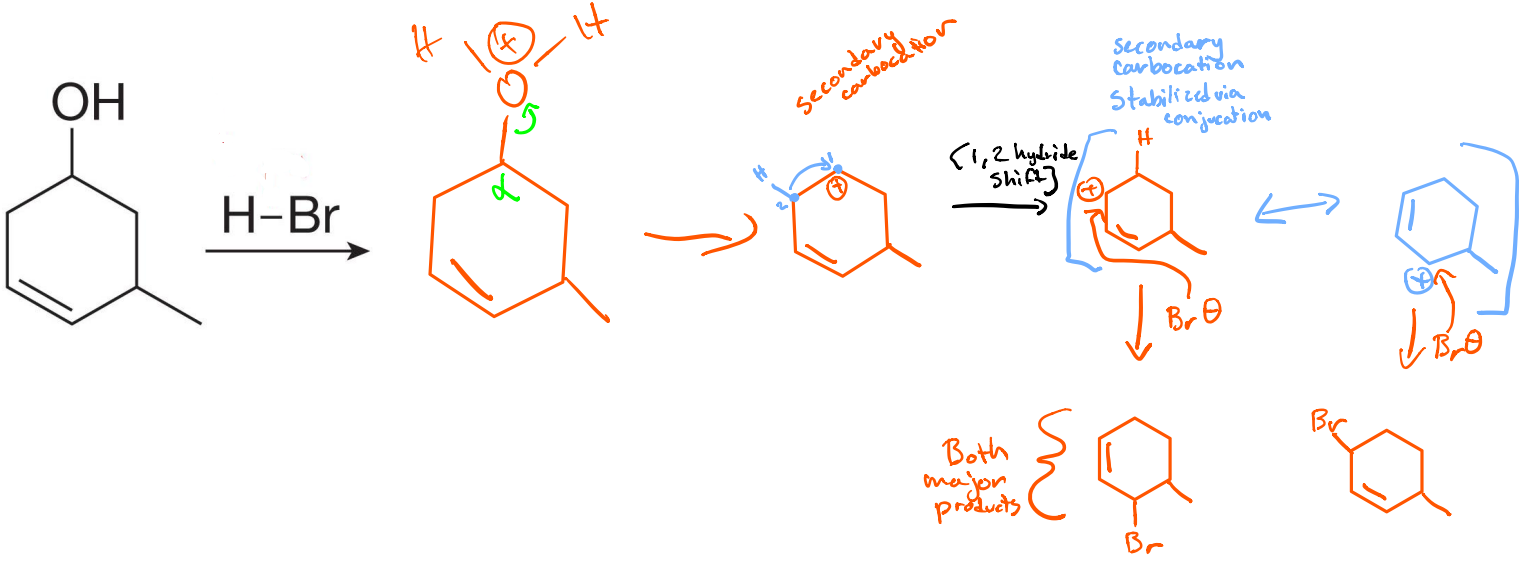


→ only way is S_N2

Under basic conditions → can't form carbocation

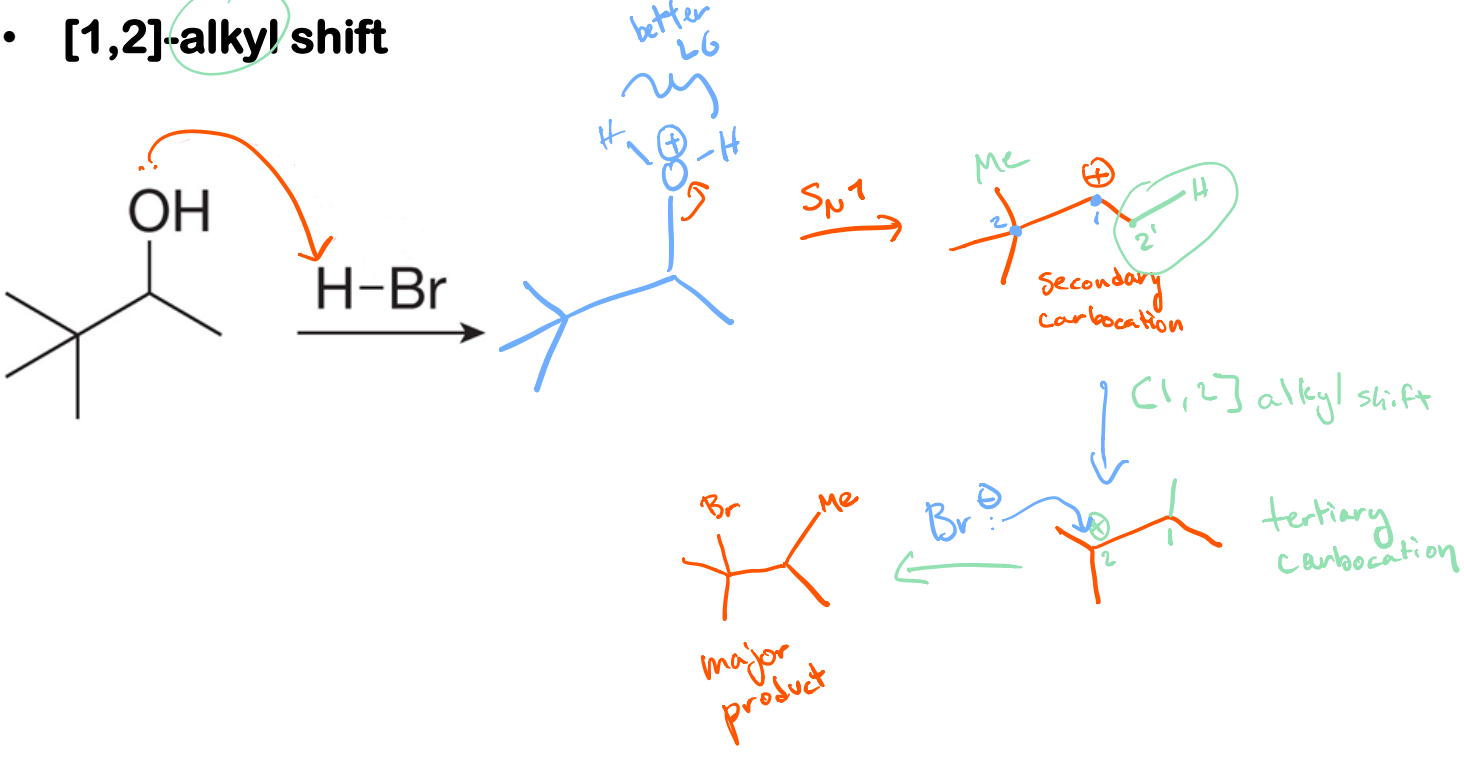
Possible Rearrangements: via 1,2 shift

- **[1,2]-hydride shift**



Possible Rearrangements: via 1,2 shift

- [1,2]-alkyl shift



Effect of Leaving Group

approximate order of leaving group ability

$$Cl < Br < \begin{matrix} I \\ OTs \end{matrix} < H_2O < OMs < OTf$$

good better best

- In general, good leaving groups accelerate S_N1 reactions.

Predict mechanism for a Nucleophilic Substitution Reactions (S_N2 or S_N1):

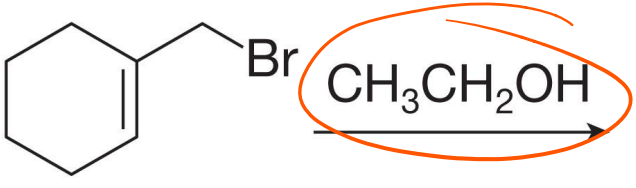
- the structure of the electrophile $1^o, 2^o, 3^o$
- the strength of the nucleophile methoxide $Br^\ominus$ $OH^\ominus$ (acidic conditions)
- the solvent used.

Structure of the electrophile: most important feature

Compound	α-Carbon structure	Symbol	
CH_3Br	methyl	Me	**S_N2 only**
CH_3CH_2Br	primary	1°	
$(CH_3)_2CHBr$	secondary	2°	both S_N1 and S_N2 possible
$(CH_3)_3CBr$	tertiary	3°	**S_N1 only**

Structure of the electrophile: most important feature

- Substrates that can form a stabilized carbocation tend to follow S_N1-type pathways.

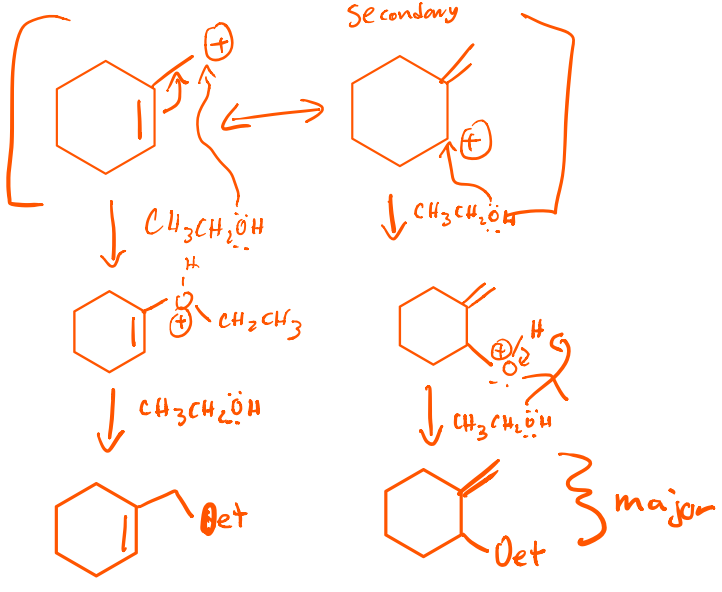


next to π bond primary

1) S_N1
S_N2 possible

2) Nu is weak alcohol
⇒ S_N1 not S_N2

3) polar protic solvent



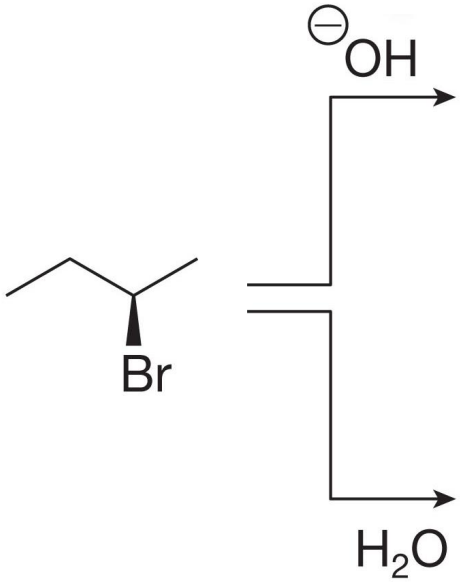
Strength of the nucleophile

- Both S_N1 and S_N2 are **possible with secondary** electrophiles.

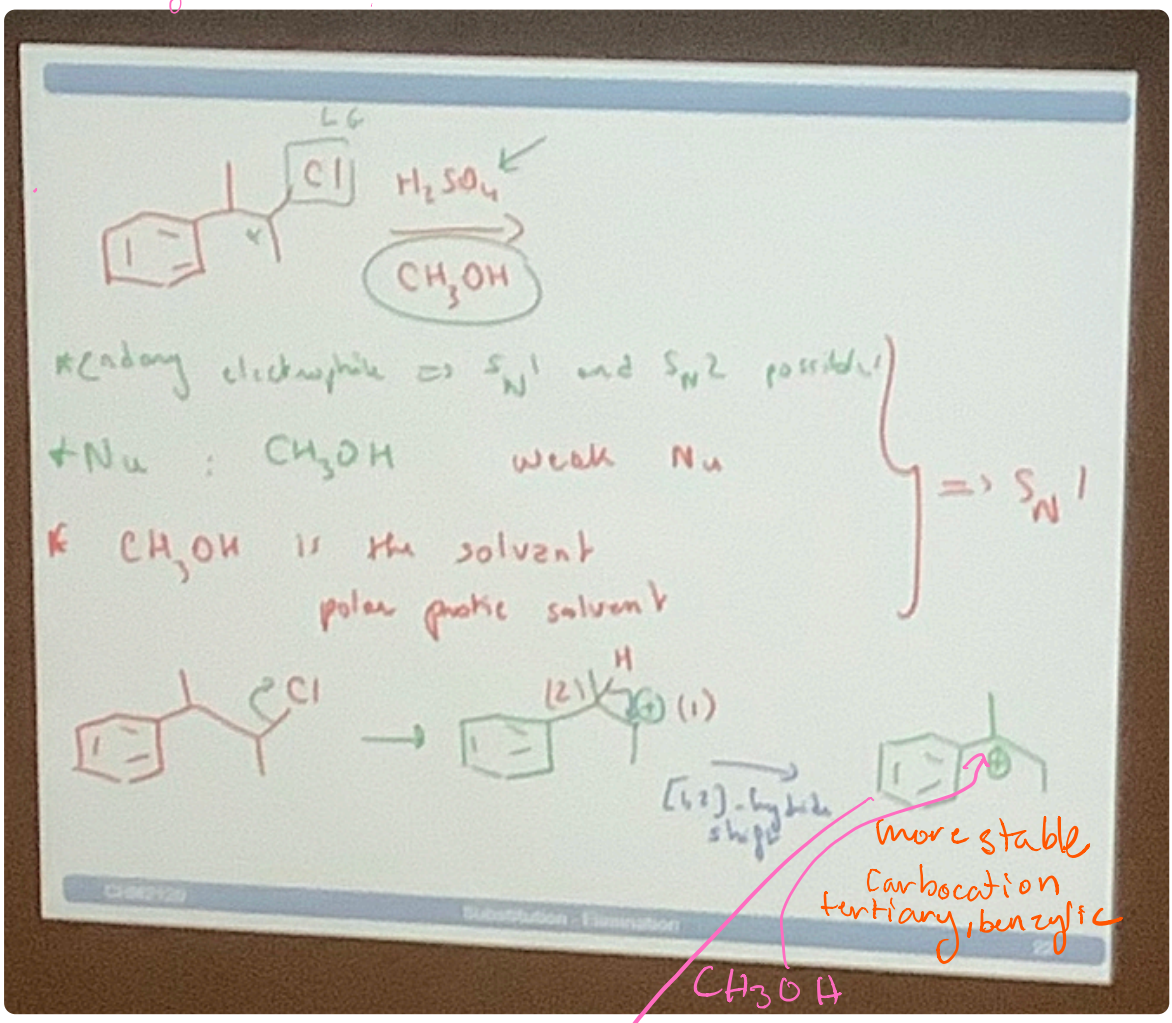
- Both S_N1 and S_N2 are **possible with** those that can form **stabilized carbocations**.

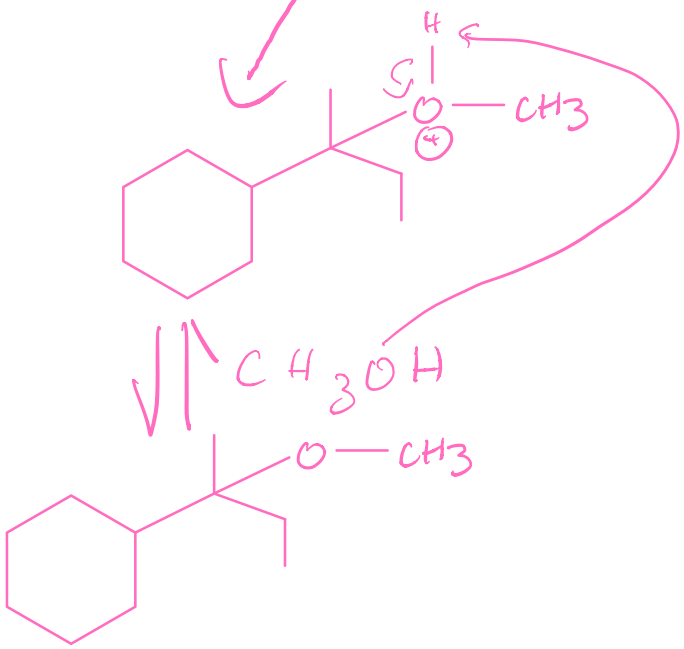
➡ In these cases, mechanism is determined by nucleophile strength.

Strength of the nucleophile



Benzylic - the most stable





Solvent used.

In general:

- polar protic solvents stabilize carbocations (favours S_N1)

- aprotic solvents increase nucleophilicity (favours S_N2)