

S_N^2 and S_N^1
4 - Exceptions in
Substitution Reactions

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Factors Affecting S_N2 and S_N1 Reactions

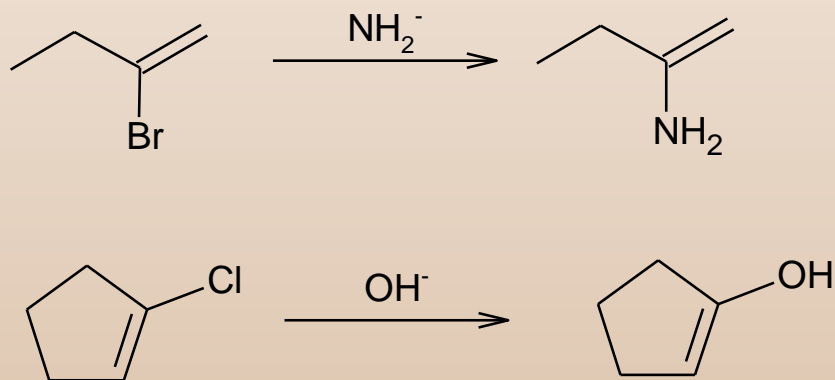
1. Nature of the Substrate (Subs)
2. Strength of the Nucleophile (Nu^-)
3. Leaving group ability (LG)
4. Solvent type

These factors will determine what kind of mechanism will occur, or will the mechanism change depending on Subs, Nu or LG. Some reaction will be more favorable than others. Favorable means, giving good yield and work as predicted.

1) Substrate – Electron Rich for S_N2

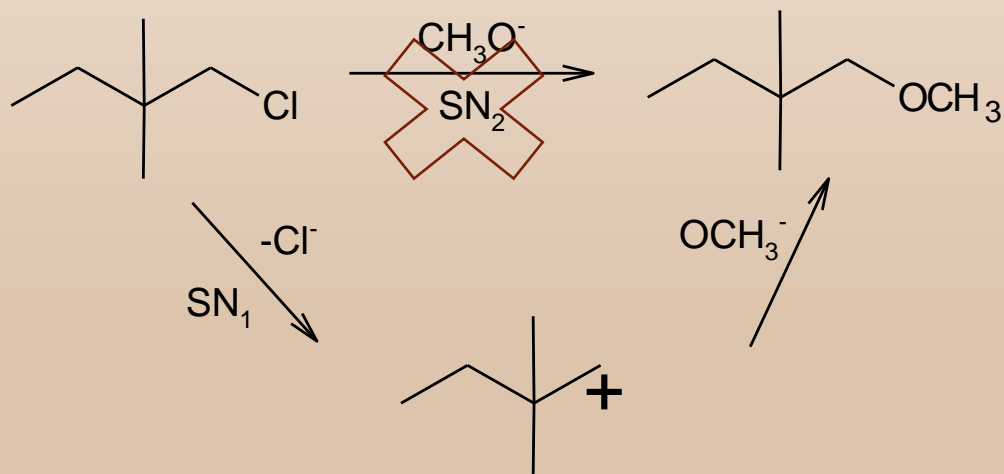
Electron rich substrates e.g. alkenes with the LG are not good substrates as the Nu is also electron rich.

Both reactions below will not work.



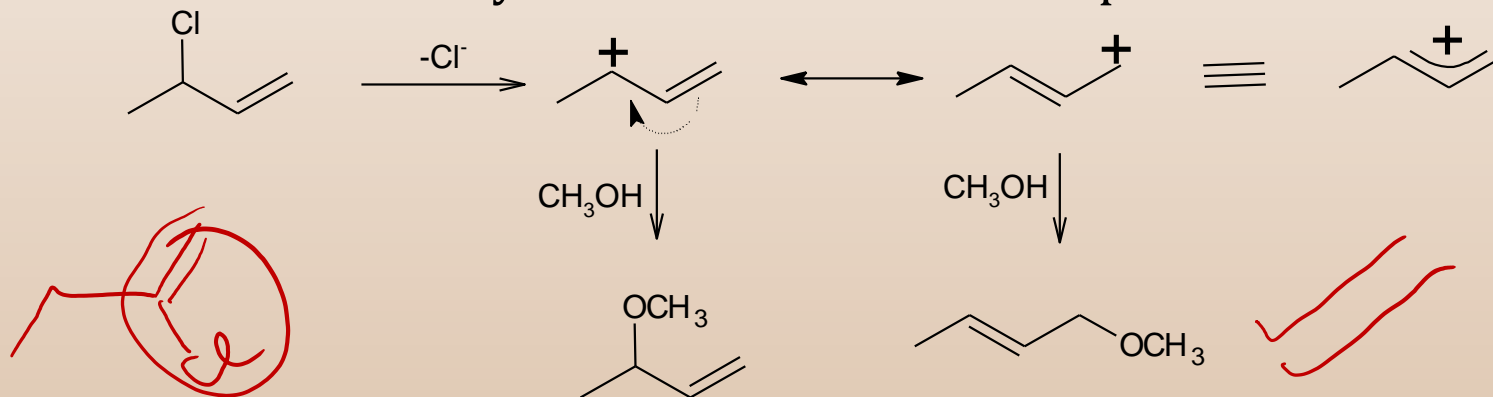
1) Substrate..contd Steric Hindrance – S_N²

- This is more critical for S_N² as Nu approaches from the back side hence the electrophilic carbon should not be hindered.
- Best substrates for S_N² are primary halides.
1° > 2° > 3°
- Exceptions in mechanism can occur if the LG is hindered. In the reaction below Subs is 1° but hindered, so the preferred mechanism is S_N¹. This just means this reaction is not favorable to give the product as written.

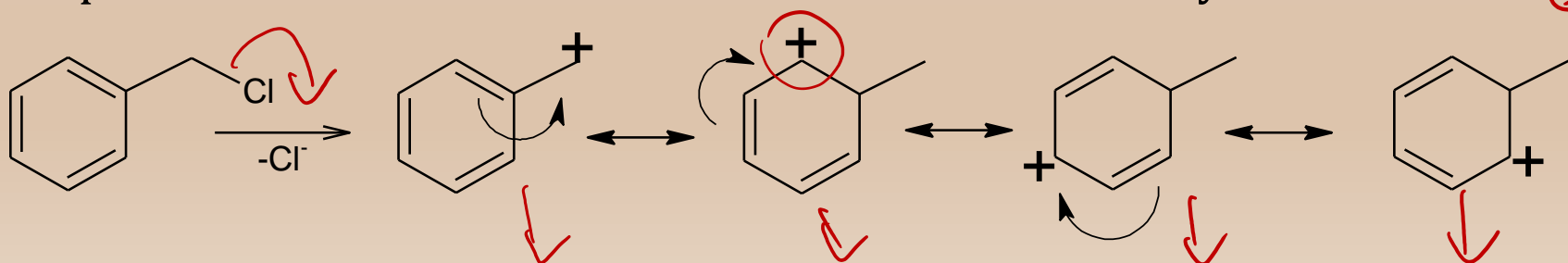


1) Substrate...contd - Resonance

- Resonance promotes S_N^1 as carbocation is the intermediate in S_N^1 .
- S_N^2 is not affected by resonance.
- In the reaction below, only S_N^1 mechanism occurs because the transition state is resonance stabilized. The only way to prove there is resonance is to isolate and study the number and kinds of products form.

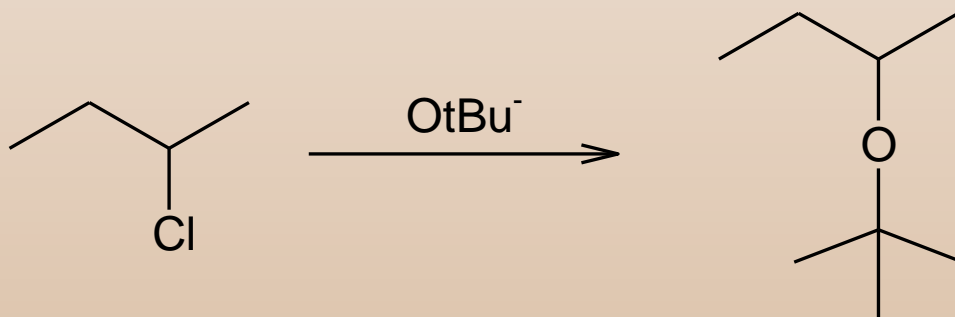


- One has to write ALL the resonance contributors to estimate the products. Below are all resonance structures for benzylic cation.



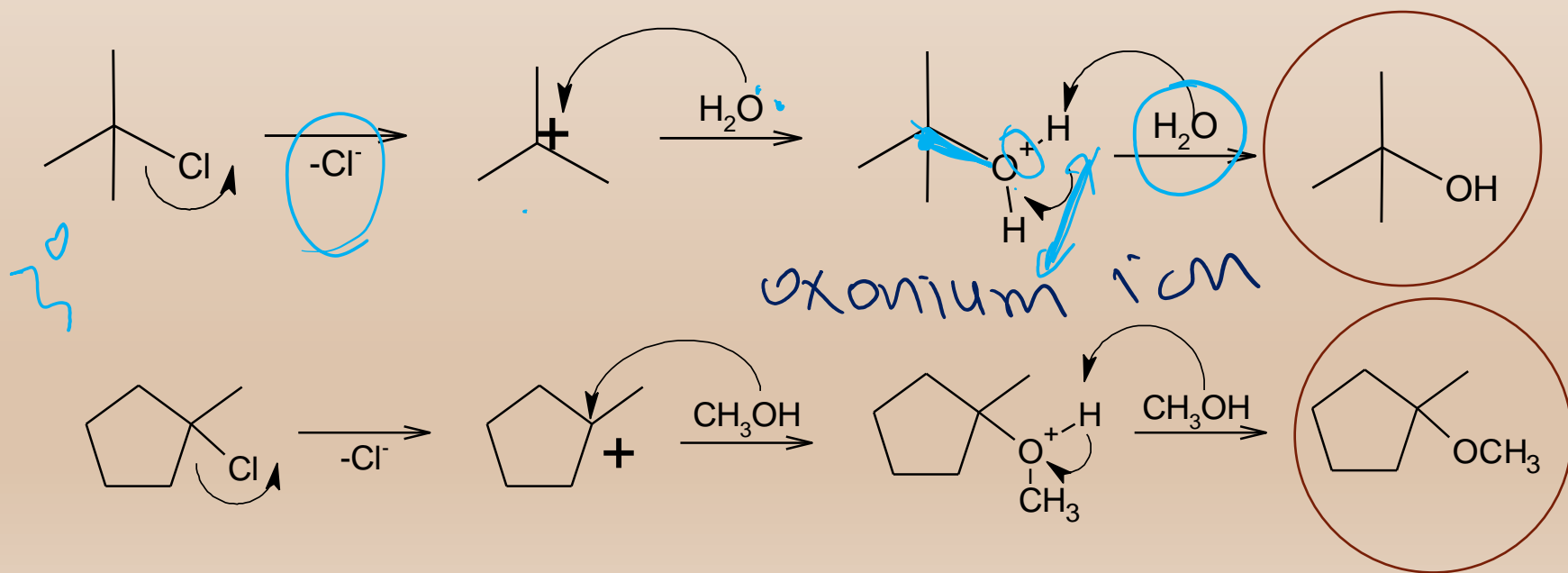
2) Nucleophile - Sterically Hindered Nu⁻

- Sterically hindered is not an issue for S_N¹ because carbocation is trigonal planar.
- In S_N² the Nu needs to access the electrophilic carbon (a carbon).
- If the Nu is too big it will experience steric hinderance and those reactions will not be favorable in S_N² mechanism.
- This is more of a problem when LG is 2°.



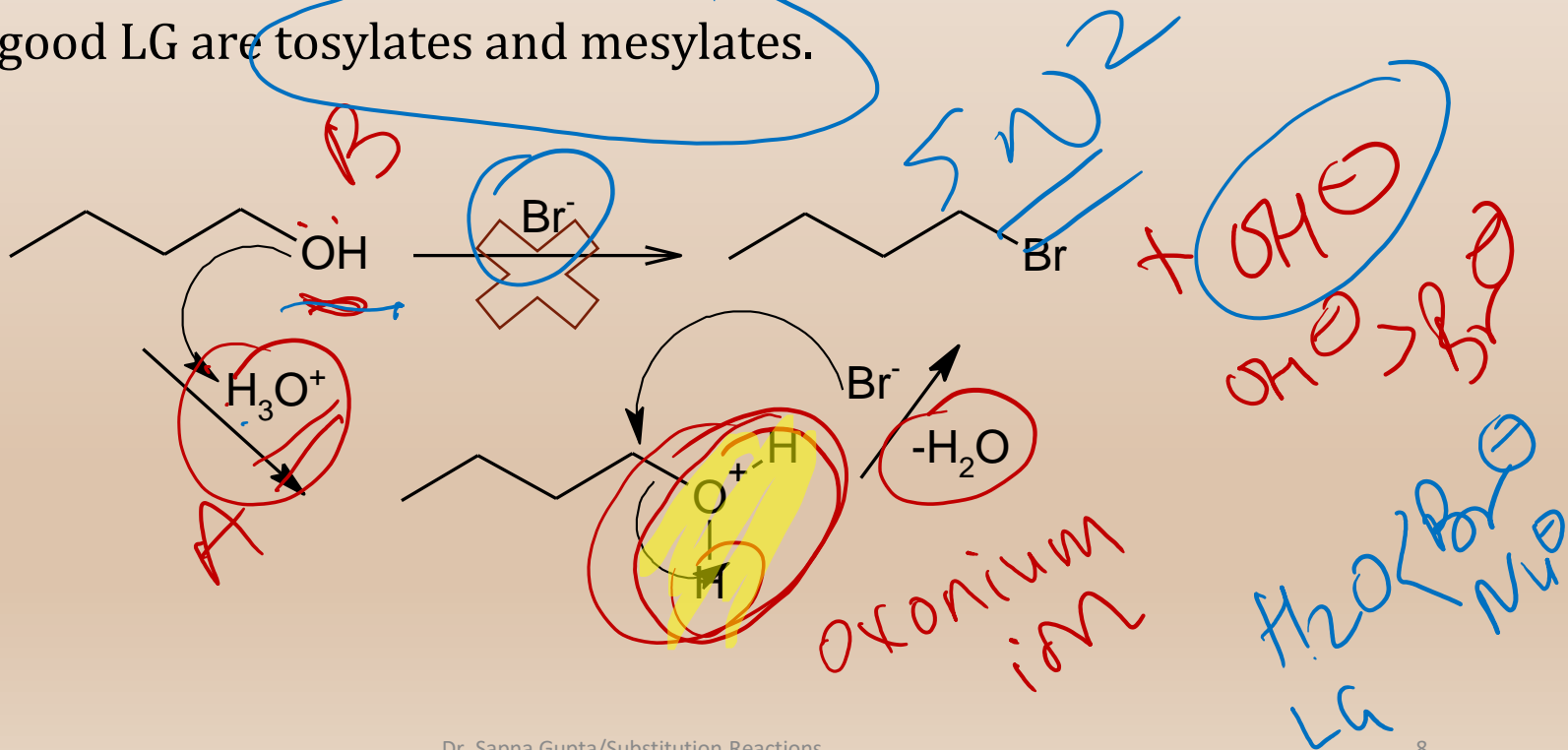
2) Nucleophile – Solvent as Nu⁻

- **Solvolysis** is when the solvent reacts with the Subs.
- This can happen only in S_N1 since nu does not need to be strong because it is not part of the rate determining step.
- Here are a couple of examples of solvolysis using water and methanol as solvents. (*Note: all arrows are double headed arrows*). The circled compounds are the products.



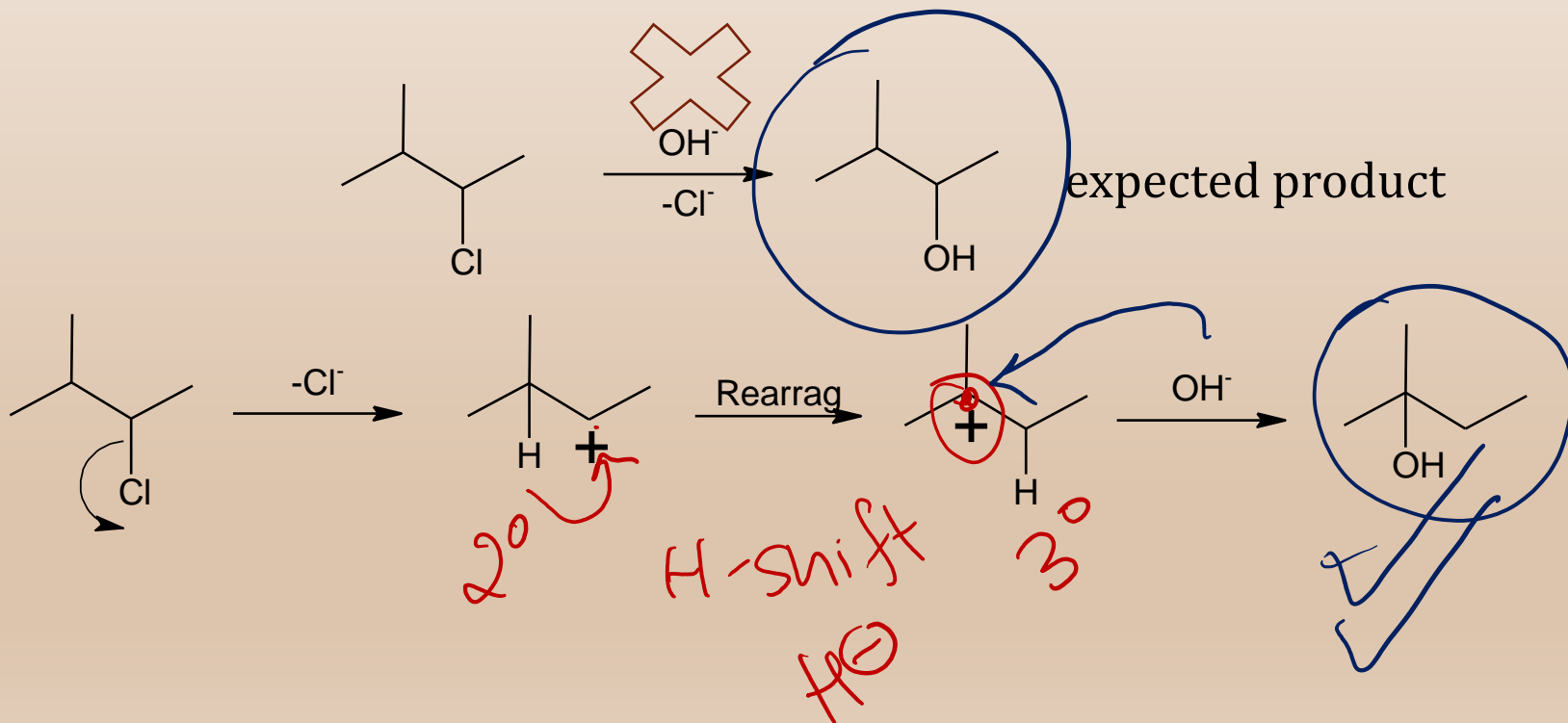
3) LG - Making a Bad LG a Good One

- Just because a LG is bad does not mean one cannot do substitution reaction.
- Some LGs can be made into good ones to promote desirable reaction.
- Here is an example of converting an alcohol (OH⁻ LG) into water (H₂O LG) a neutral LG, thus weaker base than OH⁻ thus a good LG and can be substituted with a Br⁻.
- Other good LG are tosylates and mesylates.



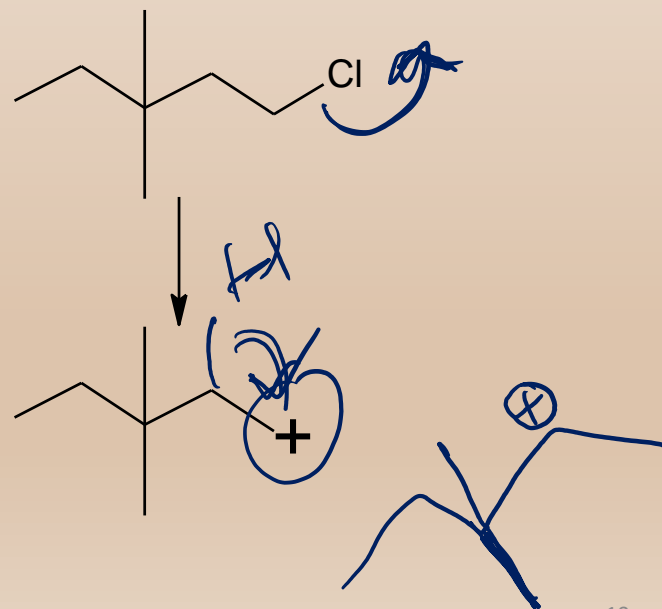
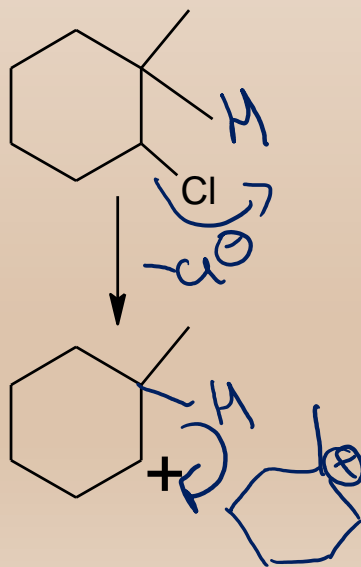
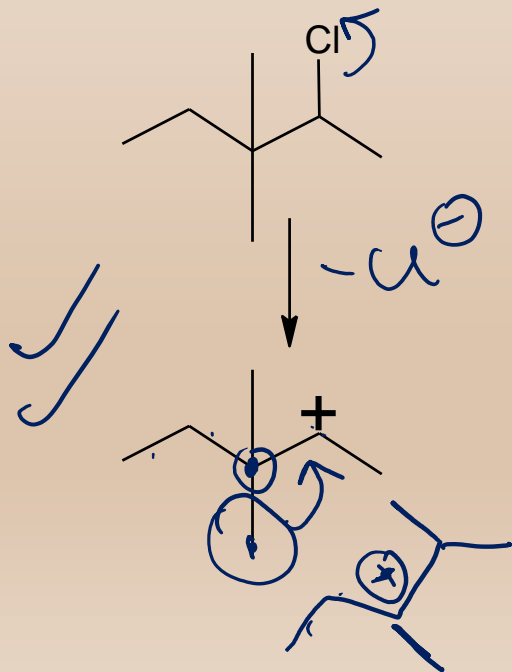
Rearrangement

- This happens in S_N1 reactions only because of carbocation formation.
- Carbocations have different stabilities, $3^\circ > 2^\circ > 1^\circ$, so if possible, rearrangement will occur to form more stable carbocation.
- This changes the carbon skeleton, thus giving a different product than expected.



Rearrangement...contd

- The only groups to shift are H, CH₃ and Ph (C₆H₅). Don't move Et, Pr etc. groups.
- Shift can happen only once.
- Shift occurs only to form a more stable ion.
- Predicting rearrangement –
 - See if the mechanism is S_N¹.
 - If yes, form the cation.
 - See if a more stable cation is possible by moving above groups, if yes, move it.



S_N2 or S_N1 ?

	S_N2	S_N1
Substrate	Primary or methyl	Tertiary
Nucleophile	Strong nucleophile	Weak nucleophile (may also be solvent)
Solvent	Polar aprotic solvent	Polar protic solvent, silver salts
Kinetics	$[\text{substrate}][\text{Nu}]$	$[\text{substrate}]$
Stereochemistry	Inversion	Racemic mixture
Rearrangement	No	Yes

Key Words/Concepts

- Substitution Reaction
- Nucleophile
- Electrophile
- Leaving group
- 1st order reaction (unimolecular)
- 2nd order reaction (bimolecular)
- Transition state
- Rate determining step
- Carbocation
- Solvolysis