Nucleophilic Substitution Reactions
continued

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Solvent Polarity

Solvents are usually classified into one of three groups.

Polar protic – a high dielectric constant and can donate hydrogen bonds. An example is CH_3CH_2OH.

Polar aprotic – a high dielectric constant and cannot donate hydrogen bonds. An example is $CH_3C{\equiv}N$.

Non Polar – a low dielectric constant and cannot donate hydrogen bonds. An example is $CH_3CH_2CH_2CH_2CH_2CH_3$.

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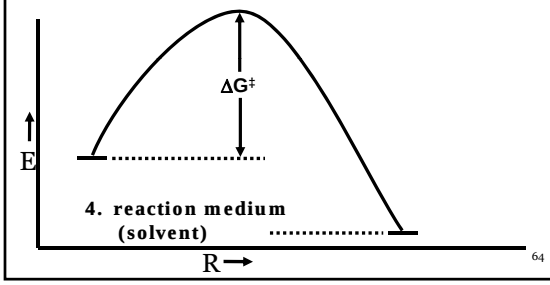
Solvent Effects in S_N2 Reactions

Solvent can stabilize reactants and/or transition state.

This stabilization can alter the rate of the reaction.



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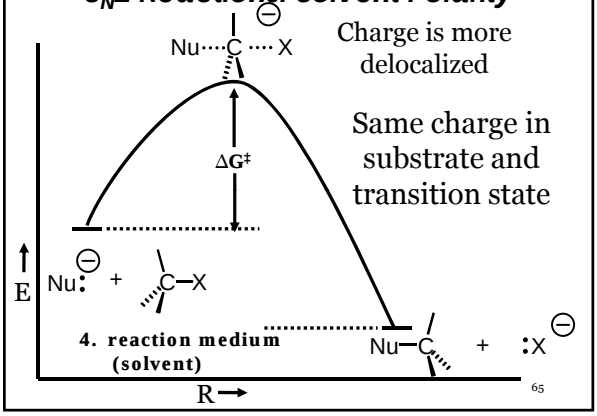
S_N2 Reactions: Solvent Polarity



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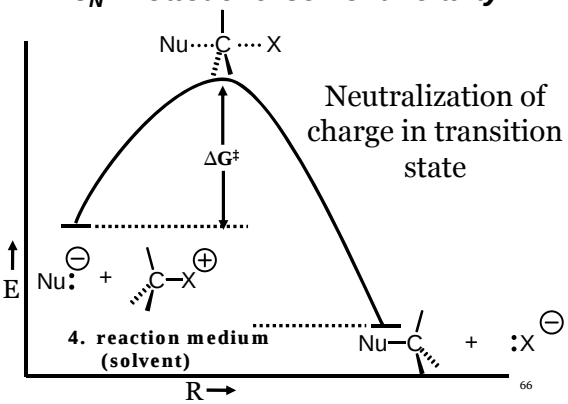
S_N2 Reactions: Solvent Polarity



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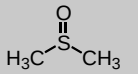
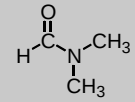
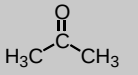
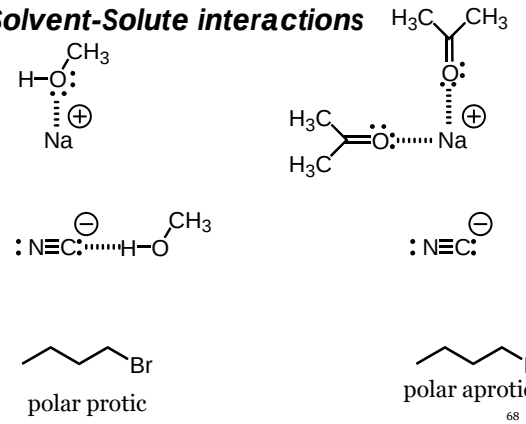
polar protic solvents

solvent	dielectric constant
$CH_3{-}OH$	33
	59
H_2O	79

polar aprotic solvents

solvent	dielectric constant
	49
	37
	21

Solvent-Solute interactions



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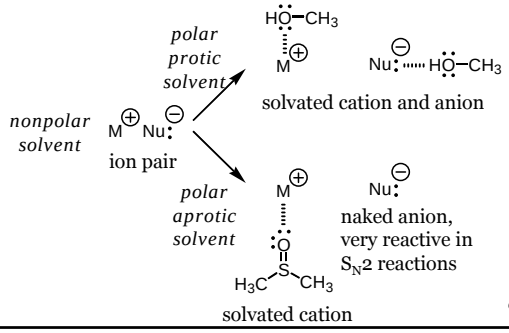
Solvation of Nucleophiles in S_N2

Anionic nucleophiles are altered by solvent



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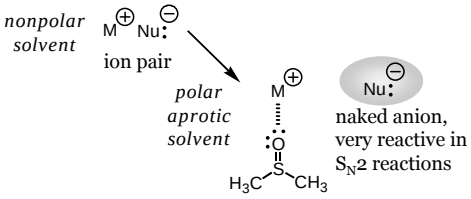
Solvation of Nucleophiles in S_N2

Anionic nucleophiles are altered by solvent

polar aprotic solvents are excellent for S_N2 reactions



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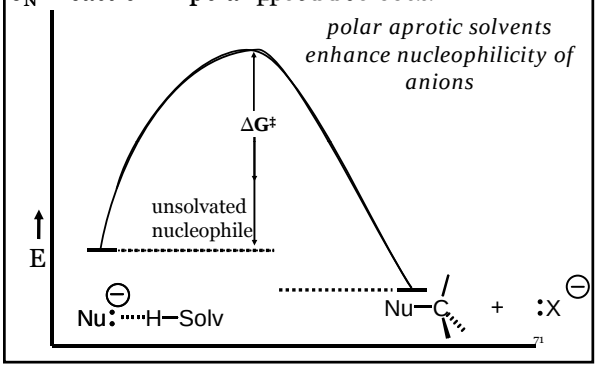
Protic vs Aprotic Solvents in S_N2

S_N2 reaction in polar aprotic solvent.



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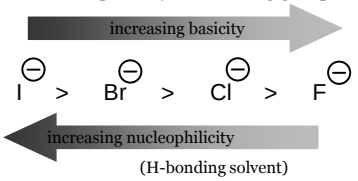
S_N2 Solvent Effects on Nucleophiles

Halides: Nucleophilicity and leaving group abilities.



Very polarizable, diffuse large anion poorly solvated

Very electronegative small anion well solvated

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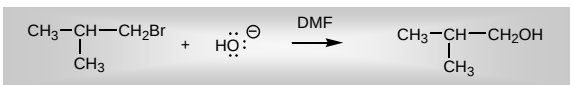
Predict, with an explanation, which one of the following reactions will occur at a faster rate.

S_N2 reaction

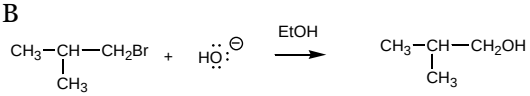
polar aprotic solvent – more reactive anionic nucleophile

DMF =

A



B



EtOH = CH_3CH_2OH

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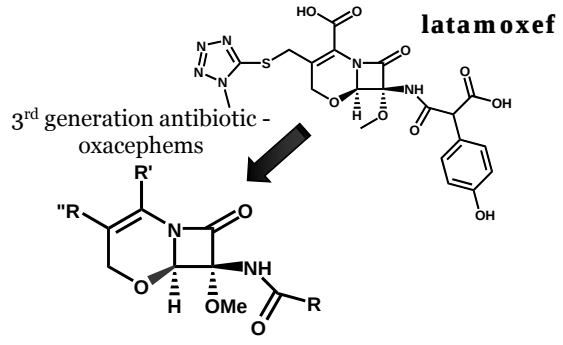
S_N2 Reactions in Synthesis



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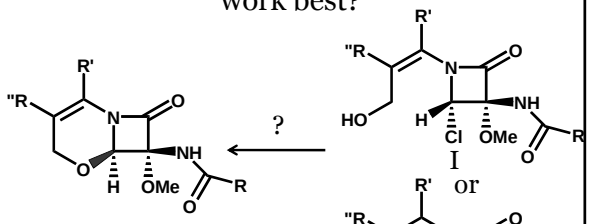
What starting material and solvent will work best?



a) I, CH_3CH_2OH b) I, CH_3CN

c) II, CH_3CH_2OH d) II, CH_3CN

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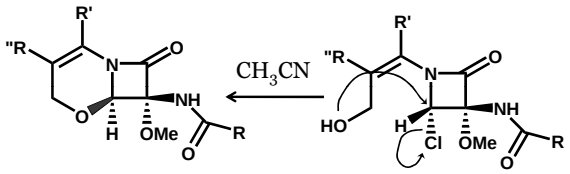
What starting material and solvent will work best?



S_N2 gives inversion
polar aprotic to improve nucleophilicity

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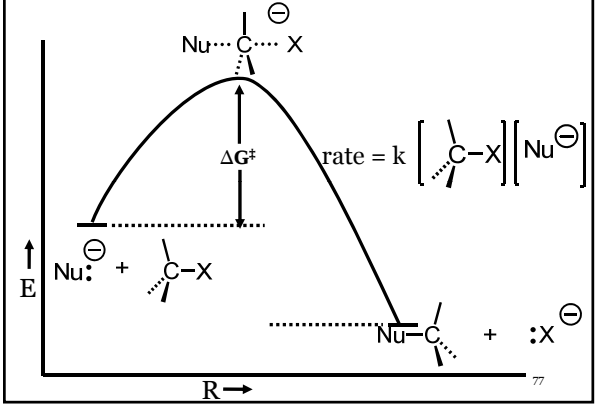
S_N2 = Substitution Nucleophilic 2nd Order



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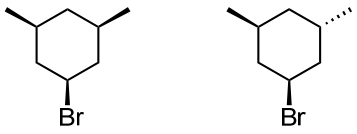
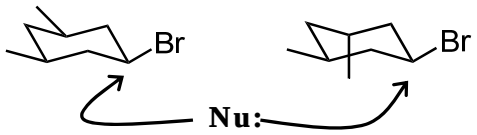
Which molecule reacts faster by S_N2?



A **B**

Steric hindrance in transition state



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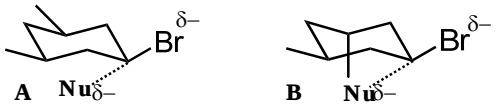
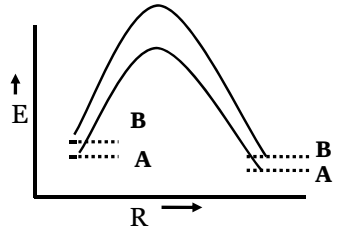
Why does A react faster than B by S_N2?

Steric hindrance in transition state





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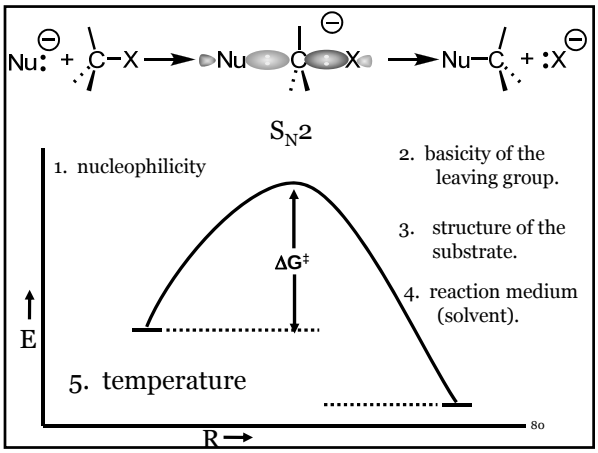
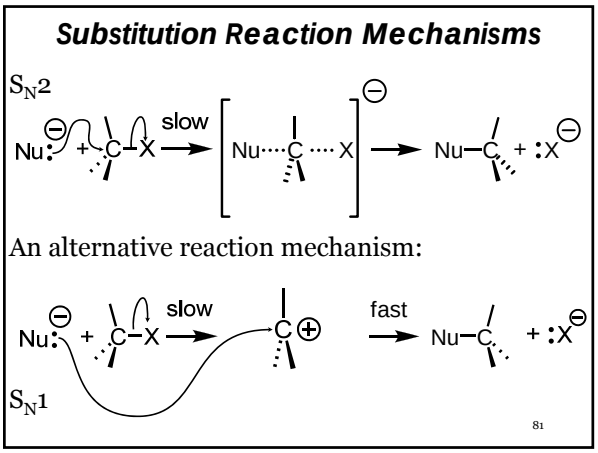
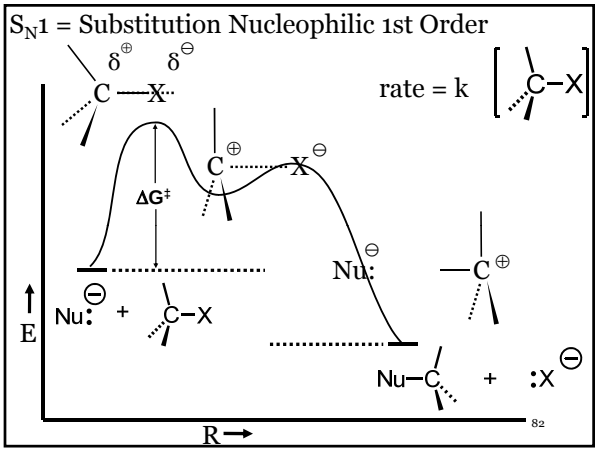

Nu: + C–X → Nu C X → Nu–C + :X
S$_N$2
1. nucleophilicity
2. basicity of the leaving group.
3. structure of the substrate.
4. reaction medium (solvent).
5. temperature
ΔG‡
E
R
80


Substitution Reaction Mechanisms
S$_N$2
Nu: + C–X slow → Nu···C···X → Nu–C + :X
An alternative reaction mechanism:
Nu: + C–X slow → C⊕ fast → Nu–C + :X
S$_N$1
81


S$_N$1 = Substitution Nucleophilic 1st Order
δ⊕ δ⊖
C—X
rate = k [C–X]
ΔG‡
C⊕ X⊖
Nu:⊖
—C⊕
Nu: + C–X
Nu–C + :X
E
R
82