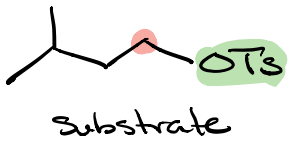


Substrate

NaOH ← Base or Nucleophile

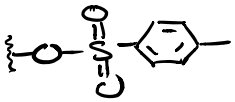
CH_3CN ← Solvent

60°C ← temp

Substrate : 1°, 2°, 3° in terms of LG location

1° Tosylate ⇒ S_N2

Base / Nucleophile : OH^- ⇒ is hydroxide ⇒ E_2

LG :  ≡ -OTs $S_N2/S_N1/E_2/E_1$ all same

Solvent : CH_3CN $CH_3C{\equiv}N$: acetonitrile S_N2/E_2

Temp : 60°C High or Low ? -OTs VG LG

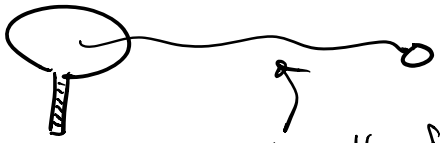
60°C ⇒ High

E_2

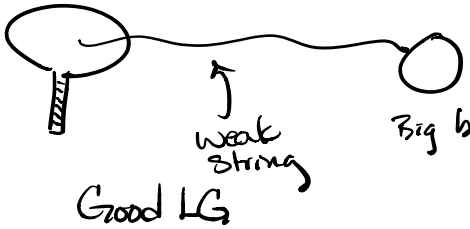
Δ = Bp of solvent = High

High vs Low

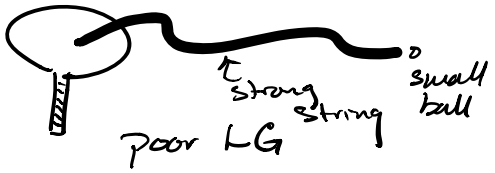
Heat = force



strength of bond ∝ how good LG is



Good LG



Poor LG

Low temp ~ 25°C might actually be high

High > 25°C

low < 25°C

High temp Δ or > 100°C

low < 100°C

1) Substrate S_N2

2) Base / nucleophile E_2

LG E_2, S_N2, E_1, S_N1

Priority

3) Solvent polar S_N2/E_2

4) Temperature High

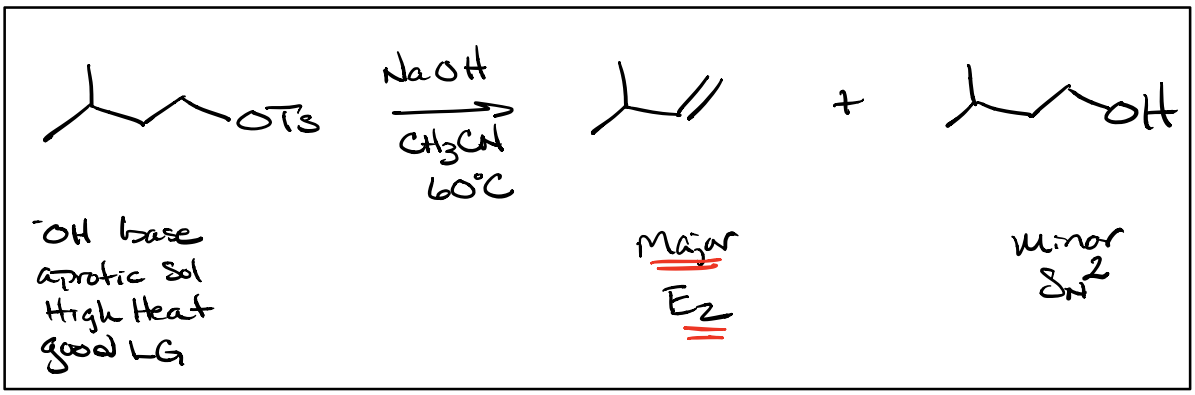
Relative OTs LG

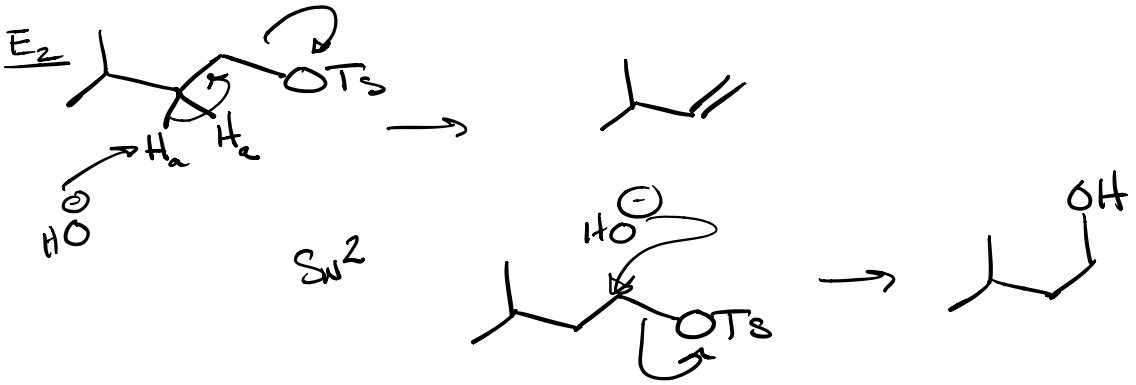
But this can change w/ factors & so this is not a hard rule

E_2

E_2 over S_N2

Major minor





NUCLEOPHILIC SUBSTITUTION AND ELIMINATION

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solvent	polar aprotic	polar aprotic
nucleophile	good nuc (weaker base than OH^-)	bulky or strong base >= OH^-
leaving group	sulfonate > I^- > Br^- > Cl^-	sulfonate > I^- > Br^- > Cl^-
Temp	low	high
	S_N1	E1
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Classification of Nucleophiles

Very good nucleophile	I^-, HS^-, RS^-
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Nucleophile	n_{CH_3I}	pK_a of conjugate acid
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Solvents Which Promote S_N2/E2 (bimolecular)

Acetone
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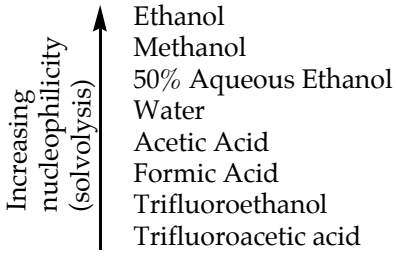
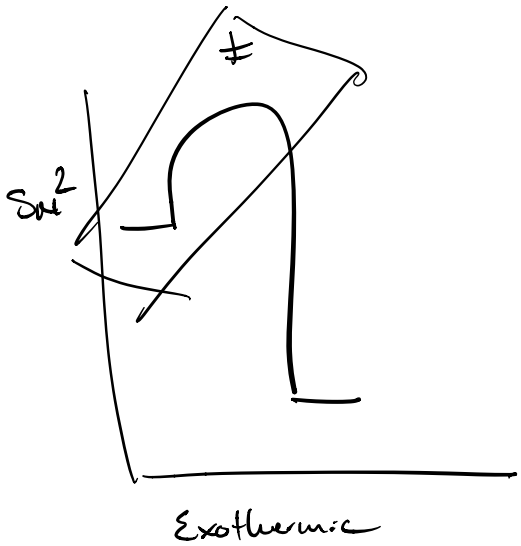
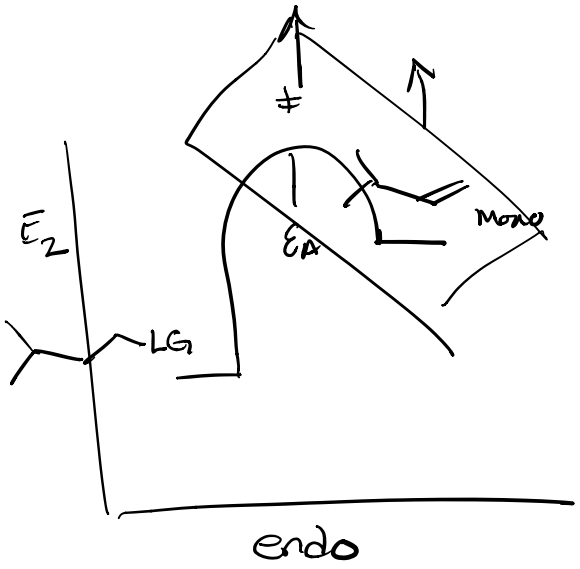
N,*N*-Dimethylformamide (DMF)
Acetonitrile
Hexamethylphosphoramide (HMPA)

Solvents Which Promote S_N1/E1 (Unimolecular/Ionizing)




‡
S_N2
Exothermic


‡
E_2
LG
E_A
More
endo


more stable

NUCLEOPHILIC SUBSTITUTION AND ELIMINATION

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nucleophile	weak nuc (no anions!)	any anionic base
leaving group	sulfonate > I^- > Br^- > Cl^-	sulfonate > I^- > Br^- > Cl^-
Temp	low	high

X

X

polar aprotic

C^+

not supported

$^-OCH_3 \approx {}^-OH$

Base vs. nucleophile

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$R-O^-$ CH_3O^-

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Better nucleophiles

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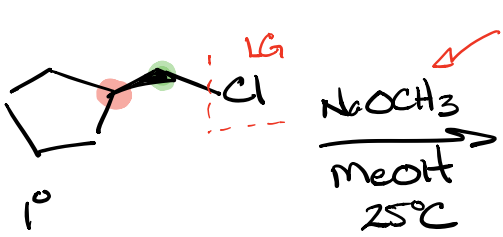
N,*N*-Dimethylformamide (DMF)
Acetonitrile
Hexamethylphosphoramide (HMPA)

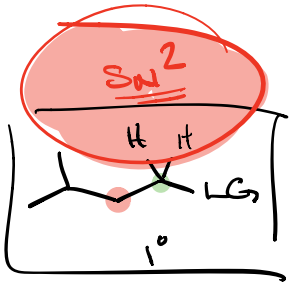
Solvents Which Promote S_N1/E1 (Unimolecular/Ionizing)

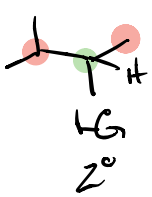
Increasing nucleophilicity (solvolysis)

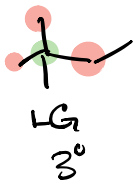
Ethanol
Methanol
50% Aqueous Ethanol
Water
Acetic Acid
Formic Acid
Trifluoroethanol
Trifluoroacetic acid



→ Substrate







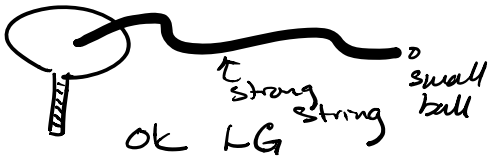
LG : Cl^- Good LG = weak base $^-OTs > I^- > Br^- > Cl^-$ ok LG

Base/nuc: $^\ominus OCH_3$? E_2 S_N2 E_1

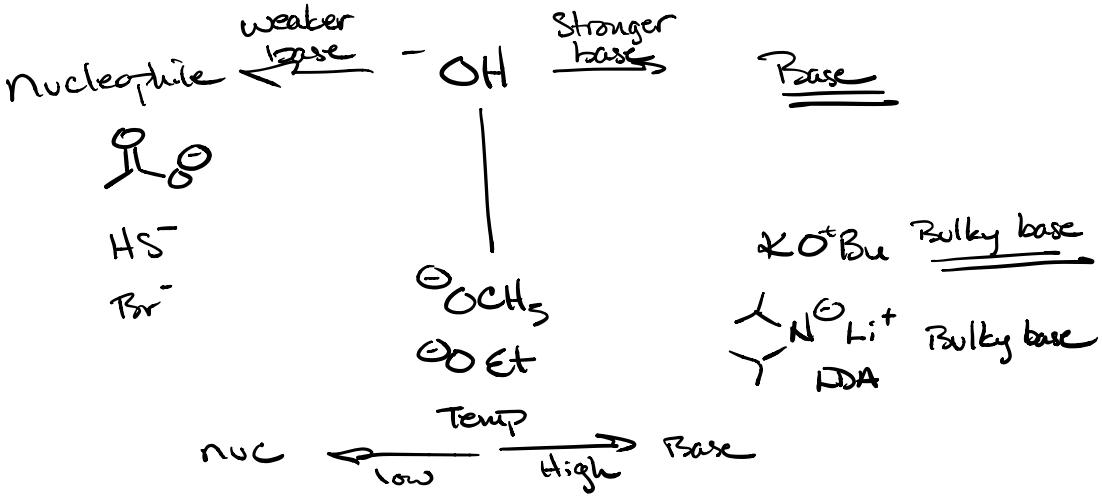
Solvent: MeOH H-bonding solvent polar protic ~~S_N1~~/E_1

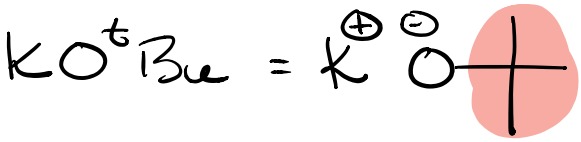
→ Temp: 25°C Low temp relative to Cl^- High/Low ∝ LG

~~S_N1~~/S_N2



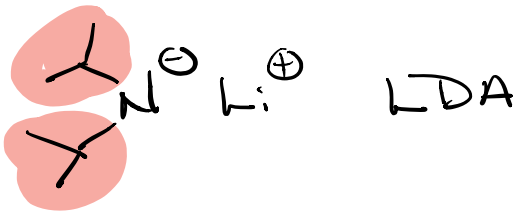
Base vs. Nucleophile

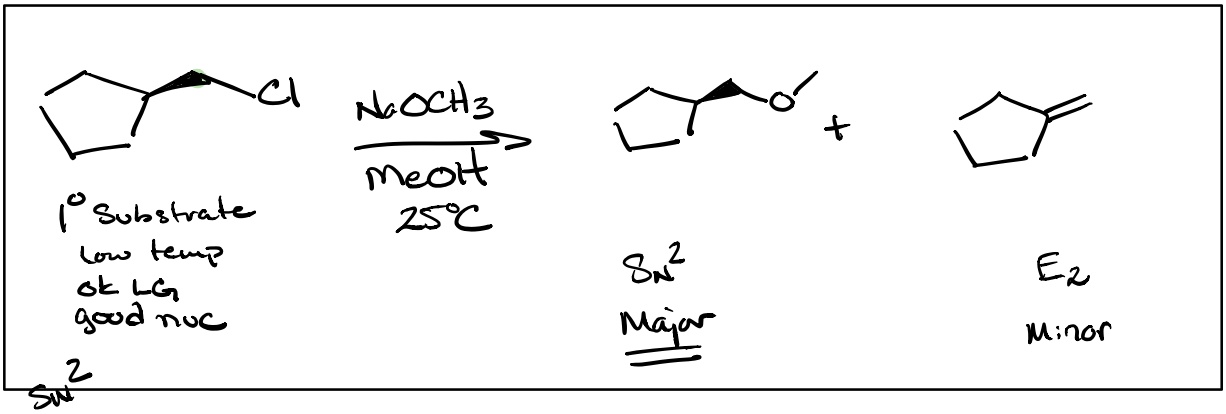


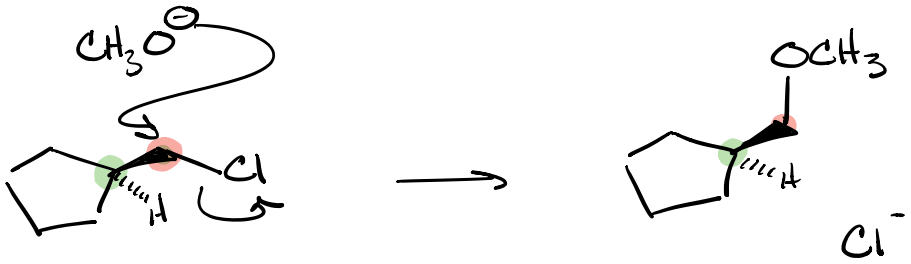
KO^tBu = 

^tBu = tert-butyl

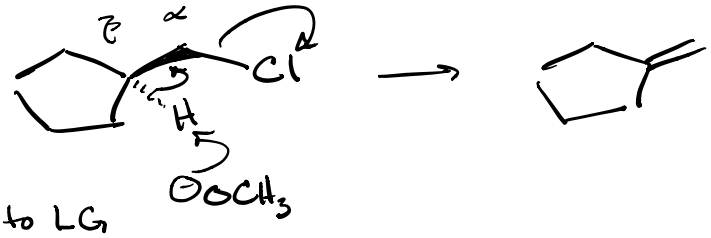
Lithium diisopropyl amide



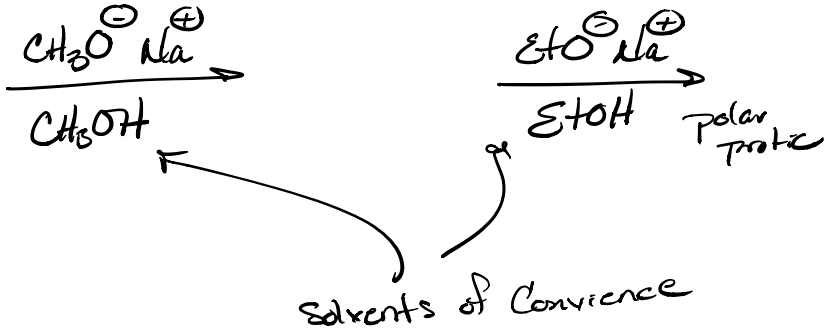

Cl
NaOCH3
MeOH
25°C
O
+
1° Substrate
low temp
ok LG
good nuc
SN2
SN2
Major
E2
Minor

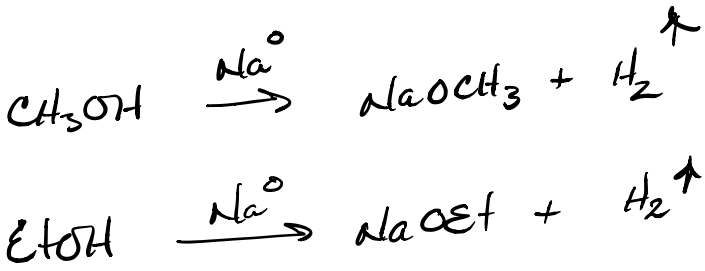

CH3O
Cl
H
OCH3
H
Cl-

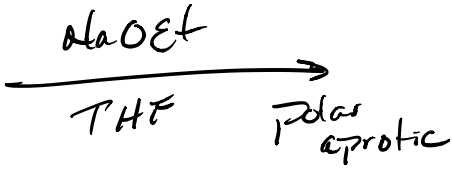
E2

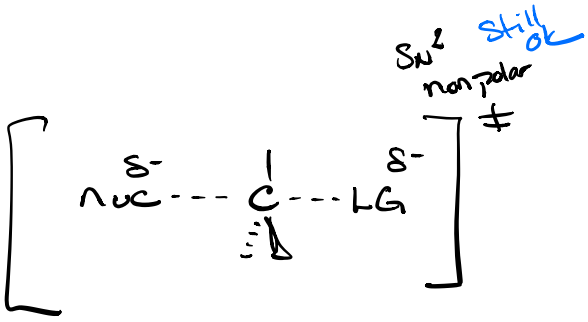

β
α
Cl
H
OCH3

H β to LG



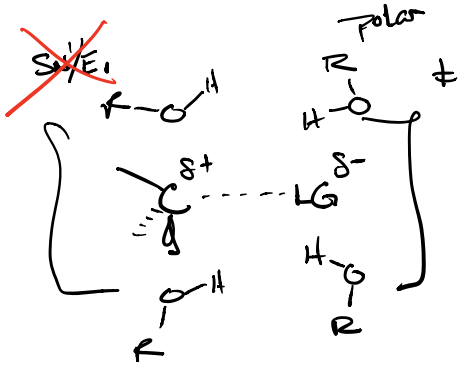




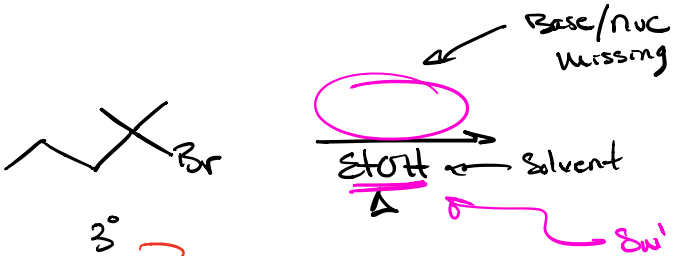


promoted by polar aprotic
but less affected by solvent

polar aprotic > protic
& not excluded



* Requires polar protic
Strongly affected by solvent



3° ⇒ SN1/E1/~~E2~~

Strong base ✗

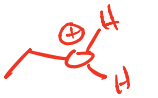
LG = $Br^{\ominus}$ good LG

Base/nuc = ? No anion ⇒ SN1 EtOH nucleophile Solvolysis ⇒ SN1

Solvent = polar protic ⇒ SN1/E1 C^+

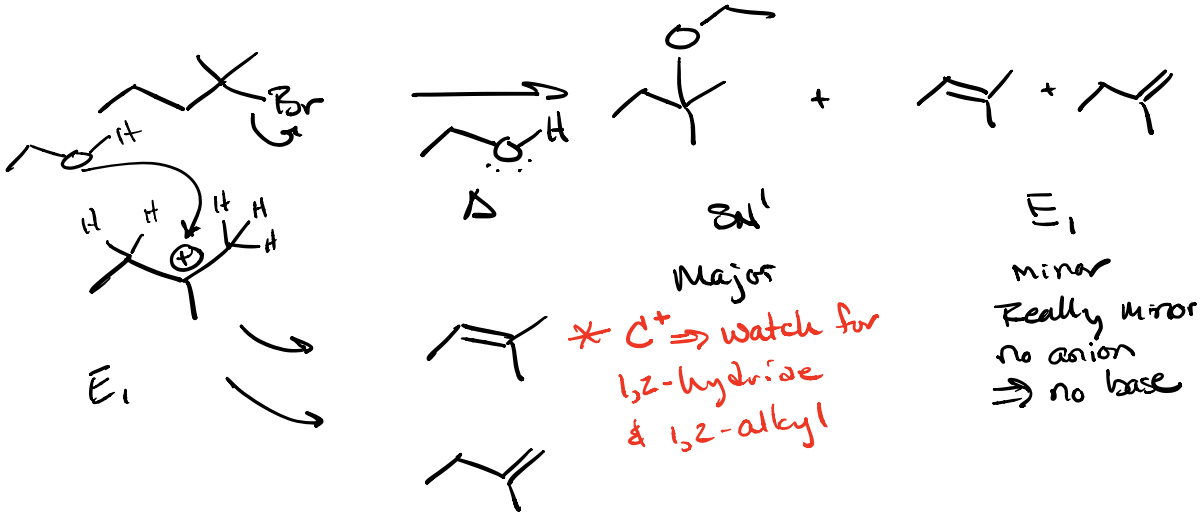
Temp = High = Δ ⇒ Elimination E1/E2

SN1 vs E1

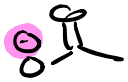


↑ HOEt

H-Br



anion $^{\ominus}OCH_3$ or $NaHCO_3$ $^{\ominus}HCO_3$

NaOAc 

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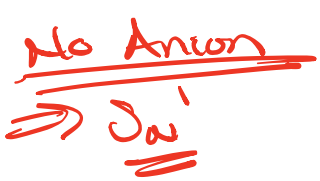

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Increasing nucleophilicity (solvolysis) ↑

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Methanol
50% Aqueous Ethanol
Water
Acetic Acid
Formic Acid
Trifluoroethanol
Trifluoroacetic acid