

NUCLEOPHILIC SUBSTITUTION AND ELIMINATION


The question is how do we discern when substitution is favored versus elimination? The answer is found partly in how we should think about reactions of alkyl halides.

*The characteristic reaction of alkyl halides (or alkyl tosylates) with a Lewis base is **elimination**, special conditions are required to promote substitution.*

Given here is a set of guidelines (not absolutes) that can be used to arrive at the probable solution to nucleophilic substitution/elimination problems.

	Substitution	Elimination
	S_N2	E2
substrate	benzyl = allyl > Me > 1° > 2° α -haloketone, α -haloester, α -halonitrile	3° > 2° > 1°
solvent	polar aprotic	polar aprotic
nucleophile	good nuc (weaker base than OH ⁻)	bulky or strong base \gg OH ⁻
leaving group	sulfonate > I ⁻ > Br ⁻ > Cl ⁻	sulfonate > I ⁻ > Br ⁻ > Cl ⁻
Temp	low	high
	S_N1	E1
substrate	3° > 2°	3° > 2° > 1°
solvent	polar protic	polar protic
nucleophile	weak nuc (no anions!)	any anionic base
leaving group	sulfonate > I ⁻ > Br ⁻ > Cl ⁻	sulfonate > I ⁻ > Br ⁻ > Cl ⁻
Temp	low	high

Classification of Nucleophiles

Very good nucleophile	I^- , HS^- , RS^-
Good nucleophile	Br^- , OH^- , RO^- , CN^- , N_3^-
<u>Fair nucleophile</u>	NH_3 , Cl^- , F^- , RCO_2^- 
Weak nucleophile	H_2O , ROH
Very weak nucleophile	RCO_2H

Nucleophilic Constants of Various Nucleophiles

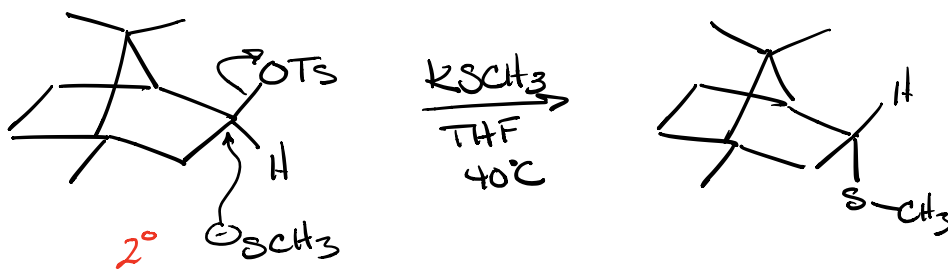
Nucleophile	n_{CH_3I}	pK_a of conjugate acid
CH_3OH	0.0	-1.7
F^-	2.7	3.45
$CH_3CO_2^-$	4.3	4.8
Cl^-	4.4	-5.7
NH_3	5.5	9.25
N_3^-	5.8	4.75
$C_6H_5O^-$	5.8	9.89
Br^-	5.8	-7.7
CH_3O^-	6.3	15.7
OH^-	6.5	15.7
$(CH_3CH_2)_3N$	6.7	10.70
CN^-	6.7	9.3
I^-	7.4	-10.7
$(CH_3CH_2)_3P$	8.7	8.69
$C_6H_5S^-$	9.9	6.5

Solvents Which Promote $S_N2/E2$ (bimolecular)

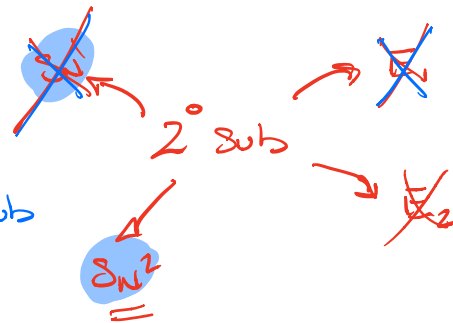
Acetone
 Dimethyl sulfoxide (DMSO)
N,N-Dimethylformamide (DMF)
 Acetonitrile
 Hexamethylphosphoramide (HMPA)

Solvents Which Promote $S_N1/E1$ (Unimolecular / Ionizing)

↑
 Increasing nucleophilicity (solvolysis)
 Ethanol
 Methanol
 50% Aqueous Ethanol
 Water
 Acetic Acid
 Formic Acid
 Trifluoroethanol
 Trifluoroacetic acid



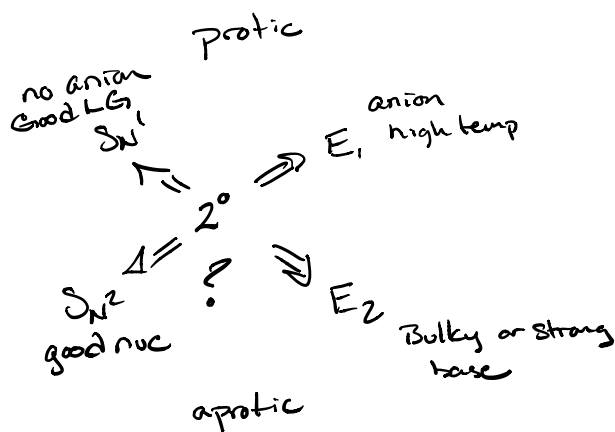
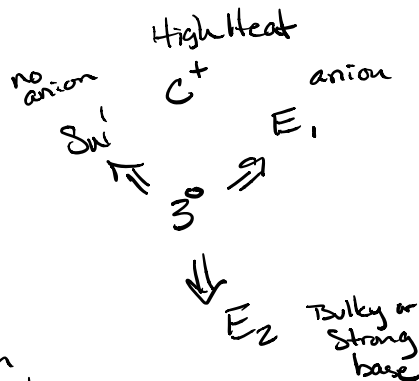
LG = Tosylate \ominus very good LG

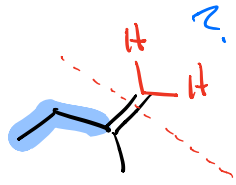


nuc/base \ominus S CCH_3 good nuc \Rightarrow Sub

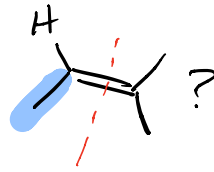
THF aprotic bp 68°C No C^+

Temp 40°C High risk

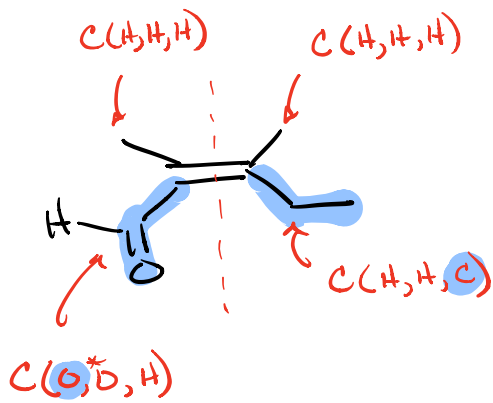
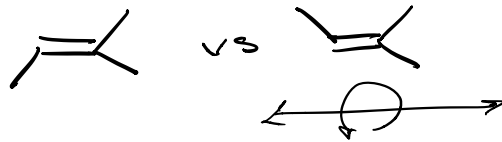




no E/Z
no cis/trans



no E/Z
no cis/trans

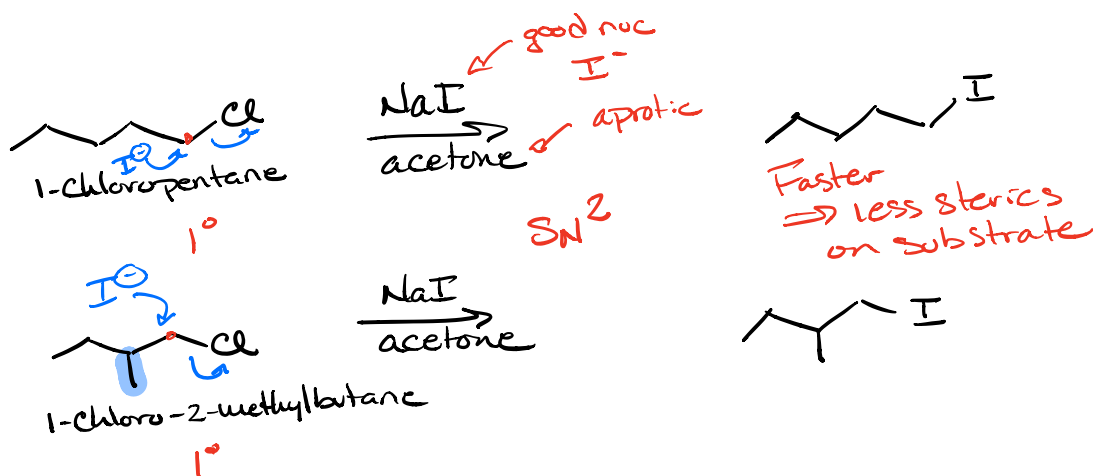


Cis or (Z)

✓ Cis = Z = Zusammen "together"

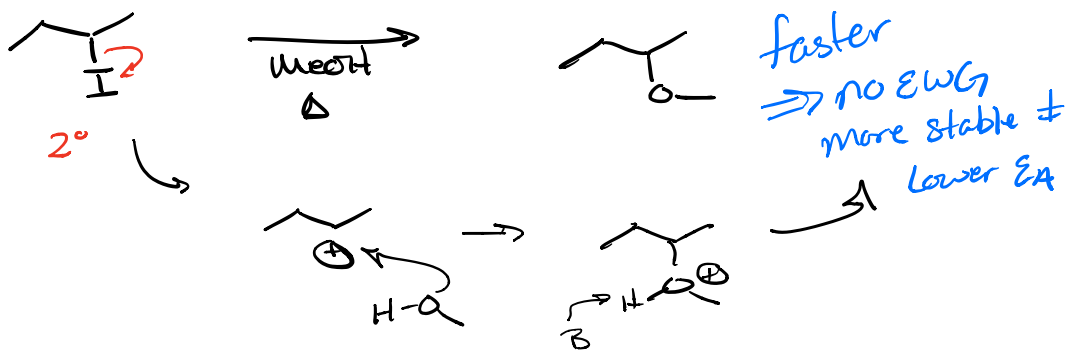
≠ trans = E = Entgegen "opposite"

Which rxn runs faster? why?

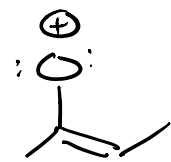
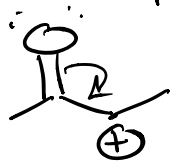


* Both rxns go by same mechanism

- ① Decide on mech
- ② Find differences
- ③ Decide on faster rxn

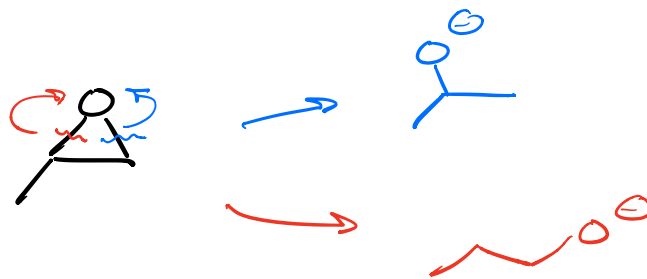
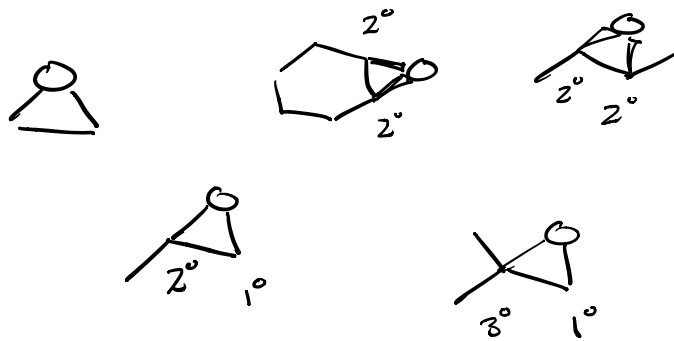
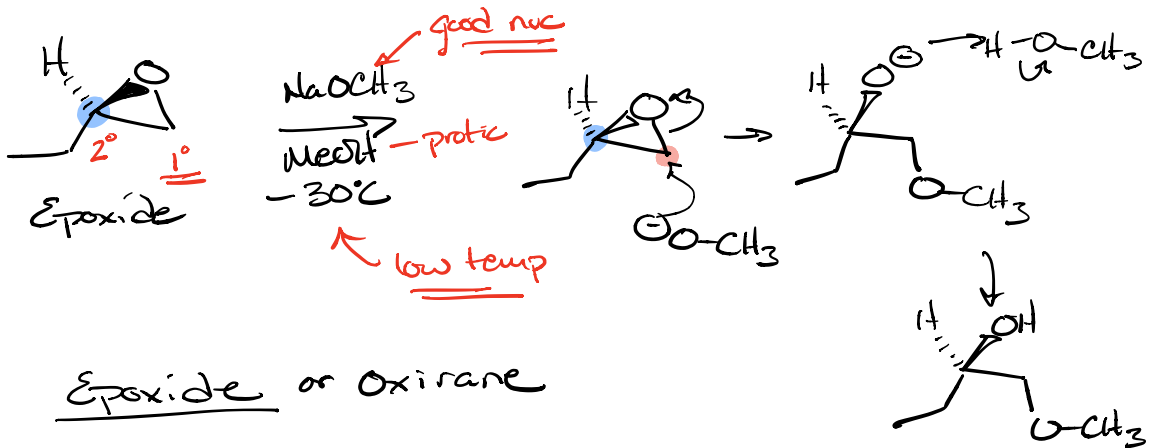


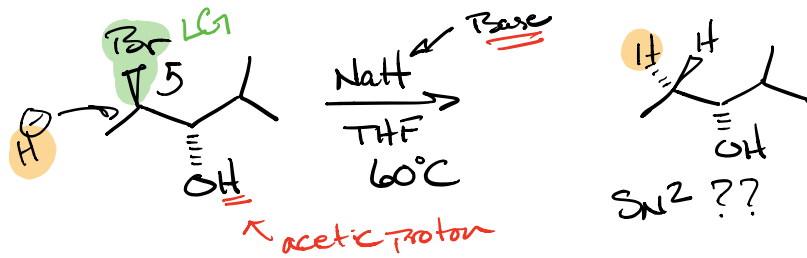
EWG not Resonance



Resonance?

Violated Octet Rule
Oxygen too EN to violate octet rule \therefore





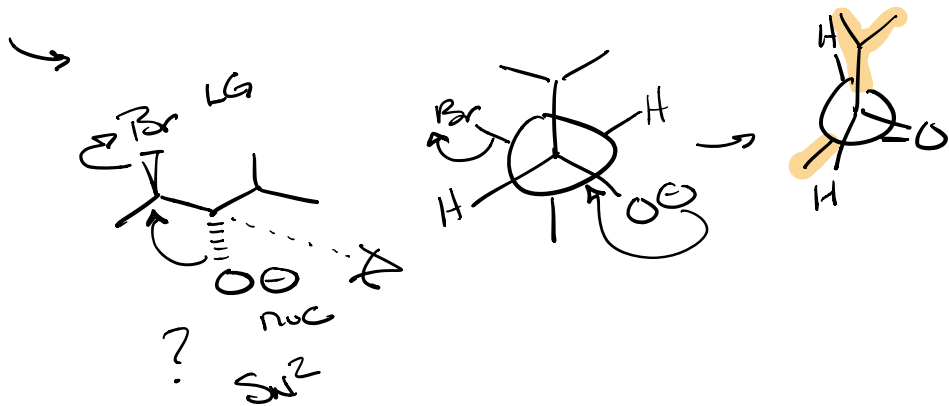
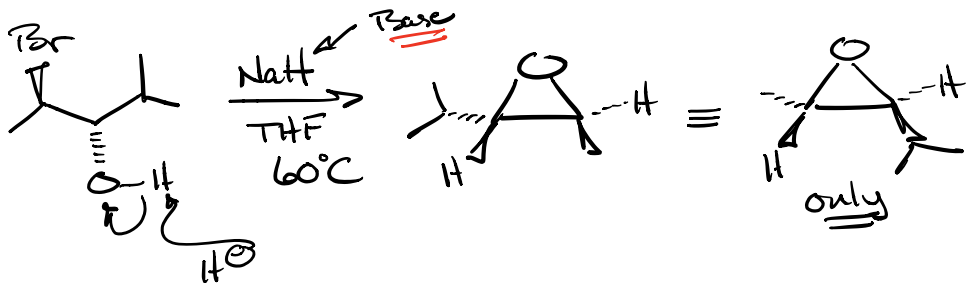
acetic proton

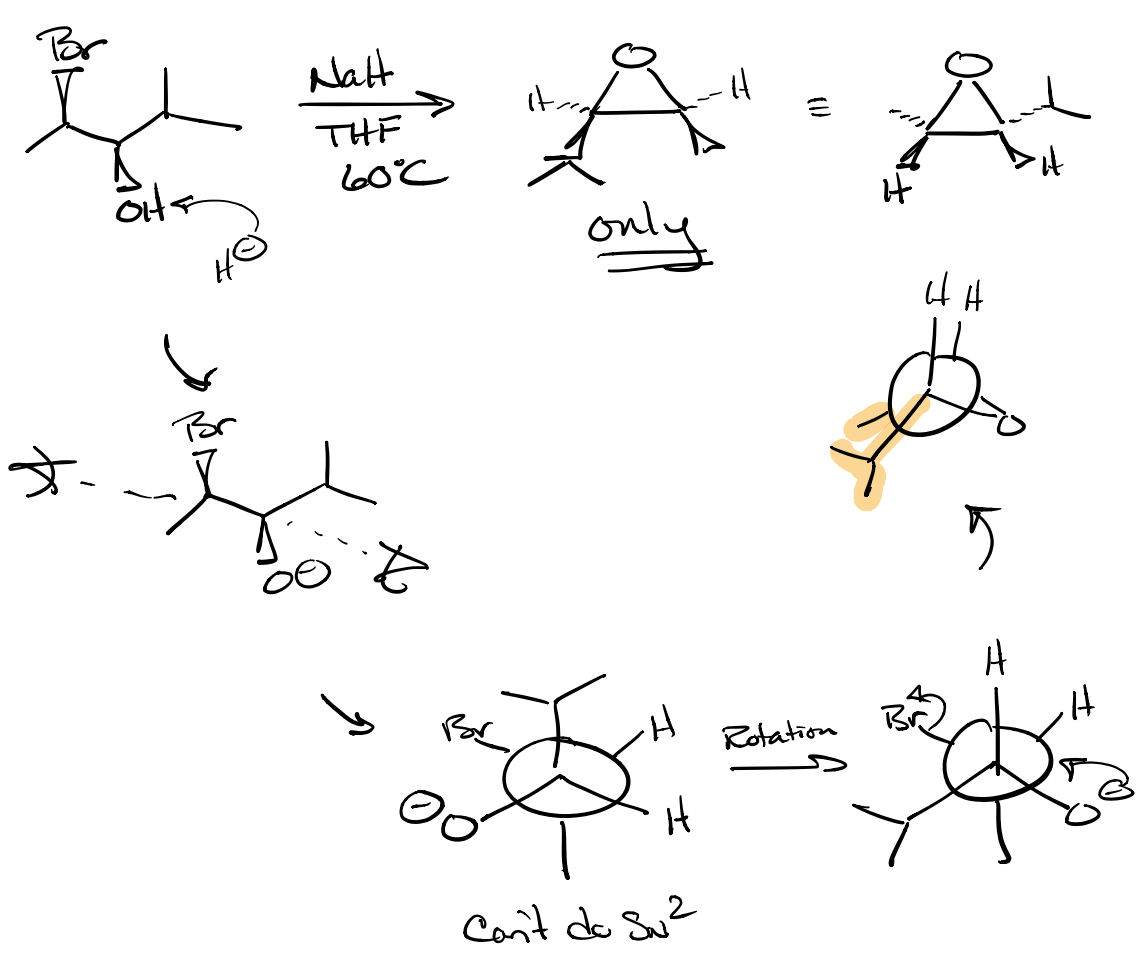
Sodium Hydride



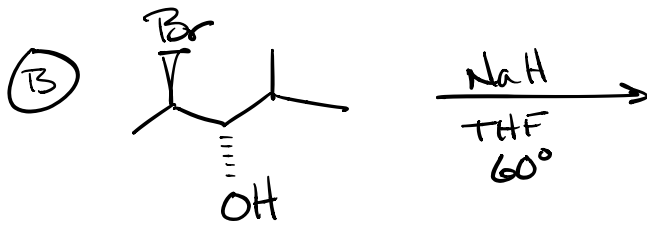
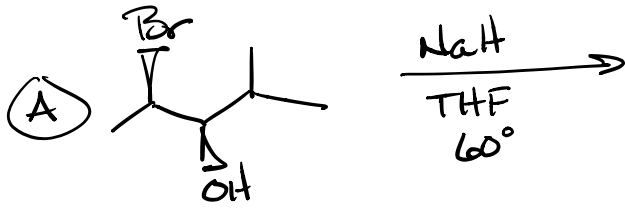
H^- hydride

⇒ good base





which Rxn is faster?



faster
Because of
Lower Sterics
in \neq

