Chapter 8

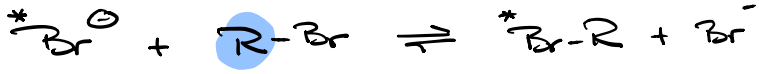
S_N2/E_2 Rate = $k[R\text{-}LG][Base/Nuc]$ (E_2: Base; S_N2: Nuc)

S_N1/E_1 Rate = $k[R\text{-}LG]$

Factors

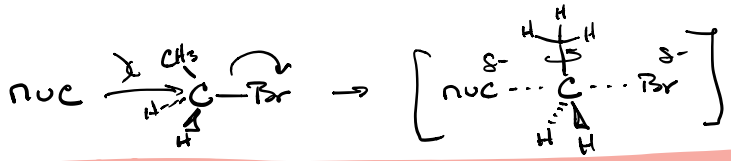
1. Substrate (S_N2: 1°, 2°, 3°, Resonance, Induction)
2. Leaving Group (Good vs poor)
   Base/Nucleophile
3. Solvent (nonpolar vs. polar vs polar protic)
4. Temperature (High vs Low)

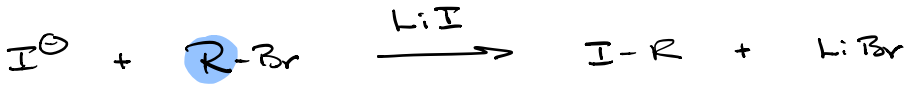
S_N2 Rates by Substrate



R	CH_3-	Et-	prop-	iprop-	tbutyl-
	methyl	1°	1°	2°	3°
	100	1.31	0.89	0.015	*0.004

* Requires protic Solvent

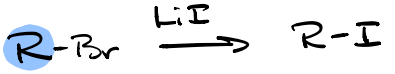


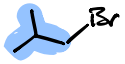


R	methyl CH_3-	1° Et-	2° iprop-	3° tbutyl-
$\frac{k_{ipr}}{k}$ Relative rate to ipr	221,000	1,350	1	—

R 1° > 2° >> 3°

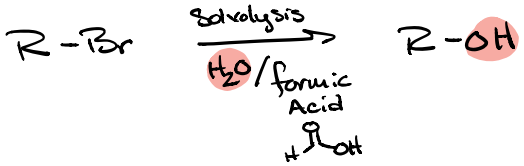
S_N2 on 1° Substrates



	Et-	prop-	ibutyl-	neopentyl-
				
$\frac{k}{k_{Et}}$	1.0	0.8	0.036	0.0002

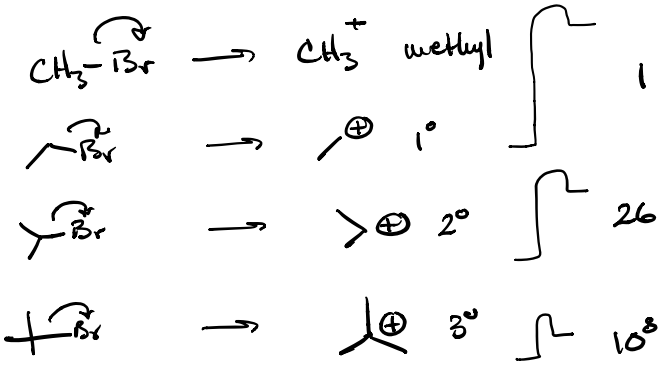
Even branching affects rates of S_N2 @ 1° center

S_N1 Rates by Substrate



R	CH_3-	Et-	iprop-	^tBu-
$\frac{k}{k_{Et}}$	0.6	1	26	10^8 !

S_N1 $3^\circ >> 2^\circ > 1^\circ$



In General S_N

$3^\circ > 2^\circ > 1^\circ$

S_N2 $1^\circ > 2^\circ > 3^\circ$ Sterics

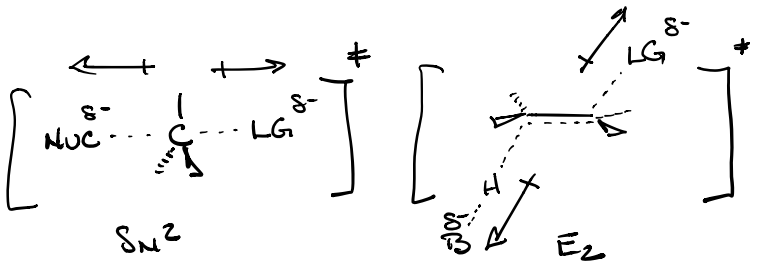
2×10^5 1000 –

S_N1 $3^\circ >> 2^\circ > 1^\circ$ Stability C^+ (Electronics)

10^8 29 1

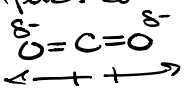
Solvent

* Bimolecular

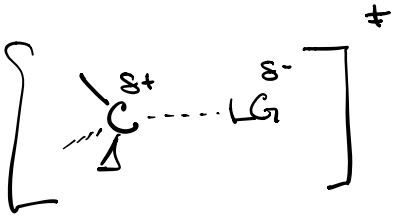


Both are non-polar → Molecular

Dipoles cancel



* Unimolecular



E_1/S_N1

Polar* → Ionic

Solvent types

nonpolar

hydrocarbons
aromatic

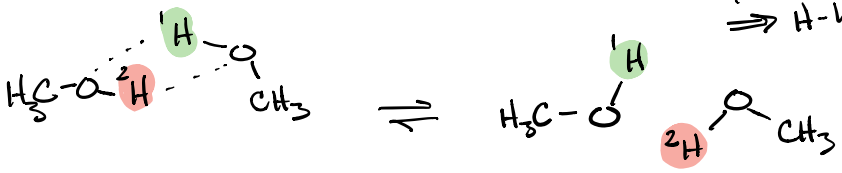
polar

CH_2Cl_2
acetone

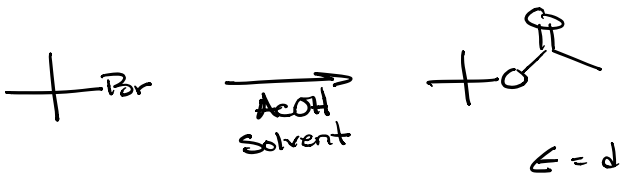
polar protic

MeOH
EtOH
H_2O
(acetic Acid
AcOH)

Have an acidic proton
⇒ H-bond protons

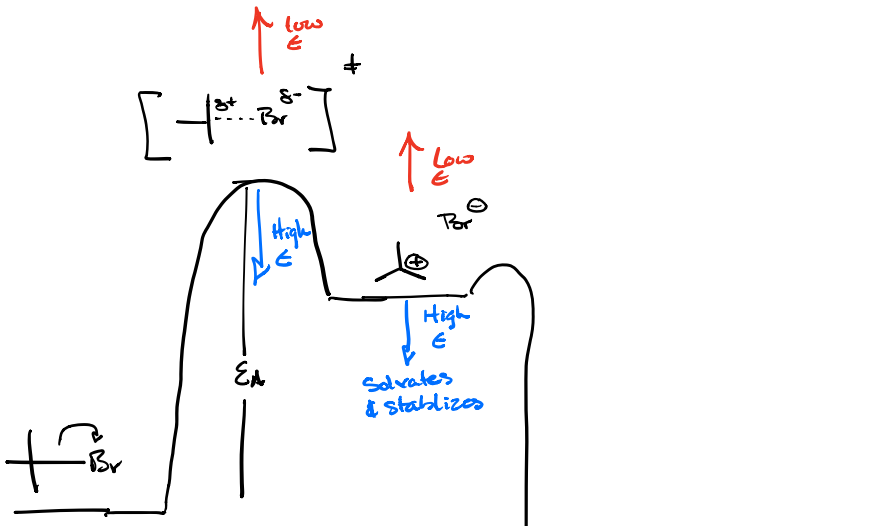


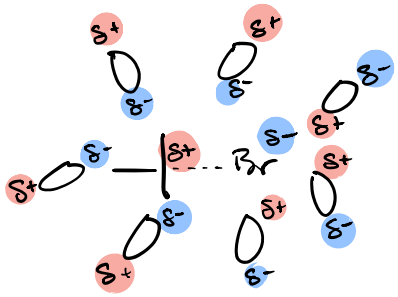
Unimolecular ≠ Strongly affected by Solvation



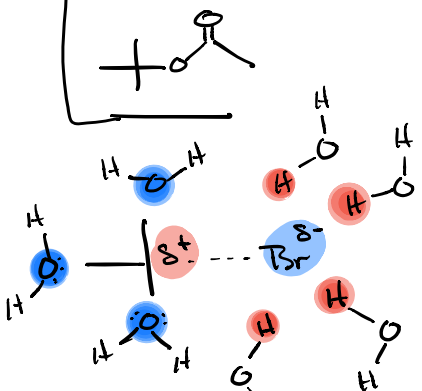
ϵ = dielectric Constant

ϵ Solvent	^{6}AcOH	^{33}MeOH	^{58}	$^{78}H_2O$
$\frac{k}{k_{AcOH}}$	1	4	5,000	150,000



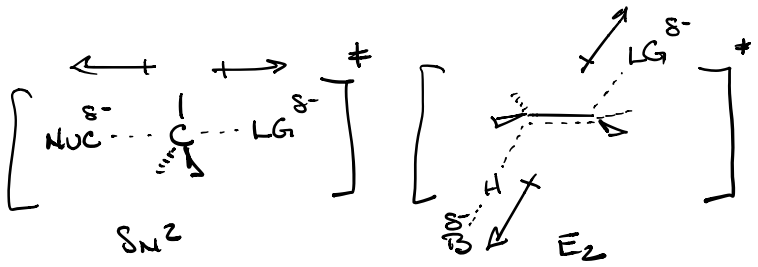


Polar Solvent attempt at solvation



Better at Solvating

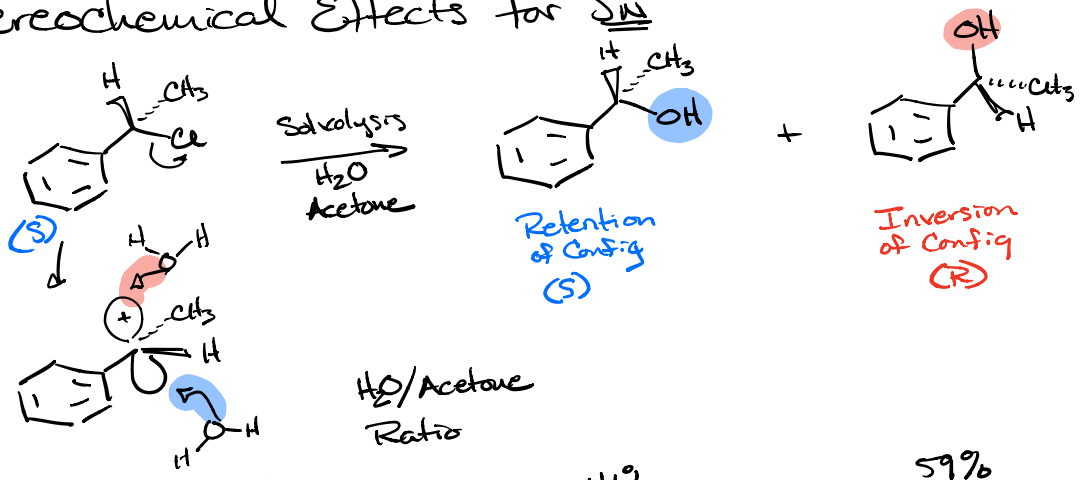
Bimolecular Solvent Effect



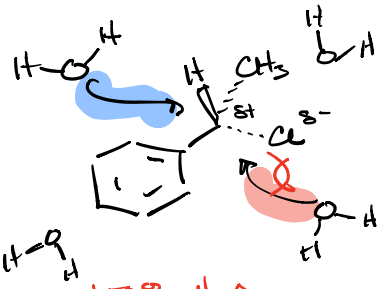
Both are non-polar → Molecular

S_N2/E_2 ≠ are less affected by solvent though polar solvents generally required for solvation of $nuc^{\ominus}$

Stereochemical Effects for S_N1

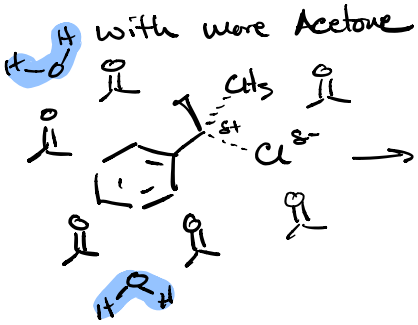


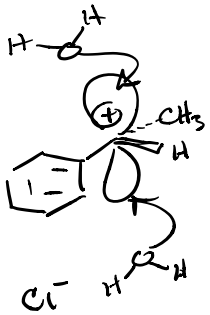
H_2O/Acetone Ratio		
"S_N2 Like" 100/0	41%	59%
40/60	47%	53%
20/80	49%	51%



100% H_2O

Inversion favored over retention





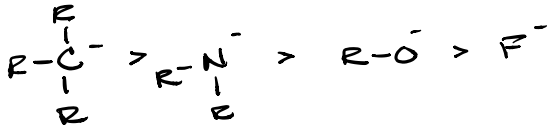
Cl^-

Equal opportunity!

Nucleophilicity

$HS^- >> {}^-CN > I^- > {}^-OH > N_3^- > Br^- >$  $>$  $\geq Cl^- > F^- > NO_3^- > H_2O$

Nucleophilicity decreases w/ increasing EN



$C^- > N^- > O^- > F^-$ ← Hold e^- more tightly, poor nucleophile

Anions more nucleophilic than Conjugates

$${}^-OH > H_2O$$

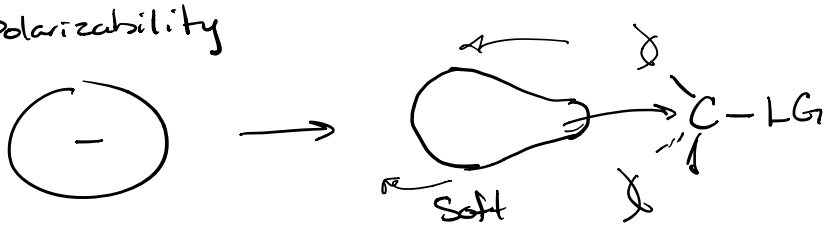
For protic solvents nucleophilicity increases going down a group

Better nuc

Better nucleophile

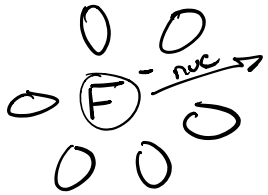
Polarizability ! Solvent !

Polarizability



Soft
Squishy
Easier time avoiding
Sterics
Better nuc

More polarizable = better nuc



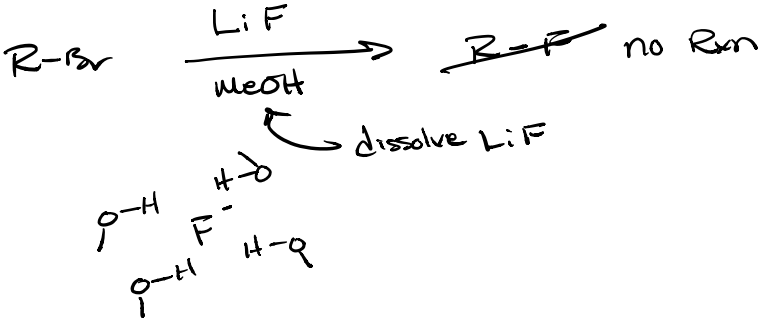
Small
Hard
unstable

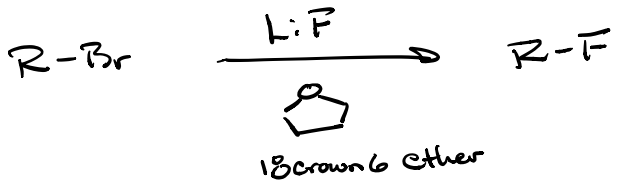
Solvent helps to
Stabilize
⇒ Cages the anion
⇒ Can't act as nucleophile

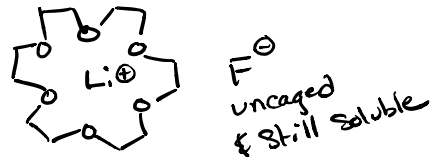
Large
Soft
delocalized
More stable

Requires less
Solvation
free → available
to act as nucleophile

* LG vs nuc
* Temp


R-Br
LiF
MeOH
R-F
no Rxn
dissolve LiF


R-Br
LiF
R-F
18crown6 ether


Li⊕
F⊖
uncaged
& still soluble