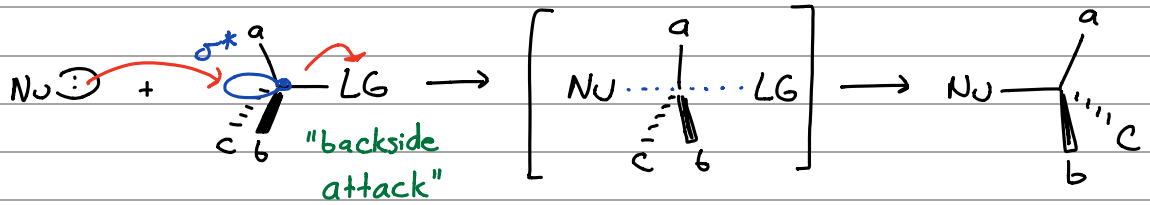
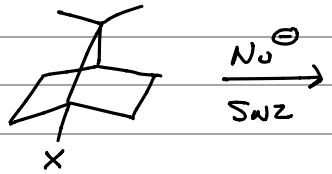
Nucleophilic Aliphatic Substitution Rxns

SN2

Concerted Rxn - Only a single transition state
Simultaneous bond making + breaking



Further support for backside attack:



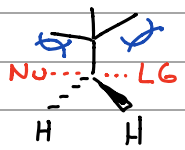
$Nu^{\ominus}$ / SN2 → No Rxn
(Ring system completely blocks access of a Nu)

The Nucleophile

- Requires a good Nu
- Slim, polarizable nucleophiles are best
  - ↳ lower down on P.T. $R\text{-}S^{\ominus}$
  - ↳ $R\text{-}{\equiv}^{\ominus}$, $NC^{\ominus}$
- Usually $Nu^{\ominus}$ better than Nu:

The Electrophile

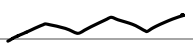
- More sterically hindered = slower rxn.



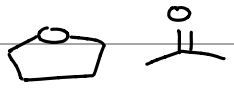
With neophyl, Sterics result in bending of the Nu···C···LG trajectory
Creating a very strained transition state

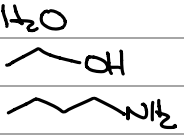
Solvent

Non-Polar: CCl_4



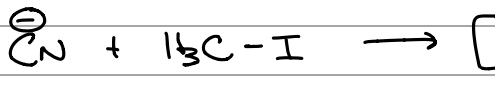
Polar Aprotic: DMSO



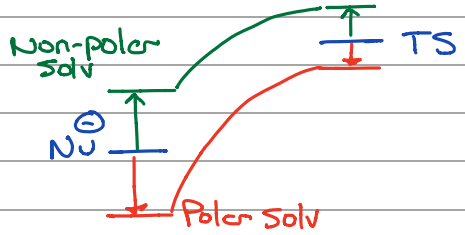
Polar Protic: H_2O, 

OH or NH

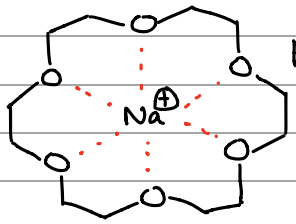
- Analyze how Solvent Stabilizes the SM relative to the TS
- Larger or more localized Charge is stabilized by ↑ Solvent polarity

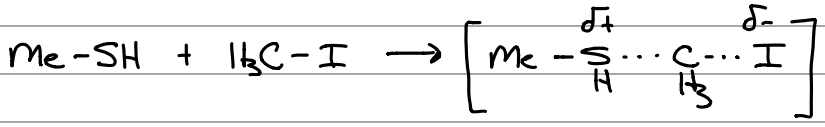


← More diffuse ⊖ Charge = Smaller Solvent effects

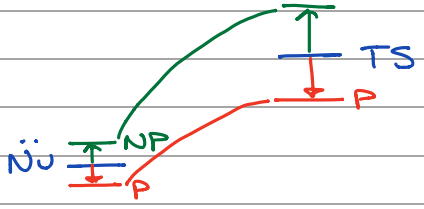


Non-Polar Solvents are best, but anions often don't dissolve well in NP Solvents
→ Addn of a Crown ether aids solubility by Solvating $M^{\oplus}$

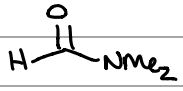




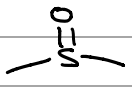
more polar than SM



Fastest in a polar aprotic Solvent

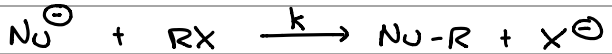


DMF



DMSO

Kinetics



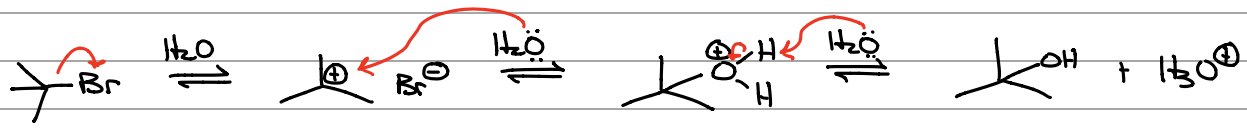
$\frac{d[P]}{dt} = k[RX][Nu^{\ominus}]$ ↑ Nu always affects the rate

If Nu in large xs ⟹

$\frac{d[P]}{dt} = k_{obs}[RX]$ ↑ k_{obs} would be linearly dependent on $[Nu^-]$

"Pseudo first order kinetics"

SN1



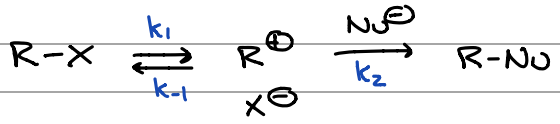
- Not Concerted
- At least two steps are involved
- Carbenium ion is trapped by the solvent

Solvent	H_2O	AcOH	MeOH
Solvolysis	Hydrolysis	acetolysis	methanolysis

Kinetics

$Rate = k[R\text{-}X]$ Does this really make sense?

↳ Leave out Nu + rate = zero



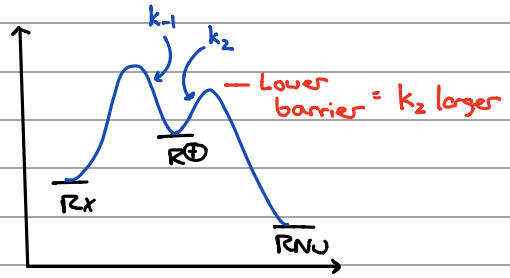
Write full kinetic expression using SSA:

$$\frac{d[P]}{dt} = \frac{k_1 k_2 [Rx][Nu^{\ominus}]}{k_{-1}[X^{\ominus}] + k_2[Nu^{\ominus}]}$$

← $[Nu^{\ominus}]$ is in the kinetic expression

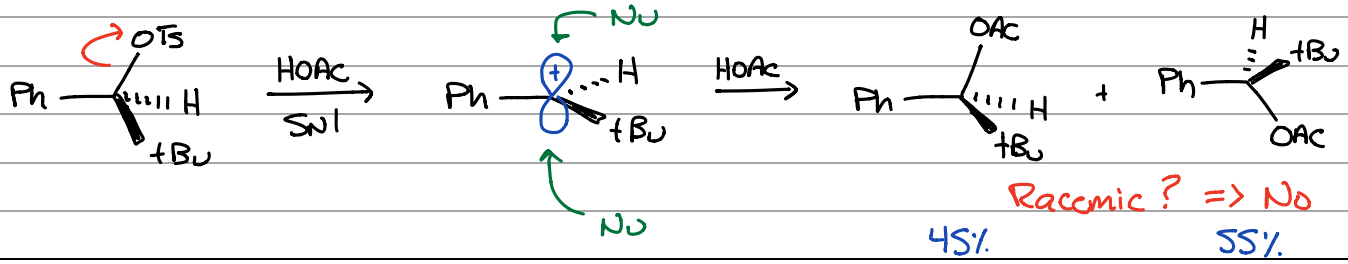
Zero order kinetics in $Nu^{\ominus}$ when:

- $Nu^{\ominus}$ is in large excess or
- $k_{-1} \ll k_2$



Common Ion Effect: Add $X^{\ominus}$, you slow down the rxn.

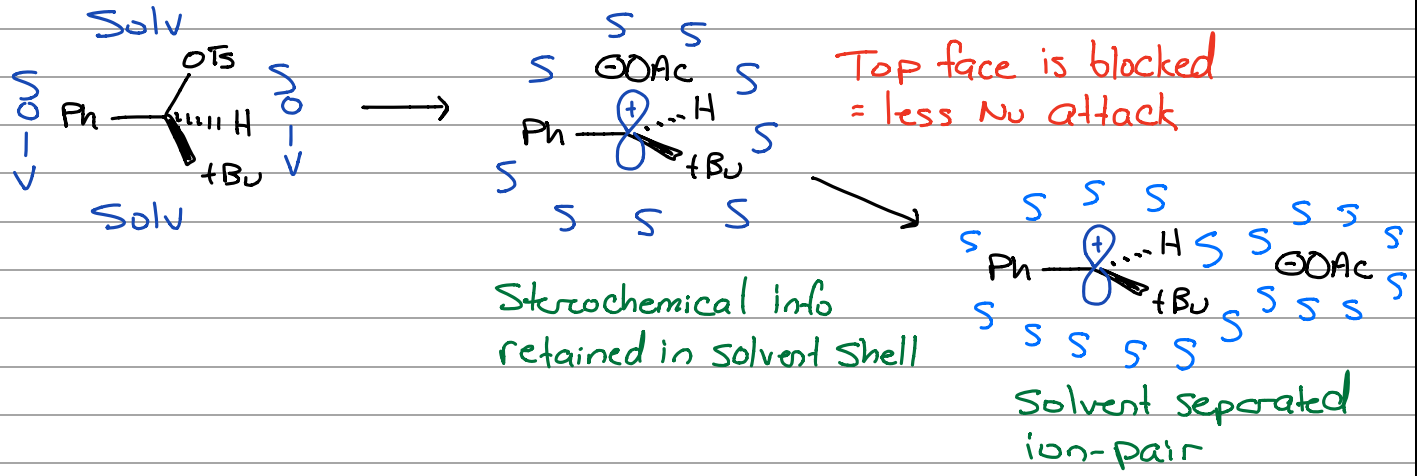
Stereochemistry



Racemic? => No

45% 55%

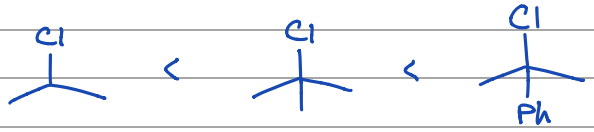
Results are Consistent with a tight ion pair



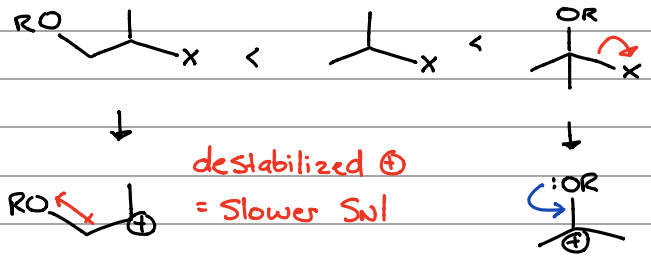
The Electrophile

- The R-group influences the lifetime of the carbenium ion

↑ Substitution → EDG
Stabilize carbenium ions
→ Speed up SN1 rxns



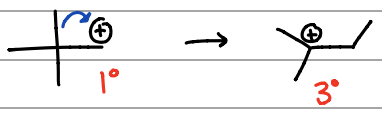
Increasing rate of solvolysis



pure inductive withdraw

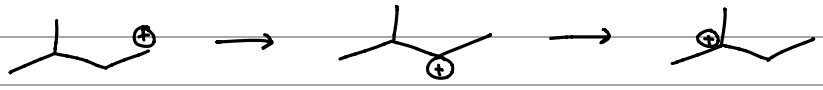
a bit of resonance donation

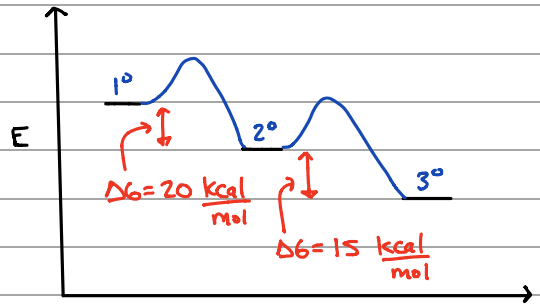
Carbocation Rearrangement



Thermodynamic Driving Force

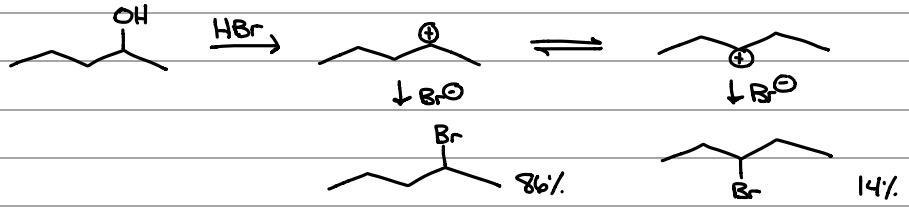
For a hypothetical:



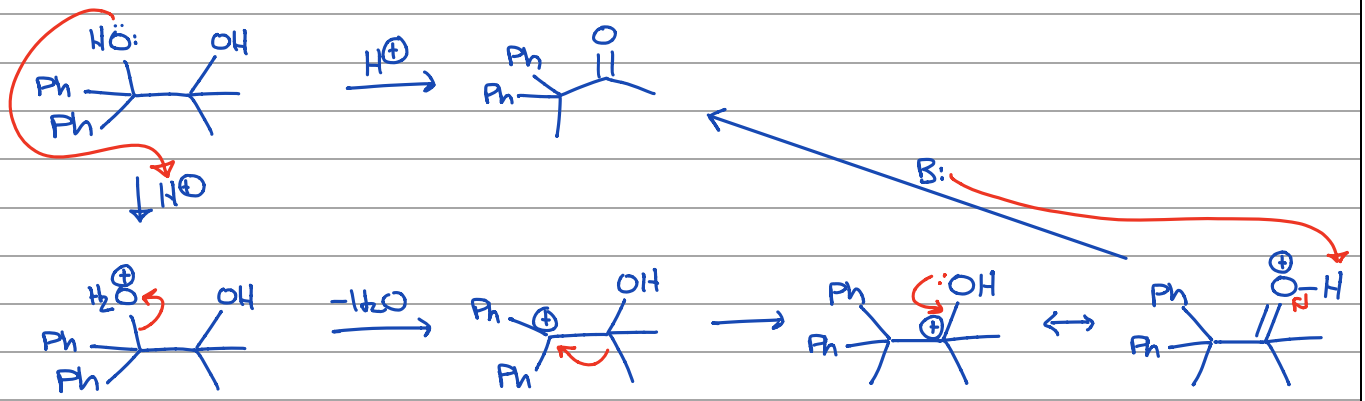


$\Delta G^{\ddagger}$ for rearrangement $< 5 \frac{kcal}{mol}$

Carbocation rearrangements occur even when the shift does not create a more stable ⊕.

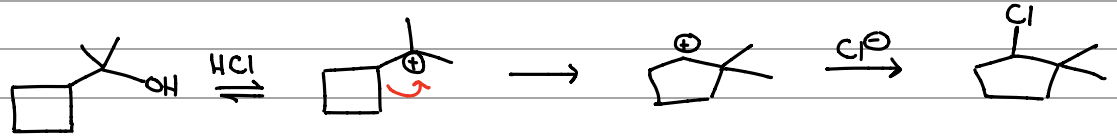


Pinacol Rearrangement:



Rearrangement can be driven by relief of ring strain

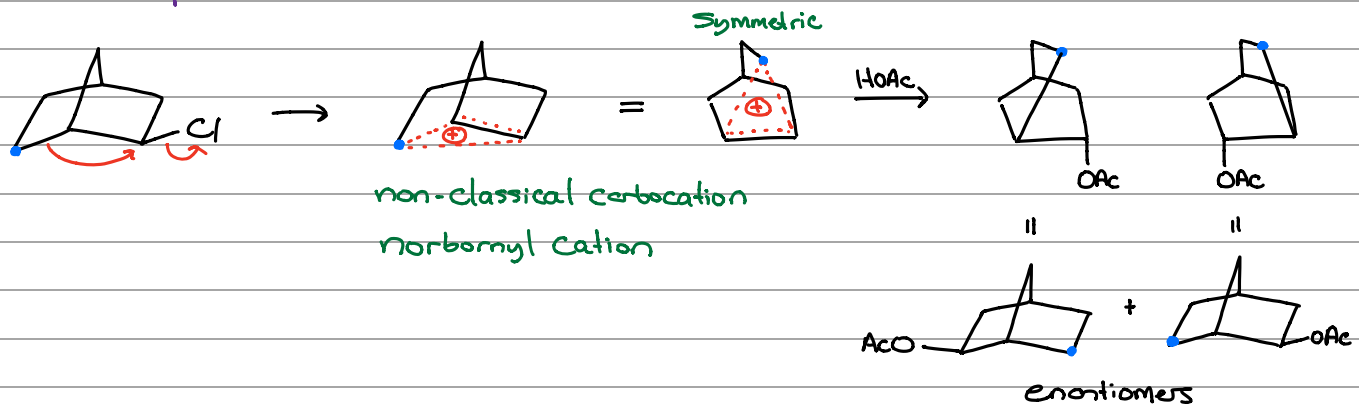
Ex 3:



Rearrangement despite 3° → 2° ⊕

Non-Classical Carbocations

Winstein Experiment



non-classical carbocation

norbornyl cation

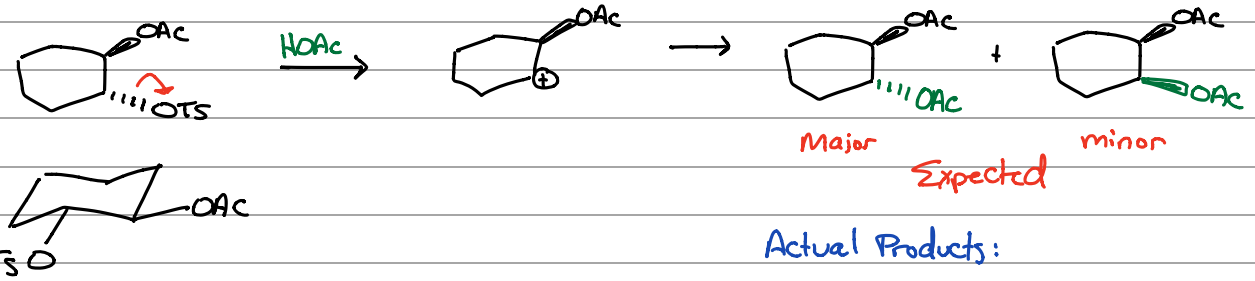
NMR equiv even at 5K

Calculations find this to be 2-4 kcal/mole more stable than the classic carbocation Strs.

Anchimeric Assistance in SN1

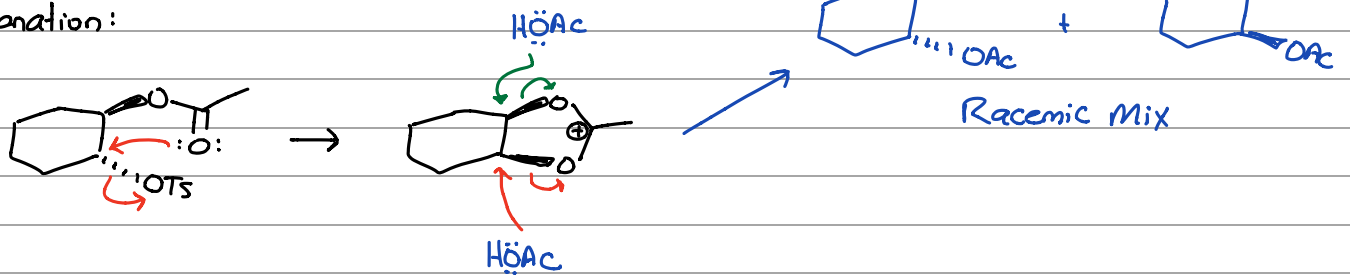
↳ aka Neighboring Group Participation

A donating pair of electrons on N, O, or S somewhere in the reactant assists in the ionization process



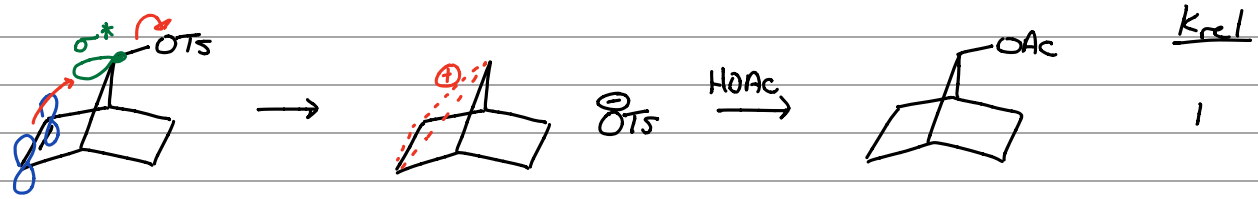
Actual Products:

Explanation:



Racemic Mix

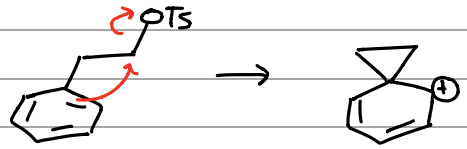
π bonds can also participate (π → σ* donation)



vs

10^{-7}

Aryl is also commonly involved in NG Participation



Leaving Group Effects

$F^{\ominus} < Cl^{\ominus} < Br^{\ominus} < I^{\ominus} < OTs \approx OMs < OH$

RF	RCl	RBr	RI	-O-S(=O)(=O)-OTol	-O-S(=O)(=O)-OMe	-O-S(=O)(=O)-OCF3
—	—	—	—	⇅		
		⇅	⇅			
	⇅					
⇅						

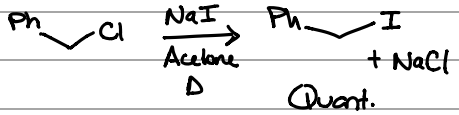
Lowest E Lumo to accept e⁻ pair

Finkelstein Rxn

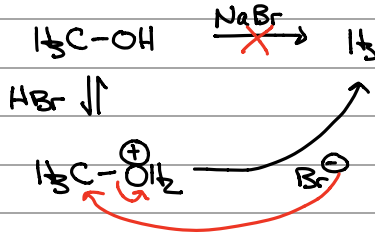
NaI + R-X' in acetone

good solubility in acetone

NaCl + NaBr have poor solubility in acetone = ppt formation drives the equilibrium



Improving a Poor L.G.



or $H_3C-OH \xrightarrow[Pyr]{TsCl} \xrightarrow{NaBr}$