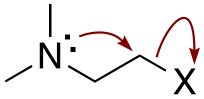
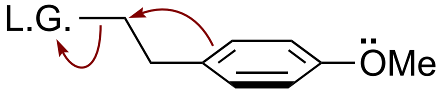
Professor David L. Van Vranken
Chemistry 201: Organic Reaction Mechanisms I

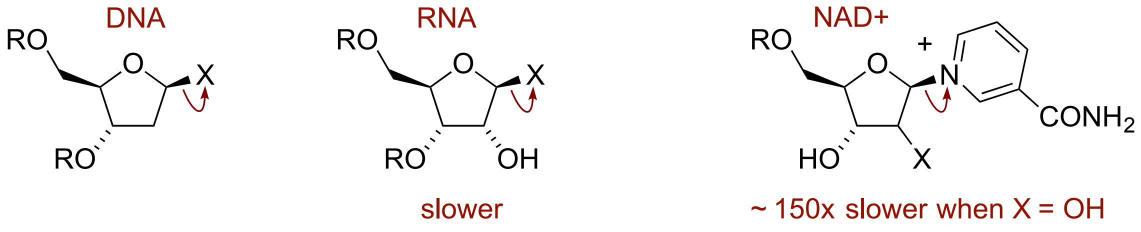
Topic 7 :
Neighboring Groups in Ionization Reactions





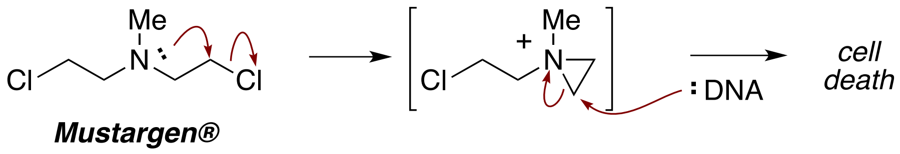
Neighboring Group Participation by Vicinal Heteroatoms

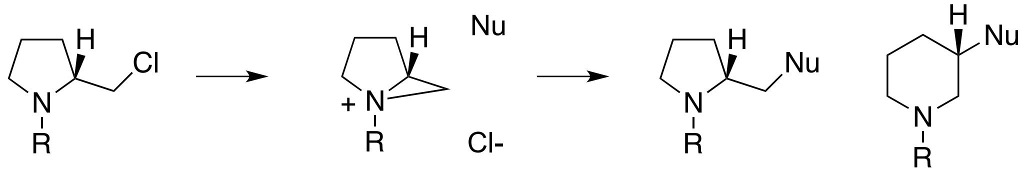
- Vicinal oxygen doesn't accelerate ionization; it slows it



Handlon, A.L.; Oppenheimer, N.J.
JOC **1991**, 5009–5010

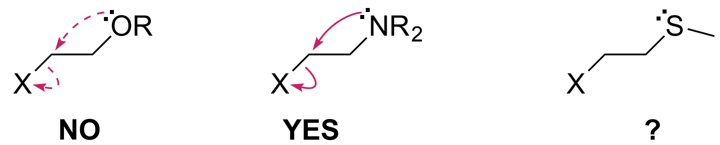
- Basic, nucleophilic amines can form strained aziridinium ions that are readily attacked.





- Intramolecular displacement reactions follow same kinetics as S_N1: rate = $\boldsymbol{k}$[R-X]
  Don't call them S_N2 reactions.

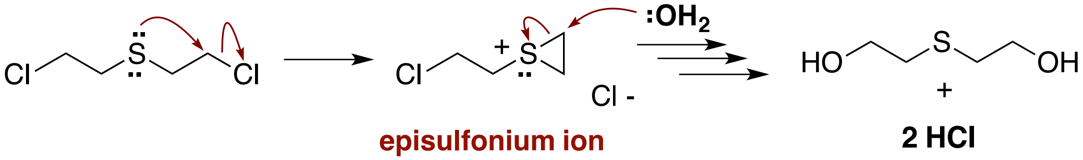
Contrast:



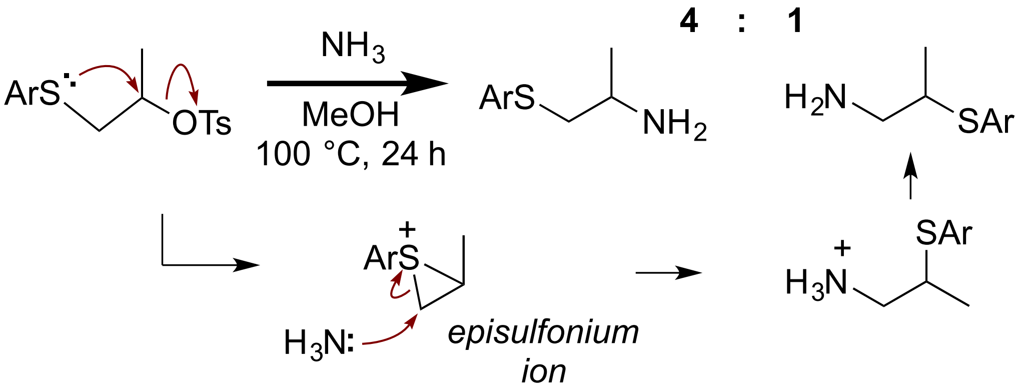
Neighboring Group Participation by 3rd Row Atoms

- British mustard gas casualties in WWI

Fatal:	4,086
Non-Fatal:	16,526



- Attack at the more substituted position of 3-membered ring "onium" ions.

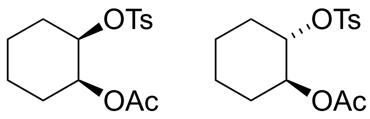


Nair, D. J.; David, J.; Nagarajan, K.
Indian J. Chem. B **1985**, *24*, 940.

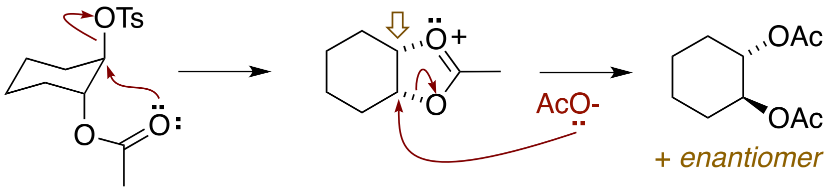
Neighboring Group Participation by Nearby Carbonyls

■ "Intramolecular S_N2" reactions follow same kinetics as S_N1: rate = $\boldsymbol{k}$[R-X]

■ Five and six-membered ring transition states are particularly favorable. Thus carbonyl oxgyen atoms can sometimes push out leaving groups five atoms away.



$\boldsymbol{k}_{rel}$	1	660



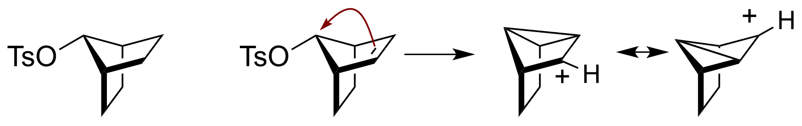
also attack here

+ *enantiomer*

Neighboring Group Participation by Pi Systems

- Pi systems separated from leaving groups by more than one carbon can not form delocalized pi carbocations.

- Homoallylic leaving groups can form cyclopropylcarbinyl cations.

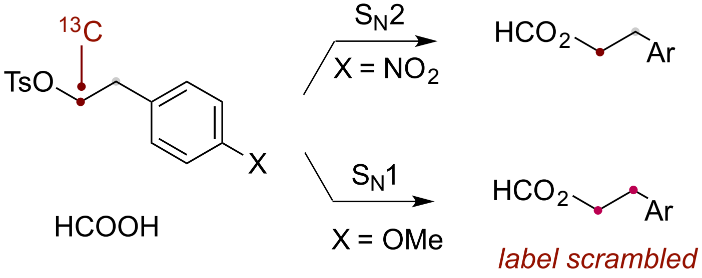


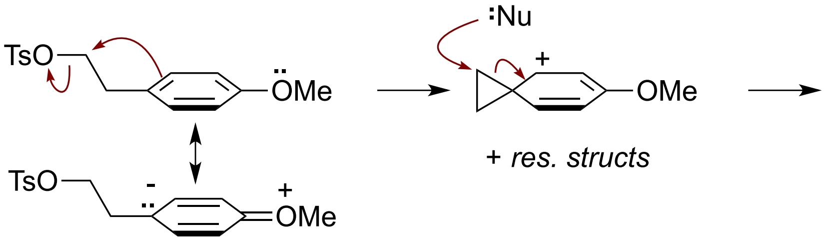
S_N1 $\boldsymbol{k}_{rel}$ 1 100,000,000,000 10^{11}

b/c cyclopropylcarbinyl

Winstein, S.; Shatavsky, M.; Norton, C.; Woodward, R. B.
J. Am. Chem. Soc. **1955**, *77*, 4183-4.

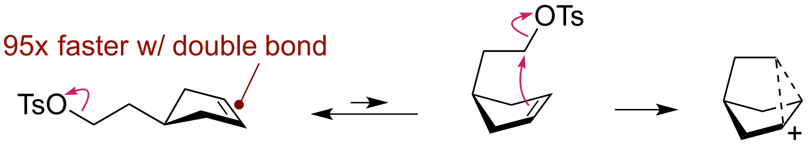
- Phenonium ions





Fujio, M.; Funatsu, M.; Goto, M.; Seki, Y.; Mishima, M.; Tsuno, Y.
Bull. Chem. Soc. Jpn. **1987**, *60*, 1091.

- Longer range participation by pi bonds.

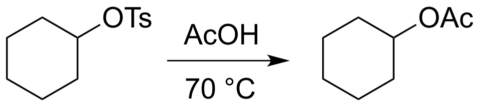


2-norbornyl
cation

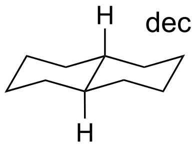
Lawton, R.G.
J. Am. Chem. Soc. **1961**, *83*, 2399.

Through-Space Hyperconjugation

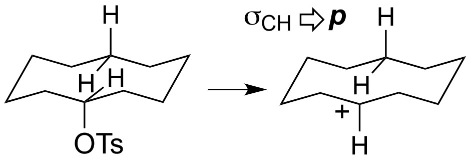
- Well aimed C-H bonds can also accelerate carbocation formation.



8,9,10-mem ring
= 200-400X faster



decalin = *no strain*

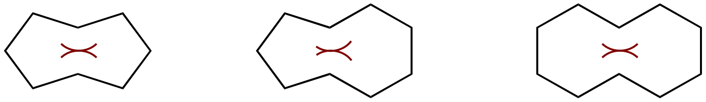


transannular interaction

ring size	k_{rel}
3	10^{-10}
4	11
5	14
6	1
7	25
8	190
9	170
10	380
11	50
12	3
>12	~1

Brown, H. C.; Ham, G.
"The Effect of Ring Size on the Rate of Acetolysis of the Cycloalkyl p-Toluene and p-Bromobenzenesulfonates."
J. Am. Chem. Soc. **1956**, *78*, 2735.

- It' very crowded in the middle of medium-sized rings (8,9,10); that makes them difficult to generate through cyclization reactions.



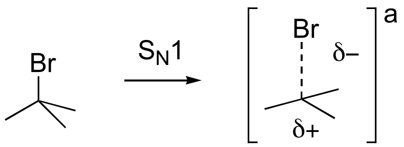
Chemistry 201: Organic Reaction Mechanisms

Lecture 8: Solvent Effects on Carbocation Formation

Read: **C&S 4.2**

Polar Solvents Speed Up S_N1

- Most ionization reactions are faster in polar solvents. Polar solvents favor charge separation.

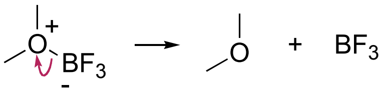


solvent	k_{rel}
$CHCl_3$	**1**
HCO_2H	**200,000**

Coulomb =

$$\Delta E = \frac{\delta^{+} \bullet \delta^{-}}{\varepsilon \, d}$$

- Not all dissociation processes are favored by polar solvents. Some do not involve creation of charge.



- The bulk dielectric constants range from 1-78. Coulomb's law doesn't explain everything.

Solvent	**ε**	
gas phase	**1**	
hexane	**1**	non-polar
Et_2O	**4**	
THF	**8**	
CH_2Cl_2	**9**	
MeOH	**33**	polar
DMF	**37**	
MeCN	**38**	
Me_2SO	**47**	
H_2O	**78**	

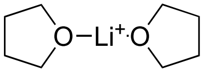
Explicit Effects of Solvent

- Even though THF has lower ε than CH_2Cl_2, it can accelerate ionization through donation

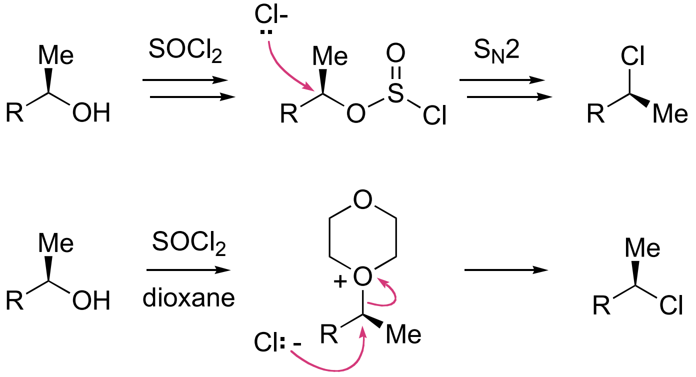
Proof that THF can donate:

LiBr
• soluble in ether
• not in CH_2Cl_2

why?



- An example of explicit solvent participation. Contrast the results of S_N2 in neat $SOCl_2$ versus dioxane



Lewis, E. S.; Boozer, C. E.
“The Kinetics and Stereochemistry of the Decomposition of Secondary Alkyl Chlorosulfites.” *J. Am. Chem. Soc.* **1952,** *74*, 308-311.

- Electronic structure calculations are good for comparing ground states, reactive intermediates, and transition states; but, they can’t anticipate solvent effects.