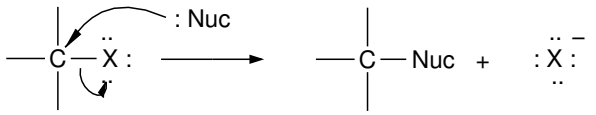
CHEM 20481 - Basic Organic Chemistry - Chapter 8 Review
Nucleophilic Substitution

General Reaction

$$\text{R-X} + :\text{Y}^- \longrightarrow \text{R-Y} + :\text{X}^-$$

R-X = Alkyl halide $\qquad$ $:\text{Y}^-$ = nucleophile

S_N2 Mechanism



rate = k[alkyl halide]^1[nucleophile]^1

This reaction proceeds with inversion of stereochemisty if the carbon atom being attacked is a stereogenic center.

Factors affected S_N2 reactivity

- **Alkyl Halide:** The transition state of this reaction requires a pseudo five-coordinate transition state, so the reaction is faster for less hindered alkyl halides.

$$\text{CH}_3\text{X} > 1^\circ > 2^\circ$$

- **Leaving Group:** This reaction involves breaking a C-X bond, so 'better' leaving groups give faster reactions.

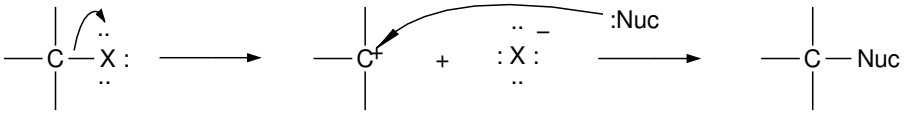
$$\text{I} > \text{Br} > \text{Cl} >> \text{F}$$

- **Nucleophile Strength:** The rate-limiting step of this reaction involves the nucleophile, so stonger (better) nucleophiles increase the rate of these reactions.

$$\text{I}^-, \text{SR}^- > \text{Br}^-, \text{OR}^-, \text{CN}^-, \text{N}_3{}^- > \text{NH}_3, \text{Cl}^-, \text{F}^-, \text{RCO}_2{}^- > \text{H}_2\text{O}, \text{ROH} > \text{RCO}_2\text{H}$$

- **Solvent:** These reactions are best (fastest) in polar, aprotic solvents

S_N1 Mechanism



rate = k[alkyl halide]^1

Due to formation of a trigonal planar carbocation intermediate, this reaction proceeds with (at least partial) racemization if the carbon atom being attacked is a stereogenic center. (A mixture of "R" and "S" forms is produced). Carbocation rearrangements can also occur with this mechanism.

Factors affected S_N1 reactivity

- **Alkyl Halide:** Since a carbocation is produced as an intermediate in the rate-limiting step of this reaction, the reaction is fastest for molecules containing more stable carbocations.

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

- **Leaving Group:** The rate-limiting step of this reaction involves breaking a C-X bond, so 'better' leaving groups give faster reactions.

$$\text{I} > \text{Br} > \text{Cl} >> \text{F}$$

- **Nucleophile Strength:** Attack of the carbocation by the nucleophile is always a fast step for these reactions, so nucleophile strength is not a significant factor in these reactions. Poor nucleophiles work just as well as good nucleophiles.
- **Solvent:** These reactions are best (fastest) in protic solvents. (Solvents containing a H-O bond).

Substitution vs. Elimination

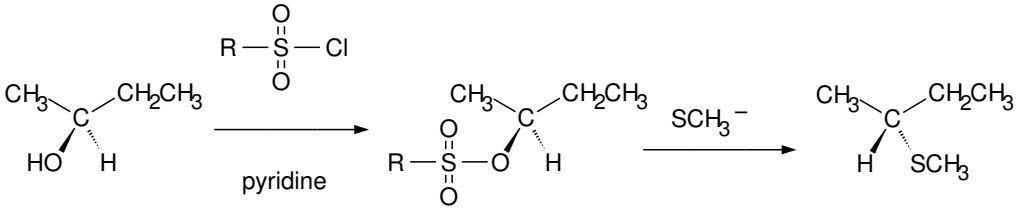
The following table summarizes the most common trends in relative reactivity

	Strong Base	**Good Nucleophile**	**Poor Nucleophile**
3°	E2	S_N1	S_N1 (and E1)
2°	E2	S_N2	S_N1 with protic solvent
		(best with aprotic solvent)	(NR with aprotic solvent)
1°	S_N2	S_N2	NR or S_N2 with aprotic solvent
	(E2 with bulky base)		(NR with protic solvent)

Sulfonate Esters

Alkyl sulfonates (RSO_2Cl) react readily with alcohols to produce sulfonic esters in a reaction that does NOT change the stereochemistry of the carbon center. The sulfonate is an excellent leaving group (better than I), and readily undergoes substitution reactions.

Ex.



S S R