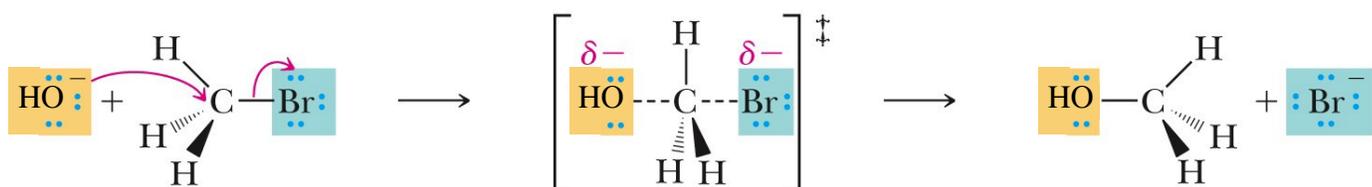


## Summary of Chapter 11

### $S_N2$ Reaction



**Reaction:** One-step, 180°, backside approach of nucleophile leads to inversion of reaction center

**Substrate/** NO  $S_N2$  ON A TERTIARY-SUBSTITUTED SUBSTRATE!!  
**Electrophile:** order of reactivity is as follows: Methyl > 1° > 2°

**Nucleophile:** Anionic nucleophiles are usually stronger than neutral ones, and favor  $S_N2$

Nucleophilicity increases moving to the left on the periodic table (i.e.  $C^- > N^- > O^-$ )

For the halogens:  $I^- > Br^- > Cl^- > F^-$

**Leaving Group:** Best leaving groups are those that can stabilize a negative charge (usually halogen or resonance delocalized anion)

Poor leaving groups include:  $F^-$ ,  $HO^-$ ,  $CH_3O^-$ ,  $H_2N^-$ ,  $R_3C^-$

The best leaving groups are:  $H_2O$  (neutral),  $TsO^-$  (resonance stabilized),  $I^-$  (larger anions stabilize negative charges better than smaller anions)

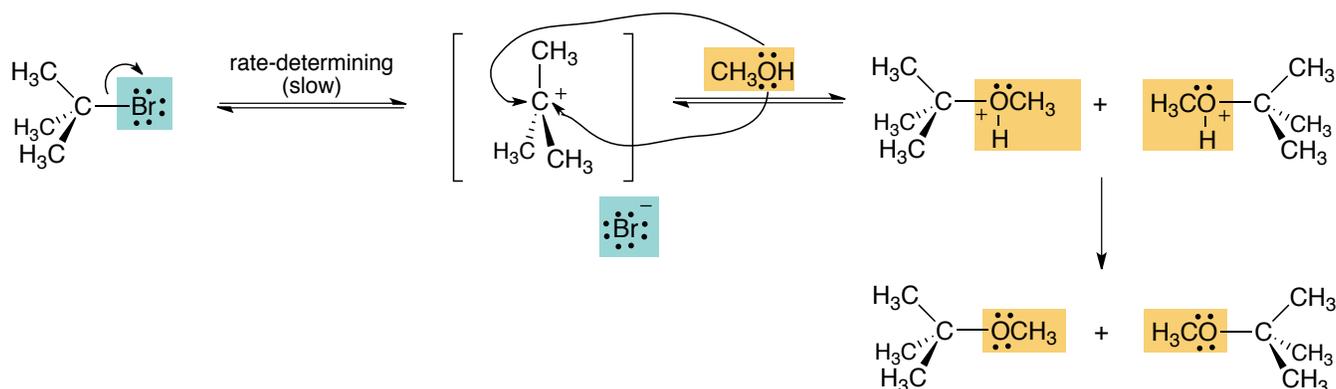
**Solvent:** Polar aprotic solvents stabilize the transition state and speed  $S_N2$  reactions up

Polar aprotic solvents include DMSO, DMF,  $CH_3CN$ , HMPA, Acetone

Polar protic solvents are the worst for  $S_N2$ ; they solvate the nucleophile, making it less likely to attack

**Rate:** The  $S_N2$  reaction is bimolecular, which means the rate depends on the concentration of two molecules (nucleophile and substrate)

## S<sub>N</sub>1 Reaction



**Reaction:** Two-step reaction; proceeds through planar sp<sup>2</sup>-hybridized intermediate; mixture of stereochemistry (racemic mixture)

**Substrate/ Electrophile:** NO S<sub>N</sub>1 ON A METHYL OR PRIMARY-SUBSTITUTED SUBSTRATE!!  
3° > 2°. Benzylic and Allylic carbons have increased reactivity because of resonance stabilization

**Nucleophile:** WEAK nucleophiles favor S<sub>N</sub>1 while STRONG nucleophiles favor S<sub>N</sub>2

**Leaving Group:** same as S<sub>N</sub>2

**Solvent:** Polar protic solvents stabilize the carbocation intermediate, but sometimes aprotic works as well

**Rate:** The S<sub>N</sub>1 reaction is unimolecular, which means the rate depends only on the concentration of one molecule (substrate/electrophile)

**Other:** Watch out for CARBOCATION REARRANGEMENTS!

## E2 Reaction

**Substrate:** Requires anti-periplanar geometry between the L.G. and hydrogen  
Relative rates of reaction:  $1^\circ > 2^\circ > 3^\circ$

**Stereochemistry/Regiochemistry** The stereochemistry of the starting material will determine whether you get the Z or E isomer when possible

Typically favors the Zaitsev product

**Rate:** This is a bimolecular reaction whose rate depends on the base and substrate used

**Bases:** The following bases give mostly E2 on  $3^\circ$  and  $2^\circ$  alkyl halides  $^-OH$ ,  $^-OCH_3$ ,  $^-OCH_2CH_3$ ,  $^-OC(CH_3)_3$

## E1 Reaction

**Substrate:** Works best on  $3^\circ$  (and  $2^\circ$ ) substrates  
Does not require the anti-periplanar geometry!

**Stereochemistry/Regiochemistry** This reaction proceeds through a carbocation intermediate!  
Typically favors the Zaitsev product

Watch out for **CARBOCATION REARRANGEMENTS!**

**Rate:** This is a unimolecular reaction whose reaction rate depends only on the concentration of the substrate.

**Other:** For substrates containing  $3^\circ$  alkyl halides or other good leaving group, this reaction can compete with the  $S_N1$

## E1cB Reaction

**Substrate:** Look for potential (resonance) stabilized anion formation

## Substrates

Methyl:	Only S <sub>N</sub> 2 is possible
Primary:	S <sub>N</sub> 2 Main reaction with non-basic nucleophiles and where pK <sub>a</sub> of conjugate acid is < 11 -SH, -SR, -CN, -N <sub>3</sub> , NH <sub>3</sub> , NR <sub>3</sub> , -X, -C≡CR, RCO <sub>2</sub> <sup>-</sup>
	E2 Main reaction with strong/bulky bases and where pK <sub>a</sub> of conjugate acid is > 11 -OH, -OR, -NH <sub>2</sub> , -NHR, -NR <sub>2</sub> , -OC(CH <sub>3</sub> ) <sub>3</sub>
	S <sub>N</sub> 2/E2 Weak nucleophiles/bases such as H <sub>2</sub> O, ROH, RCO <sub>2</sub> H give mixtures of S <sub>N</sub> 2 and E2 unless benzylic or allylic - then mixture of S <sub>N</sub> 1 and E1
Secondary:	S <sub>N</sub> 2 Main reaction with non-basic nucleophiles and where pK <sub>a</sub> of conjugate acid is < 11 -SH, -SR, -CN, -N <sub>3</sub> , NH <sub>3</sub> , NR <sub>3</sub> , -X, -C≡CR, RCO <sub>2</sub> <sup>-</sup>
	E2 Main reaction with strong/bulky bases and where pK <sub>a</sub> of conjugate acid is > 11 -OH, -OR, -NH <sub>2</sub> , -NHR, -NR <sub>2</sub> , -OC(CH <sub>3</sub> ) <sub>3</sub>
	S <sub>N</sub> 1/E1 Common in reactions with weak bases/nucleophiles in protic solvents
Tertiary:	E2 Main reaction with strong/bulky bases: -OH, -OR, -NH <sub>2</sub> , -NHR, -NR <sub>2</sub> , -OC(CH <sub>3</sub> ) <sub>3</sub>
	S <sub>N</sub> 1/E1 Main reaction with poor nucleophiles/weak bases in protic solvent