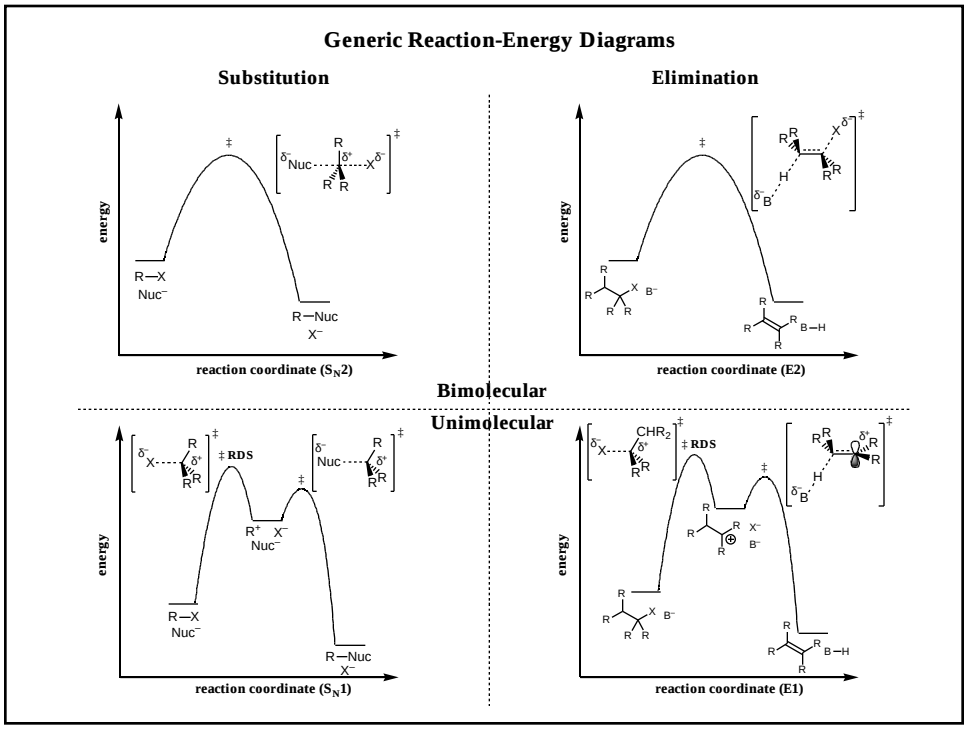
Chemistry 5.12 Spring 2003, Handout #9

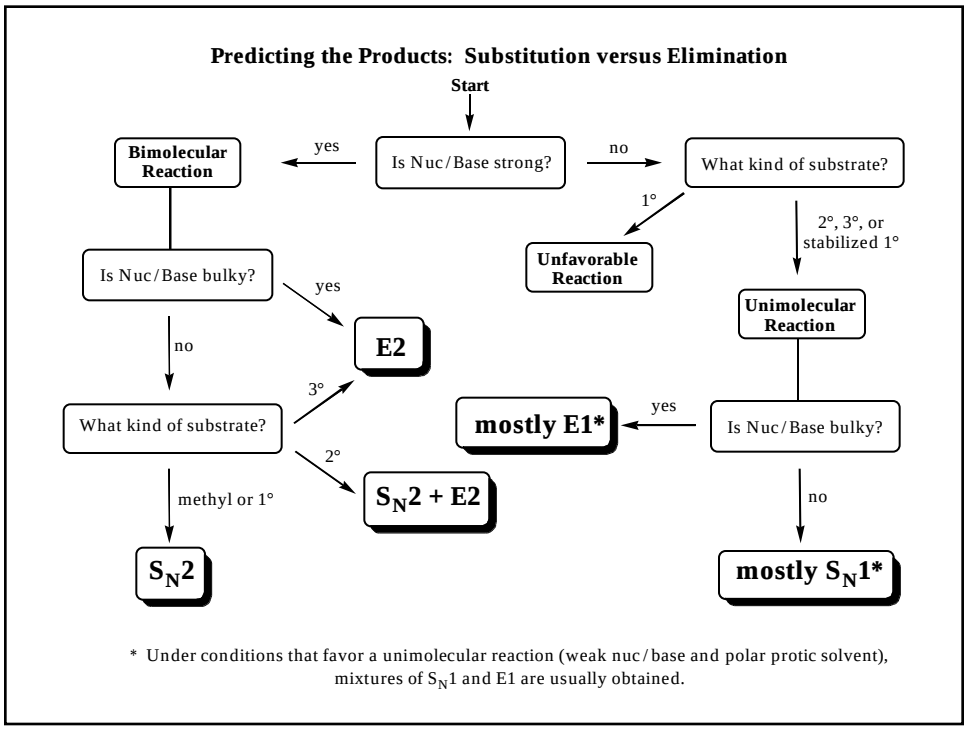
Substitution Reactions (S_N2 versus S_N1)

	S_N2	S_N1
Mechanism:	**Concerted**	**Two Steps (Look for carbocation rearrangements.)**
Rate Equation:	**Rate = k_r[R–X][Nuc]**	**Rate = k_r[R–X]**
Stereochemistry:	**Stereospecific (inversion)**	**Loss of Stereochemistry**
Substrate:	**Sterics** (methyl > 1° > 2°) **No S_N2 with 3°! Orbital Overlap** (methyl benzylic > allylic > 1°)	**Cation Stability** (benzylic > allylic > 3° > 2°) **No 1° or methyl R^+ without extra stabilization!**
Nucleophile:	**Strong/Moderate Required** strong: RS^-, I^-, R_2N^-, R_2NH, RO^-, CN^- moderate: RSH, Br^-, RCO_2^-	**Not Important**
Leaving Group:	**Moderately Important** (same trend as S_N1)	**Very Important** (–OTf >> –OTs –OMs >> –I > –Br > –Cl)
Solvent:	**Polar Aprotic**	**Polar Protic**

Elimination Reactions: E2 versus E1

	E2	E1
Mechanism:	**Concerted**	**Two Steps (Look for carbocation rearrangements.)**
Rate Equation:	**Rate = k_r[R–X][Base]**	**Rate = k_r[R–X]**
Stereochemistry:	**Stereospecific (antiperiplanar TS)**	**Not Stereospecific**
Substrate:	**Alkene Stability** (3° > 2° > 1°)	**Cation Stability** (benzylic > allylic > 3° > 2°)
Base:	**Strong Base Required** (RO^-, R_2N^-)	**Not Important: Usually Weak** (ROH, R_2NH)
Leaving Group:	**Moderately Important** (same trend as S_N1)	**Very Important** (same trend as S_N1)
Solvent:	**Wide Range of Solvents**	**Polar Protic**
Product Ratio:	**Saytzeff Rule:** The most highly substituted alkene usually predominates. **Hofmann Product:** Use of a sterically hindered base will result in formation of the least substituted alkene (Hofmann product).	





* Under conditions that favor a unimolecular reaction (weak nuc/base and polar protic solvent), mixtures of S_N1 and E1 are usually obtained.