

Organic Chemistry I
Substitution / Elimination
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 Summary table of S_N1, S_N2, E1, E2

	S _N 1	S _N 2	E1	E2
Mechanism	stepwise	concerted	stepwise	concerted
Rate	1 st order	2 nd order	1 st order	2 nd order
Substrate	3°>2°, allyl	MeX>1°>2°	3°>2°, allyl	3°>2°>1°
Leaving group	excellent	good	excellent	good
Base/Nu	nonbasic	strong Nu and unhindered	weak base	strong base (hind. favors)
Carbocation	yes	no	yes	no
Rearrangement	possible	no	possible	no
Attack	either side	back side	coplanar	coplanar
Stereochem.	racemization	inversion	Saytzeff rule	Saytzeff rule
Solvent	polar	depends	polar	depends

Saytzeff's rule: In an elimination reaction, the more highly substituted alkene, which is also the most stable alkene, will be formed predominantly.

Nucleophiles vs. bases:

Bases: Defined by thermodynamics (stability of starting material vs. products).

Basicity increases from right to left and from bottom to top on a periodic table.

(Basicity: NH₃ > H₂O and ROH > RSH)

Good bases typically are electron rich, bulky and non polarizable.

Nucleophiles: measured by kinetics and transition state.

Good nucleophiles are electron rich, polarizable, have low electronegativity, and are unhindered.

Trend of nucleophilicity: Increases from right to left, and from top to bottom.

(Nucleophile: NH₃ > H₂O and RSH > ROH)

Strong Nu that are not basic: I⁻, RS⁻, Br⁻, CN⁻, N₃⁻

Fair Nu and moderately basic: NH₃

Strong Nu but very basic: HO⁻, RO⁻

Weak Nu and weakly basic: ROH, H₂O, Cl⁻

Leaving groups: Good LGs are typically weak conjugate bases. Good LGs create strong dipole, are polarizable, and stable after departure.

Procedure:

- I. Identify the substrate (electrophile) and nucleophile / base in each reaction.
 - A. Substrate (electrophile)
 1. Identify the leaving group (LG) p. 248 (table 6.4), and decide on quality of LG.
 2. Is the carbon bonded to the LG sterically hindered? Classify as 1°, 2°, 3° (allylic or benzylic)
 3. Make initial assessment of potential pathways.
 - B. Nucleophile / Base
 1. Identify the nucleophilic portion of the nucleophile.
 2. Is it sterically hindered?
 3. Is it strongly or weakly nucleophilic?.
 4. Is it strongly or weakly basic?
- II. Combine assessment of the electrophile and nucleophile to determine potential reactions.
- III. Beware of rearrangements if a carbocation is favored under reaction conditions. Use correct stereochemistry, and remember Saytzeff's rule.

Never:

1. Form a carbocation in the presence of a strong or moderate base. If the conjugate acid of the base has a $pK_a > 8$, no carbocation!
2. Form a methyl or even a 1° carbocation unless it is resonance stabilized.
3. Perform S_N2 on a 3° carbon bearing a leaving group.

Always:

1. Form S_N2 product with unhindered electrophile with good leaving group, reacting with a strong nucleophile that is weakly basic. (I,RS')
2. E2 elimination proceeds through coplanar orientation of leaving group and proton being abstracted, and almost always in anti formation.
3. E2 product formation with strong base and hindered electrophile.
4. S_N2 and E2 proceed through concerted, stereospecific, one step, 2nd order reaction.
5. S_N1 and E1 proceed through stepwise, 1st order reaction.