

Ten Principles for learning Organic Chemistry 1

1. Carbon always has 4 bonds in any stable organic molecule

- Oxygen always has 2 bonds
- H, Cl, Br have 1 bond

2. Reactions occur at functional groups

- Not on alkane chains or rings unless activated by functional group
 - Such as hydride shifts or (next term) carbonyl groups
- Exception = free radical halogenation
- In any reaction, draw out all four substituents on the carbons at the reactive site
 - In both starting material and product

3. Nomenclature is critical

- Learn first ten hydrocarbons
- All IUPAC rules for functional groups
- Common names for compounds with 1-4 carbons
 - Cyclo - means ring
- Be familiar with frequently used terms: base, nucleophile, orbital, sp^3 , substitution, carbocation, exothermic, transition state, intermediate, etc.

4. Become comfortable with Stereochemistry

- Enantiomers (mirror images; R and S rules)
- Related principles (diastereomers, reactivity, meso compounds)
- Ring stereoisomers (cis and trans)
- Alkene isomers (cis and trans; Z and E)
- Newman projections and conformations of butane and cyclohexane

5. If the reagent is acidic (or acid-catalyzed), initiate reaction by creating a positive charge

- Put H^+ onto an oxygen or onto an unsaturated carbon
- Similar reagents can be Br^+ , Hg^{+2}

6. Know your nucleophiles (N: or N: -)

- They have a pair of electrons and are also bases
 - Nucleophile can remove a proton (eg, act as a base)
 - Nucleophile can form a bond to an electron deficient carbon
 - carbocation
 - carbon with good leaving group (C-X)
 - carbon of carbonyl group - ch. 12
 - Strong bases are more likely to remove protons ($-NH_2$, $-OH$, $-OR$)
 - Weak bases ($-Br$, $-I$, $-CN$, $-SR$, H_2O) are more likely to form a bond with C
 - Normal bases (OH^- , methoxide, ethoxide) follow Zaitsev

7. If reagent is neutral or an anion, then the first step is often attack of the nucleophile

- Can act as a base if there is an acidic hydrogen (COOH, OH, terminal alkyne)
- Can act as a base if concerted loss of leaving group (E2)
- Otherwise N attacks a carbon
- Sometimes, the organic compound may ionize first before nucleophile attacks
 - SN_1 , E1

8. Identify primary, secondary, and tertiary positions at the functional group

- Tertiary positions favor carbocation processes
 - SN_1 and E1
- Primary positions avoid carbocations, but are open to direct attack
 - SN_2 reactions
 - Less hindered, better yields in most substitution reactions
- Markovnikov's Rule - add an unsymmetrical reagent to an alkene so as to put the more positive end (H^+ , Br^+ , Hg^+ , B in BH_3) on the less substituted C.
- Relative stability of alkenes: more alkyl groups = more stable
 - Elimination with most bases produces more stable alkene (Zaitsev)
 - Sterically hindered base ($KO-t-Bu$) gives Hofman product
- Free radical reactions also favor tertiary (bromine is most selective)

9. Consider Stereochemistry of reactions

- **Inversion at reaction center in Sn2 reactions**
 - (racemization if Sn1)
- **Addition to double bonds can be syn, anti, or mixed**
 - **Syn** if simultaneous addition of both halves of a reagent
 - H₂ + cat., OsO₄ and KMnO₄, BH₃,
 - **Anti** if bridged ion
 - Br⁺, opening of epoxides
 - exception: Hg²⁺ adds anti, but loses configuration when Hg removed by reduction

10. Synthesis principles

- For a complex series of steps, work backwards (retrosynthesis)
- Look carefully at the needed positions of functional groups
 - Including regioselectivity
 - And stereochemistry
- Be especially comfortable with key conversions
- Alkane = can brominate selectively at tertiary
- Cis alkene: alkyne + hydrogen + nickel boride (P-2) catalyst
- Trans alkene: alkyne + reduction with Na or Li in ammonia or amine
- To extend carbon chains: terminal alkyne with NaH or NaNH₂
 - Then primary alkyl halide or other group susceptible to Sn₂ (e.g., epoxide)
- **KOtBu** for Hoffman elimination, KOH or KOEt
- After devising a synthesis that might work, review each step