ORGANIC CHEMISTRY

BY

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Preface

Organic Chemistry and General Chemistry are totally different animals. While Gen Chem is almost entirely conceptual, details in OChem only serve to separate the A's from the A-minuses, A-minuses from the B-pluses. Sometimes details will save you, but the bulk of understanding comes through practice problems (much like maths).

That being said, I still compiled this book because the beginning of OChem (at least at UC Berkeley) is very much like Gen Chem review, and details were quite important for the first one-third of the class. I will be adding OChem practice questions once I figure out how to integrate ChemDraw into LaTeX.....

Until then, feel free to reach out to me at derek.wan11[*at*]berkeley.edu if you find any blatant mistakes or would like to offer any suggestions.

Contents

Chapter 1

Structure and Bonding in Organic Molecules

**No details for this section.

1.1 Recommended Book Problems

- 25b
- 25f
- 25h
- 25i
- 27i
- 29b
- 29c
- 31d
- 34
- 53-57

Chapter 2

Structure and Reactivity

2.1 Details

1. Prefixes: Neo vs. Iso? Sec vs. Tert?
2. What are Vollhardt's versions of the equilibrium formulas?
3. Define: nucleophile and electrophile
4. What are four factors that affect reaction rates?
5. How do you relate the reaction constant k to the activation energy?
6. What are some ways to determine relative acidity?
7. Define a constitutional isomer.
8. Prefixes for multiple branched substituents that are the same? (i.e., the equivalent of di/tri in branched substituents?)

2.2 Recommended Book Problems

- 27a through 27c
- 30a through 30f
- 36
- **37**
- 38
- 41
- 44
- 46b and 46c
- 48

Chapter 3

Reactions of Alkanes

3.1 Details

1. Why does hyperconjugation stabilize molecules?
2. Describe the two ways you can make the initial bond break in the initiation step of radical halogenation.
3. Describe the three steps of radical halogenation.
4. Describe the differences among alkane halogenation reactions (differences among different halogens).
5. What is the relationship between exothermic/endothermic reactions and early/late transition states?

3.2 Recommended Book Problems

- 20-27
- 30 (heard of some reports of an error in the solutions book for this one)
- 34
- 38
- 46-49

Chapter 4

Cycloalkanes

4.1 Details

1. Two main rules to keep in mind when naming alkanes attached to cyclic compounds?
2. How does numbering in cyclic compounds work?
3. Define stereoisomer.
4. Why do cyclic compounds have higher heats of combustion than predicted from looking at individual CH_2 bonds?
5. Three factors that contribute to ring strain?
6. What is "banana bonding"?
7. Describe the potential energy diagram of cyclohexane stereoisomers.
8. How do you draw the cyclohexane chair conformer?
9. Why are isomers with equatorial substituents favored over isomers with axial ones?
10. Why does the largest substituent "win" in the competition between substituents to grab equatorial positions?
11. Name the stereochemical relationships: cis-1,2; trans-1,2; cis-1,3; trans-1,3; cis-1,4; trans-1,4.
12. How do you tell whether a ring with 2 substituents, drawn in its 3-dimensional form, is cis or trans?
13. Why are methyl groups more likely to be in equatorial positions instead of halogens?

4.2 Recommended Book Problems

- 23-26
- 30
- 32b and 32d
- 34
- 41a
- 54-57

Chapter 5

Stereoisomers

5.1 Details

1. Define racemate/racemic mixture
2. Quick shortcut to determine chirality?
3. What does it mean for a molecular to be dextrorotary or levorotatory?
4. Rules for determining R/S?
5. Talk about relationship between tweaking Fischer projections and enantiomers.
6. Can you get an optically active mixture from an optically inactive mixture?
7. Can you get an optically inactive mixture from an optically active mixture?

5.2 Tips

- When checking for planes of symmetry, don't forget about coplanar planes
- Hierarchy to determining chirality/meso (to save time on exams):
  (a) If there is a plane of symmetry, it is definitely achiral (chiral molecules CANNOT have a plane of symmetry)
  (b) If two of the substituents on a carbon atom are the same, the atom is NOT a stereocenter.
  (c) If there is no stereocenter, the molecule is achiral. Therefore, all non-substituted alkanes/alkenes/alkynes are achiral, combining concepts (c) and (b).
  (d) If there is a stereocenter, first check if the molecule is meso. If it's not meso, it is chiral.
  (e) (only as a last resort) If it can be superimposed on its mirror image it is definitely achiral–otherwise it is chiral.
- When drawing a substituent with stereochemistry, first draw the substituent as facing toward you (wedged). Check if this makes the molecule R or S. If it's in the wrong orientation, then flip the substituent so it is dashed. This may seem obvious–but this is far more efficient than the alternative, which is to imagine your head as being within the page–facing outward–and trying to visualize whether a dashed substituent makes the molecule R or S.

5.3 Recommended Book Problems

- 33-34
- 36

- 38-39
- 41
- 44-45

Chapter 6

Haloalkanes

6.1 Details

1. Bond strength of haloalkanes going down the periodic table? Boiling point trends going down the periodic table?
2. Discuss the placement of charges when you have an incoming negatively charged nucleophile vs. an incoming neutral nucleophile.
3. What do you call the nucleophile in acid-base reaction?
4. Why can't you use ΔH^o values for nucleophilic substitution in haloalkanes?
5. Why are tertiary halides notably absent from the list of reactions?
6. How many intermediates are formed in S_N2 reactions? What is the reaction order of S_N2?
7. What is an example of a concerted reaction?
8. Are S_N2 reactions stereospecific?
9. Can you replace a substituent without inverting the molecule?
10. Does inversion guarantee R-to-S or S-to-R?
11. Does halogenation of a molecule with two or more stereocenters invert the entire molecule?
12. What are the three consequences of inversion?
13. What are some characteristics of a good leaving group?
14. Halides as leaving groups–increasing leaving group ability going UP or DOWN the periodic table?
15. Moving across from left to right of the periodic table–increasing ability to leave or decreasing?
16. More resonance in the leaving group–increasing ability to leave or decreasing?
17. What are 2 examples of good leaving groups that "defy" the rules?
18. What is the relationship between charge and nucleophilic character?
19. What is the relationship between basicity and nucleophilic character? How does this manifest in the periodic table?
20. Does basicity increase or decrease down the periodic table? What about nucleophilicity, in protic solvents? Why?

21. Give another reason for the increasing nucleophilicity moving down the table (you may have already answered this).
22. Nucleophilic trends in polar aprotic solvents?
23. Three rules about steric effects? (leaving groups, attacking groups, branching about the carbon atoms)
24. Seven common good nucleophiles?

6.2 Recommended Book Problems

- 31c to 31f
- 36d to 36g
- 38c to 38f
- 41a
- 41f
- 42
- 44 to 48
- 56c and 56d
- 57
- 63 to 66

Chapter 7

More On Haloalkanes

7.1 Details

1. How many steps in S_N1?
2. Five characteristics of S_N1?
3. How do the potential energy graphs of S_N1 compare to those of S_N2?
4. Discuss the stereospecificity of the S_N1 reaction.
5. Intuitive way to understand the effect of solvent polarity on the rate of S_N1 reactions?
6. What effect does the nucleophile have on the rate of the S_N1 reaction?
7. Why is S_N1 possible?
8. With secondary carbocations, which is favorable for S_N2/S_N1: good leaving group in polar protic solvent? High concentration of good nucleophile in polar aprotic solvent?
9. What is the relationship between the ratio of S_N1:E1 and the leaving group?
10. Which C-H bonds become acidic once the leaving group is gone?
11. How do you increase the E1:S_N1 ratio?
12. Which is fastest? E2, S_N1, E1, or S_N2?
13. What is removed in the transition state of E2?
14. What effect does changing hydrogen to deuterium have on the rate of the E2 reaction?
15. What kind of stereochemistry is best for E2?
16. How stereospecific is the E2 reaction?
17. What happens to nucleophilic strength if you take something like cyanide and replace Na^+ with H^+? (as in NaCN vs HCN)
18. Discuss reaction predictions with secondary alkanes. Highly polar medium, good leaving group, weak nucleophiles means? High concentrations of good weakly basic nucleophiles? High concentration of strong base?

7.2 Recommended Book Problems

- 25
- 26f
- 27
- 30 to 37
- 38a, 38c, 38d
- 39a, 39c
- 40a (all of it), 40b to 40d just identify
- 41 to 43
- 46 and 47
- 49
- 53
- 57
- 62 to 66

Chapter 8

Intro to Alcohols

8.1 Details

1. What is the difference between methoxy and hydroxymethyl?
2. Three ways to make alcohols?
3. How do you name cyclic alcohols that have cis/trans orientations? (actually applies to all cyclic compounds–even for warmup questions this one may be excessively redundant...)
4. Three factors that affect the acidity of alcohols?
5. How do you find K when given the pK_a values of both sides of an equilibrium?
6. How do you solve the common problems in alcohol synthesis?
7. What are the two reagents most commonly used in reducing aldehyde and ketones? What are the differences between them?
8. Best ways to oxidize alcohols in different situations? (i.e., primary alcohol vs secondary alcohol)
9. What kind of solvent does the Grignard reagent need to be in?
10. Two properties of organometallics?
11. Can lithium make R-X into RLi?
12. What happens in the hydrolysis of a Grignard reagent?
13. General rules of thumb when doing retrosynthesis?

8.2 Recommended Book Problems

- 24
- 25 (not a)
- 26
- 28 and 29
- 30b
- 32
- 34

- 36
- 38
- 39a
- 40
- 43a, b, and e
- 46
- 48
- 51a, d, and g
- 52a and g
- 53
- 54 (especially c)
- 55a and 55b
- 56
- 63-66

Chapter 9

Further Reactions of Alcohols

9.1 Details

1. What are some bases that are strong enough to deprotonate R-OH?
2. When and why do you use PBr_3 instead of HBr? (or $SOCl_2$ and PCl_2 instead of HCl)
3. How do you make ethers in different conditions (i.e., primary + primary vs. secondary + tertiary, symmetrical, etc)
4. When do hydride shifts occur?
5. When are alkyl shifts fast?
6. How do you add a good sulfonate leaving group to ROH?
7. What's a good hint that a molecule will cyclize?
8. What are the relative rates of ring closure?
9. When do you protect alcohols?
10. In cyclic molecules, when are nucleophiles added to the more substituted side? The less substituted side?
11. Name different ways of naming sulfur groups
12. Compare the acidity of thiols to that of alcohols
13. Why is RS^- a better nucleophile than RO^-?
14. What is the leaving group ability of neutral sulfides?
15. How do you combine R-S-H and R-S-H into R-S-S-R?
16. How do you perform the reverse reaction of #15?

Chapter 10

Alkenes

10.1 Details

1. Order of priority for alcohols, thiols, and alkenes? (nomenclature)
2. How do you name exocyclic alkenes?
3. Alternate names for ethenyl and propenyl?
4. How does the strength of sigma bonds in alkenes compare to the strength of alkane bonds?
5. How does the acidity of alkenes compare to the acidity of alkanes?
6. Satzev's and Hofman's rules?
7. Discuss relationship between diastereomers and E/Z products

Chapter 11

Reactions of Alkenes

11.1 Details

1. Discuss the sign of ΔH and ΔS in addition reactions with alkenes.
2. What catalyst do you use to add H_2 to an alkene?
3. Does the addition reaction proceed without catalyst?
4. How stereospecific is the addition H_2 reaction?
5. How stereospecific is halogenation?
6. Describe the mechanism of halogenation.
7. Which two solvents can outcompete halonium ions?
8. When you have two halogens attached to each other (Cl-Br for example), which one takes the more substituted area?
9. When do you use oxymercuration?
10. When do you use hydroboration-oxidation?
11. List all the ways you can add to an alkene

Chapter 12

Solutions

12.1 Structure and Bonding in Organic Molecules

* All book solutions in the Schore book

12.2 Structure and Reactivity

12.2.1 Details

1. Neo: All atoms are in a straight chain except for 2
   Iso: All atoms are in a straight chain except for one ("I" am alone)
   Sec: When the group is bonded to a secondary carbon
   Tert: When the group is bonded to a tertiary carbon

2. ΔG^o = -RT lnK = -2.3RT logK (R being 1.986 cal/mol K)
   (Remember to use $\frac{kcal}{mol}$ for all answers, not Joules)
   @ 25^{o}C ΔG is -1.36logK

3. Nucleophile: Something that attacks positively charged nuclei, a Lewis base
   Electrophile: Lewis acid, wants to gain negative charges, attracts nucleophiles

4. Temperature, activation energy, concentration, probability factor (probability that two molecules will collide)

5. k = $Ae^{-\frac{E_a}{RT}}$
   Note that at high T, k = a.

6. Increasing acidity means
   a) more electronegative atoms (when comparing horizontally across the periodic table)
   b) larger orbital size (when comparing vertically across the periodic table)
   c) resonance

7. Same molecular formula, different connectivity

8. 2 = Bis, 3 = tris, 4 = tetrakis

12.3 Reactions of Alkanes

12.3.1 Details

1. The lone pair on a radical overlaps slightly with neighboring C-H bonding orbitals. Those slight interactions with the bonding orbitals lower the energy of the lone pair and therefore help stabilize it.

2. **(a)** Thermal excitation: Atoms vibrate so much that they separate
   (b) Photochemical: excite one electron from a bonding MO to an anti-bonding MO

3. **Initiation**: Light or energy breaks the X-X bond, where X is a halogen.
   Propagation: X attacks methane and abstracts a hydrogen atom -¿ Becomes methyl radical and HX. Then, the methyl radical meets another X-X, and they exchange electrons, becoming CH_3X + X radical, which restarts the propagation step.
   **Initiation step does not factor into the overall equation.
   Termination: Methyl radicals react, X radicals react, or methyl radical reacts with X radical.

4. Fluorine reacts with a ratio 1 : 1.2 : 1.4 with primary/secondary/tertiary hydrogen atoms.
   Chlorine reacts with ratio 1 : 4 : 5 with primary/secondary/tertiary hydrogen atoms.
   Bromine reacts with ratio 1 : 80 : 1700.
   Bigger halogens are less electronegative and release less energy when reacting, so the endothermic step of abstracting a hydrogen matters more (takes less energy to break off tertiary H than secondary H because of hyperconjugation; the transition state has radical character). Therefore, the ratios become more dramatic as the halogens get bigger.

5. An early transition state is characteristic of an exothermic, fast reaction. A late transition state is characteristic of an endothermic, slow reaction.

12.4 Cycloalkanes

12.4.1 Details

1. Carbon of attachment is C1. The alkane is the main chain if it has more carbons than the cyclic compound. Vice versa is true

2. Lowest digit numbering, and alphabetical order

3. Same connectivity, different arrangement in space (includes rotamers (i.e., anti, gauche))

4. Ring strain raises the potential energy of cyclic compounds

5. Bond angle that deviates from perfect 109.5^o (because every carbon atom is sp^3 hybridized), transannular strain (repulsion in substituents that are close to each other "within" the ring), eclipsing and gauche interactions among substituents

6. Description of the cyclopropane bond—-it is not a perfect 120^o as would be predicted from the Lewis dot structure. It is 104^o because its bonds are kinda floppy like bananas

7. Most stable: Chair conformation.
   Least stable: Half-chair
   2nd-most stable: Twist-boat
   2nd-least stable: Boat

8. Draw two parallel lines, the bottom slightly to the right of the top. Then draw two "triangles" connecting the ends of those parallel lines, one pointing down and the other pointing up. Then, starting from the bottom left, alternate hydrogens pointing down/up. Then alternate equatorial hydrogens that are parallel to the C-C bond "one over."
   *Note that the equatorial hydrogens point AWAY from the ring

9. Equatorial substituents have gauche strain with other hydrogen atoms and/or other substituents

10. Largest substituent in an axial position raises the potential energy of the compound—-the smaller substituents in axial positions don't raise potential energy as much. Therefore, the largest substituent in the axial position is more energetically favorable.

11. Axial-equatorial, axial-axial/eq-eq, axial-axial/eq-eq, axial-equatorial, axial-equatorial, axial-axial/eq-eq

12. One way is to draw in the hydrogens. If the hydrogen is in-line with the other substituent, then the molecule is trans (if the hydrogen is in line with the other substituent, that means the two substituents are not in line and are thus trans). Otherwise, the molecule is cis. Another way is to memorize #11

13. Take into account trans annular strain and gauche interactions. Even though halogens as big as iodine have much higher mass than methyl groups, they have far less gauche/ transannular strain. Basically just assume that all methyl/ethyl/propyl groups are higher in energy than other halogens/COOH/H_2N groups unless told otherwise because alkyl chains have many atoms that can rotate around and create steric hindrance.

12.5 Stereoisomers

12.5.1 Details

1. Mixture of enantiomers that are present in equal ratio. Racemates are not optically active, meaning they do not rotate light

2. Chiral molecules have no mirror plane. Achiral molecules have a mirror plane (plane can go through atoms). But keep in mind that the definition of chirality is the inability to superimpose the mirror image

3. Dextrorotary—-means the molecule rotates light clockwise. This means it is the (+) enantiomer
Levorotary—-means the molecule rotates light counterclockwise. This means it is the (—) enantiomer
**Direction of rotation does not tell you the absolute configuration of the molecule. It only gives you the +/— sign

4. Order molecules by priority—-biggest atoms are highest priority, smallest atoms are lowest priority. If there are identical atoms on all sides of the central atom, then look for the first point of difference. If there are multiple bonds, make all the pi bonds single sigma bonds with the other atom bonded to the ends of those single bonds (i.e., if the molecule is C=O, then erase one of the bonds between C and O and draw an extra single bond on C attached to O, and draw an extra single bond on O attached to another C atom). Then, look at the molecule so that the lowest priority atom is facing away from you. Look at the order of a-b-c. If a-b-c is clockwise, it is the R enantiomer. If counterclockwise, it is the S enantiomer.

5. Single mutual replacement of substituents = switch to other enantiomer. Double mutual replacement = same molecule. 90^o rotation makes it the other enantiomer. 180^o rotation makes it the same molecule.

6. No–memorize this. The intermediate radical is achiral, so you cannot get optically active products from optically inactive starting materials **(this concept was actually the basis for a question on the first midterm of Spring 2017.** Many people missed the question because they were trying to reason through sterics and reactivity–just knowing this fact would've let them speed through the question)

7. Yes-—the radical of an enantiomer is achiral, and you can form a racemic mixture

12.6 Haloalkanes

12.6.1 Details

1. Bond strength decreases (orbitals get bigger). BP goes UP because LDF dominates as the halogens get bigger. BP of haloalkane is also bigger than the alkane without the halogen

2. Negatively charged nucleophile: Creates a neutral compound, but leaving group is negative.
   Neutral nucleophile: Creates a positively charged salt, but leaving group is negative (must preserve net charge)

3. Nucleophile is the base in acid-base reactions.

4. Enthalpy values only apply to homolytic cleavage, but these reactions are heterolytic

5. Reaction speed proceeds as follows in S_N2 reactions: Primary > secondary > tertiary (steric hindrance)

6. Zero intermediates are formed in this type of reaction. Bimolecular nucleophilic substitution (i.e., S_N2) goes in one step and has one transition state. It also follows second-order kinetics because both leaving group and nucleophile are involved in the transition state.

7. S_N2 reaction is an example of a concerted reaction. Bond making occurs at the same time as bond breaking

8. Yes–experiments show that inversion occurs with halogenation (only backside attack). This means we can construct specific enantiomers

9. Yes–double inversion = retention

10. No–the incoming nucleophile may be smaller than the original halogen, which would change the R/S configuration

11. No–halogenation only inverts at the carbon it is attacking

12. Retention by double substitution, inversions are not guaranteed, and diastereoisomerization

13. Good leaving groups are weak bases. They can accommodate negative charge well by:
    a) having high electronegativity
    b) resonance
    c) large size (higher polarizability)
    ****Just look at whether it's a good acid or not. Good acid means easy to leave

14. Increasing ability to leave going DOWN the periodic table (think of acids: HI is the strongest acid). This means that orbital size dominates electronegativity in the case of halogens

15. Moving across to the right = INCREASING ability to leave. This means that electronegativity dominates moving across (just like in acids)

16. More resonance means better ability to leave

17. Neutral leaving groups (like the H_2O that leaves alcohols after being protonated) and N_2 which is a "superleaving" group (aka diazonium ions)

18. More charge (assuming all other factors are constant) means more nucleophilicity

19. Increasing basicity means more nucleophilicity. Nucleophilicity increases to the left

20. Basicity decreases down the periodic table, but nucleophilic character increases down the table. More electronegative atoms attract the solvent more strongly, and the solvation shells cause steric hindrance when attacking. Moving down the table, the atoms become less electronegative and thus have fewer solvent molecules blocking the way

21. Larger elements have larger, more polarizable electron clouds. This allows for more effective overlap in the transition state. (assuming that other atoms are the same. i.e., $H_2O < H_2S < H_2Se$)

22. Increasing nucleophilicity going UP the periodic table. The anions are "naked," and now we can follow the more basic = more nucleophilic rule.

23. Larger leaving group is a better leaving group (think of acids). Larger nucleophile is a worse nucleophile (***Earlier we saw that nucleophilic character increases going DOWN the periodic table because that was assuming we were changing the "base" atom while leaving the surrounding hydrogen atoms there (i.e., H_2O vs H_2S vs H_2Se). THIS rule is referring to the SAME "base" atom while increasing the size of its substituents, like CH_3O vs CH_3OCH_3). Sterics around the reacting carbon are the most significant (branching at the site of reaction slows down S_N2 reactions the most. Branching at neighboring carbons also slows the reaction, but not by that much).

24. Hydroxide, I^-, CN^-, CH_3O^-, SCH_3^-, NH_3, $P(CH_3)_3$ (for determining better nucleophile, remember that size matters first if it's a neutral compound. Basicity/solvent matter only when it's charged.)

12.7 More On Haloalkanes

12.7.1 Details

1. There are three steps: L group leaves, solvent comes in, then solvent is deprotonated ("optional"-occurs if there is H-bond)

2. (a) First-order
   (b) rate depends only on rate of leaving group
   (c) rate increases as polarity of solvent increases
   (d) NOT stereospecific (racemization)
   (e) product determining step occurs after rate determining step

3. S_N2 has one hump, exothermic (because only one transition state). S_N1 has three humps (first transition state is breaking off the L, second transition state is attack by the Nu molecule, third transition state is breaking off the H^+, if there is one) (not sure about this, but I believe the third hump is "optional"–it only appears if the nucleophile has an H^+ attached to N/O/F)

4. It is generally racemic. After the L group is gone, the remaining empty p-orbital on the carbon is symmetric and can be attacked from either side. In practice, there is actually slight inversion because the leaving group is negative (and compound is positive), so there's slight steric hindrance on the side of the leaving group.

5. Polar solvent will allow L to leave faster. Think of NaCl in H_2O — highly polar solvent allows for better dissociation if solute is strongly polar (when you form a carbocation and L, it is ionic, so very strongly "polar")

6. The nucleophile has no effect on the S_N1 reaction. The better nucleophile will win in competition though

7. Alpha-branching slows the S_N2 reaction so much that only S_N2 is possible. Also, with more substituents the carbocation becomes more stabilized, and it's more favorable for the radical to form (whereas in methyl/primary carbocations there is no such stability, so it's more likely for a concerted reaction to occur)

8. Good leaving group in polar protic = S_N1 (polar solvent will grab at the leaving group quickly and induce solvolysis) ; good nucleophile in polar aprotic is S_N2

9. There is no relationship. S_N1:E1 ratio is independent of the leaving group.

10. The C-H bonds next to the carbon that was attached to the leaving group become acidic.

11. a) Increase the temperature. $\Delta G = \Delta H - T\Delta S$. Since E1 increases entropy (RX becomes alkene + HX), higher temperature makes G more negative (more spontaneous, more favorable).
    b) Use a poorly nucleophilic medium to slow S_N1 (nonhydroxylic solvent, poor nucleophiles (e.g., SO_4^{2-}, CO_3^{2-}))
    ***if you use a strong base, it becomes E2

12. E2 is fastest if S_N2 is sterically hindered–otherwise it's only guaranteed to be faster than S_N1 and E1
13. H^+ and the leaving group are removed
14. Deuterium makes the reaction 7 times slower than it would be with hydrogen
15. It is best when L and H^+ are anti to each other. This creates less e-repulsion and gives the best overlap for the incoming base
16. The two pairs of diastereomers give distinct structures. R/R and S/S give the same E2 product (let's call the product A). R/S and S/R also have the same product, but it is not the same as A
17. Swapping the sodium for a hydrogen proton makes the molecule covalent, whereas with sodium it is ionic. The resulting nucleophile is much weaker in the covalent case (H^+)
18. Highly polar medium, good leaving group, weak nucleophiles = S_N1/E1. High concentrations of good weakly basic nucleophiles = S_N2. High concentration of strong base = E2

12.8 Intro to Alcohols

12.8.1 Details

1. Methoxy = CH_3O. Hydroxymethyl is CH_3OH
2. S_N2/S_N1, reduction, organometallics
3. Use R and S for every substituent (unless meso or achiral)
4. (a) Length of alcohol
   (b) Steric hindrance as a result of branching (more branching = lower acidity)
   (c) electronegativity of substituents (i.e., halogens) (also, distance of halogens from the OH group)
5. Let x = pK_a of products $-pK_a$ of reactants
   K = 10^x
6. For S_N2 reactions, there's the problem of beta branching, which can be solved by using a non-basic OH equivalent, like acetate (which becomes OH in the aqueous workup). For S_N1 reactions, the problem of E1 side effects can be fixed by lowering the temperature.
7. $LiAlH_4$ and $NaBH_4$. $NaBH_4$ is LESS reactive and MORE selective. $LiAlH_4$ is super reactive and needs APROTIC or rigorously dry solvents (i.e., ethers). $LiAlH_4$ will reduce halides, but $NaBH_4$ won't. $NaBH_4$ occurs in ONE step (termolecular between carbonyl group, $NaBH_4$, and solvent). $LiAlH_4$ occurs in a step wise fashion (H^- then H^+ and so on)
8. If it's a secondary alcohol, use $Na_2Cr_2O_7$ with H_2SO_4. (will change OH to a double bonded O). You could also use CrO_3 in H_2SO_4. If it's a primary alcohol, use PCC, otherwise the two hydrogens on the carbon just become a double bonded O and the other OH remains.
9. Must be in an ether to make RMgX.
10. They are basic and nucleophilic.
11. Yes
12. The H or D takes over the MgBr position (not OH).
13. Whenever you see a carbonyl group, make it into an alcohol (PCC or $Na_2Cr_2O_7$ in reverse). Whenever you want to combine two chains, use a Grignard or RLi + carbonyl group. If the final product is not an alcohol and they ask to work backward, start by throwing in a random halogen (the reverse reaction $LiAlH_4$ which we said can reduce R-X groups in #7). Replace the halogen with OH group (reverse reaction of H-X acid replacement). Try to divide molecules as evenly as possible.

12.9 Further Reactions of Alcohols

12.9.1 Details

1. LiH, KH, $(CH_3)COH$, LDA, NH_2^-, RLi
2. Avoid H-X when making alcohols in anything other than methyl group (meaning $R_{primary \hookrightarrow tertiary}$). Primary/secondary/tertiary carbons will undergo alkyl/hydride shifts after the H_2O leaves, so use an intermediate to prevent that from happening
3. Symmetrical ethers can be made using their corresponding alcohols + acid (acid removes an OH from one, the O on the other attacks the carbocation, then the H^+ is ripped off by solvent). Same for unsymmetrical ethers
4. During S_N1 reactions.
5. When they relieve ring strain
6. Use CH_3SO_2Cl
7. There is a base in solution, and the molecule has a good leaving group on one side and an -OH group on the other side. The (strong) base in solution will deprotonate the OH, and the remaining O will attack the carbon on the opposite end of the molecule, kicking out the leaving group.
8. $3 > 5 > 6 > 4 > 7 > 8$ (tradeoff between proximity and ring strain)
9. Protect alcohols when you want to modify the R group in an ROH compound and leave the OH intact.
10. A basic nucleophile will attack the LESS hindered side. A neutral nucleophile will add to the MORE hindered side in acidic conditions (more hindered side can accommodate positive charge better)
11. Alkanethiol is the "base" way. Mercapto is used when -SH is a substituent. Alkylthio is used when -SR is a substituent. Ignore the thing about alkyl sulfide. $-OH > -SH$ in priority
12. -SH is more acidic because it's larger/more polarizable.
13. RS^- is less basic and more polarizable than RO^-. There is no E2 problem with $R_{secondary}X$
14. Leaving ability of neutral sulfides is very good.
15. Use I_2
16. Use Li, NH_3 liquid

12.10 Alkenes

12.10.1 Details

1. -OH > -SH > -ene
2. Alkylidenecycloalkane or alkylenecycloalkane
3. Ethenyl: Vinyl; Propenyl: allyl
4. Alkene sigma bonds are stronger because they are sp^2 hybridized (33% s character, whereas alkanes have 25% s character)
5. Alkenes are more acidic because the greater s character draws electrons away from the hydrogens
6. Satzev: non-bulky base leads to more stable internal bond.
   Hofman: bulky base leads to less stable bond (bulky base can't get past the crowding substituents, so it "settles" for a terminal hydrogen)

7. The R/S S/R diastereomers will only give E or Z products. The R/R and S/S diastereomers will only give the other one. So if R/S S/R diastereomers give the E product, the R/R and S/S diastereomers will give the Z product

12.11 Reactions of Alkenes

12.11.1 Details

1. $\Delta H < 0$ (usually). $\Delta S < 0$ (two molecules becomes one).
2. Pd/C (palladium on carbon) or PtO_2 (becomes Pt after H_2 reacts with it)
3. No, the addition reaction MUST have a catalyst
4. Syn addition for adding H_2 (means adding from the same 3-d side)
5. Anti reaction for halogenation
6. First there's a cyclic molecule with the halogen at the "top." Then the other halogen from the molecule attacks and the molecule "opens up" into the anti conformation
7. ROH and H_2O
8. The more electronegative atom takes the more substituted spot
9. Use oxymercuration to avoid cations
10. Use hydroboration-oxidation to do anti-maokovnikov hydrations. Boron attaches to the less substituted end, one H attaches to more substituted end of the pi bond. Treat the molecule with H_2O_2 and OH^- and it becomes ROH.
11. a) Catalytic hydrogenation
    b) H-X (X attaches to more substituted end)
    c) Hydration (-OH attaches to more substituted end, need H^+ catalyst)
    d) X-X (anti addition)
    dd) X-X intercepted by other Nu (anti X/Nu relationship, the other Nu is markovnikov)
    e) Markovnikov hydration using oxymercuration-demercuration to avoid cations
    f) Anti-Markovnikov hydration using hydroboration-oxidation
    g) Carbene additions (cis-cyclopropanes, use hv/Cu for the one with nitrogen, tert-butyl alkoxide for $CHCl_3$, and Zn-Cu for CH_2I_2)
    h) Use RCOOH to generate oxacyclic molecules
    i) $OsO_4 + H_2S$, H_2O becomes syn-dihydroxation
    j) Ozonolysis to cleave double bonds and replace both with double-bonded O's
    k) RADICAL hydrobromination using R-O-O-R solvent (anti-markovnikov)
    l) Polymerization via H^+, ROOR, or OH^-
    m) Ozonolysis