

CHM 5224  
Basic Principles for Organic Chemistry  
Fall 2003

*Final Exam Review Topics*

**The exam is on Saturday, December 13<sup>th</sup> at 10 a.m. in LEI 142 (unless it's occupied and we need to make last minute arrangements).** The exam will be cumulative, although *emphasis* will be placed on the material covered since Exam #2. The topics below should serve to guide your study efforts — I have identified them as key points from my own review of the material. However, in theory, you are responsible for all that we have discussed! The topics, by and large, are those that have been covered on the exams . . . As for the name reactions, I have provided a list at the end that may facilitate your efforts (sort of my personal favorites).

*Physical organic chemistry and basic principles:*

(There will not be any explicit “general chemistry” questions, e.g. Lewis dot structures, formal charges, what is the molecular orbital description of H<sub>3</sub>?)

- 1) Resonance
  - a. primarily in the context of mechanism, reactivity, and intermediate stability
  - b. which species is the better leaving group? which is a better acylating agent?
- 2) Aromaticity
  - a. aromatic, antiaromatic, nonaromatic
  - b. we have seen many cases where a gain in aromaticity is the driving force in a chemical transformation
  - c. aromaticity has consequences on reactivity (i.e.  $pK_a$  values!)
- 3)  $pK_a$ 
  - a. we have routinely seen between 10–15 different  $pK_a$  values. Know them.
  - b. given that you know the  $pK_a$  values, what is the equilibrium constant for a particular acid-base reaction?
  - c. conjugate base stability
  - d. resonance versus induction
- 4) Isomers
  - a. identify the types of isomers (i.e. structural versus stereochemical, enantiomers versus diastereomers)
  - b. what makes a molecule chiral? optically active?
  - c. assigning absolute configuration
  - d. conversion between Newman projections, Fisher projections, and traditional representations
- 5) Cyclohexane conformation and energetics (what is an *A*-value? given one, can you calculate  $\Delta G$ ?)
- 6) Anomeric effect
- 7) Substitution and elimination reactions
  - a.  $S_N2$ ,  $S_N1$ ,  $S_{RN}1$ , E2, E1, E1<sub>cb</sub> and aromatic substitution
  - b. what makes a good leaving group? a good nucleophile? when you have a □-hydroxy carbonyl compound why do you write the E2 mechanism for acid-catalyzed dehydration but the E1<sub>cb</sub> for base-promoted dehydration (to give the □, □-unsaturated carbonyl)?
  - c. carbocation/carbanion stability

- d. base effects . . . bulky bases (like *t*-butoxide) versus smaller bases (methoxide/ethoxide) and the competition between substitution and elimination
- 8) Neighboring Group Participation
- a.  $\pi$ -,  $\sigma$ -, and n-type
  - b. non-classical carbocations (Chapter 22)
- 9) Reaction thermodynamics
- a. What is the Hammond postulate? What is the difference between an early and a late transition state? Look at this in relation to elimination reactions. Why do ammonium and sulfonium leaving groups give primarily the Hofmann product rather than the Saytzeff?
  - b. Identify other occurrences of product development control that we have discussed. For example, radical halogenation of hydrocarbons ( $\text{Cl}_2$  versus  $\text{Br}_2$ ).
- 10) Addition to carbon-carbon double bonds
- a. onium intermediates (e.g. bromonium, sulfonium, etc.)! H-X and X-X addition to alkenes and alkynes
  - b. oxymercuration/demercuration, hydroboration
  - c. peroxyacid epoxidation
  - d. synthesis of *trans* and *cis* glycols (Exam #2 bonus question)
- 11) Aromatic substitution (from Jones)
- a. *o,p* versus *meta* directors and synthetic strategy
  - b. an example or two of nucleophilic aromatic substitution
- 12) Carbenes
- a. how are carbenes generated?
  - b. how do they react, in general (e.g. insert into C-H and O-H bonds, add to double bonds, rearrangement chemistry), and what's the difference between a singlet and a triplet carbene?
- 13) Radicals
- a. generation (initiation), stability, and reactivity
  - b. radical chain mechanisms (don't forget termination!)
- 14) Carbonyl addition reactions (1,2-addition)
- a. can you write good mechanisms for acid- and base-catalyzed hydrolyses?
  - b. what is the relationship between resonance energy and electrophilicity (in acylation)?
  - c. carbonyl hydrate stability
  - d. acetal/hemiacetal formation and cleavage
  - e. 1,3-dithiane chemistry! *umpolung*!
  - f. carboxylic acid activation and amide bond formation (PS #8)
- 15) Imines and enamines
- a. how are they formed?
  - b. Stork's enamine chemistry . . . enamines as masked enolates! How is an enamine converted back to a carbonyl compound?
  - c. why is the less substituted enamine generally preferred?
  - d. related to the above question: What types of strain have we seen?
    - i. 1,3-diaxial and 1,3-allylic interactions
    - ii. torsional strain
      - 1. syn-pentane interactions
      - 2. eclipsing and gauche interactions
    - iii. angle strain (ring systems)
- 16) Organometallics

- a. Grignards versus organolithium reagents. What are the differences? What results upon 1,2-addition to a carbonyl? What happens if you add MeLi to a carboxylic acid? Know the general Grignard/RLi reactions.
- b. lithium-halogen exchange and directed *ortho*-lithiation
- c. cuprates
  - i. how do you make a cuprate reagent?
  - ii. these species generally do not add 1,2 to a carbonyl, but do conjugate (1,4) additions
  - iii. what other reactions do cuprates participate in that Grignards/RLi do not?

#### 17) Oxidation

- a. know a few ways to oxidize an alcohol to the acid . . . which reagents stop at the aldehyde and why?
- b. reagents for alkene dihydroxylation and oxidative cleavage
- c. ozonolysis (know the mechanism! cycloaddition!)

#### 18) Reduction

- a. we discussed NaBH<sub>4</sub> and LAH in class, primarily for the reduction of carbonyl compounds and nitriles. Don't forget about other reductions:
  - i. Wolff-Kishner and Clemmensen
  - ii. catalytic hydrogenation of alkenes
  - iii. Lindlar versus dissolving metal (Birch-type) reduction of alkynes. What stereochemistry results from these?

#### 19) $\alpha$ -Carbonyl chemistry\*

- a. this is covered extensively in the condensation name reactions! (see below)
- b. KINETIC versus THERMODYNAMIC enolate generation and trapping enolates with electrophiles
- c. silyl enol ethers (Mukaiyama reactions)
- d. all conjugate addition chemistry (1,4-addition): what nucleophiles participate in this? Enolates, for sure, but also enamines and cuprates.

#### 20) Pericyclic reactions\*

- a. definition and general classes . . . can you draw an example of each?
- b. this is where (frontier) molecular orbital theory (Fukui) becomes important!
- c. electrocyclic reactions
  - i. Woodward-Hoffmann rules
  - ii. conrotatory versus disrotatory
  - iii. you must look at orbital symmetry but also the stability of the final products! Is there a *trans* double bond in a 7-membered ring? How about a *trans* ring junction between a 6- and 4-membered ring? Be careful!
- d. cycloadditions
  - i. W-H rules, suprafacial versus antarafacial, and stereochemical consequences
  - ii. photochemical [2+2], thermal [4+2]
  - iii. Diels-Alder regiochemistry and stereochemistry! Think retrosynthetically!
  - iv. ketene cycloadditions ([s+a]!) and 1,3-dipolar cycloadditions (can you list the common 1,3-dipoles?)
- e. sigmatropic rearrangements
  - i. W-H rules, suprafacial versus antarafacial, and stereochemical consequences
  - ii. [1,5], [2,3] . . . where do these numbers come from?

#### 21) Photochemistry

- a. general concepts
  - i. Jablonski diagram

- ii. photosensitization
  - iii. Frank-Condon principle
  - b. singlets versus triplets, their energies, reactivity, and interconversion
  - c. carbene and carbonyl photochemistry (what happens when you irradiate a carbonyl group?)
- 22) Synthetic strategy: We have highlighted the process of retrosynthesis, synthons, and retrons throughout the last part of the course. Keep these concepts in mind as you look at particular transformations.

\*Sections 19–21 will be emphasized as they have not been covered extensively on Exams #1 and #2.

*Name reactions to take a close look at (other than those listed above):*

- All condensations: These follow many of the same basic mechanisms.
- Baylis-Hillman
- Friedel-Crafts alkylation/acylation
- Mitsunobu (we have seen many ways to activate acids and alcohols . . . can you think of them?)
- Beckman R. (we have seen many examples of 1,2-alkyl shifts onto heteroatoms . . . think of the occurrences)
- Pinacol R., Wagner-Meerwein R., and associated 1,2-shifts (generally the same mechanism! However, there have been differences in whether the reaction is concerted or not . . .)
- Curtius rearrangement: How do isocyanates react after you prepare them?
- Hofmann rearrangement
- Wittig and Horner-Wadsworth-Emmons
- Vilsmeier-Haack
- Favorskii-type rearrangements
- Grob fragmentation
- Pummerer R.
- Simmons-Smith
- Arndt-Eistert/Wolff: Carbene chemistry!
- McMurry Reaction and Pinacol coupling
- Barton-McCombie Deoxygenation (what is a xanthate ester? how is one prepared?)
- All Pd-Mediated cross-coupling reactions
- Baeyer-Villiger (competition with epoxidation!)
- Swern oxidation (and related sulfur-based oxidations)
- Wolff-Kishner reduction (hydrazone chemistry!)
- Birch reduction: General reaction conditions and consequences
- All reactions from PS #11 and PS #12