Chemistry 657: Organic Synthesis

The College of William & Mary
Spring 2008
Prof. Rob Hinkle
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Office Hours: by appt. or anytime

Required Materials: (a) Carey and Sundberg, *Advanced Organic Chemistry*, 4th Ed., **Part B.**
(b) Model Kit: available at the Bookstore with Chem. 206 supplies.

Valuable Resources:
(a) SciFinder Scholar software—available on Chem. computers.
(b) Paquette, L. A. *Encyclopedia of Reagents for Organic Synthesis*, Wiley: New York, 1995.
(c) Mahrwald, R., Ed., *Modern Aldol Reactions*, Volumes I and II, Wiley-VCH: New York, 2004.
(d) Otera, J., *Modern Carbonyl Chemistry*, Wiley-VCH: New York, 2000.
(e) Prof. David A. Evans' Website at Harvard University: http://www2.lsdiv.harvard.edu/labs/evans/
(f) Larock, R. C. *Comprehensive Organic Transformations*, VCH Publishers: New York, 1989.
(g) Corey, E. J.; Cheng, X.-M. *The Logic of Chemical Synthesis*, Wiley: New York, 1989.
(h) Nicolaou, K. C.; Sorensen, E. J. *Classics in Total Synthesis*, VCH Publishers: New York, 1996.
(i) Nicolaou, K. C.; Snyder, S. A. *Classics in Total Synthesis, II*, VCH Publishers: New York, 2003.
(j) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed. Wiley: New York, 1999.

The last five books (f-j) are on reserve in the library

Grading (Pts in parenthesis): In Class Midterm I (200) on Thursday 07 February; Take-Home Midterm (200) due on Thursday, 28 February (200); In-Class exam II (200) Thursday 03 April; Final Exam (200) on Tuesday, 29 April at 08:30; Take-Home Final Exam (200) due by 4:00 p.m. on Friday 1 May. Homework assignments (50 each X 6 + presentations/molecule projects = 500 pts) and final paper (200) round out the **total course points = 1900**. *Presentations on 10 and 15 April; Molecule synthesis on 24 April*. **Eight to ten page paper due on 07 May (200).**

Coverage:

This course will focus on the reactions necessary to "build" moderately complex molecules. The beginning of the course will be devoted to synthesizing and modifying particular functional groups including stereochemical control of the reactions. The second part of the

course will incorporate these "tools" into larger and more complex molecules with an emphasis on stereocontrol and stategy.

The text will be heavily supplemented by the instructor and will include many of the following topics with some additions/deletions during the evolution of the course.

Course Topics

I. Review of Chemistry 209/307.
- A. Basic Nomenclature
- B. Hybridization and conventions
- C. Isomers and their relationships
- D. Stereoelectronic relationships
- E. Reactions:
  1. S_N1, S_N2 and Elimination
  2. Reduction and Oxidation
  3. Reactions of Grignards, Lithium reagents and Cuprates
  5. Acyl Substitution
  6. Aldol addition and condensation
  7. Oxonium (oxocarbenium) ion formation.

II. Organometallics (Simple)
- A. Grignards
- B. Lithium Reagents
- C. Transmetallation
- D. Cuprates
- E. Chelation Control

III. Alkene Syntheses/degradation
- A. Dehydration/Elimination
- B. Wïttig
- C. Horner-Emmons-Wadsworth
- D. Peterson Olefination
- E. Ozonolysis/Oxidative Cleavage
- F. Ring Closing Metathesis

IV. Diastereo- and Enantioselective Reactions
- A. Alkylations and Aldols
- B. Reduction w/ Organometallics
- C. Corey Reduction
- D. Sharpless Epoxidation

V. Organometallic transformations
- A. Heck Reaction
- B. Suzuki Coupling
- C. Negishi Coupling
- D. Stille Coupling

VI. Cyclic Ether Synthesis
- A. Lewis Acid Catalysis
- B. Kishi & Woerpel models for stereoselection

VII. Total Syntheses (Molecular Architecture).