

Chemistry 634: Advanced Organic Chemistry – Synthesis and Reactivity
Fall 2009, University of Delaware
Lecture Thursday, 7-10 PM Colburn Lab (CLB) 109

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Office hour: Friday 12-1pm, LDL 205

Website: www.udel.edu/chem/dawatson/classes/Chem634_F09/Chem634_F09-home.html

Required Texts:

Advanced Organic Chemistry, Part B: Reactions and Synthesis. (5th Edition Recommended) Carey, F. A.; Sundberg, R. J. ISBN 978-0-387-68354-6

Strategic Applications of Names Reactions in Organic Synthesis. Kurti, L.; Czako, B. ISBN 978-0-12-429785-2

Recommend Texts (Optional):

Organic Synthesis: Strategy and Control. Wyatt, P.; Warren, S. ISBN 978-0-471-92963-5

Workbook for Organic Synthesis: Strategy and Control. Wyatt, P.; Warren, S. ISBN 978-0-471-92964-2

Advanced Organic Chemistry · Part A: Structure and Mechanisms Carey, F. A.; Sundberg, R. J. ISBN 978-0-387-68346-1

The following texts will also be on reserve in the Chemistry Library (and are good books to consider owning if you plan to continue in synthetic organic chemistry).

Comprehensive Organic Transformations: A Guide to Functional Group Preparations, 2nd Edition Larock, R. C.
Stereochemistry of Organic Compounds Eliel, E.; Wilen, S. H.

March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, 6th Edition Smith, M. B.; March, J.

Protective Groups in Organic Synthesis, 4th Ed, Greene and Wuts

Transition Metals in the Synthesis of Complex Organic Molecules, 2nd Ed, Hegedus, L. S.

Model Kit (required):

I do not care which brand you buy, but if you are looking for recommendations, here are two (also check with the bookstore, Amazon, or the like):

HGS 4010/Student Set – Expensive but very nice (they are a smaller set of the same models I use – I like them because they are pretty rigid. Be warned, however, they tend to be fragile).

http://www.maruzen.info/hgs/catalog/product_info.php?cPath=11&products_id=596

Darling Models – Cheaper, but very floppy (which is not great for studying stereochemistry).

http://www.darlingmodels.com/item--KIT-1-ISBN-0-9648837-1-6-Plastic-Box-Organic-Inorganic-Organometallic--kit_1_plastic_student.html

Important Online Resources

Reaction and Structure Searching:

Scifinder: <http://www2.lib.udel.edu/database/scifind.html>

Beilstein: <http://www2.lib.udel.edu/database/beilstein.html>

Citation Searching:

Web of Science: <http://apps.isiknowledge.com/>

Listing of review articles compiled by Phillip Kocienski (most useful with Endnote format):

Synthesis Reviews: <http://www.thieme-chemistry.com/en/products/journals/supplements/synthesis-reviews.html>

Time and interest permitting, a tutorial will be scheduled to demonstrate the use of these tools.

Approximate Class Outline (exact dates of topics may vary with class progress):

Week 1	Sept 3rd	Lecture 1	Introduction, Nucleophilic Substitution Chemistry
Week 2	Sept 10th	Lecture 2	Intro to Organometallic Reactions
Week 3	Sept 17th	Lecture 3	Protecting Groups, Alcohol and Carbonyl Oxidation
Week 4	Sept 24th	Lecture 4	Enolate Alkylations
Week 5	Oct 1st	Lecture 5	Reductions of Carbonyls and Imines
Week 6	Oct 8th	Lecture 6	Reactions of Carbonyls with Carbon Nucleophiles
Week 7	Oct 15th		MIDTERM EXAM
Week 8	Oct 22th	Lecture 7	Alkene Synthesis and Reactivity
Week 9	Oct 29th	Lecture 8	Alkyne Synthesis and Reactivity
Week 10	Nov 5th	Lecture 9	Pericyclic Reactions (Part 1)
Week 11	Nov 12th	Lecture 10	Pericyclic Reactions (Part 2)
Week 12	Nov 19th	Lecture 11	Strained Rings, Aromatic and Heteroaromatic Chemistry
Week 13	Nov. 26 th	No Class	Thanksgiving
Week 14	Dec 3rd	Lecture 12	Radical Reactions, C-H Functionalization
Finals Week			FINAL EXAM

Grading

Breakdown:

Midterm Exam 300 points, 30%

Final Exam 400 points, 40%

Problem Sets 300 points (10 sets, 30 points each), 30%

Total: 1000 points

Problem sets will be graded either in whole or part. If only part is graded, the same questions will be graded for all students in the class, which questions will be graded will not be pre-announced. Please note, at least 10 points will be awarded (all or nothing) for completing the problem set, so it strongly to your benefit to at least try all of the problems. You are free to work in study groups when working on the problem sets, but each student must turn in their own work. *Do not use Beilstein, Scifinder or other search engines to look up answers on the homework!* You will not have these tools when you take the exams (nor on interviews when you look for a job in a few years), so you are best served by *actually learning* the material.

Problem sets will be due at the *beginning* of class one week after they are assigned. Late problem sets will not be accepted as we may discuss the answers in class after it is due.

Exams will be closed book, closed note, but a model set is allowed. Exams will cover lecture material, problem sets, assigned reading, as well as current literature discussed in class.

All requests for regrades must be submitted in writing within 24 hours of the material being returned. Please note, the entire exam will be regraded – if grading errors are found the final grades may be higher *or lower* than original score. Also note, photocopies may be made prior to returning exams. If answers are altered, it will be obvious and provable (see below).

Academic Dishonesty

Academic dishonesty will not be tolerated. Not only is such behavior unethical, but also cheating in this class will result in you not learning material that will be critical to your chosen career path. Simply put, learn this material; you will need it to be a functional synthetic chemist. Please review the University of Delaware's Academic Dishonesty Policy, which can be found at <http://www.udel.edu/stuguide/09-10/code.html#honesty>. On assigned problem sets, study groups are allowed, but each person must turn in their own work.

Mechanism and Synthesis

Understanding a reaction at a mechanistic level is necessary in order to be able to apply it to effect the desired outcome. If you do not know how it works, you might not understand what can go wrong, or how to fix it when it does. If you encounter a mechanism that you do not understand – take the time to work out a reasonable mechanism. It is assumed that you are familiar with elementary arrow pushing and we will not be covering this in class in any depth. For those that need a refresher, the following approach is very useful.

The 12-step guide to arrow pushing (adapted from Prof. Keith Woerpel, UC Irvine):

- 1) Electrons flow from sites of high electron density to sites of low electron density (show arrows accordingly).
- 2) Balance the equation. It helps.
- 3) Don't violate basic rules of physics.
 - a. Conserve mass and energy (see rule 2)
 - b. Conserve charge
- 4) Three Arrow Rule: Don't push more than 3 arrows at one time
- 5) Draw out all intermediates.
 - a. It may seem tedious at time, but it will avoid mistakes and often reveal new insights.
 - b. 3-D depictions may help. Use models if needed.
- 6) Use your lone pairs (often the site of FMO's).
- 7) All steps are, in principle, reversible.
- 8) Contemplate your options and carry each to its conclusion before discarding (this is seriously useful advice).
- 9) The correct mechanism gives the observed product (should not be taken to mean that all mechanisms that lead to the product are *necessarily* correct).
- 10) Use connectivity to tell you how the puzzle fits together.
 - a. Number atoms logically
 - b. "Principle of least action" usually holds.
- 11) Always identify the nucleophiles and electrophiles at each step.
 - a. At times it may be useful to substitute oxidants and reductants above.
- 12) Work backwards from the product to the likely precursors.

Basic Guide to Retrosynthetic Analysis

- 1) Maximize convergence
- 2) Minimize steps by exploring multiple options before deciding on a plan (avoid FGI and protecting groups, if possible)
- 3) Add functional groups if they can lead to a simplifying disconnection
- 4) Disconnect stereocenters (clear stereocenters) where possible
- 5) C-C and C-CX bonds usually make good disconnections
- 6) Minimize medium and large rings formation
- 7) Disconnect unstable functional groups early in retrosynthesis
- 8) Recognize embedded symmetry
- 9) ID embedded complex molecules (particularly chiral pool)
- 10) Use topology to your advantage (particularly in caged molecules, make a model before starting)