

CHEM 544(1)
ADVANCED TOPICS IN ORGANIC CHEMISTRY
(COMPLEX MOLECULAR SYNTHESIS)
FALL 2015

Instructor: Dr. Philip Garner, Fulmer 337, 335-7620, ppg@wsu.edu

Class Meeting: M/W/F 12:10 pm - 1:00 pm, Fulmer 432

Course Description: Synthesis is one of the distinguishing features of chemistry as a science. It is the synthetic chemist who uses his/her intimate understanding of molecular structure and properties to produce materials of great value to society (polymers, pharmaceuticals, etc.). Thus, it is important for the serious student of chemistry to study the art and science of synthesis. Given a molecular target, how does one formulate a plan for its synthesis? One may draw an analogy between target-oriented synthesis and the game of chess. In both cases, a particular problem can be analyzed in terms of a goal to be achieved (synthesis of target = checkmate), a strategy to be followed (evolving synthetic plan = evolving game plan), and the tactics used to implement the strategy (specific reactions = individual chess moves). However, the chess analogy is not sufficient to describe the process. For example, issues such as the chemical compatibility of ancillary functional groups and the reagents to be used must be considered. There is also an element of human creativity involved, which is often easier to appreciate than to quantify. As with chess, the best way to learn how to plan and execute a successful synthesis is to analyze the work of masters. This will be our approach as well. Each synthesis covered will begin with a discussion of why the target was important, followed by a retrosynthetic analysis (strategy and tactics) and, finally, a detailed discussion of the synthesis that was actually executed (chemical reactions) as well as problems that were encountered along the way.

Lectures: The lectures were developed from the primary literature, which is cited. To fully understand the work presented, students should read the primary references associated with each synthesis. The majority of the syntheses have been summarized in the following three RECOMMENDED books: (1) *Classics in Total Synthesis – Targets, Strategies, and Methods*, Nicolaou, K. C.; Sorensen, E. J.; VCH: New York, 1996 (ISBN: 3-527-29284-4). (2) *Classics in Total Synthesis II – More Targets, Strategies, and Methods*, Nicolaou, K. C.; Snyder, S. A.; WILEY-VCH: Weinheim, 2003 (ISBN: 3-527-30685-4). (3) *Classics in Total Synthesis III – Further Targets, Strategies, and Methods*, Nicolaou, K. C.; Chen, J. S.; WILEY-VCH: Weinheim, 2011 (ISBN: 3-527-32958-8). The relevant chapters in these books provide an overview of the problem, synopsis of the synthesis, and primary literature references. These books are available for purchase both new and used online. Copies will also be held on reserve in the Owen Science & Engineering Library.

Communication: Dr. Garner will generally be available to answer questions immediately after class or by appointment. The use of e-mail is encouraged.

Learning outcomes: Students who successfully complete this course will have learned how to (1) critically analyze a published total synthesis and (2) plan and present an original total synthesis proposal.

Assessment/Grading: Learning outcomes will be assessed via (1) student participation in scheduled problem solving sessions (20%), (2) a written analysis of a published total synthesis (project 1, 40%), and (3) a written total synthesis proposal (project 2, 40%).

Academic Integrity: Academic dishonesty, such as cheating, plagiarism, fabrication, and fraud is prohibited. The work will receive a failing grade and this action will be reported to the Office of Student Conduct. Consult the Office of Student Conduct (<http://www.conduct.wsu.edu>) for additional information.

Students with Disabilities: Reasonable accommodations are available for students with a documented disability. If you have a disability and need accommodations to fully participate in this class, please either visit or call the Access Center to schedule an appointment with an Access Advisor. All accommodations MUST be approved through the Access Center. Location: Washington Building 217; Phone: 509-335-3417. Contact: Meredyth Goodwin (m.goodwin@wsu.edu)

Topics to be Covered:

1. Retrosynthetic Analysis Primer
2. Reserpine (Classics I, Chapter 4)
3. Quinine (Classics II, Chapter 15)
4. Prostaglandins (Classics I, Chapters 5 & 9)
5. Progesterone (Classics I, Chapter 6)
6. Yuzuriha Alkaloids (Classics I, Chapter 26)
7. Erythronolide B (Classics I, Chapter 11)
8. Cytovaricin (Classics I, Chapter 28)
9. Discodermolide (Classics III, Chapter 3)
10. Taxol (Classics I, Chapter 34)
11. Ecteinascidin 743 (Classics II, Chapter 5)
12. Vancomycin (Classics II, Chapter 9)
13. Glycoprotein Synthesis

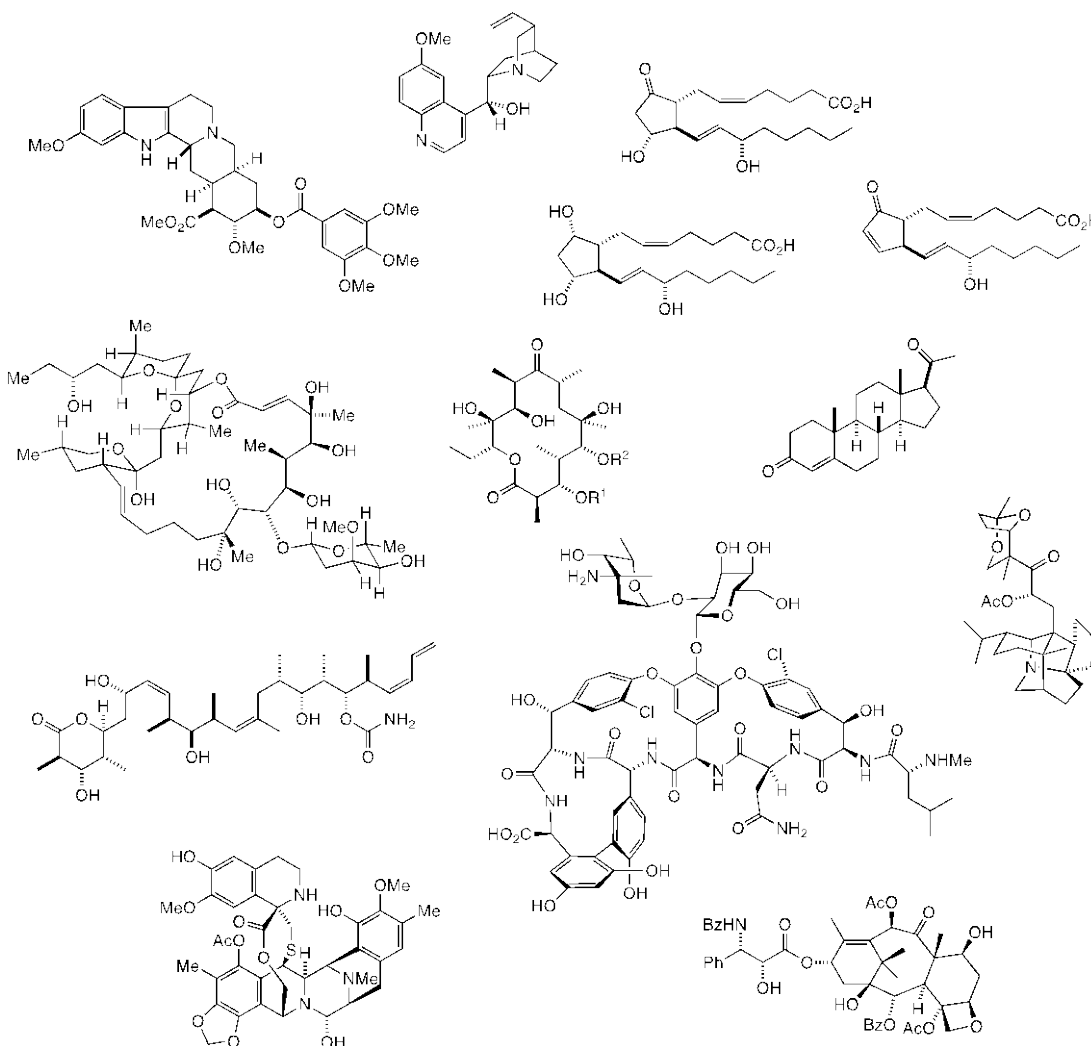


Figure 1. Structures of natural products to be covered.

Detailed Class Schedule

mon	8/24/15	lecture 1	course introduction equilenin (Bachmann), tropinone (Robinson)
wed	8/26/15	lecture 2	retrosynthetic analysis (part 1)
fri	8/28/15	lecture 3	retrosynthetic analysis (part 2)
mon	8/31/15	problem set 1	in-class solution by students
wed	8/2/15	lecture 4	reserpine (Woodward, part 1)
fri	9/4/15	lecture 5	reserpine (Woodward, part 2)
mon	9/7/15	Labor Day	no class
wed	9/9/15	lecture 6	reserpine (other approaches)
fri	9/11/15	lecture 7	quinine (intro, Woodward)
mon	9/14/15	problem set 2	in-class solution by students
wed	9/16/18	lecture 8	quinine (Uskokovic, Stork)
fri	9/18/15	lecture 9	quinine (Jacobsen)
mon	9/21/15	lecture 10	prostaglandins (Corey)
wed	9/23/15	lecture 11	prostaglandins (Stork)
fri	9/25/15	lecture 12	prostaglandins (other approaches)
mon	9/28/15	problem set 3	in-class solution by students
wed	9/30/15	lecture 13	progesterone (part 1)
fri	10/2/15	lecture 14	yuzuriha alkaloids (Heathcock)
mon	10/5/15	lecture 15	FR182877 (Sorensen, Evans)
wed	10/7/15	lecture 16	erythronolides (Corey)
fri	10/9/15	lecture 17	erythronolides (Stork)
mon	10/12/15	problem set 4	in-class solution by students project 1 information
wed	10/14/15	lecture 18	cytovaricin (Evans)
fri	10/16/15	lecture 19	discodermolide (Novartis)
mon	10/19/15	lecture 20	taxol (Nicolaou, part 1)
wed	10/21/15	lecture 21	taxol (Nicolaou, part 2)
fri	10/23/15	lecture 22	taxol (Holton)
mon	10/26/15	problem set 5	in-class solution by students

wed	10/28/15	lecture 23	taxol (Danishefsky)
fri	10/30/15	lecture 24	taxadiene (Baran)
mon	11/2/15	lecture 25	ecteinasidin 743 (Corey)
wed	11/4/15	lecture 26	ecteinasidin 743 (Fukuyama 1st)
fri	11/6/15	lecture 27	ecteinasidin 743 (Fukuyama 2nd, semi)
mon	11/9/15	problem set 6	in-class solution by students turn in project 1, project 2 information
wed	11/11/15	lecture 28	vancomycin (Nicolaou, part 1)
fri	11/13/15	lecture 29	vancomycin (Nicolaou, part 2)
mon	11/16/15	lecture 30	vancomycin (Evans)
wed	11/18/15	lecture 31	chloropectin I (Snapper & Hoyveda)
fri	11/20/15	lecture 32	introduction to glycoproteins
mon	11/23/15	no class	thanksgiving break
wed	11/25/15	no class	thanksgiving break
fri	11/27/15	no class	thanksgiving break
mon	11/30/15	project 2 help session	
wed	12/2/15	lecture 33	to be announced
fri	12/4/15	lecture 34	to be announced
mon	12/7/15	lecture 35	to be announced
wed	12/9/15	lecture 36	to be announced
fri	12/11/15	course summary	turn in project 2