

**CHEM 544-1
COMPLEX MOLECULAR SYNTHESIS
SPRING 2018**

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 = checkmate¹), 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 of synthesis. 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 in chess, a good way to learn the game (i.e. how to plan a successful synthesis) involves analyzing the work of masters. This will be our approach as well. Each synthesis covered will begin with a discussion of the target molecule, 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 and their solution.

Lectures: The lectures were developed from the primary literature. In order to fully understand the work presented, students should read the primary references associated with each synthesis - and cited literature therein as needed. 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. They are also on reserve at the Owen Science & Engineering Library.

Workshops: The class includes 12 regularly scheduled workshops. These interactive workshops will be used to answer questions, discuss useful concepts, and practice solving problems.

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) develop an original total synthesis proposal.

Assessment/Grading: Learning outcomes will be assessed via (1) student participation in scheduled workshops (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)

¹ This is not a perfect analogy since there is one precisely defined molecular target that is known at the start but many possible checkmate board positions that will depend on how the game evolves.

Class Schedule

mon	1/8/18	lecture 1	course introduction
wed	1/10/18	lecture 2	synthesis design part 1
fri	1/12/18	lecture 3	synthesis design part 2
mon	1/15/18	mlk day	no class
wed	1/17/18	workshop	synthesis design practice
fri	1/19/18	lecture 4	reserpine part 1 (Woodward)
mon	1/22/18	lecture 5	reserpine part 2 (others)
wed	1/24/18	lecture 6	quinine (Woodward)
fri	1/26/18	lecture 7	quinine (Stork)
mon	1/29/18	workshop	project 1 details
wed	1/31/18	lecture 8	quinine (Jacobsen)
fri	2/2/18	lecture 9	prostaglandins (Corey)
mon	2/5/18	workshop	
wed	2/7/18	lecture 10	prostaglandins (Stork)
fri	2/9/18	lecture 11	prostaglandins (others)
mon	2/12/18	workshop	
wed	2/14/18	lecture 12	erythronolide (Corey)
fri	2/16/18	lecture 13	cytovaricin (Evans)
mon	2/19/18	president's day	no class
wed	2/21/18	lecture 14	discodermolide (Novartis)
fri	2/23/18	lecture 15	taxol (Nicolaou)
mon	2/26/18	workshop	
wed	2/28/18	lecture 16	taxol (Holton)

fri	3/2/18	lecture 17	taxol (Baran)
mon	3/5/18	workshop	turn in project 1, project 2 details
wed	3/7/18	lecture 18	yuzuriha alkaloids (Heathcock)
fri	3/9/18	lecture 19	progesterone (Johnson)
mon	3/12/18	spring break	no class
wed	3/14/18	spring break	no class
fri	3/16/18	spring break	no class
mon	3/19/18	workshop	
wed	3/21/18	lecture 20	FR182877 (Sorensen, Evans)
fri	3/23/18	lecture 21	saframycin (Meyers)
mon	3/26/18	workshop	
wed	3/28/18	lecture 22	ecteinascidin 743 (Corey)
fri	3/30/18	lecture 23	ecteinascidin 743 (Fukuyama)
mon	4/2/18	workshop	
wed	4/4/18	lecture 24	vancomycin part 1 (Nicolaou)
fri	4/6/18	lecture 25	vancomycin part 2 (Nicolaou)
mon	4/9/18	workshop	
wed	4/11/18	lecture 26	vancomycin (Evans)
fri	4/13/18	lecture 27	EPO part 1 (Danishefsky)
mon	4/16/18	workshop	
wed	4/18/18	lecture 28	EPO part 2 (Danishefsky)
fri	4/20/18	lecture 29	EPO part 3 (Danishefsky)
mon	4/23/18	workshop	
wed	4/25/18	lecture 30	to be determined

fri 4/27/18 course summary turn in project 2