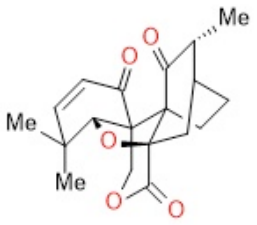
CHEM 408
Organic Synthesis – Fall 2015

Contact Information:



Professor: Emily C. McLaughlin
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Phone: extension 2355

Time and Place: Class meets Tuesdays from 4:40 to 7:00 pm in RKC 122

Office Hours: Tuesdays 10-11 am, Wednesdays 3-4 pm, and by appointment

Suggested Material: Nicolaou and Sorenson, Classics in Total Synthesis: Targets, Strategies, Methods, VHC: Weinheim, Germany, 1996. (ISBN-13: 978-3527292318) (*also on reserve in the library*)

Additional Resources (on reserve in the library):

1. Nicolaou and Snyder, Classics in Total Synthesis II: Further Targets, Strategies, Methods, Wiley-VHC: Weinheim, Germany, 2003.
2. Zweifel and Nantz, Modern Organic Synthesis: An Introduction, W.H. Freeman and Co., 2007.
3. Kürti, and Czakó, Strategic applications of named reactions in organic synthesis; Elsevier Academic Press, 2005.
4. Carey and Sundberg, Advanced organic chemistry: part B; Kluwer Academic/Plenum Pub. 2001.
5. March, Advanced organic chemistry: reactions, mechanisms, and structure, 4th ed.; J. Wiley, 1992.
6. Li, Name reactions: a collection of detailed reaction mechanisms, 3rd, ed.; Springer, 2003.
7. Mundy, Ellerd, Favaloro, Named Reactions and Reagents in Organic Synthesis, 2nd, ed.; Wiley, 2005.
8. Greene, Protective Groups in Organic Synthesis; Wiley, 1999.
9. ***Feel compelled to browse***: there are a number of other useful texts concerning organic synthesis *(see section QD.251-QD.262 in the library)*

Course Objectives:

- To develop an understanding of synthetic design and strategy in the preparation of complex, bio-active molecules.

  Instead of a rigorous introduction to reaction types and detailed mechanisms, we will work together in analysis of specific syntheses and key reaction methodologies. The molecules (outlined below) are a sampling of classes of natural (and one non-natural) products that have attracted much attention from synthetic chemists in recent years.

- To gain exposure to the excitement and challenges of modern organic synthesis while you acquire knowledge about the historical, medical, and industrial significance of certain molecules.

- To be challenged in the comprehension of the primary literature within the field of organic synthesis as well as your own (and collaborative) written and oral analyses of this work.

- To refine your skills and creativity in analyzing a recent total synthesis.

Course Topics (tentative due dates underlined):

September	1	Synthetic Design – Retrosynthetic analysis and planning a synthesis
	8	Special Topic: Photoredox catalysis – the new "*it reaction*" in synthesis
	15	Group A – β-Lactams: Penicillin *(Shehan)*
	22	Group B – β-Lactams: Thienamycin *(Merck)*
	29	Group A – Tetracyclines *(Stork)*
October	6	Group B – Tetracyclines *(Myers)*
	13	FALL BREAK – No Class ------ *Comparative Writing Assignment Due*
	20	SEMINAR - Jeffrey Winkler – University of Pennsylvania
	27	Group A – Tamiflu *(Roche)* ----- *Synthesis Proposal Abstract Due*
November	3	Group B – Tamiflu *(Hayashi)*
	10	Group A – Nakadomarin A *(Funk)*
	17	Group A – Nakadomarin A *(Evans)* ---- *Retrosynthesis Due*
	24	Jason Dutra, Pfizer Neuroscience – Design and Synthesis of BACE inhibitors
December	2	Special Topic: Maoecrystal V ----- *Rough Draft Synthesis Proposal Due*
	8	Synthesis Presentations
	15	Synthesis Presentations/Final Draft of Proposal Due

Rationale/Topic Design: The class has been divided into two groups, A and B. As outlined in the calendar, each group will be responsible for the presentation of 4 different synthetic strategies. Each group will have a significant amount of freedom in the presentation format (should be about 60 minutes) and dividing the "labor." Each topic should include:

1. The historical, commercial, medicinal, and biological *significance* of the target.
2. A thorough *retrosynthetic analysis*
3. A detailed outline of the forward synthesis and explanations ready for any/all of the mechanisms, if requested
4. Analysis of the key methodology used in the synthesis
5. A summary of the highlights and take-home messages from the synthesis

The presenting group should feel free to use the whiteboards, powerpoint slides, handouts, worksheets, molecular models or group activities for the rest of the class. Be creative!

Sub-Group Meetings: Each week, the presenting sub-group (A or B) will arrange a short meeting with Emily for consultation, direction, and questions about the synthesis. This meeting should not take place during regular office hours.

Questions and Comments: During the presentations, the non-presenting group should be active in asking questions pertaining to the topic as well as clarification. This is a small class - don't be shy.

After the presentation, the non-presenters (including myself) will have the opportunity to post further questions and comments about the synthesis through the **Discussion Forum** on Moodle. These questions/discussions/comments are **required** and will be *part of your grade for the course*.

During the next meeting, these questions will be addressed to the best of the presenting group's abilities in the first 10-15 minutes of class. This should add some continuity to reviewing our topics.

Comparative Writing Assignment: In the first half of the semester and following each pair of presentations, you will have the opportunity to submit **one** short (typewritten) assignment that compares and contrasts the two related syntheses. This should not be more than 3-4 pages of analysis and suggested topics for consideration include, but are not limited to: elegance, ingenuity, convergency, divergency, flexibility, number of steps, overall yield, stereocontrol, cost or availability of materials, scalability, safety, toxicity of reagents, new/interesting reactions, biosynthetic insights, and value of the final product.

Some ideas –

- Imagine that you are an industrial process chemist and need to make kilos of product. Which route would you choose? Maybe a combination of the two routes? Defend your decision in a report to your supervisor.
- Write a dialogue or mini-play in which two chemists with different opinions argue about the drawbacks and merits of each approach.
- More straightforward → Summarize each approach and describe the relative strengths and weaknesses of each

Homework Assignments: Throughout the semester you will be assigned 2-3 BREIF homework assignments in which you will practice your synthetic and mechanistic chemistry skills. These will be announced in class.

Synthesis Proposals: The course culminates with individual synthesis proposals! As outlined in the calendar, you will choose your own molecule as a synthetic target and propose a reasonable synthesis.

The process:

1. Choose a reasonable target from any source (try the Journal of Natural Products)
2. Have the target approved by Emily and provide a brief abstract describing your interest in the molecule (*it may be helpful to have a few possibilities before writing your abstract*)
3. Devise a reasonable retrosynthetic analysis.
4. Provide the retrosynthesis to Emily for feedback.
5. Turn the retrosynthesis into a forward strategy with solid rationale.
6. Present this to the class during the last three weeks of the semester.
7. Turn this into a final written proposal *(don't forget your references!!!)*

Grading: You will be graded on your group presentations, discussion board questions and comments (online posts), class participation, the comparative writing assignment and synthesis proposal.

Breakdown:	Group presentations	40%
	Participation and commentary	20%
	Comparative Writing Assignment	10%
	2-3 Brief Homework Assignments	10%
	Final Synthesis Presentation and Proposal	20%

Website: I have set up a website for our course at **moodle2.bard.edu**. You will need a password to join the class website. I will post all pertinent course documents on Moodle, book excerpts, reading from the primary literature, and links to useful websites/blogs/etc.. This also includes a *required* discussion forum. Please send a test message to the first thread on the discussion board ASAP.
The Moodle2 password is: **structuresF15**

Please familiarize yourself with the use of ChemDraw and SciFinder Scholar.
(download/login instructions for these programs can be found on the Moodle website.)