Chem 242 Syllabus

Chem 242: Advanced Organic Chemistry: Asymmetric Synthesis of Natural Products
Instructor: Jose S. Madalengoitia (he/him)
Office: Innovation E345
Office Hours: Monday 1:00-2:00, Tuesday 1:00-2:00, Wednesday 2:00-3:00 or by appointment
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Recommended Reference Books:

Eliel, E. L.; Wilen, S.H.; Mander, L.N.; *Stereochemistry of Organic Compounds*, Wiley, New York, 1994
Green, W. W.; Wuts, P. G. M. *Protective Groups in Organic Chemistry*, 1987.
March, J. *Advanced Organic Chemistry*, Wiley, New York, 1985.
Warren, S. G. *Organic Synthesis, the Disconnection Approach*, New York, 1982.
Encyclopedia of Reagents for Organic Synthesis, Paquette, Ed.; Wiley: New York, 1995.
Comprehensive Organic Chemistry, Barton, ed.; New York, Volumes 1-6.
Comprehensive Organic Transformations Larock, R. C.; VCH: New York, 1989.

Coursework Grading

The standard benchmark for the competence of a synthetic organic chemist is the ability to propose a potential multistep synthesis of a complex natural product target. Accordingly, this course will include two proposed synthesis of two different natural products. The first synthesis will be of a bridged polycyclic natural product, while the second synthesis will be of a polyketide.

Each proposed synthesis will be subjected to three drafts. The first draft will be a carefully prepared retrosynthetic analysis that will identify the major problems to be addressed in the synthesis and propose key bond disconnections to deal with these problems. The second draft will require a complete forward synthetic route showing all steps required to complete the target from appropriate sources of enantiopure building blocks. I will provide the critical review of this draft. The final draft will be a formal written proposal. This draft should be clear and concise. For your proposal, begin with your schemes and figures. Structures in schemes sand figures should be drawn with ChemDraw. Structures should be numbered in bold. Refer to your structure numbers in the text (or example, "Chemoselective reduction of α-amino ester **7** with $NaBH_4$ will furnish aminol **8**"). Provide references for all transformations. Only this draft will receive a grade, but failure to make the earlier draft dates will adversely affect your score. The synthesis of the first bridged polycyclic natural product need not be asymmetric, however, there must be clear control of relative stereochemistry. Where appropriate provide a figure that explains the control of relative stereochemistry.

Graduate students will do a 15 minute oral presentation of their synthesis to the class.

The natural products that you will have to provide a total synthesis for have been previously synthesized, but you will need to come up with your own unique total synthesis.

		Date
Synthesis 1.	1st draft	2/27
Synthesis 1.	2nd draft	3/6
Synthesis 1.	Final draft	3/22
	Presentation	3/24, 3/27
Synthesis 2.	1st draft	4/17
Synthesis 2.	2nd draft	4/24
Synthesis 2.	Final draft	5/5
	Presentation	5/11

Course Outline

Section 1. Introduction: background and terminology

Section 2. Strategic bond analysis

Section 3. Total synthesis examples

Section 4 Fragment coupling reactions

Section 5. Chiral building blocks: chiron approach

Section 6. Chiral building blocks: auxiliary stereocontrol

Section 7. Chiral building blocks: reagent stereocontrol

Section 8. Chiral building blocks: catalyst stereocontrol

Section 9. Total synthesis examples