CHEMISTRY 155/255
Synthesis of Complex Molecules

Winter 2008
Tu/Th 8:00-9:20am SOLIS 110

Professor K. C. Nicolaou
TSRI, Beckman Building
kcn@ucsd.edu

Professor Emmanuel Theodorakis
PACHALL 5225A
etheodor@ucsd.edu

Office Hours: By appointment

Grading:

	Chem 255	***Chem 155***
Midterm	25%	33%
Report (see below)	25%	33%
Proposal (see below)	25%	NA
Final exam	25%	33%

Prerequisites: The students of this class are expected to know how to work with ChemDraw and also how to use scientific databases such as Beilstein and SciFinder to retrieve any appropriate information. In addition, knowledge of reaction mechanisms and synthetic methods is necessary.

Books (required):
Classics in Total Synthesis K.C. Nicolaou and E. J. Sorensen VCH, **1996**. ISBN 3-527-29231-4.
Classics in Total Synthesis II K.C. Nicolaou and S. Snyder VCH, **2003**. ISBN 3-527-30684-6
Additional recommended reading:
E.J. Corey and X. Cheng, "*The Logic of Chemical Synthesis*", John Wiley & Sons, **1989**

Class Assignments:
Report (all students): Each student will prepare a short overview of a published synthesis of a natural product that was published in the literature between 2007-present. The review should be about 4-6 pages long, formatted following the NIH style, and composed as suggested below. This review should not be a repetition of the selected paper but a concise presentation of the synthesis, similarly to the way the synthesis is presented in the "Classics". The target selection should be completed by January 24 and the review should be ready by February 7.
Note: *Knowledge of Chemdraw is essential.*

Proposal (only for 255 students-graduate level class): The 255 students will need to find a new natural product of interest and write a proposal on its synthesis. Each student will need to look at the recent literature dealing with natural products isolation and select a few molecules of interest. Upon consultation with Professor Theodorakis, the student will select his synthesis target and will prepare the proposal as a word document with incorporated ChemDraw schemes. The proposal should be about 4-6 pages long, formatted using the NIH style and composed as suggested below. The target selection should be completed by February 7 and the proposal should be ready by February 28.
Note: *Knowledge of Chemdraw and Beilstein/SciFinder search engines are essential.*

Further information on Class assignments:

Before you decide on the natural product synthesis you would like to review, please consult with either Professor Nicolaou and/or Theodorakis. We will try to help you with your choice.

Your synthesis review should include the following (4-5 pages of formatted document including schemes):

1. Introduction (Background, biological properties, related syntheses (if any), other new developments related to the synthesis).

2. Retrosynthetic analysis (In one scheme indicate the key disconnections that are critical for the synthesis of the reported molecule. Comment on the key reactions and if appropriate show any modifications as reported in the paper).

3. Synthesis (In 1-3 schemes present the reported synthesis. Use one reaction per arrow and indicate the structures of products or even key reactive intermediates. If during this process you are creating new asymmetric centers comment of the reasons for stereoselectivity. If applicable, explain why the authors decided to pursue a particular strategy or set of reaction conditions. Explain the reasoning of the authors).

4. Conclusion

Conclude with what we should remember from the reported synthesis; how this strategy or a reaction addressed a synthetic limitation. In 2-3 sentences explain why this synthesis deserved to be published in that journal.

Similar information should be included in the proposal (applicable only to 255 students).

Exams (all students):

During the midterm and final, the students will be asked to propose a synthesis of a target molecule and propose missing reagents and/or synthetic intermediates of a recently synthesized natural product.

Lecture Outline (tentative)

Selected total syntheses will be discussed. Special emphasis will be placed on retrosynthetic analysis, synthetic strategies, synthetic tactics and methodologies, and asymmetric synthesis. The presentations will be as follows (tentative):

January 8:	Atoms, Molecules & Synthesis/Urea & Acetic Acid/Aspirin	(Handouts)
January 10:	Tropinone/Terpineol/Morphine	(Handouts)
January 15:	Steroids & The Pill/Penicillin	(Handouts)
January 17:	Taxol/Brevetoxin B	(Handouts)
January 22:	Small Molecule Drugs/Biologics	(Handouts)
January 24:	Total Synthesis of Taxol	(Book 1, Chapter 34)
January 29:	Tetrodotoxin	(Handouts)
January 31:	Pentacycloanammoxic Acid/Biyouyanagin A	(Handouts)
February 5:	Tetracyclin/Maduropeptin	(Handouts)

February 7: Midterm

February 12:	calicheamicin	(Book 1, chapter 30)
February 14:	Rapamycin	(Book 1, chapter 31)
February 19:	Quadrigemine C and Psycholeine	(Book 2, chapter 19)
February 21:	isochrysohermidin, resiniferatoxin	(Book 2, chapters 2 and 6)
February 26:	Okaramine N	(Book 2, chapter 22)
February 28:	longithorone, (-)-FR182877	(Book 2, chapters 16 and 17)
March 4:	aspidophytin, vinblastin	(Book 2, chapters 12 and 18)
March 6:	TBA	
March 11:	TBA	
March 13:	TBA	

March 20: Final exams

Note that a substantial amount of new material will be presented in each class.
It is strongly recommended that you review the chapters before each presentation, so that you feel somewhat familiar with the content of the lectures.