

CHEM 424 - Organic Synthesis - Winter 2016**GENERAL INFORMATION**

This course will develop the use of retrosynthetic analysis as a tool for designing practical multi-step syntheses of organic molecules. The concept of retrosynthesis has been used implicitly and explicitly in organic chemistry courses at the 300 level. In this course, you will learn a formal way of applying retrosynthetic analysis to the synthesis of complex target molecules, and you will receive considerable opportunity to practice its use. The focus of CHEM 424 will be on synthesis design and on specific reactions used in executing a synthesis. All students should recognize that these two aspects of synthesis are not independent. Familiarity with basic organic transformations plus the ability to learn more advanced reactions will be essential, especially in preparing the final synthesis proposal. The course is presented in a "reading" format supported by some lectures, discussions and presentations by students. Class discussions and lectures will not necessarily "cover" the textbook material. We will focus on key points, but also examine issues that arise from the material in the book and from recent literature. We will also talk about some important organic reactions that have changed how chemists approach synthesis design. In the event of extraordinary circumstances beyond the University's control, the content and/or evaluation scheme in this course is subject to change.

Instructor**Dr. Pat Forgione**

Office hours: Open door policy, unless I have a visitor.

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Course Format

Lectures: 1.25 h / week, 26 sessions; T/Th 11:45-13:00 in CC-101

Suggested Materials

- 1) Classics in Total Synthesis, Nicolau, Sorenson, Wiley-VCH, 1996, paperback ISBN 3-527-29284-5
- 2) The above book and twenty others have been placed on 2-hour reserve at the Vanier library. These will provide useful resources throughout the course. You can find the list of these books on the library website by searching with the course number.

Useful resources

- 1) Comprehensive Organic Synthesis: Selectivity, Strategy and Efficiency in Modern Organic Chemistry QD 262 C535 1991
- 2) Fieser and Fieser's reagents for organic synthesis, QD 262 F5.
- 3) Comprehensive organic functional group transformations, QD 262 C534 1995.
- 4) A very interesting read on the state of organic synthesis: K.C. Nicolaou: The Art and Science of Organic Synthesis at the Dawn of the Twenty-First Century - *Angew. Chem. Int. Ed.* **2000**, 39, 44-122.
- 5) Interesting Read: Molecules that Changed the World, Nicolaou, K.C. Montagnon, T. Wiley-VCH, 2008 ISBN 978-3-527-30983-2

Molecular models: Using models helps considerably with many aspects of organic chemistry – many concepts require you to picture, rotate and draw 3D objects. Models **are** permitted in exams. You are strongly advised to buy a model kit.

Advice: The best way to do well in this course is to solve problems. The more you read and think about the different ways molecules can be constructed the easier and more systematic synthesis will appear. While memorization of reactions may provide you with a larger synthetic 'tool-box', there is a certain degree of art in the design of total syntheses that should not be overlooked.

GRADING SCHEME, DEADLINES & ABSENCES

To pass the course, you must earn $\geq 50\%$ on the exams (midterm and final exam). The final grade will be weighted as follows:

Presentation Participation	5 %
Total Synthesis Assignment:	20 % (5 % for preliminary retrosynthesis, 15% for final synthesis report)
In-Class Tests:	45 % (Jan 19th , Feb 2nd , Feb 16th , March 9th , March 23rd , April 6th , in-class)
Final Exam:	30 % (<i>covers entire course content</i> , scheduled by Exams Office)

Presentation Participation: As part of this course, the graduate students will present literature presentations. Each student is required to ask (at least) 2 questions over the entire presentation periods. Question will be evaluated on quality and questions that engage the class in learning. You may not obtain more points by asking more than two questions but you are certainly welcome to ask more. Each student must also evaluate all the presentations and assign a grade, if this is not done by 1 week after the final presentation is completed, the student will receive a grade of "0" for the presentation portion of the course. If a

student misses more than 25% of the presentations without a suitable note provided within 1 week of the missed class(es), they will obtain a score of 0 for the participation grade.

Total Synthesis: Each student is required to provide a total synthesis of a molecule that has not been previously synthesized. The best way to find such a molecule is to search the Journal of Natural Products, Journal of Natural Products, Natural Product Reports or Natural Product Updates for recently isolated compounds. The instructor must approve the molecule that is chosen by **January 23rd**. Although highly unlikely, if two students choose the same molecule, this will be assigned on a first come, first served basis. **As we all have access to search engines, simply replicating a published synthesis is unacceptable and will be graded with a zero!** Three examples of what is expected can be found in the textbook by Michael Smith, *Organic Synthesis*, Chapter 14. The level of molecular complexity in the targets will be similar to that of the first example (the *isocedrene ester*) shown in Smith (on page 1493 in the first edition and page 1237 in the second edition). Smith provides a *poor* proposal, followed by two reasonable ones. Look at both the poor example and the good proposals before deciding how to approach your own proposal. Another good example can be found here: <http://pubs.acs.org/doi/pdf/10.1021/ja9024403>. The first step will be to hand in a **full retrosynthetic analysis** of your molecule (due **February 2nd**). Late submissions will result in a penalty of -10% / day! I will evaluate this and constructive comments will be provided to help you with potential pitfalls that may be present in your disconnections. The final report should contain the summarized retrosynthesis, the **full** forward synthesis, multiple possibilities for transformations that you anticipate may be problematic and must include the copies of the journal articles you used as precedence for your key transformations. This should not be a huge document, but it should be 10-15 double spaced pages including schemes in addition to any photocopied reference articles. Grading will be based on the originality of the proposal (10%), the legibility and quality of the writing/chemical structures (20%), proper referencing (ACS style) formatting (20%) and feasibility of the proposal (50%). Please see me if you need additional information for the expectations. Each step in your proposal should have a "predicted" yield that estimates how successful you feel each transformation will be. **Due April 6th, in-class (late submissions – 10% / day!).**

In-Class Tests: This will be based on the material covered in class in addition to the material in the student presentations. The focus will be on the transformations covered both in independent reading and in-class. The test will be in two parts. Part A is an individual test and will be for the first 50 minutes of class. Part B will be a group test and will constitute the last 25 minutes of class. The in-class test grade for each will be 80% from Part A and 20% from Part B, and in no case can Part B reduce the grade obtained in Part A.

Final Exam: The same format as the mid-term, but only on the material covered since the mid-term and students presentations since the mid-term. Scheduled by the registrar.

If absent from an examination, you must produce a written excuse on letterhead paper, appropriately signed (e.g., by doctor or employer), **no later than one week** after the exam. The Department determines the validity of the absence and necessary arrangements will be made. If **no valid excuse** is produced, the student will receive a **zero** grade for the missed test.

PLAGIARISM AND OTHER FORMS OF ACADEMIC DISHONESTY – Highly Encouraged QUIZ AND SEMINAR

As part of this course, you are **encouraged** to (i) attend a Chemistry and Biochemistry Departmental Seminar on the academic conduct code and the appropriate use of information sources and (ii) pass the online quiz associated with this seminar (note: passing grade for the quiz is 100%). The aim of this seminar is to clarify the academic conduct code in terms of what practices will be considered unacceptable with regards to work submitted for grading in Chemistry and Biochemistry courses. Should you have already attended these sessions you are not required to repeat them this semester. This short seminar (1 hour) will be held at the times as posted outside the main Chemistry and Biochemistry office (SP-201.01). The academic code of conduct can be found in section 16.3.14 of the academic calendar in either printed or the online (<http://registrar.concordia.ca/calendar/pdf/sec16.pdf>) versions. Any form of cheating, copying or plagiarism found in this course will be reported and the appropriate sanctions applied. The mandatory seminar is a clear and fair opportunity to learn what our faculty regards as academic misconduct. Failure to take part in this learning opportunity and thus ignorance of these regulations is no excuse and will not result in a reduced sanction in any case where academic misconduct is observed.

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Class notes will be posted on the course moodle site throughout the term.

How to search the organic synthesis literature:

1. Useful reference texts that relate closely to the content of this course

“The Logic of Chemical Synthesis.” Corey and Chang, Wiley, 1989.

2. Encyclopedias and Reference Books:

- **Strategic Applications of Named Reactions in Organic Synthesis**

Laszlo Kurti and Barbara Czako (Elsevier Academic Press)

- **Reagents for Organic Synthesis** (Fieser and Fieser, Vol 1-16)

(provides references and summaries of reagents used in organic synthesis)

- **Encyclopedia of Reagents for Organic Synthesis** (Paquette)

(a more modern treatment of the subject than Fieser and Fieser)

- **Organic Synthesis**

(a multi-volume series as well as collective volumes that survey useful / common organic syntheses)

- **Compendium of Organic Synthetic Methods**

(a multi-volume series that illustrates synthetic methods in reaction schemes, arranged by functional group)

- **Comprehensive Organic Synthesis** (Trost and Fleming, Pergamon Press, 1991) (a comprehensive review of modern synthetic chemistry arranged by reaction type)

- **Comprehensive Heterocyclic Chemistry** (Katritzky and Rees, Pergamon Press, 1984)

(a comprehensive review of modern heterocyclic chemistry)

- **Comprehensive Functional Group Transformations** (Larock, VCH, 1989) (Review of functional group interconversions arranged by functional group types with citations to primary literature)

- **Protective Groups in Organic Synthesis, 3rd Ed.** (Greene, Wuts, John Wiley and Sons, 1999)

(a survey of protecting groups used in organic synthesis)

- **Catalogues of chemical suppliers:** (e.g. Aldrich, Lancaster, VWR, Fluka, BDH and Acros)

(these catalogues often cite useful lead references along with their reagents)

3. Journals

- Journal of the American Chemical Society

- Angewandte Chemie, International Edition, English

- Journal of Organic Chemistry

- Organic Letters

- Chemical Communications

(These journals often have excellent examples of total synthesis and new methods useful for total synthesis)

4. Journals (Reviews)

- Chemical Reviews

- Accounts of Chemical Research

(These journals provide detailed review articles relating to various topics in organic synthesis)

5. How to search the chemical literature:

SciFinder Scholar and Beilstein: The library has access to SciFinder Scholar but Beilstein is another very useful

search engine. In both cases, structures or partial structures are drawn and the search engine provides references relating the synthesis or use of the drawn compound. Danielle Dennie is willing to provide training on the use of refresher course on the use of SciFinder Scholar, please see me if you are interested.

PARTIAL LIST OF CONCORDIA UNIVERSITY SERVICES...take advantage, they are there for your benefit!

1. Concordia Counselling and Development offers career services, psychological services, student learning services, etc. <http://cdev.concordia.ca/>
2. The Concordia Library Citation and Style Guides: <http://library.concordia.ca/help/howto/citations.html>
3. Advocacy and Support Services: <http://supportservices.concordia.ca/>
4. Student Transition Centre: <http://stc.concordia.ca/>
5. New Student Program: <http://newstudent.concordia.ca/>
6. Access Centre for Students with Disabilities: <http://supportservices.concordia.ca/disabilities/>
7. Student Success Centre: <http://studentsuccess.concordia.ca/>
8. The Academic Integrity Website: <http://provost.concordia.ca/academicintegrity/>
9. Financial Aid & Awards: <http://web2.concordia.ca/financialaid/>
10. Health Services: <http://www-health.concordia.ca/>
11. etc. etc. etc.