Synthetic Organic Chemistry - CHEM 4021 & CHEM 5021 Syllabus - W2023-2024

SC/CHEM 5021 3.0 (graduate)
SC/CHEM 4021 3.0 (undergraduate)

Three lecture hours per week
Term: Winter 2023-2024
Prerequisite: SC/CHEM 3021 or permission from the course director.
Time: Mon, Wed and Fri 12:30 PM
Location: ACE002 Monday and Friday
ACE013 Wednesday

Course Director

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Office hours: Flexible within reason
Appointment by e-mail if needed

Course Description. This course is designed to introduce you to the science of complex molecule synthesis. It includes a brief introduction to retrosynthetic analysis, practical issues in synthesis, and selectivity issues. The bulk of the course consists of a survey of some important classes of reactions, with particular emphasis on mechanistic understanding and rationale for observed selectivity when appropriate. The strategic use of some reactions in complex molecule synthesis will be highlighted.

Course Objectives. The purpose of this course is to provide the student with an appreciation of complex molecule synthesis and some tools to analyze and solve synthetic problems.
At the end of the course the student should:

i) Be able to analyze the synthetic problem and provide a reasonable synthetic solution based on known (or reasonable) chemical transformations.
ii) Have a good knowledge of some important modern synthetic methods, including their mechanisms and stereochemical implications.

Tools and Textbooks. *The use of chemical model kits is strongly encouraged* as a study tool as you review, solve problems and write exams. Your ability to appreciate molecules as three-dimensional entities will greatly enhance your understanding of the material.
Course notes will be provided in the form of PDF files as the course progresses. Although they are fairly comprehensive, there will be discussion that is not included in the notes.

Delivery. In-person lectures. Lectures will not be recorded. Attendance is essential.

Evaluation. Evaluation will be according to the scheme below.

Course	CHM 4021	CHEM 5021
Practice problems[1]	Not marked	Not marked
Midterm exams[2]	50 % (2 x 25 %)	50 % (2 x 25 %)
Final written exam[2]	50 %	50 %

[1] I will pose many questions during the course and I will take up the solution in a future lecture. You will benefit most from this by attempting the problem on your own before I take it up. I will not provide assignments.

[2] Midterm exams will be on **Monday February 12** and **Monday March 11** The final exam date will be determined by the registrar.

Learning Objectives

1. Identify the structural components (functional groups, functional group relationships, stereochemical relationships) in a synthetic target (a complex organic molecule).
2. Understand the theory and terminology of retrosynthetic analysis. Apply retrosynthetic analysis to a target molecule in order to devise a plan for its synthesis
3. Understand the fundamental principles leading to selectivity in organic reactions (e.g. kinetic vs. thermodynamic control, conformation effects, stereoelectronic effects).
4. Apply these concepts to achieve regioselectivity, chemoselectivity, diastereoselectivity and/or enantioselectivity in a synthetic sequence leading to a target molecule.
5. Implement a practical approach in developing a synthesis plan, taking into account the effects of step count, divergent vs. convergent synthesis, and optimization of yield.
6. Apply conformational analysis to synthetic planning, and appreciate the effect of conformation on the selectivity of reactions.
7. Appreciate the relative acidity of a range of functional groups (pKa values) and use these in the design of reactions.
8. Appreciate all the factors involved in the formation and alkylation of ketone enolates. These factors include i) relative acidities, ii) kinetic vs. thermodynamic control, iii) stereoelectronic effects of enolate formation and enolate alkylation, iv) models for enolate formation (Ireland model) and alkylation (Stevens model), and v) medium effects (solvent/salt effects).
9. Understand and apply the concept of chiral auxiliary, and use chiral auxiliaries in diastereoselective reactions used to prepare enantioenriched products.
10. Appreciate the different variations of the aldol reaction, and the factors that affect the outcome of these reactions (e.g. enolate geometry, facial selectivity, etc). Understand the

Zimmerman-Traxler model for aldol reactions and use it to predict relative configuration in aldol products.

11. Understand the fundamental principles underlying additions of nucleophiles to carbonyl groups (chelation effects, substrate effects, geometric requirements), the stereochemical models that arise from them (Felkin-Anh-Eisenstein, Conforth model, chelation controlled additions, directed additions), and apply these in the synthesis of complex molecules. These include alkylations (carbon based nucleophiles such as allyl metal reagents, and enolates) and reductions (hydride reagents).
12. Understand and apply the concept of protecting groups in synthesis. Understand the underlying reaction mechanism for installation and removal of a range of protecting groups.
13. Suggest reagents required for the oxidation of a variety of functional groups, especially alcohols. Understand the mechanism of a range of oxidation methods (DMSO-based oxidation, metal oxide oxidations (Mn, Cr, Ru), hypervalent iodine oxidations, peroxide oxidations).
14. Suggest reagents required for the installation of double bonds in complex synthetic targets. Understand the underlying mechanism and stereochemical aspects of these reactions, and how they control the geometry of the double bond in the product.
15. Become familiar with a variety of reactions to exploit C=C bonds in synthesis
16. Understand the logic of protecting groups, the mechanism of protection and deprotection, and their use in complex molecules.
17. Understand the factors that favour or disfavour ring-formation (Baldwin's rules)

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University Policies

Academic Honesty and Integrity

York students are required to maintain the highest levels of academic honesty and they are subject to the Senate Policy on Academic Honesty (http://secretariat-policies.info.yorku.ca/policies/academichonesty-senate-policy-on). The Policy affirms the responsibility of faculty members to foster acceptable standards of academic conduct and of the student to abide by such standards.

There is also an academic integrity website with comprehensive information about academic honesty and how to find resources at York to improve students' research and writing skills, and cope with university life. Students are expected to review the materials on the Academic Integrity website (https://spark.library.yorku.ca/academic-integrity-what-is-academic-integrity).

Numerous students in Faculty of Science courses have been charged with academic misconduct when materials they uploaded to third party repository sites (e.g. Course Hero, One Class, etc.) were taken and used by unknown students in later offerings of the course. The Faculty's Committee on Examinations and Academic Standards (CEAS) found in these cases that the burden of proof in a charge of aiding and abetting had been met, since the uploading students had been found in all cases to be wilfully blind to the reasonable likelihood of supporting plagiarism in this manner. Accordingly, to avoid this risk, students are urged not to upload their work to these sites. Whenever a student submits work obtained through Course Hero or One Class, the submitting student will be charged with plagiarism and the uploading student will be charged with aiding and abetting. Note also that exams, tests, and other assignments are the copyrighted works of the professor assigning them, whether copyright is overtly claimed or not (i.e. whether the © is used or not). Scanning these documents constitutes copying, which is a breach of Canadian copyright law, and the breach is aggravated when scans are shared or uploaded to third party repository sites.

Universal Access and Equity

York University is committed to the principles of respect, inclusion and equality of all persons with disabilities across campus. The university provides services for students with disabilities (including physical, medical, learning and psychiatric disabilities) needing accommodation relating to teaching and evaluation methods/materials. These services are made available to students in all faculties and programs at York University.

Students in need of these services are encouraged to register with counselling and disability services (CDS) as early as possible to ensure that appropriate accommodation can be provided

with advance notice. Students may wish to discuss the nature of their accommodations with their professor early in the term.

Many students registered with CDS are entitled to midterm and final exam accommodations such as extra time. These students must register and book their tests and exams with the Alt Exam Centre at York as soon as possible.

Additional information is available at the following websites:

Counselling and Disability Services: http://cds.info.yorku.ca York Accessibility Hub: http://accessibilityhub.info.yorku.ca Alternate Exam Centre: http://altexams.students.yorku.ca

Religious Observance Accommodation

York University is committed to respecting the religious beliefs and practices of all members of the community, and making accommodations for observances of special significance to adherents.

Please note that to arrange an alternative date or time for an examination scheduled in the formal examination periods (December and April/May), students must complete an Examination Accommodation Form, which can be obtained from Student Client Services, Student Services Centre or online at https://registrar.yorku.ca/sites/registrar/files/pdf/exam_accommodation.pdf at least 3 weeks before the final exam and submitted to the course director.

Student Conduct in Academic Situations

Students and instructors are expected to maintain a professional relationship characterized by courtesy and mutual respect. Moreover, it is the responsibility of the instructor to maintain an appropriate academic atmosphere in the classroom and other academic settings, and the responsibility of the student to cooperate in that endeavour. Further, the instructor is the best person to decide, in the first instance, whether such an atmosphere is present in the class. The policy and procedures governing disruptive and/or harassing behaviour by students in academic situations is available at : http://secretariat-policies.info.yorku.ca/policies/disruptive-andorharassing-behaviour-in-academic-situations-senate-policy