

Faculty of Science Course Syllabus Fall 2020 (revised June 2020)**Department of Chemistry**

Chemistry 4401/5401 (CRN 10480/13251) (Online)

Synthesis in Organic Chemistry

Fall 2020

Instructors: **Lecture:** Dr. Alex Speed; aspeed@dal.ca;**Office Hours:** Office hours will be by accessible by appointment on Teams or Zoom.**Lectures:** The course content will be delivered in an asynchronous manner on Brightspace.
September 8th 2020 to December 8th 2020

Course Description: A number of important organic reactions are examined in depth with particular attention to regioselectivity and the development of relative or absolute stereochemistry. Applications of these reactions in the synthesis of complex molecules are illustrated with recent examples from the literature.**Course Prerequisites:** The prerequisite to this course is CHEM 3401 or an equivalent from another university. CHEM 3404 is helpful, but not required. **Organic synthesis is a cumulative discipline, and it is expected that you have retained knowledge of reactions and concepts covered in preceding courses.****Course Exclusion:** CHEM 4401 and CHEM 5401 are the cross-listed classes for undergraduate students and graduate students respectively. Credit cannot be obtained for both CHEM 4401 and CHEM 5401. Students enrolled in CHEM 5401 will write tests with slightly different questions to CHEM 4401.**Learning Objectives:** At the end of this course you will be able to predict and rationalize the stereochemical outcome of processes including pericyclic reactions, chiral auxiliary chemistry, and asymmetric catalysis. You will gain knowledge of reactivity and selectivity in radical chemistry, including modern photoredox reactions. You will be able to use these reactions to design syntheses of moderate complexity.**Course Content:** The aim of this class is to provide the tools to understand advanced concepts in selectivity in organic chemistry. We will begin by discussing stereochemical terminology, and retrosynthetic analysis. We will then cover reactivity and stereoselectivity in pericyclic reactions. We will then explore acyclic stereocontrol of selected reactions through three-dimensional consideration of reagent approach and conformation. The main examples will include aldol and allylation reactions, and substrate controlled (or directed) reactions. Asymmetric catalysis will then be discussed, including asymmetric epoxidation, hydrogenation, and organocatalysis. We will finish by discussing free-radical chemistry, including photoredox chemistry. During the course will refine concepts of chemoselectivity that have been taught in preceding organic courses. A theme throughout the course will be the use of these concepts in the synthesis of molecules of moderate complexity such as pharmaceuticals and select natural products. A more detailed list of potential topics is found at the end of the first part of the syllabus.**Class Structure:** The class will be in an asynchronous format using Brightspace software. Lectures will consist of videos of annotated powerpoint slides with voice over which will be hosted on Panopto

(accessible through Brightspace). In general, I will try to upload a week's worth of lectures once a week on Monday, while problem sets will be uploaded by Wednesday, and problem set answers will be uploaded on Fridays. If your internet connection is not fast enough to properly display the materials, please let Dr. Speed know as soon as possible so that lower fidelity course materials can be provided. PDF files of the annotated and non-annotated lectures will also be made available. Occasionally literature references may be given for assigned reading. Evaluation material will be returned via e-mail. You will require some method of drawing structures to return to me. Acceptable options include:

1) Drawing the answers either free-hand or on a printout of the evaluations and returning the answers by either photographing or scanning them. Note there is free software (for example CamScanner) that allows you to generate high-quality scanned PDF files using your phone camera. I will prefer this option to ensure that the file-sizes of returned work is manageable. I recognize most people will not have access to a printer, so detailed instructions for organizing your free-hand drawings on blank paper will be provided on the tests.

2) Drawing the answers on the test PDF using a tablet equipped with stylus and drawing function. If you have the appropriate equipment and can draw legibly with this technique, this will be a good option.

3) If you do not have access to a camera, scanner, or tablet, completing the answers using Chemdraw will be permissible. Dalhousie has a site licence for Chemdraw. Please let me know if this option is the case, as you may require a time-extension to be able to produce legible answers using this technique. This is the least preferred option.

Office Hours: Office hours may be set up using either Teams or Zoom by e-mailing me first. In-person office hours will not be possible, even if you are on campus, to promote physical distancing.

Course Materials: A computer with an internet connection will be required to view the course presentations. As stated above, one of a camera, scanner, tablet/stylus, or ChemDraw will be required to return test answers. If using a scanner or camera, you will require blank or lined paper.

There is no required textbook for this course, however the following resources may be beneficial in the course:

- *"Organic Chemistry"* by Jonathan Clayden, Nick Greeves, Stuart Warren. Oxford University Press, 2nd Edition, 2012.

- **A comparable textbook is available online:**

"Advanced Organic Chemistry, Part B: Reactions and Synthesis", 5th Edition, by Carey and Sundberg, Springer, 2007.

This book is available on-line courtesy of the Canadian Research Knowledge Network.

To Dal students in the library or logged-in, this text-book is available at the following URL:

- <https://link.springer.com/book/10.1007/978-0-387-44899-2>
- **for home use of this**, or any other Dalhousie Library resource, modify URL to include the proxy server as follows. If the URL starts with https://, remove this, otherwise an error will be encountered:
<http://link.springer.com.ezproxy.library.dal.ca/book/10.1007/978-0-387-44899-2>
- I encourage using molecular models to understand conformation and selectivity, and these will be permitted during examinations, however they are not required.

- Avogadro is free software that allows models of molecules to be constructed and rotated. It is available at: <https://avogadro.cc/>
- Practice problems and their solutions will be made available on a weekly basis.
- Successful study habits in organic chemistry typically involve actively practicing drawing mechanisms for the reactions under study, rather than simply reviewing the mechanism and attempting to reproduce the mechanism for the first time under evaluation.

Useful Websites

Various websites are available containing information that complements that presented in the course, or may be of use in assignments.

- **Primary literature:**

There are many journals. A small set of important chemistry journals are shown below:

Home Access: See above for how to modify URLs to use Dalhousie's proxy server. Otherwise you will encounter a paywall.

American Chemical Society Journals: <http://pubs.acs.org>

Royal Society of Chemistry Journals: <http://www.rsc.org/journals-books-databases/>

Angewandte: [http://onlinelibrary.wiley.com/journal/10.1002/\(ISSN\)1521-3773](http://onlinelibrary.wiley.com/journal/10.1002/(ISSN)1521-3773)

Dalhousie Scifinder http://libraries.dal.ca/research/sciences_research/sfs.html

Scifinder is a useful, although sometimes frustrating tool for searching the chemical literature

- **Databases**

<http://www.sigmaaldrich.com> Catalogue of large chemical supplier, with physical properties and select NMR spectra of compounds

http://sdfs.db.aist.go.jp/sdfs/cgi-bin/direct_frame_top.cgi Database of NMR spectra.

http://ccc.chem.pitt.edu/wipf/MechOMs/evans_pKa_table.pdf Convenient table of pKas

<http://www.chem.wisc.edu/areas/reich/pkatable/> Extensive database of pKas

Course Assessment

Component	Weight (% of final grade)	Date
Three Assignments	15 % (5% each)	F, Sept 25 th , M, Oct 26 th , F, Nov 20 th
Three tests	45 % (15 % each)	M, Oct 5 th ; W, Nov 4 th , M, Nov 30 th
Final exam	40 %	(Scheduled during examination period by the Registrar)

The tests will be e-mailed to you around noon, Atlantic time, and will be accepted over a 6 hour window, starting from when the test is sent. Test answers will be returned digitally using either scanned or photographed, or electronically produced answers. The test will be open-book, however collaboration with others will not be permitted. **Your test will be unique to you, so you must return the answers based on the copy you have been sent.**

The final exam will be e-mailed to you around noon, Atlantic time, on the day scheduled by the registrar. It will be of the typical length that a 3 hour in-person exam would be, but it will be accepted over a 24 hour window, ending at noon, Atlantic Time, the day following its distribution. The final exam



will be open-book, however collaboration with others will not be permitted. **Your final exam will be unique to you, so you must return the answers based on the copy you have been sent.**

For 4401:

Conversion of numerical grades to Final Letter Grades follows the Dalhousie Common Grade Scale

A+ (90-100)	B+ (77-79)	C+ (65-69)	D	(50-54)
A (85-89)	B (73-76)	C (60-64)	F	(<50)
A- (80-84)	B- (70-72)	C- (55-59)		

For 5401:

The following grading scheme for graduate students will be used:

A+ (90-100)	B+ (77-79)	
A (85-89)	B (73-76)	F(<70)
A- (80-84)	B- (70-72)	

Course Policies

If you are ill or experiencing a personal emergency at the time of a midterm test, e-mail Dr. Speed to inform him of the situation, and fill out a Student Declaration of Absence (SDA) form on Brightspace when you are able. If you are experiencing technical issues that prevent completion of an online test, exam, or assignment, please also e-mail Dr. Speed, and I will attempt to accommodate the issue. Sick notes are neither required nor permitted during the 2020/2021 academic year because of the current burden on the healthcare system. I do not typically offer make-up midterm tests, however in the case of excused absences for midterm test due to illness or another appropriate situation, the grading evaluation will remain 15% per midterm test, with the balance shifting to the final. Students suffering prolonged illness may wish to contact me or the Assistant Dean of Student Affairs to explore their options. Since I wish to recognize improvement, this alternate grading scheme may also be applied to a student showing substantial improvement on the final exam relative to in-class tests at my discretion (ie the lowest test will be dropped). For this to happen, the grade on the final exam would have to be higher than at least two of the midterm tests. Students who miss the final exam for a valid reason will be offered the opportunity to write a make-up final exam.

Course Content: The following topics may be covered in the course. The order of the topics in each subsection may vary.

Part 1: Introduction to synthesis/ stereochemical terminology

- Stereochemistry- Terminology refresher
- The importance of stereochemistry
- Resolution (salts, kinetic, dynamic kinetic)
- Determination of configuration/ enantiomeric excess
- Overview of strategies to control stereochemistry
- Overview of modern synthetic chemistry
- Linear vs convergent synthesis
- Retrosynthetic analysis/ synthetic planning

Part 2: Pericyclic Chemistry

- Overview of classes of pericyclic reaction
- Frontier Molecular Orbital Analysis
- Dewar Zimmerman Analysis
- Photochemical vs. Thermal processes
- Cycloadditions: Diels-Alder reaction- regio and stereoselectivity
- Cycloadditions: Dipolar cycloadditions
- Sigmatropic Reactions: The Cope and Claisen variants
- Electrocyclic reactions
- Group Transfer and Cheletropic Reactions

Part 3: Acyclic Stereocontrol

- Contrast with cyclic stereocontrol
- Conformational analysis
- Carbonyl addition models
- Diastereoselective Aldol (Zimmerman Traxler and Ireland Models)
- Diastereoselective (and enantioselective) allylation
- A1,3 Strain

Directed Reactions (epoxidation, hydrogenation, cyclopropanation)
Directed 1,3 diol reductions
The Evans Auxiliary
Asymmetric Alkylation
Asymmetric Aldol
Asymmetric Auxiliary Diels-Alder

Part 4: Asymmetric Catalysis

CBS Catalysts
BOX Ligand
Asymmetric Hydrogenation
Sharpless epoxidation and dihydroxylation
Jacobsen epoxidation and HKR
Iminium and enamine catalysis
Chiral Brønsted Catalysis
Copper Carbene catalysis
Diastereoselective Olefin Metathesis
Diazaphospholene case-study

Part 5: Radical Chemistry

Terminology and distinctions (arrows, initiation, propagation, termination)
Classical Tin hydride chemistry
Norrish and Barton photochemistry
Minisci Chemistry
Photoredox chemistry
HAT/Photoredox chemistry
Metallaphotoredox chemistry

University Policies and Statements

This course is governed by the academic rules and regulations set forth in the University Calendar and by Senate

Missed or Late Academic Requirements due to Student Absence

As per Senate decision instructors may not require medical notes of students who must miss an academic requirement, **including the final exam**, for courses offered during fall or winter 2020-21 (until April 30, 2021).

Information on regular policy, including the use of the Student Declaration of Absence can be found here: https://www.dal.ca/dept/university_secretariat/policies/academic/missed-or-late-academic-requirements-due-to-student-absence.html.

Academic Integrity

At Dalhousie University, we are guided in all of our work by the values of academic integrity: honesty, trust, fairness, responsibility and respect (The Center for Academic Integrity, Duke University, 1999). As a student, you are required to demonstrate these values in all of the work you do. The University

provides policies and procedures that every member of the university community is required to follow to ensure academic integrity.

Information: https://www.dal.ca/dept/university_secretariat/academic-integrity.html

Accessibility

The Advising and Access Services Centre is Dalhousie's centre of expertise for student accessibility and accommodation. The advising team works with students who request accommodation as a result of a disability, religious obligation, or any barrier related to any other characteristic protected under Human Rights legislation (Canada and Nova Scotia).

Information: https://www.dal.ca/campus_life/academic-support/accessibility.html

Student Code of Conduct

Everyone at Dalhousie is expected to treat others with dignity and respect. The Code of Student Conduct allows Dalhousie to take disciplinary action if students don't follow this community expectation. When appropriate, violations of the code can be resolved in a reasonable and informal manner—perhaps through a restorative justice process. If an informal resolution can't be reached, or would be inappropriate, procedures exist for formal dispute resolution.

Code: https://www.dal.ca/dept/university_secretariat/policies/student-life/code-of-student-conduct.html

Diversity and Inclusion – Culture of Respect

Every person at Dalhousie has a right to be respected and safe. We believe inclusiveness is fundamental to education. We stand for equality. Dalhousie is strengthened in our diversity. We are a respectful and inclusive community. We are committed to being a place where everyone feels welcome and supported, which is why our Strategic Direction prioritizes fostering a culture of diversity and inclusiveness

Statement: <http://www.dal.ca/cultureofrespect.html>

Recognition of Mi'kmaq Territory

Dalhousie University would like to acknowledge that the University is on Traditional Mi'kmaq Territory. The Elders in Residence program provides students with access to First Nations elders for guidance, counsel and support. Visit or e-mail the Indigenous Student Centre (1321 Edward St) (elders@dal.ca).

Information: https://www.dal.ca/campus_life/communities/indigenous.html

Important Dates in the Academic Year (including add/drop dates)

https://www.dal.ca/academics/important_dates.html

University Grading Practices

https://www.dal.ca/dept/university_secretariat/policies/academic/grading-practices-policy.html

Student Resources and Support

Advising

General Advising https://www.dal.ca/campus_life/academic-support/advising.html

Science Program Advisors: <https://www.dal.ca/faculty/science/current-students/academic-advising.html>

Indigenous Student Centre: https://www.dal.ca/campus_life/communities/indigenous.html

Black Students Advising Centre: https://www.dal.ca/campus_life/communities/black-student-advising.html

International Centre: https://www.dal.ca/campus_life/international-centre/current-students.html

Academic supports

Library: <https://libraries.dal.ca/>

Writing Centre: https://www.dal.ca/campus_life/academic-support/writing-and-study-skills.html

Studying for Success: https://www.dal.ca/campus_life/academic-support/study-skills-and-tutoring.html

Copyright Office: <https://libraries.dal.ca/services/copyright-office.html>

Fair Dealing Guidelines <https://libraries.dal.ca/services/copyright-office/fair-dealing.html>

Other supports and services

Student Health & Wellness Centre: https://www.dal.ca/campus_life/health-and-wellness/services-support/student-health-and-wellness.html

Student Advocacy: <https://dsu.ca/dsas>

Ombudsperson: https://www.dal.ca/campus_life/safety-respect/student-rights-and-responsibilities/where-to-get-help/ombudsperson.html

Safety

Biosafety: <https://www.dal.ca/dept/safety/programs-services/biosafety.html>

Chemical Safety: <https://www.dal.ca/dept/safety/programs-services/chemical-safety.html>

Radiation Safety: <https://www.dal.ca/dept/safety/programs-services/radiation-safety.html>

Scent-Free Program: <https://www.dal.ca/dept/safety/programs-services/occupational-safety/scent-free.html>