

## Advanced Organic Chemistry: Synthesis and Mechanisms, CHEM 395, Fall 2024

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**Class Meeting** Tue & Thur 2:30-3:45 PM Dumbach 235 CHEM 395-002 (6511)

*Office Hours:* Tuesdays 11:00 a.m. – 12:00 noon in Flanner 217A, or via appointment. Appointments may be made to meet in person or via Zoom ID 235 110 7365.

### Required Texts

1) The Art of Drug Synthesis. 1st Edition by Douglas S. Johnson and Jie Jack. Li. Wiley-Interscience, 2007. Cudahy Library has an online version freely available, and there is a complete PDF version on our Sakai site. If you prefer a hard copy, the text is available for sale online, new or used.

2) Contemporary Drug Synthesis 1st Edition by Jie Jack Li, Douglas S. Johnson, Drago R. Sliskovic, Bruce D. Roth, Wiley-Interscience, 2004. Cudahy Library has an online version freely available, and there is a complete PDF version on our Sakai site. If you prefer a hard copy, the text is available for sale online, new or used online.

*Other Recommended Texts; These were candidates for texts for this class.*

1) Selected Organic Syntheses: A Guidebook for Organic Chemists, Ian Fleming, Wiley-Interscience, N.Y., 1973, reprinted 1983. ISBN: 0471263915, ISBN13: 9780471263913. Well written, clear, historical perspective, a real treasure.

2) Art in Organic Synthesis, 2<sup>nd</sup> Edition, Nitya Anand, Jasjit S. Bindra, Subramania Ranganathan. New York, Wiley, 1988. A very nice collection of syntheses including natural products as well as compounds of theoretical interest with very little prose. This text unfortunately has an awkward depiction of reagents in brackets rather than above and below the reaction arrows.

3) Recent Synthetic Developments in Polyquinane Chemistry, Paquette, Leo A., Berlin Germany ; New York N.Y. : Springer-Verlag, 1984. Cudahy Library Available , Main Stacks QD1 .F58 vol. 119 1984. This is Volume 119 of "Topics in Current Chemistry, Springer-Verlag, Berlin, New York, Managing Editor: F.L. Boschke. In particular, we may include syntheses from Chapters VII through IX (of 9 chapters total, i.e. pages 89-134 out of 161 pages). This volume is organized and well written, and depicts syntheses very clearly. Covers 5-membered ring (quinine) natural products as well as molecules of theoretical interest, such as dodecahedrane. There is a PDF copy posted on our Sakai site, and here is a stable link to the ebook:

<http://flagship.luc.edu/login?url=http://www.degruyter.com/isbn/9783112539286>

4) Classics in Total Synthesis by Nicolaou, Volumes I, II, and III. Each entry is a Mount Everest of synthesis.  
 i) Classics in Total Synthesis: Targets, Strategies, Methods by K. C. Nicolaou and E. J. Sorensen, Apr 11, 1996.  
 ii) Classics in Total Synthesis II: More Targets, Strategies, Methods by K. C. Nicolaou and S. A. Snyder, Oct 17, 2003. iii) Classics in Total Synthesis III: Further Targets, Strategies, Methods by K. C. Nicolaou and Jason S. Chen, Mar 14, 2011.

*Prerequisites:* CHEM 221 & 222 or CHEM 223 & 224, eg. Organic Chemistry I & II

*Extra Resources* *Organic Chemistry as a 2<sup>nd</sup> Language I* (1<sup>st</sup> semester topics), David R. Klein  
*Organic Chemistry as a 2<sup>nd</sup> Language II* (2<sup>nd</sup> semester topics), David R. Klein  
*Pushing Electrons* by Daniel Weeks a workbook for extra help with *mechanisms*

*Why Orgo?* Do you have an interest in human health, prescription medicines and drugs? Organic chemistry is utilized by medicinal organic chemists for the design and construction of new molecules (drugs!) that are prescribed by doctors and dispensed by pharmacists to treat diseases. Organic chemistry is also essential for inventing new dyes, plastics, resins, and detergents, and it is also used in creating new photoreceptors for renewable solar energy and LEDs for display panels (organic LEDs = OLEDs).

1. *Course Description:* This 3-credit course covers synthetic organic reactions & mechanisms as explored through the synthesis of top selling drugs. We will follow the order of two excellent texts by Jie-Jack Li and collaborators who have compiled syntheses of important drugs, organized by therapeutic indication. We will discuss most of these syntheses in order of the texts (2004, then 2007), and within the context of presenting the complete syntheses we will discuss the key reactions and mechanisms. We will very briefly discuss key features of the drug targets and druggability aspects of the individual molecules and metabolism, as we cover in much greater detail in Medicinal Chemistry 323/423. We will take turns presenting the syntheses and mechanisms on the board. Homework assignments will be designed primarily to reinforce the synthetic reactions and mechanisms, and will echo only some key medicinal chemistry aspects. Periodically there will be “Cultural Connections” handouts assigned that relate course material to broader societal and ethical questions and issues.

2. *Expected Outcomes:* The primary outcome of this class is to learn the synthetic organic reactions and mechanisms that we discuss, and to effectively present to the class the assigned drug syntheses and “arrow pushing” mechanisms. We will also learn some aspects about medicinal chemistry to provide some background for the syntheses we will cover, to provide context and significance, and we will also touch on some societal and ethical aspects to broaden our understanding of pharmaceutical drugs and the role they play in our society.

3. *Syllabus:* The current syllabus is posted on Sakai and is subject to change (dated at the top) during the semester. *You are responsible for all changes announced whether or not you are in attendance.*

4. *Exams and Grading:* There are one mid-term exam and one 2-hour final exam. This grading standard will be applied: 90% A, 88.5% A-, 87% B+, 83% B, 80% B-, 77% C+, 73% C, 70% C-, 65% D, 60% D-, <60% F. A curve for each individual exam may be applied based on the specific average and standard deviation, and will be provided upon return of the exam, along with exam grade distribution statistics.

Course Component	Percentage
Regular Presentations & Participation	30
Homework	30
Midterm exam	20
Cumulative Final	20
<b>Total</b>	<b>100%</b>

5. *Homework:* Organic chemistry is a new language that is spoken in structures. The best way to learn a language is to practice speaking and writing it, therefore the best way to learn this new language of organic chemistry is to work and hand-write out the syntheses and mechanisms.

6. *Sakai Materials:* All handouts provided in class will be mirrored on Sakai.

7. *Academic Honesty:* All exams are closed book and closed note. Academic dishonesty includes using notes or books during exams, looking at another student's test during the exam period, or talking during an exam. The consequence of academic dishonesty is failure of the exam, and the incident will be reported to the Chemistry Department Chair and the Office of the Dean. Additional sanctions including expulsion from the University may be imposed. Anything you submit that is incorporated as part of your grade in this course (quiz, exam, lab report, etc.) must represent your own work. Any student caught cheating will, at the very minimum, receive a grade of F for the item that was submitted. Cheating on any lab material results in zero points for the lab portion of the course. All students in this course are expected to have read and to abide by the appropriate standard of personal honesty and integrity, drafted by the College of Arts & Sciences that can be viewed online at

<https://www.luc.edu/cas/advising/academicintegritystatement/>

8. *Student Accommodations*: The Student Accessibility Center (SAC), Sullivan Center (773-508-3700), <http://www.luc.edu/sac>, has the mission “to support, service, and empower Loyola University Chicago students with disabilities” and to “Partner with faculty and staff to provide opportunities for collaboration, professional development, personal growth, and staff interaction, as they relate to students with disabilities.” Please direct all questions concerning accommodations to the SAC. Accommodations afforded to students require documentation and review. The SAC will issue accommodation letters for registered students to present to their instructors: accommodations are not active until students present these letters to their instructors. If students’ accommodations involve attendance or deadlines, instructors and students will jointly complete and execute an Agreement Form articulating their terms. See <https://www.luc.edu/sac/faculty/facilitatingaccommodations/> for guidance about implementing various kinds of accommodations in a way that is appropriate to your class. The Student Accessibility Center stands ready to work with you.

9. *Absence Policy for Students in Co-Curricular Activities, ROTC, and Religious Observations*: Students missing classes while representing LUC in an official capacity (e.g. intercollegiate athletics, debate team, model government organization) shall be allowed by the faculty member of record to make up any assignments and to receive notes or other written information distributed in the missed classes. Students should discuss with faculty the potential consequences of missing lectures and the ways in which they can be remedied. Students must provide their instructors with proper documentation (develop standard form on web) describing the reason for and date of the absence. This documentation must be signed by an appropriate faculty or staff member, and it must be provided as far in advance of the absence as possible. It is the responsibility of the student to make up any assignments. If the student misses an examination, the instructor is required to give the student the opportunity to take the examination at another time. (<https://www.luc.edu/athletheadvising/attendance.shtml>) If you have observances of religious holidays that will cause you to miss class or otherwise effect your performance in the class you must alert the instructor within 10 calendar days of the first class meeting of the semester to request special accommodations, which will be handled on a case-by-case basis.

10. *Synchronous Class Recordings*: The plan presently is to meet in person with no remote (Zoom) connection or recording. However, if the need arises, software may be used in this class to record live class lectures and discussions, particularly if sessions need to be conducted remotely. As a student in this class, if Zoom is employed, your participation in synchronous class lecture and discussion will be recorded. These recordings will be made available only to students enrolled in the class, to assist those who cannot attend the live session or to serve as a resource for those who would like to review content that was presented. All recordings will become unavailable to students in the class when the Sakai course is unpublished (i.e. shortly after the course ends, per the Sakai administrative schedule). Students who prefer to participate via audio only will be allowed to disable their video camera so only audio will be captured. Please discuss this option with your instructor. The use of all video recordings will be in keeping with the University Privacy Statement shown below.

11. *Loyola University Privacy Statement*: Assuring privacy among faculty and students engaged in online and face-to-face instructional activities helps promote open and robust conversations and mitigates concerns that comments made within the context of the class will be shared beyond the classroom. As such, recordings of instructional activities occurring in online or face-to-face classes may be used solely for internal class purposes by the faculty member and students registered for the course. Students will be informed of such recordings by a statement in the syllabus for the course in which they will be recorded. Instructors who wish to make subsequent use of recordings that include student activity may do so only with informed written consent of the students involved or if all student activity is removed from the recording. Recordings including student activity that have been initiated by the instructor may be retained by the instructor only for individual instructor use.

12. For important information about Title IX see

<https://www.luc.edu/equity/otherresources/resourcesforfacultystaff/syllabuslanguage/>

**Organic Chemistry 395 Tentative Schedule (subject to change)**See the official Loyola University Chicago Academic Calendar at [www.luc.edu/academics/schedules](http://www.luc.edu/academics/schedules).

Wk	Mon	Tuesday	Wed	Thursday	Fri
1	8-26	8-27 1) Introductions; 2) Paxlovir® (nirmatrelvir+ritonavir)	8-28	8-29 1) Nirmatrelvir/EDCI/HOBt; 2) Ch 1-2 rxns & solvents	8-30
2	9-2 Labor	9-3 1) solvent & reagent select; 2) clopidogrel (Plavix®)	9-4	9-5	9-6
3	9-9	9-10 1) celecoxib/Celebrex®; 2) esomeprazole/Nexium®	9-11	9-12 1) imatinib/Gleevec®; 2) loratidine/Claritin® & Clarinex®	9-13
4	9-16	9-17 1) fexofenadine/Allegra®; 2) cetirizine/Zyrtec®	9-18	9-19 1) isotretinoin/Accutane®; 2) tazarotene/Tazorac®	9-20
5	9-23	9-24 1) minoxidil/Rogaine®; 2) finasteride/Propecia®	9-25	9-26 1) ciprofloxacin/Cipro®; 2) linezolid/Zyvox®	9-27
6	9-30	10-1 <b>Midterm</b>	10-2	10-3 1) risperidone/Risperdal®; 2) olanzapine/Zyprexa®	10-4
7	10-7 Break	10-8 <b>Mid-semester Break</b>	10-9	10-10 1) aripiprazole/Abilify®; 2) atorvastatin/Lipitor®	10-11
8	10-14	10-15 1) fluoxetine/Prozac®; 2) sertraline/Zoloft®	10-16	10-17 1) paroxetine/Paxil®; 2) orlistat/Xenical®	10-18
9	10-21	10-22 1) sumatriptan/Imitrex®; 2) sildenafil/Viagra®	10-23	10-24 1) fluticasone/Flonase®; 2) salmeterol/Serevent®	10-25
10	10-28	10-29 1) montelukast/Singulair®; 2) exemestane/Aromasin®	10-30	10-31 1) anastrozole/Arimidex®; 2) levofloxacin/Levaquin®	11-1
11	11-4	11-5 1) itraconazole/Sproanox®; fluconazole/Diflucan®	11-6	11-7 1) nevirapine/Viramune®; 2) efavirenz/Sustiva®	11-8
12	11-11	11-12 1) delavirdine/Rescriptor®; 2) oseltamivir/Tamiflu®	11-13	11-14 1) rosiglitazone/Avandia®; 2) losartan/Cozaar®	11-15
13	11-18	11-19 1) enalapril/Vasotec®; 2) lisinopril/Zestril®	11-20	11-21 1) nifedipine/Adalat®; 2) ezetimibe/Zetia®	11-22
14	11-25	11-26 2) venlafaxine/Effexor®; 2) duloxetine/Cymbalta®	11-27 Thanks-giving Break	11-28 <b>Thanksgiving Break</b>	11-29 Thanks
15	12-2	12-3 1) zolpidem/Ambien® 2) pregabalin/Lyrica®	12-4	12-5 1) amphetamine/Adderol®; 2) methylphenidate/Ritalin®	12-6
16	12-9	12-10	12-11 Study Day	12-12	12-13
Saturday, December 14, 2024 from 4:15-6:15 p.m. <b>Final Exam</b>					