CEM 852: "Methods of Organic Synthesis" — Spring 2022

Course Content: According to the course catalog, the course content is as follows: "In-depth coverage of the principle reactions leading to carbon-carbon bond formation, along with functional group transformations. Strategies and methods for organic synthesis." We will cover the reactivity, methodology, and mechanistic aspects of the reactions of alkenes and alkynes, oxidations and reductions, enolates and related nucleophiles, pericyclic reactions, transition-metal chemistry, etc.

Instructor: Robert Maleczka Office: 528 Chemistry; office hours: by appointment
phone: 353-0834; email: maleczka@msu.edu

Course Coordinator: Ms. Nancy Lavrik (email: lavrik@chemistry.msu.edu)

Class Time: MWF 9:10–10:00 am, January by zoom, then room 127 Chemistry Building
& Monday 7–9 pm, January 31st by zoom, then room 581W
Zoom info will be sent by email.

Web-page: https://www2.chemistry.msu.edu/courses/cem852/index.html

Recommended Texts:

1. Your undergraduate organic text.
2. George S. Zweifel, Michael H. Nantz, and Peter Somfai, *Modern Organic Synthesis: An Introduction*, 2017, Wiley. ISBN-978-1-119-08653-6.
3. Paul Wyatt & Stuart Warren, *Organic Synthesis: Strategy and Control*, Wiley, 2007. ISBN-978-0-470-92963-5.
4. K. C. Nicolaou & E. J. Sorensen, *Classics in Total Synthesis, Targets, Strategies, Methods*, VCH, 1996. ISBN-3-527-29231-4. (On reserve in the MSU library)
5. The ACS Organic Division is an excellent resource for organic chemists. The Reich Collection of Resources (https://organicchemistrydata.org/) includes ~700 Total Syntheses searchable and categorized by compound name, named reactions used, chemoselectivity, rings formed, reaction types, and reagents used, etc.; a comprehensive Topics in NMR database, and information on pKa tables, electron pushing, A-values, nomenclature, organometallic chemistry, etc.

Grading Scheme:

Exam/Assignment	pts	
Midterm Exam 1	100	Monday Feb. 21 (6:00–9:00 pm); room TBD
Midterm Exam 2	100	Monday March 28 (6:00–9:00 pm); room TBD
Classic Synthesis Presentation	50	
Total Synthesis First Oral Report	10	
Total Synthesis Final Oral Report	50	
Total Synthesis Written Report:	40	
Final Exam:	150	Tuesday May 3 (time tentative); room TBD
Total	500	

Tentative Lecture Schedule*:

Dates	**Subject**	**Reading**
January 10	Course Intro	
January 12	Rapamycin & Methyl Homosecodaphniphyllate	Nicolaou & Sorensen
January 14–31	Classics in Total Synthesis	Nicolaou & Sorensen
February 2	Synthetic Design	Zweifel/Nance Chapter 1
February 4, 7	Conformational Analysis	Zweifel/Nance Chapter 2
February 9, 11	Protective Groups / Chemoselectivity	Zweifel/Nance Chapter 3
Feb. 14 am, 16, 18	Oxidations & Reductions	Zweifel/Nance Chapter 4
February 21	**Exam 1, 6:00–9:00 pm, room 127**	**(100 pts)**
Feb. 23–28. March 2	Reactions of C–C π-Bonds	Zweifel/Nance Chapter 5
March 4, 14	Formation of C–C π-Bonds	Zweifel/Nance Chapter 8
March 16, 18, 21	Formation of C–C bonds via Enolate Anions	Zweifel/Nance Chapter 6
March 23, 25	Formation of C–C bonds via Organometallics	Zweifel/Nance Chapter 7
Mar. 28	**Exam 2, 6:00–9:00 pm, room 127**	**(100 pts)**
March 30, April 1,	Pericyclic Reactions	Zweifel/Nance Chapter 9
April 4, 6	Asymmetric Catalysis	Warren Chapter 25, 26
April 8	Organocatalysis	Warren Chapter 28, 29
April 11, 15, 13	Aromatic Substitution / CH activation	Warren Chapters 7, 33
April 11	Synthesis Presentations I, 7 pm, Room TBD	(10 pts)
April 18, 20, 22	Reactive Intermediates	Zweifel/Nance Chapter 9
April 25, 27, 29	Heterocycles	Warren Chapters 32, 34, 35
April 25	Written Reports Due, 6 pm, Room TBD	(40 pts)
April 25–27	Synthesis Presentations II, 6 pm, Room TBD	(40 pts)
May 3	**Final Exam, Tuesday, time TBD (150 pts)**	**all inclusive**

Notes: No makeup exams will be given. If you miss an hourly examination due to *religious holidays, unavoidable personal commitments, grief absences, illness*, etc., your course grade will be calculated by adding the point value (100 pts) of each missed exam to the Final Exam (MSU Final Exam Policy). If you know you will have a conflict with the dates indicated above AND you let me know by January 17, I will arrange for a makeup date. *Subject to Change

Grade Scale (I reserve the right to adjust this scale downward):

Grade	pts
4.0	>400
3.5	300–400
3.0	200–299
2.5	150–199
0.0	<150

Supplemental Material: See the course web page for handouts, including old exams. You may also find Professor Reusch's Virtual Textbook of Organic Chemistry and the associated interactive problems and tutorials helpful. Furthermore, please check the announcements link on the 852 web frequently for important information, course up-dates, and additional materials.

Classic Syntheses (50 points): Students will each present a synthesis from Nicolaou's "Classics in Total Synthesis" (on reserve in the MSU library). In years past, these presentations would be spread out over the semester. However, owing to President Stanley's mandate, these presentations will occur throughout the month of January. Plan for your presentation to take about **20 minutes**, *excluding* questions. Your lecture will be graded using the same criteria used for the Organic Seminars, including input from your classmates. I also expect you to provide a PDF file no later than three days following your presentation for placement on the web. (Note: please use white backgrounds for your presentation.)

Schedule

1.	January 10	Rapamycin (Chapter 31)	Robert Maleczka
2.	January 14	Erythronolide B (Chapter 11)	Nick Wills
3.	January 14	Reserpene (Chapter 4)	Nikita
4.	January 19	Strychnine (Chapter 2)	Sodiq Nafiu
5.	January 19	Strychnine (Chapter 33)	Nathan Slater
6.	January 21	Monensin (Chapter 12)	Hanin Sarhan
7.	January 21	Monensin (Chapter 15)	Yasiru Alwis
8.	January 24	Periplanone B (Chapter 13)	Sonam Shivtarkar
9.	January 24	Periplanone B (Chapter 21)	Anuki Wethalawe
10.	January 26	Progesterone (Chapter 6)	Rosemary Augustine
11.	January 26	Endiandric Acids A–D (Chapter 17)	Shannon Cartwright
12.	January 28	Amphotericin B (Chapter 24)	Bahareh Ghaffari
13.	January 28	Zaragozic Acid (Chapter 35)	Sydney Cobb
14.	January 31 am	Indolizomycin (Chapter 27)	Keyvan Pedrood
15.	January 31 am	Theinamycin (Chapter 16)	Keshav Prahaladi
16.	January 31 pm	Asteltoxin (Chapter 20)	Milad Pedarpourvajargahy
17.	January 31 pm	Hirsutene (Chapter 23)	Salma Begum

If you know you of a conflict with the dates indicated above AND you let me know by January 11, I will arrange a makeup date. If you miss your "Classic Synthesis" presentation, we will pro-rate your final.

Total Synthesis (100 pts): In early March, each of you will be given a natural product for which you are to design a synthesis. We will first meet on at 7 pm on Monday April 11. At that meeting, you are to present a retrosynthesis (10-minutes max!) of your molecule highlighting what you view will be the key points of your proposed synthesis, including the means by which your synthesis will be made asymmetric. An electronic copy of your retrosynthesis is due at 7 pm that day.

A written report describing your synthesis is part of this assignment. This report should resemble a second-year oral exam written report with a ≤4000-word limit, not counting Scheme captions and references (no limit on the number of Schemes). An electronic of your written report is due at 6 pm on

April 25. On the evenings of April 25–27 we will meet at 6 pm (room TBD) for a full presentation of your synthesis (30 minutes maximum!).

Each synthesis will be graded on the basis of your presentation, how you respond to questions, chemical soundness, creativity, thoroughness, the clarity of your final report, and your attendance. More details on this assignment will be given later in the semester.

Total Synthesis Schedule:

First Oral Report (10 pts): Presented on zoom Monday April 11 starting at 7 pm.

Written Report: (40 pts): An electronic copy is due at 6 pm Monday April 25

Final Oral Report (50 pts): Presented over three evenings Monday April 25, Tuesday April 26, and Wednesday April 27, starting at 6 pm each night. These meetings are tentatively scheduled to take place in-person in room 136 (subject to change). Electronic copies (PDF) of all presentations are due at 6 pm on April 25. Those giving their oral report on April 26 or 27 are not to present an edited version of what was handed in on April 25. Doing so will result in a 0 for the assignment.

Special Assistance: Any students requiring special assistance must identify themselves to the instructor at the beginning of the semester.

Class Conduct: Professional, courteous, and ethical conduct is expected of all students at all times. Likewise, diversity among students should be respected. Finally, please turn off your cell phones before entering the classroom.

Policy on Cheating: In order to discourage cheating, the instructor may make copies of some pages of some exams. Any student caught cheating will receive a grade of 0.0 for that test. In addition, a letter describing the incident will be sent to the chairperson of the Chemistry department, as well as that student's Department Chair, College Dean, and each member of the student's Ph.D. committee.

COVID-19 Information: The novel coronavirus, which causes the disease COVID-19, has been declared a worldwide pandemic. The COVID-19 virus is extremely contagious and is believed to spread mainly from person-to-person contact. The COVID-19 pandemic represents an unprecedented public health crisis that has impacted every facet of life, including the classroom environment. The most up to date information from MSU is available at: https://msu.edu/together-we-will/covid19-guidance/.

Instructional format: In response to omicron, instruction will be by zoom throughout the month of January. Come February, significant changes in how we conduct in-person classes may be on the horizon. Should in classroom attendance be impacted by COVID-19, modifications may be made to the class format and/or instructor. Similarly, were MSU to halt in-person graduate study modifications will be made to the class format.

Face coverings: Face coverings must be worn by everyone (including all faculty, staff, students, vendors, and visitors) indoors while on property owned or governed by MSU and while participating in MSU-related or MSU-sponsored activities. Thus, unless you have a University issued exemption, you must wear a face covering in class. **This face covering must cover your mouth and nose**.

Physical distancing: As best as our room assignment allows, we will be practicing physical distancing in the classroom. Thus, all students should attempt to maintain at least six feet distance between themselves and others (excluding those with whom they live). This applies to all aspects of the classroom setting, including seating arrangements, informal conversations, and dialogue between faculty and students.

Exposure to COVID-19: If a student is exposed to someone who is ill or has tested positive for the COVID-19 virus, they will stay home and follow MSU guidelines (see below) to determine what steps should be taken. Students who miss assignments or exams will have their final pro-rated. Cases of extended absence will be handled on an individual basis

Self-Monitoring: Students will self-monitor for flu-like symptoms (for example, cough, shortness of breath, difficulty breathing, fever, sore throat or loss of taste or smell). If a student experiences any flu-like symptoms, they will stay home and follow MSU guidelines (see below) to determine what steps should be taken.

Personal Hygiene. All students must maintain proper hygiene and health practices, including:

- Washing hands frequently with soap and water or, if soap is unavailable, using hand sanitizer with at least 60% alcohol
- Routinely cleaning and sanitizing living spaces and/or workspace
- Using the bend of the elbow or shoulder to shield a cough or sneeze
- Refraining from shaking hands

Adherence to Signage and Instructions: Students will (a) look for instructional signs posted by MSU or public health authorities, (b) observe instructions from MSU or public health authorities that are emailed to my "msu.edu" account, and (c) follow those instructions.

Compliance and reporting: Those who come to MSU facilities must commit to the personal responsibility necessary for us to remain as safe as possible, including following the specific guidelines outlined in this syllabus and provided by MSU more broadly (see below). There may be times when action will be necessary to reinforce expectations. If you do not wear appropriate face coverings (see MSU's guidelines), do not wear your face covering appropriately (i.e., over your mouth and nose), or do not adhere to physical distancing guidelines (i.e., six feet apart), you will be asked to correct the situation or leave the facility. In addition, MSU will utilize the processes already in place to respond to any issues of noncompliance with standards established for the health and safety of our community. For classroom disruptions or issues, the responses and processes that have been used previously remain the first line of action. If necessary, the student conduct system will be the avenue used to adjudicate student disciplinary situations.

Additional COVID-19 information. See https://msu.edu/together-we-will/keeping-spartans-safe/ for details about these new policies and procedures and see https://ehs.msu.edu/_assets/docs/fact-sheets/cloth-face-covering-fact-sheet.pdf for more details about the cloth face coverings guidelines.