

Texas A & M University-Kingsville
CHEM 5327, Advanced Organic Synthesis

Syllabus

Course Description:

The course is for graduate students majoring in a field of chemistry, biochemistry or engineering. The course highlights the recent practical methods that currently enjoy widespread application to the synthesis of organic compounds in the laboratory. The course is designed to provide the students an appreciation of the usefulness of the reactions, their versatility and in some cases their selectivity. Reaction mechanisms are not discussed except in so far as is necessary for understanding the course or stereochemistry of a reaction. The course is addressed principally to graduate students at the beginning of their research careers with an aim to bring out the salient features of the reactions and reagents rather than to provide a comprehensive account.

Name of Instructor:

Dr. Apurba Bhattacharya

Office Location:

Nierman Hall, Room 156B. Telephone: (361) 593-2664

Office Hours:

2:00- 4:00 PM, Monday through Friday, or by appointment.

Course Lecture Location:

TBA

Required Texts:

Some Modern Methods of Organic Synthesis, by W. Carruthers, Third Edition:
Cambridge University Press, 1986.

Recommended Readings:

Some Modern Methods of Organic Synthesis, by W. Carruthers, Fourth Edition:
Cambridge Texts in Chemistry and Biochemistry, 2004.

Modern Synthetic Reactions, by H.O.House, Second Edition: W.A.Benjamin, Inc, 1972.

Advanced Organic Chemistry, by J. March, Fourth Edition: Wiley Interscience, 1992.

Selected Journal Articles.

Course Objectives:

- Develop a fundamental understanding of carbon-carbon single and double bond formation.
- Development of highly stereoselective reactions and their applications in complex syntheses. These reactions include stereoselective alkylation of carbonyl compounds, stereoselective aldol condensations, stereoselective oxidations, epoxidations and reductions.
- Discussion of newer methods for the stereoselective formation of carbon-carbon double bonds, and the modern application of the Diels Alder reaction, particularly its use in the control of stereochemistry in the synthesis of natural products.
- Determine which strategic bond constructions can be used most effectively to obtain synthetic targets with high selectivity.
- Become adept at identifying strengths and weaknesses of particular methods, and determine which one will be optimal for particular synthetic operations.
- Learn various commercial processes from individual case studies involving organic synthesis currently practiced in the agrochemical and pharmaceutical sectors.

Course Outline:

Formation of carbon-carbon single bonds.

Alkylation of enolate anions, dianions, α -thio and α -seleno carbanions.

Enamines and related reactions.

Umpolung(dipole inversion)

The aldol reaction

Allylic alkylation of alkenes

The dihydro-1,3-oxazine synthesis of aldehydes and ketones

Coupling of organonickel and organocopper complexes.

Organocuprates

Carbenes and carbaenoids

Addition of free radicals to alkenes

Photocyclization.

---4 weeks.

1st Exam.

Formation of carbon-carbon double bonds.

β -elimination, Pyrolytic syn elimination. Sulfoxide-sulfenate rearrangement; synthesis of allylic alcohols.

Wittig and related reactions.

Alkenes from sulfones

Decarboxylation of β -lactones

Synthesis of tri- and tetrasubstituted alkenes.

Fragmentation Reactions

Oxidative decarboxylation.

Alkenes from arylsulfonyl hydrazones

Stereospecific synthesis from 1,2 diols

Claisen rearrangement of allyl vinyl ethers

Reductive dimerization of carbonyl compounds

----4 weeks.

2nd Exam.

Diels Alder and related reactions.

Dienes and Dienophiles.

Intramolecular Diels Alder reactions.

Retro Diels Alder reactions.

Catalysis by Lewis Acids.

Regiochemistry of the Diels Alder reactions.

Stereochemistry of the Diels Alder reactions.

Asymmetric Diels Alder reaction.

The ene reaction

Cyclo additions with allyl cations and allyl anions.

1,3-dipolar cycloaddition.

----- 2 weeks

Formal presentation.

Synthetic applications of organo boranes and organosilanes.

Hydroboration, reactions of organoboranes.

Carbonylation of organoboranes, reaction with α -bromo ketones α -bromoesters.

Application of organosilicon compounds in synthesis-protection of functional groups.

Alkenyl silanes and allyl silanes

Control of rearrangement of carbonium ions by silicon-the β -effect.

α -silyl carbanions, β -silyl carbonyl compounds.

TMS cyanide, TMS iodide and TMS triflate.

----2 weeks

Formal presentation.

Oxidation

Oxidation of hydrocarbons
Oxidation of alcohols.
Oxidation of carbon-carbon double bonds.
Photosensitized oxidation of alkenes
Palladium Catalyzed alkylation of alkenes.
Oxidation of ketones
 α,β -unsaturated ketones.
Bayer-Villiger oxidation.
RuO₄ oxidation, Thallium nitrate oxidation

Reduction.

Catalytic Hydrogenation
Reduction by dissolving metals
Reduction by hydride transfer reagents
Reduction with boranes and dialkyl boranes
Other methods:
Wolff-Kishner reduction, desulphurisation. Di-imide, low-valent Ti, Trialkyl tin hydrides, Trialkylsilanes

-----3 weeks

Final exam.

Student learner outcomes:

At the successful completion of this course, you will demonstrate understanding of the key elements of molecular orbital interpretation of various types of concerted pericyclic reactions by successful completion of an assessment exam.

Method(s) of evaluation and grading procedures:

- Evaluation of the course objectives will be assessed by the evaluation of two major examinations (hour exams) and a comprehensive final examination.

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|--------------------------------------|---------|
| Examination 1 | 100pts |
| Examination 2 | 100pts |
| Examination 3, Comprehensive (Final) | 200pts |
| ----- | |
| Total | 400 pts |

- Due to time constraints no make-up examinations will be given. A student who can document an excused absence receives a grade based on his/her exam average. A

grade of zero will be recorded for unexcused absences. From time to time there will be unannounced quizzes.

- **Seminar Program.** Students are strongly encouraged to attend the seminars offered in the Department of Chemistry. They will earn 10(bonus points)/1000 points basis if they attend the seminars.

Policies for attendance, excused absences, make-up exams, late assignments, early final exams, cell phones, etc.:

Successful performance in this class requires that you attend class. Make-ups for missed exams are granted only for excused (official university) absences. Please note that attendance policies may vary by college. No late assignments will be accepted. Graduating seniors who need to schedule an early final should inform the instructor early in the semester. Students should turn off and stow their cell phones during class.

Disability statement (See pages 2 & 11 of Student Handbook):

The Americans with Disabilities Act (ADA) is a federal anti-discrimination statute that provides comprehensive civil rights protection for persons with disabilities. Among other things, this legislation requires that all students with disabilities be guaranteed a learning environment that provides for reasonable accommodation of their disability. If you believe you have a disability requiring an accommodation please contact the Disability Resource Center (DRC) as early as possible in the term. DRC is located in the Life Service and Wellness building at 1210 Retama Drive, or call (361) 593-3024.

Academic misconduct statement (see page 23, section 100 of student handbook):

You are expected to adhere to the highest academic standards of behavior and personal conduct in this course and all other courses. Students who engage in academic misconduct are subject to university disciplinary procedures. Make sure you are familiar with your Student Handbook, especially the section on academic misconduct, which discusses conduct expectations and academic dishonesty rules.

Forms of academic dishonesty:

- 1) **Cheating:** Using unauthorized notes or study aids, allowing another party to do one's work/exam and turning in that work/exam as one's own; submitting the same or similar work in more than one course without permission from the course instructors; deception in which a student misrepresents that he/she has mastered information on an academic exercise that he/she has not mastered; giving or receiving aid unauthorized by the instructor on assignments or examinations.
- 2) **Aid of academic dishonesty:** Intentionally facilitating any act of academic dishonesty. Tampering with grades or taking part in obtaining or distributing any part of a scheduled test.
- 3) **Fabrication:** Falsification or creation of data, research or resources, or altering a graded work without the prior consent of the course instructor.
- 4) **Plagiarism:** Portrayal of another's work or ideas as one's own. Examples include unacknowledged quotation and/or paraphrase of someone else's words, ideas, or data as one's own in work submitted for credit. Failure to identify information or essays from the Internet and submitting them as one's own work also constitutes plagiarism.

- 5) **Lying:** Deliberate falsification with the intent to deceive in written or verbal form as it applies to an academic submission.
- 6) **Bribery:** Providing, offering or taking rewards in exchange for a grade, an assignment, or the aid of academic dishonesty.
- 7) **Threat:** An attempt to intimidate a student, staff or faculty member for the purpose of receiving an unearned grade or in an effort to prevent reporting of an Honor Code violation. Please be aware that the University subscribes to the Turnitin plagiarism detection service. Your paper may be submitted to this service at the discretion of the instructor.

Other Forms of Academic Misconduct:

- 1) Failure to follow published departmental guidelines, professor's syllabi, and other posted academic policies in place for the orderly and efficient instruction of classes, including laboratories, and use of academic resources or equipment.
- 2) Unauthorized possession of examinations, reserved library materials, laboratory materials or other course related materials.
- 3) Failure to follow the instructor or proctor's test-taking instructions, including but not limited to not setting aside notes, books or study guides while the test is in progress, failing to sit in designated locations and/or leaving the classroom/ test site without permission during a test.
- 4) Prevention of the convening, continuation or orderly conduct of any class, lab or class activity. Engaging in conduct that interferes with or disrupts university teaching, research or class activities such as making loud and distracting noises, repeatedly answering cell phones/text messaging or allowing pagers to beep, exhibiting erratic or irrational behavior, persisting in speaking without being recognized, repeatedly leaving and entering the classroom or test site without authorization, and making physical threats or verbal insults to the faculty member, or other students and staff.
- 5) Falsification of student transcript or other academic records; or unauthorized access to academic computer records.
- 6) Nondisclosure or misrepresentation in filling out applications or other university records.
- 7) Any action which may be deemed as unprofessional or inappropriate in the professional community of the discipline being studied.

Non-academic misconduct (see page 23, section 100 of the student handbook):

The university respects the rights of instructors to teach and of students to learn. Maintenance of these rights requires campus conditions that do not impede their exercise. Campus behavior that interferes with these rights will not be tolerated; examples include

- 1) interfering with the instructor's ability to conduct the class,
- 2) causing inability of other students to profit from the instructional program, or
- 3) any interference with the rights of others.

An individual engaging in such disruptive behavior may be subject to disciplinary action. Such incidents will be adjudicated by the Dean of Students under non-academic procedures.

Ongoing behaviors or single behaviors considered distracting (e.g., coming late to class, performing a repetitive act that is annoying, sleeping or reading a newspaper in class, etc.) will be addressed by the faculty member initially either generally or individually. Cases in which such annoying behavior becomes excessive and the student refuses to respond to the faculty member's efforts can be referred to the Dean of Students. In the case of serious disruptive behavior in a classroom the instructor may first request compliance from the student and if it is not received, an instructor has the authority to ask the student to leave the classroom. If the student fails to leave after being directed to do so, assistance may be obtained from other university personnel, including University Police Department. An individual engaging in such disruptive behavior is subject to disciplinary action. Such incidents will be adjudicated by the Dean of Students under non-academic procedures to determine if the student should be allowed to return to the classroom.

Harassment /Discrimination (See page 23, section 200 of Student Handbook):

Texas A&M University-Kingsville will investigate all complaints that indicate sexual harassment, harassment, or discrimination may have occurred by the facts given by the complainant. Sexual harassment of anyone at Texas A&M University-Kingsville is unacceptable and will not be tolerated. Any member of the university community violating this policy will be subject to disciplinary action. A person who believes he/she has been the victim of sexual harassment, harassment, or discrimination may pursue either the informal or the formal complaint resolution procedure. A complaint may be initially made to the complainant's immediate supervisor, a department head, any supervisory employee, the Dean of Students (593-3606), or the Office of Compliance (593-4758). Regardless of who the complaint is filed with, the Compliance Office will be notified of the complaint so it can be investigated.

Six-drop policy:

The following provision (new in Fall 2007) does not apply to students with Texas public college or university credits prior to Fall 2007. The Texas legislature has enacted a limit to the number of course drops allowed to a student without penalty. After a student has dropped six courses, a grade of QF will normally be recorded for each subsequent drop. If you need additional information on Senate Bill 1231 and how it affects you, please contact the Registrar's Office in College Hall, Room 105.

Comments:

- I will not take formal attendance but class attendance is a very practical necessity. Please note that attendance policies may vary by college). No late assignments will be accepted. Graduating seniors who need to schedule an early final should inform the instructor early in the semester. Students should turn off their cell phones during class.
- The syllabus is intended to be informational and not contractual. The instructor reserves the right to amend, alter, change, delete, or modify the syllabus with notice (announced during the lecture season) in any manner that is deemed necessary and in the best interest of the Department of chemistry and Texas A & M University-Kingsville.

- It is the responsibility of the student to keep the original graded copies of all materials (exams, problem set, in-class assignments, etc.) that have been returned for his/her records. Graded final exams are retained by the instructor for his/her permanent records.

- Classroom Policies:
 1. You are expected to conduct yourselves as mature professionals in class. Questions and discussions regarding the material are welcomed. Chatting and visiting are best done before or after class.
 2. **PLEASE TURN OFF YOUR CELL PHONES AND PUT IT AWAY WHEN YOU COME TO CLASS!**
 3. I don't mind if you bring food or drinks to class, but please make sure you dispose properly of anything you bring.