Chem 5331: Advanced Organic (NMR) Spectroscopy
Class Syllabus....Spring, 2012

Class M, W, F, 10:00 to 10:50 am, Room 165 Ekeley (Conference Room)

Course will be taught by :
Dr. Rich Shoemaker, Room 02 Cristol, E-mail: Richard.Shoemaker@colorado.edu , Phone: (303) 492-7062

Office Hours: Arranged as needed on an individual basis.

Web-Page: Look for course materials on the NMR website: http://chemnmr.colorado.edu/class .

Overview: This course is intended for those who are using (or will be using) NMR spectroscopy as a primary characterization tool in their research. There will be two principle areas of emphasis (not necessarily in order):

1. How do we determine the structure of a compound, and what is required to say that a compound has been thoroughly characterized?
2. The "nuts and bolts" of NMR spectroscopy, including how the signals are generated and detected, how the instrumentation works, and a functional understanding of pulse-sequences. Emphasis will be placed on the optimal processing and analysis of 1D and 2D NMR data.

Textbook: There will be NO books ordered for this course by the University Bookstore. You will need to use online resources such as Amazon.com, BarnesandNoble.com, or other sites to get your books. BOTH BOOKS ARE REQUIRED! This year we will be using two texts:

- Tim Claridge, *High-Resolution NMR Techniques in Organic Chemistry, Volume 2*, Elsevier (2009) [ISBN 978-0-08-054818-0 (paperback)]. (this is Volume 27 of the Tetrahedron Organic Chemistry Series).
- Crews, Rodriguez, & Jaspars: *Organic Structure Analysis, Second Edition*, Oxford University Press (2010) [ISBN 978-0-19-533604-7]. This is a completely re-written and updated text pertaining to NMR interpretation, as well as other instrumental methods for structure elucidation of organic molecules.
- A third text: *Organic Structure Determination Using 2-D NMR Spectroscopy*, by Jeffrey H. Simpson (Elsevier, 2008) [ISBN 978-0-12-088522-0], is recommended. Problems from this text will be assigned for practice, and it is a good book to purchase to get extra practice with NMR structure elucidation.

There is far too much information to be covered in lectures, and it is expected that you will read the assigned chapters and work the assigned problems. The lectures will be intended to supplement/enhance the information in the texts, and are not to be a substitute for reading. Unannounced "Pop" Quizzes may be given at any time on the assigned reading.

Grading Policy The course grade will be based on a combination of graded problem sets & pop-quizzes (totalling 40% of the final grade), 2 in-class exams (20% each) and a take-home final exam (20%). Some problems in the book (and supplemental problem sets) will be assigned, and answer keys provided. Although not every problem set will be graded, every problem set should be approached as if it will be graded. Prior notice may not be given regarding which problem sets will be turned in for a grade. Although subject to change, it is planned that the first exam will be a 1-hour, in-class exam, and the second exam be likely be included as part of the take-home exam. This is subject to change, so we *could* have the final exam in-class at the scheduled time. The take-home final exam will be distributed on or before the last day of class (Friday, May 4th), and will be required to be completed and turned in by 5:00 pm on Thursday, May 10th. The specific details of the take-home final exam will be provided before it is distributed.

Policy for Disputing Grades: If you feel a problem or question was scored unfairly, you may re-submit the entire exam or problem-set for re-grading. After re-scoring the entire exam or problem set, you will receive the new grade (whether higher or lower than the original score) *hint... few have ever done this and earned a higher overall score.*

Goals and Objectives: Students in this course should gain an understanding of NMR techniques as applied to molecular structure determination and to the study of molecular dynamics. In addition to learning to derive structures from spectra, students will gain a basic understanding of NMR spectroscopy in one and two dimensions. Upon successful completion of the course, students will know what techniques are available to answer specific, key questions about molecular structure. Concepts including instrumentation, shimming, pulse-sequences, magnetization, relaxation, polarization transfer, coherence transfer will be addressed in this course. Upon successful completion of this course, students should be prepared to apply modern NMR spectroscopic techniques to their research problems.

Calendar: Due to Dr. Shoemaker's responsibilities involving management of the NMR Facility, certain situations might arise that could require class cancellations or rescheduling. Should this happen, it will be announced as far in advance as possible. The detailed calendar below includes all class cancellations that are known at the time of this writing. If it becomes necessary, Dr. Shoemaker reserves the right to schedule extra, required lectures outside of the normal class time; however, this will be avoided if possible.

Below is a general, *approximate* overview/outline of the course. This represents the initial plan, but it is subject to change. Sections may be added or omitted as necessary to cover the material deemed most important. The dates are tentative estimates because one never knows for sure how long it will take to adequately cover each topic.

Jan 18: **Review the relationships between NMR spectral data and structure** (Chemical Shifts, J-couplings, and the basic concepts of NMR that should have been learned in undergraduate organic chemistry). {Read *Crews*, Ch.1, and Ch. 1 in *Simpson* }

Jan 20 – 23: **Introduction to experimental NMR spectroscopy** {If you haven't read Ch. 1-2 in *Claridge* & Ch. 2 in *Crews*, do it now} Nuts and Bolts of NMR: magnetization, relaxation, pulsed-excitation. Introduce the "rotating frame of reference", as it applies to the net magnetization, excitation, and detection.

Jan 25 – Jan 27: **Detecting the NMR signal**: Dynamic Range, Spectral width vs. Dwell Time, Signal Averaging, and Signal:Noise ratio. {Read Ch. 3 in *Claridge* }.

Jan 30 – Feb 3: **The time-frequency connection: understanding the FFT**, its uses and consequences. Understanding the principles of the Fourier-transform, and the relationship between time-domain and frequency-domain in 1D NMR is crucial to understanding 2D NMR concepts. Apodization, Digital Resolution, Zero-Filling, Phasing, Baseline Correction, Integration will all be covered. {Review Chapters 2 & 3 in *Claridge*}

Feb 6-10: **Instrumentation**: getting to know your NMR spectrometer. We will hopefully shine some light into the traditional "Black Box" called the NMR spectrometer. We'll cover superconducting magnets, pulse generation, signal detection, probe design/performance issues, probe-tuning, shimming. {Chapter 3 in *Claridge*, Section 3.4, 3.5}

Feb 13-29:

- **Interpreting 1D NMR spectra**: Chemical Shifts, J-couplings, and structure. Interpretation/prediction of chemical shifts, and interpretation of first-order J-coupling patterns coupling constants as related to structure. Chemical Equivalence & Structure, including symmetry, chirality. {Chapter 3 and beginning of Chapter 4 in *Crews*, Chapters 4-5, and 6.1-6.8 in *Simpson*}
- **Dynamic NMR & Advanced J-Coupling.** Understanding simple chemical exchange, and introduce complex spin systems, recognizing first-order coupling vs. strong-coupling. Common spin-systems, and "magnetic equivalence" vs. "chemical equivalence" (i.e. AX, AB, AMX, ABX, …etc.) For Dynamic NMR: http://chemnmr.colorado.edu/manuals/DNMR_Calculations.pdf , Chapter 4 in *Crews* .. esp. 4.4-4.8 }.

March 2-9:

- **More on NMR Relaxation, NOE**: Quantitation in NMR: getting reliable peak integrations. The Nuclear Overhauser Effect (NOE), how we measure it. Through-space proximity via cross-relaxation {Review *Claridge*, 2.4 & 2.5, and READ Sections 8.1-8.6 in *Claridge*}. Note: we'll introduce Transient 1D NOE concepts now, and address 2D-NOE experiments later in the course.
- **Advanced 1-Dimensional NMR**: Having read chapter 4 in *Claridge*, we will discuss the important points including polarization transfer (INEPT), spectral editing (DEPT/APT), and important aspects of decoupling. And, by the way, yes… this will likely be on the Exam on Monday.

March 12: **Exam #1** (tentative, the exact day will be announced at least 1 week prior to the Exam). The exam will cover basic experimental NMR spectroscopy, and interpretation of 1D-NMR spectra.

March 14-19: **Introduction to 2D-NMR**, experimental concepts and applying the FFT in two dimensions. {READ *Claridge*, Chs. 5 & 6}. We'll start with 2D-COSY, then move to heteronuclear experiments (HETCOR, HMQC/HSQC, HMBC, …etc.). Emphasize optimal 2D-NMR data processing, presentation, and analysis.

March 21-23: **Using 2D NMR to determine structures**, and assigning NMR resonances. the "alphabet soup" of NMR acronyms {*Claridge* Ch. 9, Chapter 5 in *Crews*, Chapter 9-10 in *Simpson* }

March 26-30: **Spring Break**, No Classes… No Assigned Homework.

April 2 - 13: **More 2D NMR Applications**, including 2D-NOESY/ROESY & Dynamic Exchange measurements in 2-Dimensions (NOESY/ROESY/EXCHSY) {*Claridge*, 8.7 through 8.10}… Note, Ch. 8 in *Claridge* may be the best single place to go to know what you need to know about the NOE experiments for small molecules. Spend a lot of time with this chapter, now or later (when you use NOE experiments in your research).

April 15-20: **No Class**, Dr. Shoemaker will be attending the Experimental NMR Conference (ENC) in Miami, FL. **More Structure Determination and Assignment**, bringing it all together. I will assign problems using NMR data from a variety of NMR experiments to assign the structure and all NMR resonances. {Lots of problems to work while I am away}

April 23-May 4:

- **Using Pulsed Field Gradients** (PFGs) and selective pulses in 2D NMR experiments… basic principles and practical applications, including measuring diffusion (DOSY), coherence selection, and artifact suppression.
- **1D Analogues to 2D NMR experiments** (Using selective pulses), 1D-COSY/TOCSY, 1D-NOESY/GOESY.
- **Additional Topics**, possibly including Solid-State NMR concepts and techniques, semi-solid phase (gel phase), Diffusion-NMR/DOSY, BioMolecular NMR concepts… depending on what we've accomplished
- **Practice problems for Final Exam…**

Final Examination Information:

Take-Home Final Exam to be distributed on (or before) May 4th (Last Day of Class).

We will probably ignore the scheduled Final Exam time, and a written exam will likely be included as part of the take-home exam. This is subject to change, so we *could* have the final exam in class at the schedule time. This will be the Instructor's decision.

University Required Syllabus Information:

If you qualify for accommodations because of a disability, please submit to me a letter from Disability Services in a timely manner so that your needs may be addressed. Disability Services determines accommodations based on documented disabilities. Contact: 303-492-8671, Willard 322, and http://www.Colorado.EDU/disabilityservices.

Campus policy regarding religious observances requires that faculty make every effort to reasonably and fairly deal with all students who, because of religious obligations, have conflicts with scheduled exams, assignments or required attendance. In this class, please see me if you need to miss any class due to a resigious observance, and we will make the appropriate arrangements. See full details at http://www.colorado.edu/policies/fac_relig.html .

Students and faculty each have responsibility for maintaining an appropriate learning environment. Students who fail to adhere to such behavioral standards may be subject to discipline. Faculty have the professional responsibility to treat all students with understanding, dignity and respect, to guide classroom discussion and to set reasonable limits on the manner in which they and their students express opinions. Professional courtesy and sensitivity are especially important with respect to individuals and topics dealing with differences of race, culture, religion, politics, sexual orientation, gender, gender variance, and nationalities. Class rosters are provided to the instructor with the student's legal name. I will gladly honor your request to address you by an alternate name or gender pronoun. Please advise me of this preference early in the semester so that I may make appropriate changes to my records. See polices at:
http://www.colorado.edu/policies/classbehavior.html and at http://www.colorado.edu/studentaffairs/judicialaffairs/code.html#student_code

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All students of the University of Colorado at Boulder are responsible for knowing and adhering to the academic integrity policy of this institution. Violations of this policy may include: cheating, plagiarism, aid of academic dishonesty, fabrication, lying, bribery, and threatening behavior. All incidents of academic misconduct shall be reported to the Honor Code Council (honor@colorado.edu; 303-725-2273). Students who are found to be in violation of the academic integrity policy will be subject to both academic sanctions from the faculty member and non-academic sanctions (including but not limited to university probation, suspension, or expulsion). Other information on the Honor Code can be found at http://www.colorado.edu/policies/honor.html and at http://www.colorado.edu/academics/honorcode/ .