Chemistry 421. Physical Methods in Organic Chemistry

Fall 2005: Dr. Charles DeBrosse

Text:	Organic Structure Analysis
Authors:	Phillip Crews, Jaime Rodriguez, and Marcel Jaspars
Publisher:	Oxford University Press, New York, (1998)
ISBN	0-19-510102-2

Course Description: This is a "tools" course, intended to provide students with background, understanding and practice in applying spectroscopic methods to problems of structure determination in organic chemistry. The methods considered in this course are nuclear magnetic resonance (NMR), mass spectrometry (MS), vibrational spectroscopy (IR, Raman) and electronic (UV, chiroptical) spectroscopy. Students will acquire a working knowledge of the theory in these areas, but the emphasis will be on data analysis and interpretation. The logical flow of structure determination will be presented. Students will develop competency in this area by solving problems in which unknown structures are elucidated.

As well, we will learn the limitations of these techniques, and the advantages obtained by integrating the frequently complementary information obtainable from different methods. The scope, limitations and potential in so-called "hyphenated" techniques will be discussed.

Prerequisites: This course is intended for first-year graduate students in Chemistry. It will be assumed that the students have completed a year's course in Organic Chemistry, and have retained the spectroscopic components of that course. Upper division undergraduates in Chemistry with the appropriate background may take this class in consultation with the instructor. The instructor will assume that the students have a firm grasp of organic nomenclature, characteristics of functional groups, stereochemistry and the nature of isomers in organic chemistry.

Course Organization:This course will meet Tuesday evenings from 6:10-9pm. There will be one hour-exam and a final examination. The course will make extensive use of the "Blackboard" utility available through the Temple University Portal system. Students will need to set up their own access via the Portal. Class attendance is encouraged by the instructor in the strongest possible terms, and active participation by question and discussion is welcome.

Homework: Several homework sets will be assigned during the course. These will be collected and marked. Assigned readings are indicated in the syllabus. Please read the material before coming to class. Certain materials in addition to the text may be placed on reserve in the Chemistry library. The lecture notes will be available on the Temple Blackboard system as .ppt files, typically on the Sunday evening prior to the week's lecture.

Grading: The point totals will be apportioned in approximately equal parts from the homework sets, the midterm and the final examination. These will be added and the grades curved according to the distribution within the class.

Office Hours: The instructor, Dr. Charles DeBrosse is generally available in 232 Beury Hall, or in the NMR Lab (001 Beury) Monday-Friday, and welcomes students throughout the day and will make appointments for longer consultations. Telephone 215-204-1082, email debrosse@temple.edu.

Disability Policy Any student who has a need for accommodation based on the impact of a disability should contact the instructor privately to discuss the specific situation as soon as possible. Contact Disability Resources and Services at 215-204-1280 in 100 Ritter Annex to coordinate reasonable accommodation for students with documented disabilities.

Individual Lecture Schedule

The reading assignments for each evenings lecture are captioned in parentheses)

30 August 2005. (Read Crews, Chapters **1**, **2**)
Also, review the sections in any appropriate sophomore organic text related to NMR, IR and Mass Spectrometry.
Lecture 1. **The problem of structure determination in organic Chemistry.**
Definitions, pure compounds, mixtures, what does it mean to define a structure? Knowns, unknowns, partially known. Why do we need to know structures? Total synthesis as a structure proof. Using knowledge of reactions and mechanisms. The classical approach via degradation to known compounds and their derivatives. Molecular formula as a keystone. Molecular weights, exact masses and microanalyses. Isotope contributions. Valency, sites of unsaturation, exchangeable H, and the nitrogen rule. Spectroscopic approaches and orthogonal views. Spectroscopy and structure. Spectroscopic measurements and data. How are the methods similar yet different? The electromagnetic spectrum; frequency, wavelength, energy. Frequency dispersion. Response of detectors. Width of spectral signals. Signal-to-noise, digital resolution,

dynamic range. Dispersive methods vs. Pulse methods and Fourier transforms. Beer's Law. Introducing NMR.

6 September 2005 (Read Crews, Chapter **3**)
Lecture 2. **NMR and the Chemical Shift**
Chemical Shifts. Quantitative aspects. How NMR spectrometers work. (theory, experiment, sample prep, parameters) Vector Pictures and Spectra. Chemical shifts for ^{1}H, ^{13}C, ^{31}P, ^{15}N Practical knowledge and theory of shift effects. Correlation with structures. Reading an NMR spectrum. (inventory approach). Time scales in NMR.

13 September 2005 (Crews, Chapter **4**)
Lecture 3. **Fine Structure in NMR Spectroscopy**
Couplings in NMR spectra. Equivalent nuclei. Multiplicity rules. Second-order spectra. Couplings and geometry. Long-range coupling. ^{13}C-^{1}H coupling. Couplings involving ^{31}P, ^{19}F. Deuterium substitution. Pulse sequences and relaxation effects. Solvent suppression methods. The NOe experiment. Multiple Pulse methods. Spectral editing. The use of the Structure Solver Template explained.

20 September 2005 (Crews Chapter **6**)
Lecture 4. **Beginning Mass Spectrometry**
Introducing Mass Spectrometry. Ionization methods, EI and CI. Identifying the molecular ion. The nitrogen rule. Exchangeable hydrogens. Fragmentation pathways. Cluster analysis. Speciating fragments and the "rule of 13". Ion-molecule chemistry; acidity, basicity and energy considerations. Problem Set I handed in.

27 September 2005 (Crews, Chapter **7**)
Lecture 5. **Mass Spectrometry continued.**
Sample introduction, ionization methods, mass analyzers. Scope and limitations of different types of mass spectrometry. Mass Spectrometry (LCMS, GCMS) as a detector for analytical chemistry. Interpreting Mass Spectral data. On-line databases. MS^{N} data to clarify origins of fragments. Problem Set II handed in.

4 October 2005. (Crews, Chapter **5**)
Lecture 6. **2-Dimensional NMR Spectroscopy**
2-Dimensional NMR. Where does it come from? Encoding a second dimension. The nature of 2D data. How do we interpret 2D spectra? Types of structural information available from various 2D NMR measurements. Problem Set III handed in.

11 October 2005
A Problem-Solving Session, and Review

18 October 2005
Mid-Term Examination

25 October 2005 (Crews, Chapter **8**)
Lecture 7. **Vibrational Spectra and Structural Analysis**.

Structural effects on functional group absorbances. Strain, hybridization, and electronic effects. Symmetry and polarizability in IR. The Raman effect and IR vs. Raman. General ranges for bands. Tautomers and hydrogen bonding in IR spectra. Instrumental requirements. How FT-IR works. Scope, limitations and complementary nature of the methods. Calculations of frequencies. Gas-phase vs. condensed phase effects. Using databases for identity matching. Problem Set IV handed in.

1 November 2005 (Crews, chapter **9.1–9.4)**
Lecture 8. **Electronic Spectroscopy**
UV/vis chromophores. Analysis by UV. Spectrophotometry experiments. Chemically-induced shifts. The Woodward-Fieser rules and applications to structure determination. Use of UV detectors in analytical chemistry. Problem Set V handed in.

8 November 2005 (Crews, chapter **9.5–9.7**)
Lecture 9. **Chiroptical spectra. CD/ORD.**
The Cotton effect and chiral perturbations. Octant rules, Brewster's Rule. Exciton coupling. Determination of absolute configuration. VCD. Chiral NMR methods. Problem Set VI handed in.

15 November 2005(Crews, chapter 10**)**
***Lecture 10*. An Integrated Approach to Problem Solving.**
Putting the data together in structure elucidation. A systematic approach. Worked examples. Recognizing blind spots.

22 November 2005
(No Class, Thursday schedule)

29 November 2005
***Lecture 11*. An Overview of Organic Analysis in the Solid State.**
FTIR, solids NMR, powder pattern XRD. Thermal methods (DSC, TGA). What do we probe, how do the methods tie together? Polymorphism, solvation and hydration, purity assessment. Problem Set VII handed in.

6 December 2005
Lecture 12. **Review and Discussion**
Q&A, problem solving, Problem Set VIII handed in.

13December 2005
Final Examination