Improving the Undergraduate Chemistry Curriculum through NMR Spectroscopy: a Hands-on, Discovery-Based Approach

In an effort to meet the challenges of undergraduate curriculum reform and to promote active learning in the sciences, the Chemistry Department at DePaul is committed to developing opportunities for integrating technology into education, especially in the laboratory. As part of a rapidly growing university, the Chemistry Department recognizes the need to provide students with the necessary exposure to state-of-the-art analytical instrumentation and techniques. In that regard, we are reexamining the way we teach molecular structure in the first and second quarters of organic chemistry, primarily through discovery-based laboratories that incorporate NMR spectroscopy in the in the context of developing other fundamental analytical skills. The primary objective of this proposal is to obtain a modern, high-field FT-NMR spectrometer to implement our pedagogical plan and to enhance the successful research-oriented, project-based experiments already in place in the third quarter of the organic laboratory sequence. In order to make maximum use of the requested instrument, we will adapt NMR experiments for the upper-level laboratory courses in physical chemistry, instrumental analysis and biochemistry, as well. A gradual increase in the number of chemistry majors and minors is anticipated as a result of the proposed curriculum reform. In addition, it is expected that students' understanding of molecular structure will markedly increase with hands-on exposure to an NMR spectrometer.

PROJECT DESCRIPTION

- **Background, Goals and Objectives**

Founded in 1898, DePaul University is a private, comprehensive university situated in urban Chicago. DePaul is committed to providing outstanding educational opportunities to a diverse population of undergraduate students. The University's curriculum, based on a Liberal Studies Program, emphasizes reflective intellectual activity, value-consciousness and critical inquiry as well as active participation in the exploration and discovery of knowledge. With a total enrollment of 20,548 students in 2000, DePaul is currently the largest catholic university and the ninth-largest private university in the country.[1] Between 1999 and 2000 DePaul experienced a 5% growth in enrollment, making it the fastest growing university of its size and type in the country. The number of undergraduate students in 2001 is 12,436, with approximately 30 % minority and 60 % women.

The Department of Chemistry, which is part of the College of Liberal Arts and Sciences, offers standard concentrations in chemistry and biochemistry as well as a concentration accredited by the American Chemical Society (ACS). The department also contributes to an interdisciplinary concentration in environmental science, and administers annually to about 350 science majors and 700 non-science majors. A chemistry/education program is offered in cooperation with the School of Education to prepare students for careers in teaching science. The department also offers a pre-engineering program in chemical engineering. About one-third of our graduating majors go on to graduate school in chemistry or biochemistry, while the remaining two-thirds are split evenly between those attending medical or other professional schools and those pursuing job opportunities, including secondary education.

The common core of the departmental program requirements includes introductory courses in general, organic and physical chemistry, biochemistry and instrumental analysis. Integral components of these courses are weekly laboratories, through which students not only learn laboratory techniques of each sub-discipline, but also become familiar with the experimental nature of chemistry. The ten full-time faculty members in the department regard undergraduate laboratory instruction as essential to the preparation of students for success in many professional fields and graduate studies.

As part of the University's efforts to meet the challenges of undergraduate curriculum reform and to promote active learning in the sciences, the Chemistry Department is committed to developing opportunities for integrating technology into education, especially in the laboratory. Effective implementation of such reform requires state-of-the-art analytical equipment, and towards that end the department has acquired several new instruments (listed separately; the department's annual equipment budget is $75,000). The faculty pays special attention to the development of innovative methods for improving students' understanding of basic principles through laboratory experiments that stress interactive instrumental analysis and discovery.

The primary objective of this proposal is to obtain a modern, high-field FT-NMR spectrometer to develop a method for using NMR spectroscopy as a platform for teaching molecular structure. A hands-on, discovery-based approach to spectroscopic analysis in the introductory organic chemistry course sequence will be investigated. In order to make maximum use of the requested instrument, experiments that incorporate NMR spectroscopy in upper-level laboratory courses, such as biochemistry, physical chemistry and instrumental analysis will also be developed or adapted. The requested instrument will significantly enhance current and planned undergraduate research programs in the Chemistry Department at DePaul, as well.

While the full power of modern NMR technology is being utilized in undergraduate laboratories around the country, as evidenced by NSF-supported experiments that are continuously documented in the literature,[2] DePaul's refurbished 90 MHz JEOL NMR spectrometer (originally manufactured in 1979) no longer functions for routine use. After many repairs, the magnet has lost its field and temperature stability and is absolutely unsuitable for the hands-on, discovery-based approach to spectroscopic analysis we are attempting to implement into our curriculum. Presently, though students are instructed on the principles and applications of NMR spectroscopy, lack of an appropriate instrument has inhibited our full-scale development of the proposed curriculum improvements.

Results of a recent national survey suggest that spectroscopic analysis is, indeed, an increasingly important part of the introductory organic chemistry curriculum, and recent guidelines established by the ACS's Committee on Professional Training, in fact, recommend hands-on use of NMR spectroscopy in the undergraduate organic laboratory.[3] In an effort to comply with the ACS guidelines and to better serve the educational needs of the growing number of science students at DePaul, a pedagogical plan is presented that requires a reliable NMR spectrometer.

- **Detailed Project Plan**

The Chemistry Department at DePaul University is currently experiencing a period of substantial growth and reform under the direction of Associate Professor Wendy Wolbach, who is in her second year as Chair. As part of Dr. Wolbach's initiative to increase student enrollment in chemistry, and with the hiring of two new tenure-track assistant professors, the department is becoming more research-oriented. Within the last three years, the number of chemistry majors and minors at DePaul has increased substantially and continues to increase with active recruiting efforts by the department and the university.

Integration of technology into student learning is essential for preparing students to meet the challenges of research. As part of a growing university, the Chemistry Department at DePaul recognizes the need to provide students with the necessary background and preparation to be successful in scientific endeavors. We are reexamining the way we teach molecular structure, primarily through a discovery-based approach to NMR spectroscopy, in conjunction with project-based laboratories that have been well established here and else where.[4]

Hands-on NMR spectroscopy will most significantly affect the organic laboratory course sequence. DePaul University operates on a quarter system, and organic chemistry is traditionally taken in the sophomore year over three quarters. The sophomore year is often a turning point in students' careers, when they make decisions about their futures and officially declare their majors. The sophomore year is also a critical time for recruiting talented chemists, and exposure to instrumentation in the context of discovery- and project-based experiments is a strong selling point. Studies have demonstrated that students' interest in developing fundamental analytical skills is markedly enhanced with active involvement.[5]

As a fundamental tool of modern organic chemistry, it is our premise that hands-on NMR spectroscopy should be integrated into the curriculum much earlier than it is traditionally. We envision incorporating NMR analysis as a routine tool as early as the second or third week of classes in the fall quarter, before any formal discussion of spectroscopic theory has taken place. This approach is similar to the "guided inquiry" approach to NMR spectroscopy that was developed by Parmentier and co-workers at Beloit College.[6] During the first ten weeks of classes, students will engage in a number of discovery-based projects for structure determination, and begin to learn spectroscopy in the context of developing other fundamental laboratory techniques like distillation, extraction and recrystallization.

Solomons *Organic Chemistry* (7^{th} ed) is one of the first modern organic texts to incorporate IR spectroscopy in an introductory chapter.[7] We have found that Solomons's treatment of IR spectroscopy has greatly facilitated incorporation of routine IR analysis early in the laboratory sequence. However, without a reliable NMR spectrometer at their disposal, our students have become overly reliant on IR for structure determination, often where inappropriate. NMR spectroscopy is discussed separately, much later in Solomons, as in most organic texts. And while it is not necessarily a short-coming to hold off on comprehensive discussions of spectroscopic theory until students have a more solid understanding of organic chemistry, it is perhaps a disadvantage for students not to begin incorporating NMR analysis earlier in the development of their repertoire of laboratory skills.

As an example of our discovery-based approach to integrating hands-on NMR spectroscopy into the organic laboratory, the following identification project is described. Students will be challenged to identify the components of a two-component sample of volatile liquids. The samples will be prepared ahead of time by the laboratory instructor or teaching assistants to contain a 1:1 mixture of a higher- and lower-boiling component. These are simple, volatile organic compounds as shown in the table below.

LOW-BOILING SAMPLES	**HIGH-BOILING SAMPLES**
tetrahydrofuran (66 °C)	bromobenzene (156 °C)
ethyl acetate (77 °C)	benzaldehyde (179 °C)
ethanol (78 °C)	phenol (182 °C)

A total of nine (low/high) combinations are possible with the above compounds. Students will be instructed first to analyze their mixtures by IR and ^{1}H NMR spectroscopy, and then separate the components by fractional distillation, noting the boiling ranges of each component. Finally, the students will analyze their purified components again by IR and ^{1}H NMR. From their collective spectral data the class will generate IR and ^{1}H NMR data tables.

The primary objectives of the laboratory exercise are traditional: to learn the technique of purification by distillation and the notion of boiling point as a physical property that can be used as one means of structure identification. The underlying, and ultimately more important objective of the project, however, is to establish a foundation for spectroscopic analysis as a method for structure determination. The details of the IR and NMR spectra will certainly be mysterious to students looking at these data for the first time. They will, however, be able to discover trends and correlations in their data: one of the low-boiling components (ethanol) shows a similar signal in the IR as one of the higher-boiling components (phenol); all three high-boiling components show signals in the region of 7 ppm of the ^{1}H NMR, but only one of them shows a signal in the region of 9 ppm, and so on. This discovery process will take place primarily in guided post-lab discussion sections, during which students will make observations of the data they have gathered and formulate conclusions about the identity of the unknown compounds.

Similar projects will be conducted with mixtures of simple solid compounds that will be separated by extraction techniques and purified by recrystallization. These projects will also incorporate melting point determination and TLC analysis. By the end of their first quarter of organic chemistry, students will have developed the usual laboratory techniques inherent to most curricula, but will also have begun to develop an intuition about spectroscopy, the theoretical details of which will be discussed in greater depth in the following quarter.

As their skills in structure determination develop, students will be much more prepared to analyze and identify products of the reactions that will be explored in lab during the following quarter. Students will carry out "traditional" reactions[8] in the second quarter, but with perhaps greater insight having developed strong analytical skills in the first quarter. In lecture, they will also begin to understand the theory of NMR and IR spectroscopy, which will perhaps be much more tangible from the point of reference established during the first and second quarters. The details of ^{1}H NMR spectroscopy (relative chemical shift, splitting patterns, integration) will no doubt seem less remote than they almost certainly do to our students at present.

The laboratory component of third-quarter organic chemistry has already evolved into a project-based experience that emphasizes an understanding of the scientific method and gives students first-hand exposure to research.[4] This is largely due to the NSF-supported efforts of Associate Professor Gregory Kharas (NSF-DUE 9455681, "Undergraduate Organic Chemistry Model: Experiencing Research in an Instructional Laboratory"). Students are engaged in the synthesis and characterization of novel trisubstituted ethylene (TSE) polymers. Incorporating hands-on NMR analysis into these projects would immeasurably enhance the research experiences of our students.

These discovery projects are structured to provide genuine research experience, including: manual and computer literature searches for information on targeted compounds; synthesis and characterization of a monomer; copolymerization and characterization of the copolymer; communication and interpretation of results in a formal (ACS publication format) report. The projects involve micro- and macroscale synthetic techniques based on two reactions, (1) synthesis of a family of TSE monomers via base-catalyzed Knovenagel condensation of substituted aldehydes with activated methylene compounds, followed by (2) copolymerization of a TSE monomer with styrene in the presence of a radical initiator. The results of the discovery projects are checked subsequently by undergraduate and graduate students prior to submission for publication.[9] The availability of a high-field NMR spectrometer will give students the opportunity to get first-hand experience in the structure analysis of the monomers and copolymers they have prepared. This will reinforce the students' ability to make the connection between the theory of organic chemistry learned in lecture, the analytical techniques learned in the laboratory, and the application of organic chemistry in the research of new materials (polymers).

Since organic chemistry is a pre-requisite for all upper level chemistry courses, including physical chemistry, instrumental analysis and biochemistry, our plan is to ensure that chemistry students are thoroughly knowledgeable about NMR spectroscopy by the time they have finished with introductory organic. In this way they will be fully prepared to engage in more sophisticated NMR experiments in their upper level courses and faculty-directed research projects. This will allow for maximum use of the requested instrument.

Students enrolled in instrumental analysis, for instance, will learn about 2D NMR capabilities and perform DEPT , HETCOR and other 2D experiments. Biochemistry students will study enzyme activity using ^{19}F NMR,[10] and the three-dimensional structure of small proteins.[11] In physical chemistry, students will use NMR spectroscopy to solve problems regarding reaction thermodynamics, kinetics, conformation and molecular complexation.[12] Another experiment will be adapted to calculate equilibrium constants for the complexation of donor-acceptor π-complexes by NMR through application of the Benisi-Hildebrand method.[13]

A modern NMR spectrometer will tremendously enhance the Chemistry Department's undergraduate research program, which currently includes a number of projects requiring the routine characterization of organic compounds and polymers. Most of he NMR analysis associated with these projects is currently done outside the department. Availability of a modern NMR spectrometer will facilitate the undertaking of more challenging research problems and provide the necessary foundation for personal and professional advancement for students and faculty.

In Dr. Kharas's laboratory students are working on the synthesis and characterization of novel monomers and polymers based on trisubstituted ethylenes.[14] Kharas's research interests also include the synthesis and characterization of resorbable polymers for biomedical applications.[15] Students involved in research projects with Kharas will greatly benefit by having the opportunity to perform NMR analyses on new compounds synthesized in the laboratory. Professor Kharas has supervised the research of more than 50 students since arriving at DePaul in 1992. His students regularly present their research results at professional meetings and appear as co-authors on his publications.[9]

In Dr. Dintzner's laboratory students synthesize haptens (protein-conjugated molecules capable of stimulating a specific immune response) for the development of potential catalytic antibodies.[16] Dintzner's haptens are submitted to the hybridoma facilities at The Scripps Research Institute, where they are used to immunize mice. Antibodies generated in response to the haptens are isolated and purified at Scripps and sent back to Dintzner's laboratory for screening. Antibodies found to be catalytic are employed in the syntheses of physiologically active natural products. Dintzner's research involves multi-step synthesis of small molecules, which necessitates routine structure determination, principally by NMR spectroscopy.

Other research groups that will benefit from a new NMR spectrometer include the laboratories of Assistant Professors Kathleen Helm-Bychowski, and Richard Niedziela. Helm-Bychowski is a biochemist working on the molecular evolution of mitochondrial and nuclear DNA sequences in birds and mammals. Neidziela's research involves the development of spectroscopic methods for the characterization of organic and inorganic aerosols. Both will incorporate some form of NMR spectroscopy into their research.

- **Experience and Capability of the Principal Investigators**

Faculty involved in teaching laboratory chemistry courses are strongly committed to curriculum improvement through integration of hands-on NMR spectroscopy. The project directors have considerable experience in the application of NMR spectroscopy for the characterization of organic compounds, and are proficient with the routine upkeep and operation of the requested instrument. Professor Tom Murphy, who is the Director of the Environmental Science Department and Professor of Chemistry, has considerable experience in teaching spectral interpretation, organic chemistry and instrumental analysis, and is fully committed to integrating hands-on NMR technology in these laboratory courses. Kharas, who teaches organic, polymer chemistry and instrumental analysis, has almost twenty years of experience in the application of NMR spectroscopy in organic, physical and polymer chemistry, including the use of high resolution techniques (DEPT, HETCOR, COSY) for the analysis of microstructure of polymers.[12] Dintzner, who teaches organic and advanced organic chemistry, is a synthetic chemist with considerable experience in the NMR analysis of organic compounds and a strong commitment to the development of undergraduate research at DePaul.[17]

- **Evaluation Plan and Dissemination of Results**

In order to evaluate our hypothesis that a hands-on, discovery-based approach to NMR spectroscopy is an effective way to develop an understanding of molecular structure, early in the introductory organic laboratory sequence, a summative evaluation process will be conducted for this project. We will assess the project's success primarily on the basis of ACS standardized organic chemistry examination test scores on an annual basis, beginning in the current year (before the project is initiated). These are selected answer (multiple-choice) exams that are reliable, well-established and contain specific questions regarding structure determination on the basis of NMR spectroscopy. We will administer the same exam at the end of each academic year for five years and pay particular attention to how students' performance on the NMR spectroscopy-related questions improve with integration of hands-on exposure to an NMR spectrometer in discovery-based laboratories, as the project proceeds. We will be cognizant of possible unanticipated outcomes that might deveolp as the project proceeds, as well, which may be evident by overall increasing test scores.

While the standardized ACS examinations will provide "hard" data for evaluation of the project's success, our evaluation will seek to examine additional components by observing the extent to which the following project goals are met: (1) increasing the number of chemistry majors and minors, (2) increasing the research productivity of chemistry students and faculty, (3) increasing the number of students who pursue advanced degrees in chemistry after graduation, and (4) improving the chemistry laboratory sequences. Progress towards the first three goals will be quantified on an annual basis for five years using a survey approach: the total number of chemistry majors and minors will be counted per annum; research productivity will be measured by the number of scholarly papers and presentations generated by the department each year; the number of students who go on to graduate school will also be counted each year. Improvement of the chemistry laboratory sequences is a qualitative consideration, but can be evaluated quantitatively through judgement coding in the form of anonymous course evaluation forms that ask the students to rate the level by which the laboratory experience has enhanced their understanding of chemistry using a numerical scale. In these ways we will assess the project's success towards meeting the overall objectives and benefiting the students involved. We will ultimately establish a new approach for teaching molecular structure that we will incorporate into a laboratory manual that may be adopted by other undergraduate institutions around the country.

The dissemination of our results will be on-going and target an audience of faculty at undergraduate institutions nationwide. Our reports will be primarily in the form of articles submitted to the *Journal of Chemical Education* and presentations at national ACS meetings through the Division of Chemical Education. We will work with DePaul's public relations department to publicize our curriculum reform more widely to the community. In conjunction with DePaul's Interdisciplinary Science & Technology Center we will establish a week-long summer program through which local high school students and teachers will experience the power of NMR technology and learn about the exciting opportunities offered through the Chemistry Department at DePaul.

The project-based experiments in polymer synthesis instituted by Dr. Kharas and funded by the NSF in the mid-1990s (NSF-DUE 9455681, "Undergraduate Organic Chemistry Model: Experiencing Research in an Instructional Laboratory") have been tremendously successful here at DePaul and have resulted in numerous publications.[9] Integration of hands-on NMR spectroscopy early in the introductory organic laboratory sequence, through well designed discovery-based experiments, will further enhance the chemistry curriculum at DePaul. Results of our investigation will be carefully evaluated and thoroughly disseminated as described herein.

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