Putting NMR in the Hands of the Undergraduate Chemistry Student

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Reigniting the interest in students wishing to study chemistry at degree level and beyond is very much about offering interesting courses and practical sessions which allow the students to use modern instrumentation that put the theory of the text book into their hands in a straightforward, easy-to-use manner. This challenge is one for both teachers and suppliers of instrumentation working together to develop relevant programs that excite the chemists of tomorrow. In this article, we look at the response of universities and students to a new benchtop solution (Spinsolve™ benchtop NMR spectrometer from Magritek).

Figure 1. Cryogen-free Spinsolve benchtop NMR spectrometer

Putting the System to the Test

The School of Chemistry at the University of Melbourne was one of the first teaching departments to invest in a Spinsolve system. It was bought to support undergraduate teaching. The unit was installed in early 2013 and is being used in the Advanced Practical Course (called CHEM30015: Advanced Practical Chemistry). This is a course in experimental chemistry that is undertaken by students who are majoring in chemistry in the final year of a 3-year BSc course. The unit was purchased through Wilsmore and teaching support funding and championed by Dr Paul Donnelly and colleagues. NMR plays an important role in Donnelly's research work too. His multidisciplinary research involves inorganic/organic synthesis and the application of a wide range of analytical techniques including: multinuclear NMR, mass spectrometry, electronic and fluorescent spectroscopy, EPR, electrochemical techniques and X-ray crystallography. He focuses on the application of synthetic inorganic/organic chemistry to biology and materials science. In particular, he is interested in the application of coordination chemistry to metal-based drugs and the study of metal ions in biological systems.

Figure 2 shows an example from a Third Year Chemistry Experiment and demonstrates the reaction of coordinated ligands using the conversion of diamagnetic $[Co(phen)^3]^{3+}$ (top) to paramagnetic $[Co(phen)^3]^{2+}$ (bottom) complexes. Many organometallic complexes contain paramagnetic ions. These extend the chemical shift range of proton spectra to hundreds of ppm. The analysis of such samples is an important spectroscopic skill to teach students so they are aware that paramagnetic samples exhibit a wide chemical shift range and broadened signals in comparison to diamagnetic complexes. The Paramagnetic protocol in the Spinsolve software is particularly tailored for scanning such samples.

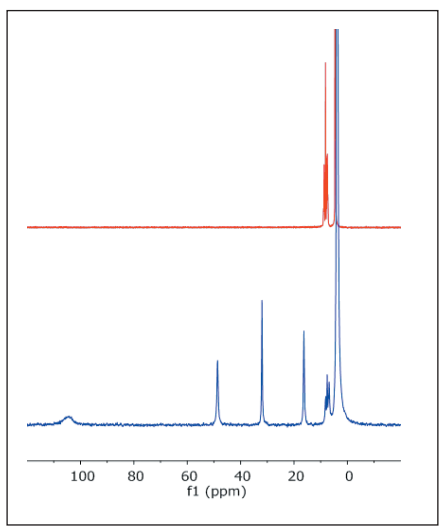

Figure 2. 3rd year teaching experiment: the reaction of coordinated ligands (conversion of diamagnetic to paramagnetic complex)

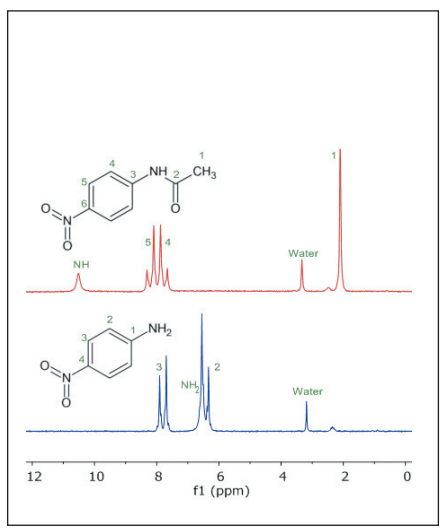

Figure 3. 2nd year teaching experiment: the synthesis of p-nitroaniline through the hydrolysis of p-nitroacetanilide

Figure 3 shows a Second Year Chemistry experiment where students synthesise p-nitroaniline through the hydrolysis of p-nitroacetanilide. In industry, this compound is used in the manufacture of dyes. The two graphs below show the Proton NMR spectra of both starting (top) and final (bottom) products dissolved in deuterated DMSO. The disappearance of the methyl peak (top, 1) and the conversion of the NH peak from 10.5 ppm into a NH2 at 6.6 ppm are evidence of a successful reaction.

Melbourne's third year Advanced Practical Chemistry course is designed as a comprehensive programme that provides experience across multiple traditional chemical disciplines whilst highlighting the importance of these disciplines in diverse 'real world' applications such as materials science and medicinal chemistry. The course consists of a series of laboratory-based experiments aimed at developing and refining students' experimental skills in the safe handling, synthesis and analysis of chemical substances of a range of different classes of compounds; an understanding of modern characterisation techniques (e.g. chromatography, atomic and molecular spectroscopy); the operation of instrumentation for the acquisition of advanced spectroscopic and physical data; and the interpretation and reporting of scientific observations including kinetic, structural and thermodynamic data. On completion of the course, the students' practical skills base should be sufficient to enable them to undertake independent research-based studies.

Professor Frances Separovic, Head of Chemistry and a leading researcher in NMR spectroscopy and biophysical chemistry, is delighted to see how well the NMR integrates into the students' practical classes. "Now the students are able to acquire their own NMR spectra as well as carry out the analysis of the compounds they have made. This makes their undergraduate experiment more applicable to both research and industry settings and increases their enthusiasm for Chemistry. The University of Melbourne is a leading research and teaching university and we all very pleased to have our undergraduate students, using a benchtop NMR that mimics well the high field instruments in our research laboratories."

The Stake-Holder's View

Senior Technical Officer, Sioe See Volaric, is responsible for technical support and training of the undergraduate students to use the spectrometer. Sioe See has played a key role in the successful integration of chemistry practical courses that occurred upon introduction of the Melbourne Model.

With her sixteen years' experience within the School of Chemistry, Sioe See's comments are extremely relevant reflecting the reactions of the department, both staff and students.

"This is the first time our 3rd year Chemistry students have encountered and used an NMR instrument at first hand. The Spinsolve has added value to our new Melbourne Model practical subject which is now in its third year. The NMR is used by students in the characterisation of organic compounds they synthesise in the laboratory. The students have developed skills in sample preparation, choice of deuterated solvents to be used, an appreciation of what a good NMR spectrum should look like, how to tell apart solvent peaks from analyte peaks and how to integrate NMR signals using the Mestralab MNova software that came with the system. The NMR practical skills will prepare them for later years when they progress to studies towards an MSc or PhD.

"Other spectroscopic techniques which students run routinely include FTIR and UV-Visible. They also have the opportunity to perform experiments involving Cyclic Voltammetry, Fluorescence, Phosphorescence, Magnetic Susceptibility, Mass Spectrometry, X-ray crystallography, Laser

spectroscopy, and Colloid and Surface Chemistry using the Wilhelmy Plate and or Tensiometer apparatus. There is also a compulsory computational component which uses a Gaussian03 computer package which students may access through a web interface called WebMO."

"We chose the Spinsolve instead of other commercial benchtop systems because the sample delivery is very like the conventional NMR instrument. It uses NMR tubes which we can buy very cheaply. The sample concentration of ~10-20 mg/0.4 mL is sufficient for a very good signal to noise spectrum. Spectra can be acquired, peaks picked and signals integrated within 3 minutes. When we tried other systems where the sample is delivered via infusion through a fine capillary, we saw blockages which can be problem particularly in a teaching lab environment. We cannot have too many interruptions in a teaching environment because students are constrained with time."

"The system can also do neat liquid samples and hence the sample is not destroyed and can be recovered, particularly if they are difficult to synthesise. No sample preparation is needed for such samples. With the latest software, students can run paramagnetic organometallic cobalt complexes, 1H 2D COSY and JRES and, if the samples are dilute or insoluble, they can choose to collect their FID to infinity. It is entirely up to the users' control. The NMR data are saved on the School prac server and students can retrieve them for analysis in their own time using iNMR software which is installed in the 20 Imacs in the Multimedia Room. This makes it a truly multi-user facility for the department."

"Maintenance and cleaning is very straightforward. I only need to shim it once a day and if the signals drift a bit or the signals are broad, a powershim (45 minutes) is all I need to get it working to specifications. We had an incident whereby a student broke the sample tube with its contents in the cavity of the NMR. After retrieving all the broken pieces, our Spinsolve was back in operation within 90 minutes. Importantly, the NMR is shielded and students are not exposed to any stray magnetic fields."

The Students' View

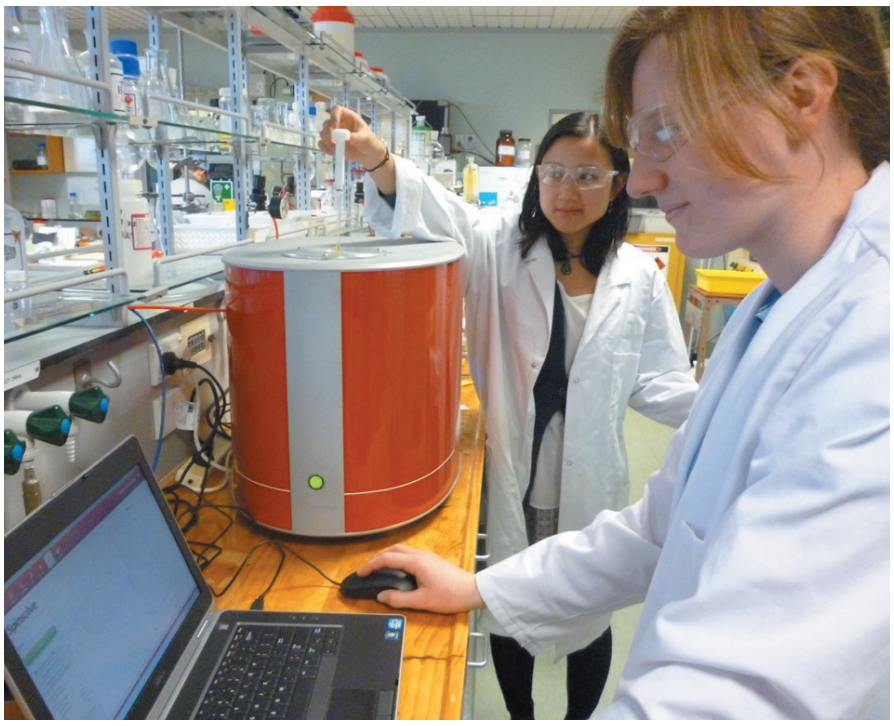

Figure 4. Undergraduate chemistry students performing practical NMR experiments in a standard laboratory environment

The real proof of the concept behind the development and adoption of Spinsolve in undergraduate teaching is going to be judged by the reaction of the users – the students themselves. After all, if they are not motivated and interested to learn more, the design goals will have been missed. Here is a selection of remarks from the Melbourne third year student group.

"It's a good thing to have in the lab for undergraduate students have a chance to learn new stuff. I don't know whether it's just me or not, but I would like my undergraduate degree to prepare me for post-graduate studies e.g. master's degree. So I think I need and I want to learn everything that I need to know beforehand."

"It was actually exciting to run our own NMR samples. It was a good experience to be able to operate the spectrometer and analyse the sample. It made analysing the compound easier, although it was kind of complicated at first. The NMR sample preparation was definitely useful because I learned more about the choice of solvents when analysing different samples. The software was easy to operate too."

"It was nice to have the experience with a new type of instrument, preparing the samples and getting real spectra. The software was easy to use, at least by the standards of lab software."

"The NMR is good actually. It's very exciting to be able to run our own sample and do the analysis of the spectra."

"The sample preparation is a very good skill to acquire. I'm assuming it's the same way we do for the 400 MHz NMR. So it will be useful when we do our higher degree research (honours, masters, or even PhD!)."

And…The Future

Melbourne's Sioe See looks ahead as to how use will grow. "In the future we intend to use the spectrometer to support other teaching courses (2nd year courses as well as third year) as will our Public Outreach program. Michael Moylan, our Chemistry Outreach Fellow, plans to use the NMR system in part of his school program for Year 12 students. Students in Year 12 study NMR in theory but this will give them the opportunity to run neat samples of ethanol and learn to interpret and integrate the signals.

It is noted that Spinsolve has been adopted in other renowned institutions worldwide. These include Temple University (Philadelphia), Rochester Institute of Technology, the Technical University of Delft (Netherlands), the German Federal Institute of Materials & Testing (Berlin) and the University of Glasgow.

Acknowledgments

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Addressing the Challenge – The Magritek Development Story

The world of nuclear magnetic resonance (NMR) spectroscopy has long been on the wish list of the undergraduate teacher. However, the expense both in terms of the initial capital purchase and subsequent running costs, due to the liquid helium consumption, made this a non-starter for the majority of colleges. Enter Magritek and the work of research teams at the RWTH University in Aachen, Germany, together with New Zealand's Massey and Victoria Universities to address this challenge. Their first product was released in 2005 when the university spinout company launched its first teaching product, the Terranova-MRI, the world's first and only 3D MRI-capable teaching system for students and teachers in a normal laboratory environment. MRI experiments can now safely be done anywhere -- the Terranova-MRI uses the Earth's magnetic field.

An operator places a standard NMR sample tube inside the Spinsolve benchtop NMR system

Now, in 2013, the step to provide a system to the world of chemistry was launched, the Spinsolve benchtop NMR spectrometer. It attacks all the negative reasons for adding NMR spectroscopy to the undergraduate practical curriculum. Because there is no superconducting magnet, the system costs a fraction of traditional high field system to purchase and requires no expensive cryogen refills. Only a standard mains power supply is required and it consumes no more power than a regular PC. Safety is a key issue: stray magnetic fields are entirely inside the enclosure making it safe to deploy in a regular chemistry lab next to other analytical instruments. It also offers many of the benefits of the more expensive system. For example, it uses standard 5 mm NMR test tubes, exactly the same as high field instruments, so sample handling is familiar and convenient. The system can be deployed in the lab where the experimenter wishes to work so there is no more waiting for NMR results with samples sent out. No expert operator required and thus the students can use it themselves to gain the experience to take into their future career.

Now, students can have powerful, high resolution NMR spectroscopy, in the chemistry lab, alongside other analytical techniques such as IR, GC, LC, MS, FTIR and Raman. The Spinsolve delivers incredible sensitivity through intuitive, easy-to-use software. The system has the best signal-to-noise ratio of any benchtop high resolution NMR instrument and can easily measure normal student laboratory samples in 10 seconds. This means no wasting time waiting for results. This is perfect for when there is a queue of students waiting to measure their samples in a practical lab class. Supplied with 2D COSY, students can perform both standard and advanced NMR experiments.