University of Barcelona
Department of Organic Chemistry

UNDERSTANDING NMR SPECTROSCOPY

James Keeler

University of Cambridge, Department of Chemistry

1 What this course is about

This course is aimed at those who are already familiar with using NMR on a day-to-day basis, but who wish to deepen their understanding of how NMR experiments work and the theory behind them. It will be assumed that you are familiar with the concepts of chemical shifts and couplings, and are used to interpreting proton and ^{13}C spectra. It will also be assumed that you have at least come across simple two-dimensional spectra such as COSY and HMQC and perhaps may have used such spectra in the course of your work. Similarly, some familiarity with the nuclear Overhauser effect (NOE) will be assumed. That NMR is a useful for chemists will be taken as self evident.

This course will always use the same approach. We will first start with something familiar – such as multiplets we commonly see in proton NMR spectra – and then go deeper into the explanation behind this, introducing along the way new ideas and new concepts. In this way the new things that we are learning are always rooted in the familiar, and we should always be able to see *why* we are doing something.

In NMR there is no escape from the plain fact that to understand all but the simplest experiments we need to use *quantum mechanics*. Luckily for us, the quantum mechanics we need for NMR is really rather simple, and if we are prepared to take it on trust, we will find that we can make quantum mechanical calculations simply by applying a set of rules. Also, the quantum mechanical tools we will use are quite intuitive and many of the calculations can be imagined in a very physical way. So, although we will be using quantum mechanical ideas, we will not be using any heavy-duty theory. It is not necessary to have studied quantum mechanics at anything more than the most elementary level.

Inevitably, we will have to use some mathematics in our description of NMR. However, the level of mathematics we need is quite low and should not present any problems for a science graduate. Occasionally we will use a few ideas from calculus, but even then it is not essential to understand this in great detail.

Course structure

The course is accompanied by a detailed set of handouts, which for convenience is divided up into “chapters”. You will notice an inconsistency in the style of these chapters; this comes about because they have been prepared (or at least the early versions of them) over a number of years for a variety of purposes. The notes are sufficiently complete that you should not need to take many extra notes during the lectures.

Each chapter has associated with it some exercises which are intended to illustrate the course material; unless you do the exercises you will not understand the material. These exercises will give you a feel for what you can do with NMR data and how what you see relates to the theory you have studied.

Chapter 2 considers how we can understand the form of the NMR spectrum in terms of the underlying nuclear spin energy levels. Although this approach is more complex than the familiar "successive splitting" method for constructing multiplets it does help us understand how to think about multiplets in terms of "active" and "passive" spins. This approach also makes it possible to understand the form of multiple quantum spectra, which will be useful to us later on in the course. The chapter closes with a discussion of strongly coupled spectra and how they can be analysed.

Chapter 3 introduces the vector model of NMR. This model has its limitations, but it is very useful for understanding how pulses excite NMR signals. We can also use the vector model to understand the basic, but very important, NMR experiments such as pulse-acquire, inversion recovery and most importantly the spin echo.

Chapter 4 is concerned with data processing. The signal we actually record in an NMR experiment is a function of time, and we have to convert this to the usual representation (intensity as a function of frequency) using Fourier transformation. There are quite a lot of useful manipulations that we can carry out on the data to enhance the sensitivity or resolution, depending on what we require. These manipulations are described and their limitations discussed.

Chapter 5 is concerned with how the spectrometer works. It is not necessary to understand this is great detail, but it does help to have some basic understanding of what is going on when we "shim the magnet" or "tune the probe". In this chapter we also introduce some important ideas about how the NMR signal is turned into a digital form, and the consequences that this has.

Chapter 6 introduces the product operator formalism for analysing NMR experiments. This approach is quantum mechanical, in contrast to the semi-classical approach taken by the vector model. We will see that the formalism is well adapted to describing pulsed NMR experiments, and that despite its quantum mechanical rigour it retains a relatively intuitive approach. Using product operators we can describe important phenomena such as the evolution of couplings during spin echoes, coherence transfer and the generation of multiple quantum coherences.

Chapter 7 puts the tools from Chapter 6 to immediate use in analysing and understanding two-dimensional spectra. Such spectra have proved to be enormously useful in structure determination, and are responsible for the explosive growth of NMR over the past 20 years or so. We will concentrate on the most important types of spectra, such as COSY and HMQC, analysing these in some detail.

Chapter 8 considers the important topic of relaxation in NMR. We start out by considering the effects of relaxation, concentrating in particular on the very important nuclear Overhauser effect. We then go on to consider the sources of relaxation and how it is related to molecular properties.

Chapter 9 does not form a part of the course, but is an optional advanced topic. The chapter is concerned with the two methods used in multiple pulse NMR to select a particular outcome in an NMR experiment: phase cycling and field gradient pulses. An understanding of how these work is helpful in getting to grips with the details of how experiments are actually run.

Texts

There are innumerable books written about NMR. Many of these avoid any serious attempt to describe how the experiments work, but rather concentrate on the interpretation of various kinds of spectra. An excellent example of this kind of book is J. K. M. Sanders and B. K. Hunter *Modern NMR Spectroscopy* (OUP).

There are also a number of texts which take a more theory-based approach, at a number of different levels. Probably the best of the more elementary books if P. J. Hore *Nuclear Magnetic Resonance* (OUP).

For a deeper understanding you can do no better than refer to the book recently published by M. H. Levitt *Spin Dynamics* (Wiley).

Acknowledgements

Chapters 2 to 5 were prepared for a graduate course given at the Department of Chemistry, University of California Irvine in the spring of 2002. I wish to express my thanks to Professor AJ Shaka, and to his colleagues at Irvine, for the invitation to give this course and for hosting a period of sabbatical leave.

Chapters 6, 7 and 8 are modified from notes prepared for summer schools held in Mishima and Sapporo (Japan) in 1998 and 1999; thanks are due to Professor F Inagaki for the opportunity to present this material.

Chapter 9 was originally prepared (in a somewhat different form) for an EMBO course held in Turin (Italy) in 1995. It has been modified subsequently for the courses in Japan mentioned above and for another EMBO course held in Lucca in 2000. Once again I am grateful to the organizers and sponsors of these meetings for the opportunity to present this material.

Finally I wish to thank Professor Dr Miquel Pons Vallès and the Department of Organic Chemistry, University of Barcelona, for the opportunity to present this course. Financial support from the International Graduate School of Catalonia is gratefully acknowledged.

James Keeler
University of Cambridge, Department of Chemistry
March 2004
`James.Keeler@ch.cam.ac.uk`
`www-keeler.ch.cam.ac.uk`