Nuclear Magnetic Resonance Spectroscopy

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Nuclear Magnetic Resonance Spectroscopy, or NMR as we chemists call it is a powerful tool for studying molecular structure. At the University of Wyoming, the Chemistry department has three NMR spectrometers. We maintain two NMR instruments for the study of solutions, which operate with proton resonance frequencies of 270 and 400 MHz. For the study of solids, Dr. Yarger’s group is equipped with a 400 MHz instrument. The “400 liquids” instrument is arguably the most used instrument in the department.

Two-dimensional NMR Spectroscopy

Although much of the NMR spectroscopy in the department is the traditional one-dimensional variety, we have the capability to conduct two and three-dimensional experiments as well. Many of the two-dimensional techniques are easy to set up and use, and they provide a wealth of information that is not available using one-dimensional techniques. By including magnetic field gradients to the mix, the time required to perform two-dimensional experiments can often be reduced to a few minutes.

Correlation Spectroscopy, or COSY

Correlation experiments reveal connections between the atoms in a molecule. This is deduced from observations of the coupling between the nuclear spins. Spin coupling is typically observed between nuclei that are separated by one to three bonds, and most correlation experiments are designed to emphasize these short-range couplings. Experiments designed to emphasize long-range coupling can also be useful. By observing several sets of overlapping correlations, it is possible to establish the chemical structure with great certainty. In a one-dimensional spectrum, spin coupling is observed as multiplet structure in the peaks. In a two-dimensional spectrum, spin coupling causes the appearance of cross peaks, or peaks off the diagonal.

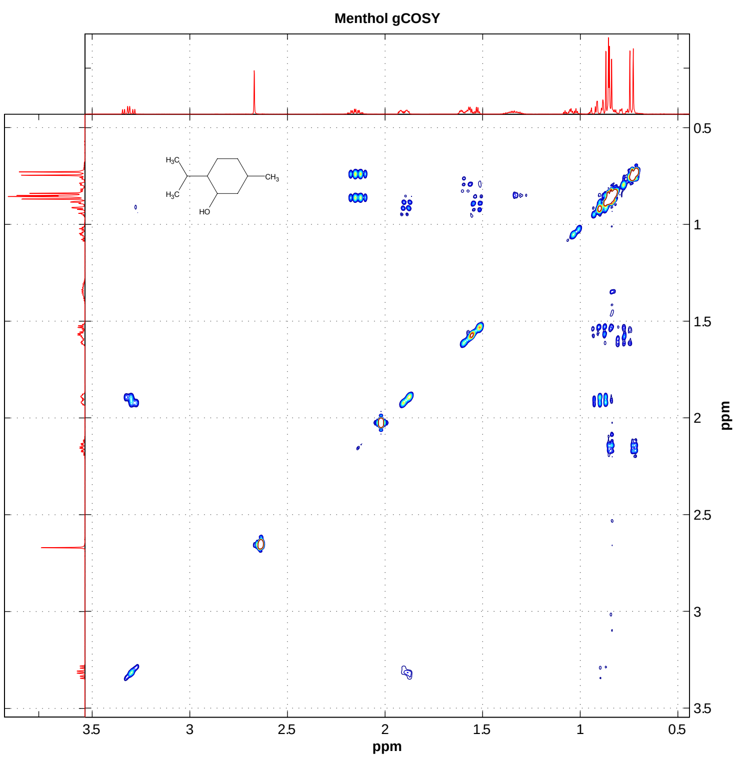


Figure 1

Gradient COSY

The gradient COSY experiment is the simplest of the two-dimensional magnetic field gradient NMR experiments. Normally, a COSY spectrum would require a minimum of four scans (per FID) to distinguish the sign of a frequency in the second dimension and select the desired coherence (in this case scalar J coupling between nuclei separated by two or three bonds). By introducing magnetic field gradients into the experiment, the desired coherence can be selected in one scan. Gradient methods thus significantly shorten the time it takes to acquire a two-dimensional spectrum. The gradient COSY spectrum of Menthol is shown in figure 1. It required about 11 minutes to collect.

Gradient HMQC

The gradient Hetero-nuclear Multiple Quantum Correlation experiment is designed to reveal connections between carbon atoms and the protons directly bonded to them. The experiment also furnishes information about carbon types.

Quaternary carbons, for instance, have no attached protons and consequently, show no correlations. Methine carbons show one peak. Methylene carbons may show one or two peaks depending on the chemical shifts of the two protons and methyl groups generally show a single intense peak or a single multiplet. HMQC is known as an "inverse" or "indirect" experiment, because the ^{13}C chemical shift information is encoded into the ^{1}H signal which is then detected. Direct experiments detect the ^{13}C nucleus. The main advantage of inverse detection is that the proton sensitivity is much greater than the sensitivity of carbon. This makes it possible to get a proton-carbon correlation spectrum in a relatively short time. The gradient HMQC spectrum of Menthol is shown in figure 2. It required about 18 minutes to collect.

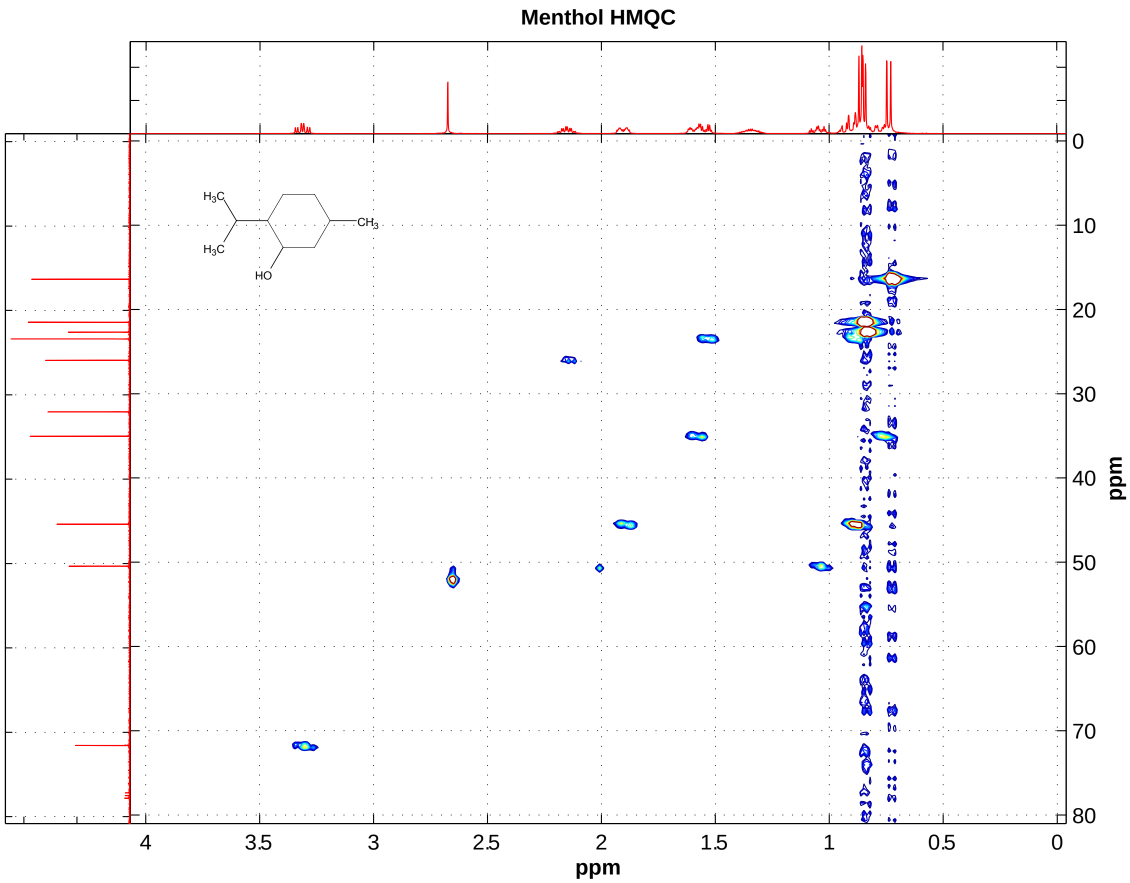
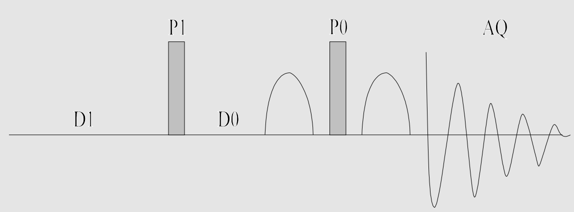


Figure 2



This is the pulse sequence for the gradient-COSY experiment. In two-dimensional NMR, we typically collect between 100 and 500 FID's. In this diagram, D0 is a delay that is small in the first FID and incremented for each new FID. It is used to encode a second time dimension into the data. D1 is referred to as the relaxation delay. It allows the nuclear spins to return to equilibrium and is usually 1 to 3 seconds in length. P1 and P0 are short pulses of approximately 10 microseconds in duration from a radio transmitter operating at the proton resonance frequency. In the case of our Bruker DRX-400 spectrometer, this is close to 400 MHz. The "humps" in the diagram represent magnetic field gradient pulses with length of 1 millisecond. AQ is the time in which we collect the data, and the squiggly line has the approximate appearance of a the free induction decay, or FID.