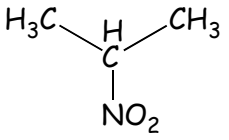
INTERPRETING 2D NMR SPECTRA[1]

How To Read COSY Spectra

2-Nitropropane: To see what type of information a COSY spectrum may provide. we shall consider several examples of increasing complexity. The first is the COSY spectrum of 2-nitropropane. In this simple molecule, we expect to observe coupling between the protons on the two methyl groups and the proton at the methine position.

Figure 1 is the COSY spectrum of 2-nitropropane. The first thing to note about the spectrum is that the proton NMR spectrum of the compound being studied is plotted along both the horizontal and vertical axes, and each axis is calibrated according to the chemical shift values (in parts per million , ppm). The COSY spectrum shows distinct spots on a diagonal. extending from the upper right corner of the spectrum down to the lower left corner. By extending vertical and horizontal lines from each spot on the diagonal, you call easily see that each spot on the diagonal corresponds with the same peak on each coordinate axis



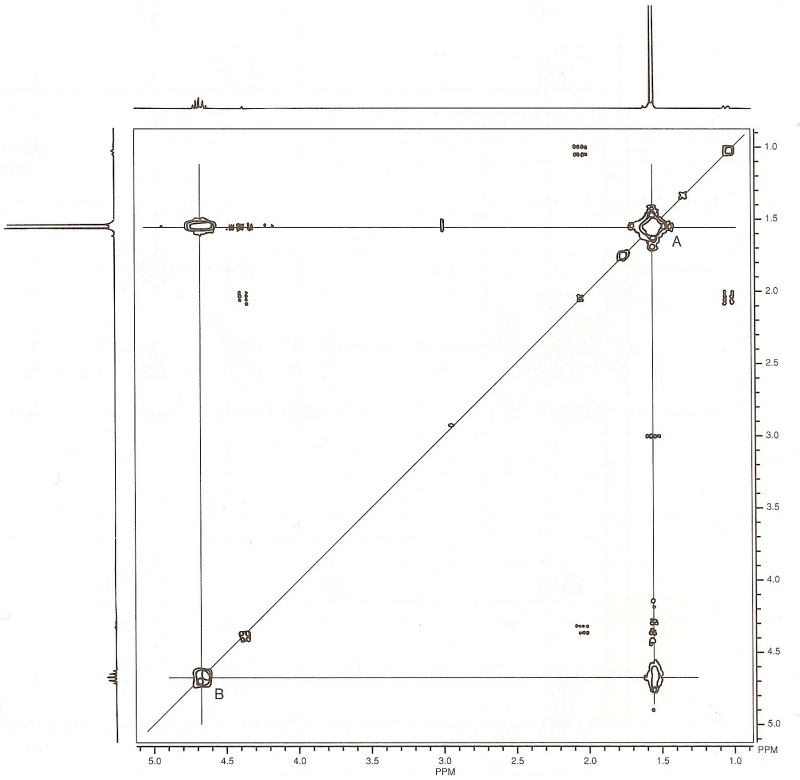
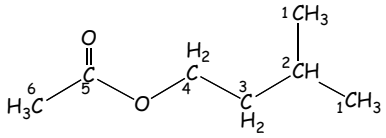


Figure 1, COSY spectrum of 2-nitropropane.

The diagonal peaks serve only as reference points. The important peaks in the spectrum are the oil-diagonal peaks. In the spectrum of 2-nitropropane, we can extend a horizontal line from the spot at 1.56 ppm (which is labeled A and corresponds to the methyl protons). This horizontal line eventually encounters an off-diagonal spot (al the upper left of the COSY spectrum) that corresponds to the methine proton peak at 4.66 ppm (labeled B). A vertical line drawn from this off diagonal spot intersects the spot on the diagonal that corresponds to the methine proton (B). The presence of this off-diagonal spot, which correlates the methyl proton spot and the methine proton spot, confirms that the methyl protons arc coupled to the methine protons. as we would have expected. A similar result would have been obtained by drawing a vertical line from the 1.56-ppm spot (A) and at horizontal line from the 4.66-ppm spot (B). The two lines would have intersected at the second off-diagonal spot (at the lower right of the COSY spectrum). The vertical and horizontal lines described in this analysis are drawn on the COSY spectrum in Figure 1.

Isopentyl Acetate. In practice, we would not require a COSY spectrum to fully interpret the NMR spectrum of 2-nitropropane. The preceding analysis illustrated how to interpret a COSY spectrum, using a simple. easy-to-understand example. A more interesting example is the COSY spectrum of isopentyl acetic (Fig. 2).

Again we see coordinate axes; the proton spectrum of isopentyl acetate is plotted along each axis. The COSY spectrum shows a distinct set of spots on a diagonal, with each spot corresponding to the same peak on each coordinate axis. Lines have been drawn to help you identify the correlations. In the COSY spectrum of isopentyl acetate, we see that the protons of the two equivalent methyl groups (1) correlate with the methine proton (2). We can also see correlation between the two methylene groups (3 and 4) and between the methine proton (2) and the neighboring methylene (3). The methyl group of the acetate moiety (6) docs not show off-diagonal peaks. because the acetyl methyl protons are not coupled to other protons in the molecule.



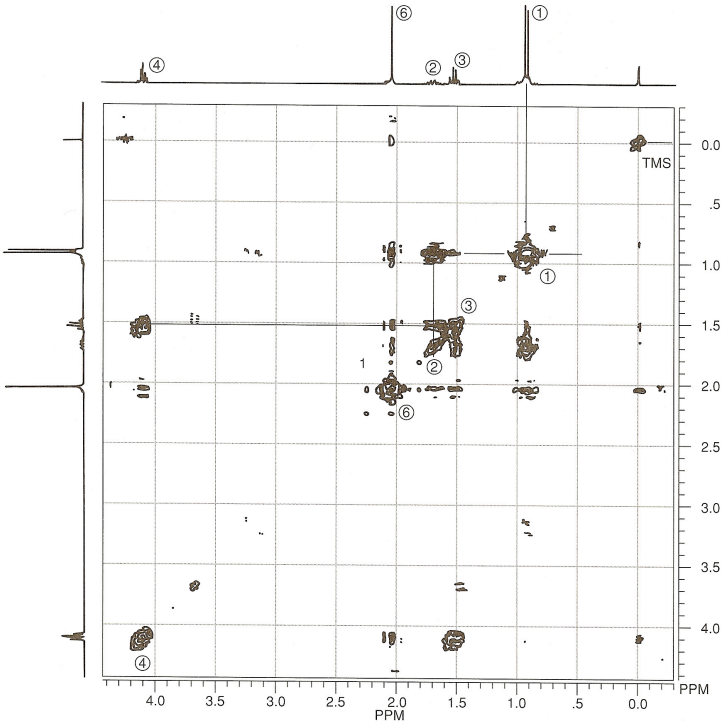
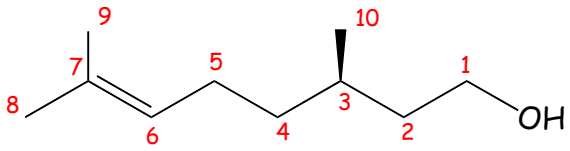


Figure 2, COSY spectrum of isopentyl acetate.

You may have noticed that each of the COSY spectra shown in this section contains additional spots besides the ones examined in our discussion. Often these "extra" spots have much lower intensities than the principal spots on the plot. The COSY method can sometimes detect interactions between nuclei over ranges that extend beyond three bonds. Besides this long-range coupling, nuclei that are several atoms apart but that are close together *spatially* also may produce off-diagonal peaks. We learn to ignore these minor peaks in our interpretation of COSY spectra. In some variations of the method, however, spectroscopist make use of such long-range interactions to produce two-dimensional NMR spectra that specifically record this type of information.

Citronellol. The COSY spectrum of citronellol is a third example. The spectrum (Figure 3) is rather complex in appearance. Nevertheless, we can identify certain important coupling interactions. Again, lines have been drawn to help you identify the correlations. The proton on C_6 is clearly coupled to the protons on C_5. Closer examination of the spectrum also reveals that the proton on C_6 is coupled through allylic (four-bond) coupling to the two methyl groups at C_8 and C_9. The protons on C_1 are coupled to two nonequivalent protons on C_2 (at 1.4 and 1.6 ppm). They are

nonequivalent, owing to the presence of a stereocenter in the molecule at C_3. The splitting of the methyl protons at C_{10} by the methine proton at C_3 can also be seen. although the C_3 spot on the diagonal line is obscured by other spots that are superimposed on it. However, from the COSY spectrum we can determine that the methine proton at C_3 must occur at the same chemical shift as one of the C_8 or C_9 methyl groups (1.6 ppm). Thus, a great deal of useful information can be obtained *even* from *a* complicated *COSY pattern.*



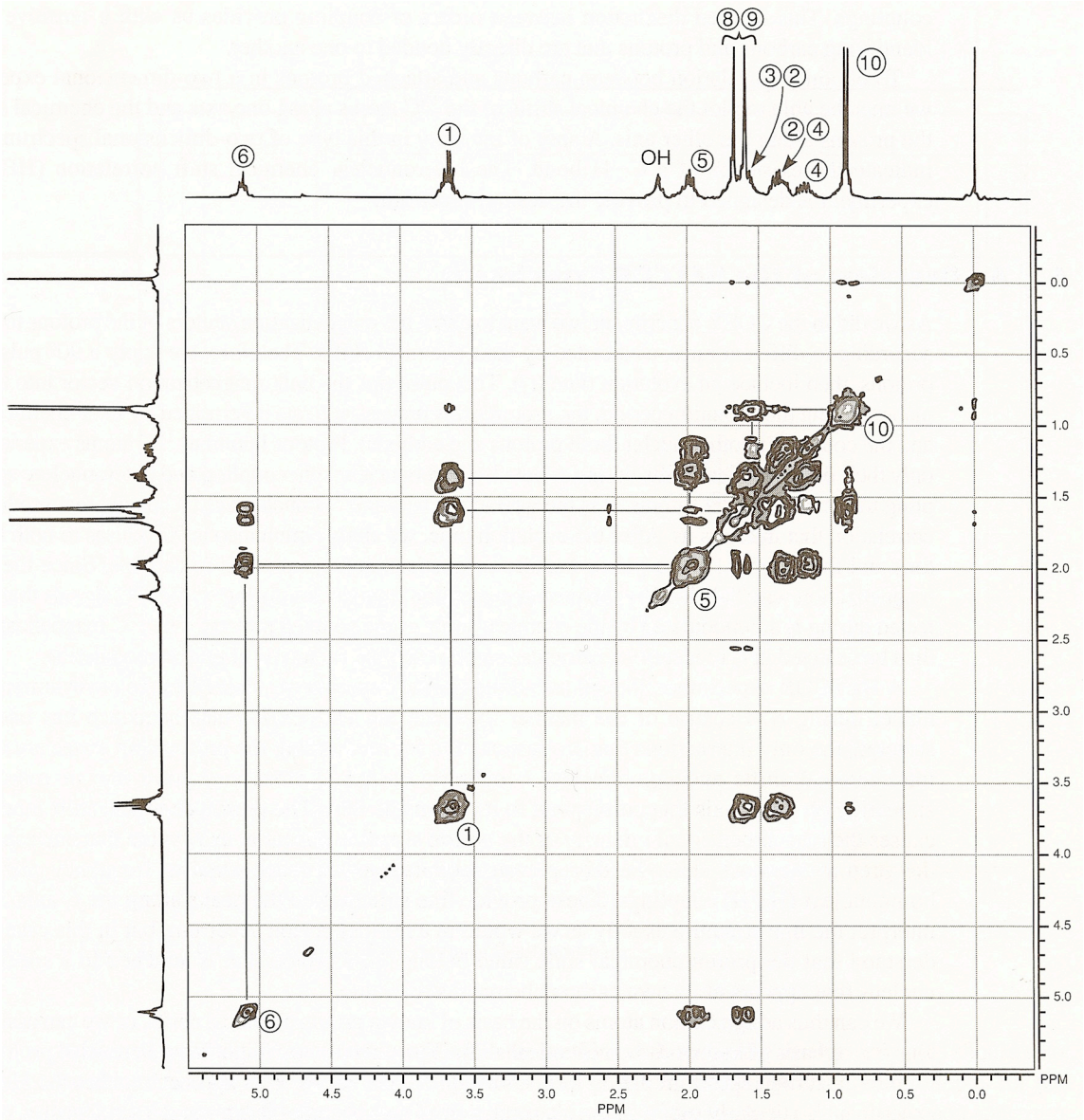
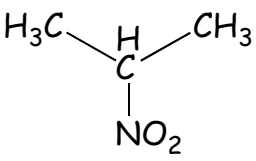


Figure 3 COSY spectrum of citronellol

How To Read HETCOR Spectra

2-Nitropropane. Figure 4 is an example of a simple HETCOR plot. In this case, the sample is 2-nitropropane.

It is common practice to plot the proton spectrum of the compound being studied along one axis and the carbon spectrum along the other axis. Each spot of intensity on the two-dimensional plot indicates a carbon atom that bears the corresponding protons. In Figure 4. you should be able to see a peak corresponding to the methyl carbons. which appear at 21 ppm in the carbon spectrum (horizontal axis), and a peak at 79 ppm corresponding to the methine carbon.



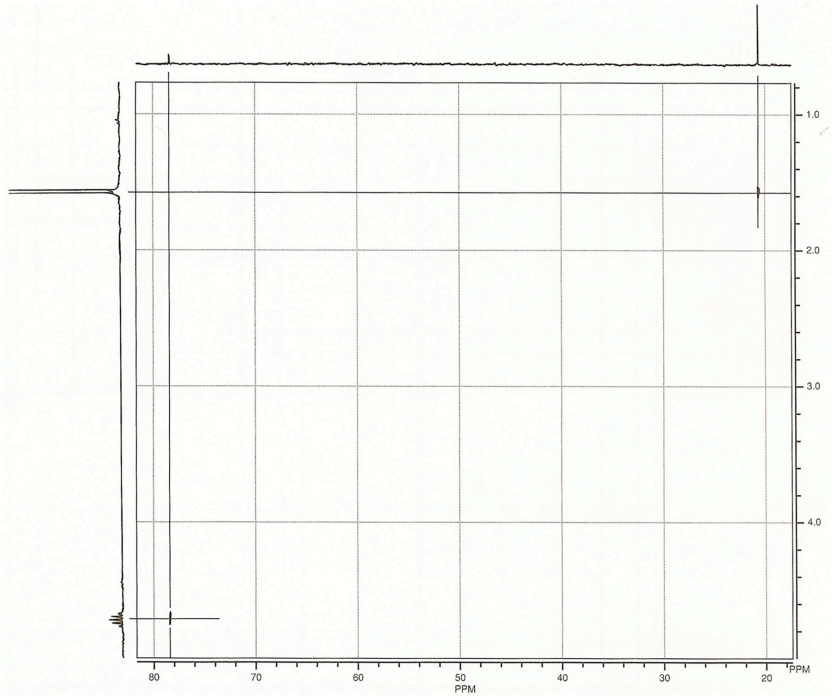
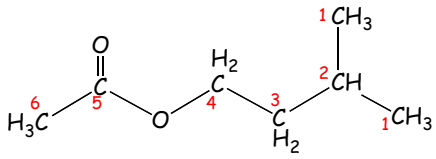


FIGURE 4 HERTCOR spectrum of 2-nitropropane.

On the vertical axis, you should also be able to find the doublet for the methyl protons at 1.56 ppm (proton spectrum) and a septet for the methine proton at 4.66 ppm. If you draw a vertical line from the methyl peak of the carbon spectrum (21 ppm) and a horizontal line from the methyl peak of the proton spectrum (1.56 ppm), the two lines would intersect at the exact point on the two-dimensional plot where a spot is marked. This spot indicates that the protons at 1.56 ppm and the carbons at 21 ppm represent the same position of the molecule. That is, the hydrogens are attached to the indicated carbon. In the same way, the spot in the lower left corner of the HETCOR plot correlates with the carbon peak at 79 ppm and the proton septet at 4.66 ppm, indicating that these two absorptions represent the same position in the molecule.

Isopentyl Acetate. A second, more complex example is isopentyl acetate. Figure 5 is the HETCOR plot for this substance. Each spot on the HETCOR plot has been labeled with a number and lines have been drawn to help you see the correlations between proton peaks and carbon peaks. The carbon peak at 23 ppm and the proton doublet at 0.92 ppm correspond to the methyl groups (1); the carbon peak at 25 ppm and the proton multiplet at 1.69 ppm correspond to the methine position (2); and the carbon peak at 37 ppm and the proton quartet at 1.52 ppm correspond to the methylene group (3). The other methylene group (4) is deshielded by the



nearby oxygen atom. Therefore, a spot on the HETCOR plot for this group appears at 63 ppm on the carbon axis and 4.10 ppm on the proton axis. It is interesting that the methyl group of the acetyl function (6) appears down field of the methyl groups of the isopentyl group (1) in the proton spectrum (2.04 ppm). We expect this chemical shift, since the methyl protons should be deshielded by the anisotropic nature of the carbonyl group. In the carbon spectrum, however. the carbon peak appears *upfield* of the methyl carbons of the isopentyl group. A spot on the HETCOR plot that correlates these two peaks confirms the assignment.

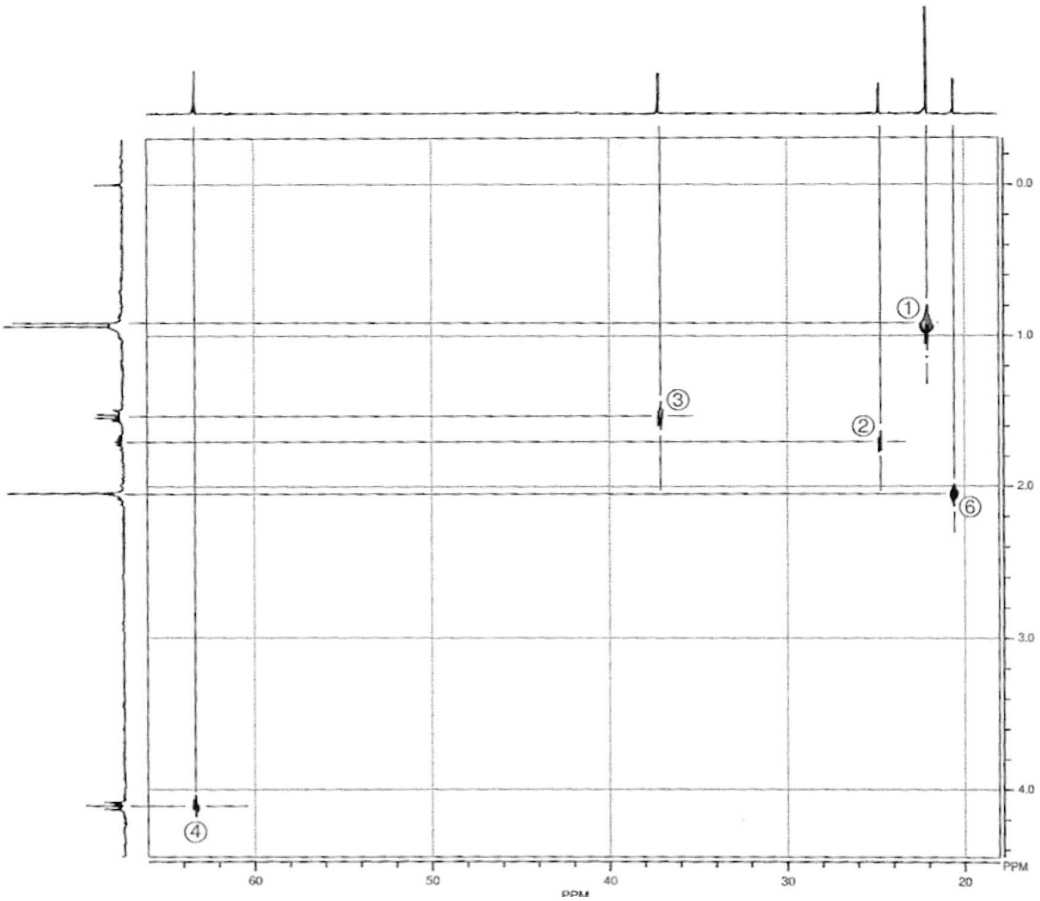
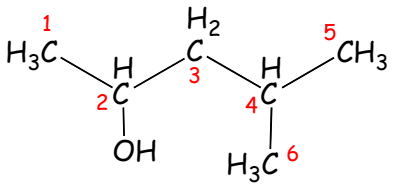
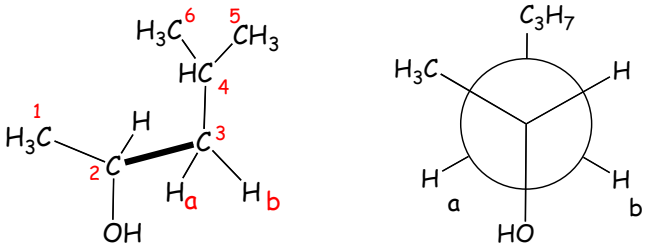


Figure 5. HETCOR spectrum of isopentyl acetate.

4-Methyl-2-Pentanol. Figure 6 shows the final example that illustrates some of the power of the HETCOR technique for 4-methyl-2-pentanol. Lines have been drawn on the spectrum to help you find the correlations. This molecule has a stereocenter at carbon 2. An examination of the HETCOR plot for 4-methyl-2-pentanol reveals *two* spots that correspond to the two methylene protons on carbon 3. At 48 ppm on the carbon axis. two contour spots appear, one at about 1.20 ppm on the proton axis and the other at about 1.40 ppm. The HETCOR plot shows that there are two nonequivalent protons attached to carbon 3. If we examine a Newman projection of this molecule, we find that the presence of the stereocenter makes the two methylene protons (a and b) nonequivalent. As a result, they appear at different values of chemical shift.





The *carbon* spectrum also reveals the effect of a stereocenter in the molecule. In the proton spectrum, the apparent doublet (actually it is a *pair* of doublets) at 0.91 ppm arises from the six protons on the methyl groups, which are labeled 5 and 6 in the preceding structure. Looking across to the right on the HETCOR plot, you will find two contour spots, one corresponding to 22 ppm and the other corresponding to 23 ppm. These two carbon peaks arise because the two methyl groups are also not quite equivalent; the distance from one methyl group to the oxygen atom is not quite the same as that from the other methyl group, when we consider the most likely conformation for the molecule.

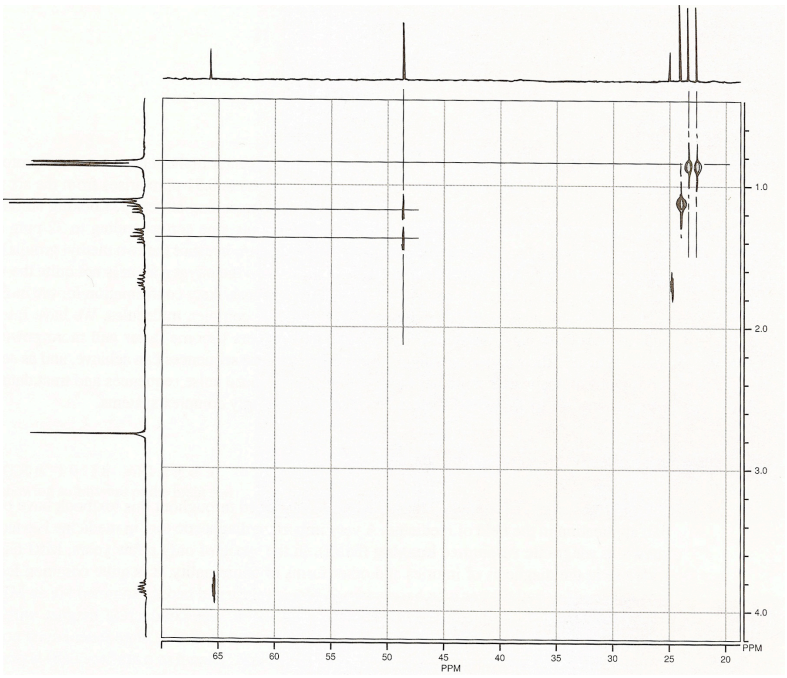


FIGURE 6 HETCOR spectrum of 4-methyl-2-pentanol.

A great many advanced techniques can be applied to complex molecules. We have introduced only a few of the most important ones here. As computers become faster and more powerful, as chemists evolve their understanding of what different pulse sequences can achieve. and as scientists write more sophisticated computer programs to control those pulse sequences and treat data, it will become possible to apply NMR spectroscopy to increasingly complex systems.

1. Pavia, Lampman and Kris, Introduction to Spectroscopy, 3rd Ed. Brooks/Cole, 2001