Lecture # 10

NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

Part Two: Carbon-13 Spectra, Including Heteronuclear Coupling with Other Nuclei

The study of carbon nuclei through nuclear magnetic resonance (NMR) spectroscopy is an important technique for determining the structures of organic molecules. Using it together with proton NMR and infrared spectroscopy, organic chemists can often determine the complete structure of an unknown compound without "getting their hands dirty" in the laboratory! Fourier transform–NMR (FT-NMR) instrumentation makes it possible to obtain routine carbon spectra easily.

Unfortunately, the resonances of ^{13}C nuclei are more difficult to observe than those of protons (^1H). They are about 6000 times weaker than proton resonances, for two major reasons.

For a given magnetic field strength, the resonance frequency of a ^{13}C nucleus is about one-fourth the frequency required to observe proton resonances (see Table 5.2). For example, in a 7.05-Tesla applied magnetic field, protons are observed at 300 MHz, while ^{13}C nuclei are observed at about 75 MHz. With modern instrumentation, it is a simple matter to switch the transmitter frequency from the value required to observe proton resonances to the value required for ^{13}C resonances.

☐ 6.2 CARBON-13 CHEMICAL SHIFTS

A. Correlation Charts

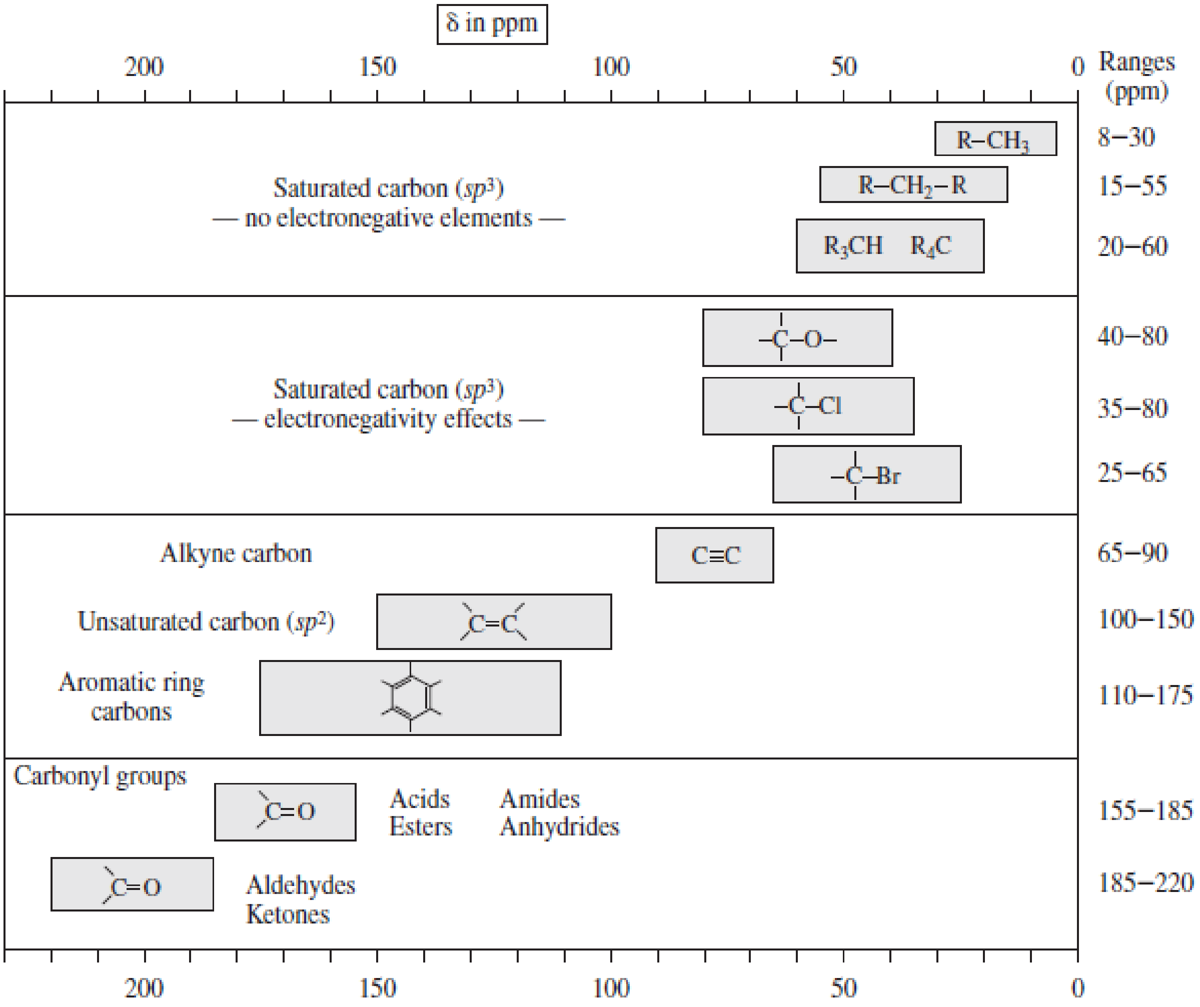
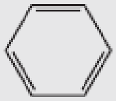
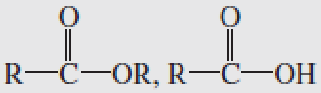
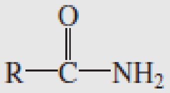
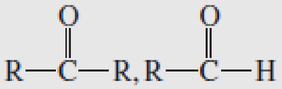


FIGURE 6.1 A correlation chart for ^{13}C chemical shifts (chemical shifts are listed in parts per million from TMS).

TABLE 6.1

APPROXIMATE ^{13}C CHEMICAL SHIFT RANGES (ppm) FOR SELECTED TYPES OF CARBON

$R-CH_3$	8–30	$C\equiv C$	65–90
R_2CH_2	15–55	$C=C$	100–150
R_3CH	20–60	$C\equiv N$	110–140
$C-I$	0–40		110–175
$C-Br$	25–65		
$C-N$	30–65	 $R-\overset{O}{\overset{\|}{C}}-OR,\ R-\overset{O}{\overset{\|}{C}}-OH$	155–185
$C-Cl$	35–80	 $R-\overset{O}{\overset{\|}{C}}-NH_2$	155–185
$C-O$	40–80	 $R-\overset{O}{\overset{\|}{C}}-R,\ R-\overset{O}{\overset{\|}{C}}-H$	185–220

In ^1H NMR, the effect of an electronegative element on chemical shift diminishes with distance, but it is always in the same direction (deshielding and downfield). In ^{13}C NMR, an electronegative element also causes a downfield shift in the α and β carbons, but it usually leads to a small *upfield* shift for the γ carbon. This effect is clearly seen in the carbons of 1-hexanol:

$$\begin{array}{cccccc} 14.2 & 22.8 & 32.0 & 25.8 & 32.8 & 61.9\text{ ppm} \\ CH_3- & CH_2- & CH_2- & CH_2- & CH_2- & CH_2-OH \\ \omega & \varepsilon & \delta & \gamma & \beta & \alpha \end{array}$$

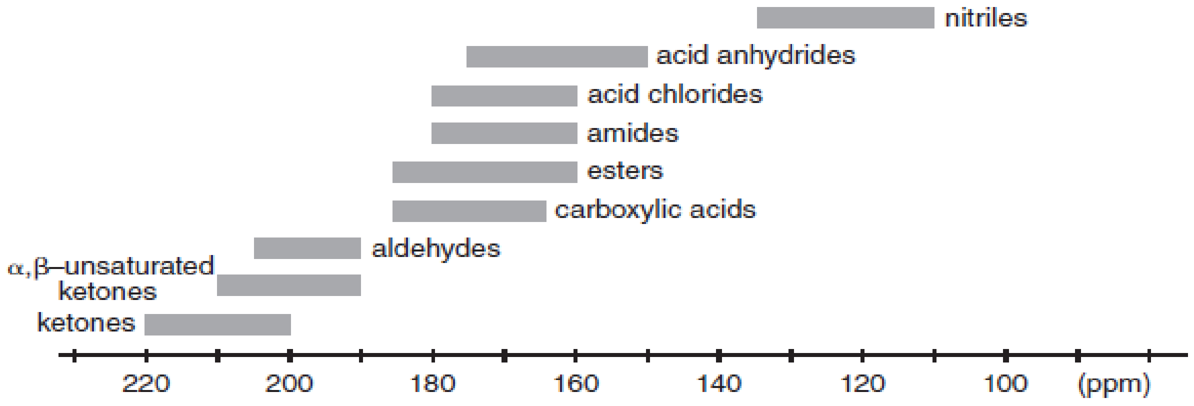
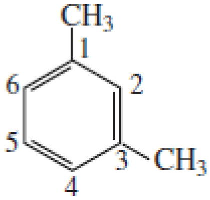


FIGURE 6.2 A ^{13}C correlation chart for carbonyl and nitrile functional groups.

B. Calculation of ^{13}C Chemical Shifts

Consider *m*-xylene (1,3-dimethylbenzene) as an example. Consulting the tables, you will find that the base value for the carbons in a benzene ring is 128.5 ppm. Next, look in the substituent tables that relate to benzene rings for the methyl substituent corrections (Table A8.7 in Appendix 8). These values are

	ipso	*ortho*	*meta*	*para*
CH_3:	9.3	0.7	– 0.1	–2.9 ppm



C1 = base + *ipso* + *meta* = 128.5 + 9.3 + (–0.1) = 137.7 ppm

C2 = base + *ortho* + *ortho* = 128.5 + 0.7 + 0.7 = 129.9 ppm

C3 = C1

C4 = base + *ortho* + *para* = 128.5 + 0.7 + (–2.9) = 126.3 ppm

C5 = base + *meta* + *meta* = 128.5 + 2(– 0.1) = 128.3 ppm

C6 = C4

The observed values for C1, C2, C4, and C5 of *m*-xylene are 137.6, 130.0, 126.2, and 128.2 ppm, respectively, and the calculated values agree well with those actually measured.

6.3 PROTON-COUPLED ^{13}C SPECTRA—SPIN–SPIN SPLITTING OF CARBON-13 SIGNALS

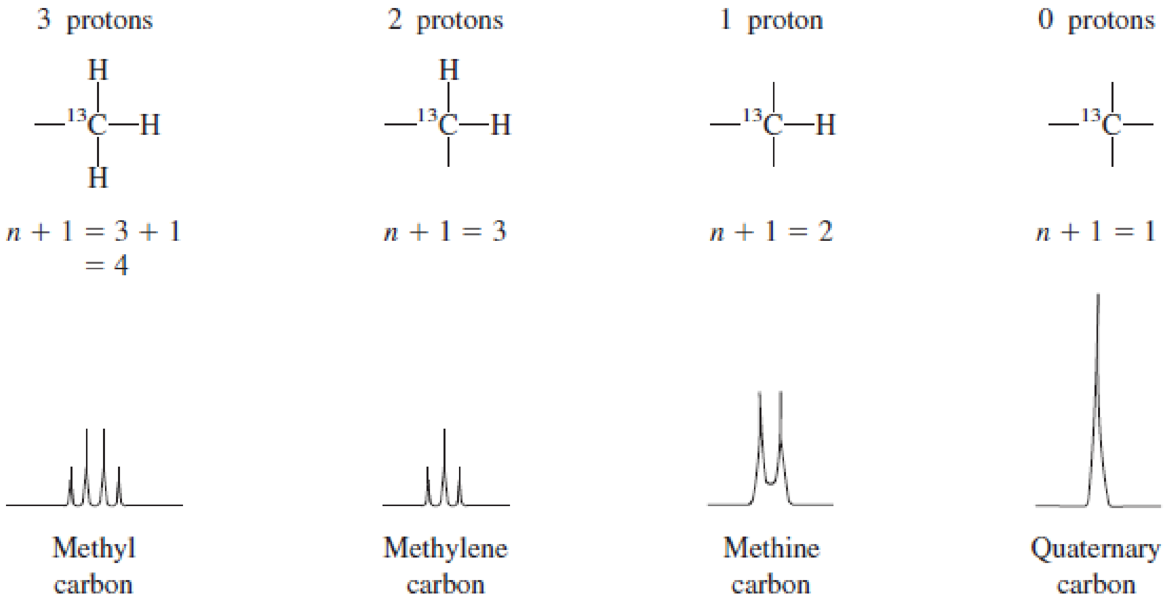


FIGURE 6.3 The effect of attached protons on ^{13}C resonances.

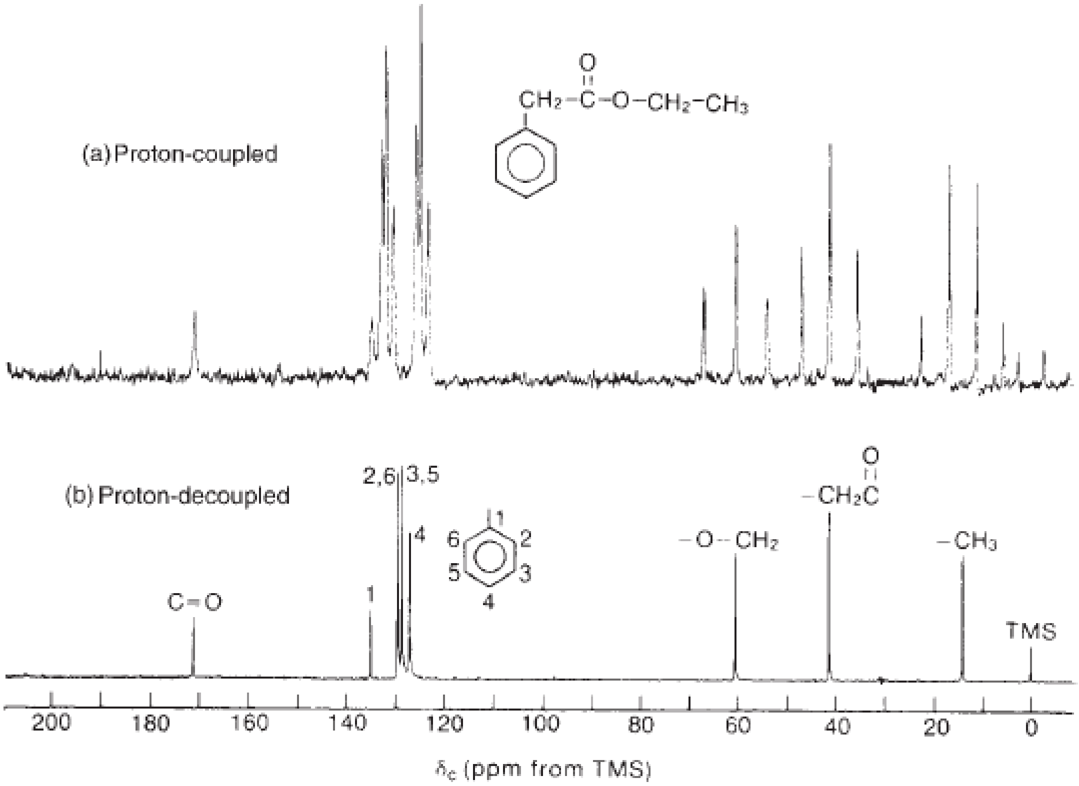


FIGURE 6.4 Ethyl phenylacetate. (a) The proton-coupled ^{13}C spectrum (20 MHz). (b) The proton-decoupled ^{13}C spectrum (20 MHz). (From Moore, J. A., and D. L. Dalrymple, *Experimental Methods in Organic Chemistry*, W. B. Saunders, Philadelphia, 1976.)

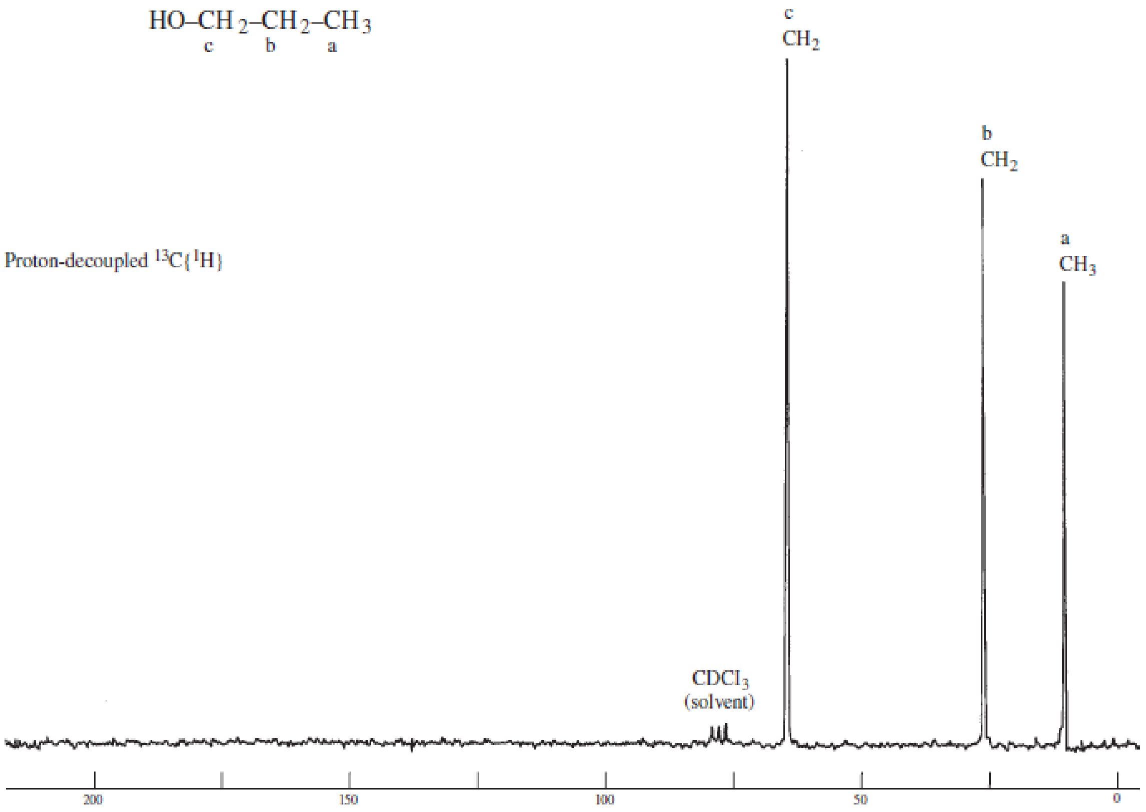


FIGURE 6.5 The proton-decoupled ^{13}C spectrum of 1-propanol (22.5 MHz).

☐ 6.5 NUCLEAR OVERHAUSER ENHANCEMENT (NOE)

When we obtain a proton-decoupled ^{13}C spectrum, the intensities of many of the carbon resonances increase significantly above those observed in a proton-coupled experiment. Carbon atoms with hydrogen atoms directly attached are enhanced the most, and the enhancement increases (but not always linearly) as more hydrogens are attached. This effect is known as the nuclear Overhauser effect, and the degree of increase in the signal is called the **nuclear Overhauser enhancement (NOE)**. The NOE effect is *heteronuclear* in this case, operating between two dissimilar atoms (carbon and hydrogen). Both atoms exhibit spins and are NMR active. The nuclear Overhauser effect is general, showing up when one of two different types of atoms is irradiated while the NMR spectrum of the other type is determined. If the absorption intensities of the observed (i.e., nonirradiated) atom change, enhancement has occurred. The effect can be either positive or negative, depending on which atom types are involved. In the case of ^{13}C interacting with ^{1}H, the effect is positive; irradiating the hydrogens increases the intensities of the carbon signals. The maximum enhancement that can be observed is given by the relationship

$$\text{NOE}_{\text{max}} = \frac{1}{2}\left(\frac{\gamma_{\text{irr}}}{\gamma_{\text{obs}}}\right) \qquad \textbf{Equation 6.1}$$

where γ_{irr} is the magnetogyric ratio of the nucleus being irradiated, and γ_{obs} is that of the nucleus being observed. Remember that NOE_{max} is the *enhancement* of the signal, and it must be added to the original signal strength:

$$\text{total predicted intensity (maximum)} = 1 + \text{NOE}_{\text{max}}$$

Equation 6.2

For a proton-decoupled ^{13}C spectrum, we would calculate, using the values in Table 5.2,

$$\text{NOE}_{\text{max}} = \frac{1}{2}\left(\frac{267.5}{67.28}\right) = 1.988$$

Equation 6.3

indicating that the ^{13}C signals can be enhanced up to 200% by irradiation of the hydrogens. This value, however, is a theoretical maximum, and most actual cases exhibit less-than-ideal enhancement.

Signal enhancement due to NOE is an example of **cross-polarization,** in which a polarization of the spin states in one type of nucleus causes a polarization of the spin states in another nucleus. Cross-polarization will be explained in Section 6.6. In the current example (proton-decoupled ^{13}C spectra), when the hydrogens in the molecule are irradiated, they become saturated and attain a distribution of spins very different from their equilibrium (Boltzmann) state. There are more spins than normal in the *excited* state. Due to the interaction of spin dipoles, the spins of the carbon nuclei "sense" the spin imbalance of the hydrogen nuclei and begin to adjust themselves to a new equilibrium state that has more spins in the *lower* state. This increase of population in the lower spin state of carbon increases the intensity of the NMR signal.

In a proton-decoupled ^{13}C spectrum, the total NOE for a given carbon increases as the number of nearby hydrogens increases. Thus, we usually find that the intensities of the signals in a ^{13}C spectrum (assuming a single carbon of each type) assume the order

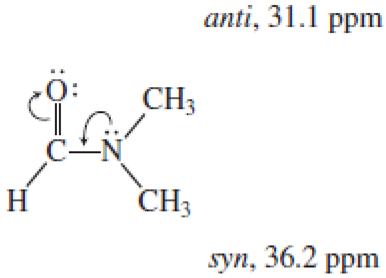
$$CH_3 > CH_2 > CH \gg C$$

Although the hydrogens producing the NOE effect influence carbon atoms more distant than the ones to which they are attached, their effectiveness drops off rapidly with distance. The interaction of the spin–spin dipoles operates through space, not through bonds, and its magnitude decreases as a function of the inverse of r^3, where r is the radial distance from the hydrogen of origin.

$$C \xrightarrow{r} H \qquad \text{NOE} = f\left(\frac{1}{r^3}\right)$$

Thus, nuclei must be rather close together in the molecule in order to exhibit the NOE effect. The effect is greatest for hydrogens that are directly attached to carbon.

In advanced work, NOEs are sometimes used to verify peak assignments. Irradiation of a selected hydrogen or group of hydrogens leads to a greater enhancement in the signal of the closer of the two carbon atoms being considered. In dimethylformamide, for instance, the two methyl groups are nonequivalent, showing two peaks at 31.1 and 36.2 ppm, because free rotation is restricted about the C—N bond due to resonance interaction between the lone pair on nitrogen and the π bond of the carbonyl group.



Dimethylformamide

Irradiation of the aldehyde hydrogen leads to a larger NOE for the carbon of the *syn* methyl group (36.2 ppm) than for that of the *anti* methyl group (31.1 ppm), allowing the peaks to be assigned. The *syn* methyl group is closer to the aldehyde hydrogen.

It is possible to retain the benefits of NOE even when determining a proton-coupled ^{13}C NMR spectrum that shows the attached hydrogen multiplets. The favorable perturbation of spin-state populations builds up slowly during irradiation of the hydrogens by the decoupler, and it persists for some time after the decoupler is turned off. In contrast, decoupling is available only while the decoupler is in operation and stops immediately when the decoupler is switched off. One can build up the NOE effect by irradiating with the decoupler during a period before the pulse and then turning off the decoupler during the pulse and free-induction decay (FID) collection periods. This technique gives an **NOE-enhanced proton-coupled spectrum,** with the advantage that peak intensities have been increased due to the NOE effect. See Section 9.1 for details.

6.6 CROSS-POLARIZATION: ORIGIN OF THE NUCLEAR OVERHAUSER EFFECT

To see how cross-polarization operates to give nuclear Overhauser enhancement, consider the energy diagram shown in Figure 6.6. Consider a two-spin system between atoms ^{1}**H** and ^{13}C. These two atoms may be spin coupled, but the following explanation is easier to follow if we simply ignore any spin–spin splitting. The following explanation is applied to the case of ^{13}C NMR spectroscopy, although the explanation is equally applicable to other possible combinations of atoms. Figure 6.6 shows four separate energy levels (N_1, N_2, N_3, and N_4), each with a different combination of spins of atoms ^{1}H and ^{13}C. The spins of the atoms are shown at each energy level.

The selection rules, derived from quantum mechanics, require that the only allowed transitions involve a change of only one spin at a time (these are called **single-quantum transitions**). The allowed transitions, proton excitations (labeled ^{1}**H**) and carbon excitations (labeled ^{13}**C**), are shown. Notice that both proton transitions and both carbon transitions have the same energy (remember that we are ignoring splitting due to *J* interactions).

Because the four spin states have different energies, they also have different *populations*. Because the spin states N_3 and N_2 have very similar energies, we can assume that their populations are approximately equal. Now use the symbol $\boldsymbol{B}$ to represent the equilibrium populations of these two spin states. The population of spin state N_1, however, will be higher (by an amount δ), and the population of spin state N_4 will be reduced (also by an amount δ). The intensities of the NMR lines will be proportional to the difference in populations between the energy levels where transitions are occurring. If we compare the populations of each energy level, we can see that the intensities of the two carbon lines (X) will be equal.

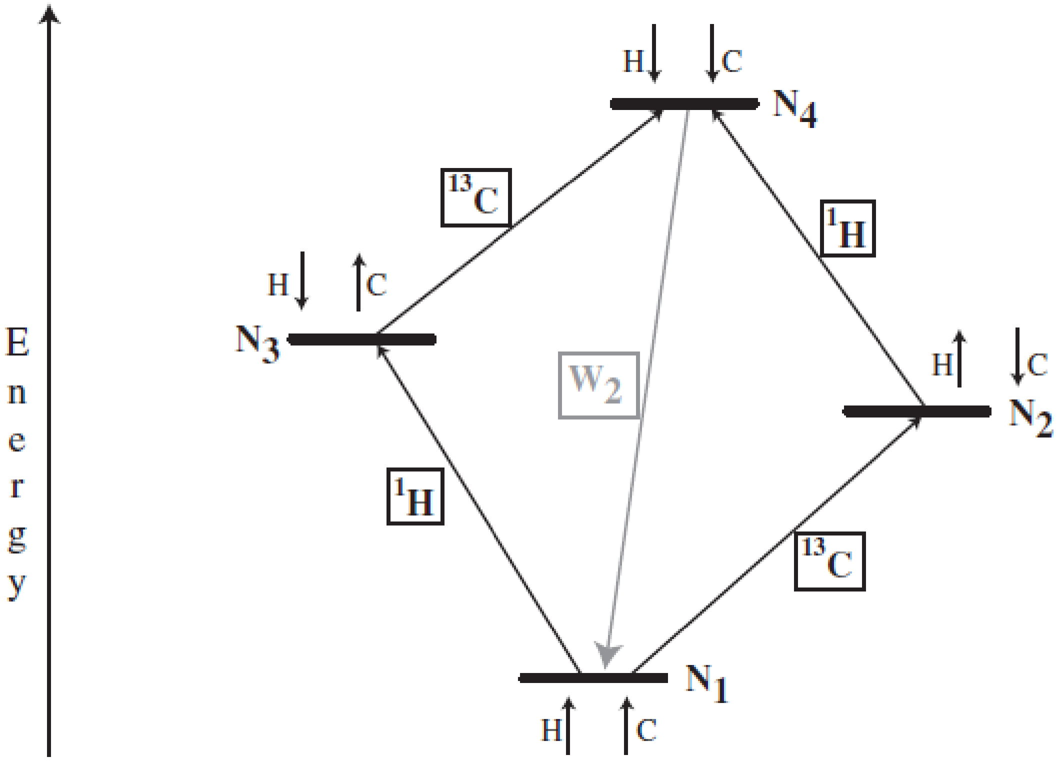


FIGURE 6.6 Spin energy level diagram for an AX System.

Level	Equilibrium Populations
N_1	$B + \delta$
N_2	B
N_3	B
N_4	$B - \delta$

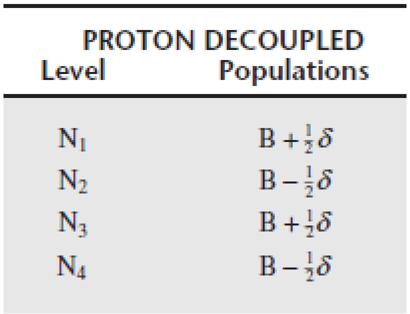
Assuming that the populations of the ^{13}C energy levels are at equilibrium, the carbon signals will have intensities:

^{13}C Energy Levels at Equilibrium

$$N_3 - N_4 = B - B + \delta = \delta$$

$$N_1 - N_2 = B + \delta - B = \delta$$

Consider now what happens when we irradiate the proton transitions during the broad-band decoupling procedure. The irradiation of the protons causes the proton transitions to become **saturated**. In other words, the probability of an upward and a downward transition for these nuclei (the proton transitions shown in Fig. 6.6) now becomes *equal*. The population of level N_4 becomes equal to the population of level N_2, and the population of level N_3 is now equal to the population of level N_1. The populations of the spin states can now be represented by the following expressions:



PROTON DECOUPLED	
Level	Populations
N_1	$B + \frac{1}{2}\delta$
N_2	$B - \frac{1}{2}\delta$
N_3	$B + \frac{1}{2}\delta$
N_4	$B - \frac{1}{2}\delta$

Using these expressions, the intensities of the carbon lines can be represented:

^{13}C Energy Levels with Broad-Band Decoupling

$$N_3 - N_4 = B + \frac{1}{2}\,\delta - B + \frac{1}{2}\delta = \delta$$

$$N_1 - N_2 = B + \frac{1}{2}\,\delta - B + \frac{1}{2}\delta = \delta$$

So far, there has been no change in the intensity of the carbon transition.

At this point, we need to consider that there is another process operating in this system. When the populations of the spin states have been disturbed from their equilibrium values, as in this case by irradiation of the proton signal, **relaxation processes** will tend to restore the populations to their equilibrium values. Unlike excitation of a spin from a lower to a higher spin state, relaxation processes are not subject to the same quantum mechanical selection rules. Relaxation involving changes of both spins simultaneously (called **double-quantum transitions**) are allowed; in fact, they are relatively important in magnitude. The relaxation pathway labeled $\mathbf{W_2}$ in Fig. 6.6 tends to restore equilibrium populations by relaxing spins from state N_4 to N_1. We shall represent the number of spins that are relaxed by this pathway by the symbol *d*. The populations of the spin states thus become as follows:

Level	Populations
N_1	$B + \frac{1}{2}\delta + d$
N_2	$B - \frac{1}{2}\delta$
N_3	$B + \frac{1}{2}\delta$
N_4	$B - \frac{1}{2}\delta - d$

The intensities of the carbon lines can now be represented:

^{13}C Energy Levels with Broad-Band Decoupling and with Relaxation

$$N_3 - N_4 = B + \frac{1}{2}\,\delta - B + \frac{1}{2}\delta + d = \delta + d$$

$$N_1 - N_2 = B + \frac{1}{2}\,\delta + d - B + \frac{1}{2}\delta = \delta + d$$

Thus, the intensity of each of the carbon lines has been enhanced by an amount *d* because of this relaxation.

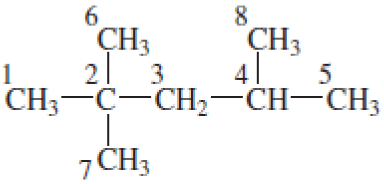
The theoretical maximum value of *d* is 2.988 (see Eqs. 6.2 and 6.3). The amount of nuclear Overhauser enhancement that may be observed, however, is often less than this amount. The preceding discussion has ignored possible relaxation from state N_3 to N_2. This relaxation pathway would involve no net change in the total number of spins (a **zero-quantum transition**). This relaxation would tend to *decrease* the nuclear Overhauser enhancement. With relatively small molecules, this second relaxation pathway is much less important than $\mathbf{W_2}$; therefore, we generally see a substantial enhancement.

6.7 PROBLEMS WITH INTEGRATION IN ^{13}C Spectra

Avoid attaching too much significance to peak sizes and integrals in proton-decoupled ^{13}C spectra. In fact, carbon spectra are usually not integrated in the same routine fashion as is accepted for proton spectra. Integral information derived from ^{13}C spectra is usually not reliable unless special techniques are used to ensure its validity. It is true that a peak derived from two carbons is larger

6.8 MOLECULAR RELAXATION PROCESSES

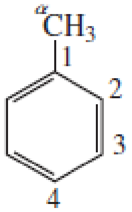
Spin–lattice relaxation times, T_1 values, are not of much use in proton NMR since protons have very short relaxation times. However, T_1 values are quite important to ^{13}C NMR spectra because they are much longer for carbon nuclei and can dramatically influence signal intensities. One can always expect quaternary carbons (including most carbonyl carbons) to have long relaxation times because they have no attached hydrogens. A common instance of long relaxation times is the carbons in an aromatic ring with a substituent group different from hydrogen. The ^{13}C T_1 values for isooctane (2,2,4-trimethylpentane) and toluene follow.



$CH_3-C(CH_3)_2-CH_2-CH(CH_3)-CH_3$

C	T_1
1, 6, 7	9.3 sec
2	68
3	13
4	23
5, 8	9.8

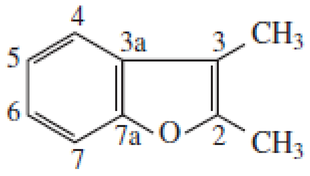
2,2,4-Trimethylpentane



C	T_1	NOE
α	16 sec	0.61
1	89	0.56
2	24	1.6
3	24	1.7
4	17	1.6

Toluene

The example of 2,3-dimethylbenzofuran will close this section. In this molecule, the quaternary (*ipso*) carbons have relaxation times that exceed 1 min. As discussed in Section 6.7, to obtain a decent spectrum of this compound, it would be necessary to extend the data acquisition and delay periods to determine the entire spectrum of the molecule and see the carbons with high T_1 values.



C	T_1	NOE
2	83 sec	1.4
3	92	1.6
3a	114	1.5
7a	117	1.3
Others	<10	1.6–2

2,3-Dimethylbenzofuran

6.9 OFF-RESONANCE DECOUPLING

In many cases, it would be helpful to have the information about the attached hydrogens that a proton-coupled spectrum provides, but frequently the spectrum becomes too complex, with overlapping multiplets that are difficult to resolve or assign correctly. A compromise technique called **off-resonance decoupling** can often provide multiplet information while keeping the spectrum relatively simple in appearance.

In an off-resonance-decoupled ^{13}C spectrum, the coupling between each carbon atom and each hydrogen attached directly to it is observed. The $n + 1$ Rule can be used to determine whether a given carbon atom has three, two, one, or no hydrogens attached. However, when off-resonance decoupling is used, the *apparent magnitude* of the coupling constants is reduced, and overlap of the resulting multiplets is a less-frequent problem. The off-resonance-decoupled spectrum retains the couplings between the carbon atom and directly attached protons (the one-bond couplings) but effectively removes the couplings between the carbon and more remote protons.

In this technique, the frequency of a second radiofrequency transmitter (the **decoupler**) is set either upfield or downfield from the usual sweep width of a normal proton spectrum (i.e., *off resonance*). In contrast, the frequency of the decoupler is set to *coincide exactly* with the range of proton resonances in a true decoupling experiment. Furthermore, in off-resonance decoupling, the power of the decoupling oscillator is held *low* to avoid complete decoupling.

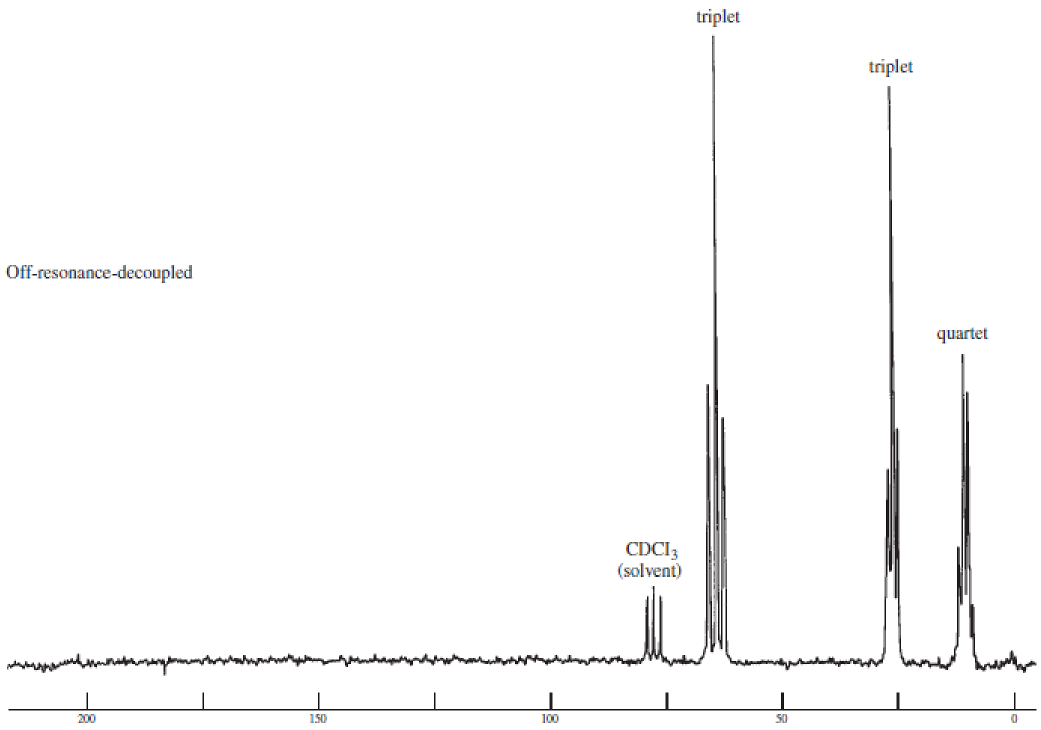


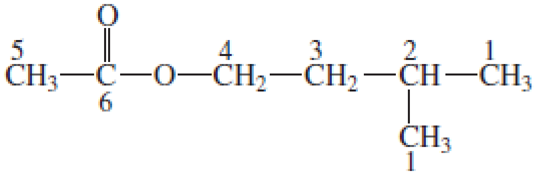
FIGURE 6.8 The off-resonance-decoupled ^{13}C spectrum of 1-propanol (22.5 MHz).

6.10 A QUICK DIP INTO DEPT

Despite its utility, off-resonance decoupling is now considered an old-fashioned technique. It has been replaced by more modern methods, the most important of which is **D**istortionless **E**nhancement by **P**olarization **T**ransfer, better known as **DEPT.** The DEPT technique requires an FT-pulsed spectrometer. It is more complicated than off-resonance decoupling, and it requires a computer, but it gives the same information more reliably and more clearly. Chapter 9 will discuss the DEPT method in detail; only a brief introduction to the method and the results it provides will be provided here.

In the DEPT technique, the sample is irradiated with a complex sequence of pulses in both the ^{13}C and ^{1}H channels. The result of these pulse sequences[3] is that the ^{13}C signals for the carbon atoms in the molecule will exhibit different **phases,** depending on the number of hydrogens attached to each carbon. Each type of carbon will behave slightly differently, depending on the **duration** of the complex pulses. These differences can be detected, and spectra produced in each experiment can be plotted.

One common method of presenting the results of a DEPT experiment is to plot four different **subspectra**. Each subspectrum provides different information. A sample DEPT plot for **isopentyl acetate** is shown in Figure 6.9.



$$\overset{5}{CH_3}-\underset{6}{\overset{\overset{\displaystyle O}{\|}}{C}}-O-\overset{4}{CH_2}-\overset{3}{CH_2}-\underset{\underset{\displaystyle \underset{1}{CH_3}}{|}}{\overset{2}{CH}}-\overset{1}{CH_3}$$

The lowest trace in the figure is the usual broad-band-decoupled ^{13}C spectrum. The second trace from the bottom is the result of a pulse sequence (called a **DEPT-45**) in which the only signals detected are those that arise from protonated carbons. You will notice that the carbonyl carbon (labeled **6**), at 172 ppm, is not seen. The solvent peaks arising from $CDC1_3$ (77 ppm) are also not seen. Deuterium (D or ^{2}H) behaves differently from ^{1}H, and as a result the carbon of $CDC1_3$ behaves as if it were not protonated. The third trace is the result of a slightly different pulse sequence (called a **DEPT-90**). In this trace, only those carbons that bear a single hydrogen are seen. Only the carbon at position **2** (25 ppm) is observed.

The uppermost trace is more complicated than the previous subspectra. The pulse sequence that gives rise to this subspectrum is called **DEPT-135**. Here, all carbons that have an attached proton provide a signal, but the **phase** of the signal will be different, depending on whether the number of attached hydrogens is an odd or an even number. Signals arising from CH or CH_3 groups will give positive peaks, while signals arising from CH_2 groups will form negative (inverse) peaks. When we examine the upper trace in Figure 6.9, we can identify all of the carbon peaks in the spectrum of isopentyl acetate. The positive peaks at 21 and 22 ppm must represent CH_3 groups as those peaks are not represented in the DEPT-90 subspectrum. When we look at the original ^{13}C spectrum, we see that the peak at 21 ppm is not as strong as the peak at 22 ppm. We conclude, therefore, that the peak at 21 ppm must come from the CH_3 carbon at position **5**, while the stronger peak at 22 ppm comes from the pair of equivalent CH_3 carbons at position **1**. We have already determined that the positive peak at 25 ppm is due to the CH carbon at position **2** as it appears in both the DEPT-135 and the DEPT-90 subspectra. The inverse peak at 37 ppm is due to a CH_2 group, and we can identify it as coming from the carbon at position **3**. The inverse peak at 53 ppm is clearly caused by the CH_2 carbon at position **4**, deshielded by the attached oxygen atom. Finally, the downfield peak at 172 ppm has already been labeled as arising from the carbonyl carbon at **6**. This peak appears only in the original ^{13}C spectrum; therefore, it must not have any attached hydrogens.

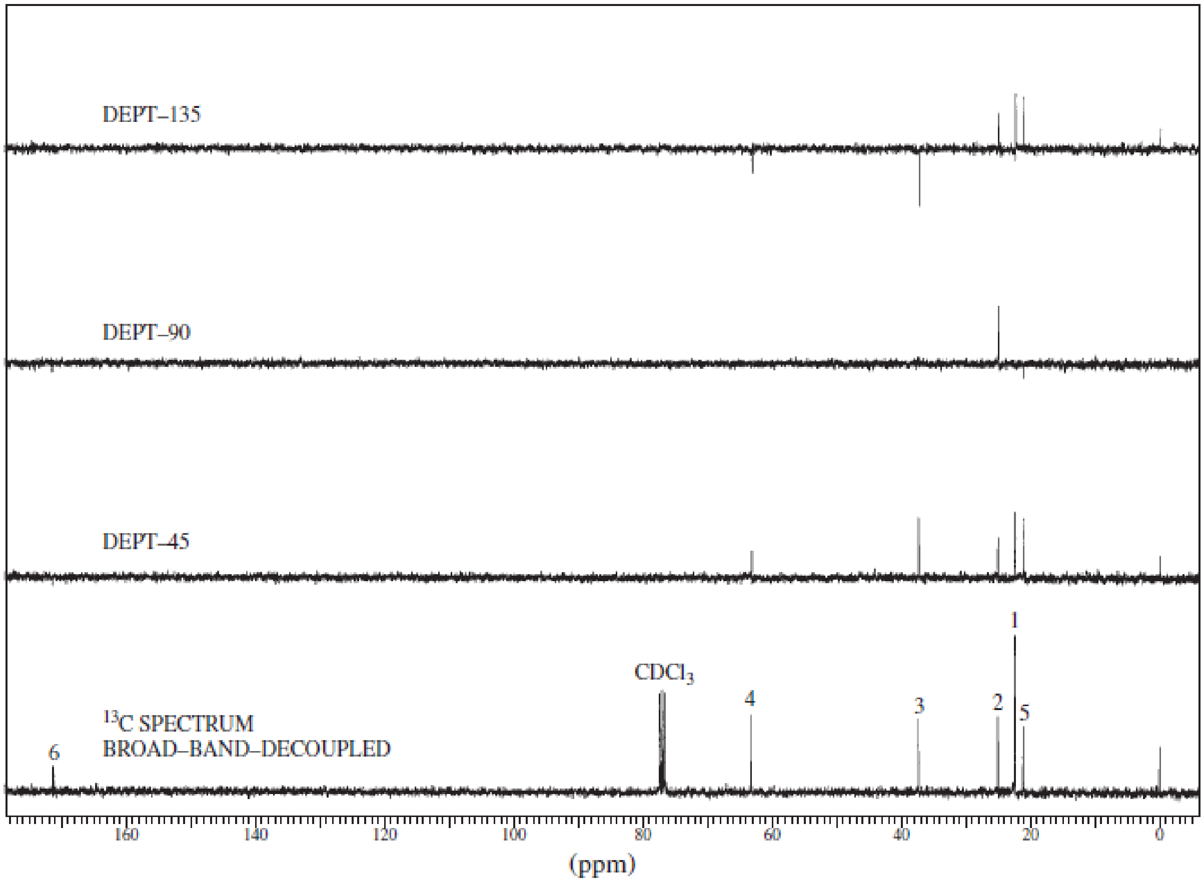


FIGURE 6.9 DEPT spectra of isopentyl acetate.