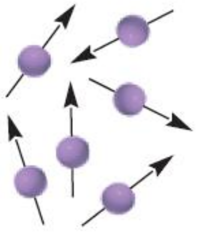
Nuclear magnetic resonance (NMR) spectroscopy

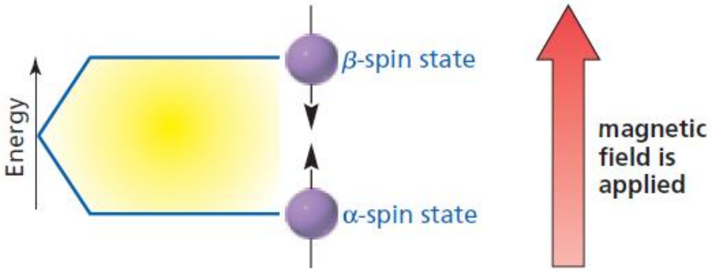
Introduction to NMR Spectroscopy

Determining the structures of compounds is an important part of organic chemistry. After a compound has been synthesized, its structure must be confirmed. NMR spectroscopy was developed by physical chemists in the late 1940s to study the properties of atomic nuclei. We have seen that electrons are charged, spinning particles with two allowed spin states: + 1/2and – 1/2. Certain nuclei also have allowed spin states of + 1/2and – 1/2. And this property allows them to be studied by NMR. Examples of such nuclei are 1H, 13C, 15N, 19F, 31P. Because hydrogen nuclei (protons) were the first nuclei studied by nuclear magnetic resonance, the acronym "NMR" is generally assumed to mean **(proton 1H NMR magnetic resonance).** Spectrometers were later developed for19F **NMR, 31P NMR, 13C NMR, 15N NMR**

Spinning charged nuclei generate a magnetic field, like the field of a small bar magnet. In the absence of an applied magnetic field, the nuclear spins are randomly oriented. However, when a sample is placed in an applied magnetic field, the nuclei twist and turn to align themselves *with* or *against* the field of the larger magnet. More energy is needed for a proton to align against the field than with it. Protons that align with the field are in the lower-energy **α-spin state** protons that align against the field are in the higher-energy **β-spin state.** More nuclei are in the state than in the state. The difference in the populations is very small (about 20 out of a million protons), but is sufficient to form the basis of NMR spectroscopy.



no applied magnetic field

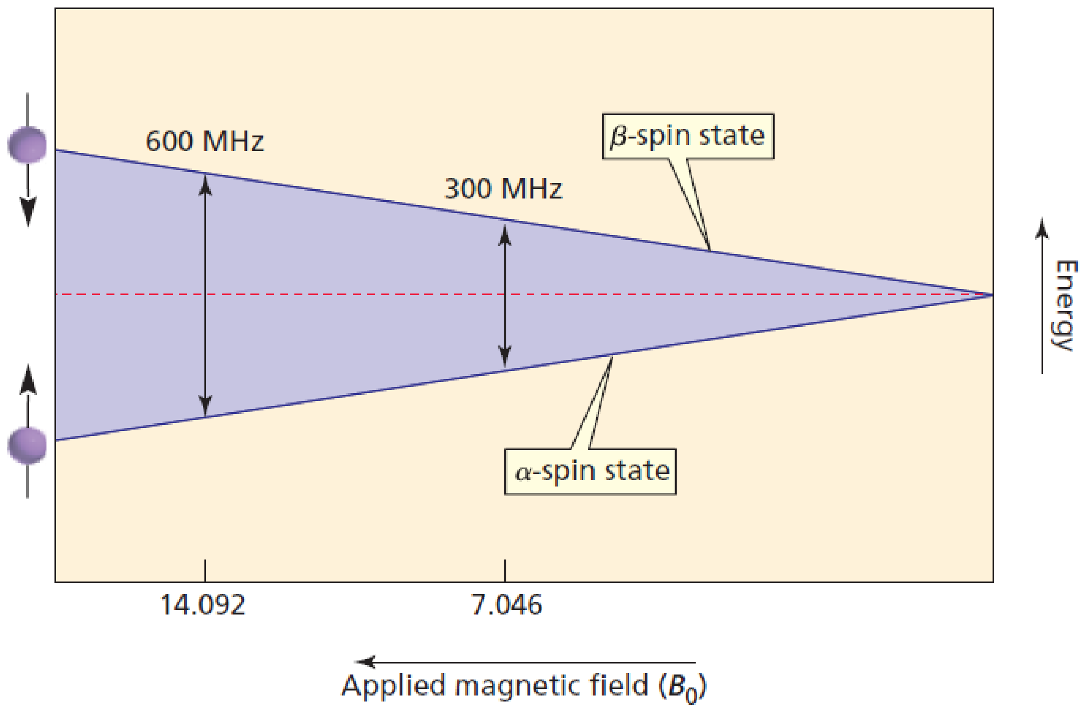


The energy difference (ΔE) between the α and β states depends on the strength of the **applied magnetic field (Bo).** The greater the strength of the magnetic field to which we expose the nucleus, the greater is the difference in energy between the α and β states

When the sample is subjected to a pulse of radiation whose energy corresponds to the difference in energy (ΔE) between the α and β states, nuclei in the α-spin state are promoted to the β state. This transition is called "flipping" the spin.

The radiation required is in the radiofrequency (rf) region of the electromagnetic spectrum and is called **rf radiation**. When the nuclei undergo relaxation (i.e., return to their original state), they emit electromagnetic signals whose frequency depends on the difference in energy (ΔE) between the α and β states.

The NMR spectrometer detects these signals and displays them as a plot of signal frequency versus intensity—an NMR spectrum



Shielding:

We have seen that when a sample in a magnetic field is irradiated with rf radiation of the proper frequency, each proton in an organic compound gives a signal at a frequency that depends on the energy difference (ΔE) between the α and β states,

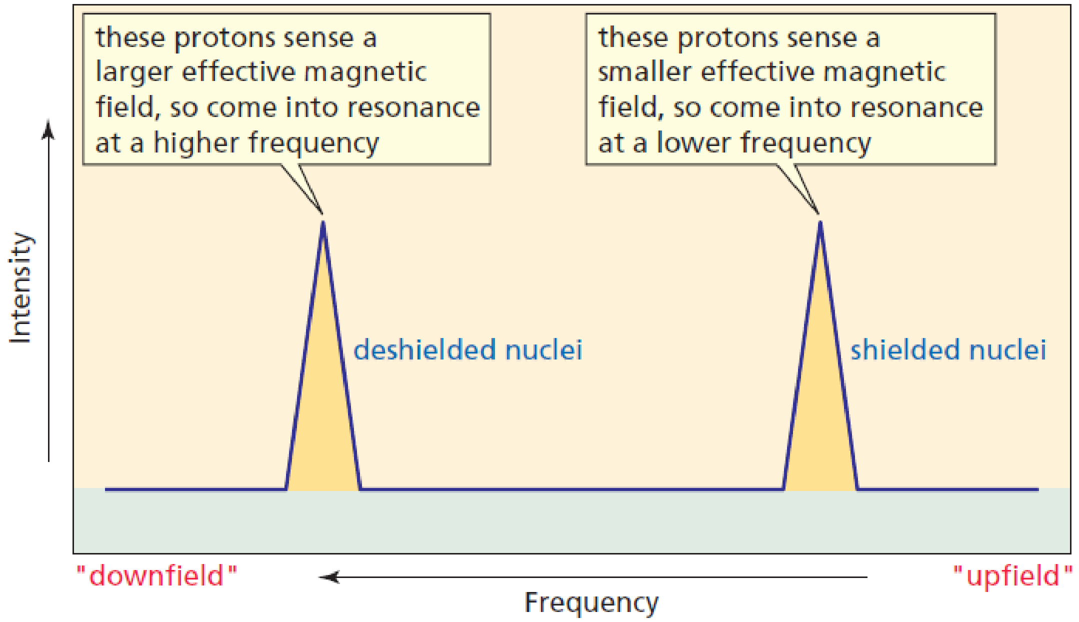
A nucleus, however, is embedded in a cloud of electrons that partly ***shields*** it from the applied magnetic field. Fortunately for chemists, the shielding varies for different protons within a molecule. In other words, all the protons do not experience the same applied magnetic field. What causes shielding? In a magnetic field, the electrons circulate about the nuclei and induce a local magnetic field that opposes (i.e., that subtracts from) the applied magnetic field. The **effective magnetic field**, therefore, is what the nuclei "sense" through the surrounding electronic environment:

$$B_{\text{effective}} = B_{\text{applied}} - B_{\text{local}}$$

This means that the greater the electron density of the environment in which the proton is located, the greater B_{local} is and the more the proton is shielded from the applied magnetic field. This type of shielding is called **diamagnetic shielding.** **Thus, protons in electron-**dense environments sense a ***smaller effective magnetic field***. They, **therefore, will require a** *lower frequency* **to come into resonance—that is, flip their spin— because (ΔE) is smaller. Protons in electron-poor environments sense a larger effective magnetic field and, therefore, will require a higher frequency to come into resonance, because (ΔE) is *larger*.**

Protons in electron-rich environments are more shielded and appear at lower frequencies—on the right-hand side of the spectrum. Protons in electron-poor environments are less shielded and appear at higher frequencies—on the left-hand side of the spectrum. (Notice that high frequency in an NMR spectrum is on the left-hand side, just as it is in IR and UV/Vis spectra.)

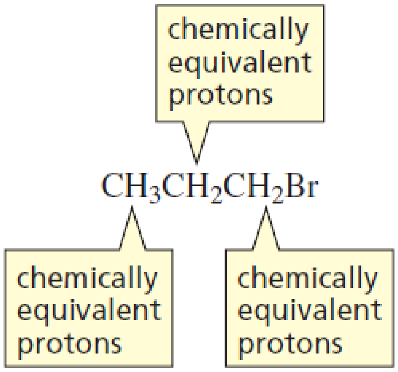
The terms "**upfield**" and "**downfield**," which came into use when continuous wave (CW) spectrometers were used (before the advent of Fourier transform spectrometers), are so entrenched in the vocabulary of NMR that you should know



Upfield means farther to the right-hand side of the spectrum, and **downfield** means farther to the left-hand side of the spectrum. In contrast to FT–NMR techniques, which hold magnetic field strength constant and vary frequency, continuous-wave techniques hold frequency constant and vary magnetic field. The magnetic field increases from left to right across a spectrum because higher magnetic fields are required for shielded protons to come into resonance at a given frequency (Figure 14.4). Therefore, upfield is toward the right and downfield is toward the left.

The Number of Signals in the ^{1}H NMR Spectrum

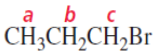
Protons in the same environment are called **chemically equivalent protons**. For example, **1-bromopropane** has three different sets of chemically equivalent protons. The three methyl protons are chemically equivalent because of rotation about the C-C bond. The two methylene protons on the middle carbon are chemically equivalent, and the two methylene protons on the carbon bonded to the bromine atom make up the third set of chemically equivalent protons.



Each set of chemically equivalent protons in a compound gives rise to a signal in the ^{1}H NMR spectrum of that compound. (Sometimes the signals are not sufficiently separated and overlap each other. When this happens, one sees fewer signals than anticipated) Because 1-bromopropane has three sets of chemically equivalent protons, it has three signals in its ^{1}H NMR spectrum.

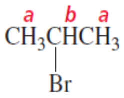
2-Bromopropane has two sets of chemically equivalent protons and, therefore, it has two signals in its ^{1}H NMR spectrum. The six methyl protons in 2-bromopropane are equivalent, so they give rise to only one signal.

Ethyl methyl ether has three sets of chemically equivalent protons: the methyl protons on the carbon adjacent to the oxygen, the methylene protons on the carbon adjacent to the oxygen, and the methyl protons on the carbon that is one carbon removed from the oxygen. The chemically equivalent protons in the following compounds are designated by the same letter:



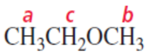
$\overset{a}{\mathrm{CH_3}}\overset{b}{\mathrm{CH_2}}\overset{c}{\mathrm{CH_2}}\mathrm{Br}$

three signals



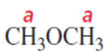
$\overset{a}{\mathrm{CH_3}}\underset{\mathrm{Br}}{\overset{b}{\mathrm{CH}}}\overset{a}{\mathrm{CH_3}}$

two signals



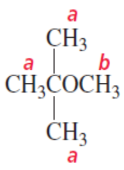
$\overset{a}{\mathrm{CH_3}}\overset{c}{\mathrm{CH_2}}\mathrm{O}\overset{b}{\mathrm{CH_3}}$

three signals



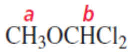
$\overset{a}{\mathrm{CH_3}}\mathrm{O}\overset{a}{\mathrm{CH_3}}$

one signal



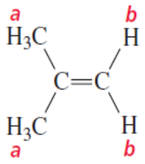
$\overset{a}{\mathrm{CH_3}}\underset{\underset{a}{\mathrm{CH_3}}}{\overset{\overset{a}{\mathrm{CH_3}}}{\mathrm{C}}}\mathrm{O}\overset{b}{\mathrm{CH_3}}$

two signals

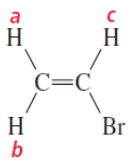


$\overset{a}{\mathrm{CH_3}}\mathrm{O}\overset{b}{\mathrm{CHCl_2}}$

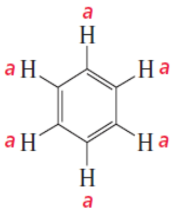
two signals



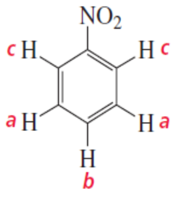
two signals



three signals



one signal



three signals

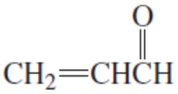
PROBLEM 3◆

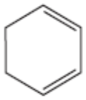
How many signals would you expect to see in the ^1H NMR spectrum of each of the following compounds?

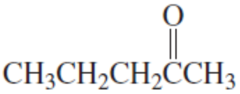
a. $CH_3CH_2CH_2CH_3$

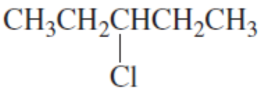
b. $BrCH_2CH_2Br$

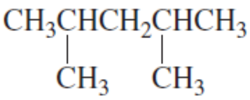
c. $CH_2{=}CHCl$

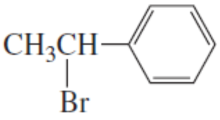
d.

$CH_2{=}CH\overset{\overset{O}{\|}}{C}H$

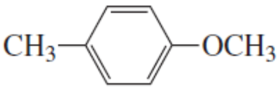
e.


f.

$CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}CH_3$

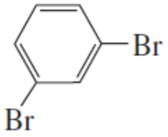
g.

$CH_3CH_2\underset{\underset{Cl}{|}}{C}HCH_2CH_3$

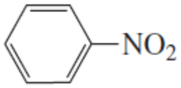
h.

$CH_3\underset{\underset{CH_3}{|}}{C}HCH_2\underset{\underset{CH_3}{|}}{C}HCH_3$

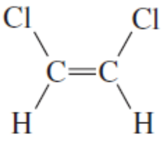
i.


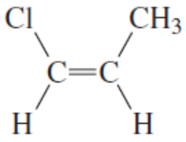
j.


k.


l.


m.


n.


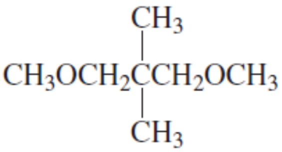
o.


PROBLEM 4

How could you distinguish the ^1H NMR spectra of the following compounds?

a. $CH_3OCH_2OCH_3$

b. CH_3OCH_3

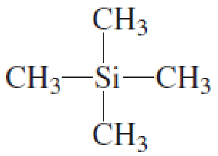
c.

$CH_3OCH_2\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{C}}CH_2OCH_3$

The Chemical Shift:

A small amount of an inert reference compound is added to the sample tube containing the compound whose NMR spectrum is to be taken. The positions of the signals in an NMR spectrum are defined according to how far they are from the signal of the reference compound. The most commonly used reference compound is tetramethylsilane (TMS). Because TMS is a **highly volatile compound**, **it can easily be removed from the sample by evaporation after the NMR spectrum is taken**.

The methyl protons of TMS are in a more electron-dense environment than are most protons in organic molecules, **because silicon is less electronegative than carbon (electronegativities of 1.8 and 2.5, respectively). Consequently, the signal for the methyl protons of TMS is at a lower frequency than most other signals (i.e., it appears to the right of the other signals).**

The position at which a signal occurs in an NMR spectrum is called the chemical shift. The chemical shift is a measure of how far the signal is from the reference TMS signal. The most common scale for chemical shifts is the **δ (delta)** scale. The TMS signal is used to define the zero position on this scale. The chemical shift is determined by measuring the distance from the TMS peak (in hertz) and dividing by the operating frequency of the instrument (in megahertz). Because the units are Hz/MHz, a chemical shift has units of parts per million (ppm) of the operating frequency:



$$CH_3-\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{Si}}-CH_3$$

tetramethylsilane
TMS

$$\delta = \text{chemical shift (ppm)} = \frac{\text{distance downfield from TMS (Hz)}}{\text{operating frequency of the spectrometer (MHz)}}$$

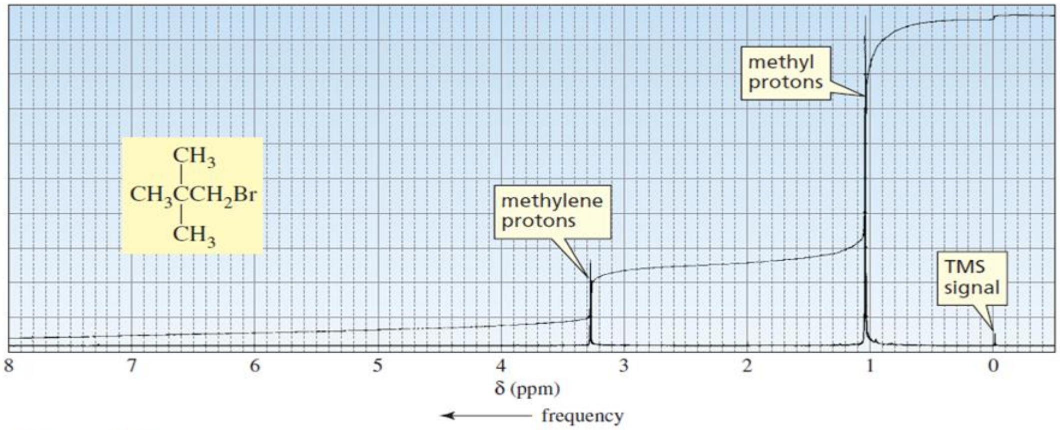


Figure 14.5
^{1}H NMR spectrum of 1-bromo-2,2-dimethylpropane. The TMS signal is a reference signal from which chemical shifts are measured; it defines the zero position on the scale.

Most proton chemical shifts fall in the range from 0 to 10 ppm. The^{1}H NMR spectrum for 1-bromo-2,2-dimethylpropane in Figure 14.5 shows that the chemical shift of the methyl protons is at 1.05 ppm and the chemical shift of the methylene protons is at 3.28 ppm. **Notice that low-frequency (upfield, shielded) signals have small δ (ppm) values, whereas high-frequency (downfield, deshielded) signals have large δ values**. The advantage of the δ scale is that the chemical shift of a given nucleus is independent of the operating frequency of the NMR spectrometer. Thus, the chemical shift of the methyl protons of 1-bromo-2,2-dimethylpropane is at 1.05 ppm in both a 60-MHz and a 360-MHz instrument. In contrast, if the chemical shift were reported in hertz, it would be at 63 Hz in a 60-MHz instrument and at 378 Hz in a 360-MHz (63/60 = 1.05; 378/360 = 1.052). Instrument The following diagram will help you keep track of the terms associated with NMR spectroscopy:

protons in electron-poor environments	protons in electron-dense environments
deshielded protons	shielded protons
downfield	upfield
high frequency	low frequency
large δ values	small δ values

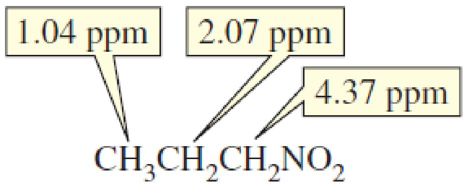
← δ

← frequency

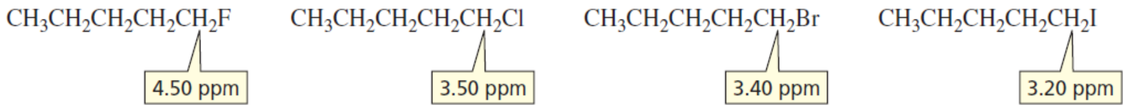
The Relative Positions of ^{1}H NMR Signals

The ^{1}H NMR spectrum of 1-bromo-2,2-dimethylpropane in Figure 14.5 has two signals because the compound has two different kinds of protons. The methylene protons are in a less electron-dense environment than the methyl protons are because the methylene protons are closer to the electron-withdrawing bromine. Because the methylene protons are in a less electron-dense environment, they are less shielded from the applied magnetic field. The signal for these protons therefore occurs at a higher frequency than the signal for the more shielded methyl protons. ***Remember that the right-hand side of an NMR spectrum is the low-frequency side, where protons in electron-dense environments (more shielded) show a signal. The left-hand side is the high-frequency side, where less***

shielded protons show a signal (Figure 14.4). We would expect the ^1H NMR spectrum of 1-nitropropane to have three signals because the compound has three different kinds of protons. The closer the protons are to the electron-withdrawing nitro group, the less they are shielded from the applied magnetic field, so the higher the frequency (i.e., the farther downfield) at which their signals will appear. Thus, the protons closest to the nitro group show a signal at the highest frequency (4.37 ppm), and the ones farthest from the nitro group show a signal at the lowest frequency (1.04 ppm).



Compare the chemical shifts of the methylene protons immediately adjacent to the halogen in each of the following alkyl halides. The position of the signal depends on the **electronegativity of the halogen**—the more electronegative the halogen, the higher is the frequency of the signal. Thus, the signal for the methylene protons adjacent to fluorine (the most electronegative of the halogens) occurs at the highest frequency, whereas the signal for the methylene protons adjacent to iodine (the least electronegative of the halogens) occurs at the lowest frequency.



Characteristic Values of Chemical Shifts:

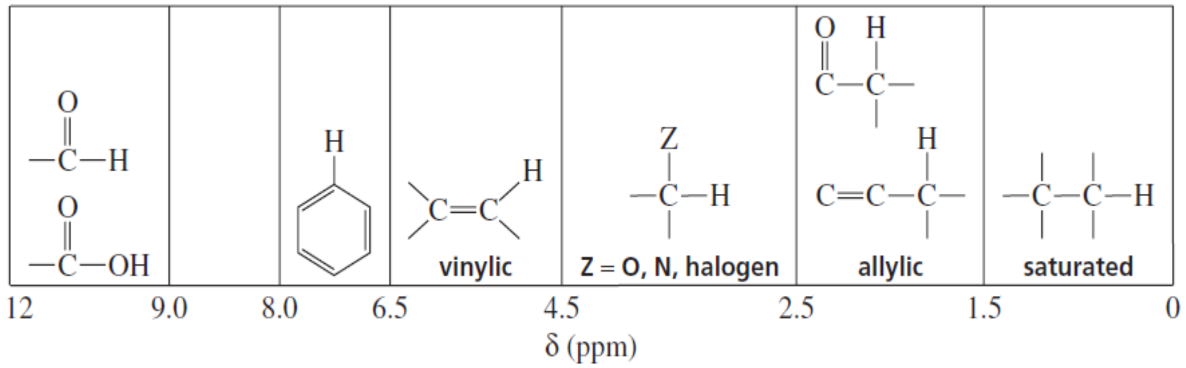
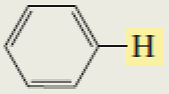
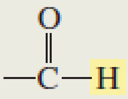
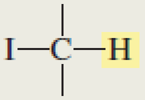
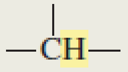
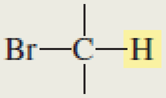
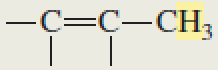
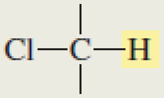
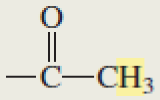
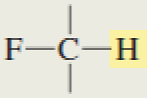
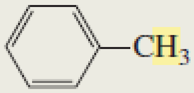
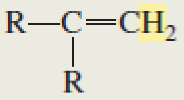
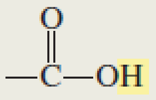
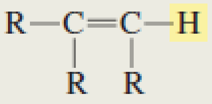
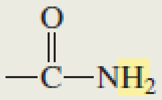


Table 14.1 Approximate Values of Chemical Shifts for ^{1}H NMR[a]

Type of proton	Approximate chemical shift (ppm)	Type of proton	Approximate chemical shift (ppm)
$(CH_3)_4Si$	0		6.5–8
$-CH_3$	0.9	 $-\overset{O}{\overset{\|}{C}}-H$	9.0–10
$-CH_2-$	1.3	 $I-\overset{\|}{\underset{\|}{C}}-H$	2.5–4
 $-\overset{\|}{C}H-$	1.4	 $Br-\overset{\|}{\underset{\|}{C}}-H$	2.5–4
 $-\underset{\|}{C}=\underset{\|}{C}-CH_3$	1.7	 $Cl-\overset{\|}{\underset{\|}{C}}-H$	3–4
 $-\overset{O}{\overset{\|}{C}}-CH_3$	2.1	 $F-\overset{\|}{\underset{\|}{C}}-H$	4–4.5
	2.3	RNH_2	Variable, 1.5–4
$-C\equiv C-H$	2.4	ROH	Variable, 2–5
$R-O-CH_3$	3.3	ArOH	Variable, 4–7
 $R-\underset{\underset{R}{\|}}{C}=CH_2$	4.7	 $-\overset{O}{\overset{\|}{C}}-OH$	Variable, 10–12
 $R-\underset{\underset{R}{\|}}{C}=\underset{\underset{R}{\|}}{C}-H$	5.3	 $-\overset{O}{\overset{\|}{C}}-NH_2$	Variable, 5–8

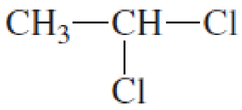
[a] The values are approximate because they are affected by neighboring substituents.

Integration of NMR Signals:

The two signals in the NMR spectrum of 1-bromo-2,2-dimethylpropane in Figure 14.5 are not the same size because the **area under each signal** is **proportional to the number of protons** that gives rise to the signal. The area under the signal occurring at the lower frequency is larger because the signal is caused by **nine** methyl protons, while the smaller, higher-frequency signal results from **two** methylene protons.

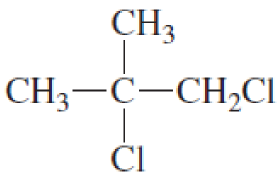
You probably remember from a calculus course that the **area under a curve can be determined by integration**. An ^{1}HNMR spectrometer is equipped with a computer that calculates the integrals electronically. **Modern spectrometers print out the integrals as numbers on the spectrum.** The integrals can also be displayed by a line of integration superimposed on the original spectrum (Figure 14.7). **The height of each integration step is proportional to the area under that signal, which, in turn, is proportional to the number of protons giving rise to the signal**. By measuring the heights of the integration steps, you can determine that the ratio of the integrals is approximately (1.6: 7.0 = 1: 4.4).

(The measured integrals are approximate by as much as 10% because of experimental error.) The ratios are multiplied by a number that will cause all the numbers to be close to whole numbers—in this case, we multiply by 2—as there can be only whole numbers of protons. That means that the ratio of protons in the compound is (2: 8.8), which is rounded (2: 9). to The integration tells us the relative number of protons that give rise to each signal, not the absolute number. For example, integration could not distinguish between 1,1-dichloroethane and 1,2-dichloro-2-methylpropane because both compounds would show an integral ratio of 1 : 3.



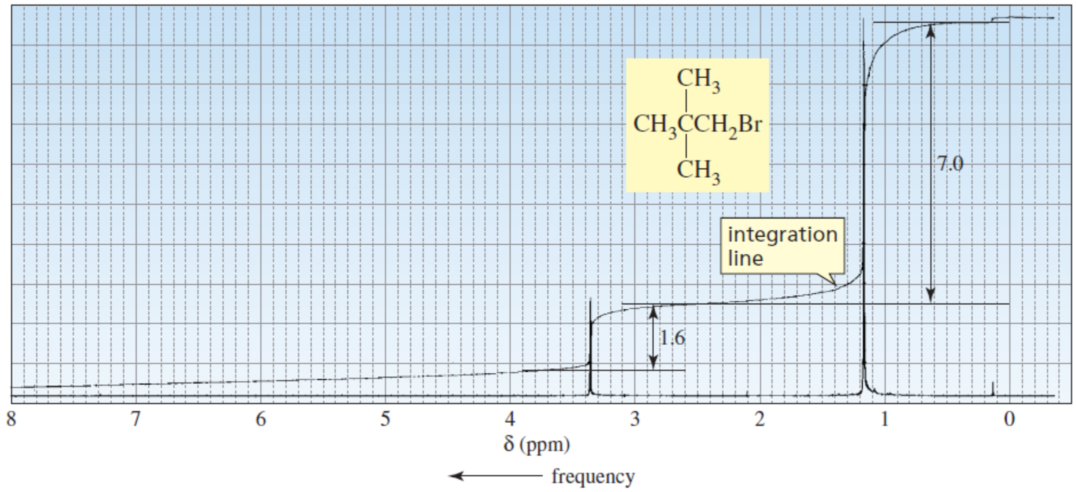
$$CH_3-\underset{\underset{Cl}{|}}{CH}-Cl$$

1,1-dichloroethane
ratio of protons = 1:3



$$CH_3-\overset{\overset{CH_3}{|}}{\underset{\underset{Cl}{|}}{C}}-CH_2Cl$$

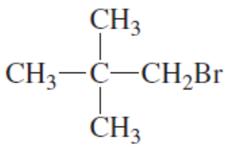
1,2-dichloro-2-methylpropane
ratio of protons 2:6 = 1:3

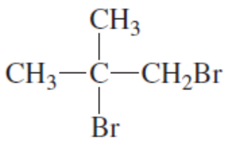


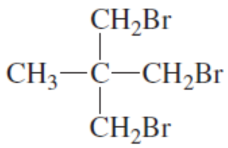
▲ Figure 14.7
Analysis of the integration line in the ^{1}H NMR spectrum of 1-bromo-2,2-dimethylpropane.

PROBLEM 14◆

How would integration distinguish the ^{1}H NMR spectra of the following compounds?


$CH_3-\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}-CH_2Br$


$CH_3-\overset{\displaystyle CH_3}{\underset{\displaystyle Br}{C}}-CH_2Br$


$CH_3-\overset{\displaystyle CH_2Br}{\underset{\displaystyle CH_2Br}{C}}-CH_2Br$

PROBLEM 15 SOLVED

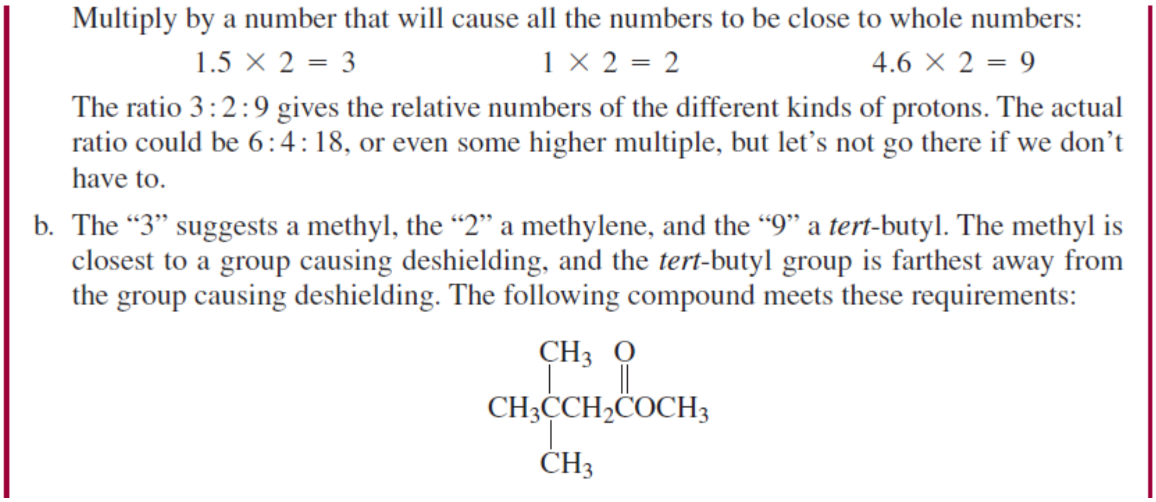
a. Calculate the ratios of the different kinds of protons in a compound with an integral ratio of 6 : 4 : 18.4 (going from left to right across the spectrum).

b. Determine the structure of a compound that would give these relative integrals in the observed order.

SOLUTION

a. Divide each by the smallest number:

$$\frac{6}{4} = 1.5 \qquad \frac{4}{4} = 1 \qquad \frac{18.4}{4} = 4.6$$



Multiply by a number that will cause all the numbers to be close to whole numbers:

$1.5 \times 2 = 3 \qquad 1 \times 2 = 2 \qquad 4.6 \times 2 = 9$

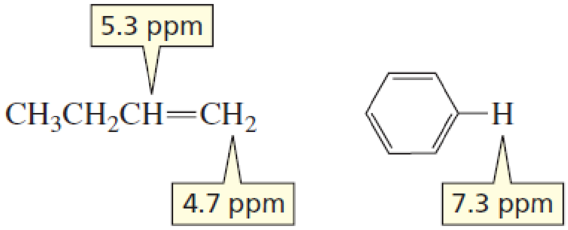
The ratio 3 : 2 : 9 gives the relative numbers of the different kinds of protons. The actual ratio could be 6 : 4 : 18, or even some higher multiple, but let's not go there if we don't have to.

b. The "3" suggests a methyl, the "2" a methylene, and the "9" a *tert*-butyl. The methyl is closest to a group causing deshielding, and the *tert*-butyl group is farthest away from the group causing deshielding. The following compound meets these requirements:

$$CH_3\overset{CH_3}{\underset{CH_3}{C}}CH_2\overset{O}{\overset{\|}{C}}OCH_3$$

Diamagnetic Anisotropy:

The chemical shifts of hydrogen bonded to sp2 hybridized carbons are at a higher frequency than one would predict, based on the electronegativity of the sp2 carbons. For example, hydrogen bonded to a terminal sp2carbon of an alkene appears at 4.7 ppm, hydrogen bonded to an internal sp2 carbon appears at 5.3 ppm, and hydrogen on a benzene ring appears at 6.5–8.0 ppm.



The unusual chemical shifts associated with hydrogens bonded to carbons that form π bonds are due to ***diamagnetic anisotropy.***

Anisotropic is Greek for "different in different directions." Because π electrons are less tightly held by nuclei than are σ electrons, π electrons are more free to move in response to a magnetic field. When a magnetic field is applied to a compound with π electrons, the π **electrons move in a circular path**. This electron motion causes an induced magnetic field**. How this induced magnetic field affects the chemical shift of a proton depends** on the direction of the induced magnetic field—in the region where the proton is located—relative to the direction of the applied magnetic field. The magnetic field induced by the π electrons of a benzene ring—in the region where benzene's protons are located—is **oriented in the same direction** as the applied field (Figure 14.9). The magnetic field induced by the π electrons of an alkene—in the region where the protons bonded to the sp2 carbons of the alkene are located—is also oriented in the same direction as the applied field. Thus, in both cases, a **larger effective magnetic field—the sum of the strengths of the applied field and the induced field—is sensed by the protons**. Because frequency is proportional to the strength of the magnetic field experienced by the protons, the protons resonate at higher frequencies than they would have if the π electrons had not induced a magnetic field.

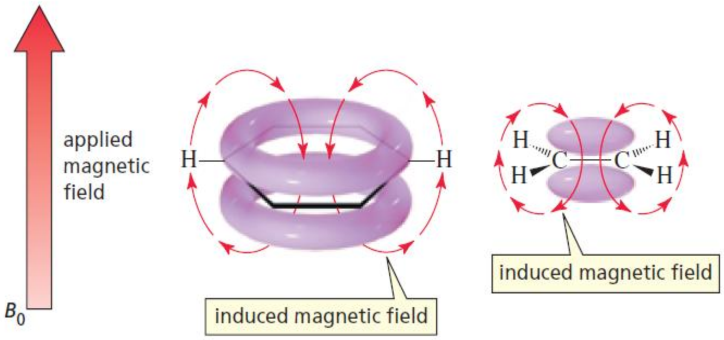


Figure 14.9
The magnetic fields induced by both the π electrons of a benzene ring and the π electrons of an alkene in the vicinity of the aromatic or vinylic protons are in the same direction as the applied magnetic field. Since a larger effective magnetic field is sensed b the protons, they resonate at higher frequencies.