CHAPTER

13 Spectroscopy

CHAPTER OUTLINE

Many organosilicon compounds such as tetramethylsilane [$(CH_3)_4Si$] are made from SiO_2, which occurs naturally in many forms, including quartz. The hydrogens and carbons of tetramethylsilane are the references to which other hydrogens and carbons are compared in nuclear magnetic resonance spectroscopy.

Until the second half of the twentieth century, the structure of a substance—a newly discovered natural product, for example—was determined using information obtained from chemical reactions. This information included the identification of functional groups by chemical tests, along with the results of experiments in which the substance was broken down into smaller, more readily identifiable fragments. Typical of this approach is the demonstration of the presence of a double bond in an alkene by catalytic hydrogenation and determination of its location by ozonolysis. After considering all the available chemical evidence, the chemist proposed a candidate structure (or structures) consistent with the observations. Proof of structure was provided either by converting the substance to some already known compound or by an independent synthesis.

Qualitative tests and chemical degradation have given way to instrumental methods of structure determination. The main methods and the structural clues they provide are:

- **Nuclear magnetic resonance (NMR) spectroscopy,** which tells us about the carbon skeleton and the environments of the hydrogens attached to it.
- **Infrared (IR) spectroscopy,** which reveals the presence or signals the absence of key functional groups.
- **Ultraviolet-visible (UV-VIS) spectroscopy,** which probes the electron distribution, especially in molecules that have conjugated π electron systems.
- **Mass spectrometry (MS),** which gives the molecular weight and formula, both of the molecule itself and various structural units within it.

As diverse as these techniques are, all of them are based on the absorption of energy by a molecule, and all measure how a molecule responds to that absorption. In describing these techniques our emphasis will be on their application to structure determination. We'll start with a brief discussion of electromagnetic radiation, which is the source of the energy that a molecule absorbs in NMR, IR, and UV-VIS spectroscopy. Mass spectrometry is unique in that, instead of electromagnetic radiation, its energy source is a stream of charged particles such as electrons.

13.1 Principles of Molecular Spectroscopy: Electromagnetic Radiation

Electromagnetic radiation, of which visible light is but one example, has the properties of both particles and waves. The particles are called **photons,** and each possesses an amount of energy referred to as a **quantum.** In 1900, the German physicist Max Planck proposed that the energy of a photon (E) is directly proportional to its frequency (ν).

"Modern" physics dates from Planck's proposal that energy is quantized, which set the stage for the development of quantum mechanics. Planck received the 1918 Nobel Prize in physics.

$$E = h\nu$$

The SI units of frequency are reciprocal seconds (s^{-1}), given the name *hertz* and the symbol Hz in honor of the nineteenth-century physicist Heinrich R. Hertz. The constant of proportionality h is called **Planck's constant** and has the value

$$h = 6.63 \times 10^{-34}\ \text{J} \cdot \text{s}$$

Electromagnetic radiation travels at the speed of light ($c = 3.0 \times 10^8$ m/s), which is equal to the product of its frequency ν and its wavelength λ:

$$c = \nu\lambda$$

The range of photon energies is called the *electromagnetic spectrum* and is shown in Figure 13.1. Visible light occupies a very small region of the electromagnetic spectrum. It is characterized by wavelengths of 400 nm (violet) to 800 nm (red). When examining Figure 13.1 be sure to keep the following two relationships in mind:

$1\ \text{nm} = 10^{-9}\text{m}$

1. *Frequency is inversely proportional to wavelength;* the greater the frequency, the shorter the wavelength.
2. *Energy is directly proportional to frequency;* electromagnetic radiation of higher frequency possesses more energy than radiation of lower frequency.

Gamma rays and X-rays are streams of very high energy photons. Radio waves are of relatively low energy. Ultraviolet radiation is of higher energy than the violet end of visible light. Infrared radiation is of lower energy than the red end of visible light. When a molecule is exposed to electromagnetic radiation, it may absorb a photon, increasing its energy by an amount equal to the energy of the photon. Molecules are highly selective with respect to the frequencies they absorb. Only photons of certain specific frequencies are absorbed by a molecule. The particular photon energies absorbed by a molecule depend on molecular structure and are measured with instruments called **spectrometers.** The data obtained are very sensitive indicators of molecular structure.

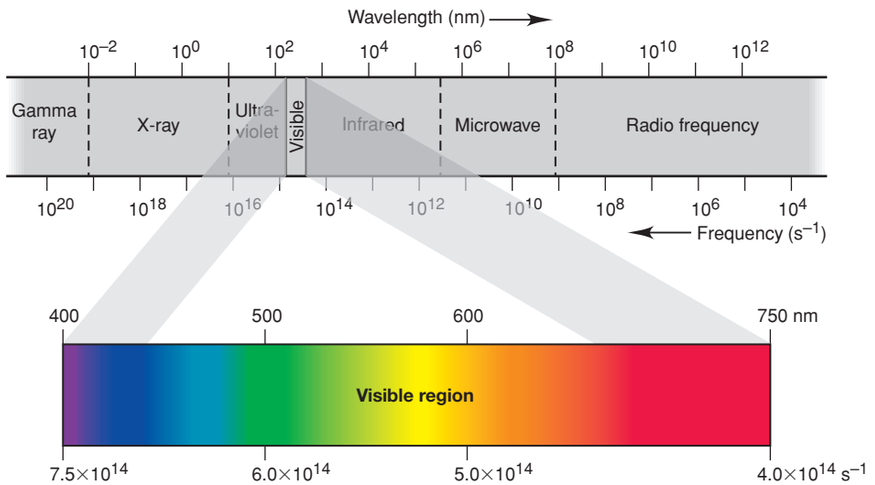


FIGURE 13.1
The electromagnetic spectrum. (Reprinted, with permission, from M. Silberberg, *Chemistry,* 4th ed., McGraw-Hill Higher Education, 2006, p. 259.)

13.2 Principles of Molecular Spectroscopy: Quantized Energy States

What determines whether electromagnetic radiation is absorbed by a molecule? The most important requirement is that the energy of the photon must equal the energy difference between two states, such as two nuclear spin states (NMR), two vibrational states (IR), or two electronic states (UV-VIS). In physics, the term for this is *resonance*—the transfer of energy between two objects that occurs when their frequencies are matched. In molecular spectroscopy, we are concerned with the transfer of energy from a photon to a molecule. Consider, for example, two energy states of a molecule designated E_1 and E_2 in Figure 13.2. The energy difference between them is $E_2 - E_1$, or ΔE. Unlike kinetic energy, which is continuous, meaning that all values of kinetic energy are available to a molecule, only certain energies are possible for electronic, vibrational, and nuclear spin states. These energy states are said to be **quantized.** More of the molecules exist in the lower energy state E_1 than in the higher energy state E_2. Excitation of a molecule from a lower state to a higher one requires the addition of an increment of energy equal to ΔE. Thus, when electromagnetic radiation strikes a molecule, only the frequency with energy equal to ΔE is absorbed. All other frequencies are transmitted.

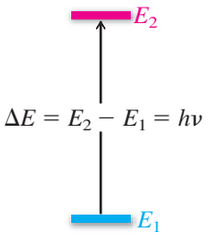


FIGURE 13.2
Two energy states of a molecule. Absorption of energy equal to $E_2 - E_1$ excites a molecule from its lower energy state to the next higher state.

Spectrometers are designed to measure the absorption of electromagnetic radiation by a sample. Basically, a spectrometer consists of a source of radiation, a compartment containing the sample through which the radiation passes, and a detector. The frequency of radiation is continuously varied, and its intensity at the detector is compared with that at the source. When the frequency is reached at which the sample absorbs radiation, the detector senses a decrease in intensity. The relation between frequency and absorption is plotted as a **spectrum,** which consists of a series of peaks at characteristic frequencies. Its interpretation can furnish structural information. Each type of spectroscopy developed independently of the others, and so the data format is different for each one. An NMR spectrum looks different from an IR spectrum, and both look different from a UV-VIS spectrum.

With this as background, we will now discuss spectroscopic techniques individually. NMR, IR, and UV-VIS spectroscopy provide complementary information, and all are useful. Among them, NMR provides the information that is most directly related to molecular structure and is the one we'll examine first.

13.3 Introduction to ^{1}H NMR Spectroscopy

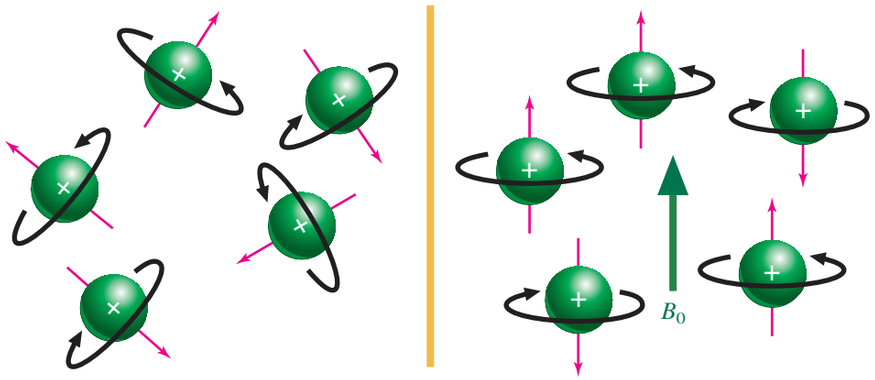
Nuclear magnetic resonance spectroscopy depends on the absorption of energy when the nucleus of an atom is excited from its lowest energy spin state to the next higher one. We should first point out that the nuclei of many elements are difficult to study by NMR, and some can't be studied at all. Fortunately though, the two elements that are the most common in organic molecules (carbon and hydrogen) have isotopes (^{1}H and ^{13}C) capable of giving NMR spectra that are rich in structural information. A proton nuclear magnetic resonance (^{1}H NMR) spectrum tells us about the environments of the various hydrogens in a molecule; a carbon-13 nuclear magnetic resonance (^{13}C NMR) spectrum does the same for the carbon atoms. Separately and together ^{1}H and ^{13}C NMR take us a long way toward determining a substance's molecular structure. We'll develop most of the general principles of NMR by discussing ^{1}H NMR, then extend them to ^{13}C NMR. The ^{13}C NMR discussion is shorter, not because it is less important than ^{1}H NMR, but because many of the same principles apply to both techniques.

Nuclear magnetic resonance of protons was first detected in 1946 by Edward Purcell (Harvard) and by Felix Bloch (Stanford). Purcell and Bloch shared the 1952 Nobel Prize in physics.

Like an electron, a proton has two spin states with quantum numbers of $+\frac{1}{2}$ and $-\frac{1}{2}$. There is no difference in energy between these two nuclear spin states; a proton is just as likely to have a spin of $+\frac{1}{2}$ as $-\frac{1}{2}$. Absorption of electromagnetic radiation can only occur when the two spin states have different energies. A way to make them different is to place the sample in a magnetic field. A spinning proton behaves like a tiny bar magnet and has a magnetic moment associated with it (Figure 13.3). In the presence

FIGURE 13.3

(*a*) In the absence of an external magnetic field, the nuclear spins of the protons are randomly oriented. (*b*) In the presence of an external magnetic field B_0, the nuclear spins are oriented so that the resulting nuclear magnetic moments are aligned either parallel or antiparallel to B_0. The lower energy orientation is the one parallel to B_0, and more nuclei have this orientation.



(*a*) No external magnetic field (*b*) Apply external magnetic field B_0

of an external magnetic field B_0, the spin state in which the magnetic moment of the nucleus is aligned with B_0 is lower in energy than the one in which it opposes B_0.

As shown in Figure 13.4, the energy difference between the two states is directly proportional to the strength of the applied field. Net absorption of electromagnetic radiation requires that the lower state be more highly populated than the higher one, and quite strong magnetic fields are required to achieve the separation necessary to give a detectable signal. A magnetic field of 4.7 T, which is about 100,000 times stronger than Earth's magnetic field, separates the two spin states of ^{1}H by only 8×10^{-5} kJ/mol (1.9×10^{-5} kcal/mol). From Planck's equation $\Delta E = h\nu$, this energy gap corresponds to radiation having a frequency of 2×10^8 Hz (200 MHz), which lies in the radio-frequency (rf) region of the electromagnetic spectrum (Figure 13.1).

The SI unit for magnetic field strength is the tesla (T), named after Nikola Tesla, a contemporary of Thomas Edison and who, like Edison, was an inventor of electrical devices.

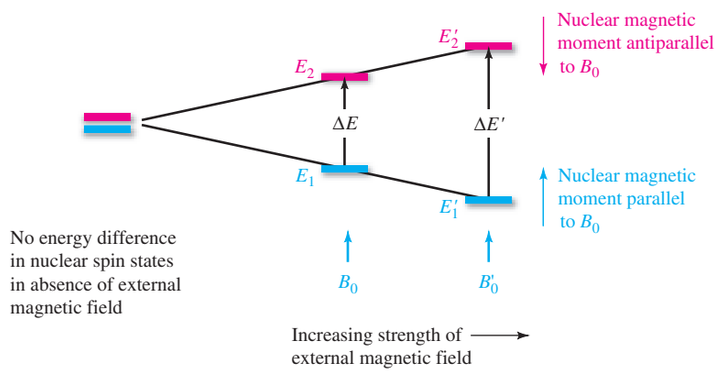
Frequency of electromagnetic radiation (s^{-1} or Hz) → is proportional to → Energy difference between nuclear spin states (kJ/mol or kcal/mol) → is proportional to → Magnetic field (T)

PROBLEM 13.1

Most of the NMR spectra in this text were recorded on a spectrometer having a field strength of 4.7 T (200 MHz for ^{1}H). The first generation of widely used NMR spectrometers were 60-MHz instruments. What was the magnetic field strength of these earlier spectrometers? What is the field strength of the 920-MHz instruments now commercially available?

FIGURE 13.4

An external magnetic field causes the two nuclear spin states to have different energies. The difference in energy ΔE is proportional to the strength of the applied field.



The response of an atom to the strength of the external magnetic field is different for different elements, and for different isotopes of the same element. The resonance frequencies of most nuclei are sufficiently different that an NMR experiment is sensitive only to a particular isotope of a single element. The frequency for ^{1}H is 200 MHz at 4.7 T, but that of ^{13}C is 50.4 MHz. Thus, when recording the NMR spectrum of an organic compound, we see signals only for ^{1}H or ^{13}C, but not both; ^{1}H and ^{13}C NMR spectra are recorded in separate experiments with different instrument settings.

PROBLEM 13.2

What will be the ^{13}C frequency of an NMR spectrometer that operates at 100 MHz for protons?

The essential features of an NMR spectrometer consist of a powerful magnet to align the nuclear spins, a radiofrequency (rf) transmitter as a source of energy to excite a nucleus from its lowest energy state to the next higher one, and a way to monitor the absorption of rf radiation and display the spectrum.

Among the variations on this general theme, we could, for example, keep the magnetic field constant and continuously vary the radiofrequency until it matched the energy difference between the nuclear spin states. Or, we could do the reverse; keep the rf constant and adjust the energy levels by varying the magnetic field strength. Both methods work, and the instruments based on them are called *continuous wave* (CW) spectrometers. Many of the terms we use in NMR spectroscopy trace their origin to the way CW instruments operate. But CW instruments are rarely used anymore.

CW-NMR spectrometers have been replaced by *pulsed Fourier-transform* nuclear magnetic resonance (FT-NMR) spectrometers (Figure 13.5). Rather than sweeping through a range of frequencies (or magnetic field strengths), the sample is placed in a magnetic field and irradiated with a short, intense burst of rf radiation (the *pulse*), which excites *all* of the protons in the molecule at the same time. The magnetic field associated with the new orientation of nuclear spins induces an electrical signal in the receiver that decreases as the nuclei return to their original orientation. The resulting *free-induction decay* (FID) is a composite of the decay patterns of all of the protons in the molecule. The FID pattern is stored in a computer and converted into a spectrum by a mathematical process known as a *Fourier transform.* The pulse-relaxation sequence takes only about a second, but usually gives signals too weak to distinguish from background noise. The signal-to-noise ratio is enhanced by repeating the sequence many times, then averaging the data. Noise is random and averaging causes it to vanish; signals always appear at the same frequency and accumulate. All of the operations—the interval between pulses, collecting, storing, and averaging the data and converting it to a spectrum by a Fourier transform—are under computer control, which makes the actual recording of an FT-NMR spectrum a routine operation.

Not only is pulsed FT-NMR the best method for obtaining proton spectra, it is the only practical method for many other nuclei, including ^{13}C. It also makes possible a large number of sophisticated techniques that have revolutionized NMR spectroscopy.

Richard R. Ernst of the Swiss Federal Institute of Technology won the 1991 Nobel Prize in chemistry for devising pulse-relaxation NMR techniques.

13.4 Nuclear Shielding and ^{1}H Chemical Shifts

Our discussion so far has concerned ^{1}H nuclei in general without regard for the environments of individual protons in a molecule. Protons in a molecule are connected to other atoms—carbon, oxygen, nitrogen, and so on—by covalent bonds. The electrons in these bonds, indeed all the electrons in a molecule, affect the magnetic environment of the protons. Alone, a proton would feel the full strength of the external field, but a proton in an organic molecule responds to both the external field plus any local fields within the molecule. An external magnetic field affects the motion of the electrons in a molecule, inducing local fields characterized by lines of force that circulate in the *opposite*

1. Dissolve sample in $CDCl_3$ and place in NMR tube.
2. Insert NMR tube into vertical cavity (bore) of the magnet.
3. Bore of magnet contains a probe that acts as a transmitter of radiofrequency (RF) pulses and receiver of signals from the sample. The transmitter is housed in a console along with other electronic equipment.
4. A short (5 μs), intense RF pulse is sent from the RF transmitter in the console to the probe. Absorption of RF energy tips the magnetic vector of the nuclei in the sample.
5. The magnetic field associated with the new orientation of the nuclei returns (relaxes) to the original state. Nuclei relax rapidly but at different rates that depend on their chemical environment. As the magnetic field changes, it generates an electrical impulse that is transmitted from the probe to a receiver in the console as a "free induction decay."
6. The pulse–relax sequence is repeated many times and the free-induction decay data stored in a computer in the console.
7. A mathematical operation called a Fourier transform carried out by the computer converts the amplitude-versus-time data of the free-induction decay to amplitude versus frequency and displays the resulting spectrum on the screen or prints it.

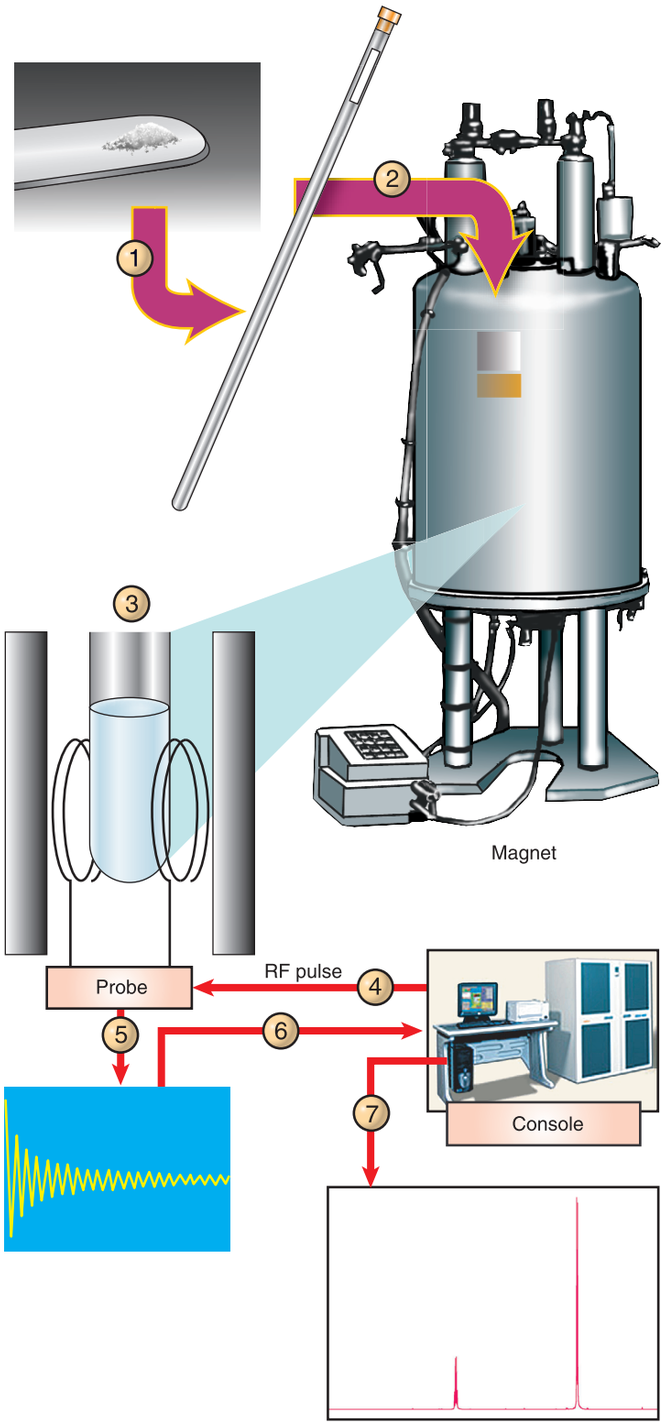


FIGURE 13.5

How an NMR spectrum is acquired using a pulse-Fourier transform (FT) NMR spectrometer.

direction from the applied field (Figure 13.6). Thus, the net field felt by a proton in a molecule will always be less than the applied field, and the proton is said to be **shielded.** All of the protons of a molecule are shielded from the applied field by the electrons, but some are less shielded than others. The term *deshielded* is often used to describe this decreased shielding of one proton relative to another.

The more shielded a proton is, the greater must be the strength of the applied field in order to achieve resonance and produce a signal. A more shielded proton absorbs rf radiation at higher field strength **(upfield)** compared with one at lower field strength **(downfield).** Different protons give signals at different field strengths. *The dependence of the resonance position of a nucleus that results from its molecular environment is called its* **chemical shift.** This is where the real power of NMR lies. The chemical shifts of various protons in a molecule can be different and are characteristic of particular structural features.

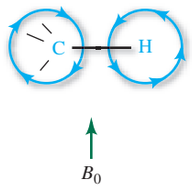


FIGURE 13.6

The induced magnetic field of the electrons in the carbon–hydrogen bond opposes the external magnetic field. The resulting magnetic field experienced by the proton and the carbon is slightly less than B_0.

Figure 13.7 shows the ^{1}H NMR spectrum of chloroform ($CHCl_3$) to illustrate how the terminology just developed applies to a real spectrum.

Instead of measuring chemical shifts in absolute terms, we measure them with respect to a standard—*tetramethylsilane* $(CH_3)_4Si$, abbreviated *TMS.* The protons of TMS are more shielded than those of most organic compounds, so all of the signals in a sample ordinarily appear at lower field than those of the TMS reference. When measured using a 100-MHz instrument, the signal for the proton in chloroform ($CHCl_3$), for example, appears 728 Hz downfield from the TMS signal. But because frequency is proportional to magnetic field strength, the same signal would appear 1456 Hz downfield from TMS on a 200-MHz instrument. We simplify the reporting of chemical shifts by converting them to parts per million (ppm) downfield from TMS, which is assigned a value of 0. The TMS need not actually be present in the sample, nor even appear in the spectrum in order to serve as a reference. When chemical shifts are reported this way, they are identified by the symbol δ and are independent of the field strength.

$$\text{Chemical shift } (\delta) = \frac{\text{position of signal} - \text{position of TMS peak}}{\text{spectrometer frequency}} \times 10^6$$

Thus, the chemical shift for the proton in chloroform is:

$$\delta = \frac{1456 \text{ Hz} - 0 \text{ Hz}}{200 \times 10^6 \text{ Hz}} \times 10^6 = 7.28$$

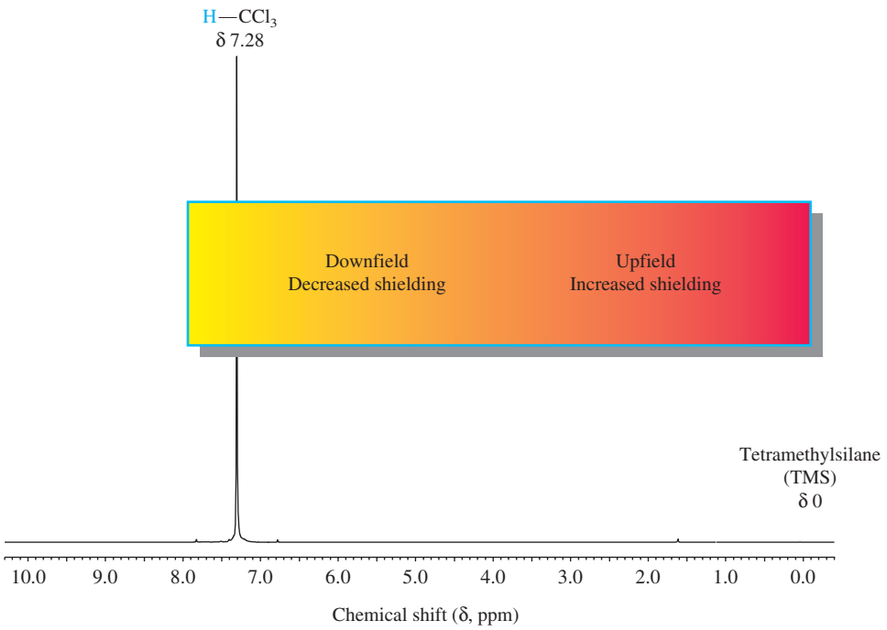


FIGURE 13.7

The 200-MHz ^{1}H NMR spectrum of chloroform ($HCCl_3$). Chemical shifts are measured along the *x*-axis in parts per million (ppm) from tetramethylsilane as the reference, which is assigned a value of zero.

PROBLEM 13.3

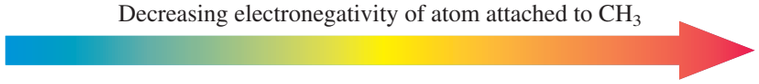
The ^1H NMR signal for bromoform ($CHBr_3$) appears at 2065 Hz when recorded on a 300-MHz NMR spectrometer. (a) What is the chemical shift of this proton? (b) Is the proton in $CHBr_3$ more shielded or less shielded than the proton in $CHCl_3$?

NMR spectra are usually run in solution and, although chloroform is a good solvent for most organic compounds, it's rarely used because its own signal at δ 7.28 would be so intense that it would obscure signals in the sample. Because the magnetic properties of deuterium (D = ^2H) are different from those of ^1H, $CDCl_3$ gives no signals at all in a ^1H NMR spectrum and is used instead. Indeed, $CDCl_3$ is the most commonly used solvent in ^1H NMR spectroscopy. Likewise, D_2O is used instead of H_2O for water-soluble substances such as carbohydrates.

13.5 Effects of Molecular Structure on ^1H Chemical Shifts

Nuclear magnetic resonance spectroscopy is such a powerful tool for structure determination because *protons in different environments experience different degrees of shielding and have different chemical shifts.* In compounds of the type CH_3X, for example, the shielding of the methyl protons increases as X becomes less electronegative.

Increased shielding of methyl protons
Decreasing electronegativity of atom attached to CH_3



CH_3F	CH_3OCH_3	$(CH_3)_3N$	CH_3CH_3	$(CH_3)_4Si$
Methyl fluoride	Dimethyl ether	Trimethylamine	Ethane	Tetramethylsilane
Chemical shift of methyl protons (δ):				
4.3	3.2	2.2	0.9	0.0

Problem 13.3 in the preceding section was based on the chemical shift difference between the proton in $CHCl_3$ and the proton in $CHBr_3$ and its relation to shielding.

Inasmuch as the shielding is due to the electrons, it isn't surprising to find that the chemical shift depends on the degree to which X draws electrons away from the methyl group. A similar trend is seen in the methyl halides, in which the protons in CH_3F are the least shielded (δ 4.3) and those of CH_3I (δ 2.2) are the most.

The decreased shielding caused by electronegative substituents is primarily an inductive effect and, like other inductive effects, falls off rapidly as the number of bonds between the substituent and the proton increases. Compare the chemical shifts of the protons in propane and 1-nitropropane.

δ 0.9 δ 1.3 δ 0.9	δ 4.3 δ 2.0 δ 1.0
$H_3C—CH_2—CH_3$	$O_2N—CH_2—CH_2—CH_3$
Propane	1-Nitropropane

The strongly electron-withdrawing nitro group deshields the protons on C-1 by 3.4 ppm (δ 4.3 − 0.9). The effect is smaller on the protons at C-2 (0.7 ppm), and almost completely absent at C-3.

The deshielding effects of electronegative substituents are cumulative, as the chemical shifts for various chlorinated derivatives of methane indicate.

	CH_3Cl	CH_2Cl_2	$CHCl_3$
	Chloromethane	Dichloromethane	Trichloromethane
Chemical shift (δ):	3.1	5.3	7.3

PROBLEM 13.4

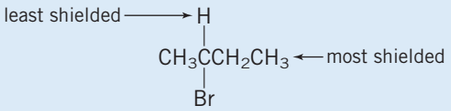
Identify the most shielded and least shielded protons in

(a) 2-Bromobutane

(b) 1,1,2-Trichloropropane

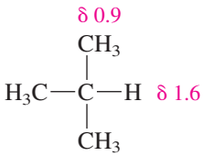
(c) Tetrahydrofuran:

Sample Solution (a) Bromine is electronegative and will have its greatest electron-withdrawing effect on protons that are separated from it by the fewest bonds. Therefore, the proton at C-2 will be the least shielded, and those at C-4 the most shielded.

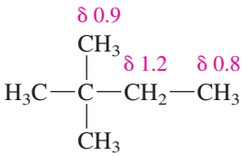


The observed chemical shifts are δ 4.1 for the proton at C-2 and δ 1.1 for the protons at C-4. The protons at C-1 and C-3 appear in the range δ 1.7–2.0.

Table 13.1 collects chemical-shift information for protons of various types. The major portion of the table concerns protons bonded to carbon. Within each type, methyl (CH_3) protons are more shielded than methylene (CH_2), and methylene protons are more shielded than methine (CH). The differences, however, are small.



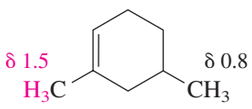
2-Methylpropane



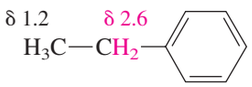
2,2-Dimethylbutane

Given that the chemical shift of methane is δ 0.2, we attribute the decreased shielding of the protons of RCH_3, R_2CH_2, and R_3CH to the number of carbons attached to primary, secondary, and tertiary carbons, respectively. Carbon is more electronegative than hydrogen, so replacing the hydrogens of CH_4 by one, then two, then three carbons decreases the shielding of the remaining protons.

Likewise, the generalization that sp^2-hybridized carbon is more electronegative than sp^3-hybridized carbon is consistent with the decreased shielding of allylic and benzylic protons.

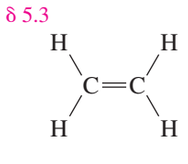


1,5-Dimethylcyclohexene

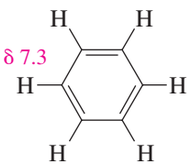


Ethylbenzene

Hydrogens that are directly attached to double bonds (vinylic protons) or to aromatic rings (aryl protons) are especially deshielded.



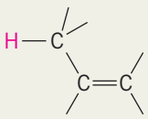
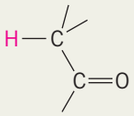
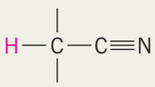
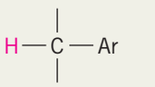
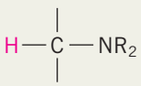
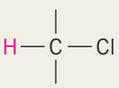
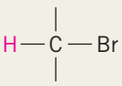
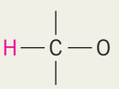
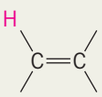
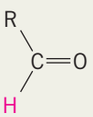
Ethylene



Benzene

The main contributor to the deshielding of vinylic and aryl protons is the induced magnetic field associated with π electrons. We saw earlier in Section 13.4 that the local field resulting from electrons in a C—H σ bond opposes the applied field and shields a molecule's protons. The hydrogens of ethylene and benzene, however, lie in a region of the

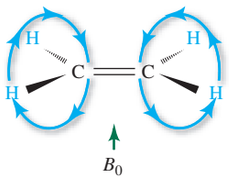
TABLE 13.1 Approximate Chemical Shifts of Representative Protons

Compound class or type of proton		Chemical shift (δ), ppm*
Protons bonded to carbon		
Alkane	RCH_3, R_2CH_2, R_3CH	0.9–1.8
Allylic		1.5–2.6
Terminal alkyne	H—C≡C	1.8–3.1
C—H adjacent to C=O		2.0–2.5
C—H adjacent to C≡N		2.1–2.3
Benzylic		2.3–2.8
Amine		2.2–2.9
Alkyl chloride		3.1–4.1
Alkyl bromide		2.7–4.1
Alcohol or ether		3.3–3.7
Vinylic		4.5–6.5
Aryl	H—Ar	6.5–8.5
Aldehyde		9–10
Protons bonded to nitrogen or oxygen		
Amine	H—NR_2	1–3†
Alcohol	H—OR	0.5–5†
Phenol	H—OAr	6–8†
Carboxylic acid		10–13†

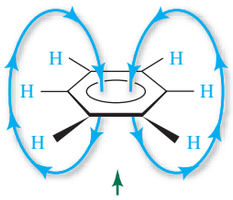
*Approximate values relative to tetramethylsilane; other groups within the molecule can cause a proton signal to appear outside of the range cited.

†The chemical shifts of O—H and N—H protons are temperature- and concentration-dependent.

molecule where the induced magnetic field of the π electrons reinforces the applied field, *deshielding* the protons (Figure 13.8). In the case of benzene, this is described as a **ring current** effect that originates in the circulating π electrons. It has interesting consequences, some of which are described in the boxed essay *Ring Currents—Aromatic and Antiaromatic.*



(*a*)



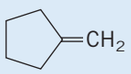
(*b*)

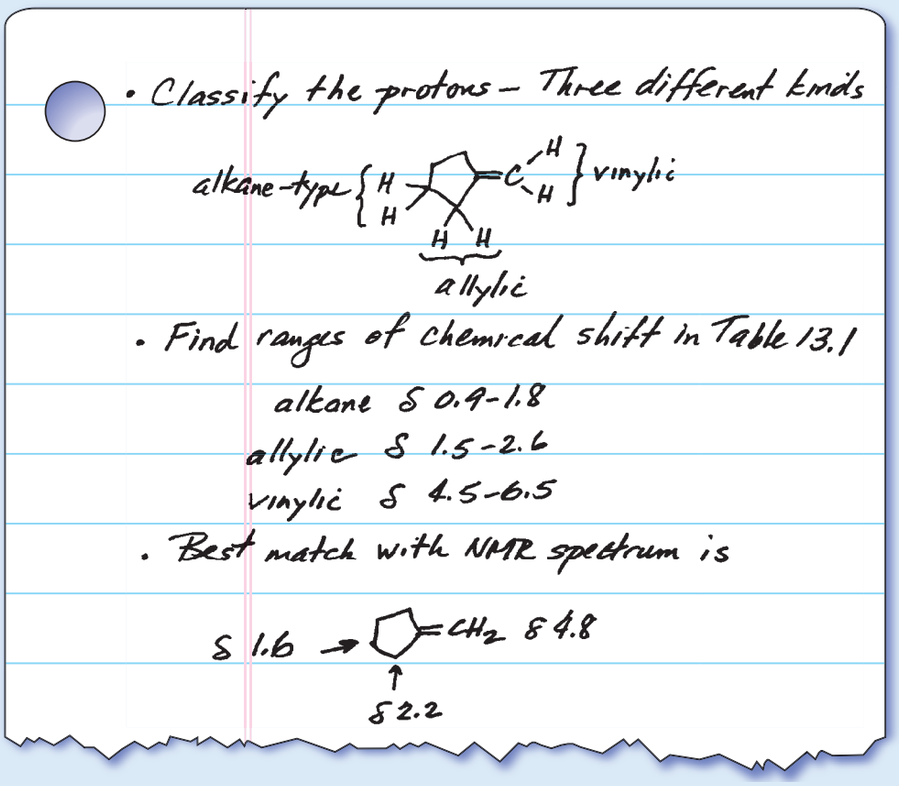
FIGURE 13.8

The induced magnetic field of the π electrons of (*a*) ethylene and (*b*) benzene reinforces the applied field in the regions near vinyl and aryl protons and deshields them.

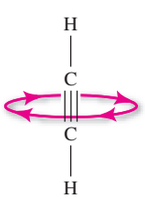
PROBLEM 13.5

Assign the chemical shifts δ 1.6, δ 2.2, and δ 4.8 to the appropriate protons of methylenecyclopentane

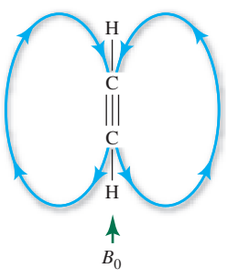




Acetylenic hydrogens are unusual in that they are more shielded than we would expect for protons bonded to *sp*-hybridized carbon. This is because the π electrons circulate around the triple bond, not along it (Figure 13.9*a*). Therefore, the induced



(*a*)

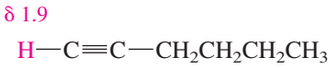


(*b*)

FIGURE 13.9

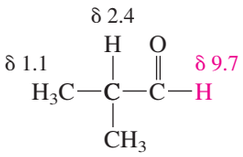
(*a*) The π electrons of acetylene circulate in a region surrounding the long axis of the molecule. (*b*) The induced magnetic field associated with the π electrons opposes the applied field and shields the protons.

magnetic field is parallel to the long axis of the triple bond and shields the acetylenic proton (Figure 13.9*b*). Acetylenic protons typically have chemical shifts in the range δ 1.8–3.1.

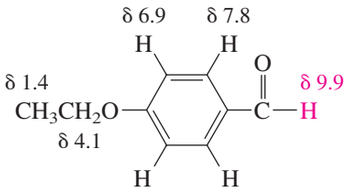


1-Hexyne

The induced field of a carbonyl group (C═O) deshields protons in much the same way that C═C does, and its oxygen makes it even more electron withdrawing. Thus, protons attached to C═O in aldehydes are the least shielded of any protons bonded to carbon. They have chemical shifts in the range δ 9–10.



2-Methylpropanal

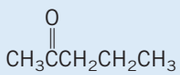


p-Ethoxybenzaldehyde

Protons on carbons adjacent to a carbonyl group are deshielded slightly more than allylic hydrogens.

PROBLEM 13.6

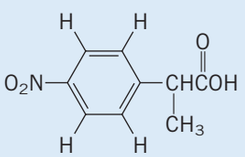
Assign the chemical shifts δ 1.1, δ 1.7, δ 2.0, and δ 2.3 to the appropriate protons of 2-pentanone.



The second portion of Table 13.1 deals with O—H and N—H protons. As the table indicates, the chemical shifts of these vary much more than for protons bonded to carbon. This is because O—H and N—H groups can be involved in intermolecular hydrogen bonding, the extent of which depends on molecular structure, temperature, concentration, and solvent. Generally, an increase in hydrogen bonding decreases the shielding. This is especially evident in carboxylic acids. With δ values in the 10–12 ppm range, O—H protons of carboxylic acids are the least shielded of all of the protons in Table 13.1. Hydrogen bonding in carboxylic acids is stronger than in most other classes of compounds that contain O—H groups.

PROBLEM 13.7

Assign the chemical shifts δ 1.6, δ 4.0, δ 7.5, δ 8.2, and δ 12.0 to the appropriate protons of 2-(*p*-nitrophenyl)propanoic acid.



As you can see from Table 13.1, it is common for several different kinds of protons to have similar chemical shifts. The range covered for ^{1}H chemical shifts is only 12 ppm, which is relatively small compared with (as we'll see) the 200-ppm range for ^{13}C chemical shifts. The ability of an NMR spectrometer to separate signals that have

Ring Currents—Aromatic and Antiaromatic

We saw in Chapter 12 that aromaticity reveals itself in various ways. Qualitatively, aromatic compounds are more stable and less reactive than alkenes. Quantitatively, their heats of hydrogenation are smaller than expected. Theory, especially Hückel's rule, furnishes a structural basis for aromaticity. Now let's examine some novel features of the NMR spectra of aromatic compounds.

We have mentioned that the protons in benzene appear at relatively low field because of deshielding by the magnetic field associated with the circulating π electrons. The amount of deshielding is sufficiently large—on the order of 2 ppm more than the corresponding effect in alkenes—that its presence is generally accepted as evidence for aromaticity. We speak of this deshielding as resulting from an *aromatic ring current.*

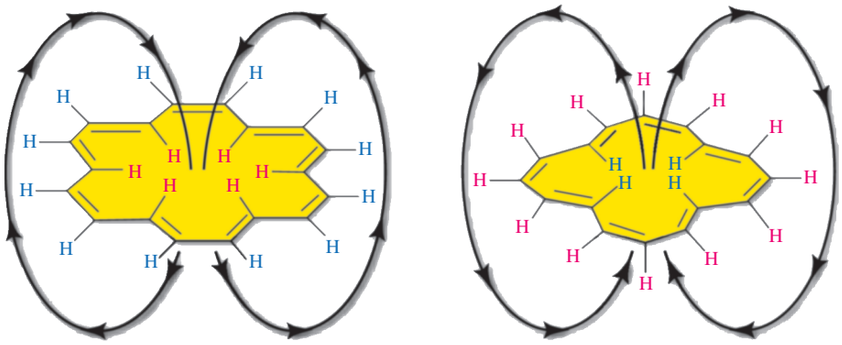
Something interesting happens when we go beyond benzene to apply the aromatic ring current test to annulenes.

[18]Annulene satisfies the Hückel $(4n + 2)$ π electron rule for aromaticity, and many of its properties indicate aromaticity (Section 11.21). As shown in Figure 13.10*a,* [18]annulene contains two different kinds of protons; 12 lie on the ring's periphery ("outside"), and 6 reside near the middle of the molecule ("inside"). The 2:1 ratio of outside/inside protons makes it easy to assign the signals in the ^{1}H NMR spectrum. The outside protons have a chemical shift δ of 9.3 ppm, which makes them even less shielded than those of benzene. The six inside protons, on the other hand, have a *negative* chemical shift (δ −3.0), meaning that the signal for these protons appears at *higher field* (to the right) of the TMS peak. *The inside protons of [18]annulene are more than 12 ppm more shielded than the outside protons.*

As shown in Figure 13.10*a*, both the shielding of the inside protons and the deshielding of the outside ones result from the same aromatic ring current. When the molecule is placed in an external magnetic field B_0, its circulating π electrons produce their own magnetic field. This induced field opposes the applied field B_0 in the center of the molecule, shielding the inside protons. Because the induced magnetic field closes on itself, the outside protons lie in a region where the induced field reinforces B_0. The aromatic ring current in [18]annulene shields the 6 inside protons and deshields the 12 outside ones.

Exactly the opposite happens in [16]annulene (Figure 13.10*b*). Now it is the outside protons (δ 5.3) that are more shielded. The inside protons (δ 10.6) are less shielded than the outside ones and less shielded than the protons of both benzene and [18]annulene. This reversal of the shielding and deshielding regions in going from [18] to [16]annulene can only mean that the directions of their induced magnetic fields are reversed. Thus [16]annulene, which has $4n$ π electrons and is antiaromatic, not only lacks an aromatic ring current, its π electrons produce exactly the opposite effect when placed in a magnetic field.

Score one for Hückel.



12 "outside" hydrogens: δ 9.3
6 "inside" hydrogens: δ −3.0
[18]Annulene

(*a*)

12 "outside" hydrogens: δ 5.3
4 "inside" hydrogens: δ 10.6
[16]Annulene

(*b*)

FIGURE 13.10

More shielded (red) and less shielded (blue) protons in (*a*) [18]annulene and (*b*) [16]annulene. The induced magnetic field associated with the aromatic ring current in [18]annulene shields the inside protons and deshields the outside protons. The opposite occurs in [16]annulene, which is antiaromatic.

similar chemical shifts is termed its *resolving power* and is directly related to the magnetic field strength of the instrument. Even though the δ values of their chemical shifts don't change, two signals that are closely spaced at 60 MHz become well separated at 300 MHz.

13.6 Interpreting ^{1}H NMR Spectra

Analyzing an NMR spectrum in terms of a unique molecular structure begins with the information contained in Table 13.1. By knowing the chemical shifts characteristic of various proton environments, the presence of a particular structural unit in an unknown compound may be inferred. An NMR spectrum also provides other useful information, including:

1. *The number of signals,* which tells us how many different kinds of protons there are.
2. *The intensity of the signals* as measured by the area under each peak, which tells us the relative ratios of the different kinds of protons.
3. *The multiplicity, or splitting, of each signal,* which tells us how many protons are vicinal to the one giving the signal.

Protons that have different chemical shifts are said to be **chemical-shift-nonequivalent** (or **chemically nonequivalent**). A separate NMR signal is given for each chemical-shift-nonequivalent proton in a substance. Figure 13.11 shows the 200-MHz ^{1}H NMR spectrum of methoxyacetonitrile (CH_3OCH_2CN), a molecule with protons in two different environments. The three protons in the CH_3O group constitute one set, the two protons in the OCH_2CN group the other. These two sets of protons give rise to the two peaks that we see in the NMR spectrum and can be assigned on the basis of their chemical shifts. The protons in the OCH_2CN group are connected to a carbon that bears two electronegative substituents (O and C≡N) and are less shielded than those of the CH_3O group, which are attached to a carbon that bears only one electronegative atom (O). The signal for the protons in the OCH_2CN group appears at δ 4.1; the signal corresponding to the CH_3O protons is at δ 3.3.

Another way to assign the peaks is by comparing their intensities. The three equivalent protons of the CH_3O group give rise to a more intense peak than the two equivalent protons of the OCH_2CN group. This is clear by simply comparing the heights of the peaks in the spectrum. It is better, though, to compare peak areas. This is done electronically at the time the NMR spectrum is recorded, and the **integrated areas** are displayed on the computer screen or printed out. Peak areas are proportional to the number of equivalent protons responsible for that signal.

It is important to remember that integration of peak areas gives relative, not absolute, proton counts. Thus, a 3:2 ratio of areas can, as in the case of CH_3OCH_2CN, correspond to a 3:2 ratio of protons. But in some other compound a 3:2 ratio of areas might correspond to a 6:4 or 9:6 ratio of protons.

PROBLEM 13.8

The 200-MHz ^{1}H NMR spectrum of 1,4-dimethylbenzene looks exactly like that of CH_3OCH_2CN except the chemical shifts of the two peaks are δ 2.2 and δ 7.0. Assign the peaks to the appropriate protons of 1,4-dimethylbenzene.

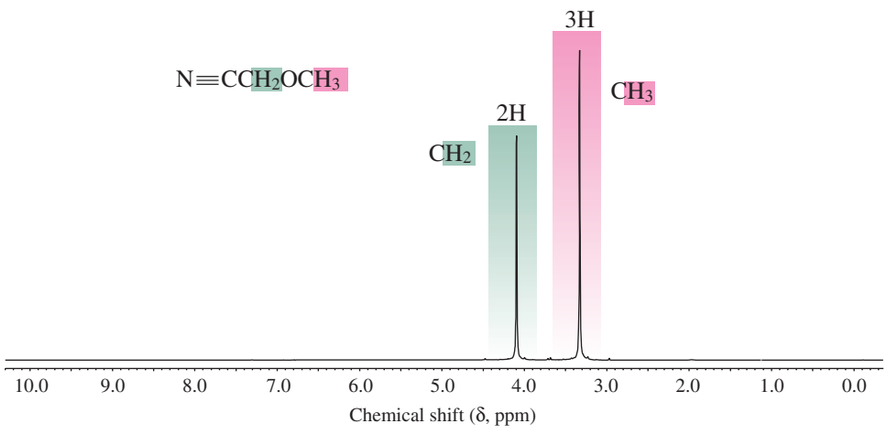


FIGURE 13.11
The 200-MHz ^{1}H NMR spectrum of methoxyacetonitrile (CH_3OCH_2CN).

Protons in equivalent environments have the same chemical shift. Often it is an easy matter to decide, simply by inspection, whether protons are equivalent or not. In more difficult cases, mentally replacing a proton in a molecule by a "test group" can help. We'll illustrate the procedure for a simple case—the protons of propane. To see if they have the same chemical shift, replace one of the methyl protons at C-1 by chlorine, then do the same thing for a proton at C-3. Both replacements give the same molecule, 1-chloropropane. Therefore the methyl protons at C-1 are equivalent to those at C-3.

$CH_3CH_2CH_3$	$ClCH_2CH_2CH_3$	$CH_3CH_2CH_2Cl$
Propane	1-Chloropropane	1-Chloropropane

If the two structures produced by mental replacement of two different hydrogens in a molecule by a test group are the same, the hydrogens are chemically equivalent. Thus, the six methyl protons of propane are all chemically equivalent to one another and have the same chemical shift.

Replacement of either one of the methylene protons of propane generates 2-chloropropane. Both methylene protons are equivalent. Neither of them is equivalent to any of the methyl protons.

The ^{1}H NMR spectrum of propane contains two signals: one for the six equivalent methyl protons, the other for the pair of equivalent methylene protons.

PROBLEM 13.9

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

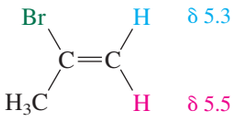
(a) 1-Bromobutane
(b) 1-Butanol
(c) Butane
(d) 1,4-Dibromobutane
(e) 2,2-Dibromobutane
(f) 2,2,3,3-Tetrabromobutane
(g) 1,1,4-Tribromobutane
(h) 1,1,1-Tribromobutane

Sample Solution (a) To test for chemical-shift equivalence, replace the protons at C-1, C-2, C-3, and C-4 of 1-bromobutane by some test group such as chlorine. Four constitutional isomers result:

$CH_3CH_2CH_2CHBrCl$	$CH_3CH_2CHClCH_2Br$	$CH_3CHClCH_2CH_2Br$	$ClCH_2CH_2CH_2CH_2Br$
1-Bromo-1-chlorobutane	1-Bromo-2-chlorobutane	1-Bromo-3-chlorobutane	1-Bromo-4-chlorobutane

Thus, separate signals will be seen for the protons at C-1, C-2, C-3, and C-4. Barring any accidental overlap, we expect to find four signals in the NMR spectrum of 1-bromobutane.

Chemical-shift nonequivalence can occur when two environments are stereochemically different. The two vinyl protons of 2-bromopropene have different chemical shifts.



2-Bromopropene

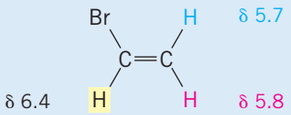
One of the vinyl protons is cis to bromine; the other trans. Replacing one of the vinyl protons by some test group, say, chlorine, gives the *Z* isomer of 2-bromo-1-chloropropene; replacing the other gives the *E* stereoisomer. The *E* and *Z* forms of 2-bromo-1-chloropropene are diastereomers. Protons that yield diastereomers on being replaced by some test group are *diastereotopic* (Section 7.13) and can have different chemical shifts. Because their environments are similar, however, the chemical shift difference is usually small, and it sometimes happens that two diastereotopic protons accidentally have the same chemical shift. Recording the spectrum on a higher field NMR spectrometer is often helpful in resolving signals with similar chemical shifts.

PROBLEM 13.10

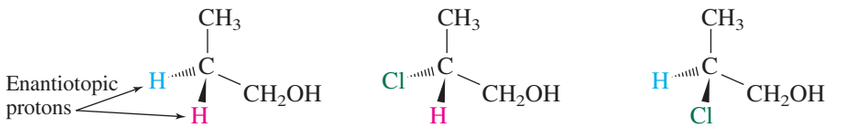
How many signals would you expect to find in the ^{1}H NMR spectrum of each of the following compounds?

(a) Vinyl bromide
(b) 1,1-Dibromoethene
(c) *cis*-1,2-Dibromoethene
(d) *trans*-1,2-Dibromoethene
(e) Allyl bromide
(f) 2-Methyl-2-butene

Sample Solution (a) Each proton of vinyl bromide is unique and has a chemical shift different from the other two. The least shielded proton is attached to the carbon that bears the bromine. The pair of protons at C-2 are diastereotopic with respect to each other; one is cis to bromine and the other is trans to bromine. There are three proton signals in the NMR spectrum of vinyl bromide. Their observed chemical shifts are as indicated.



When enantiomers are generated by replacing first one proton and then another by a test group, the pair of protons are *enantiotopic* (Section 7.9). The methylene protons at C-2 of 1-propanol, for example, are enantiotopic.



1-Propanol (*R*)-2-Chloro-1-propanol (*S*)-2-Chloro-1-propanol

Replacing one of these protons by chlorine as a test group gives (*R*)-2-chloro-1-propanol; replacing the other gives (*S*)-2-chloro-1-propanol. Enantiotopic protons have the same chemical shift, regardless of the field strength of the NMR spectrometer.

Enantiotopic protons can have different chemical shifts in an optically pure chiral solvent. Because the customary solvent ($CDCl_3$) used in NMR measurements is achiral, this phenomenon is not observed in routine work.

At the beginning of this section we noted that an NMR spectrum provides structural information based on chemical shift, the number of peaks, their relative areas, and the multiplicity, or splitting, of the peaks. We have discussed the first three of these features of ^{1}H NMR spectroscopy. Let's now turn our attention to peak splitting to see what kind of information it offers.

13.7 Spin–Spin Splitting in ^{1}H NMR Spectroscopy

The ^{1}H NMR spectrum of CH_3OCH_2CN (Figure 13.11) displayed in the preceding section is relatively simple because both signals are singlets; that is, each one consists of a single peak. It is quite common though to see a signal for a particular proton appear not as a singlet, but as a collection of peaks. The signal may be split into two peaks (a doublet), three peaks (a triplet), four peaks (a quartet), or even more. Figure 13.12 shows the ^{1}H NMR spectrum of 1,1-dichloroethane (CH_3CHCl_2), which is characterized by a doublet centered at δ 2.1 for the methyl protons and a quartet at δ 5.9 for the methine proton.

More complicated splitting patterns conform to an extension of the "$n + 1$" rule and will be discussed in Section 13.11.

The number of peaks into which the signal for a particular proton is split is called its **multiplicity.** For simple cases the rule that allows us to predict splitting in ^{1}H NMR spectroscopy is

$$\text{Multiplicity of signal for } H_a = n + 1$$

where n is equal to the number of equivalent protons that are vicinal to H_a. Two protons are vicinal to each other when they are bonded to adjacent atoms. Protons vicinal to H_a are separated from H_a by three bonds. The three methyl protons of 1,1-dichloroethane

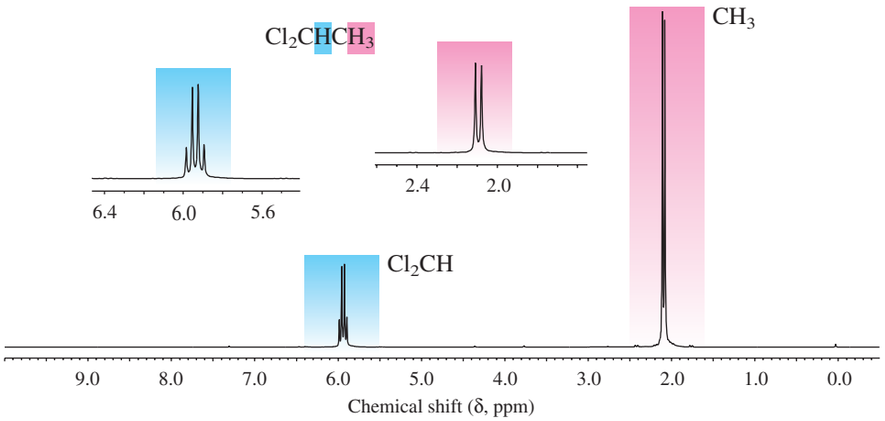
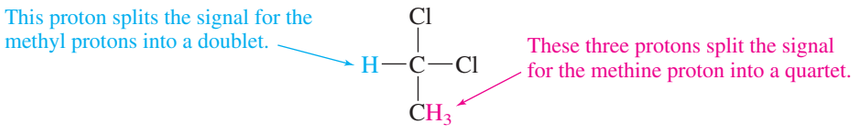


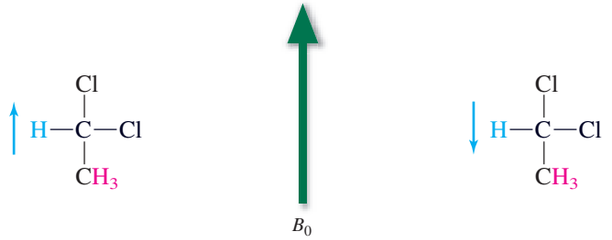
FIGURE 13.12
The 200-MHz ^{1}H NMR spectrum of 1,1-dichloroethane (Cl_2CHCH_3), showing the methine proton as a quartet and the methyl protons as a doublet. The peak multiplicities are seen more clearly in the scale-expanded insets.

are vicinal to the methine proton and split its signal into a quartet. The single methine proton, in turn, splits the methyl protons' signal into a doublet.



The physical basis for peak splitting in 1,1-dichloroethane can be explained with the aid of Figure 13.13, which examines how the chemical shift of the methyl protons is affected by the spin of the methine proton. There are two magnetic environments for the methyl protons: one in which the magnetic moment of the methine proton is parallel to the applied field, and the other in which it is antiparallel to it. When the magnetic moment of the methine proton is parallel to the applied field, it reinforces it. This decreases the shielding of the methyl protons and causes their signal to appear at slightly lower field strength. Conversely, when the magnetic moment of the methine proton is antiparallel to the applied field, it opposes it and increases the shielding of the methyl protons. Instead of a single peak for the methyl protons, there are two of approximately equal intensity: one at slightly higher field than the "true" chemical shift, the other at slightly lower field.

Turning now to the methine proton, its signal is split by the methyl protons into a quartet. The same kind of analysis applies here and is outlined in Figure 13.14. The methine proton "sees" eight different combinations of nuclear spins for the methyl protons. In one combination, the magnetic moments of all three methyl protons reinforce the applied field. At the other extreme, the magnetic moments of all three methyl protons oppose the applied field. There are three combinations in which the magnetic moments of two methyl protons reinforce the applied field, whereas one opposes it. Finally, there are three combinations in which the magnetic moments of two methyl protons oppose the applied field and one reinforces it. These eight possible combinations give rise to four distinct peaks for the methine proton, with a ratio of intensities of 1:3:3:1.



Spin of methine proton reinforces B_0; a weaker B_0 is needed for resonance. Methyl signal appears at lower field.

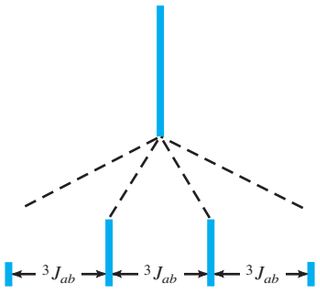
Spin of methine proton shields methyl protons from B_0. Methyl signal appears at higher field.

FIGURE 13.13
The magnetic moments (blue arrows) of the two possible spin states of the methine proton affect the chemical shift of the methyl protons in 1,1-dichloroethane. When the magnetic moment is parallel to the external field B_0 (green arrow), it adds to the external field and a smaller B_0 is needed for resonance. When it is antiparallel to the external field, it subtracts from it and shields the methyl protons.

FIGURE 13.14

The methyl protons of 1,1-dichloroethane split the signal of the methine proton into a quartet.

There are eight possible combinations of the nuclear spins of the three methyl protons in CH_3CHCl_2.



These eight combinations cause the signal of the $CHCl_2$ proton to be split into a quartet, in which the intensities of the peaks are in the ratio 1:3:3:1.

We describe the observed splitting of NMR signals as **spin–spin splitting** and the physical basis for it as **spin–spin coupling.** It has its origin in the communication of nuclear spin information via the electrons in the bonds that intervene between the nuclei. Its effect is greatest when the number of bonds is small. Vicinal protons are separated by three bonds, and coupling between vicinal protons, as in 1,1-dichloroethane, is called **three-bond coupling,** or **vicinal coupling.** Four-bond couplings are weaker and not normally observable.

A very important characteristic of spin–spin splitting is that protons that have the same chemical shift do not split each other's signal. Ethane, for example, shows only a single sharp peak in its NMR spectrum. Even though there is a vicinal relationship between the protons of one methyl group and those of the other, they do not split each other's signal because they are equivalent.

PROBLEM 13.11

Describe the appearance of the ^{1}H NMR spectrum of each of the following compounds. How many signals would you expect to find, and into how many peaks will each signal be split?

(a) 1,2-Dichloroethane
(b) 1,1,1-Trichloroethane
(c) 1,1,2-Trichloroethane
(d) 1,2,2-Trichloropropane
(e) 1,1,1,2-Tetrachloropropane

Sample Solution (a) All the protons of 1,2-dichloroethane ($ClCH_2CH_2Cl$) are chemically equivalent and have the same chemical shift. Protons that have the same chemical shift do not split each other's signal, and so the NMR spectrum of 1,2-dichloroethane consists of a single sharp peak.

Coupling of nuclear spins requires that the nuclei split each other's signal equally. The separation between the two halves of the methyl doublet in 1,1-dichloroethane is equal to the separation between any two adjacent peaks of the methine quartet. The extent to which two nuclei are coupled is given by the **coupling constant *J*** and in simple cases is equal to the separation between adjacent lines of the signal of a particular proton. The three-bond coupling constant $^3J_{ab}$ in 1,1-dichloroethane has a value of 7 Hz. *The size of the coupling constant is independent of the field strength;* the separation between adjacent peaks in 1,1-dichloroethane is 7 Hz, irrespective of whether the spectrum is recorded at 200 MHz or 500 MHz.

13.8 Splitting Patterns: The Ethyl Group

At first glance, splitting may seem to complicate the interpretation of NMR spectra. In fact, it makes structure determination easier because it provides additional information. It tells us how many protons are vicinal to a proton responsible for a particular signal.

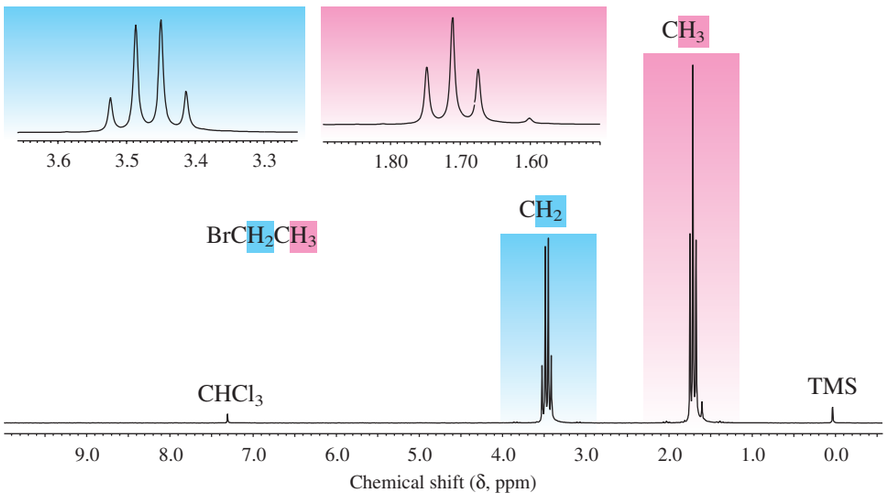
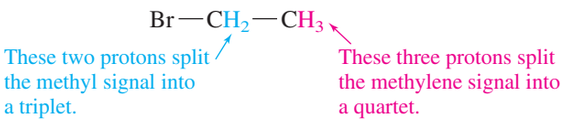


FIGURE 13.15
The 200-MHz ^{1}H NMR spectrum of ethyl bromide ($BrCH_2CH_3$), showing the characteristic triplet–quartet pattern of an ethyl group. The small peak at δ 1.6 is an impurity.

With experience, we learn to pick out characteristic patterns of peaks, associating them with particular structural types. One of the most common of these patterns is that of the ethyl group, represented in the NMR spectrum of ethyl bromide in Figure 13.15.

In compounds of the type CH_3CH_2X, especially where X is an electronegative atom or group, such as bromine in ethyl bromide, the ethyl group appears as a *triplet–quartet pattern.* The signal for the methylene protons is split into a quartet by coupling with the three methyl protons. The signal for the methyl protons is a triplet because of vicinal coupling to the two protons of the adjacent methylene group.



We have discussed in the preceding section why methyl groups split the signals due to vicinal protons into a quartet. Splitting by a methylene group gives a triplet corresponding to the spin combinations shown in Figure 13.16 for ethyl bromide. The relative intensities of the peaks of this triplet are 1:2:1.

PROBLEM 13.12

Describe the appearance of the ^{1}H NMR spectrum of each of the following compounds. How many signals would you expect to find, and into how many peaks will each signal be split?

(a) $ClCH_2OCH_2CH_3$
(b) $CH_3CH_2OCH_3$
(c) $CH_3CH_2OCH_2CH_3$
(d) *p*-Diethylbenzene
(e) $ClCH_2CH_2OCH_2CH_3$

Sample Solution (a) Along with the triplet–quartet pattern of the ethyl group, the NMR spectrum of this compound will contain a singlet for the two protons of the chloromethyl group.

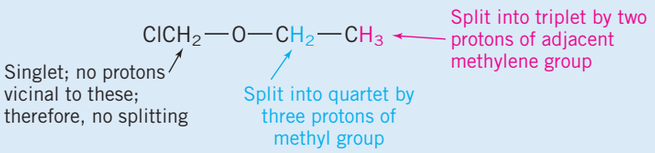
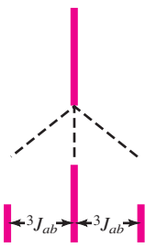


Table 13.2 summarizes the splitting patterns and peak intensities expected for coupling to various numbers of protons.

There are four possible combinations of the nuclear spins of the two methylene protons in CH_3CH_2Br.



These four combinations cause the signal of the CH_3 protons to be split into a triplet, in which the intensities of the peaks are in the ratio 1:2:1.

FIGURE 13.16
The methylene protons of ethyl bromide split the signal of the methyl protons into a triplet.

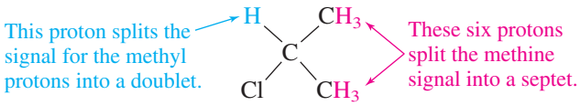
TABLE 13.2 Splitting Patterns of Common Multiplets

Number of protons to which nucleus is equally coupled	Appearance of multiplet	Intensities of lines in multiplet
1	Doublet	1:1
2	Triplet	1:2:1
3	Quartet	1:3:3:1
4	Pentet	1:4:6:4:1
5	Sextet	1:5:10:10:5:1
6	Septet	1:6:15:20:15:6:1

The intensities correspond to the coefficients of a binomial expansion (Pascal's triangle).

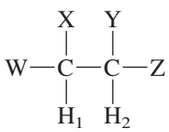
13.9 Splitting Patterns: The Isopropyl Group

The NMR spectrum of isopropyl chloride (Figure 13.17) illustrates the appearance of an isopropyl group. The signal for the six equivalent methyl protons at δ 1.5 is split into a doublet by the proton of the H—C—Cl unit. In turn, the H—C—Cl proton signal at δ 4.2 is split into a septet by the six methyl protons. A *doublet–septet* pattern is characteristic of an isopropyl group.



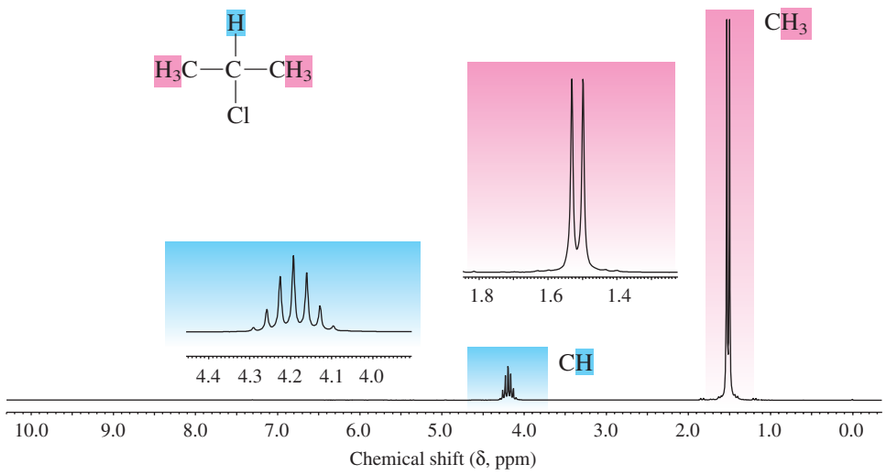
13.10 Splitting Patterns: Pairs of Doublets

We often see splitting patterns in which the intensities of the individual peaks do not match those given in Table 13.2, but are distorted in that the signals for coupled protons "lean" toward each other. This leaning is a general phenomenon, but is most easily illustrated for the case of two nonequivalent vicinal protons as shown in Figure 13.18.



The appearance of the splitting pattern of protons 1 and 2 depends on their coupling constant J and the chemical shift difference $\Delta\nu$ between them. When the ratio $\Delta\nu/J$ is large, two symmetrical 1:1 doublets are observed. We refer to this as the "AX"

FIGURE 13.17
The 200-MHz ^{1}H NMR spectrum of isopropyl chloride, showing the doublet–septet pattern of an isopropyl group.



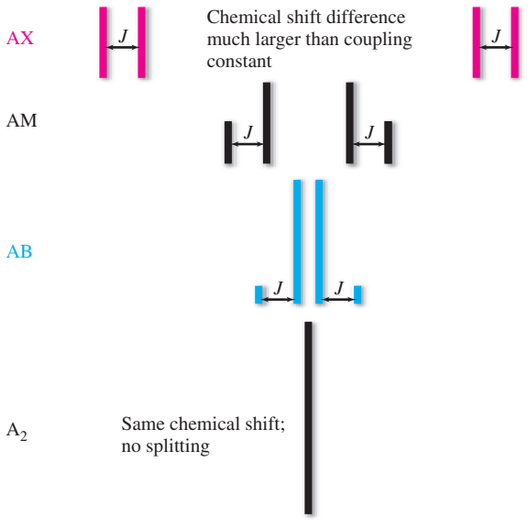
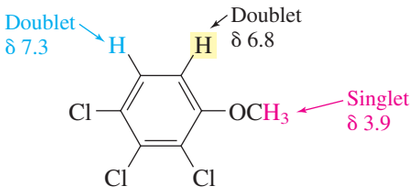


FIGURE 13.18

The appearance of the splitting pattern of two coupled protons depends on their coupling constant J and the chemical shift difference $\Delta\nu$ between them. As the ratio $\Delta\nu/J$ decreases, the doublets become increasingly distorted. When the two protons have the same chemical shift, no splitting is observed.

case, using two letters that are remote in the alphabet to stand for signals well removed from each other on the spectrum. Keeping the coupling constant the same while reducing $\Delta\nu$ leads to a steady decrease in the intensity of the outer two peaks with a simultaneous increase in the inner two as we progress from AX through AM to AB. At the extreme (A_2), the two protons have the same chemical shift, the outermost lines have disappeared, and no splitting is observed. Because of its appearance, it is easy to misinterpret an AB or AM pattern as a quartet, rather than the pair of skewed doublets it really is.

A skewed doublet of doublets is clearly visible in the ^{1}H NMR spectrum of 2,3,4-trichloroanisole (Figure 13.19). In addition to the singlet at δ 3.9 for the protons of the —OCH_3 group, we see doublets at δ 6.8 and δ 7.3 for the two protons of the aromatic ring.



2,3,4-Trichloroanisole

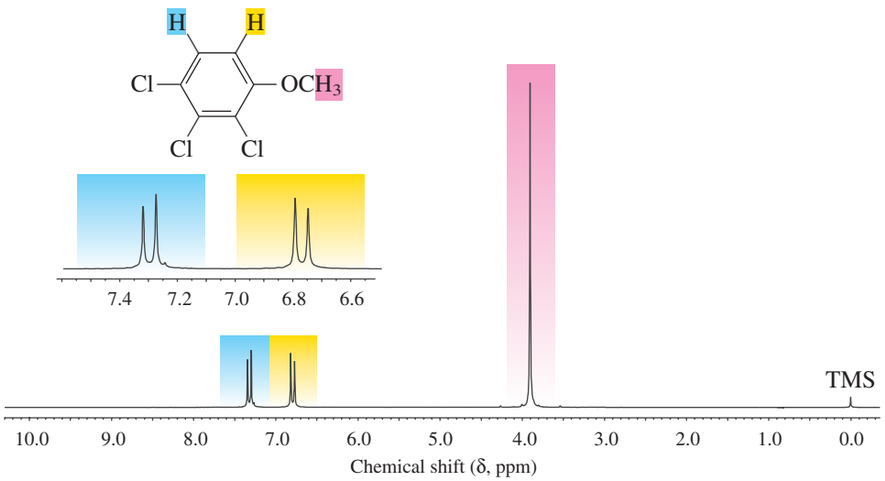
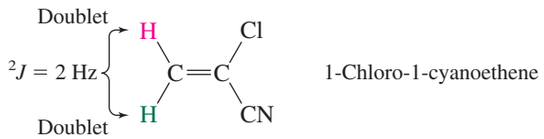


FIGURE 13.19

The 200-MHz ^{1}H NMR spectrum of 2,3,4-trichloroanisole, showing the splitting of the ring protons into a pair of doublets that "lean" toward each other.

A doublet of doublets frequently occurs with *geminal* protons (protons bonded to the same carbon). Geminal protons are separated by two bonds, and geminal coupling is referred to as *two-bond coupling* (^2J) in the same way that vicinal coupling is referred to as *three-bond coupling* (^3J). An example of geminal coupling is provided by the compound 1-chloro-1-cyanoethene, in which the two hydrogens appear as a pair of doublets. The splitting in each doublet is 2 Hz.

The protons in 1-chloro-1-cyanoethene are *diastereotopic* (Section 13.6). They are nonequivalent and have different chemical shifts. Remember, splitting can only occur between protons that have different chemical shifts.



1-Chloro-1-cyanoethene

Splitting due to geminal coupling is seen only in CH_2 groups and only when the two protons have different chemical shifts. All three protons of a methyl (CH_3) group are equivalent and cannot split one another's signal, and, of course, there are no protons geminal to a single methine (CH) proton.

13.11 Complex Splitting Patterns

All the cases we've discussed so far have involved splitting of a proton signal by coupling to other protons that were equivalent to one another. Indeed, we have stated the splitting rule in terms of the multiplicity of a signal as being equal to $n + 1$, where n is equal to the number of equivalent protons to which the proton that gives the signal is coupled. What if all the vicinal protons are *not* equivalent?

Figure 13.20*a* shows the signal for the proton marked Ar**C**$\mathbf{H}_a$=CH_2 in *m*-nitrostyrene, which appears as a set of four peaks in the range δ 6.7–6.9. These four peaks are in fact a "doublet of doublets." The proton in question is *unequally coupled* to the two protons at the end of the vinyl side chain. The size of the vicinal coupling constant between protons trans to each other on a double bond is normally larger than that between cis protons. In this case the trans coupling constant is 16 Hz and the cis coupling constant is 12 Hz. Thus, as shown in Figure 13.20*b,* the signal for H_a is split into a doublet with a spacing of 16 Hz by one vicinal proton, and each line of this doublet is then split into another doublet with a spacing of 12 Hz.

You will find it revealing to construct a splitting diagram similar to that of Figure 13.20 for the case in which the cis and trans **H**—C=C—**H** coupling constants are equal. Under those circumstances the four-line pattern simplifies to a triplet, as it should for a proton equally coupled to two vicinal protons.

The "$n + 1$ rule" should be amended to read: *When a proton* H_a *is coupled to* H_b, H_c, H_d, *etc., and* $J_{ab} \neq J_{ac}$, $\neq J_{ad}$, *etc., the original signal for* H_a is split into $n + 1$ *peaks by* n H_b *protons, each of these lines is further split into* $n + 1$ *peaks by* n H_c *protons, and each of these into* $n + 1$ *lines by* n H_d *protons, and so on.* Bear in mind that because of overlapping peaks, the number of lines actually observed can be less than that expected on the basis of the splitting rule.

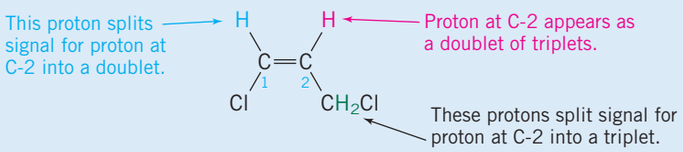
PROBLEM 13.13

Describe the splitting pattern expected for the proton at

(a) C-2 in (*Z*)-1,3-dichloropropene

(b) C-2 in $CH_3\overset{\displaystyle O}{\overset{\|}{C}}H\overset{\displaystyle Br}{\overset{|}{C}}H$

Sample Solution (a) The signal of the proton at C-2 is split into a doublet by coupling to the proton cis to it on the double bond, and each line of this doublet is split into a triplet by the two protons of the CH_2Cl group.



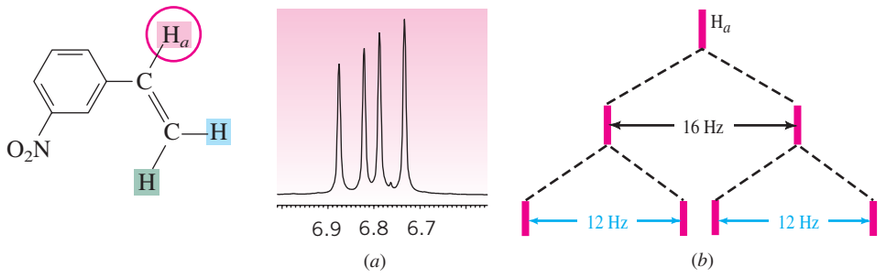


FIGURE 13.20

Splitting of a signal into a doublet of doublets by unequal coupling to two vicinal protons. (*a*) Appearance of the signal for the proton marked H_a in *m*-nitrostyrene as a set of four peaks. (*b*) Origin of these four peaks through successive splitting of the signal for H_a.

13.12 ^{1}H NMR Spectra of Alcohols

The —OH proton of a primary alcohol RCH_2OH is vicinal to two protons, and its signal would be expected to be split into a triplet. Under certain conditions signal splitting of alcohol protons is observed, but usually it is not. Figure 13.21 presents the NMR spectrum of benzyl alcohol, showing the methylene and hydroxyl protons as singlets at δ 4.7 and 2.5, respectively. (The aromatic protons also appear as a singlet, but that is because they all accidentally have the same chemical shift and so cannot split each other.)

The reason that splitting of the hydroxyl proton of an alcohol is not observed is that it is involved in rapid exchange reactions with other alcohol molecules. Transfer of a proton from an oxygen of one alcohol molecule to the oxygen of another is quite fast and effectively *decouples* it from other protons in the molecule. Factors that slow down this exchange of OH protons, such as diluting the solution, lowering the temperature, or increasing the crowding around the OH group, can cause splitting of hydroxyl resonances.

PROBLEM 13.14

Splitting of hydroxyl protons can be observed when the solvent in which the spectrum is recorded is dimethyl sulfoxide (DMSO) because hydrogen bonding to the oxygen of $(CH_3)_2\overset{+}{S}—\ddot{O}\!:^-$ slows down the rate of proton exchange between —OH groups. Explain how you could use this fact to distinguish among primary, secondary, and tertiary alcohols.

The chemical shift of the hydroxyl proton is variable, with a range of δ 0.5–5, depending on the solvent, the temperature at which the spectrum is recorded, and the

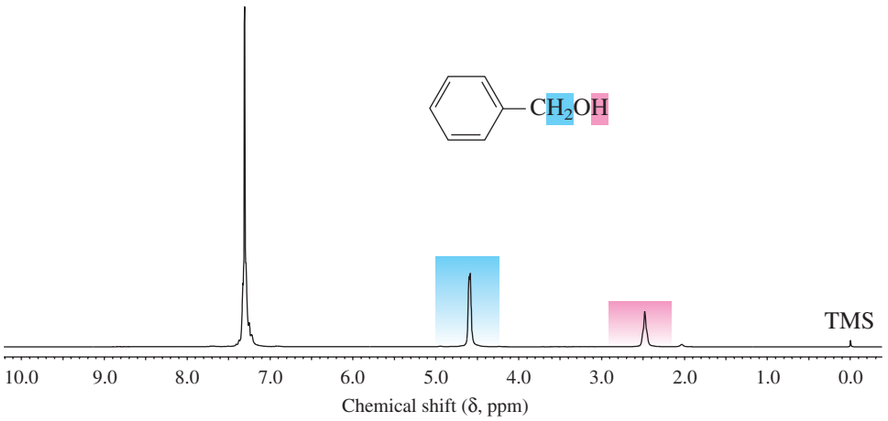


FIGURE 13.21

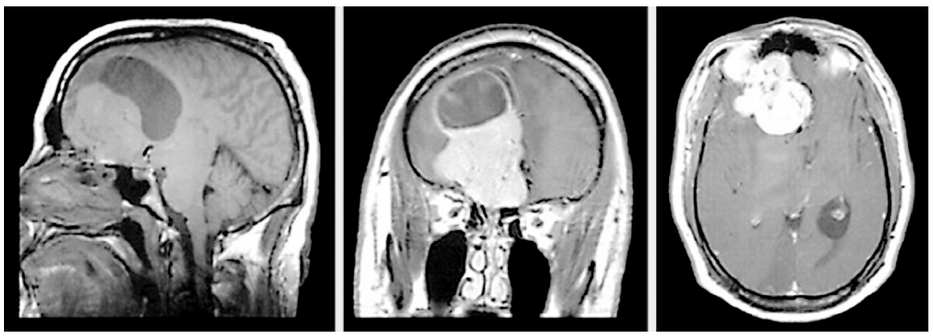
The 200-MHz ^{1}H NMR spectrum of benzyl alcohol. The hydroxyl proton and the methylene protons are vicinal but do not split each other because of the rapid intermolecular exchange of hydroxyl protons.

Magnetic Resonance Imaging (MRI)

It isn't often that someone goes to the emergency room because of a headache, and when the staff discovered that the man who did was due in court for sentencing the next day, some of them felt that there might not be anything wrong with him at all. There was.

The man's behavior toward the staff soon convinced them that he should be admitted, kept overnight, and seen by a neurologist the next day. After a preliminary examination, a magnetic resonance image, or MRI, was ordered which revealed the brain tumor shown in Figure 13.22. The tumor was located in the right frontal cortex, a portion of the brain known to be involved in controlling impulsive behavior.

The man had behaved normally until middle age; then his personality underwent significant changes, involving certain impulsive behaviors and criminal tendencies. These, as well as other behaviors, had not responded to drugs or counseling.



(*a*) (*b*) (*c*)

FIGURE 13.22

MRI scans of a brain tumor in the prefrontal cortex. The tumor is in the right hemisphere. The contrast-enhanced views (*b* and *c*) distinguish between the tumor (bright white) and a large accompanying cyst (gray oval with white outline in *b*). The tumor itself begins just beyond the nose (black shadow at top of *c*). (*a*) Sagittal view (patient facing left, head in profile). (*b*) Coronal view (view from the top of the head). (*c*) Axial view (diagonal section from the top of the head). (Images used, with permission, from J.M. Burns, R.H. Swerdlow: Right orbitofrontal tumor with pedophilia symptom and constructional apraxia sign. *Archives of Neurology,* vol. 60:437–440; 2003. © Copyright, American Medical Association.

—Continued

concentration of the solution. The alcohol proton shifts to lower field in more concentrated solutions.

An easy way to verify that a particular signal belongs to a hydroxyl proton is to add D_2O. The hydroxyl proton is replaced by deuterium according to the equation:

$$RCH_2OH + D_2O \rightleftharpoons RCH_2OD + DOH$$

Deuterium does not give a signal under the conditions of ^1H NMR spectroscopy. Thus, replacement of a hydroxyl proton by deuterium leads to the disappearance of the OH peak of the alcohol. Protons bonded to nitrogen and sulfur also undergo exchange with D_2O. Those bound to carbon normally do not, which makes this a useful technique for assigning the proton resonances of OH, NH, and SH groups.

13.13 NMR and Conformations

We know from Chapter 3 that the protons in cyclohexane exist in two different environments: axial and equatorial. The NMR spectrum of cyclohexane, however, shows only a single sharp peak at δ 1.4. All the protons of cyclohexane appear to be equivalent in the NMR spectrum. Why?

(Continued)

Even though he had earned a master's degree, the man performed poorly on some simple mental tests and was unable to sketch the face of a clock or write a legible, coherent sentence.

Once the tumor was found, it was surgically removed. The man's ability to curb his impulses was restored, his mental, graphical, and writing skills improved to the normal range, and he successfully completed a rehabilitation program. About a year later though, the headaches and some of the earlier behaviors returned. When a new MRI showed that the tumor had regrown, it was removed and again the symptoms disappeared.

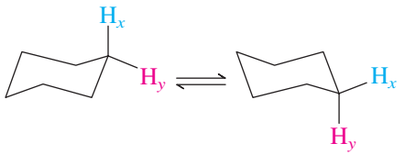
At a turning point in this man's life, an MRI made all the difference. MRI is NMR. The word *nuclear* is absent from the name to avoid confusion with nuclear medicine, which involves radioactive isotopes. MRI is noninvasive, requires no imaging or contrast agents, and is less damaging than X-rays. In the time since the first MRI of a living creature—a clam—was successfully obtained in the early 1970s, MRI has become a standard diagnostic tool. Two of its early developers, Paul Lauterbur (University of Illinois) and Peter Mansfield (University of Nottingham) were recognized with the 2003 Nobel Prize in physiology or medicine.

An MRI scanner is an NMR machine large enough to accommodate a human being, has a powerful magnet, operates in the pulse-FT mode, and detects protons—usually the protons in water and, to a lesser extent, lipids. The principles are the same as those of conventional FT-NMR spectroscopy but, because the goal is different, the way the data are collected and analyzed differs too. Some key features of MRI include:

1. A selective pulse is used in order to excite protons in a particular slice of the object to be imaged.
2. Unlike conventional NMR, the magnetic field in MRI is not uniform. A linear gradient is applied in addition to the static field so that the field strength varies as a function of position in the object but is precisely known. Because the frequency of a proton signal is directly proportional to the strength of the applied magnetic field, the measured resonance frequency is linearly related to the position in the magnetic field gradient.
3. Computer software carries out the essential task of reconstructing the 2D or 3D image from the NMR signals. The data are generally presented as a series of slices through the imaged object. Three different views of a tumor are shown in Figure 13.22 with different slice orientations.
4. The intensity of the signal—its relative lightness or darkness in the image—depends on the concentration and spin relaxation times of the various protons. Spin relaxation time is the time it takes for the perturbed magnetization associated with a proton to return to its equilibrium value. The relaxation time is quite sensitive to the environment and is different for water in blood and various tissues.

New applications of nuclear magnetic resonance in biomedical science continue to appear. Functional MRI (fMRI) is an offshoot of MRI. Unlike MRI, which is used for diagnosis in a clinical setting, fMRI is a research tool that detects regions of the brain that are actively responding to stimuli. Increased brain activity is accompanied by an increase in blood flow to the region involved. This alters the ratio of oxygenated hemoglobin to its nonoxygenated counterpart. Because the two hemoglobins have different magnetic properties, the nuclear spin relaxation times of the protons in water are affected and can be studied by MRI. In the short time since its development, fMRI has been used successfully to study memory and cognition in relation to brain activity.

The answer is related to the very rapid rate of ring flipping in cyclohexane.



NMR is too slow to "see" the individual conformations of cyclohexane, but sees instead the *average* environment of the protons. Because chair–chair interconversion in cyclohexane converts each axial proton to an equatorial one and vice versa, the average environments of all the protons are the same. A single peak is observed that has a chemical shift midway between the true chemical shifts of the axial and the equatorial protons.

The rate of ring flipping can be slowed down by lowering the temperature. At temperatures of about -100°C, separate signals are seen for the axial and equatorial protons of cyclohexane.

13.14 ^{13}C NMR Spectroscopy

We pointed out in Section 13.3 that both ^{1}H and ^{13}C are nuclei that can provide useful structural information when studied by NMR. Although a ^{1}H NMR spectrum helps us infer much about the carbon skeleton of a molecule, a ^{13}C NMR spectrum has the

obvious advantage of probing the carbon skeleton directly. ^{13}C NMR spectroscopy is analogous to ^{1}H NMR in that the number of signals informs us about the number of different kinds of carbons, and their chemical shifts are related to particular chemical environments.

However, unlike ^{1}H, which is the most abundant of the hydrogen isotopes (99.985%), only 1.1% of the carbon atoms in a sample are ^{13}C. Moreover, the intensity of the signal produced by ^{13}C nuclei is far weaker than the signal produced by the same number of ^{1}H nuclei. In order for ^{13}C NMR to be a useful technique in structure determination, a vast increase in the signal-to-noise ratio is required. Pulsed FT-NMR provides for this, and its development was the critical breakthrough that led to ^{13}C NMR becoming the routine tool that it is today.

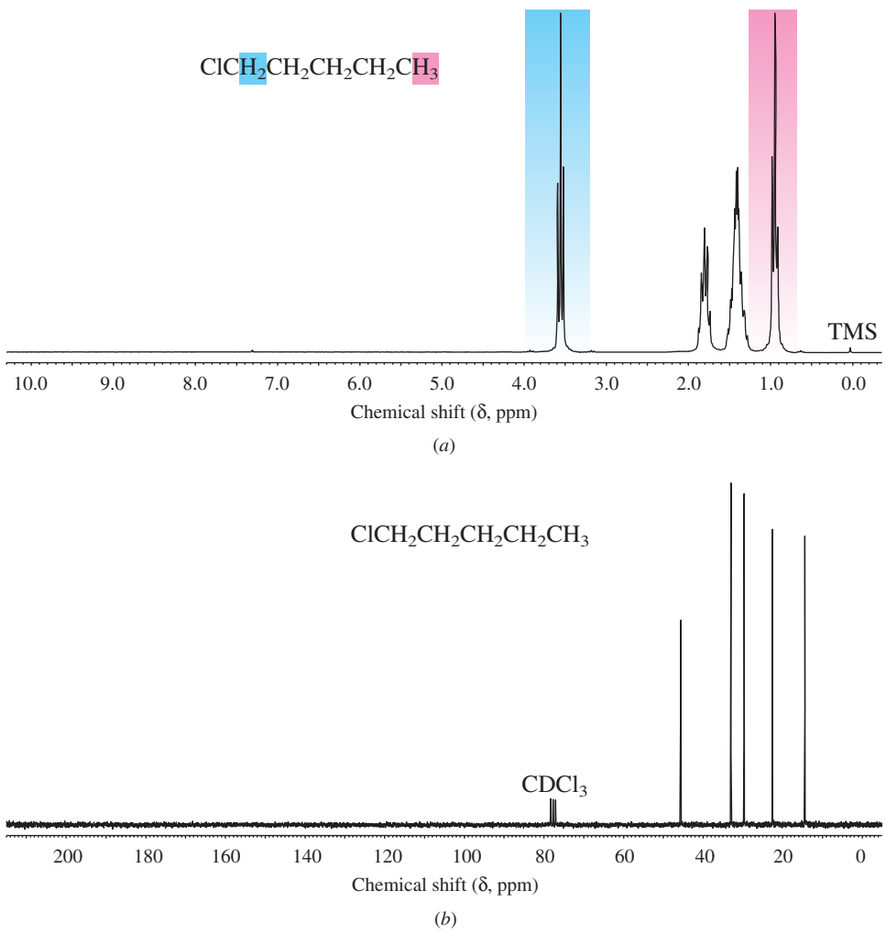
To orient ourselves in the information that ^{13}C NMR provides, let's compare the ^{1}H and ^{13}C NMR spectra of 1-chloropentane (Figures 13.23*a* and 13.23*b,* respectively). The ^{1}H NMR spectrum shows reasonably well-defined triplets for the protons of the CH_3 and CH_2Cl groups (δ 0.9 and 3.55, respectively). The signals for the six CH_2 protons at C-2, C-3, and C-4 of $CH_3CH_2CH_2CH_2CH_2Cl$, however, appear as two unresolved multiplets at δ 1.4 and 1.8.

The ^{13}C NMR spectrum, on the other hand, is very simple: *a separate, distinct peak is observed for each carbon.*

Notice, too, how well-separated these ^{13}C signals are: they cover a range of over 30 ppm, compared with less than 3 ppm for the proton signals of the same compound. In general, the window for proton signals in organic molecules is about 12 ppm; ^{13}C chemical shifts span a range of over 200 ppm. The greater spread of ^{13}C chemical shifts makes it easier to interpret the spectra.

FIGURE 13.23

(*a*) The 200-MHz ^{1}H NMR spectrum and (*b*) the ^{13}C NMR spectrum of 1-chloropentane.

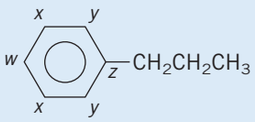


PROBLEM 13.15

How many signals would you expect to see in the ^{13}C NMR spectrum of each of the following compounds?

(a) Propylbenzene
(b) Isopropylbenzene
(c) 1,2,3-Trimethylbenzene
(d) 1,2,4-Trimethylbenzene
(e) 1,3,5-Trimethylbenzene

Sample Solution (a) The two ring carbons that are ortho to the propyl substituent are equivalent and so must have the same chemical shift. Similarly, the two ring carbons that are meta to the propyl group are equivalent to each other. The carbon atom para to the substituent is unique, as is the carbon that bears the substituent. Thus, there will be four signals for the ring carbons, designated *w, x, y,* and *z* in the structural formula. These four signals for the ring carbons added to those for the three nonequivalent carbons of the propyl group yield a total of seven signals.



Propylbenzene

13.15 ^{13}C Chemical Shifts

Just as chemical shifts in ^{1}H NMR are measured relative to the *protons* of tetramethylsilane, chemical shifts in ^{13}C NMR are measured relative to the *carbons* of tetramethylsilane. Table 13.3 lists typical chemical-shift ranges for some representative types of carbon atoms.

In general, the factors that most affect ^{13}C chemical shifts are

1. The electronegativity of the groups attached to carbon
2. The hybridization of carbon

Electronegativity Effects. Electronegative substituents affect ^{13}C chemical shifts in the same way as they affect ^{1}H chemical shifts, by withdrawing electrons. For ^{1}H NMR, recall that because carbon is more electronegative than hydrogen, the protons in methane (CH_4)

TABLE 13.3 Chemical Shifts of Representative Carbons

Type of carbon	Chemical shift (δ) ppm*	Type of carbon	Chemical shift (δ) ppm*
Hydrocarbons		**Functionally substituted carbons**	
RCH_3	0–35	RCH_2Br	20–40
R_2CH_2	15–40	RCH_2Cl	25–50
R_3CH	25–50	RCH_2NH_2	35–50
R_4C	30–40	RCH_2OH and RCH_2OR	50–65
$RC\equiv CR$	65–90	$RC\equiv N$	110–125
$R_2C=CR_2$	100–150	$RCOH$ and $RCOR$	160–185
	110–175	RCH and RCR	190–220

*Approximate values relative to tetramethylsilane.

are more shielded than primary hydrogens (RCH_3), primary hydrogens are more shielded than secondary (R_2CH_2), and secondary more shielded than tertiary (R_3CH). The same holds true for carbons in ^{13}C NMR, but the effects can be 10–20 times greater.

	$(CH_3)_4C$	$(CH_3)_3CH$	$CH_3CH_2CH_3$	CH_3CH_3	CH_4
Classification:	Quaternary	Tertiary	Secondary	Primary	
Chemical shift (δ), ppm:					
H		1.7	1.3	0.9	0.2
C	28	25	16	8	−2

Likewise, for functionally substituted methyl groups:

	CH_3F	CH_3OH	CH_3NH_2	CH_4
Chemical shift (δ), ppm:				
H	4.3	3.4	2.5	0.2
C	75	50	27	−2

Figure 13.23 compared the appearance of the ^1H and ^{13}C NMR spectra of 1-chloropentane and drew attention to the fact each carbon gave a separate peak, well separated from the others. Let's now take a closer look at the ^{13}C NMR spectrum of 1-chloropentane with respect to assigning these peaks to individual carbons.

	Cl—CH_2—CH_2—CH_2—CH_2—CH_3				
^{13}C chemical shift (δ), ppm:	45	33	29	22	14

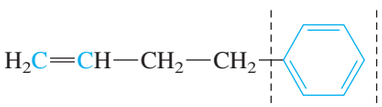
The most obvious feature of these ^{13}C chemical shifts is that the closer the carbon is to the electronegative chlorine, the more deshielded it is. Peak assignments will not always be this easy, but the correspondence with electronegativity is so pronounced that *spectrum simulators* are available that allow reliable prediction of ^{13}C chemical shifts from structural formulas. These simulators are based on arithmetic formulas that combine experimentally derived chemical shift increments for the various structural units within a molecule.

The Descriptive Passage and Interpretive Problems at the end of this chapter illustrate the spectrum simulator approach to calculating ^{13}C chemical shifts.

PROBLEM 13.16

The ^{13}C NMR spectrum of 1-bromo-3-chloropropane contains peaks at δ 30, δ 35, and δ 43. Assign these signals to the appropriate carbons.

Hybridization Effects. Here again, the effects are similar to those seen in ^1H NMR. As illustrated by 4-phenyl-1-butene, sp^3-hybridized carbons are more shielded than sp^2-hybridized ones.

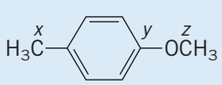


^{13}C chemical shift (δ), ppm:	114	138	36	36	126–142

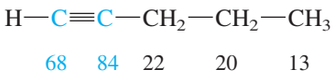
Of the sp^2-hybridized carbons, C-1 is the most shielded because it is bonded to only one other carbon. The least shielded carbon is the ring carbon to which the side chain is attached. It is the only sp^2-hybridized carbon connected to three others.

PROBLEM 13.17

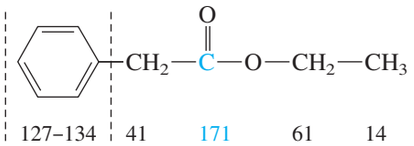
Consider carbons *x*, *y*, and *z* in *p*-methylanisole. One has a chemical shift of δ 20, another has δ 55, and the third δ 157. Match the chemical shifts with the appropriate carbons.



Acetylenes are anomalous in ^{13}C, as in ^{1}H NMR. *sp*-Hybridized carbons are less shielded than sp^3-hybridized ones, but more shielded than sp^2-hybridized ones.



Electronegativity and hybridization effects combine to make the carbon of a carbonyl group especially deshielded. Normally, the carbon of C═O is the least shielded one in a ^{13}C NMR spectrum.



PROBLEM 13.18

Which would you expect to be more shielded, the carbonyl carbon of an aldehyde or a ketone? Why?

We will have more to say about ^{13}C chemical shifts in later chapters when various families of compounds, especially those that contain carbonyl groups, are discussed in more detail.

13.16 ^{13}C NMR and Peak Intensities

Two features that are fundamental to ^{1}H NMR spectroscopy—integrated areas and splitting patterns—are not very important in ^{13}C NMR.

Although it is a simple matter to integrate ^{13}C signals, it is rarely done because the observed ratios can be more misleading than helpful. The pulsed FT technique that is standard for ^{13}C NMR has the side effect of distorting the signal intensities, especially for carbons that lack attached hydrogens. Examine Figure 13.24, which shows the ^{13}C NMR spectrum of 3-methylphenol (*m*-cresol). Notice that, contrary to what we might expect for a compound with seven peaks for seven different carbons, the intensities of these peaks are not nearly the same. The two least intense signals, those at δ 140 and δ 157, correspond to carbons that lack attached hydrogens.

PROBLEM 13.19

To which of the compounds of Problem 13.15 does the ^{13}C NMR spectrum of Figure 13.25 belong?

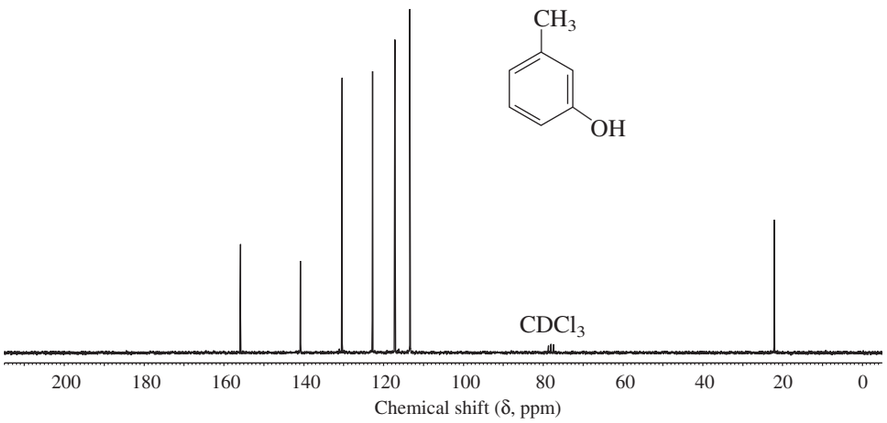
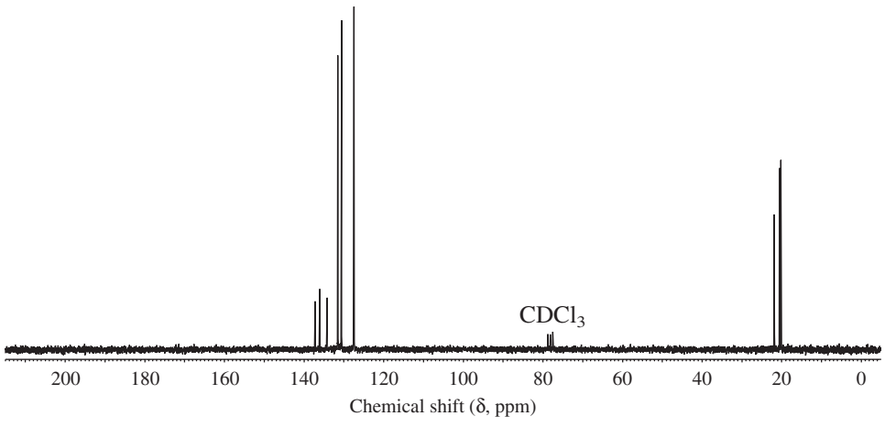


FIGURE 13.24

The ^{13}C NMR spectrum of *m*-cresol. Each of the seven carbons of *m*-cresol gives a separate peak. Integrating the spectrum would not provide useful information because the intensities of the peaks are so different, even though each one corresponds to a single carbon.

FIGURE 13.25
The ^{13}C NMR spectrum of the unknown compound of Problem 13.19.



13.17 ^{13}C—^{1}H Coupling

You may have noticed another characteristic of ^{13}C NMR spectra—all of the peaks are singlets. With a spin of $\pm\frac{1}{2}$, a ^{13}C nucleus is subject to the same splitting rules that apply to ^{1}H, and we might expect to see splittings due to ^{13}C—^{13}C and ^{13}C—^{1}H couplings. We don't. Why?

The lack of splitting due to ^{13}C—^{13}C coupling is easy to understand. ^{13}C NMR spectra are measured on samples that contain ^{13}C at the "natural abundance" level. Only 1% of all the carbons in the sample are ^{13}C, and the probability that any molecule contains more than one ^{13}C atom is quite small.

Splitting due to ^{13}C—^{1}H coupling is absent for a different reason, one that has to do with the way the spectrum is run. Because a ^{13}C signal can be split not only by the protons to which it is directly attached, but also by protons separated from it by two, three, or even more bonds, the number of splittings might be so large as to make the spectrum too complicated to interpret. Thus, the spectrum is measured under conditions, called **broadband decoupling,** that suppress such splitting. In addition to pulsing the sample by a radiofrequency tuned for ^{13}C, the sample is continuously irradiated by a second rf transmitter that covers the entire frequency range for all the ^{1}H nuclei. The effect of this second rf is to decouple the ^{1}H spins from the ^{13}C spins, which causes all the ^{13}C signals to collapse to singlets.

What we gain from broadband decoupling in terms of a simple-looking spectrum comes at the expense of some useful information. For example, being able to see splitting corresponding to one-bond ^{13}C—^{1}H coupling would immediately tell us the number of hydrogens directly attached to each carbon. The signal for a carbon with no attached hydrogens (a *quaternary* carbon) would be a singlet, the hydrogen of a CH group would split the carbon signal into a doublet, and the signals for the carbons of a CH_2 and a CH_3 group would appear as a triplet and a quartet, respectively. Although it is possible, with a technique called *off-resonance decoupling,* to observe such one-bond couplings, identifying a signal as belonging to a quaternary carbon or to the carbon of a CH, CH_2, or CH_3 group is normally done by a method called DEPT, which is described in the next section.

13.18 Using DEPT to Count Hydrogens Attached to ^{13}C

In general, a simple pulse FT-NMR experiment involves the following stages:

1. Equilibration of the nuclei between the lower and higher spin states under the influence of a magnetic field
2. Application of a radiofrequency pulse to give an excess of nuclei in the higher spin state
3. Acquisition of free-induction decay data during the time interval in which the equilibrium distribution of nuclear spins is restored
4. Mathematical manipulation (Fourier transform) of the data to plot a spectrum

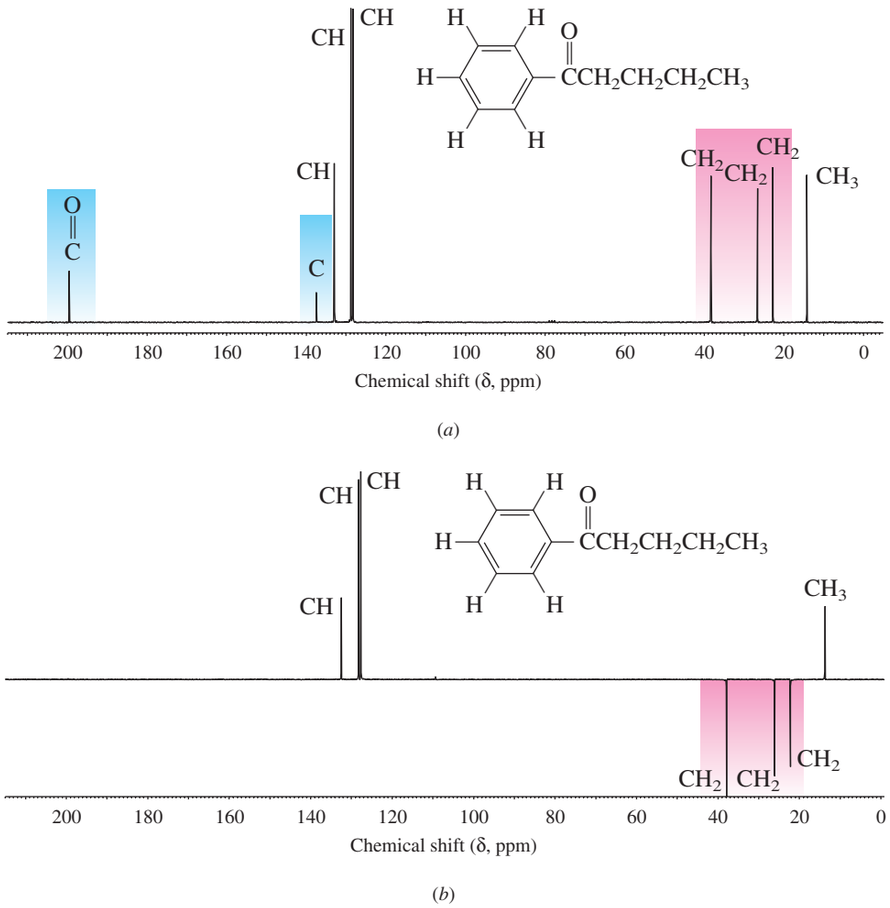


FIGURE 13.26

^{13}C NMR spectra of 1-phenyl-1-pentanone. (*a*) Normal spectrum. (*b*) DEPT spectrum recorded using a pulse sequence in which CH_3 and CH carbons appear as positive peaks, CH_2 carbons as negative peaks, and carbons without any attached hydrogens are nulled.

The pulse sequence (stages 2–3) can be repeated hundreds of times to enhance the signal-to-noise ratio. The duration of time for stage 2 is on the order of milliseconds, and that for stage 3 is about 1 second.

Major advances in NMR have been made by using a second rf transmitter to irradiate the sample at some point during the sequence. There are several such techniques, of which we'll describe just one, called **distortionless enhancement of polarization transfer,** abbreviated as **DEPT.**

In the DEPT routine, a second transmitter excites ^1H, which affects the appearance of the ^{13}C spectrum. A typical DEPT experiment is illustrated for the case of 1-phenyl-1-pentanone in Figure 13.26. In addition to the normal spectrum shown in Figure 13.26*a,* four more spectra are run using prescribed pulse sequences. In one (Figure 13.26*b*), the signals for carbons of CH_3 and CH groups appear normally, whereas those for CH_2 groups are inverted and those for C without any attached hydrogens are nulled. In the others (not shown) different pulse sequences produce combinations of normal, nulled, and inverted peaks that allow assignments to be made to the various types of carbons with confidence.

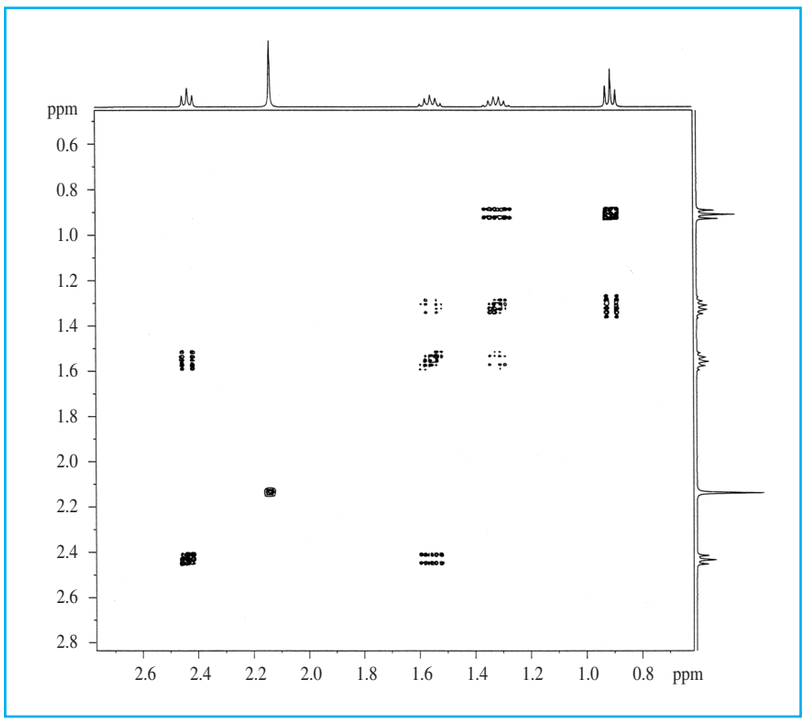
13.19 2D NMR: COSY and HETCOR

The more information you can extract from an NMR spectrum, the better your chances at arriving at a unique structure. Like spin–spin splitting, which complicates the appearance of an ^1H NMR spectrum but provides additional information, 2D NMR looks more complicated than it is while making structure determination easier.

The key dimension in NMR is the frequency axis. All of the spectra we have seen so far are 1D spectra because they have only one frequency axis. In 2D NMR a standard pulse sequence adds a second frequency axis. Only pulsed FT-NMR spectrometers are capable of carrying out 2D experiments.

The theoretical aspects, including pulse sequences, that underlie 2D NMR are discussed in the May 1990 issue of the *Journal of Chemical Education,* pp. A125–A137.

FIGURE 13.27
^{1}H-^{1}H COSY NMR spectrum of 2-hexanone.

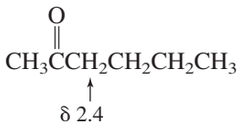


One kind of 2D NMR is called **COSY,** which stands for **correlated spectroscopy.** With a COSY spectrum you can determine by inspection which signals correspond to spin-coupled protons. Identifying coupling relationships is a valuable aid to establishing a molecule's *connectivity*.

Figure 13.27 is the COSY spectrum of 2-hexanone. Both the *x*- and *y*-axes are frequency axes expressed as chemical shifts. Displaying the 1D ^{1}H NMR spectrum of 2-hexanone along the *x*- and *y*-axes makes it easier to interpret the 2D information, which is the collection of contoured objects contained within the axes. To orient ourselves, first note that many of the contours lie along the diagonal that runs from the lower left to the upper right. This diagonal bisects the 2D NMR into two mirror-image halves. The off-diagonal contours are called *cross peaks* and contain the connectivity information we need.

Each cross peak has *x* and *y* coordinates. One coordinate corresponds to the chemical shift of a proton, the other to the chemical shift to a proton to which it is coupled. Because the diagonal splits the 2D spectrum in half, each cross peak is duplicated on the other side of the other diagonal with the same coordinates, except in reverse order. This redundancy means that we really need to examine only half of the cross peaks.

To illustrate, start with the lowest field signal (δ 2.4) of 2-hexanone. We assign this signal, a triplet, to the protons at C-3 on the basis of its chemical shift and the splitting evident in the 1D spectrum.



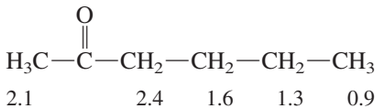
We look for cross peaks with the same *x* coordinate by drawing a vertical line from δ 2.4, finding a cross peak with a *y* coordinate of δ 1.6. *This means that the protons responsible for the signal at δ 2.4 are coupled to the ones at δ 1.6.* Therefore, the chemical shift of the C-4 protons is δ 1.6.

Now work from these C-4 protons. Drawing a vertical line from δ 1.6 on the *x*-axis finds two cross peaks. One cross peak simply confirms the coupling to the protons at C-3. The other has a *y* coordinate of δ 1.3 and, therefore, must correspond to the protons at C-5.

A vertical line drawn from δ 1.3 intersects the cross peaks at both δ 1.6 and δ 0.9. The former confirms the coupling of C-5 to C-4; the latter corresponds to the C-5 to C-6 coupling and identifies the signal at δ 0.9 as belonging to the protons at C-6.

Finally, a vertical line drawn from δ 2.1 intersects no cross peaks. The singlet at δ 2.1, as expected, is due to the protons at C-1, which are not coupled to any of the other protons in the molecule.

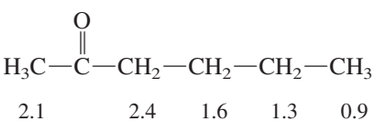
The complete connectivity and assignment of ^{1}H chemical shifts is



Although the 1D ^{1}H spectrum of 2-hexanone is simple enough to be interpreted directly, you can see that COSY offers one more tool we can call on in more complicated cases.

A second 2D NMR method called **HETCOR (heteronuclear chemical shift correlation)** is a type of COSY in which the two frequency axes are the chemical shifts for different nuclei, usually ^{1}H and ^{13}C. With HETCOR it is possible to relate a peak in a ^{13}C spectrum to the ^{1}H signal of the protons attached to that carbon. As we did with COSY, we'll use 2-hexanone to illustrate the technique.

The HETCOR spectrum of 2-hexanone is shown in Figure 13.28. It is considerably simpler than a COSY spectrum, lacking diagonal peaks and contoured cross peaks. Instead, we see objects that are approximately as tall as a ^{1}H signal is wide, and as wide as a ^{13}C signal. As with the COSY cross peaks, however, it is their coordinates that matter, not their size or shape. Interpreting the spectrum is straightforward. The ^{13}C peak at δ 30 correlates with the ^{1}H singlet at δ 2.1, which because of its multiplicity and chemical shift corresponds to the protons at C-1. Therefore, this ^{13}C peak can be assigned to C-1 of 2-hexanone. Repeating this procedure for the other carbons gives:



^{1}H chemical shift (δ), ppm:	2.1	2.4	1.6	1.3	0.9
^{13}C chemical shift (δ), ppm:	30	43	26	22	14

The July 1995 issue of the *Journal of Chemical Education* (pp. 659–661) contains an undergraduate laboratory experiment in which COSY is used to analyze the products of a chemical reaction.

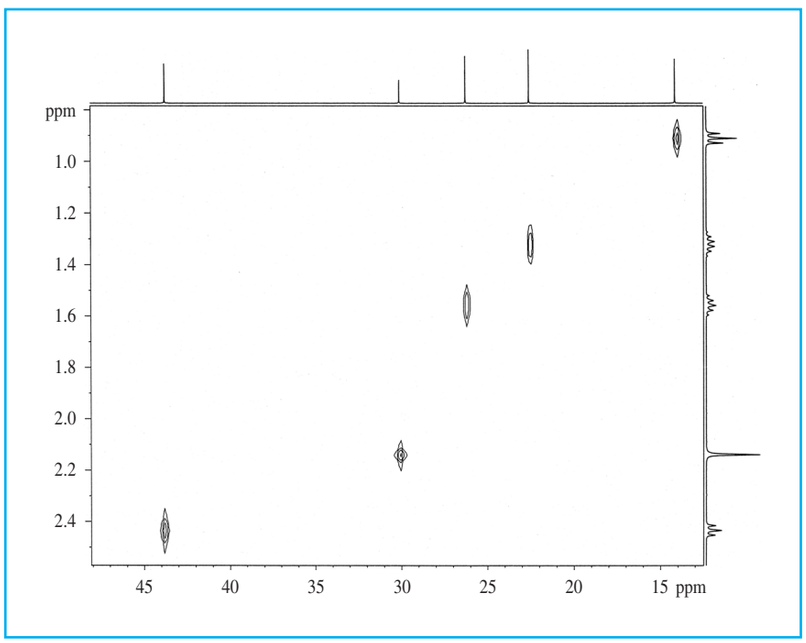


FIGURE 13.28

^{1}H-^{13}C HETCOR NMR spectrum of 2-hexanone.

The chemical shift of the carbonyl carbon (δ 209) is not included because it has no attached hydrogens.

Because the digitized areas of the ^{1}H spectrum give the relative number of protons responsible for each signal, HETCOR serves as an alternative to DEPT for counting the number of protons bonded to each carbon.

A number of 2D NMR techniques are available for a variety of purposes. They are especially valuable when attempting to determine the structure of complicated natural products and the conformations of biomolecules.

13.20 Introduction to Infrared Spectroscopy

IR's earliest recognition came during World War II when it provided a key clue to the unusual β-lactam structure of the "miracle drug" penicillin.

Before the advent of NMR spectroscopy, infrared (IR) spectroscopy was the instrumental method most often applied to organic structure determination. Although NMR, in general, tells us more about the structure of an unknown compound, IR remains an important tool because of its usefulness in identifying the presence of certain *functional groups* within a molecule. Structural units, including functional groups, vibrate in characteristic ways and it is this sensitivity to *group vibrations* that is the basis of IR spectroscopy.

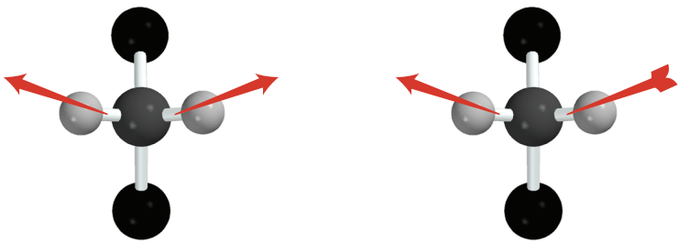
Among the ways a molecule responds to the absorption of energy is by vibrational motions such as the stretching and contracting of bonds and the opening and closing (bending) of bond angles. Vibrational motion and its energy are quantized. Only certain vibrational energy states are allowed.

We can visualize molecular vibrations by thinking of atoms and bonds as balls and springs.

Zero-point energy is the term given to the energy of a molecule at absolute zero.

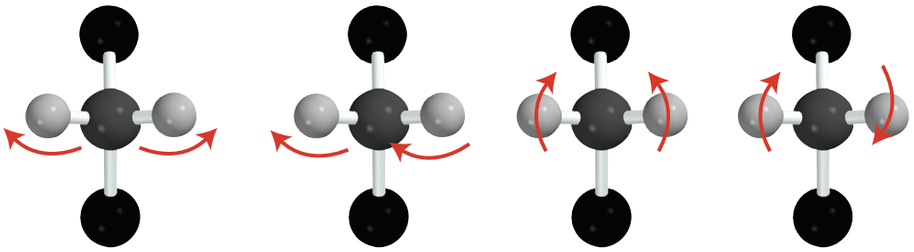
Even at the absolute zero of temperature, atoms in a molecule vibrate with respect to the bonds that connect them. At room temperature, the molecules are distributed among various vibrational energy states. *Frequency* is a property of the vibration and is related to the difference between vibrational energy states by $\Delta E = h\nu$ (Section 13.1). Promoting a molecule from a lower to a higher vibrational energy state increases the *amplitude* of the vibration.

For a sense of the variety of vibrational modes available to a molecule, consider a CH_2 group. Stretching and contracting the pair of C—H bonds can occur in two different ways. In the *symmetric* stretch, both C—H bonds stretch at the same time and contract at the same time. In the *antisymmetric* stretch, one C—H bond stretches while the other contracts.



Stretching vibrations: Symmetric Antisymmetric

In addition to stretching vibrations, a CH_2 group can bend, and each bending mode has its own set of energy states.



Bending vibrations: Scissoring Rocking Wagging Twisting

Spectra by the Thousands

The best way to get good at interpreting spectra is by experience. Look at as many spectra and do as many spectroscopy problems as you can.

Among Web sites that offer spectroscopic problems, two stand out (Figure 13.29). One, called *WebSpectra,* was developed by Professor Craig A. Merlic (UCLA):*

http://www.chem.ucla.edu/~webspectra

The other is the *Organic Structure Elucidation* workbook, created by Professor Bradley D. Smith (Notre Dame):

http://www.nd.edu/~smithgrp/structure/workbook.html

WebSpectra includes 75 problems. All the problems display the ^{1}H and ^{13}C spectra, several with DEPT or COSY enhancements. A number include IR spectra. *Organic Structure Elucidation* contains 64 problems, all with ^{1}H and ^{13}C NMR, IR, and mass spectra. The exercises in both *WebSpectra* and *Organic Structure Elucidation* are graded according to difficulty. Give them a try.

Vast numbers of NMR, IR, and mass spectra are freely accessible via the *Spectral Data Base System* (SDBS) maintained by the Japanese National Institute of Advanced Industrial Science and Technology at:

http://www.aist.go.jp/RIODB/SDBS/menu-e.html

The SDBS contains 14,000 ^{1}H NMR, 12,300 ^{13}C NMR, 49,800 IR, and 22,900 mass spectra.† Not only does the SDBS contain more spectra than anyone could possibly browse through, it incorporates some very useful search features. If you want spectra for a particular compound, entering the name of the compound calls up links to its spectra, which can then be displayed. If you don't know what the compound is, but know one or more of the following:

- Molecular formula
- ^{1}H or ^{13}C chemical shift of one or more peaks
- Mass number of mass spectra fragments

entering the values singly or in combination returns the names of the best matches in the database. You can then compare the spectra of these candidate compounds with the spectra of the sample to identify it.

As extensive as the SDBS is, don't be disappointed if the exact compound you are looking for is not there. There are, after all, millions of organic compounds. However, much of structure determination (and organic chemistry in general) is based on analogy. Finding the spectrum of a related compound can be almost as helpful as finding the one you really want.

These Web resources, in conjunction with the figures and problems in your text, afford a wealth of opportunities to gain practice and experience in modern techniques of structure determination.

*For a complete description of *WebSpectra* see pp. 118–120 of the January 2001 issue of the *Journal of Chemical Education.*

†Using the SDBS as the basis for student exercises in organic spectroscopy is described in the September 2001 issue of the *Journal of Chemical Education,* pp. 1208–1209.

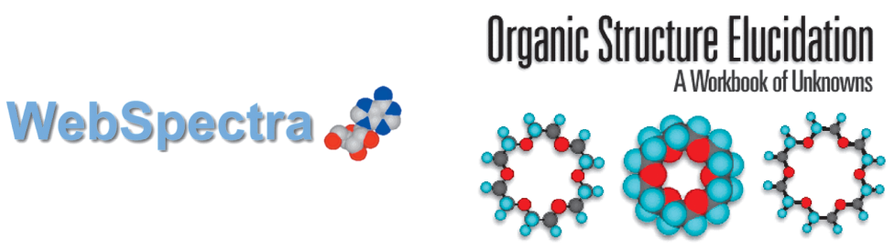


FIGURE 13.29

These two welcome screens open the door to almost 150 spectroscopy problems. The screens are used with permission of Professors Craig A. Merlic (*WebSpectra*) and Bradley D. Smith (*Organic Structure Elucidation*). See the text for the respective URLs.

A molecule absorbs that portion of electromagnetic radiation having a frequency that matches the energy difference between two vibrational energy levels. This radiation lies in the infrared region of the electromagnetic spectrum (Figure 13.1). The wavelength λ of the infrared region that is the most useful for structure determination is 2.5–16 μm, where 1 μm $= 10^{-6}$ m. Instead of wavelengths or SI units of frequency (s^{-1}), IR spectroscopy uses **wavenumbers,** which are equal to λ^{-1} and expressed in units of reciprocal centimeters (cm^{-1}). Thus, the region 2.5–16 μm corresponds to 4000–625 cm^{-1}. Wavenumbers are directly proportional to energy; 4000 cm^{-1} is the high-energy end of the scale for IR spectra, and 625 cm^{-1} is the low-energy end.

The energy difference between adjacent vibrational states is tens of thousands of times larger than what we saw for nuclear spin states in NMR.

PROBLEM 13.20

Vibrational frequencies are sensitive to isotopic replacement. The O—H stretching frequency is near 3600 cm^{-1}, but that of O—D is about 2630 cm^{-1}. Which are closer in energy, two adjacent O—H or two adjacent O—D vibrational states?

Most molecules have many more vibrational modes than the ones shown in this section for a single CH_2 group. Some involve relatively simple structural units, others a substantial fraction of the atoms in a molecule. Thus the infrared spectrum of each compound is unique, and superimposability of their IR spectra is convincing evidence that two substances are the same.

13.21 Infrared Spectra

IR spectra can be obtained regardless of the physical state of a sample—solid, liquid, gas, or dissolved in some solvent. If the sample is a liquid, a drop or two is placed between two sodium chloride disks, through which the IR beam is passed. Solids may be dissolved in a suitable solvent such as carbon tetrachloride or chloroform. More commonly, a solid sample is mixed with potassium bromide and the mixture pressed into a thin wafer, which is placed in the path of the IR beam. Newer instruments require little or no sample preparation.

The evolution of instrumentation in IR spectroscopy bears a similarity to that of NMR in that modern spectrometers collect data differently from the methods used by older instruments and convert it to a spectrum by Fourier transform (FT) methods. Older spectrometers used a prism or grating to separate the radiation from an IR source into its component wavelengths and compared the intensity of a beam after it had passed through a sample to that of a reference beam. A continuous sweep through the wavelength range, followed by plotting absorption or transmittance versus wavenumbers, furnished the spectrum. The present generation of IR spectrometers employs a technique known as attenuated total reflectance (ATR) coupled with FT data analysis. The whole range of vibrational states is sampled at once and transformed by Fourier analysis to give a spectrum formatted in the custom of traditional instruments. Recording an FT-IR spectrum takes about 1 min, compared with the 10–15 min needed for older instruments.

All IR spectra in this text were recorded without solvent using an ATR instrument.

Figure 13.30 orients us with respect to where we can expect to find IR absorptions for various structural units. Peaks in the range of 4000–1600 cm^{-1} are usually emphasized because this is the region in which the vibrations characteristic of particular functional groups are found. We'll look at some of these functional groups in more detail in Section 13.22. The region 1500–500 cm^{-1} is known as the **fingerprint region;** it is here that the pattern of peaks varies most from compound to compound.

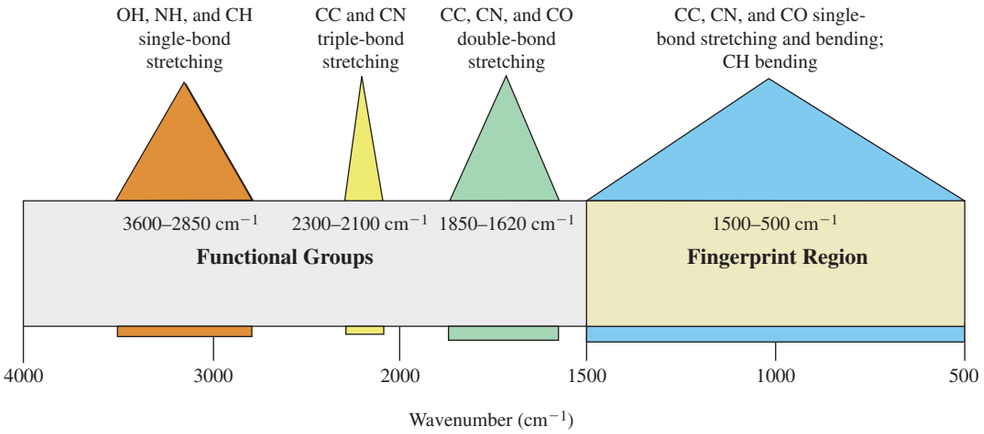


FIGURE 13.30

Structural units are commonly found in specific regions of the infrared spectrum.

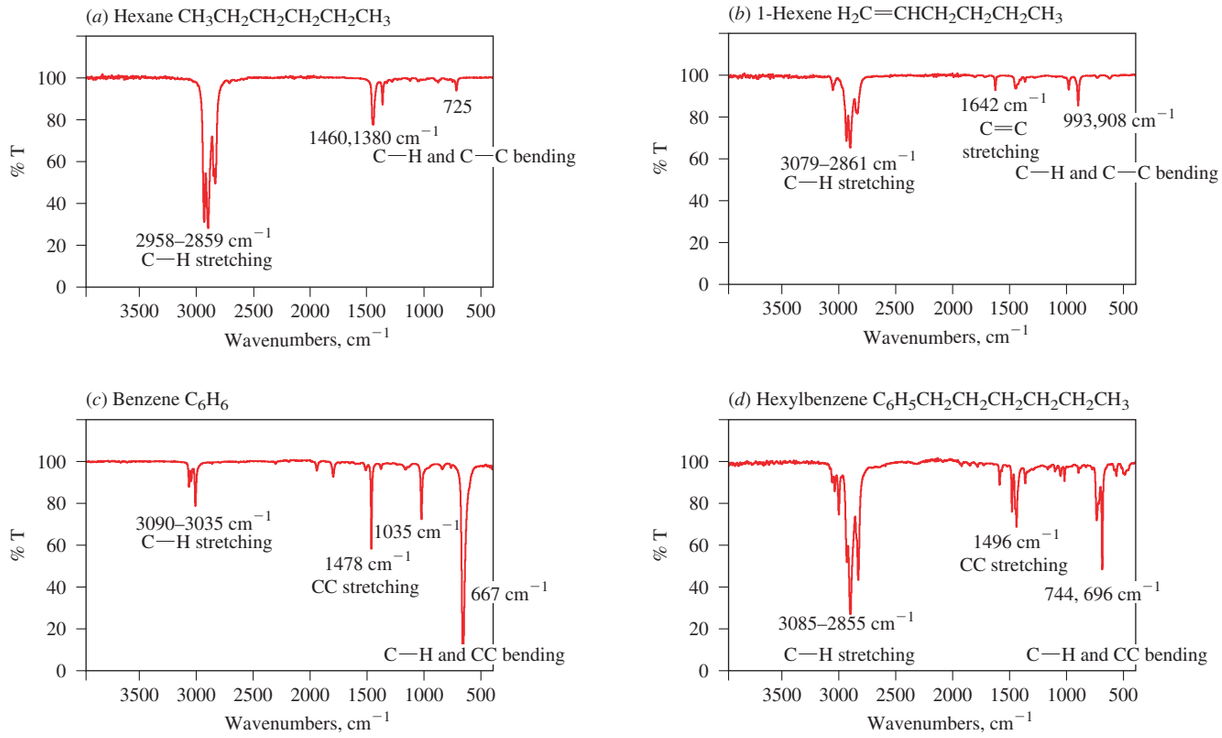


FIGURE 13.31

IR spectra of the hydrocarbons: (*a*) hexane, (*b*) 1-hexene, (*c*) benzene, and (*d*) hexylbenzene.

An IR spectrum usually contains more peaks that we can assign, or even need to assign. We gain information by associating selected absorptions with particular structural units and functional groups, as well as noting what structural units can be excluded from consideration because a key peak that characterizes it is absent from the spectrum.

Figure 13.31*a–d* shows the IR spectra of four hydrocarbons: hexane, 1-hexene, benzene, and hexylbenzene. Each spectrum consists of a series of absorption peaks of varying shape and intensity. Unlike NMR, in which intensities are related to the number of nuclei responsible for each signal, some IR vibrations give more intense peaks than others. To give an observable peak in the infrared, a vibration must produce a change in the molecular dipole moment, and peaks are usually more intense when they involve a bond between two atoms of different electronegativity. Consequently, C—C single-bond stretching vibrations normally give peaks of low intensity. The intensities of IR peaks are usually expressed in terms of percent transmittance (%T) and described as weak, medium, or strong.

All of the spectra in this text are displayed on a common %T scale to better show how peak intensities differ among various groups.

The IR spectrum of hexane (Figure 13.31*a*) is relatively simple, characterized by several peaks near 3000 cm^{-1} due to C—H stretching, along with weaker peaks at 1460, 1380, and 725 cm^{-1} from C—H and C—C bending.

Among the several ways in which the spectrum of the alkene 1-hexene differs from hexane (Figure 13.31*b*), the most useful from the perspective of structure determination is found in the C—H stretching region. Although all the peaks for C—H stretching in *hexane* appear below 3000 cm^{-1}, *1-hexene* exhibits a peak at 3079 cm^{-1}. Peaks for C—H stretching above 3000 cm^{-1} are characteristic of hydrogens bonded to sp^2-hybridized carbon. The IR spectrum of 1-hexene also displays a weak peak at 1642 cm^{-1} corresponding to its C=C stretching vibration. The peaks at 993 and 908 cm^{-1} in the spectrum of 1-hexene, absent in the spectrum of hexane, are bending vibrations of the $H_2C{=}C$ group.

PROBLEM 13.21

Ethylene lacks a peak in its IR spectrum for C=C stretching. Why?

Benzene (Figure 13.31*c*) has *only* sp^2-hybridized carbons, and *all* of its peaks for C—H stretching lie above 3000 cm^{-1}. CC stretching gives a weak peak at 1478 cm^{-1}. The most intense peak in benzene (667 cm^{-1}) results from a vibration in which one of the C—H bonds bends out of the plane of the ring.

The hexylbenzene spectrum (Figure 13.31*d*) bears similarities to those of hexane and benzene. Peaks for C—H stretching are found both above and below 3000 cm^{-1} for sp^2 and sp^3 C—H stretching, respectively. The benzene ring is represented in the weak peak at 1496 cm^{-1}. The three peaks between 750 and 690 cm^{-1} include bending modes for the hexyl chain and the ring.

Rarely can the structure of a hydrocarbon ever be determined by IR alone. Figure 13.31 alerts us to the fact that most organic compounds give IR spectra in which many of the peaks are due to the carbon skeleton and its attached hydrogens. Chemists pay less attention to these peaks now that ^1H and ^{13}C NMR are available to gain the same information. What IR does best—identifying the presence or absence of functional groups—is described in the following section.

13.22 Characteristic Absorption Frequencies

Table 13.4 lists the **characteristic absorption frequencies** (in wavenumbers) for a variety of structural units found in organic compounds. Generally, absorptions above 1500 cm^{-1} for functional groups such as OH, C=O, and C≡N are the easiest to assign and provide the most useful information.

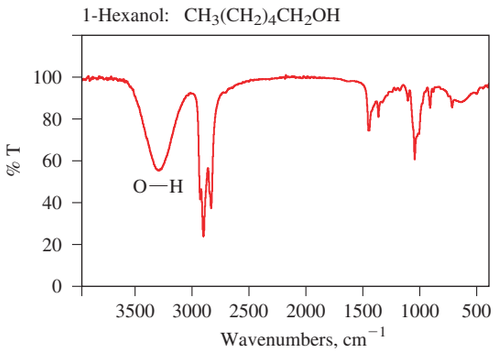
Some of these characteristic absorptions are reflected in the IR spectra of eight functional-group classes in Figure 13.32: alcohol, nitrile, carboxylic acid, ketone, ester, ether, amine, and amide. None of the specific compounds represented contains

TABLE 13.4 Infrared Absorption Frequencies of Some Common Structural Units

Structural unit	Frequency, cm^{-1}	Structural unit	Frequency, cm^{-1}
Stretching vibrations			
Single bonds		**Double bonds**	
—O—H (alcohols)	3200–3600		1620–1680
—O—H (carboxylic acids)	2500–3600		
	3350–3500		
		Aldehydes and ketones	1710–1750
sp C—H	3310–3320	Carboxylic acids	1700–1725
sp^2 C—H	3000–3100	Acid anhydrides	1800–1850 and 1740–1790
sp^3 C—H	2850–2950	Acyl halides	1770–1815
sp^2 C—O	1200	Esters	1730–1750
sp^3 C—O	1025–1200	Amides	1680–1700
		Triple bonds	
		—C≡C—	2100–2200
		—C≡N	2240–2280
Bending vibrations of diagnostic value			
Alkenes:		***Substituted derivatives of benzene:***	
$RCH{=}CH_2$	910, 990	Monosubstituted	730–770 and 690–710
$R_2C{=}CH_2$	890	Ortho-disubstituted	735–770
cis-RCH=CHR′	665–730	Meta-disubstituted	750–810 and 680–730
trans-RCH=CHR′	960–980	Para-disubstituted	790–840
$R_2C{=}CHR'$	790–840		

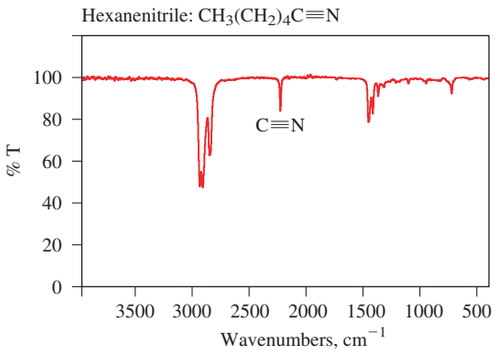
(*a*) **Alcohols:** A broad peak at 3200–3400 cm^{-1} is characteristic of hydrogen-bonded OH groups. In dilute solution, hydrogen bonding is less, and a sharp second peak for "free" OH groups appears near 3600 cm^{-1}.

The peak at 1070 cm^{-1} lies in the range given in Table 13.4 (1025–1200 cm^{-1}) for C—O stretching and can be assigned to it.

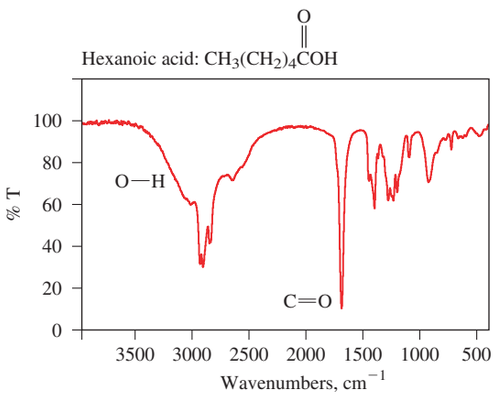


(*b*) **Nitriles:** The C≡N triple bond absorption is easily identifiable in the IR spectrum of a nitrile as a sharp peak of medium intensity at 2240–2280 cm^{-1}.

Very few other groups absorb in this region, the most notable being C≡C triple bonds (2100–2200 cm^{-1}).



(*c*) **Carboxylic acids:** Carboxylic acids have two characteristic absorptions: a broad peak for O—H stretching in the range 2500–3600 cm^{-1} and a strong peak for C=O stretching at 1700–1725 cm^{-1}.



(*d*) **Aldehydes and ketones:** As in other carbonyl-containing compounds, the C=O stretching vibration gives the strongest peak in the IR spectra of aldehydes and ketones.

The C=O stretching frequencies of aldehydes are similar to those of ketones.

The C—H stretch of the CH=O group in aldehydes appears as a pair of bands in the range 2700–2900 cm^{-1}.

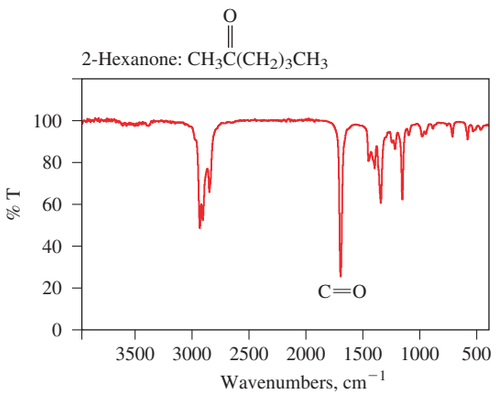
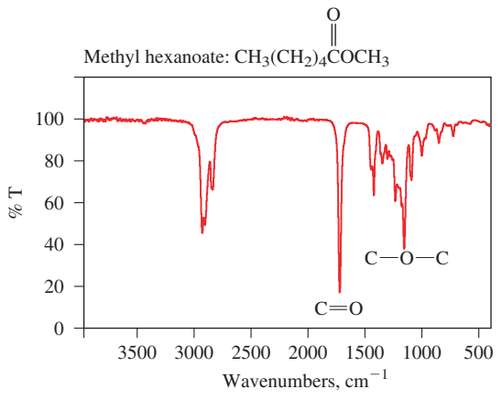


FIGURE 13.32

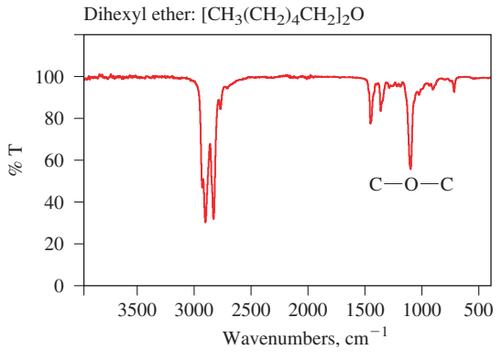
IR spectra of (*a*) 1-hexanol, (*b*) hexanenitrile, (*c*) hexanoic acid, (*d*) 2-hexanone, (*e*) methyl hexanoate, (*f*) dihexyl ether, (*g*) hexylamine, and (*h*) hexanamide.

(Continued)

(*e*) **Esters:** In addition to a strong C═O absorption (1730–1750 cm^{-1}), esters exhibit peaks for symmetric and antisymmetric C—O—C stretching at 1050–1300 cm^{-1}.



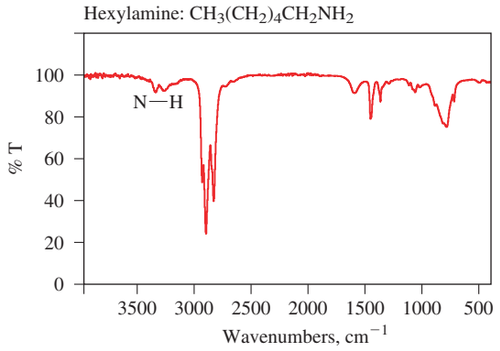
(*f*) **Ethers:** Peaks for C—O—C stretching in ethers appear in the range 1070–1150 cm^{-1}. Ethers of the type ROR′ where R and R′ are different have two peaks in this region.



(*g*) **Amines:** Primary amines (RNH_2) have two peaks for the NH_2 group in the 3300–3500 cm^{-1} region, one for symmetric and the other for antisymmetric N—H stretching. Secondary amines (RNHR′) have only one peak (3310–3350 cm^{-1}).

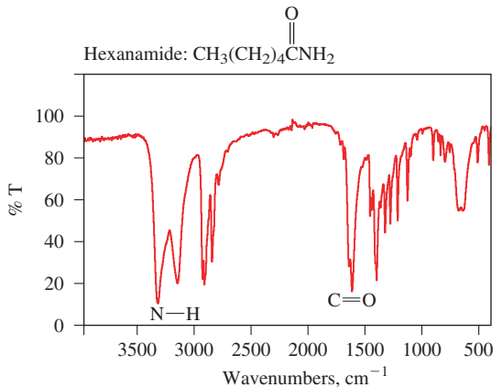
An NH bending peak at 650–900 cm^{-1} occurs in both RH_2 and RNHR′. Primary amines also have an NH bending absorption at 1580–1650 cm^{-1}.

C—N stretching peaks are found at 1020–1250 cm^{-1}.



(*h*) **Amides:** Amides of the type $RC(O)NH_2$ have peaks for both symmetric (3400 cm^{-1}) and antisymmetric (3500 cm^{-1}) N—H stretching.

The C═O absorption for amides appears at slightly lower frequency (1650–1700 cm^{-1}) than for ketones. Amides have a peak for NH_2 bending at a slightly lower frequency (1600–1650 cm^{-1}) than C═O.



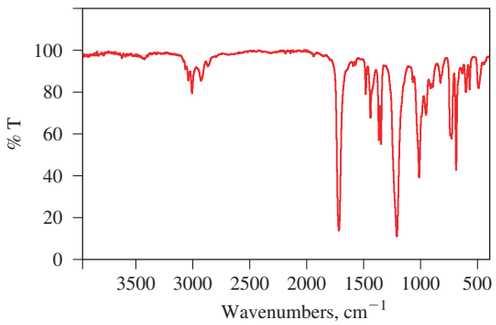
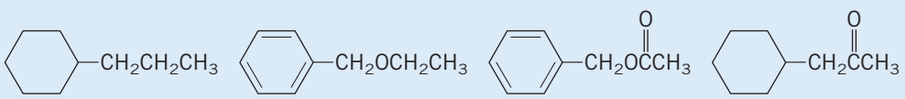


FIGURE 13.33
The IR spectrum of the unknown compound in Problem 13.22.

hydrogens bonded to sp^2-hybridized carbon, so all of the C—H absorbances lie below 3000 cm^{-1}. The compounds are related in that all have an unbranched six-carbon chain and, except for the peaks associated with the functional group, their spectra are similar, though not identical.

PROBLEM 13.22

Which of the following is the most likely structure of the compound characterized by the IR spectrum shown in Figure 13.33?



In later chapters, when families of compounds are discussed in detail, the IR frequencies associated with each type of functional group will be revisited.

13.23 Ultraviolet-Visible (UV-VIS) Spectroscopy

The main application of UV-VIS spectroscopy, which depends on transitions between electronic energy levels, is in identifying conjugated π electron systems.

Much greater energies separate electronic states than vibrational states. The energy required to promote an electron from one electronic state to the next lies in the visible and ultraviolet range of the electromagnetic spectrum (Figure 13.1). We usually identify radiation in the UV-VIS range by its wavelength in nanometers. Thus, the visible region corresponds to 400–800 nm. Red light is the low-energy (long wavelength) end of the visible spectrum, violet light the high-energy (short wavelength) end. Ultraviolet light lies beyond the visible spectrum with wavelengths in the 200–400-nm range.

An important enzyme in biological electron transport called *cytochrome P450* gets its name from its UV absorption. The "P" stands for "pigment" because it is colored, and the "450" corresponds to the 450-nm absorption of one of its derivatives.

Figure 13.34 shows the UV spectrum of the conjugated diene *cis,trans*-1,3-cyclooctadiene, measured in ethanol as the solvent. As is typical of most UV spectra, the absorption is rather broad and is often spoken of as a "band" rather than a "peak." The wavelength at an absorption maximum is referred to as the λ_{max} of the band. For 1,3-cyclooctadiene, λ_{max} is 230 nm. In addition to λ_{max}, UV-VIS bands are characterized by their **absorbance** (A), which is a measure of how much of the radiation that passes through the sample is absorbed. To correct for concentration and path length effects, absorbance is converted to **molar absorptivity** (ϵ) by dividing it by the concentration c in moles per liter and the path length l in centimeters.

$$\epsilon = \frac{A}{c \cdot l}$$

Molar absorptivity, when measured at λ_{max}, is cited as ϵ_{max}. It is normally expressed without units. Both λ_{max} and ϵ_{max} are affected by the solvent, which is therefore included

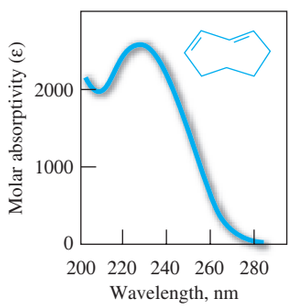
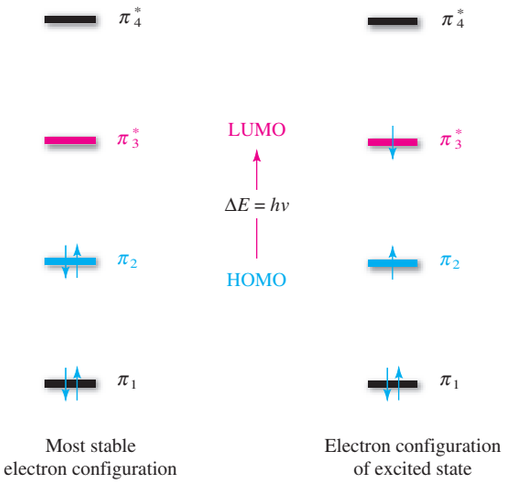


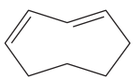
FIGURE 13.34
The UV spectrum of *cis,trans*-1,3-cyclooctadiene.

FIGURE 13.35

The $\pi \rightarrow \pi^*$ transition in *cis,trans*-1,3-cyclooctadiene involves excitation of an electron from the highest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO).



when reporting UV-VIS spectroscopic data. Thus, you might find a literature reference expressed in the form



cis,trans-1,3-Cyclooctadiene
$\lambda_{max}^{ethanol}$ 230 nm
$\epsilon_{max}^{ethanol}$ 2630

Figure 13.35 illustrates the transition between electronic energy states responsible for the 230-nm UV band of *cis,trans*-1,3-cyclooctadiene. Absorption of UV radiation excites an electron from the highest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO). In alkenes and polyenes, both the HOMO and LUMO are π type orbitals (rather than σ); the HOMO is the highest energy π orbital and the LUMO is the lowest energy π^* orbital. Exciting one of the π electrons from a bonding π orbital to an antibonding π^* orbital is referred to as a $\pi \rightarrow \pi^*$ transition.

PROBLEM 13.23

λ_{max} for the $\pi \rightarrow \pi^*$ transition in ethylene is 170 nm. Is the HOMO–LUMO energy difference in ethylene greater than or less than that of *cis,trans*-1,3-cyclooctadiene (230 nm)?

The HOMO–LUMO energy gap and, consequently, λ_{max} for the $\pi \rightarrow \pi^*$ transition varies with the substituents on the double bonds. The data in Table 13.5 illustrate two substituent effects: adding methyl substituents to the double bond, and extending

TABLE 13.5 Absorption Maxima of Some Representative Alkenes and Polyenes*

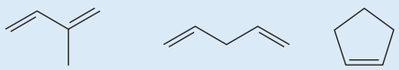
Compound	Structure	λ_{max} (nm)
Ethylene	$H_2C{=}CH_2$	170
2-Methylpropene	$H_2C{=}C(CH_3)_2$	188
1,3-Butadiene	$H_2C{=}CHCH{=}CH_2$	217
4-Methyl-1,3-pentadiene	$H_2C{=}CHCH{=}C(CH_3)_2$	234
2,5-Dimethyl-2,4-hexadiene	$(CH_3)_2C{=}CHCH{=}C(CH_3)_2$	241
(2*E*,4*E*,6*E*)-2,4,6-Octatriene	$CH_3CH{=}CHCH{=}CHCH{=}CHCH_3$	263
(2*E*,4*E*,6*E*,8*E*)-2,4,6,8-Decatetraene	$CH_3CH{=}CH(CH{=}CH)_2CH{=}CHCH_3$	299
(2*E*,4*E*,6*E*,8*E*,10*E*)-2,4,6,8,10-Dodecapentaene	$CH_3CH{=}CH(CH{=}CH)_3CH{=}CHCH_3$	326

*The value of λ_{max} refers to the longest wavelength $\pi \rightarrow \pi^*$ transition.

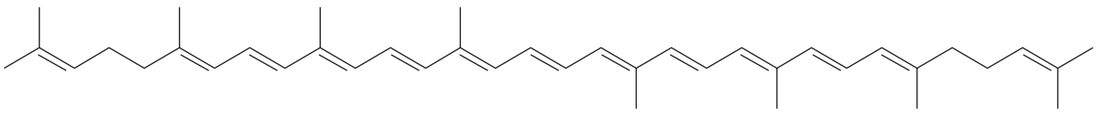
conjugation. Both cause λ_{max} to shift to longer wavelengths, but the effect of conjugation is the larger of the two. Based on data collected for many dienes it has been found that each methyl substituent on the double bonds causes a shift to longer wavelengths of about 5 nm, whereas extending the conjugation causes a shift of about 36 nm for each additional double bond.

PROBLEM 13.24

Which one of the C_5H_8 isomers shown has its λ_{max} at the longest wavelength?



A striking example of the effect of conjugation on light absorption occurs in *lycopene,* one of the pigments in ripe tomatoes. Lycopene has a conjugated system of 11 double bonds and absorbs *visible light.* It has several UV-VIS bands, each characterized by a separate λ_{max}. Its longest wavelength absorption is at 505 nm.



Lycopene

Many organic compounds such as lycopene are colored because their HOMO–LUMO energy gap is small enough that λ_{max} appears in the visible range of the spectrum. All that is required for a compound to be colored, however, is that it possess some absorption in the visible range. It often happens that a compound will have its λ_{max} in the UV region but that the peak is broad and extends into the visible. Absorption of the blue-to-violet components of visible light occurs, and the compound appears yellow.

A second type of absorption that is important in UV-VIS examination of organic compounds is the $n \rightarrow \pi^*$ transition of the carbonyl (C═O) group. One of the electrons in a lone-pair orbital of oxygen is excited to an antibonding orbital of the carbonyl group. The n in $n \rightarrow \pi^*$ identifies the electron as one of the nonbonded electrons of oxygen. This transition gives rise to relatively weak absorption peaks ($\epsilon_{max} < 100$) in the region 270–300 nm.

Don't confuse the n in $n \rightarrow \pi^*$ with the n of Hückel's rule.

The structural unit associated with an electronic transition in UV-VIS spectroscopy is called a **chromophore.** Chemists often use *model compounds* to help interpret UV-VIS spectra. An appropriate model is a simple compound of known structure that incorporates the chromophore suspected of being present in the sample. Because remote substituents do not affect λ_{max} of the chromophore, a strong similarity between the spectrum of the model compound and that of the unknown can serve to identify the kind of π electron system present in the sample. There is a substantial body of data concerning the UV-VIS spectra of a great many chromophores, as well as empirical correlations of substituent effects on λ_{max}. Such data are helpful when using UV-VIS spectroscopy as a tool for structure determination.

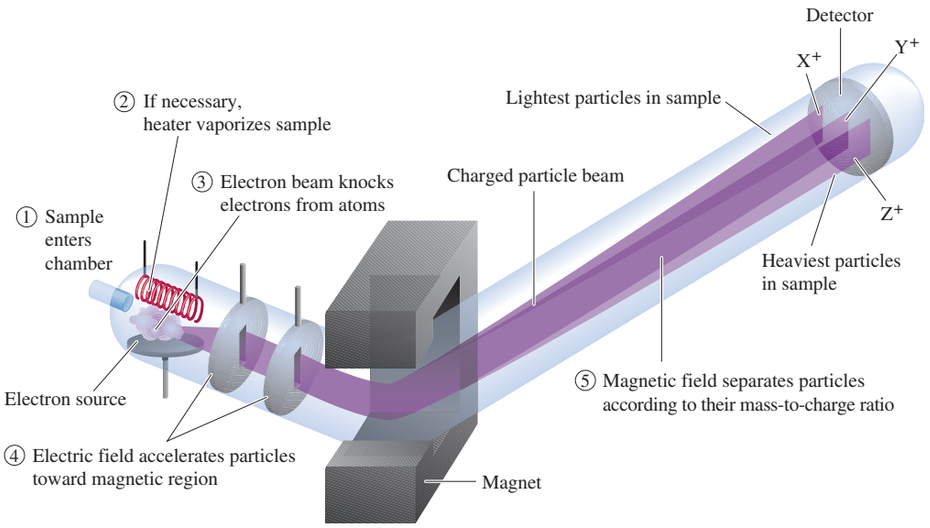
13.24 Mass Spectrometry

Mass spectrometry differs from the other instrumental methods discussed in this chapter in a fundamental way. It does not depend on the absorption of electromagnetic radiation but rather examines what happens when a molecule is bombarded with high-energy electrons. If an electron having an energy of about 10 electronvolts (10 eV = 230.5 kcal/mol) collides with an organic molecule, the energy transferred as a result of that collision is sufficient to dislodge one of the molecule's electrons.

$$\underset{\text{Molecule}}{A{:}B} + \underset{\text{Electron}}{e^-} \longrightarrow \underset{\text{Cation radical}}{A^{\overset{+}{\cdot}}B} + \underset{\text{Two electrons}}{2e^-}$$

FIGURE 13.36

Diagram of a mass spectrometer. Only positive ions are detected. The cation X^+ has the lowest mass-to-charge ratio and its path is deflected most by the magnet. The cation Z^+ has the highest mass-to-charge ratio and its path is deflected least. (Adapted, with permission, from M. Silberberg, *Chemistry,* McGraw-Hill Higher Education, 2003, p. 54.)



We say the molecule AB has been ionized by **electron impact.** The species that results, called the **molecular ion,** is positively charged and has an odd number of electrons—it is a **cation radical.** The molecular ion has the same mass (less the negligible mass of a single electron) as the molecule from which it is formed.

Although energies of about 10 eV are required, energies of about 70 eV are used. Electrons this energetic not only cause ionization of a molecule but also impart a large amount of energy to the molecular ion, enough energy to break chemical bonds. The molecular ion dissipates this excess energy by dissociating into smaller fragments. Dissociation of a cation radical produces a neutral fragment and a positively charged fragment.

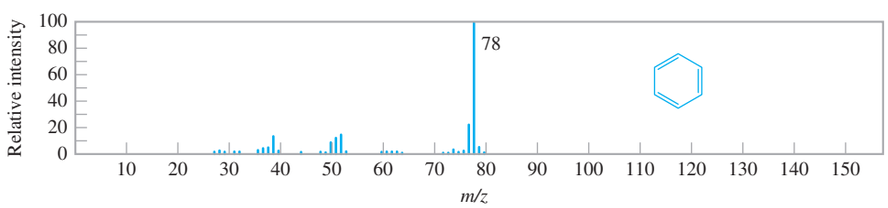
$$\underset{\text{Cation radical}}{A\overset{+}{\cdot}B} \longrightarrow \underset{\text{Cation}}{A^+} + \underset{\text{Radical}}{B\cdot}$$

Ionization and fragmentation produce a mixture of particles, some neutral and some positively charged. To understand what follows, we need to examine the design of an electron-impact mass spectrometer, shown in Figure 13.36. The sample is bombarded with 70-eV electrons, and the resulting positively charged ions (the molecular ion as well as fragment ions) are directed into an analyzer tube surrounded by a magnet. This magnet deflects the ions from their original trajectory, causing them to adopt a circular path, the radius of which depends on their mass-to-charge ratio *(m/z).* Ions of small *m/z* are deflected more than those of larger *m/z.* By varying either the magnetic field strength or the degree to which the ions are accelerated on entering the analyzer, ions of a particular *m/z* can be selectively focused through a narrow slit onto a detector, where they are counted. Scanning all *m/z* values gives the distribution of positive ions, called a **mass spectrum,** characteristic of a particular compound.

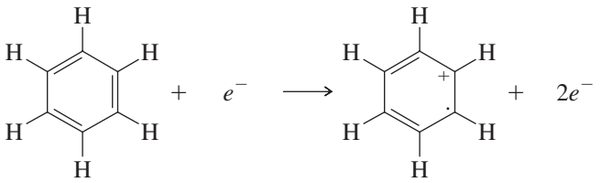
Modern mass spectrometers are interfaced with computerized data-handling systems capable of displaying the mass spectrum according to a number of different formats. Bar graphs on which relative intensity is plotted versus *m/z* are the most common. Figure 13.37 shows the mass spectrum of benzene in bar graph form.

FIGURE 13.37

The mass spectrum of benzene. The peak at $m/z = 78$ corresponds to the C_6H_6 molecular ion.

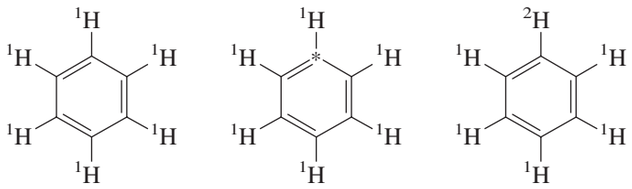


The mass spectrum of benzene is relatively simple and illustrates some of the information that mass spectrometry provides. The most intense peak in the mass spectrum is called the **base peak** and is assigned a relative intensity of 100. Ion abundances are proportional to peak intensities and are reported as intensities relative to the base peak. The base peak in the mass spectrum of benzene corresponds to the molecular ion (M^+) at $m/z = 78$.



Benzene does not undergo extensive fragmentation; none of the fragment ions in its mass spectrum are as abundant as the molecular ion.

There is a small peak one mass unit higher than M^+ in the mass spectrum of benzene. What is the origin of this peak? What we see in Figure 13.37 as a single mass spectrum is actually a superposition of the spectra of three isotopically distinct benzenes. Most of the benzene molecules contain only ^{12}C and ^{1}H and have a molecular mass of 78. Smaller proportions of benzene molecules contain ^{13}C in place of one of the ^{12}C atoms or ^{2}H in place of one of the protons. Both these species have a molecular mass of 79.



Not only the molecular ion peak but all the peaks in the mass spectrum of benzene are accompanied by a smaller peak one mass unit higher. Indeed, because all organic compounds contain carbon and most contain hydrogen, similar **isotopic clusters** will appear in the mass spectra of all organic compounds.

Isotopic clusters are especially apparent when atoms such as bromine and chlorine are present in an organic compound. The natural ratios of isotopes in these elements are

$$\frac{^{35}Cl}{^{37}Cl} = \frac{100}{32.7} \qquad \frac{^{79}Br}{^{81}Br} = \frac{100}{97.5}$$

Figure 13.38 presents the mass spectrum of chlorobenzene. There are two prominent molecular ion peaks, one at m/z 112 for $C_6H_5{}^{35}Cl$ and the other at m/z 114 for $C_6H_5{}^{37}Cl$. The peak at m/z 112 is three times as intense as the one at m/z 114.

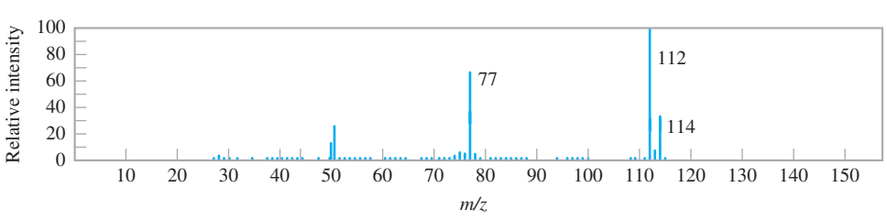


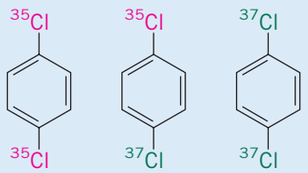
FIGURE 13.38
The mass spectrum of chlorobenzene.

PROBLEM 13.25

Knowing what to look for with respect to isotopic clusters can aid in interpreting mass spectra. How many peaks would you expect to see for the molecular ion in each of the following compounds? At what *m/z* values would these peaks appear? (Disregard the small peaks due to ^{13}C and ^{2}H.)

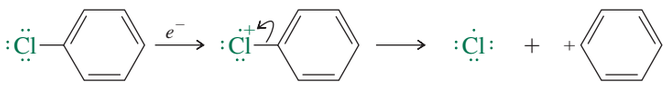
(a) *p*-Dichlorobenzene
(b) *o*-Dichlorobenzene
(c) *p*-Dibromobenzene
(d) *p*-Bromochlorobenzene

Sample Solution (a) The two isotopes of chlorine are ^{35}Cl and ^{37}Cl. There will be three isotopically different forms of *p*-dichlorobenzene present. They have the structures shown as follows. Each one will give an M^+ peak at a different value of *m/z*.



m/z 146 *m/z* 148 *m/z* 150

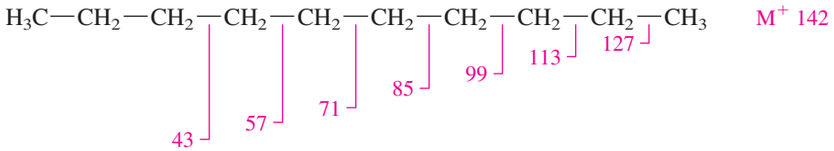
Unlike the case of benzene, in which ionization involves loss of a π electron from the ring, electron-impact-induced ionization of chlorobenzene involves loss of an electron from an unshared pair of chlorine. The molecular ion then fragments by carbon–chlorine bond cleavage.



Chlorobenzene — Molecular ion of chlorobenzene — Chlorine atom — Phenyl cation *m/z* 77

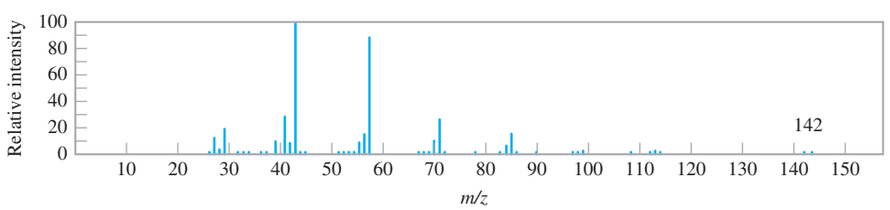
The peak at *m/z* 77 in the mass spectrum of chlorobenzene in Figure 13.38 is attributed to this fragmentation. Because there is no peak of significant intensity two atomic mass units higher, we know that the cation responsible for the peak at *m/z* 77 cannot contain chlorine.

Some classes of compounds are so prone to fragmentation that the molecular ion peak is very weak. The base peak in most unbranched alkanes, for example, is *m/z* 43, which is followed by peaks of decreasing intensity at *m/z* values of 57, 71, 85, and so on. These peaks correspond to cleavage of each possible carbon–carbon bond in the molecule. This pattern is evident in the mass spectrum of decane, depicted in Figure 13.39. The points of cleavage are indicated in the following diagram:



Many fragmentations in mass spectrometry proceed so as to form a stable carbocation, and the principles that we have developed regarding carbocation stability apply.

FIGURE 13.39
The mass spectrum of decane. The peak for the molecular ion is extremely small. The most prominent peaks arise by fragmentation.



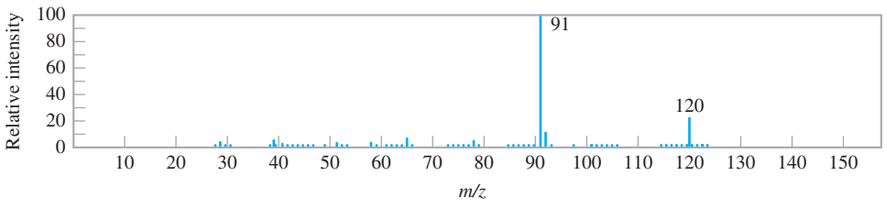
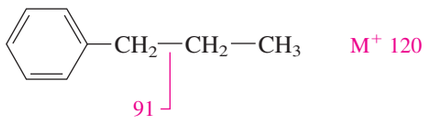


FIGURE 13.40
The mass spectrum of propylbenzene. The most intense peak is $C_7H_7^+$.

Alkylbenzenes of the type $C_6H_5CH_2R$ undergo cleavage of the bond to the benzylic carbon to give *m/z* 91 as the base peak. The mass spectrum in Figure 13.40 and the following fragmentation diagram illustrate this for propylbenzene.

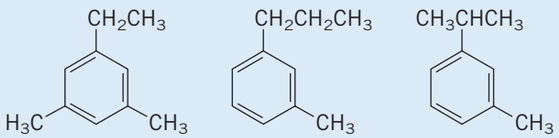


Although this cleavage is probably driven by the stability of benzyl cation, evidence has been obtained suggesting that tropylium cation, formed by rearrangement of benzyl cation, is actually the species responsible for the peak.

The structure of tropylium cation is given in Section 11.22.

PROBLEM 13.26

The base peak appears at *m/z* 105 for one of the following compounds and at *m/z* 119 for the other two. Match the compounds with the appropriate *m/z* values for their base peaks.

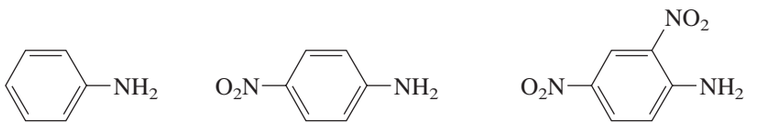


Understanding how molecules fragment upon electron impact permits a mass spectrum to be analyzed in sufficient detail to deduce the structure of an unknown compound. Thousands of compounds of known structure have been examined by mass spectrometry, and the fragmentation patterns that characterize different classes are well documented. As various groups are covered in subsequent chapters, aspects of their fragmentation behavior under conditions of electron impact will be described.

13.25 Molecular Formula as a Clue to Structure

As we have just seen, interpreting the fragmentation patterns in a mass spectrum in terms of a molecule's structural units makes mass spectrometry much more than just a tool for determining molecular weights. Nevertheless, even the molecular weight can provide more information than you might think.

A relatively simple example is the **nitrogen rule.** A molecule with an odd number of nitrogens has an odd molecular weight; a molecule with only C, H, and O or with an even number of nitrogens has an even molecular weight.



	Aniline (C_6H_7N)	*p*-Nitroaniline ($C_6H_6N_2O_2$)	2,4-Dinitroaniline ($C_6H_5N_3O_4$)
Molecular weight:	93	138	183

Gas Chromatography, GC/MS, and MS/MS

All of the spectra in this chapter (^{1}H NMR, ^{13}C NMR, IR, UV-VIS, and MS) were obtained using pure substances. It is much more common, however, to encounter an organic substance, either formed as the product of a chemical reaction or isolated from natural sources, as but one component of a mixture. Just as the last half of the twentieth century saw a revolution in the methods available for the *identification* of organic compounds, so too did it see remarkable advances in methods for their *separation* and *purification.*

Classical methods for separation and purification include fractional distillation of liquids and recrystallization of solids, and these two methods are routinely included in the early portions of laboratory courses in organic chemistry. Because they are capable of being adapted to work on a large scale, fractional distillation and recrystallization are the preferred methods for purifying organic substances in the pharmaceutical and chemical industries.

Some other methods are more appropriate when separating small amounts of material in laboratory-scale work and are most often encountered there. Indeed, it is their capacity to deal with exceedingly small quantities that is the strength of a number of methods that together encompass the various forms of **chromatography.** The first step in all types of chromatography involves adsorbing the sample onto some material called the *stationary phase.* Next, a second phase (the *mobile phase*) is allowed to move across the stationary phase. Depending on the properties of the two phases and the components of the mixture, the mixture is separated into its components according to the rate at which each is removed from the stationary phase by the mobile phase.

In **gas chromatography** (GC), the stationary phase consists of beads of an inert solid support coated with a high-boiling liquid, and the mobile phase is a gas, usually helium. Figure 13.41 shows a typical gas chromatograph. The sample is injected by syringe onto a heated block where a stream of helium carries it onto a coiled column packed with the stationary phase. The components of the mixture move through the column at different rates. They are said to have different *retention times.* Gas chromatography is also referred to as *gas–liquid partition chromatography,* because the technique depends on how different substances partition themselves between the gas phase (dispersed in the helium carrier gas) and the liquid phase (dissolved in the coating on the beads of solid support).

Typically the effluent from a gas chromatograph is passed through a detector, which feeds a signal to a recorder whenever a substance different from pure carrier gas leaves the column. Thus, one determines the number of components in a mixture by counting the number of peaks on a strip chart. It is good practice to carry out the analysis under different conditions by varying the liquid phase, the temperature, and the flow rate of the carrier gas so as to ensure that two substances have not eluted together and given a single peak under the original conditions. Gas chromatography can also be used to identify the components of a mixture by comparing their retention times with those of authentic samples.

In **gas chromatography/mass spectrometry** (GC/MS), the effluent from a gas chromatograph is passed into a mass spectrometer and a mass spectrum is taken every few milliseconds. Thus gas chromatography is used to separate a mixture, and mass spectrometry used to analyze it. GC/MS is a very powerful

—Continued

A second example concerns different compounds that have the same molecular weight, but different molecular formulas, such as heptane and cyclopropyl acetate.

Heptane (C_7H_{16}) Cyclopropyl acetate ($C_5H_8O_2$)

Because we normally round off molecular weights to whole numbers, both have a molecular weight of 100 and both have a peak for their molecular ion at *m/z* 100 in a typical mass spectrum. Recall, however, that mass spectra contain isotopic clusters that differ according to the isotopes present in each ion. Using the exact values for the major isotopes of C, H, and O, we calculate *exact masses* of *m/z* of 100.1253 and 100.0524 for the molecular ions of heptane (C_7H_{16}) and cyclopropyl acetate ($C_5H_8O_2$), respectively. As similar as these values are, it is possible to distinguish between them using a *high-resolution mass spectrometer.* This means that the exact mass of a molecular ion can usually be translated into a unique molecular formula.

You can't duplicate these molecular weights for C_7H_{16} and $C_5H_8O_2$ by using the atomic weights given in the periodic table. Those values are for the natural-abundance mixture of isotopes. The exact values are 12.00000 for ^{12}C, 1.00783 for ^{1}H, and 15.9949 for ^{16}O.

Once we have the molecular formula, it can provide information that limits the amount of trial-and-error structure writing we have to do. Consider, for example, heptane and its molecular formula of C_7H_{16}. We know immediately that the molecular formula belongs to an alkane because it corresponds to C_nH_{2n+2}.

What about a substance with the molecular formula C_7H_{14}? This compound cannot be an alkane but may be either a cycloalkane or an alkene, because both these classes

(Continued)

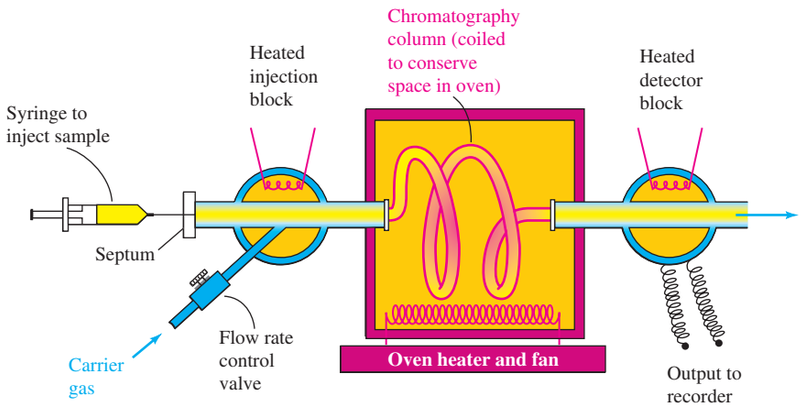


FIGURE 13.41

Diagram of a gas chromatograph. When connected to a mass spectrometer as in GC/MS, the effluent is split into two streams as it leaves the column. One stream goes to the detector, the other to the mass spectrometer. (Adapted, with permission, from H. D. Durst and G. W. Gokel, *Experimental Organic Chemistry,* 2nd ed., McGraw-Hill, New York, 1987.)

analytical technique. One of its more visible applications involves the testing of athletes for steroids, stimulants, and other performance-enhancing drugs. These drugs are converted in the body to derivatives called *metabolites,* which are then excreted in the urine. When the urine is subjected to GC/MS analysis, the mass spectra of its organic components are identified by comparison with the mass spectra of known metabolites stored in the instrument's computer. Using a similar procedure, the urine of newborn infants is monitored by GC/MS for metabolite markers of genetic disorders that can be treated if detected early in life. GC/MS is also used to detect and measure the concentration of halogenated hydrocarbons in drinking water.

Although GC/MS is the most widely used analytical method that combines a chromatographic separation with the identification power of mass spectrometry, it is not the only one. Chemists have coupled mass spectrometers to most of the instruments that are used to separate mixtures. Perhaps the ultimate is **mass spectrometry/mass spectrometry** (MS/MS), in which one mass spectrometer generates and separates the molecular ions of the components of a mixture and a second mass spectrometer examines their fragmentation patterns!

of hydrocarbons correspond to the general molecular formula C_nH_{2n}. *Any time a ring or a double bond is present in an organic molecule, its molecular formula has two fewer hydrogen atoms than that of an alkane with the same number of carbons.*

The relationship between molecular formulas, multiple bonds, and rings is referred to as the *index of hydrogen deficiency* and can be expressed by the equation:

$$\text{Index of hydrogen deficiency} = \tfrac{1}{2}\,(C_nH_{2n+2} - C_nH_x)$$

where C_nH_x is the molecular formula of the compound.

Other terms that mean the same thing as the index of hydrogen deficiency include *elements of unsaturation, sites of unsaturation,* and *the sum of double bonds and rings.*

A molecule that has a molecular formula of C_7H_{14} has an index of hydrogen deficiency of 1:

$$\text{Index of hydrogen deficiency} = \tfrac{1}{2}\,(C_7H_{16} - C_7H_{14})$$

$$\text{Index of hydrogen deficiency} = \tfrac{1}{2}\,(2) = 1$$

Thus, the compound has one ring or one double bond. It can't have a triple bond.

A molecule of molecular formula C_7H_{12} has four fewer hydrogens than the corresponding alkane. It has an index of hydrogen deficiency of 2 and can have two rings, two double bonds, one ring and one double bond, or one triple bond.

What about substances other than hydrocarbons, 1-heptanol $[CH_3(CH_2)_5CH_2OH]$, for example? Its molecular formula ($C_7H_{16}O$) contains the same carbon-to-hydrogen ratio as heptane and, like heptane, it has no double bonds or rings. Cyclopropyl acetate ($C_5H_8O_2$), the structure of which was given at the beginning of this section, has one ring

A more detailed discussion of hydrogen deficiency can be found in the May 1995 issue of the *Journal of Chemical Education,* pp. 245–248.

and one double bond and an index of hydrogen deficiency of 2. *Oxygen atoms have no effect on the index of hydrogen deficiency.*

A halogen substituent, like hydrogen, is monovalent and when present in a molecular formula is treated as if it were hydrogen for counting purposes.

How does one distinguish between rings and double bonds? This additional piece of information comes from catalytic hydrogenation experiments in which the amount of hydrogen consumed is measured exactly. Each of a molecule's double bonds consumes one molar equivalent of hydrogen, but rings are unaffected. For example, a substance with a hydrogen deficiency of 5 that takes up 3 mol of hydrogen must have two rings.

PROBLEM 13.27

How many rings are present in each of the following compounds? Each consumes 2 mol of hydrogen on catalytic hydrogenation.

(a) $C_{10}H_{18}$
(b) C_8H_8
(c) $C_8H_8Cl_2$
(d) C_8H_8O
(e) $C_8H_{10}O_2$
(f) C_8H_9ClO

Sample Solution (a) The molecular formula $C_{10}H_{18}$ contains four fewer hydrogens than the alkane having the same number of carbon atoms ($C_{10}H_{22}$). Therefore, the index of hydrogen deficiency of this compound is 2. Because it consumes two molar equivalents of hydrogen on catalytic hydrogenation, it must have either a triple bond or two double bonds and no rings.

13.26 SUMMARY

Section 13.1 Structure determination in modern organic chemistry relies heavily on instrumental methods. Several of the most widely used ones depend on the absorption of electromagnetic radiation.

Section 13.2 Absorption of electromagnetic radiation causes a molecule to be excited from its most stable state (the *ground* state) to a higher energy state (an *excited* state).

Spectroscopic method	*Transitions between*
Nuclear magnetic resonance	Spin states of an atom's nucleus
Infrared	Vibrational states
Ultraviolet-visible	Electronic states

Mass spectrometry is not based on absorption of electromagnetic radiation, but monitors what happens when a substance is ionized by collision with a high-energy electron.

^{1}H Nuclear Magnetic Resonance Spectroscopy

Section 13.3 In the presence of an external magnetic field, the $+\frac{1}{2}$ and $-\frac{1}{2}$ nuclear spin states of a proton have slightly different energies.

Section 13.4 The energy required to "flip" the spin of a proton from the lower energy spin state to the higher state depends on the extent to which a nucleus is shielded from the external magnetic field by the molecule's electrons.

Section 13.5 Protons in different environments within a molecule have different **chemical shifts;** that is, they experience different degrees of shielding. Chemical shifts (δ) are reported in parts per million (ppm) from tetramethylsilane (TMS). Table 13.1 lists characteristic chemical shifts for various types of protons.

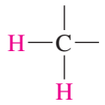
Section 13.6 In addition to *chemical shift,* a ^{1}H NMR spectrum provides structural information based on:

Number of signals, which tells how many different kinds of protons there are

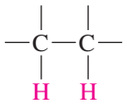
Integrated areas, which tells the ratios of the various kinds of protons

Splitting pattern, which gives information about the number of protons that are within two or three bonds of the one giving the signal

Section 13.7 **Spin–spin splitting** of NMR signals results from coupling of the nuclear spins that are separated by two bonds (*geminal coupling*) or three bonds (*vicinal coupling*).



Geminal hydrogens are separated by two bonds



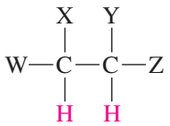
Vicinal hydrogens are separated by three bonds

In the simplest cases, the number of peaks into which a signal is split is equal to $n + 1$, where n is the number of protons to which the proton in question is coupled. *Protons that have the same chemical shift do not split each other's signal.*

Section 13.8 The methyl protons of an ethyl group appear as a *triplet* and the methylene protons as a *quartet* in compounds of the type CH_3CH_2X.

Section 13.9 The methyl protons of an isopropyl group appear as a *doublet* and the methine proton as a *septet* in compounds of the type $(CH_3)_2CHX$.

Section 13.10 A *doublet of doublets* characterizes the signals for the protons of the type shown (where W, X, Y, and Z are not H or atoms that split H themselves).



Section 13.11 Complicated splitting patterns can result when a proton is unequally coupled to two or more protons that are different from one another.

Section 13.12 Splitting resulting from coupling to the O—H proton of alcohols is not normally observed, because the hydroxyl proton undergoes rapid intermolecular exchange with other alcohol molecules, which "decouples" it from other protons in the molecule.

Section 13.13 Many processes such as conformational changes take place faster than they can be detected by NMR. Consequently, NMR provides information about the *average* environment of a proton. For example, cyclohexane gives a single peak for its 12 protons even though, at any instant, 6 are axial and 6 are equatorial.

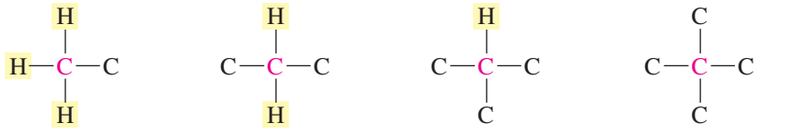
^{13}C Nuclear Magnetic Resonance Spectroscopy

Section 13.14 ^{13}C has a nuclear spin of $\pm\frac{1}{2}$ but only about 1% of all the carbons in a sample are ^{13}C. Nevertheless, high-quality ^{13}C NMR spectra can be obtained by pulse FT techniques and are a useful complement to ^{1}H NMR spectra.

Section 13.15 ^{13}C signals are more widely separated from one another than proton signals, and ^{13}C NMR spectra are relatively easy to interpret. Table 13.3 gives chemical shift values for carbon in various environments.

Section 13.16 ^{13}C NMR spectra are rarely integrated because the pulse FT technique distorts the signal intensities.

Section 13.17 Carbon signals normally appear as singlets, but several techniques are available that allow one to distinguish among the various kinds of carbons shown.



3 attached hydrogens (Primary carbon) | 2 attached hydrogens (Secondary carbon) | 1 attached hydrogen (Tertiary carbon) | no attached hydrogens (Quaternary carbon)

Section 13.18 One of the special techniques for distinguishing carbons according to the number of their attached hydrogens is called **DEPT.** A series of NMR measurements using different pulse sequences gives normal, nulled, and inverted peaks that allow assignment of primary, secondary, tertiary, and quaternary carbons.

Section 13.19 2D NMR techniques are enhancements that are sometimes useful in gaining additional structural information. A ^{1}H-^{1}H COSY spectrum reveals which protons are spin-coupled to other protons, which helps in determining connectivity. A HETCOR spectrum shows the C—H connections by correlating ^{13}C and ^{1}H chemical shifts.

Infrared Spectroscopy

Section 13.20 IR spectroscopy probes molecular structure by examining transitions between quantized vibrational energy levels using electromagnetic radiation in the 625–4000-cm^{-1}range, where cm^{-1} are units of **wavenumbers,** defined as λ^{-1}. Wavenumbers are proportional to frequency. The simplest vibration is the stretching of the bond between two atoms, but more complex vibrations can involve movement of many of a molecule's atoms.

Section 13.21 IR spectra are commonly regarded as consisting of a functional-group region (1500–4000 cm^{-1}) and a fingerprint region (500–1500 cm^{-1}). Included in the functional-group region are absorptions due to C—H stretching. In general, C—H stretching frequencies lie below 3000 cm^{-1} for sp^3-hybridized carbon and above 3000 cm^{-1} for sp^2. The fingerprint region is used less for determining structure than for verifying whether two compounds are identical or not.

Section 13.22 Functional-group identification is the main contribution of IR spectroscopy to organic chemistry. Various classes of compounds exhibit peaks at particular frequencies characteristic of the functional groups they contain. (Table 13.4).

Ultraviolet-Visible Spectroscopy

Section 13.23 Transitions between electronic energy levels involving electromagnetic radiation in the 200–800-nm range form the basis of UV-VIS spectroscopy. The absorption peaks tend to be broad but are often useful in indicating the presence of particular π electron systems within a molecule.

Mass Spectrometry

Section 13.24 Mass spectrometry exploits the information obtained when a molecule is ionized by electron impact and then dissociates to smaller fragments. Positive ions are separated and detected according to their mass-to-charge

(*m/z*) ratio. By examining the fragments and by knowing how classes of molecules dissociate on electron impact, one can deduce the structure of a compound. Mass spectrometry is quite sensitive; as little as 10^{-9} g of compound is sufficient for analysis.

Section 13.25 A compound's molecular formula gives information about the number of double bonds and rings it contains and is a useful complement to spectroscopic methods of structure determination.

PROBLEMS

13.28 Each of the following compounds is characterized by a ^{1}H NMR spectrum that consists of only a single peak having the chemical shift indicated. Identify each compound.

(a) C_8H_{18}; δ 0.9
(b) C_5H_{10}; δ 1.5
(c) C_8H_8; δ 5.8
(d) C_4H_9Br; δ 1.8
(e) $C_2H_4Cl_2$; δ 3.7
(f) $C_2H_3Cl_3$; δ 2.7
(g) $C_5H_8Cl_4$; δ 3.7
(h) $C_{12}H_{18}$; δ 2.2
(i) $C_3H_6Br_2$; δ 2.6

13.29 Each of the following compounds is characterized by a ^{1}H NMR spectrum that consists of two peaks, both singlets, having the chemical shifts indicated. Identify each compound.

(a) C_6H_8; δ 2.7 (4H) and 5.6 (4H)
(b) $C_5H_{11}Br$; δ 1.1 (9H) and 3.3 (2H)
(c) $C_6H_{12}O$; δ 1.1 (9H) and 2.1 (3H)
(d) $C_6H_{10}O_2$; δ 2.2 (6H) and 2.7 (4H)

13.30 Deduce the structure of each of the following compounds on the basis of their ^{1}H NMR spectra and molecular formulas:

(a) C_8H_{10}; δ 1.2 (triplet, 3H); δ 2.6 (quartet, 2H); δ 7.1 (broad singlet, 5H)
(b) $C_{10}H_{14}$; δ 1.3 (singlet, 9H); δ 7.0 to 7.5 (multiplet, 5H)
(c) C_6H_{14}; δ 0.8 (doublet, 12H); δ 1.4 (septet, 2H)
(d) C_6H_{12}; δ 0.9 (triplet, 3H); δ 1.6 (singlet, 3H); δ 1.7 (singlet, 3H); δ 2.0 (pentet, 2H); δ 5.1 (triplet, 1H)
(e) $C_4H_6Cl_4$; δ 3.9 (doublet, 4H); δ 4.6 (triplet, 2H)
(f) $C_4H_6Cl_2$; δ 2.2 (singlet, 3H); δ 4.1 (doublet, 2H); δ 5.7 (triplet, 1H)
(g) C_3H_7ClO; δ 2.0 (pentet, 2H); δ 2.8 (singlet, 1H); δ 3.7 (triplet, 2H); δ 3.8 (triplet, 2H)
(h) $C_{14}H_{14}$; δ 2.9 (singlet, 4H); δ 7.1 (broad singlet, 10H)

13.31 From among the isomeric compounds of molecular formula C_4H_9Cl, choose the one having a ^{1}H NMR spectrum that

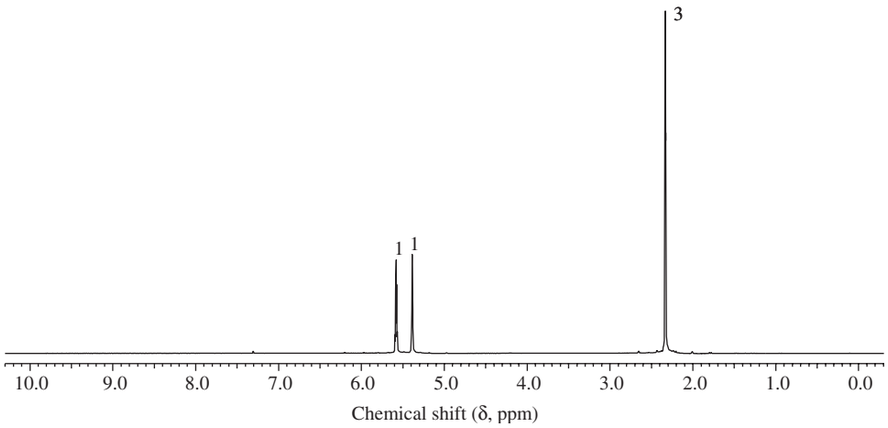
(a) Contains only a single peak
(b) Has several peaks including a doublet at δ 3.4
(c) Has several peaks including a triplet at δ 3.5
(d) Has several peaks including two distinct three-proton signals, one of them a triplet at δ 1.0 and the other a doublet at δ 1.5

13.32 Identify the C_3H_5Br isomers on the basis of the following information:

(a) Isomer A has the ^{1}H NMR spectrum shown in Figure 13.42.
(b) Isomer B has three peaks in its ^{13}C NMR spectrum: δ 32.6 (CH_2); 118.8 (CH_2); and 134.2 (CH).
(c) Isomer C has two peaks in its ^{13}C NMR spectrum: δ 12.0 (CH_2) and 16.8 (CH). The peak at lower field is only half as intense as the one at higher field.

FIGURE 13.42

The 200-MHz ^{1}H NMR spectrum of isomer A (Problem 13.32a).



13.33 Identify each of the $C_4H_{10}O$ isomers on the basis of their ^{13}C NMR spectra:

(a) δ 18.9 (CH_3) (two carbons)
δ 30.8 (CH) (one carbon)
δ 69.4 (CH_2) (one carbon)

(b) δ 10.0 (CH_3)
δ 22.7 (CH_3)
δ 32.0 (CH_2)
δ 69.2 (CH)

(c) δ 31.2 (CH_3) (three carbons)
δ 68.9 (C) (one carbon)

13.34 Identify the C_6H_{14} isomers on the basis of their ^{13}C NMR spectra:

(a) δ 19.1 (CH_3)
δ 33.9 (CH)

(b) δ 13.7 (CH_3)
δ 22.8 (CH_2)
δ 31.9 (CH_2)

(c) δ 11.1 (CH_3)
δ 18.4 (CH_3)
δ 29.1 (CH_2)
δ 36.4 (CH)

(d) δ 8.5 (CH_3)
δ 28.7 (CH_3)
δ 30.2 (C)
δ 36.5 (CH_2)

(e) δ 14.0 (CH_3)
δ 20.5 (CH_2)
δ 22.4 (CH_3)
δ 27.6 (CH)
δ 41.6 (CH_2)

13.35 A compound (C_4H_6) has two signals of approximately equal intensity in its ^{13}C NMR spectrum; one is a CH_2 carbon at δ 30.2, the other a CH at δ 136. Identify the compound.

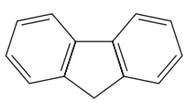
13.36 A compound ($C_3H_7ClO_2$) exhibited three peaks in its ^{13}C NMR spectrum at δ 46.8 (CH_2), δ 63.5 (CH_2), and δ 72.0 (CH). Excluding compounds that have Cl and OH on the same carbon, which are unstable, what is the most reasonable structure for this compound?

13.37 From among the compounds chlorobenzene, *o*-dichlorobenzene, and *p*-dichlorobenzene, choose the one that

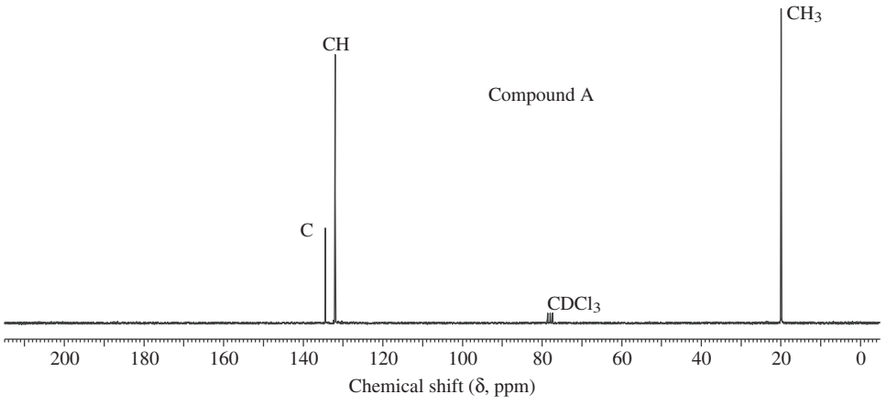
(a) Gives the simplest ^{1}H NMR spectrum
(b) Gives the simplest ^{13}C NMR spectrum
(c) Has three peaks in its ^{13}C NMR spectrum
(d) Has four peaks in its ^{13}C NMR spectrum

Problem 13.38 is taken from an experiment designed for introductory organic chemistry laboratories described in the March, 2003, issue of the *Journal of Chemical Education,* pp. 311–312.

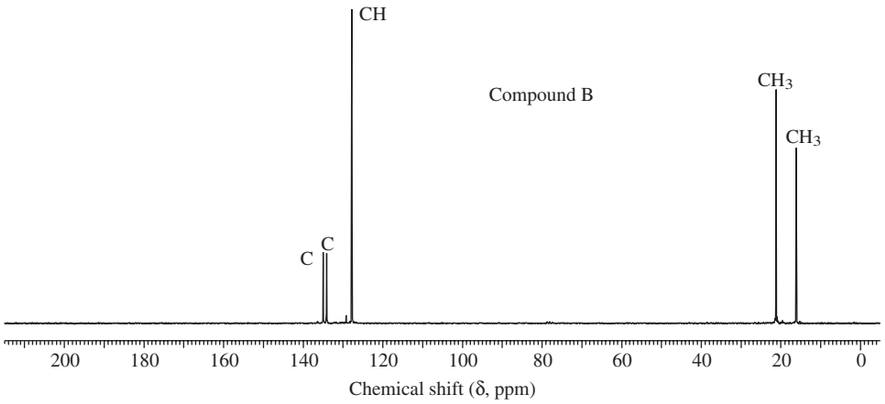
13.38 The ^{1}H NMR spectrum of fluorene has signals at δ 3.8 and δ 7.2–7.7 in a 1:4 ratio. After heating with $NaOCH_3$ in CH_3OD at reflux for 15 minutes the signals at δ 7.2–7.7 remained, but the one at δ 3.8 had disappeared. Suggest an explanation and write a mechanism for this observation.



Fluorene



(*a*)



(*b*)

FIGURE 13.43
The ^{13}C NMR spectrum of (*a*) compound A and (*b*) compound B, isomers of $C_{10}H_{14}$ (Problem 13.39).

13.39 Compounds A and B are isomers of molecular formula $C_{10}H_{14}$. Identify each one on the basis of the ^{13}C NMR spectra presented in Figure 13.43.

13.40 Identify the hydrocarbon that gives the IR spectrum shown in Figure 13.44 and has an M^+ peak at *m/z* 102 in its mass spectrum.

13.41 A compound ($C_8H_{10}O$) has the IR and ^1H NMR spectra presented in Figure 13.45. What is its structure?

13.42 Deduce the structure of a compound having the mass, IR, and ^1H NMR spectra presented in Figure 13.46 (page 573).

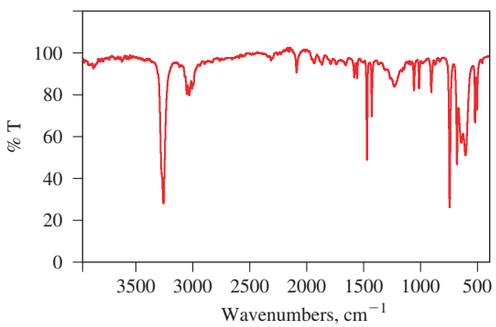
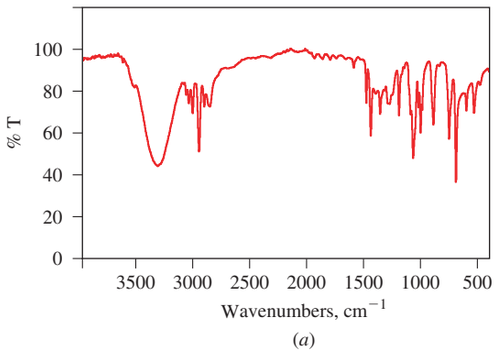


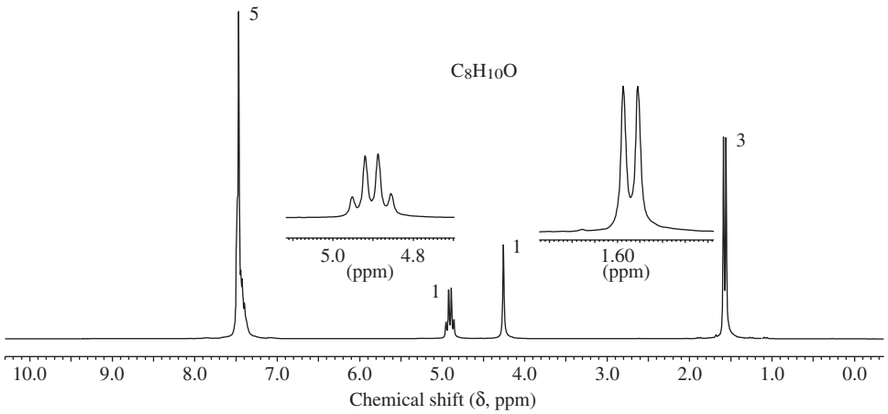
FIGURE 13.44
The IR spectrum of the hydrocarbon in Problem 13.40.

FIGURE 13.45

(*a*) IR and (*b*) 200-MHz ^{1}H NMR spectra of a compound $C_8H_{10}O$ (Problem 13.41).



(*a*)



(*b*)

13.43 Figure 13.47 (page 574) presents IR, ^{1}H NMR, ^{13}C NMR, and mass spectra for a particular compound. What is it?

13.44 Which would you predict to be more shielded, the inner or outer protons of [24]annulene?

13.45 ^{19}F is the only isotope of fluorine that occurs naturally, and it has a nuclear spin of $\pm\frac{1}{2}$.

(a) Into how many peaks will the proton signal in the ^{1}H NMR spectrum of methyl fluoride be split?

(b) Into how many peaks will the fluorine signal in the ^{19}F NMR spectrum of methyl fluoride be split?

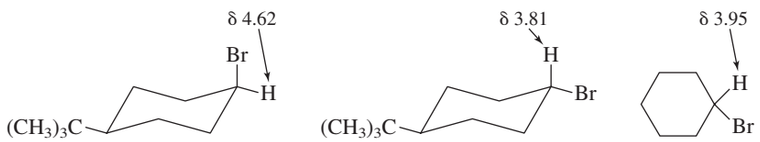
(c) The chemical shift of the protons in methyl fluoride is δ 4.3. Given that the geminal ^{1}H—^{19}F coupling constant is 45 Hz, specify the δ values at which peaks are observed in the proton spectrum of this compound at 200 MHz.

13.46 ^{31}P is the only phosphorus isotope present at natural abundance and has a nuclear spin of $\pm\frac{1}{2}$. The ^{1}H NMR spectrum of trimethyl phosphite, $(CH_3O)_3P$, exhibits a doublet for the methyl protons with a splitting of 12 Hz.

(a) Into how many peaks is the ^{31}P signal split?

(b) What is the difference in chemical shift (in hertz) between the lowest and highest field peaks of the ^{31}P multiplet?

13.47 We noted in Section 13.13 that an NMR spectrum is an average spectrum of the conformations populated by a molecule. From the following data, estimate the percentages of axial and equatorial bromine present in bromocyclohexane.



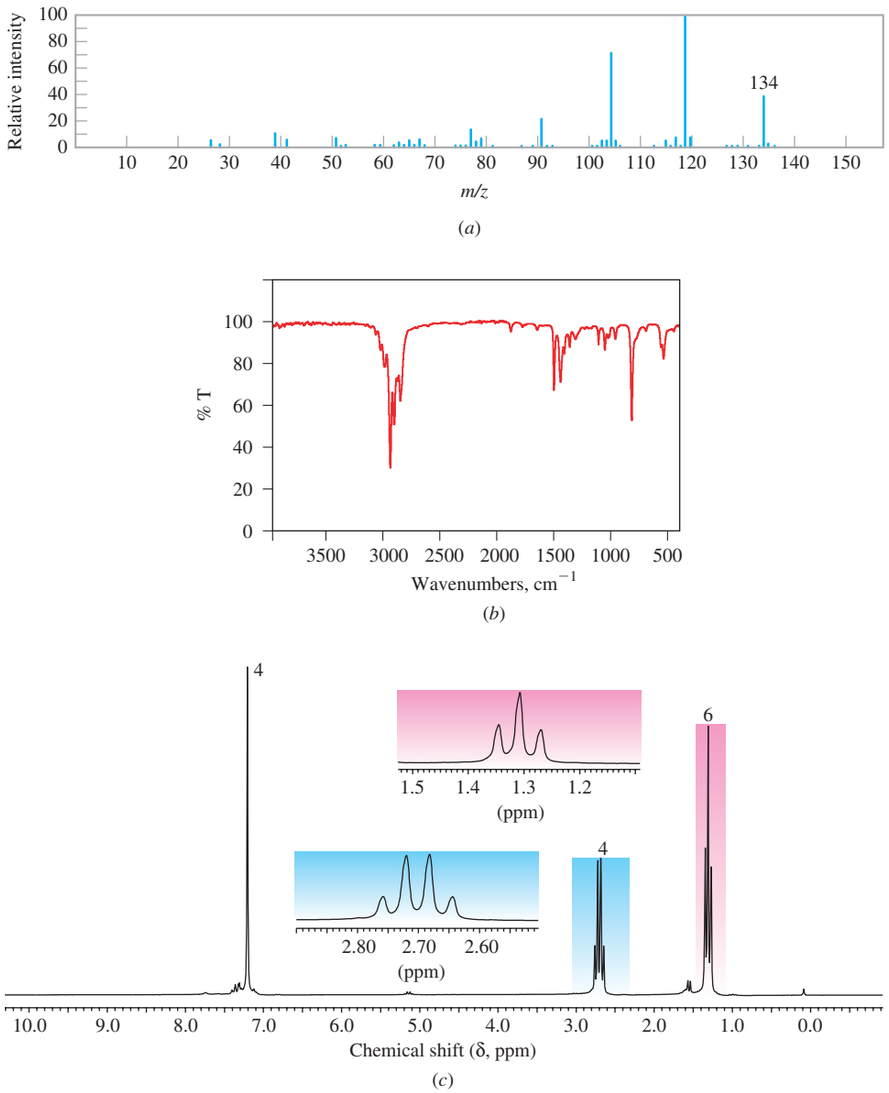


FIGURE 13.46
(*a*) Mass, (*b*) IR, and (*c*) 200-MHz ^{1}H NMR spectra of a compound (Problem 13.42).

13.48 IR spectroscopy is an inherently "faster" method than NMR, and an IR spectrum is a superposition of the spectra of the various conformations, rather than an average of them. When 1,2-dichloroethane is cooled below its freezing point, the crystalline material gives an IR spectrum consistent with a single species that has a center of symmetry. At room temperature, the IR spectrum of liquid 1,2-dichloroethane retains the peaks present in the solid, but includes new peaks as well. Explain these observations.

13.49 *Microwave spectroscopy* is used to probe transitions between rotational energy levels in molecules.

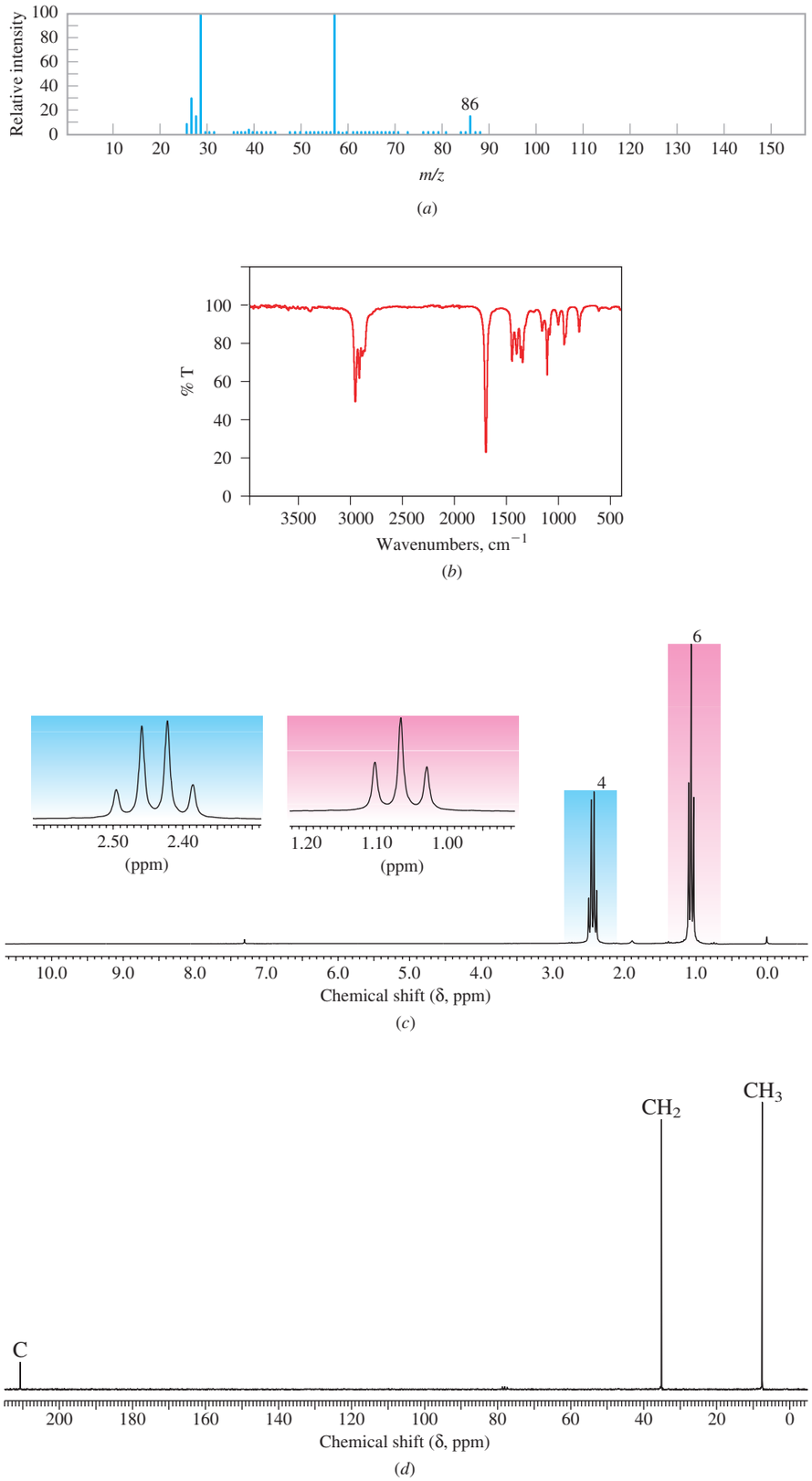
(a) A typical wavelength for microwaves is 10^{-2} m, compared with 10^{-5} m for IR radiation. Is the energy separation between rotational energy levels in a molecule greater or less than the separation between vibrational energy levels?

(b) Microwave ovens cook by heating the water in the food. Absorption of microwave radiation by the water excites it to a higher rotational energy state, and it gives off this excess energy as heat when it relaxes to its ground state. Why are vibrational and electronic energy states not involved in this process?

13.50 The peak in the UV-VIS spectrum of acetone [$(CH_3)_2C{=}O$] corresponding to the $n \rightarrow \pi^*$ transition appears at 279 nm when hexane is the solvent, but shifts to 262 nm in water. Which is more polar, the ground electronic state or the excited state?

FIGURE 13.47

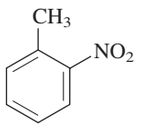
(*a*) Mass, (*b*) IR, (*c*) 200-MHz ^{1}H NMR, and (*d*) ^{13}C NMR spectra for the compound of Problem 13.43.



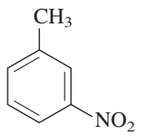
DESCRIPTIVE PASSAGE AND INTERPRETIVE PROBLEMS 13

Calculating Aromatic ^{13}C Chemical Shifts

Although chemical-shift tables such as Table 13.3 (Section 13.15) are useful guides to where we expect to find peaks for various structural units, they quote ranges rather than specific values. The value cited for aromatic ring carbons, for example, is 110–175 ppm. Information this general cannot discriminate between isomers such as *o*- and *m*-nitrotoluene solely on the basis of their ^{13}C NMR spectra. Both isomers have six nonequivalent ring carbons and similar, though not identical, ^{13}C NMR spectra.



o-Nitrotoluene



m-Nitrotoluene

This passage describes a simple method for predicting chemical shifts for carbons on a substituted benzene ring, based on the ^{13}C chemical shift of benzene (δ 128.5) as a standard. Substituents increase (+) or decrease (−) that value for the carbon to which they are attached and the carbons ortho, meta, and para to it. The direction (+ or −) and size (Δ) of substituent effects are determined experimentally; values for some common substituents are given in Table 13.6. When using this table, C-1 refers specifically to the carbon for which the chemical shift is being calculated without regard to its IUPAC number.

TABLE 13.6 Incremental ^{13}C Chemical Shift Effects of Substituents (δ), ppm*

Substituent	$\Delta_{C\text{-}1}$	Δ_{ortho}	Δ_{meta}	Δ_{para}
H	0	0	0	0
CH_3	+9.1	+0.7	−0.1	−3.0
Cl	+5.3	+0.4	+1.4	−1.9
OH	+28.8	−12.8	+1.4	−7.4
OCH_3	+33.5	−14.4	+1.0	−7.7
NH_2	+18.2	−13.4	+0.8	−10.0
CO_2CH_3	+2.0	+1.2	−0.1	+4.3
C(O)Cl	+4.7	+2.7	+0.3	+6.5
$C(O)NH_2$	+5.0	−1.2	+0.1	+3.4
NO_2	+19.9	−4.9	+0.9	+6.1

*Values calculated from http://www.stephanbird.org.uk/Chemistry/Carbon/AreneNMR-C13.html.

Be careful. This URL is case-sensitive.

^{13}C-substituent effects are additive for as many substituents as are present on the ring. Thus, for the carbon that bears the methyl group in *o*-nitrotoluene:

$$\delta = 128.5 + (\Delta \text{ for C-1} = CH_3) + (\Delta \text{ for ortho } NO_2)$$

$$\delta = 128.5 + (+9.1) + (-4.9) = 132.7$$

Likewise for the nitro-bearing carbon in *o*-nitrotoluene:

$$\delta = 128.5 + (\Delta \text{ for C-1} = NO_2) + (\Delta \text{ for ortho } CH_3)$$

$$\delta = 128.5 + (+19.9) + (+0.7) = 149.1$$

Analogous arithmetic gives the calculated chemical shifts for all the ring carbons (Table 13.7).

TABLE 13.7 Calculated and Observed ^{13}C Chemical Shifts for the Ring Carbons in *o*- and *m*-Nitrotoluene

		^{13}C Chemical Shift of Carbon, δ^*					
		1	**2**	**3**	**4**	**5**	**6**
o-Nitrotoluene	Calculated	132.7	149.1	123.5	126.4	134.5	130.1
	Observed	133.5	149.4	124.6	126.9	133.0	132.8
m-Nitrotoluene	Calculated	139.6	124.3	148.3	120.6	129.3	135.3
	Observed	139.9	123.8	148.4	120.6	129.1	135.4

*Column numbers 1–6 are IUPAC locants of ring carbons.

The match between the calculated ^{13}C chemical shifts and those actually observed for the two isomers is quite good. The major difference between the two isomers is the chemical shift of the methyl-bearing carbon, which is both large enough and in the direction predicted by the calculation to serve to identify each isomer.

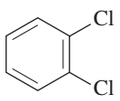
The URL referenced as a footnote in Table 13.6 provides an easy, automatic way to do these calculations. One simply selects substituents at the carbons of the benzene ring on the screen and is rewarded with the chemical shifts of all six ring carbons.

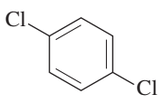
The problems that follow illustrate some of the ways that chemical shift calculations can assist in structure determination among compounds that contain benzene rings. The purpose of the first problem is to acquaint you with the online calculator at the URL referenced in Table 13.6. You will need the calculator for the substituent effect Δ of fluorine. With the exception of fluorine, substituent effects for the other atoms and groups are listed in the table.

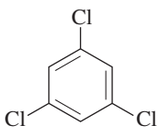
13.51 Which carbons of 1-chloro-4-fluorobenzene are the most shielded?

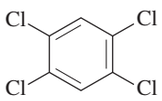
A. C-1
B. C-2 and C-6
C. C-3 and C-5
D. C-4

13.52 A chlorinated derivative of benzene had only two peaks for aromatic carbons in its ^{13}C NMR spectrum. Of the following, which compound can be eliminated on the basis of this information?


A.

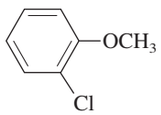

B.

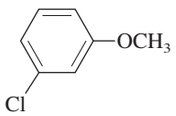

C.

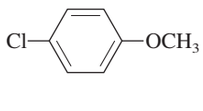

D.

13.53 Of the remaining possible compounds from Problem 13.52, which one is most consistent with the observed ^{13}C shifts of δ 127.2 and 135.6?

13.54 The ^{13}C NMR spectrum of a C_7H_7ClO isomer has peaks for a methyl carbon and six aromatic ring carbons. Which compound can you exclude based solely on the number of peaks?

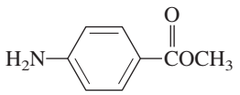

A.


B.

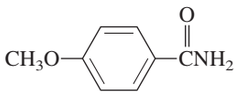

C.

13.55 The ^{13}C NMR spectrum of one of the chloroanisole isomers shown in the preceding problem has peaks at δ 112.6, 114.4, 120.9, 130.2, 135.0, and 160.5. Which isomer fits the data best?

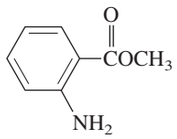
13.56 A compound of molecular formula $C_8H_9NO_2$ had peaks for its benzene ring carbons at δ 113.8, 119.3, 131.6, and 151.4. No other peaks for benzene ring carbons were present. Which compound is most consistent with the ^{13}C NMR data?



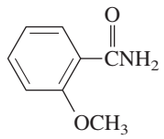
A.



B.

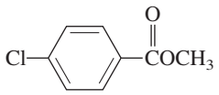


C.

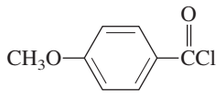


D.

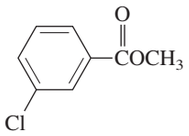
13.57 A compound of molecular formula $C_8H_7ClO_2$ had peaks for its benzene ring carbons at δ 114.3, 125.3, 134.0, and 165.5. No other peaks for benzene ring carbons were present. Which compound is most consistent with the ^{13}C NMR data?



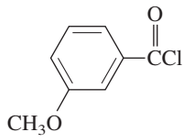
A.



B.



C.



D.

13.58 There is one peak too few, and one of the peaks is too large in the ^{13}C NMR spectrum of 2-chloro-5-methylphenol. The reason for this is that two of the carbons, although nonequivalent, have the same chemical shift and appear as a single peak. For which two carbons are the calculated chemical shifts the closest?

A. C-1 and C-6
B. C-2 and C-6
C. C-1 and C-3
D. C-4 and C-5