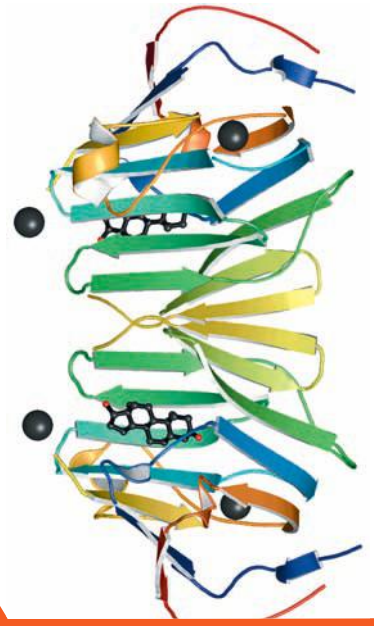
CHAPTER

13

The anabolic steroids sometimes taken by athletes are transported to their target tissues in the body by binding to a protein called human sex hormone–binding globulin. The chemical structures of this and other complex organic molecules are generally determined by x-ray crystallography.



Structure Determination

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OWL

Online homework for this chapter can be assigned in OWL, an online homework assessment tool.

Every time a reaction is run, the products must be identified, and every time a new compound is found in nature, its structure must be determined. Determining the structure of an organic molecule was a difficult and time-consuming process in the early days of chemistry, but powerful techniques and specialized instruments developed in the mid-1900s greatly simplified the task. We'll look at four of the most useful such techniques—mass spectrometry (MS), infrared spectroscopy (IR), ultraviolet spectroscopy (UV), and nuclear magnetic resonance spectroscopy (NMR)—each of which yields a different kind of structural information.

Mass Spectrometry	What is the molecular formula?
Infrared (IR) spectroscopy	What functional groups are present?
Ultraviolet (UV) spectroscopy	Is a conjugated π electron system present?
Nuclear magnetic resonance (NMR) spectroscopy	What is the carbon–hydrogen framework?

WHY THIS CHAPTER

Finding the structures of new molecules, whether small ones synthesized in the laboratory or large proteins and nucleic acids found in living organisms, is central to progress in chemistry and biochemistry. We'll only scratch the surface of structure determination in this book, but after reading

this chapter you should have a good idea of some techniques that are available and of how and when each is used.

13.1 Mass Spectrometry

At its simplest, **mass spectrometry (MS)** is a technique for measuring the molecular weight, and therefore the formula, of a molecule. Whether you know it or not, you see a mass spectrometer every time you pass through airport security and watch a security person swabbing a piece of luggage and putting the swab into an instrument. The instrument is a specialized mass spectrometer, and it can detect explosives by measuring the molecular weight of volatile materials on the swab and comparing the result to the molecular weights of known explosives.

More than 20 different kinds of commercial mass spectrometers are available depending on the intended application, but all have three basic parts: an *ionization source* in which sample molecules are given an electrical charge; a *mass analyzer* in which ions are separated by their mass-to-charge ratio, *m/z;* and a *detector* in which the separated ions are observed and counted. Since the number of charges z on each ion is usually 1, the value of m/z for an ion is simply its mass, m. Masses up to approximately 2500 atomic mass units (amu) can be analyzed with an accuracy up to four decimal places.

A typical mass spectrum, like that of hexane in Figure 13.1, is normally presented as a bar graph with m/z on the horizontal axis and relative abundance of ions on the vertical axis. The tallest peak, assigned an intensity of 100%, is called the *base peak,* and the peak that corresponds to the unfragmented ion is called the *parent peak,* or the *molecular ion* (M^+). Hexane, for instance, shows $M^+ = 86$, corresponding to a formula of C_6H_{14}.

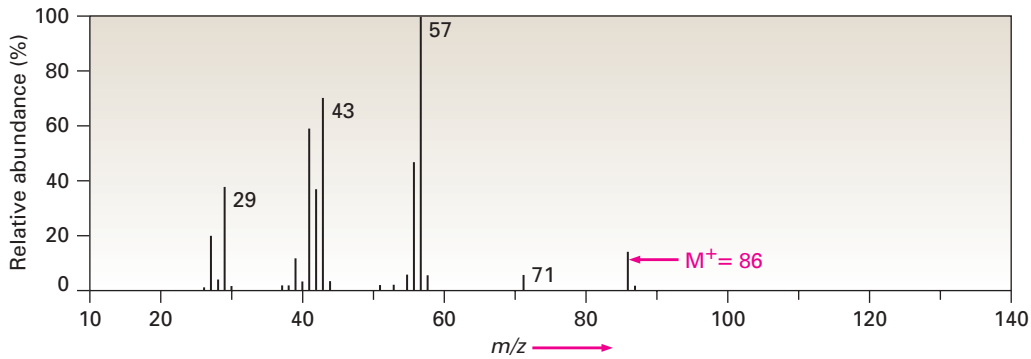


Figure 13.1 Mass spectrum of hexane (C_6H_{14}; MW = 86). The molecular ion is at $m/z = 86$, the base peak is at $m/z = 57$, and numerous other ions are present.

In addition to giving a molecular ion, most molecules fragment in the mass spectrometer, giving rise to numerous other ions that can provide structural information when interpreted. Hexane, for instance, shows peaks at $m/z = 71$ corresponding to loss of a CH_3- group, $m/z = 57$ corresponding to loss of an CH_3CH_2- group, $m/z = 43$ corresponding to loss of a $CH_3CH_2CH_2-$ group, and so forth.

You might also note in Figure 13.1 that in addition to the peak for the molecular ion at $m/z = 86$, there is also a small peak at $m/z = 87$ because of the presence of different isotopes in molecules. Although ^{12}C is the most

abundant carbon isotope, a small amount (1.10% natural abundance) of ^{13}C is also present. Thus, a certain percentage of the molecules analyzed in the mass spectrometer contain a ^{13}C atom, giving rise to the observed M+1 peak.

Problem 13.1 The mass spectrum of the product formed in the addition of a halogen X_2 to but-2-ene showed a peak at $m/z = 310$. What halogen was used?

Problem 13.2 Oxidation of butan-1-ol to give butanal gives a by-product whose mass spectrum shows peaks at $m/z = 88$ and $m/z = 72$. What do you think the impurity might be?

13.2 Spectroscopy and the Electromagnetic Spectrum

Visible light, X rays, microwaves, radio waves, and so forth, are all different kinds of *electromagnetic radiation.* Collectively, they make up the **electromagnetic spectrum**, shown in Figure 13.2. The electromagnetic spectrum is arbitrarily divided into regions, with the familiar visible region accounting for only a small portion of the overall spectrum, from 3.8×10^{-7} to 7.8×10^{-7} m in wavelength. The visible region is flanked by the infrared and ultraviolet regions.

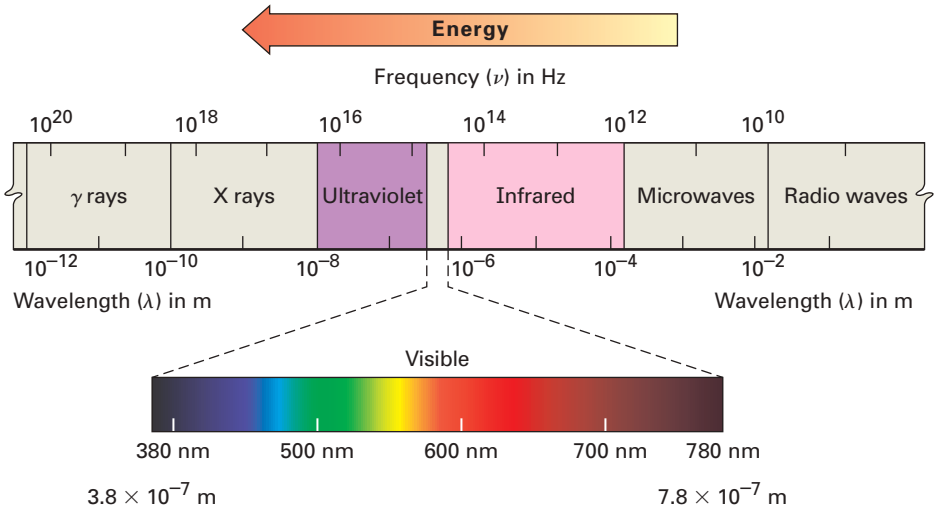


Figure 13.2 The electromagnetic spectrum covers a continuous range of wavelengths and frequencies, from radio waves at the low-frequency end to gamma (γ) rays at the high-frequency end. The familiar visible region accounts for only a small portion near the middle of the spectrum.

Electromagnetic radiation is often said to have dual behavior. In some respects it has the properties of a particle, called a *photon,* yet in other respects it behaves as an energy wave. Like all waves, electromagnetic radiation is characterized by a frequency, a wavelength, and an amplitude (Figure 13.3). The **wavelength, λ** (Greek lambda), is the distance from one wave maximum to the next. The **frequency, ν** (Greek nu), is the number of waves that pass by a fixed point per unit time, usually given in reciprocal seconds (s^{-1}), or **hertz, Hz** (1 Hz = 1 s^{-1}). The **amplitude** is the height of a wave, measured from midpoint to peak. The intensity of radiant energy, whether a

feeble glow or a blinding glare, is proportional to the square of the wave's amplitude.

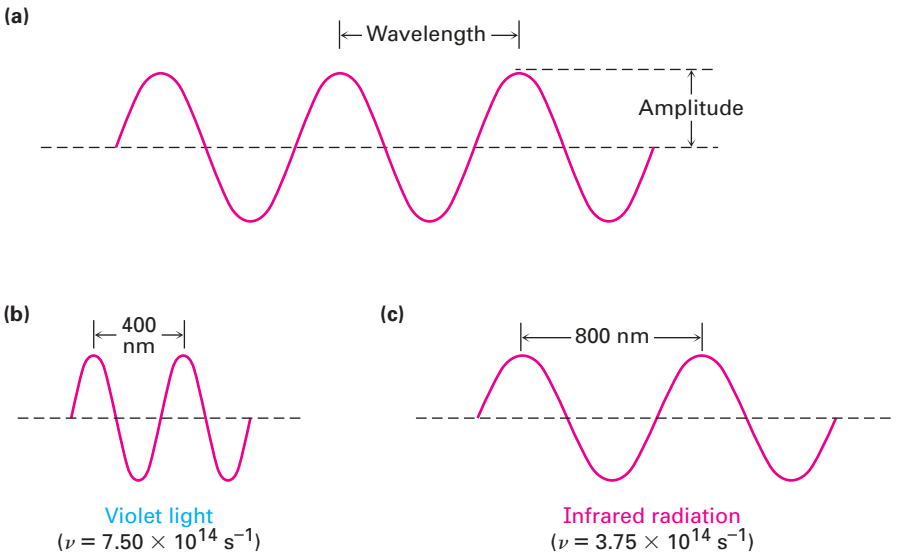


Figure 13.3 Electromagnetic waves are characterized by a wavelength, a frequency, and an amplitude. **(a)** Wavelength (λ) is the distance between two successive wave maxima. Amplitude is the height of the wave measured from the center. **(b), (c)** What we perceive as different kinds of electromagnetic radiation are simply waves with different wavelengths and frequencies.

Multiplying the length of a wave in meters (m) by its frequency in reciprocal seconds (s^{-1}) gives the speed of the wave in meters per second (m/s). The rate of travel of all electromagnetic radiation in a vacuum is a constant value, commonly called the "speed of light" and abbreviated c. Its numerical value is defined as exactly 2.997 924 58 $\times$ 10^8 m/s, usually rounded off to 3.00 $\times$ 10^8 m/s.

$$\text{Wavelength} \times \text{Frequency} = \text{Speed}$$
$$\lambda\ (\text{m}) \times \nu\ (\text{s}^{-1}) = c\ (\text{m/s})$$
$$\lambda = \frac{c}{\nu} \quad \text{or} \quad \nu = \frac{c}{\lambda}$$

Just as matter comes only in discrete units, called atoms, electromagnetic energy is transmitted only in discrete amounts, called *quanta*. The amount of energy, ϵ, corresponding to 1 quantum of energy, or 1 *photon*, of a given frequency ν is expressed by the Planck equation

$$\varepsilon = h\nu = \frac{hc}{\lambda}$$

where h = Planck's constant [6.62×10^{-34} (J · s) = 1.58×10^{-34} (cal · s)]
c = speed of light (3.00×10^8 m/s)
λ = wavelength in meters

The Planck equation says that the energy of a given photon varies directly with its frequency ν but inversely with its wavelength λ. High frequencies and short wavelengths correspond to high-energy radiation such as gamma rays; low frequencies and long wavelengths correspond to low-energy radiation such as radio waves. Multiplying ϵ by Avogadro's number, N_A, gives the same

equation in more familiar units, where E represents the energy of Avogadro's number (one "mole") of photons of wavelength λ:

$$E = \frac{N_A hc}{\lambda} = \frac{1.20 \times 10^{-4} \text{ kJ/mol}}{\lambda \text{ (in meters)}} \quad \text{or} \quad \frac{2.86 \times 10^{-5} \text{ kcal/mol}}{\lambda \text{ (in meters)}}$$

Infrared radiation with a wavelength 1.0×10^{-5} m, for instance, has an energy of 12 kJ/mol (2.9 kcal/mol).

When an organic compound is exposed to electromagnetic radiation, it absorbs energy of certain wavelengths but passes, or transmits, energy of other wavelengths. If we irradiate an organic compound with energy of many wavelengths and determine which are absorbed and which are transmitted, we can determine the **absorption spectrum** of the compound. The results are displayed on a plot of wavelength versus the amount of radiation transmitted.

An example of an absorption spectrum—that of ethanol exposed to infrared radiation—is shown in Figure 13.4. The horizontal axis records the wavelength, and the vertical axis records the intensity of the various energy absorptions in percent transmittance. The baseline corresponding to 0% absorption (or 100% transmittance) runs along the top of the chart, so a downward spike means that energy absorption has occurred at that wavelength.

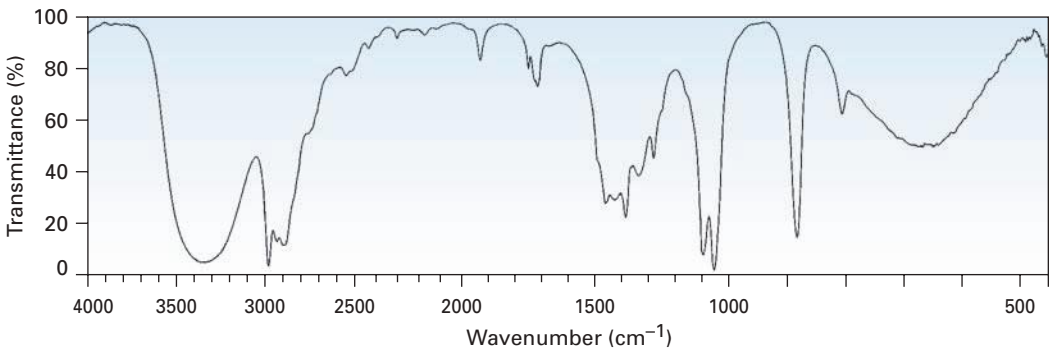


Figure 13.4 The infrared absorption spectrum of ethanol, CH_3CH_2OH. A transmittance of 100% means that all the energy is passing through the sample. A lower transmittance means that some energy is being absorbed. Thus, each downward spike corresponds to an energy absorption.

Worked Example 13.1

Converting from Frequency to Wavelength

What is the wavelength in meters of visible light with a frequency of 4.5×10^{14} Hz?

Strategy

Frequency and wavelength are related by the equation $\lambda = c/\nu$, where c is the speed of light (3.0×10^8 m/s).

Solution

$$\lambda = \frac{3.0 \times 10^8 \text{ m/s}}{4.5 \times 10^{14} \text{ s}^{-1}} = 6.7 \times 10^{-7} \text{ m}$$

Worked Example 13.2

Calculating the Energy of Electromagnetic Waves

Which is higher in energy, FM radio waves with a frequency of 1.015×10^8 Hz (101.5 MHz) or visible light with a frequency of 5×10^{14} Hz?

Strategy Remember the equations $\epsilon = h\nu$ and $\epsilon = hc/\lambda$, which say that energy increases as frequency increases and as wavelength decreases.

Solution Because visible light has a higher frequency than radio waves, it is higher in energy.

Problem 13.3 How does the energy of infrared radiation with $\lambda = 1.0 \times 10^{-6}$ m compare with that of an X ray having $\lambda = 3.0 \times 10^{-9}$ m?

Problem 13.4 Which is higher in energy, radiation with $\nu = 4.0 \times 10^{9}$ Hz or radiation with $\lambda = 9.0 \times 10^{-6}$ m?

Problem 13.5 Cellphones use microwave radiation of around 1.9×10^{9} Hz.

(a) What is the wavelength of cellphone radiation?

(b) Use the equation $E = 1.20 \times 10^{-4}$ (kJ/mol)/λ to calculate the amount of energy in cellphone radiation in kJ/mol. How does the amount of energy you calculated for a cellphone compare with the energy of visible red light (200 kJ/mol).

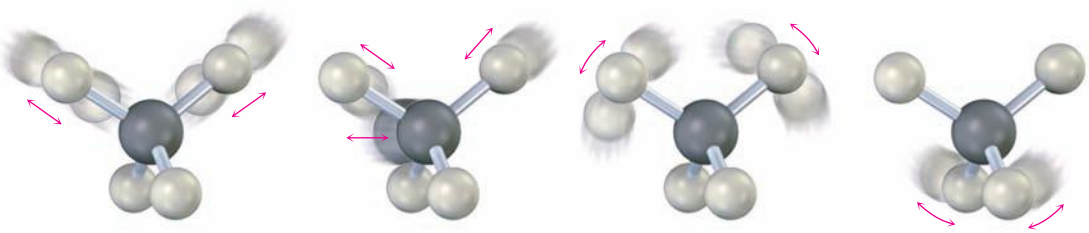
13.3 Infrared Spectroscopy of Organic Molecules

The **infrared (IR)** region of the electromagnetic spectrum covers the range from just above the visible (7.8×10^{-7} m) to approximately 10^{-4} m, but only the midportion from 2.5×10^{-6} m to 2.5×10^{-5} m is used by organic chemists. Wavelengths within the IR region are usually given in micrometers ($1\ \mu\text{m} = 10^{-6}$ m), and frequencies are given in *wavenumbers* rather than in hertz. The **wavenumber ($\tilde{\nu}$)** is the reciprocal of the wavelength in centimeters and is therefore expressed in units of cm^{-1}.

$$\text{Wavenumber:} \quad \tilde{\nu}\,(\text{cm}^{-1}) = \frac{1}{\lambda\ (\text{cm})}$$

Thus, the useful IR region is from 4000 to 400 cm^{-1}, corresponding to energies of 48.0 kJ/mol to 4.80 kJ/mol (11.5–1.15 kcal/mol).

Why does an organic molecule absorb some wavelengths of IR radiation but not others? All molecules have a certain amount of energy and are in constant motion. Their bonds stretch and contract, atoms wag back and forth, and other molecular vibrations occur. Some of the kinds of allowed vibrations are shown.



Symmetric stretching | **Antisymmetric stretching** | **In-plane bending** | **Out-of-plane bending**

The amount of energy a molecule contains is not continuously variable but is *quantized*. That is, a molecule can stretch or bend only at specific frequencies

corresponding to specific energy levels. Take bond stretching, for instance. Although we usually speak of bond lengths as if they were fixed, the numbers given are really averages. In fact, a typical C–H bond with an average bond length of 110 pm is actually vibrating at a specific frequency, alternately stretching and contracting as if there were a spring connecting the two atoms.

When the molecule is irradiated with electromagnetic radiation, *energy is absorbed if the frequency of the radiation matches the frequency of the vibration.* The result of this energy absorption is an increased amplitude for the vibration; in other words, the "spring" connecting the two atoms stretches and compresses a bit further. Since each frequency absorbed by a molecule corresponds to a specific molecular motion, we can find what kinds of motions a molecule has by measuring its IR spectrum. By then interpreting those motions, we can find out what kinds of bonds (functional groups) are present in the molecule.

IR spectrum → What molecular motions? → What functional groups?

13.4 Interpreting Infrared Spectra

The full interpretation of an IR spectrum is difficult because most organic molecules are so large that they have dozens of different molecular motions and thus have dozens of absorptions. Fortunately, we don't need to interpret an IR spectrum fully to get useful information because most functional groups have characteristic IR absorptions that don't change from one compound to another. The C=O absorption of a ketone is almost always in the range 1670 to 1750 cm^{-1}, the O–H absorption of an alcohol is almost always in the range 3400 to 3650 cm^{-1}, the C=C absorption of an alkene is almost always in the range 1640 to 1680 cm^{-1}, and so forth. By learning where characteristic functional-group absorptions occur, it's possible to get structural information from IR spectra. Table 13.1 lists the characteristic IR bands of some common functional groups.

Table 13.1 Characteristic Infrared Absorptions of Some Functional Groups

Functional Group	Absorption (cm^{-1})	Intensity
Alkane		
C–H	2850–2960	Medium
Alkene		
=C–H	3020–3100	Medium
C=C	1640–1680	Medium
Alkyne		
≡C–H	3300	Strong
C≡C	2100–2260	Medium
Alkyl halide		
C–Cl	600–800	Strong
C–Br	500–600	Strong
Alcohol		
O–H	3400–3650	Strong, broad
C–O	1050–1150	Strong
Arene		
C–H	3030	Weak
Aromatic ring	1660–2000	Weak
	1450–1600	Medium
Amine		
N–H	3300–3500	Medium
C–N	1030–1230	Medium
Carbonyl compound		
C=O	1670–1780	Strong
Aldehyde	1725	Strong
Ketone	1715	Strong
Ester	1735	Strong
Amide	1690	Strong
Carboxylic acid	1710	Strong, broad
Carboxylic acid		
O–H	2500-3100	Strong, broad
Nitrile		
C≡N	2210–2260	Medium
Nitro		
NO_2	1540	Strong

Look at the spectra of cyclohexanol and cyclohexanone in Figure 13.5 to see how IR spectroscopy can be used. Although both spectra contain many peaks, the characteristic absorptions of the different functional groups allow the compounds to be distinguished. Cyclohexanol shows a characteristic alcohol O–H absorption at 3300 cm^{-1} and a C–O absorption at 1060 cm^{-1}; cyclohexanone shows a characteristic ketone C=O peak at 1715 cm^{-1}.

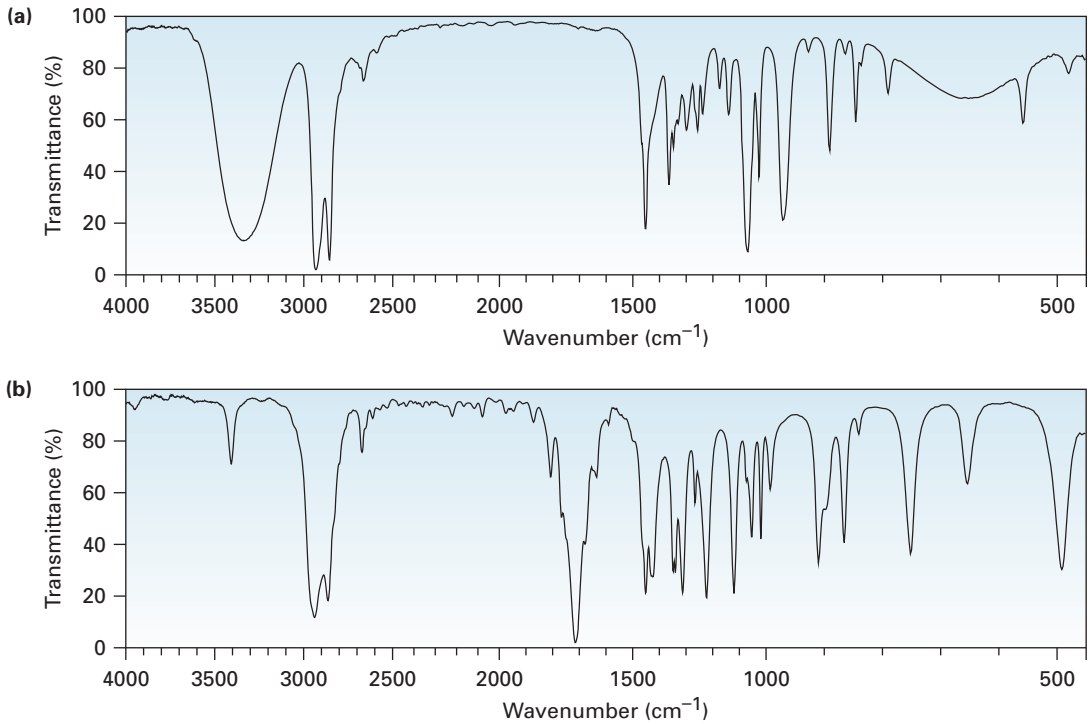


Figure 13.5 Infrared spectra of **(a)** cyclohexanol and **(b)** cyclohexanone. Spectra like these are easily obtained in minutes with milligram amounts of material.

One further point about infrared spectroscopy: it's also possible to obtain structural information from an IR spectrum by noticing which absorptions are *not* present. If the spectrum of an unknown does *not* have an absorption near 3400 cm^{-1}, the unknown is not an alcohol; if the spectrum does not have an absorption near 1715 cm^{-1}, the unknown is not a ketone; and so on.

It helps in remembering the positions of various IR absorptions to divide the infrared range from 4000 to 200 cm^{-1} into four parts, as shown in Figure 13.6.

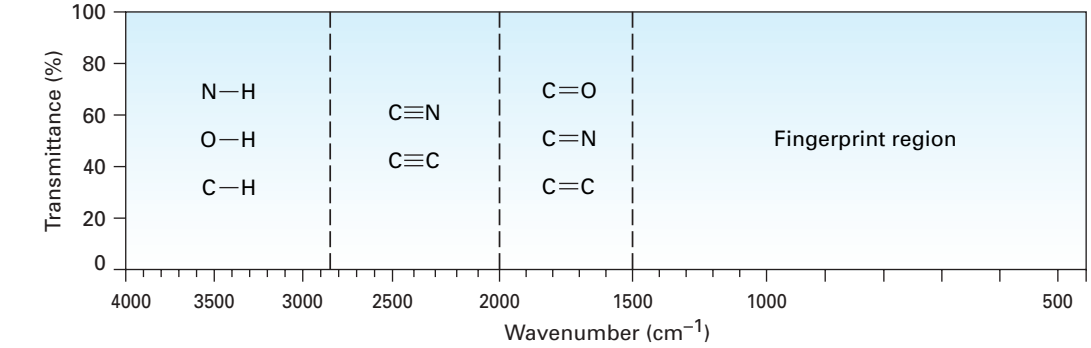


Figure 13.6 The four regions of the infrared spectrum—single bonds to hydrogen, triple bonds, double bonds, and fingerprint.

- The region from 4000 to 2500 cm^{-1} corresponds to absorptions caused by N–H, C–H, and O–H single-bond stretching motions. N–H and O–H bonds absorb in the 3300 to 3600 cm^{-1} range; C–H bond stretching occurs near 3000 cm^{-1}.

- The region from 2500 to 2000 cm^{-1} is where triple-bond stretching occurs. Both C≡N and C≡C bonds absorb here.
- The region from 2000 to 1500 cm^{-1} is where double bonds (C=O, C=N, and C=C) absorb. Carbonyl groups generally absorb in the range 1670 to 1780 cm^{-1}, and alkene stretching normally occurs in the narrow range 1640 to 1680 cm^{-1}.
- The region below 1500 cm^{-1} is the fingerprint portion of the IR spectrum. A large number of absorptions due to a variety of C–C, C–O, C–N, and C–X single-bond vibrations occur here, forming a unique pattern that acts as an identifying fingerprint of each organic compound.

Worked Example 13.3 Predicting Infrared Absorptions

Refer to Table 13.1 and make educated guesses about the functional groups that cause the following IR absorptions:

(a) 1735 cm^{-1} **(b)** 3500 cm^{-1}

Solution

(a) An absorption at 1735 cm^{-1} is in the carbonyl-group region of the IR spectrum, probably an ester.
(b) An absorption at 3500 cm^{-1} is in the –OH (alcohol) region.

Worked Example 13.4 Using Infrared Spectroscopy

Acetone and prop-2-en-1-ol ($H_2C{=}CHCH_2OH$) are isomers. How could you distinguish them by IR spectroscopy?

Strategy Identify the functional groups in each molecule, and refer to Table 13.1.

Solution Table 13.1 shows that acetone has a strong C=O absorption at 1715 cm^{-1}, while prop-2-en-1-ol has an –OH absorption at 3500 cm^{-1} and a C=C absorption at 1660 cm^{-1}.

Problem 13.6 What functional groups might molecules contain if they show IR absorptions at the following frequencies?

(a) 1715 cm^{-1}
(b) 1540 cm^{-1}
(c) 2210 cm^{-1}
(d) 1720 and 2500–3100 cm^{-1}
(e) 3500 and 1735 cm^{-1}

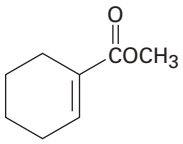
Problem 13.7 How might you use IR spectroscopy to help distinguish between the following pairs of isomers?

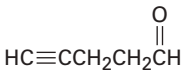
(a) CH_3CH_2OH and CH_3OCH_3

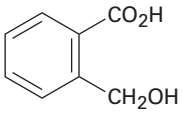
(b)  and $CH_3CH_2CH_2CH_2CH{=}CH_2$

(c) $CH_3CH_2\overset{\overset{O}{\|}}{C}OH$ and $HOCH_2CH_2\overset{\overset{O}{\|}}{C}H$

Problem 13.8 Where might the following compound have IR absorptions?

(a) 

(b) 

(c) 

13.5 Ultraviolet Spectroscopy

The **ultraviolet (UV)** region of the electromagnetic spectrum extends from the low-wavelength end of the visible region (4×10^{-7} m) to the long-wavelength end of the X-ray region (10^{-8} m). The part of greatest interest to organic chemists, though, is the narrow range from 2×10^{-7} m to 4×10^{-7} m. Absorptions in this region are measured in *nanometers* (nm), where 1 nm = 10^{-9} m = 10^{-7} cm. Thus, the ultraviolet range of interest is from 200 to 400 nm.

We saw in the previous section that when a molecule is subjected to IR irradiation, the energy absorbed corresponds to the amount necessary to increase molecular vibrations. When UV radiation is used, the energy absorbed corresponds to the amount necessary to raise the energy level of a π electron in a conjugated molecule.

A typical UV spectrum—that of buta-1,3-diene—is shown in Figure 13.7. Unlike IR spectra, which generally have many peaks, UV spectra are usually quite simple. Often, there is only a single broad peak, which is identified by noting the wavelength at the very top, indicated as λ_{max}. For buta-1,3-diene, λ_{max} = 217 nm. Note that UV spectra differ from IR spectra in the way they are presented. For historical reasons, IR spectra are usually displayed so that the baseline corresponding to zero absorption runs across the top of the chart and a valley indicates an absorption, whereas UV spectra are displayed with the baseline at the bottom of the chart so that a peak indicates an absorption.

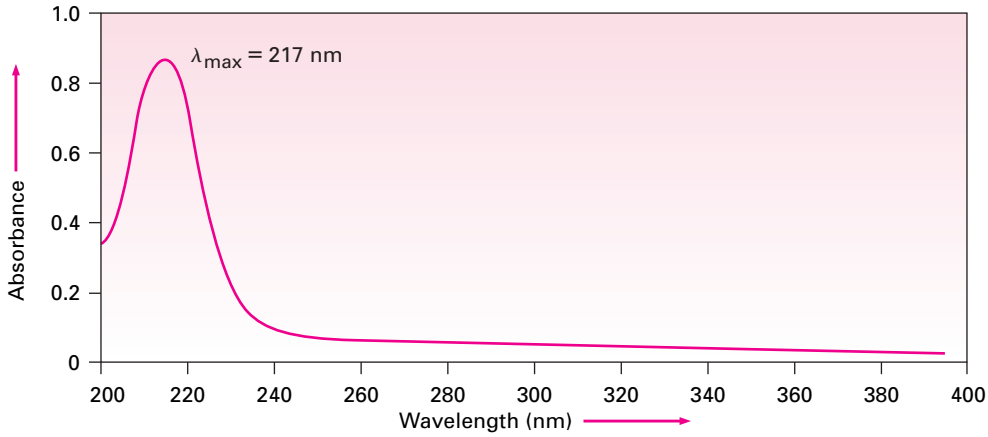


Figure 13.7 Ultraviolet spectrum of buta-1,3-diene.

The amount of UV light absorbed by a sample is expressed as the sample's absorbance (A), defined by the equation

$$A = \epsilon \cdot c \cdot l$$

where ϵ = the *molar absorptivity* of the molecule in units of L/(mol · cm)
The higher the molar absorptivity, the greater the amount of radiation absorbed by the compound.
c = the concentration of a solution of sample in mol/L
l = the sample pathlength in cm

A particularly important use of this equation comes from rearranging it to the form $c = A/(\epsilon \cdot l)$, which lets us measure the concentration of a sample in solution when A, ϵ, and l are known. As an example, β-carotene, the pigment responsible for the orange color of carrots, has $\epsilon = 138{,}000$ L/(mol · cm). If a sample of β-carotene is placed in a cell with a pathlength of 1.0 cm and the UV absorbance reads 0.37, then the concentration of β-carotene in the sample is

$$c = \frac{A}{\epsilon l} = \frac{0.37}{\left(1.38 \times 10^5 \dfrac{\text{L}}{\text{mol} \cdot \text{cm}}\right)(1.00\ \text{cm})}$$
$$= 2.7 \times 10^{-6}\ \text{M}$$

Problem 13.9 What is the concentration of cytosine, a constituent of nucleic acids, if its molar absorptivity is 6.1×10^3 L/(mol · cm) and its absorbance is 0.20 in a cell with a 1.0 cm pathlength?

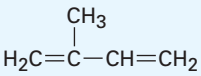
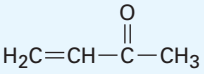
13.6 Interpreting Ultraviolet Spectra: The Effect of Conjugation

The wavelength of radiation necessary to raise the energy of a π electron in a conjugated molecule depends on the nature of the molecule's π electron system. One of the most important factors is the extent of conjugation (Section 4.8). Thus, by measuring the UV spectrum of an unknown, we can derive structural information about the nature of any conjugated π electron system present in a molecule.

It turns out that the energy required for an electronic transition decreases as the extent of conjugation increases. Thus, buta-1,3-*di*ene absorbs at $\lambda_{max} = 217$ nm, hexa-1,3,5-*tri*ene absorbs at $\lambda_{max} = 258$ nm, and octa-1,3,5,7-*tetra*ene absorbs at $\lambda_{max} = 290$ nm. (Remember: longer wavelength means lower energy.)

Other kinds of conjugated π electron systems besides dienes and polyenes also show ultraviolet absorptions. Conjugated enones, such as but-3-en-2-one, and aromatic molecules, such as benzene, also have characteristic UV absorptions that aid in structure determination. The UV absorption maxima of some representative conjugated molecules are given in Table 13.2.

Table 13.2 Ultraviolet Absorption Maxima of Some Conjugated Molecules

Name	Structure	λ_{max} (nm)
2-Methybuta-1,3-diene		220
Cyclohexa-1,3-diene		256
Hexa-1,3,5-triene	$H_2C{=}CH{-}CH{=}CH{-}CH{=}CH_2$	258
Octa-1,3,5,7-tetraene	$H_2C{=}CH{-}CH{=}CH{-}CH{=}CH{-}CH{=}CH_2$	290
But-3-en-2-one		219
Benzene		203

Worked Example 13.5 Using Ultraviolet Spectroscopy

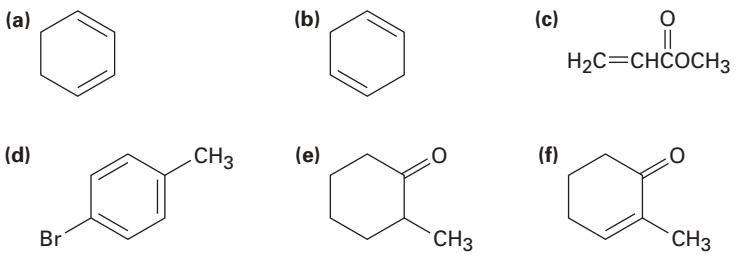
Hexa-1,5-diene and hexa-1,3-diene are isomers. How can you distinguish them by UV spectroscopy?

Hexa-1,5-diene **Hexa-1,3-diene**

Strategy Remember that only conjugated molecules show UV absorptions.

Solution Hexa-1,3-diene is a conjugated diene, but hexa-1,5-diene is nonconjugated. Only the conjugated isomer shows a UV absorption above 200 nm.

Problem 13.10 Which of the following compounds show UV absorptions in the range 200 to 400 nm?



Problem 13.11 How can you distinguish between hexa-1,3-diene and hexa-1,3,5-triene by UV spectroscopy?

13.7 Nuclear Magnetic Resonance Spectroscopy

We've seen up to this point that IR spectroscopy provides information about a molecule's functional groups and that UV spectroscopy provides information about a molecule's conjugated π electron system. **Nuclear magnetic resonance (NMR) spectroscopy** complements these techniques by providing a "map" of the carbon–hydrogen framework in an organic molecule. Taken together, IR, UV, and NMR spectroscopies often make it possible to find the structures of even very complex molecules.

How does NMR spectroscopy work? Many kinds of nuclei, including ^{1}H and ^{13}C, behave as if they were spinning about an axis. Because they're positively charged, these spinning nuclei act like tiny magnets and interact with an external magnetic field (denoted $\boldsymbol{B}_0$). In the absence of an external magnetic field, the nuclear spins of magnetic nuclei are oriented randomly. When a sample containing these nuclei is placed between the poles of a strong magnet, however, the nuclei adopt specific orientations, much as a compass needle orients in the earth's magnetic field.

A spinning ^{1}H or ^{13}C nucleus can orient so that its own tiny magnetic field is aligned either with (parallel to) or against (antiparallel to) the external field. The two orientations don't have the same energy and therefore aren't equally likely. The parallel orientation is slightly lower in energy, making this spin state slightly favored over the antiparallel orientation (Figure 13.8).

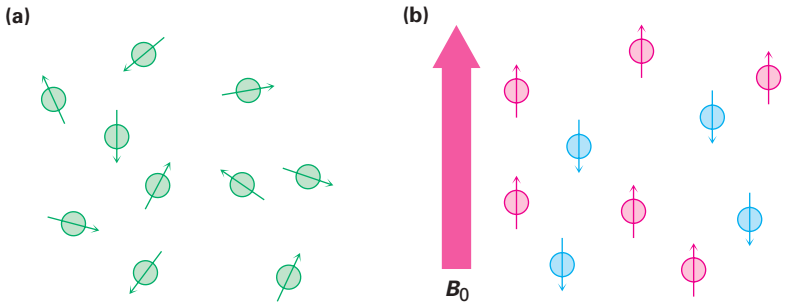


Figure 13.8 **(a)** Nuclear spins are oriented randomly in the absence of an external magnetic field but **(b)** have a specific orientation in the presence of an external field $\boldsymbol{B}_0$. Some of the spins (red) are aligned parallel to the external field and others (blue) are antiparallel. The parallel spin state is lower in energy and therefore favored.

If the oriented nuclei are now irradiated with electromagnetic radiation of the right frequency, energy absorption occurs and the lower-energy state "spin-flips" to the higher-energy state. When this spin-flip occurs, the nuclei are said to be in resonance with the applied radiation—hence the name *nuclear magnetic resonance*.

The exact frequency necessary for resonance depends both on the strength of the external magnetic field and on the identity of the nuclei. If a very strong field is applied, the energy difference between the two spin states is larger so

that higher-energy (higher-frequency) radiation is required. If a weaker magnetic field is applied, less energy is needed to effect the transition between nuclear spin states.

In practice, superconducting magnets that produce enormously powerful fields up to 21.2 tesla (T) are sometimes used, but field strengths in the range of 4.7 to 7.0 T are more common. At a magnetic field strength of 4.7 T, so-called radiofrequency (rf) energy in the 200 MHz range (1 MHz = 10^6 Hz) brings a ^{1}H nucleus into resonance, and rf energy of 50 MHz brings a ^{13}C nucleus into resonance. At the highest field strength currently available in commercial instruments (21.2 T), 900 MHz energy is required for ^{1}H spectroscopy.

Problem 13.12 NMR spectroscopy uses electromagnetic radiation with a frequency of 1×10^8 Hz. Is this a greater or lesser amount of energy than that used by IR spectroscopy?

13.8 The Nature of NMR Absorptions

From the description thus far, you might expect all ^{1}H nuclei in a molecule to absorb energy at the same frequency and all ^{13}C nuclei to absorb at the same frequency. If so, we would observe only a single NMR absorption band in the ^{1}H or ^{13}C spectrum of a molecule, a situation that would be of little use. In fact, the absorption frequency is not the same for all ^{1}H or all ^{13}C nuclei.

All nuclei are surrounded by electrons. When an external magnetic field is applied to a molecule, the moving electrons around nuclei set up tiny local magnetic fields of their own. These local fields act in opposition to the applied field, so that the *effective* field actually felt by the nucleus is a bit weaker than the applied field.

$$\boldsymbol{B}_{\text{effective}} = \boldsymbol{B}_{\text{applied}} - \boldsymbol{B}_{\text{local}}$$

In describing this effect of local fields, we say that the nuclei are **shielded** from the full effect of the applied field by their surrounding electrons. Because each specific nucleus in a molecule is in a slightly different electronic environment, each nucleus is shielded to a slightly different extent and the effective magnetic field felt by each is slightly different. These slight differences can be detected, and we therefore see a different NMR signal for each chemically distinct ^{1}H or ^{13}C nucleus in a molecule.

Figure 13.9 shows both the ^{1}H and the ^{13}C NMR spectra of methyl acetate, $CH_3CO_2CH_3$. The horizontal axis shows the effective field strength felt by the nuclei, and the vertical axis indicates the intensity of absorption of rf energy. Each peak in the NMR spectrum corresponds to a chemically distinct ^{1}H or ^{13}C nucleus in the molecule. Note, though, that ^{1}H and ^{13}C spectra can't be observed at the same time on the same spectrometer because different amounts of energy are required to spin-flip the different kinds of nuclei. The two spectra must be recorded separately.

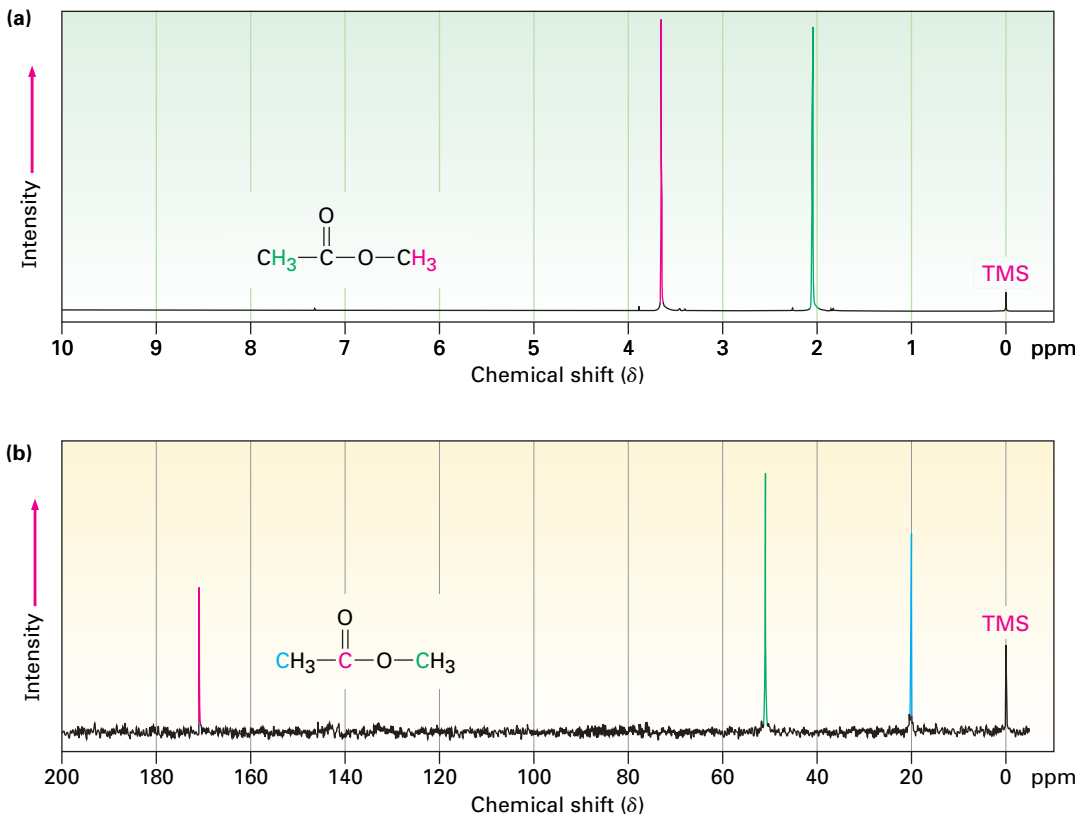


Figure 13.9 **(a)** The ^{1}H NMR spectrum and **(b)** the ^{13}C NMR spectrum of methyl acetate, $CH_3CO_2CH_3$. The small peak marked "TMS" at the far right of each spectrum is a calibration peak, as explained shortly.

The ^{13}C spectrum of methyl acetate in Figure 13.9b has three peaks, one for each of the three chemically distinct carbons in the molecule. The ^{1}H spectrum shows only *two* peaks, however, even though methyl acetate has *six* hydrogens. One peak is due to the $CH_3C{=}O$ hydrogens and the other to the $-OCH_3$ hydrogens. Because the three hydrogens in each methyl group have the same chemical (and magnetic) environment, they are shielded to the same extent and are said to be *equivalent*. Chemically equivalent nuclei always show a single absorption. The two methyl groups themselves, however, are nonequivalent, so the two sets of hydrogens absorb at different positions.

Worked Example 13.6

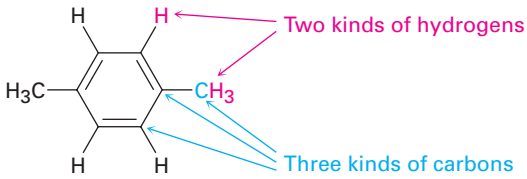
Predicting the Number of NMR Absorptions

How many signals would you expect *p*-dimethylbenzene to show in its ^{1}H and ^{13}C NMR spectra?

Strategy Look at the structure of the molecule, and count the number of kinds of chemically distinct ^{1}H and ^{13}C nuclei.

Solution Because of the molecule's symmetry, the two $-CH_3$ groups in *p*-dimethylbenzene are equivalent and all four ring hydrogens are equivalent. Thus, there are only two absorptions in the ^{1}H NMR spectrum. Also because of symmetry, there are only three absorptions in the ^{13}C NMR spectrum: one for the two equivalent

methyl-group carbons, one for the four equivalent C–H ring carbons, and one for the two equivalent ring carbons bonded to the methyl groups.



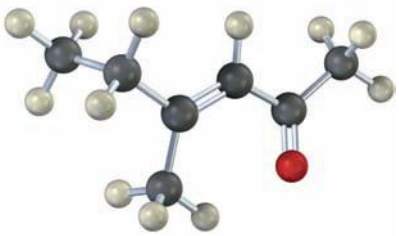
***p*-Dimethylbenzene**

Problem 13.13 How many absorptions would you expect each of the following compounds to show in its ^{1}H and ^{13}C NMR spectra?

(a) Methane **(b)** Ethane **(c)** Propane
(d) Cyclohexane **(e)** Dimethyl ether **(f)** Benzene
(g) $(CH_3)_3COH$ **(h)** Chloroethane **(i)** $(CH_3)_2C{=}C(CH_3)_2$

Problem 13.14 2-Chloropropene shows signals for three kinds of hydrogens in its ^{1}H NMR spectrum. Explain.

Problem 13.15 How many signals would you expect the following compound to show in its ^{1}H and ^{13}C NMR spectra?



13.9 Chemical Shifts

NMR spectra are displayed on charts that show the applied field strength increasing from left to right (Figure 13.9). Thus, the left side of the chart is the low-field (or **downfield**) side, and the right side is the high-field (or **upfield**) side. Nuclei that absorb on the downfield side of the chart require a lower field strength for resonance, implying that they have relatively little shielding. Nuclei that absorb on the upfield side require a higher field strength for resonance, implying that they have more shielding.

To define the position of an absorption, the NMR chart is calibrated and a reference point is used. In practice, a small amount of tetramethylsilane [TMS; $(CH_3)_4Si$] is added to the sample so that a reference absorption peak is produced when the spectrum is run. TMS is used as reference for both ^{1}H and ^{13}C spectra because it produces in both a single peak that occurs upfield of most other absorptions in organic compounds. The ^{1}H and ^{13}C spectra of methyl acetate shown previously in Figure 13.9 have the TMS reference peak indicated.

The exact position on the chart at which a nucleus absorbs is called its **chemical shift**. The chemical shift of TMS is set as the zero point, and other peaks normally occur downfield, to the left on the chart. NMR charts are calibrated using an arbitrary scale called the **delta (δ) scale**, where 1 δ equals 1 part per million (ppm) of the spectrometer operating frequency. For example, if we were measuring the ^{1}H NMR spectrum of a sample using an instrument operating at 200 MHz, 1 δ would be 1 millionth of 200 million Hz, or 200 Hz. If we were measuring the spectrum using a 500 MHz instrument, 1 δ would be 500 Hz.

Although this method of calibrating NMR charts may seem complex, there's a good reason for it. As we saw earlier, the rf frequency required to bring a given nucleus into resonance depends on the spectrometer's magnetic field strength. But because there are many different kinds of spectrometers with many different magnetic field strengths, chemical shifts given in frequency units (Hz) vary greatly from one instrument to another. Thus, a resonance that occurs at 120 Hz downfield from TMS on one spectrometer might occur at 600 Hz downfield from TMS on another spectrometer with a more powerful magnet.

By using a system of measurement in which NMR absorptions are expressed in relative terms (parts per million relative to spectrometer frequency) rather than absolute terms (Hz), it's possible to compare spectra obtained on different instruments. *The chemical shift of an NMR absorption in δ units is constant, regardless of the operating frequency of the spectrometer.* A ^{1}H nucleus that absorbs at 2.0 δ on a 200 MHz instrument also absorbs at 2.0 δ on a 500 MHz instrument.

Worked Example 13.7 **Converting between Hertz and δ Units**

Cyclohexane shows an absorption at 1.43 δ in its ^{1}H NMR spectrum. How many hertz away from TMS is this on a spectrometer operating at 200 MHz? On a spectrometer operating at 300 MHz?

Strategy Remember that 1 δ = 1 ppm of spectrometer operating frequency.

Solution On a 200 MHz spectrometer, 1 δ = 200 Hz. Thus, 1.43 δ = 286 Hz away from the TMS reference peak. On a 300 MHz spectrometer, 1 δ = 300 Hz and 1.43 δ = 429 Hz.

Problem 13.16 When the ^{1}H NMR spectrum of acetone is recorded on a 100 MHz instrument, a single sharp resonance line at 2.1 δ is observed.

(a) How far away from TMS (in hertz) does the acetone absorption occur?
(b) What is the position of the acetone absorption in δ units on a 220 MHz instrument?
(c) How many hertz away from TMS does the absorption in the 220 MHz spectrum correspond to?

Problem 13.17 The following ^{1}H NMR resonances were recorded on a spectrometer operating at 300 MHz. Convert each into δ units.

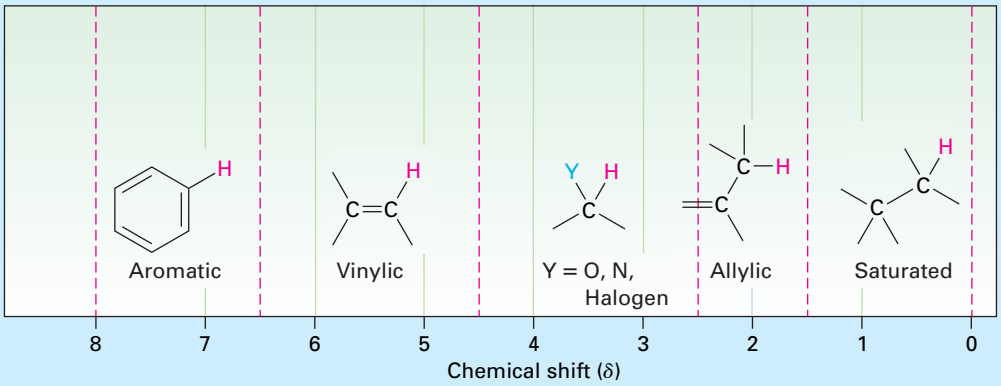
(a) $CHCl_3$, 2180 Hz **(b)** CH_3Cl, 915 Hz
(c) CH_3OH, 1040 Hz **(d)** CH_2Cl_2, 1590 Hz

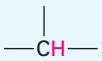
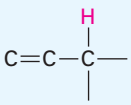
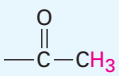
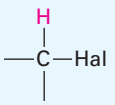
13.10 Chemical Shifts in ^{1}H NMR Spectra

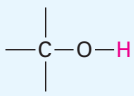
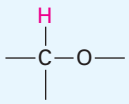
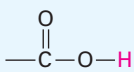
Everything we've said thus far about NMR spectroscopy applies to both ^{1}H and ^{13}C spectra. Now, let's focus only on ^{1}H NMR spectroscopy to see how it can be used in organic structure determination.

Most ^{1}H NMR absorptions occur in the range 0 to 10 δ, which can be divided into the five regions shown in Table 13.3. By remembering the positions of these regions, it's possible to tell at a glance what kinds of protons a molecule contains. (In speaking about NMR, the ^{1}H nucleus is often referred to as a *proton*.) In general, protons bonded to saturated, sp^3-hybridized carbons absorb at higher fields, whereas protons bonded to sp^2-hybridized carbons absorb at lower fields. Protons on carbons that are bonded to electronegative atoms, such as N, O, or halogen, also absorb at lower fields.

Table 13.3 Correlation of ^{1}H Chemical Shift with Environment



Type of hydrogen		Chemical shift (δ)
Reference	$Si(CH_3)_4$	0
Alkyl (primary)	$-CH_3$	0.7–1.3
Alkyl (secondary)	$-CH_2-$	1.2–1.6
Alkyl (tertiary)		1.4–1.8
Allylic		1.6–2.2
Methyl ketone		2.0–2.4
Aromatic methyl	$Ar-CH_3$	2.4–2.7
Alkynyl	$-C\equiv C-H$	2.5–3.0
Alkyl halide		2.5–4.0

Type of hydrogen		Chemical shift (δ)
Alcohol		2.5–5.0
Alcohol, ether		3.3–4.5
Vinylic		4.5–6.5
Aryl	Ar—H	6.5–8.0
Aldehyde		9.7–10.0
Carboxylic acid		11.0–12.0

Worked Example 13.8 Predicting Chemical Shifts in ^{1}H NMR Spectra

Methyl 2,2-dimethylpropanoate $(CH_3)_3CCO_2CH_3$ has two peaks in its ^{1}H NMR spectrum. At what approximate chemical shifts do they come?

Strategy Identify the types of hydrogens in the molecule, and note whether each is alkyl, vinylic, or next to an electronegative atom. Then predict where each absorbs, using Table 13.3 as necessary.

Solution The $-OCH_3$ protons absorb around 3.5 to 4.0 δ because they are on carbon bonded to oxygen. The $(CH_3)_3C-$ protons absorb near 1.0 δ because they are typical alkane-like protons.

Problem 13.18 Each of the following compounds exhibits a single ^{1}H NMR peak. Approximately where would you expect each to absorb?

(a) Ethane **(b)** Acetone **(c)** Benzene **(d)** Trimethylamine

13.11 Integration of ^{1}H NMR Spectra: Proton Counting

Look at the ^{1}H NMR spectrum of methyl 2,2-dimethylpropanoate in Figure 13.10. There are two peaks, corresponding to the two kinds of protons, but the peaks aren't the same size. The peak at 1.20 δ, due to the $(CH_3)_3C-$ protons, is larger than the peak at 3.65 δ, due to the $-OCH_3$ protons.

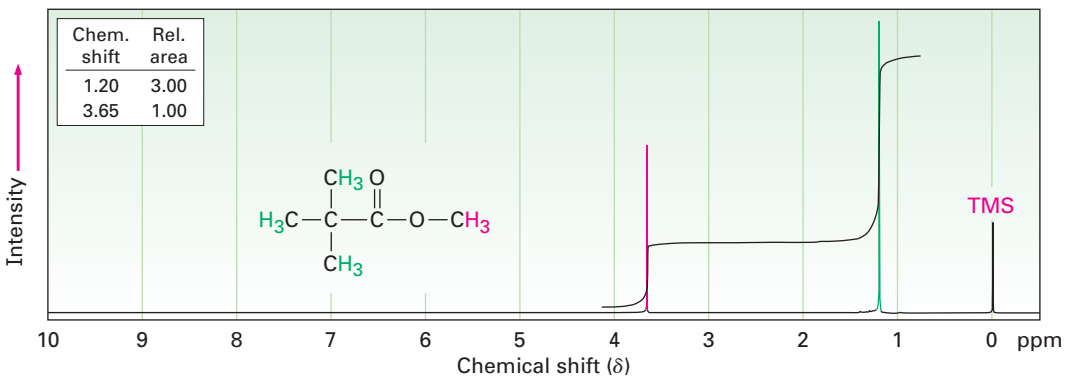


Figure 13.10 The ^{1}H NMR spectrum of methyl 2,2-dimethylpropanoate. Integrating the two peaks in a stair-step manner shows that they have a 1:3 ratio, corresponding to the 3:9 ratio of protons responsible. Modern instruments give a direct digital readout of relative peak areas.

The area under each peak is proportional to the number of protons causing that peak. By electronically measuring, or **integrating**, the area under each peak, it's possible to measure the relative numbers of the different kinds of protons in a molecule.

Modern NMR instruments provide a digital readout of relative peak areas, but an older, more visual method displays the integrated peak areas as a stair-step line, with the height of each step proportional to the area under the peak, and therefore proportional to the relative number of protons causing the peak. To compare the size of one peak against another, simply take a ruler and

measure the heights of the various steps. For example, the two steps for the peaks in methyl 2,2-dimethylpropanoate are found to have a 1:3 (or 3:9) area ratio when integrated—exactly what we expect since the three $-OCH_3$ protons are equivalent and the nine $(CH_3)_3C-$ protons are equivalent.

Problem 13.19 How many peaks would you expect in the ^1H NMR spectrum of *p*-dimethylbenzene (*p*-xylene)? What ratio of peak areas would you expect to find on integration of the spectrum? Refer to Table 13.3 for approximate chemical shift values, and sketch what the spectrum might look like.

13.12 Spin–Spin Splitting in ^1H NMR Spectra

In the ^1H NMR spectra we've seen thus far, each chemically different proton in a molecule has given rise to a single peak. It often happens, though, that the absorption of a proton splits into *multiple* peaks, called a **multiplet**. For example, the ^1H NMR spectrum of bromoethane in Figure 13.11 indicates that the $-CH_2Br$ protons appear as four peaks (a *quartet*) centered at 3.42 δ and the $-CH_3$ protons appear as three peaks (a *triplet*) centered at 1.68 δ.

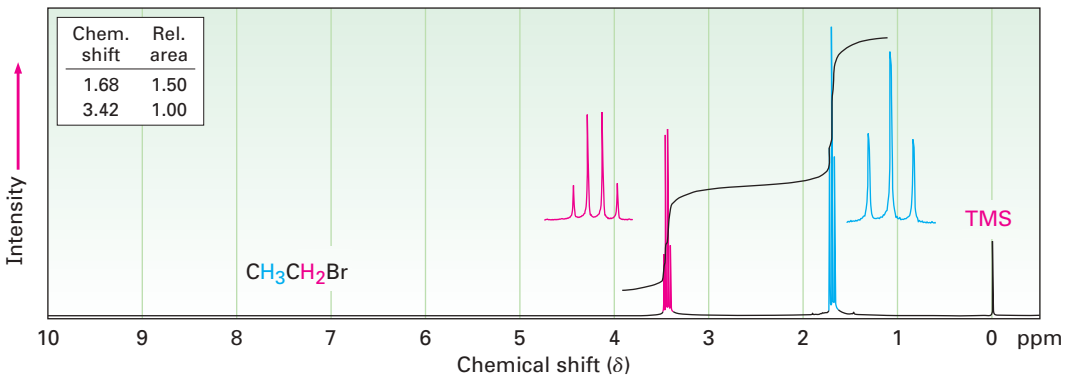


Figure 13.11 The ^1H NMR spectrum of bromoethane, CH_3CH_2Br. The $-CH_2Br$ protons appear as a quartet at 3.42 δ, and the $-CH_3$ protons appear as a triplet at 1.68 δ.

Called **spin–spin splitting**, multiple absorptions of a nucleus are caused by the interaction, or **coupling**, of the spins of nearby nuclei. In other words, the tiny magnetic field produced by one nucleus affects the magnetic field felt by neighboring nuclei. Look at the $-CH_3$ protons in bromoethane, for example. The three equivalent $-CH_3$ protons are neighbored by two other magnetic nuclei—the two protons on the adjacent $-CH_2Br$ group. Each of the neighboring $-CH_2Br$ protons has its own nuclear spin, which can align either with or against the applied field, producing a tiny effect that is felt by the $-CH_3$ protons.

There are three ways in which the spins of the two $-CH_2Br$ protons can align, as shown in Figure 13.12. If both proton spins align with the applied field, the total effective field felt by the neighboring $-CH_3$ protons is slightly

larger than it would otherwise be. Consequently, the applied field necessary to cause resonance is slightly reduced. Alternatively, if one of the $-CH_2Br$ proton spins aligns with the field and one aligns against the field, there is no effect on the neighboring $-CH_3$ protons. (There are two ways this arrangement can occur, depending on which of the two proton spins aligns which way.) Finally, if both $-CH_2Br$ proton spins align against the applied field, the effective field felt by the $-CH_3$ protons is slightly smaller than it would otherwise be and the applied field needed for resonance is slightly increased.

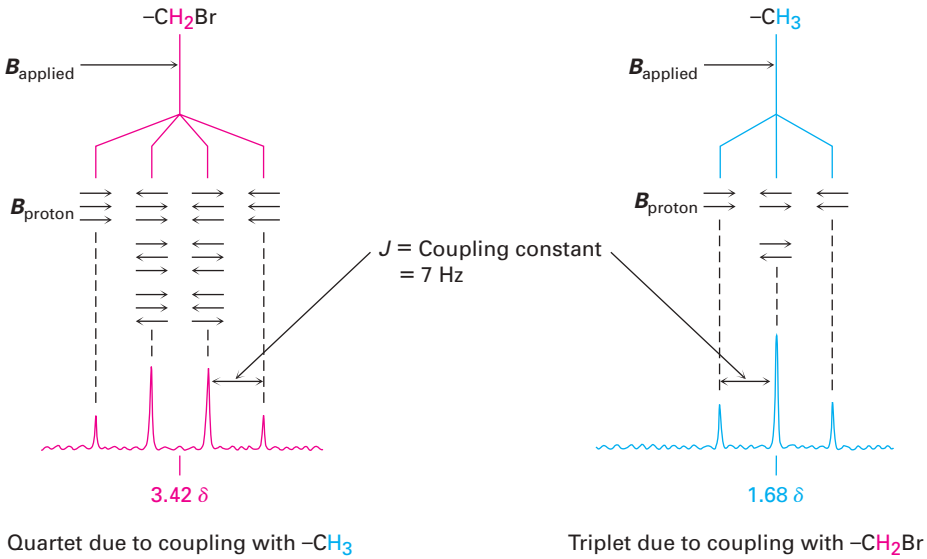


Figure 13.12 The origin of spin–spin splitting in bromoethane. The nuclear spins of neighboring protons, indicated by horizontal arrows, align either with or against the applied field, causing the splitting of absorptions into multiplets.

Any given molecule has only one of the three possible alignments of $-CH_2Br$ spins, but in a large collection of molecules, all three spin states are represented in a 1:2:1 statistical ratio. We therefore find that the neighboring $-CH_3$ protons come into resonance at three slightly different values of the applied field, and we see a 1:2:1 triplet in the NMR spectrum. One resonance is a little above where it would be without coupling, one is at the same place it would be without coupling, and the third resonance is a little below where it would be without coupling.

In the same way that the $-CH_3$ absorption of bromoethane is split into a triplet, the $-CH_2Br$ absorption is split into a quartet. The three spins of the neighboring $-CH_3$ protons can align in four possible combinations: all three with the applied field, two with and one against (three ways), one with and two against (three ways), or all three against. Thus, four peaks are produced for the $-CH_2Br$ protons in a 1:3:3:1 ratio.

As a general rule, called the ***n* + 1 rule**, protons that have n equivalent neighboring protons show $n + 1$ peaks in their NMR spectrum. For example, the spectrum of 2-bromopropane in Figure 13.13 shows a doublet at 1.71 δ and a seven-line multiplet, or *septet,* at 4.28 δ. The septet is caused by splitting of the $-CHBr-$ proton signal by six equivalent neighboring protons on the two methyl groups ($n = 6$ leads to $6 + 1 = 7$ peaks). The doublet is due to

signal splitting of the six equivalent methyl protons by the single –CHBr– proton ($n = 1$ leads to 2 peaks).

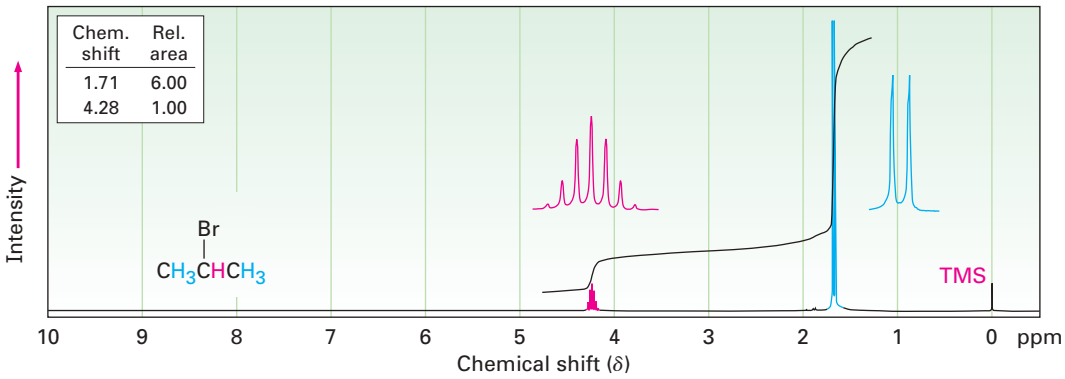
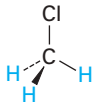


Figure 13.13 The ^{1}H NMR spectrum of 2-bromopropane. The $-CH_3$ proton signal at 1.71 δ is split into a doublet, and the –CHBr– proton signal at 4.28 δ is split into a septet. Note that the distance between peaks—the *coupling constant*—is the same in both multiplets.

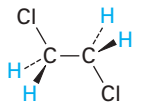
The distance between peaks in a multiplet is called the **coupling constant**, ***J***. Coupling constants are measured in hertz and generally fall in the range 0 to 18 Hz. The exact value of J between two neighboring protons depends on the geometry of the molecule, but a typical value for an open-chain alkane is $J = 6–8$ Hz. Note that the same coupling constant is shared by both groups of hydrogens whose spins are coupled and is independent of spectrometer field strength. In bromoethane, for instance, the $-CH_2Br$ protons are coupled to the $-CH_3$ protons and appear as a quartet with $J = 7$ Hz. The $-CH_3$ protons appear as a triplet with the same $J = 7$ Hz coupling constant.

Three important points about spin–spin splitting are illustrated by the spectra of bromoethane in Figure 13.11 and 2-bromopropane in Figure 13.13.

- **Chemically equivalent protons don't show spin–spin splitting.** The equivalent protons may be on the same carbon or on different carbons, but their signals don't split.

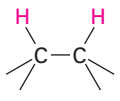


Three C–H protons are chemically equivalent; no splitting occurs.

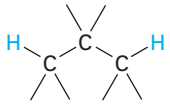


Four C–H protons are chemically equivalent; no splitting occurs.

- **The signal of a proton with *n* equivalent neighboring protons is split into a multiplet of *n* + 1 peaks.** Protons that are more than two carbon atoms apart usually don't split each other's signals.



Splitting observed



Splitting not usually observed

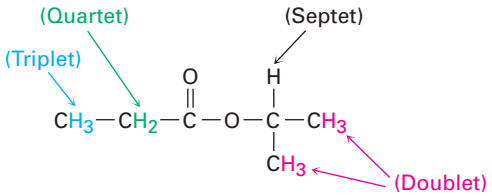
- **Two groups of protons coupled to each other have the same coupling constant *J*.**

Worked Example 13.9 **Predicting Spin–Spin Splitting Patterns**

Predict the splitting pattern for each kind of hydrogen in isopropyl propanoate, $CH_3CH_2CO_2CH(CH_3)_2$.

Strategy First, find how many different kinds of protons are present (there are four). Then, determine how many neighboring protons each kind has and apply the $n + 1$ rule.

Solution

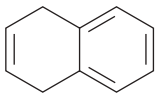


Isopropyl propanoate

Problem 13.20 Predict the splitting patterns for each proton in the following molecules:

(a) $CHBr_2CH_3$ **(b)** $CH_3OCH_2CH_2Br$ **(c)** $ClCH_2CH_2CH_2Cl$

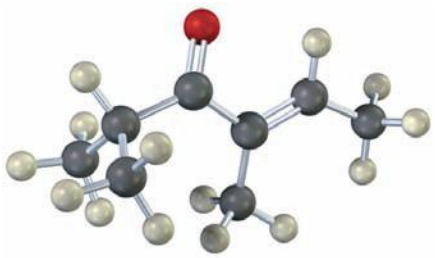
(d) $CH_3CH(CH_3)COCH_2CH_3$ **(e)** $CH_3CH_2COCH(CH_3)_2$ **(f)**



Problem 13.21 Propose structures for compounds that show the following ^{1}H NMR spectra:

(a) C_2H_6O; one singlet
(b) $C_3H_6O_2$; two singlets
(c) C_3H_7Cl; one doublet and one septet

Problem 13.22 Predict the splitting patterns for each kind of chemically distinct proton in the following molecule:

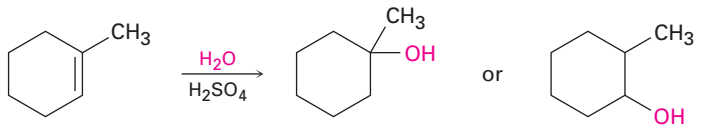


13.13 Uses of ^{1}H NMR Spectra

^{1}H NMR spectroscopy is used to help identify the product of nearly every reaction run in the laboratory. For example, we said in Section 4.3 that acid-catalyzed addition of H_2O to an alkene occurs with Markovnikov orientation

to give the more highly substituted alcohol. With the help of ^{1}H NMR, we can now prove this statement.

Does addition of H_2O to 1-methylcyclohexene yield 1-methylcyclohexanol or 2-methylcyclohexanol?



1-Methylcyclohexene **1-Methylcyclohexanol** **2-Methylcyclohexanol**

The ^{1}H NMR spectrum of the reaction product is shown in Figure 13.14. Although many of the ring protons overlap into a broad, poorly defined multiplet centered around 1.5 δ, the spectrum also shows a large singlet absorption in the saturated methyl region at 1.19 δ, indicating that the product has a methyl group with no neighboring hydrogens ($R_3C—C\mathbf{H_3}$). Furthermore, the spectrum shows no absorptions around 4 δ, where we would expect the signal of an $R_2C\mathbf{H}OH$ proton to occur. Thus, the reaction product is 1-methylcyclohexanol.

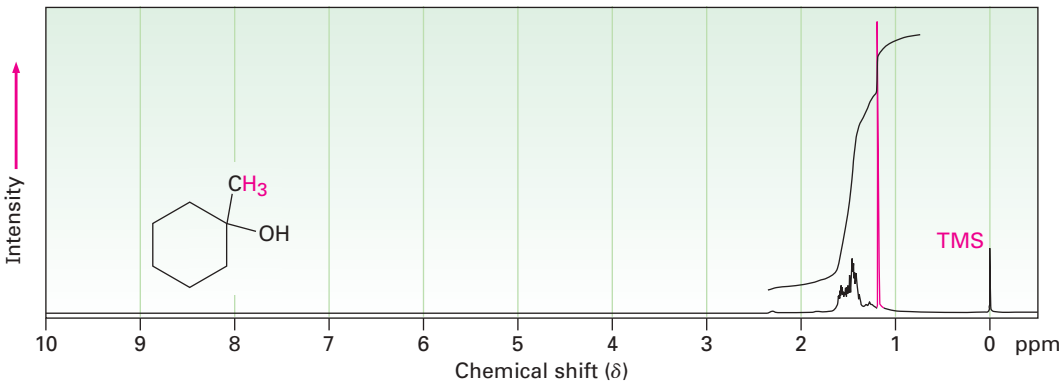


Figure 13.14 The ^{1}H NMR spectrum of the reaction product from H_2O and 1-methylcyclohexene. The presence of the $-CH_3$ absorption at 1.19 δ and the absence of any absorptions near 4 δ identify the product as 1-methylcyclohexanol.

13.14 ^{13}C NMR Spectroscopy

Having now looked at ^{1}H NMR spectroscopy, let's take a brief look at ^{13}C NMR before ending. In some ways, it's surprising that carbon NMR is even possible. After all, ^{12}C, the most abundant carbon isotope, has no nuclear spin and can't be seen by NMR. Carbon-13 is the only naturally occurring carbon isotope with a nuclear spin, but its natural abundance is only 1.1%. Thus, only about 1 of every 100 carbon atoms in an organic molecule is observable by NMR. Fortunately, the technical problems caused by this low abundance have been overcome by computer techniques, and ^{13}C NMR is a routine structural tool.

At its simplest, ^{13}C NMR makes it possible to count the number of carbon atoms in a molecule. Look at the ^{13}C NMR spectrum of methyl acetate shown previously in Figure 13.9b, for instance. Methyl acetate has three nonequivalent carbon atoms and thus has three peaks in its ^{13}C NMR spectrum.

(Coupling between adjacent carbon atoms isn't seen, because the low natural abundance of ^{13}C makes it unlikely that two such nuclei will be adjacent in a molecule.)

Most ^{13}C resonances are between 0 and 220 δ downfield from the TMS reference line, with the exact chemical shift of each ^{13}C resonance dependent on that carbon's electronic environment within the molecule. Figure 13.15 shows the correlation of chemical shift with environment.

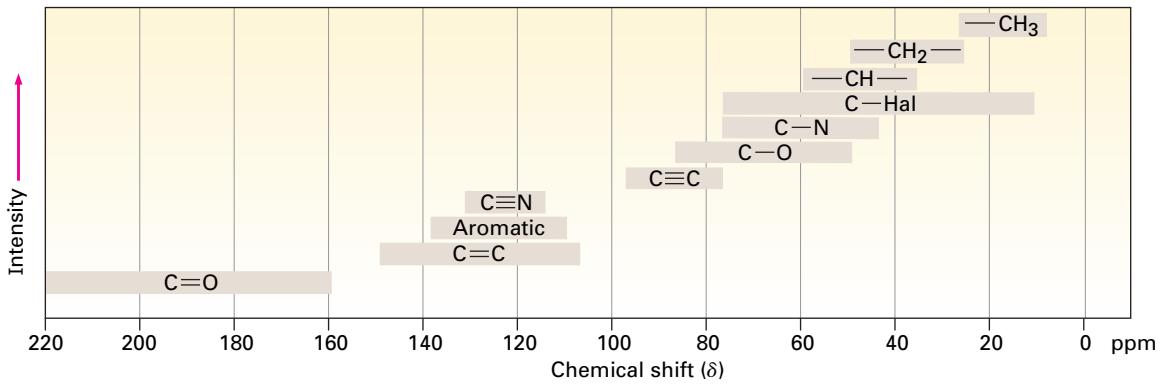


Figure 13.15 Chemical shift correlations for ^{13}C NMR.

The factors that determine chemical shifts are complex, but it's possible to make some generalizations. One trend is that a carbon's chemical shift is affected by the electronegativity of nearby atoms. Carbons bonded to oxygen, nitrogen, or halogen absorb downfield (to the left) of typical alkane carbons. Another trend is that sp^3-hybridized carbons absorb in the range 0 to 90 δ, while sp^2 carbons absorb in the range 110 to 220 δ. Carbonyl carbons (C=O) are particularly distinct in the ^{13}C NMR spectrum and are always found at the extreme low-field end of the chart, in the range 160 to 220 δ. For example, the ^{13}C NMR spectrum of *p*-bromoacetophenone in Figure 13.16 shows an absorption for the carbonyl carbon at 197 δ.

The ^{13}C NMR spectrum of *p*-bromoacetophenone is interesting for another reason as well. Note that only six absorptions are observed, even though the molecule has eight carbons. *p*-Bromoacetophenone has a symmetry plane that makes carbons 4 and 4′, and carbons 5 and 5′, equivalent. Thus, the six ring carbons show only four absorptions in the range 128 to 137 δ. In addition, the $-CH_3$ carbon absorbs at 26 δ.

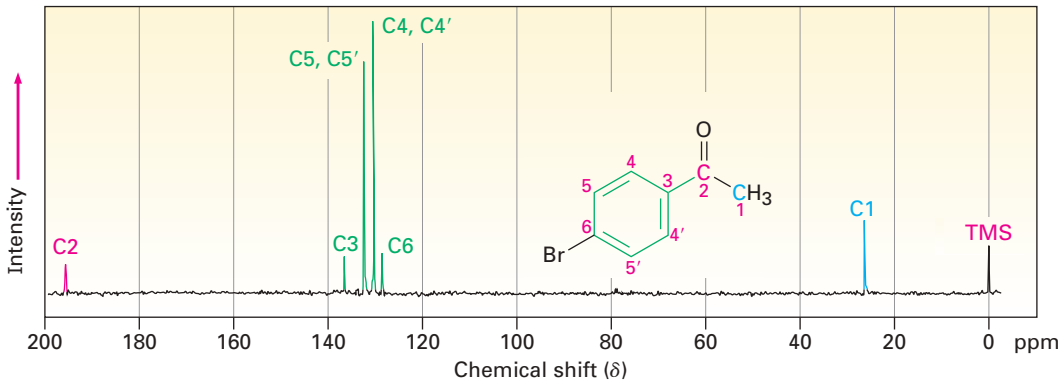


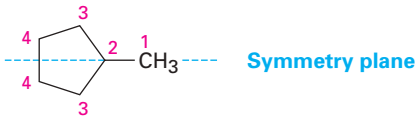
Figure 13.16 The ^{13}C NMR spectrum of *p*-bromoacetophenone, $BrC_6H_4COCH_3$.

Worked Example 13.10 Predicting the Number of ^{13}C Absorptions

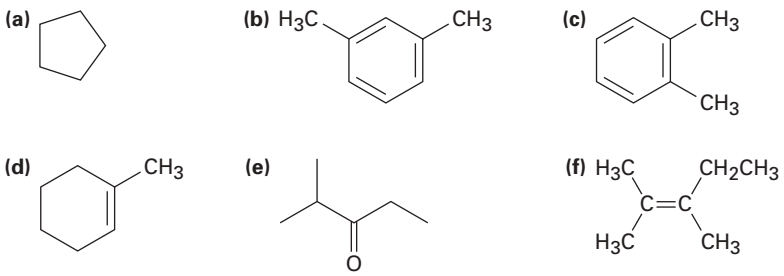
How many peaks would you expect in the ^{13}C NMR spectrum of methylcyclopentane?

Strategy Find the number of distinct types of carbons in the molecule, taking symmetry into account.

Solution Because of its symmetry plane, methylcyclopentane has only four kinds of carbons and only four peaks in its ^{13}C NMR spectrum.



Problem 13.23 How many peaks would you expect in the ^{13}C NMR spectra of the following compounds?



Problem 13.24 Propose structures for compounds whose ^{13}C NMR spectra fit the following descriptions:

(a) A hydrocarbon with seven peaks in its spectrum
(b) A six-carbon compound with only five peaks in its spectrum
(c) A four-carbon compound with three peaks in its spectrum

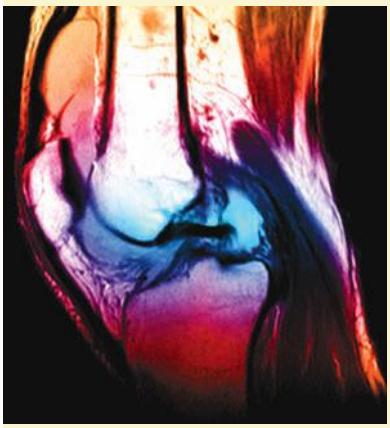
INTERLUDE

Magnetic Resonance Imaging (MRI)

As practiced by organic chemists, NMR spectroscopy is a powerful method of structure determination. A small amount of sample, typically a few milligrams or less, is dissolved in a small amount of solvent, the solution is placed in a thin glass tube, and the tube is placed into the narrow (1–2 cm) gap between the poles of a strong magnet. Imagine, though,

continued

INTERLUDE



Living Art Enterprises/Photo Researchers, Inc.

This person won't be running again soon. The MRI shows a torn posterior cruciate ligament in the knee.

that a much larger NMR instrument were available. Instead of a few milligrams, the sample size could be tens of kilograms; instead of a narrow gap between magnet poles, the gap could be large enough for a whole person to climb into so that an NMR spectrum of body parts could be obtained. That large instrument is exactly what's used for *magnetic resonance imaging (MRI),* a diagnostic technique of enormous value to the medical community.

Like NMR spectroscopy, MRI takes advantage of the magnetic properties of certain nuclei, typically hydrogen, and of the signals emitted when those nuclei are stimulated by radiofrequency energy. Unlike what happens in NMR spectroscopy, though, MRI instruments use data manipulation techniques to look at the three-dimensional *location* of magnetic nuclei in the body rather than at the chemical nature of the nuclei. As noted, most MRI instruments currently look at hydrogen, present in abundance wherever there is water or fat in the body.

The signals detected by MRI vary with the density of hydrogen atoms and with the nature of their surroundings, allowing identification of different types of tissue and even allowing the visualization of motion. For example, the volume of blood leaving the heart in a single stroke can be measured, and heart motion can be observed. Soft tissues that don't show up well on X-ray films can be seen clearly, allowing diagnosis of brain tumors, strokes, and other conditions. The technique is also valuable in diagnosing damage to knees or other joints and is a noninvasive alternative to surgical explorations.

Several types of atoms in addition to hydrogen can be detected by MRI, and the applications of images based on ^{31}P atoms are being explored. The technique holds great promise for studies of metabolism.

Summary and Key Words

absorption spectrum 437
amplitude 435
chemical shift 449
coupling 452
coupling constant (*J*) 454
delta (δ) scale 449
downfield 448
electromagnetic spectrum 435
frequency (*ν*) 435
hertz (Hz) 435
infrared (IR) spectroscopy 438
integration 451
mass spectrometry 434
multiplet 452
n + 1 rule 453
nuclear magnetic resonance (NMR) spectroscopy 445
shielding 446
spin–spin splitting 452

Finding the structure of a new molecule, whether a small one synthesized in the laboratory or a large one found in living organisms, is central to progress in chemistry and biochemistry. Four main spectroscopic methods are used to determine the structures of organic molecules. Each gives a different kind of information.

Mass Spectrometry	What is the molecular formula?
Infrared spectroscopy	What functional groups are present?
Ultraviolet spectroscopy	Is a conjugated π electron system present?
Nuclear magnetic resonance spectroscopy	What carbon–hydrogen framework is present?

In **mass spectrometry**, molecules are first ionized and then sorted according to their mass-to-charge ratio (*m/z*). The ionized sample molecule is called the *molecular ion,* M^+, and measurement of its mass gives its molecular weight. Clues about molecular structure can be obtained by interpreting the fragmentation pattern of the molecular ion.

When an organic molecule is irradiated with **infrared (IR)** energy, frequencies of light corresponding to the energies of various molecular stretching and

ultraviolet (UV) spectroscopy 442
upfield 448
wavelength (λ) 435
wavenumber ($\tilde{\nu}$) 438

bending motions are absorbed. Each functional group has a characteristic set of IR absorptions that allows the group to be identified. For example, an alkene C=C bond absorbs in the range 1640 to 1680 cm^{-1}, a saturated ketone absorbs near 1715 cm^{-1}, and a nitrile absorbs near 2230 cm^{-1}. By observing which frequencies of IR radiation are absorbed by a molecule and which are not, the functional groups in a molecule can be identified.

Ultraviolet (UV) spectroscopy is applicable to conjugated π electron systems. When a conjugated molecule is irradiated with ultraviolet light, energy absorption occurs, leading to excitation of π electrons to higher energy levels. The greater the extent of conjugation, the longer the wavelength needed for excitation.

Nuclear magnetic resonance (NMR) spectroscopy is the most valuable of the common spectroscopic techniques. When ^1H and ^{13}C nuclei are placed in a magnetic field, their spins orient either with or against the field. On irradiation with radiofrequency (rf) waves, energy is absorbed and the nuclear spins flip from the lower-energy state to the higher-energy state. This absorption of energy is detected, amplified, and displayed as an NMR spectrum. NMR spectra display four general features.

- **Number of peaks.** Each nonequivalent kind of ^1H or ^{13}C nucleus in a molecule gives rise to a different peak.
- **Chemical shift.** The exact position of each peak is correlated to the chemical environment of each ^1H or ^{13}C nucleus. Most ^1H absorptions are in the range 0 to 10 δ downfield from the TMS reference signal, and most ^{13}C absorptions are in the range 0 to 220 δ.
- **Integration.** The area under each peak can be electronically integrated to determine the relative number of protons responsible for each peak.
- **Spin–spin splitting.** Neighboring nuclear spins can **couple**, splitting an NMR absorption into a **multiplet**. The NMR signal of a ^1H nucleus neighbored by n adjacent protons splits into $n + 1$ peaks with coupling constant J.

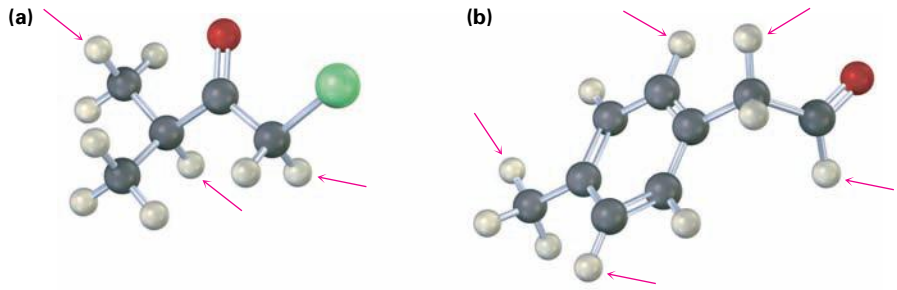
Exercises

Visualizing Chemistry

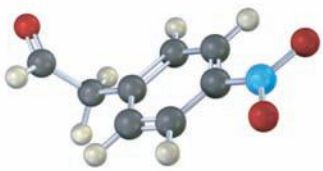
(Problems 13.1–13.24 appear within the chapter.)

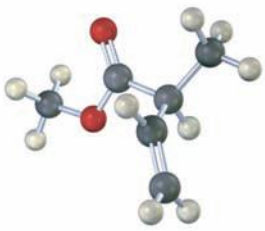
OWL
Interactive versions of these problems are assignable in OWL.

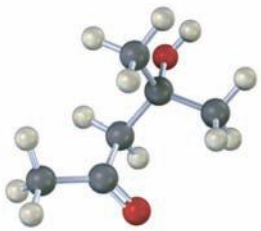
13.25 Into how many peaks would you expect the ^1H NMR signal of the indicated protons to be split? (Yellow-green = Cl.)



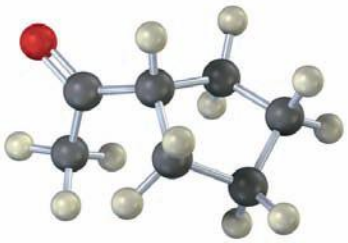
13.26 Where in the infrared spectrum would you expect each of the following compounds to absorb?

(a) 

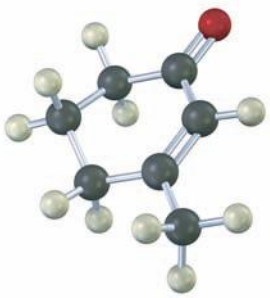
(b) 

(c) 

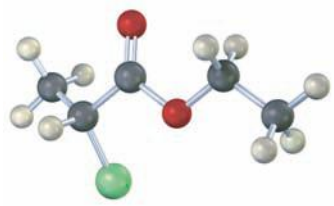
13.27 How many absorptions would you expect the following compound to have in its ^{13}C NMR spectrum?



13.28 How many absorptions would you expect the following compound to have in its ^{1}H and ^{13}C NMR spectrum?



13.29 Sketch what you might expect the ^{1}H and ^{13}C NMR spectra of the following compound to look like (yellow-green = Cl):



Additional Problems

Mass Spectrometry

13.30 The male sex hormone testosterone contains only C, H, and O and has a mass of 288.2089 amu, as determined by high-resolution mass spectrometry. What is the likely molecular formula of testosterone?

13.31 Propose structures for compounds that fit the following mass-spectral data:
(a) A hydrocarbon with $M^+ = 132$
(b) A hydrocarbon with $M^+ = 166$
(c) A hydrocarbon with $M^+ = 84$

13.32 Halogenated compounds are particularly easy to identify by their mass spectra because both chlorine and bromine occur naturally as mixtures of two abundant isotopes. Chlorine occurs as ^{35}Cl (75.8%) and ^{37}Cl (24.2%); bromine occurs as ^{79}Br (50.7%) and ^{81}Br (49.3%). At what masses do the molecular ions occur for the following formulas? What are the relative percentages of each molecular ion?
(a) Bromomethane, CH_3Br **(b)** 1-Chlorohexane, $C_6H_{13}Cl$

Electromagnetic Radiation and Spectroscopy

13.33 Tell what is meant by each of the following terms:
(a) Chemical shift **(b)** Coupling constant **(c)** λ_{max}
(d) Spin–spin splitting **(e)** Wavenumber
(f) Applied magnetic field

13.34 The energy of electromagnetic radiation in units of kJ/mol, can be determined by the formula $E = (1.20 \times 10^{-4}\ \text{kJ/mol})/\lambda$, where λ is the wavelength in meters. What is the energy of infrared radiation of wavelength 6.55×10^{-6} m?

13.35 Using the equation given in Problem 13.34, calculate the energy required to effect the electronic excitation of buta-1,3-diene ($\lambda_{max} = 217$ nm).

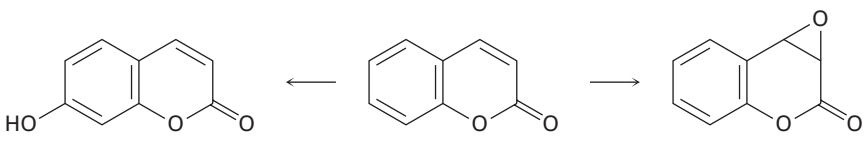
13.36 Using the equation given in Problem 13.34, calculate the amount of energy required to spin-flip a proton in a spectrometer operating at 100 MHz. Does increasing the spectrometer frequency from 100 MHz to 220 MHz increase or decrease the amount of energy necessary for resonance?

UV Spectroscopy

13.37 The active metabolite of the antiviral drug abacavir has a UV molar absorptivity of 13,260 L/(mol · cm). What absorbance would you expect for a sample in a cell with a pathlength of 1.00 cm at a concentration of 42 μM? (1 $\mu M = 10^{-6}$ M)

13.38 What is the concentration of a sample of abacavir in mg/mL if the UV absorbance measured in a cell with 1.00 cm pathlength is $A = 0.93$ and the molar absorptivity is 13,260 L/(mol · cm).

13.39 The pathway for metabolism of a drug depends on the species doing the metabolizing. Coumarin, an anticoagulant, metabolizes to a toxic compound in rats but not in humans. How would the UV spectra differ between the different metabolites?



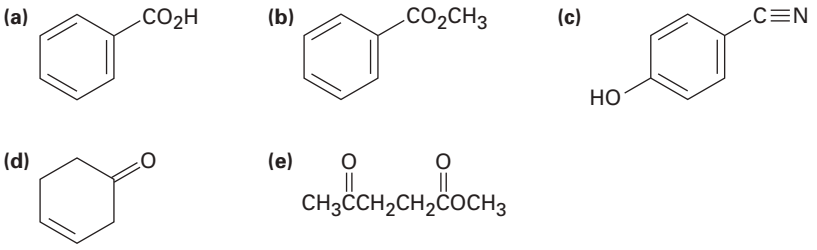
(Human metabolite) Coumarin (Rat metabolite)

13.40 The mosquito attractant oct-1-en-3-ol can be prepared by reduction of oct-1-en-3-one. How can UV spectroscopy be used to show when the reaction is complete?

IR Spectroscopy

13.41 What kinds of functional groups might compounds contain if they show the following IR absorptions?
(a) 1670 cm^{-1}
(b) 1735 cm^{-1}
(c) 1540 cm^{-1}
(d) 1715 cm^{-1} and 2500–3100 cm^{-1} (broad)

13.42 At what approximate positions might the following compounds show IR absorptions?



13.43 If C–O single-bond stretching occurs at 1000 cm^{-1} and C=O double-bond stretching occurs at 1700 cm^{-1}, which of the two requires more energy? How does your answer correlate with the relative strengths of single and double bonds?

13.44 Propose structures for compounds that meet the following descriptions:
(a) C_5H_8, with IR absorptions at 3300 and 2150 cm^{-1}
(b) C_4H_8O, with a strong IR absorption at 3400 cm^{-1}
(c) C_4H_8O, with a strong IR absorption at 1715 cm^{-1}
(d) C_8H_{10}, with IR absorptions at 1600 and 1500 cm^{-1}

NMR Spectroscopy

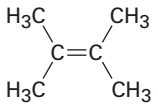
13.45 The following ^1H NMR absorptions, determined on a spectrometer operating at 100 MHz, are given in hertz downfield from the TMS standard. Convert the absorptions to δ units.
(a) 218 Hz **(b)** 478 Hz **(c)** 751 Hz

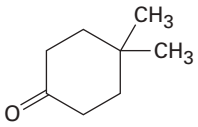
13.46 At what positions, in hertz downfield from the TMS standard, would the NMR absorptions in Problem 13.45 appear on a spectrometer operating at 220 MHz?

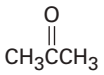
13.47 The following NMR absorptions, given in δ units, were obtained on a spectrometer operating at 300 MHz. Convert the chemical shifts from δ units into hertz downfield from TMS.
(a) 2.1 δ **(b)** 3.45 δ **(c)** 6.30 δ

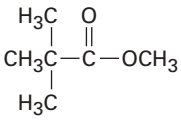
13.48 When measured on a spectrometer operating at 100 MHz, chloroform ($CHCl_3$) shows a single sharp absorption at 7.3 δ.
(a) How many parts per million downfield from TMS does chloroform absorb?
(b) How many hertz downfield from TMS does chloroform absorb if the measurement is carried out on a spectrometer operating at 360 MHz?
(c) What is the position of the chloroform absorption in δ units measured on a 360 MHz spectrometer?

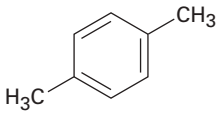
13.49 How many absorptions would you expect each of the following compounds to have in its ^1H and ^{13}C NMR spectra?

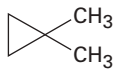
(a) 

(b) 

(c) 

(d) 

(e) 

(f) 

13.50 Describe the ^1H NMR spectra you would expect for the following compounds:
(a) CH_3CHCl_2 **(b)** $CH_3CO_2CH_2CH_3$ **(c)** $(CH_3)_3CCH_2CH_3$

13.51 The following compounds all show a single peak in their ^1H NMR spectra. List them in order of expected increasing chemical shift: CH_4, CH_2Cl_2, cyclohexane, CH_3COCH_3, $H_2C{=}CH_2$, benzene.

General Problems

13.52 How would you use IR spectroscopy to distinguish between the following pairs of isomers?
(a) $(CH_3)_3N$ and $CH_3CH_2NHCH_3$
(b) CH_3COCH_3 and $CH_2{=}CHCH_2OH$
(c) CH_3COCH_3 and CH_3CH_2CHO

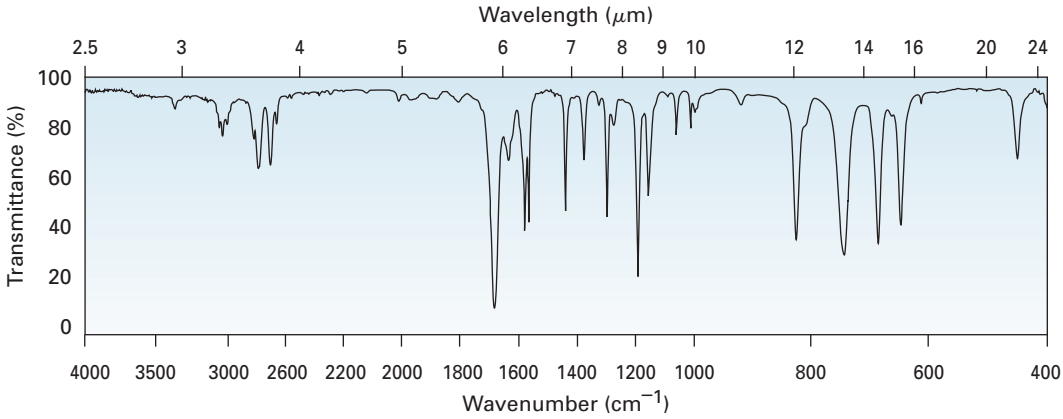
13.53 How would you use ^1H NMR spectroscopy to distinguish between the isomer pairs shown in Problem 13.52?

13.54 How could you use ^{13}C NMR spectroscopy to distinguish between the isomer pairs shown in Problem 13.52?

13.55 Assume you are carrying out the dehydration of 1-methylcyclohexanol to yield 1-methylcyclohexene. How could you use IR spectroscopy to determine when the reaction is complete? What characteristic absorptions would you expect for both starting material and product?

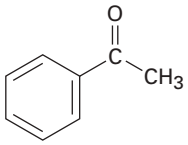
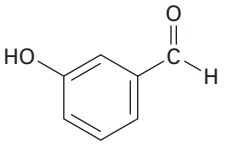
13.56 How would you expect the mass spectra of the starting material and product to differ for Problem 13.55?

13.57 The IR spectrum of a compound with the formula C_7H_6O is shown. Propose a likely structure.

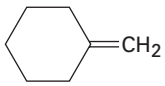


13.58 At what approximate positions might the following compounds show IR absorptions?

(a) $CH_3CH_2\overset{\overset{O}{\|}}{C}CH_3$ **(b)** $CH_3CHCH_2C{\equiv}CH$ (CH₃ on CH) **(c)** $CH_3CHCH_2CH{=}CH_2$ (CH₃ on CH)

(d) $CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}OCH_3$ **(e)**  **(f)** 

13.59 Dehydration of 1-methylcyclohexanol might lead to either of two isomeric alkenes, 1-methylcyclohexene or methylenecyclohexane. How could you use NMR spectroscopy (both ^1H and ^{13}C) to determine the structure of the product?

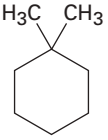
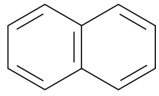


Methylenecyclohexane

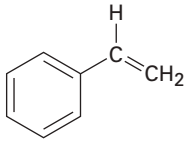
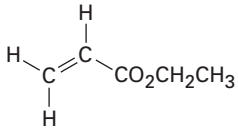
13.60 3,4-Dibromohexane can undergo base-induced loss of 2 HBr to yield either hex-3-yne or hexa-2,4-diene. How could you use UV spectroscopy to help identify the product? How could you use ^1H NMR spectroscopy?

13.61 Describe the ^1H and ^{13}C NMR spectra you expect for the following compounds:
(a) $ClCH_2CH_2CH_2Cl$ **(b)** $CH_3COCH_2CH_2Cl$

13.62 How many types of nonequivalent protons are present in each of the following compounds?

(a)  **(b)** $CH_3CH_2CH_2OCH_3$ **(c)** 

Naphthalene

(d)  **(e)** 

Styrene **Ethyl acrylate**

13.63 Propose structures for compounds with the following formulas that show only one peak in their ^1H NMR spectra:
(a) C_5H_{12} **(b)** C_5H_{10} **(c)** $C_4H_8O_2$

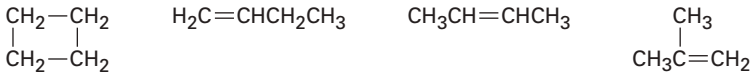
13.64 Assume you have a compound with formula C_3H_6O.
(a) Propose as many structures as you can that fit the molecular formula (there are seven).
(b) If your compound has an IR absorption at 1715 cm^{-1}, what can you conclude?
(c) If your compound has a single ^1H NMR absorption at 2.1 δ, what is its structure?

13.65 Propose structures for compounds that fit the following ^1H NMR data:

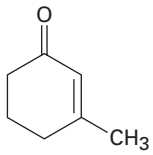
(a) $C_5H_{10}O$
6 H doublet at 0.95 δ, J = 7 Hz
3 H singlet at 2.10 δ
1 H multiplet at 2.43 δ

(b) C_3H_5Br
3 H singlet at 2.32 δ
1 H singlet at 5.25 δ
1 H singlet at 5.54 δ

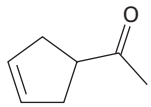
13.66 How can you use ^1H and ^{13}C NMR to help distinguish among the following four isomers?



13.67 How can you use ^1H NMR to help distinguish between the following isomers?



3-Methylcyclohex-2-enone

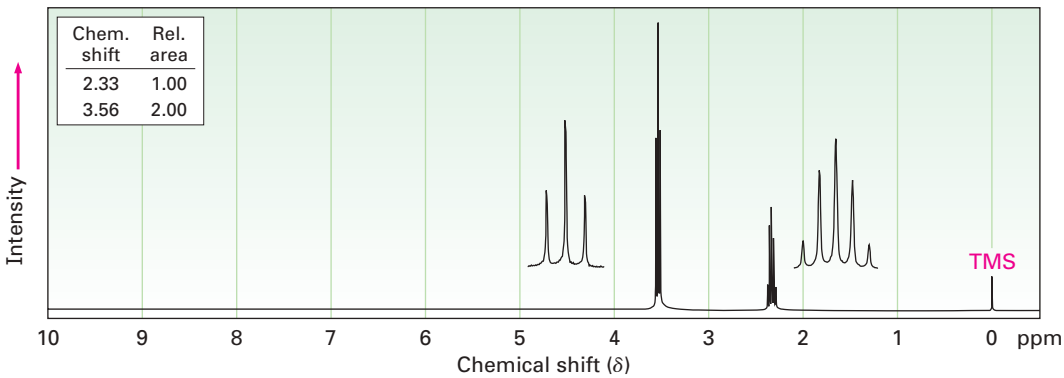


Cyclopent-3-enyl methyl ketone

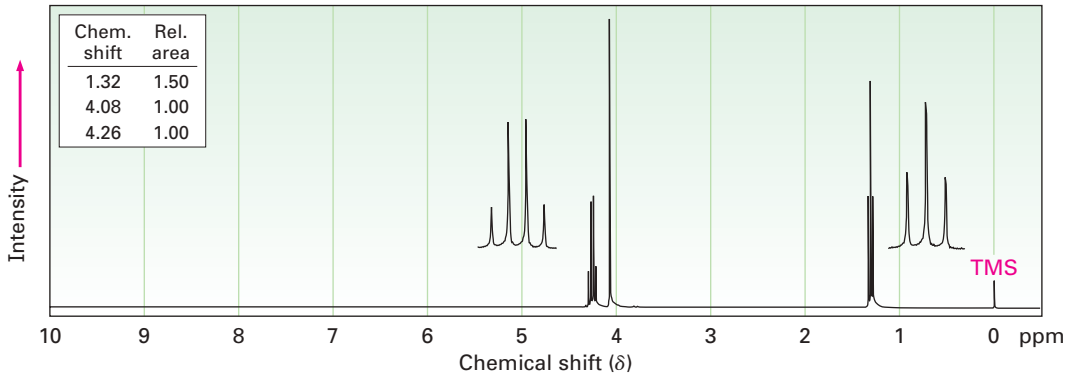
13.68 How can you use ^{13}C NMR to help distinguish between the isomers in Problem 13.67?

13.69 How can you use UV spectroscopy to help distinguish between the isomers in Problem 13.67?

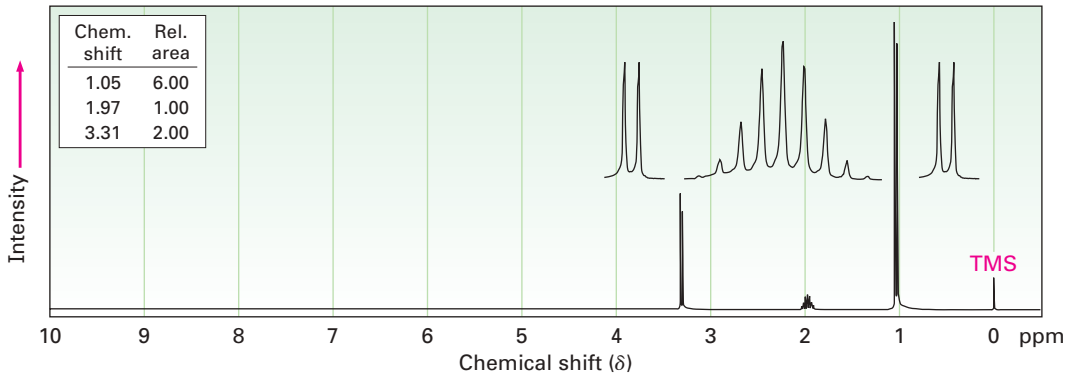
13.70 The ^1H NMR spectrum of compound **A**, $C_3H_6Br_2$, is shown. Propose a structure for **A**, and explain how the spectrum fits your structure.



13.71 The compound whose ^{1}H NMR spectrum is shown has the formula $C_4H_7O_2Cl$ and has an IR absorption peak at 1740 cm^{-1}. Propose a structure.



13.72 Propose a structure for a compound with formula C_4H_9Br that has the following ^{1}H NMR spectrum:



13.73 Propose structures for compounds that fit the following ^{1}H NMR data:

(a) $C_4H_6Cl_2$
3 H singlet at 2.18 δ
2 H doublet at 4.16 δ, J = 7 Hz
1 H triplet at 5.71 δ, J = 7 Hz

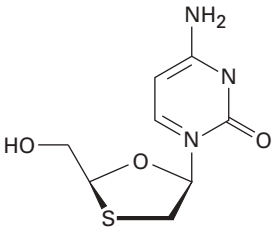
(b) $C_{10}H_{14}$
9 H singlet at 1.30 δ
5 H singlet at 7.30 δ

13.74 Nitriles (RC≡N) react with Grignard reagents (RMgBr). The reaction product from 2-methylpropanenitrile with methylmagnesium bromide has the following spectroscopic properties. Propose a structure.

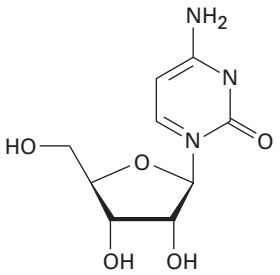
Molecular weight = 86
IR: 1715 cm^{-1}
^{1}H NMR: 1.05 δ (6 H doublet); 2.12 δ (3 H singlet); 2.67 δ (1 H septet)
^{13}C NMR: 18.2, 27.2, 41.6, 211.2 δ

IN THE MEDICINE CABINET

13.75 Lamivudine, a drug used in the management of acquired immunodeficiency syndrome (AIDS), structurally resembles the nucleoside cytidine found in nucleic acids. Lamivudine is also referred to as 3TC, an acronym for 3-thiocytosine.



Lamivudine



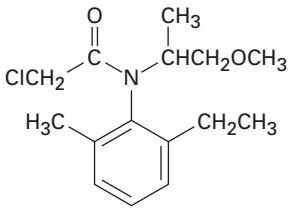
Cytidine

(a) How many chirality centers does lamivudine have?
(b) Lamivudine has two acetal-like groups that will hydrolyze on treatment with aqueous acid. Identify them.
(c) What three products arise from the acid hydrolysis of lamivudine?
(d) The concentration of lamivudine in the blood can be measured by UV spectroscopy. Assuming a molar absorptivity of 8600 L/(mol · cm), what is the concentration of drug in blood plasma if a tenfold dilution of the sample gives an absorbance of 0.195 using a sample pathlength of 1.00 cm?

IN THE FIELD

13.76 Partial analytical data for the herbicide metolachlor, seen previously in Problems 2.74, 5.61, 6.66, and 9.58, is listed. Account for each piece of the data.

IR:	Absorption at 1680 cm^{-1}
UV:	Broad absorption at 310 nm
^1H NMR:	1.11 δ (3 H doublet); 1.23 δ (3 H triplet);
	2.21 δ (3 H singlet);
	2.57 δ (2 H quartet); 3.25 δ (3 H singlet);
	3.46 δ (2 H doublet);
	3.57 δ (2 H singlet)



Metolachlor